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Abstract booklet

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T1

Preliminary results from Global Registry of Alopecia Areata Disease Severity and Treatment Safety (GRASS) International: Treatment patterns and adverse events

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Abstract

Background: The Global Registry of Alopecia Areata Disease Severity and Treatment Safety (GRASS) International is an international collaborative network of patient disease registries collecting specific data pertaining to the epidemiological, socioeconomic and treatment characteristics of AA.

Methods: Consented individuals with a diagnosis of AA were enrolled in GRASS. Statistical analysis of the data was performed using descriptive statistics.

Results: As of December 2022, 699 individuals had been recruited. Almost two-thirds were female (63.4%; 95% CI 59.7, 67.0). The majority (87.8%; 95% CI 85.2, 90.2) were adults, though eight children (<12 years) and 15 adolescents (12-17 years) were also recruited. The median age of participants was 37 (IQR=25). Two-thirds presented with patchy disease (66.5%; 95% CI 61.9, 70.8). Over 70% (95% CI 66.4, 74.9) received systemic treatment, with oral minoxidil (57.5%; 95% CI 52.9, 62.1) and corticosteroids (37.7%; 95% CI 33.2, 42.3) most frequently prescribed. Janus kinase (JAK) inhibitors were prescribed in 32.2% of cases (95% CI 28.0, 36.7), with baricitinib the most common (27.7%; 95% CI 23.6, 32.0). 159 adverse events (AEs) were reported; 114 from systemic medication. Oral minoxidil produced the most AEs (29.6%; 95% CI 22.6, 37.3), then baricitinib (16.4%; 95% CI 11.0, 23.0). Four serious AEs occurred (2 required hospitalisation; 2 were medically important events).

Conclusions: GRASS demographic data reflects that described in the AA literature. The high frequency of systemic therapy likely reflects referral bias, though AEs are low Data captured by GRASS will help understand safety and effectiveness during an AA treatment revolution.

T2

Clinical and etiological basis of comorbidities and therapy response in alopecia areata

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Abstract

Alopecia areata (AA) is an autoimmune disorder and a common cause of hair loss with a lifetime risk of about 2%. AA patients are at increased risk for developing immune-mediated comorbidities and major depressive disorder (MDD). The clinical manifestation of AA is very heterogeneous and the prognosis of disease, treatment response and presentation of associated comorbidities is very variable on an individual level. We have one of the largest AA cohorts worldwide composed of ~2800 individuals. From the majority of these individuals, we have genome-wide genotype data and phenotypic data on disease course, treatment response and comorbidities. Based on these, we performed several descriptive and genetic studies addressing the role of clinical and etiological factors in the 1) comorbid manifestation of immune-mediated diseases and MDD in AA and 2) therapy response of AA patients. Clinically, we observed associations between age of onset, severity and persistence of AA and comorbid presentation of atopy and autoimmune thyroid diseases. We identified that AA severity is also associated with MDD and there is a strong correlation between age at onset of AA and MDD. We identified suggestive genetic loci associated with the risk of developing immune-mediated comorbidities in AA and showed that there is not a broad genetic overlap between MDD and AA despite the high levels of AA-MDD comorbidity. Finally, we showed that therapy response in AA is associated clinically with disease course and genetically with several variants located in genes implicating the immune response and/or skin biology.

T3

Evidence of deregulated linoleic acid metabolism and fructose-induced tissue hyperuricemia in Alopecia Areata: A role for endothelial damage?

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Abstract

Metabolism has emerged as an important research area in immune-inflammatory diseases. To explore this in the inflammatory hair disease, Alopecia Areata (AA), we performed metabolomics using Liquid Chromatography-Mass Spectrometry (LC-MS) on scalp tissue samples from patients with AA (N=4), comparing non-lesional versus lesional biopsies.

We compared the results against an internal chemical standard library and the NIST mass spectrometry library, putatively annotating a total of 827 metabolites (inclusive of key metabolites involved in central carbon metabolism and amino acid metabolism) that we were confident were correctly annotated, based on internal criteria. Of these, 39 metabolites were found to be significantly altered between non-lesional and lesional AA scalp skin (one-way ANOVA; $p=<0.05$).

Included in these were the linoleic acid metabolites, 13-HODE and Coronaric acid, both of which were significantly decreased in lesional AA skin. 13-HODE may play a key role in the healthy hair follicle (HF) via mechanisms linked to its action on PPAR- γ and TRPV1. Interestingly, a reduction in 13-HODE levels often follows endothelial injury. Moreover, 13-HODE has been implicated in several inflammatory diseases, including asthma and arthritis.

Additionally, LC-MS also revealed that fructose and uric acid were elevated in lesional AA skin. Fructose metabolism can increase uric acid levels, which is a pro-inflammatory metabolite thought to either mark or contribute to endothelial dysfunction. Together, this work suggests a role of altered metabolic pathways in AA pathogenesis, which could be exerted via the infliction of endothelial cell damage.

T4

Integrated safety analysis of ritlecitinib for the treatment of alopecia areata (AA) from the phase 2 and phase 3 ALLEGRO clinical trial program

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Abstract

Background: This integrated safety analysis evaluated the long-term safety of the oral JAK3/TEC family kinase inhibitor ritlecitinib in patients with AA from two phase 2a studies (one ongoing), one phase 2b/3 study, and an ongoing long-term, phase 3, open-label study from the ALLEGRO program.

Methods: Safety data from two cohorts were analyzed: a placebo-controlled cohort from three studies and an any-ritlecitinib cohort including patients who received ≥1 dose of ritlecitinib in any of the four studies. Proportions and incidence rates (IR) of adverse events (AEs) are reported.

Results: In the placebo-controlled cohort (n=881), the proportion of patients with AEs ranged from 69.4% to 75.4% in the ritlecitinib groups vs 69.5% in the placebo group. Eleven patients reported serious AEs, and 19 permanently discontinued due to AEs. In the any-ritlecitinib cohort (n=1294), median duration of ritlecitinib exposure was 624 days (2091.7 total patient-years [PY]). AEs were reported in 1094 patients (84.5%; IR, 179.8/100 PY) and serious AEs in 57 (4.4%; IR, 2.6/100 PY); 78 (6.0%; IR, 3.6/100 PY) permanently discontinued due to AEs. Most common AEs: headache (17.7%), SARS-CoV-2 test positive (15.5%), and nasopharyngitis (12.4%). Two deaths occurred (breast cancer and acute respiratory failure). IRs of opportunistic infections were 0.05/100 PY, herpes zoster were 0.9/100 PY, malignancies (excluding nonmelanoma skin cancer) were 0.3/100 PY, and major adverse cardiovascular events were 0.1/100 PY.

Conclusion: Treatment with ritlecitinib in patients with AA for a median of 1.7 years was well tolerated and demonstrated no new safety signals compared with prior ritlecitinib studies.

T5

Switching between Janus kinase inhibitors in alopecia area: a review of clinical response

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Abstract

Janus kinase (JAK) inhibitors are revolutionising the treatment of alopecia areata (AA), but many uncertainties exist. Data demonstrating the effect of changing JAK inhibitor agent for an AA patient with a sub-optimal response or secondary failure are lacking.

We sought to retrospectively assess the outcomes of switching between tofacitinib and baricitinib in patients with AA in a single tertiary centre. A search of electronic patient records identified 77 patients having been on both oral baricitinib and tofacitinib.

Seventy-three patients received tofacitinib first. Of these, 30 achieved complete hair regrowth, 35 responded partially and 8 had no response. Among the 30 complete responders, 16 were switched to baricitinib during the COVID-19 pandemic (due to safety perceptions) and remained in complete remission. Nine initial tofacitinib complete responders experienced relapse on therapy and switched to baricitinb; 5 experienced full hair regrowth and 4 partial hair regrowth.

All 35 tofacitinib partial responders were switched to baricitinib. Ten experienced complete regrowth. Among the 8 patients who failed to regrow any hair despite tofacitinib therapy, 2 had a partial response and 6 no response upon switching to baricitinib.

Within the limitations of our study, our findings suggest that AA patients who are partial responders to tofacitinib, or experience secondary failure on tofacitinib may benefit from switching to baricitinib. In contrast, patients with AA who fail to regrow any hair with one JAK inhibitor may be less likely to respond to a second JAK inhibitor.

T6

Short anagen hair syndrome: Association with mono- and biallelic variants in WNT10A and a shared genetic etiology with male pattern hair loss

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Abstract

Short anagen hair (SAH) is a rare, paediatric hair disorder characterised by a short anagen phase, the inability of the scalp hair to obtain length, and a negative psychological impact. At writing, the genetic basis of SAH is unknown. Here, molecular genetic investigations were performed in 48 individuals with a clinical phenotype suggestive of SAH. The analyses revealed that 19 individuals (~40%) carried bi- or mono-allelic pathogenic variants in WNT10A. Rare WNT10A variants are associated with a phenotypic spectrum ranging from no clinical signs to severe ectodermal dysplasia. The present analyses revealed a significant association between WNT10A and a distinct SAH phenotype of abnormally short, light-coloured hair, and a regression of the fronto-parietal hairline. Notably, the most frequent variant in the cohort, c.682T>A;p.(Phe228Ile), was in linkage disequilibrium with four common WNT10A variants, all of which have a known association with male pattern hair loss (MPHL). Using UK Biobank data, our analyses showed that c.682T>A;p.(Phe228Ile), and another variant identified in the SAH cohort, are also associated with MPHL, and partially explain the known associations between WNT10A and MPHL. Our results suggest that WNT10A is associated with SAH, and that SAH has a genetic overlap with the common phenotype MPHL. The presumed shared biological effect of WNT10A variants in SAH and MPHL is a shortening of the anagen phase. Other factors, such as modifier genes and sex, may also play a role in the clinical manifestation of hair phenotypes associated with the WNT10A locus.

T7

The use of systemic minoxidil in a paediatric population: A review of 368 children with a variety of hair disorders

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Abstract

Systemic minoxidil is increasingly used off-license for multiple alopecias in adult patients. A large multicentre study reviewing oral minoxidil in adults, demonstrated a good safety profile. Paediatric alopecias can be due to a range of conditions including: disorders of hair loss/aberrant growth, congenital, hair shaft abnormalities and more. There are limited treatments available for our paediatric population.

We performed a retrospective review of all paediatric cases treated with oral minoxidil to evaluate the safety and efficacy between January 2012 to 2022. We reviewed demographics, diagnosis, previous treatments, systemic minoxidil doses, use of topical minoxidil, side effects, concomitant medications, and severity scores pre/post-treatment.

A total of 368 patients were identified. The mean age was 12 years old (range 2-18 years). There was a female predominance. Doses of sublingual minoxidil ranged from 0.1 to 4.5mg. It was well-tolerated, with 28 patients (7.6%) reporting an adverse event, the most common being hypertrichosis and dizziness with three patients discontinuing treatment. Our adverse events echo that of the adult population.

The diagnoses treated included androgenetic alopecia, alopecia areata, loose and short anagen syndromes, trichotillomania, monilethrix, woolly hair syndrome and traction alopecia. Alopecia areata and androgenetic alopecia were the most common conditions. Androgenetic alopecia patients improved on the grading scale by 1 point. Loose anagen syndrome cases showed improvement with negative hair pull post-treatment. However, not all hair disorders demonstrated a significant response.

Reviewing the use of oral minoxidil in a variety of paediatric hair disorders can enable us to further understand its mechanism.

T8

Hair ageing in Black women (age>59): impact on personal and social identity and subjective wellbeing.

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Abstract

The natural fragility of high curl types is well documented, however, the impact of ageing on such a hair is less well known. This inter-disciplinary project straddles hair science, gerontology and psychology and explores:

·The evolution of hair management practices of Black women from the perspective of ageing.
·The impact of age-related hair changes on subjective well-being.

The study was based on a mixed methods approach, beginning with an online survey (Qualtrics XM, USA) and followed by a series of in-depth semi-structured interviews and thematic analysis (NVivo12, QRS International, USA).

The quantitative data (n=46, age>60years) identified statistically significant age-related shift in hair styles away from braiding and chemical relaxing but hair colouring was not impacted. Current hair style attractiveness was positively correlated with satisfaction with hair colour, length and texture. The qualitative research (n=10, age=59-67years) identified three main themes:

·Hair ageing with subthemes: greyness/texture and health (267refs);
·Hair and identity with subthemes: social, cultural and political identity (297refs);
·Wellbeing with subthemes: scalp and fibre health, age-related practicalities, emotions (185refs).

Overall, age did not diminish the desire to maintain hair as a personal attribute important for the social and cultural identity as well as for the subjective wellbeing but impacted the time and effort that women were prepared to put into hair management. They were not prepared to accept hair greying but were concerned with hair loss due to chemical and styling processes. In conclusion, hair ageing studies can contribute to the body of science focused on ageing and wellbeing.

T9

The psychosocial impact of alopecia areata on men: A qualitative investigation

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Abstract

Men's experiences of alopecia areata (AA) are underexplored to date, so we sought to explore this question with a view to informing psychosocial and practical support for affected men. To do so, we collected qualitative data embedded within a larger mixed-methods study. Participants were men aged over 16 with AA. In an online survey, 74 men wrote about the subjectively salient aspects of their experiences of AA, which we analysed through inductive content analysis. Eighteen survey participants then participated in remotely conducted semi-structured interviews to explore their experiences in depth, analysed via reflexive thematic analysis.

Participants' survey responses generated multiple themes within the broad categories of internal experiences, practical experiences, influence of others, comparators, and treatment. The most common theme was depleted confidence and wellbeing (57%), with around a quarter also describing impacted social functioning, and adopting concealment strategies. Researchers' interview analysis generated four themes: The unknown man, which described male AA as unknown at a societal and personal level; The man in context, illustrating how participants' experiences were shaped by contextual factors like comparisons with male pattern baldness and women with AA, and demographic characteristics such as sexual orientation; The burdened man, which summarised the personal, social and physical challenges experienced by men including felt emasculation; and The grown man, describing participants' positive adjustment to AA.

Findings offer important nuance to our understanding of how men experience AA. Interpretation through the lens of masculinities may help understand findings more clearly and develop more appealing support content for men.

T10

Senescence-Associated ß-Galactosidase expression is not primarily related to cellular senescence in aggregating rat dermal papilla cells in vitro.

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Abstract

INTRODUCTION AND OBJECTIVES

Hair follicle ageing has been linked to dermal papilla cells and the phenomenon of cellular senescence, with associated loss of proliferative and migratory capacity, is a feature of cultured primary cells. We have observed an intense increase of senescence-associated-beta-galactosidase (SA-β-gal) label (the most common marker of cellular senescence) in spontaneously aggregating and aggregated primary rat vibrissae follicle dermal papillae cells (DPCs) in vitro. Here we investigated whether, in this context, SA-β-gal labelling was a reliable indicator of cellular senescence.

METHODS

Subconfluent, aggregating and cryosectioned aggregates of rat DPCs were immunolabelled with various senescence and proliferation markers including Lamin B1 (nuclear envelope), γ-H2AX (DNA double-break damage repair) and Ki 67 (cell proliferation). Aggregating cultured rat DPCs were activated by scratch wounding, and SA-β-gal stained at pH 6.0 before wounding and 24 and 48 hours post-wounding.

RESULTS

Antibody marker expression in and around DPC aggregations was not consistent with strong SA-β-gal senescence labelling. Proliferative Ki 67 positive cells were still present, Lamin B1 revealed that most cells had normal nuclear structure and the γ-H2AX DNA repair mechanism was not prominent. Interestingly, cells that had migrated from aggregates to heal scratch wounds were SA-β-gal labelled, and after enzymatic passaging most DPCs from aggregates lost SA-β-gal staining.

CONCLUSIONS

Our antibody results question whether SA-β-gal labelling genuinely reflects cellular senescence in rat DPC aggregations, particularly as SA-β-gal activity can apparently be reversed functionally.

T11

Miniaturisation of hair follicles in androgenetic alopecia may be driven by accelerated localised ageing

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Abstract

Androgenetic alopecia (AGA) is characterised by miniaturisation of hair follicles (HF) in the frontal, parietal and vertex of the scalp whilst HF in the occipital scalp are spared. The dermal papilla (DP) is the signalling centre of the HF which controls growth and cycling of the HF. In AGA, the volume of the DP decreases which correlates with decrease in the size of the hair shaft and miniaturisation of HF. To investigate the role of the DP in miniaturisation, matched donor DP from the frontal (FDP) and occipital (ODP) scalp were isolated from 4 patients with AGA and used for transcriptomic analysis. This revealed differential gene expression between the FDP and ODP with EGR1, HSPB1, DNAJB1 and APOD all significantly upregulated in the FDP versus the ODP. All 4 of these genes have previously been identified as upregulated in the DP of aged mice versus young mice. To investigate if this was coincidental or if FDP have an increased biological age relative to ODP, we looked at the methylation status of an ageing marker, ELOVL2, in FDP and ODP from HF of patients with AGA. Using an equation to calculate biological age of tissues from ELOVL2 methylation profiles, we found that FDP have a significantly higher biological age compared to ODP. We also found a significant increase in biological age of frontal HF compared to occipital HF in AGA patients. These results point towards accelerated ageing of frontal HF and the potential to utilise anti-ageing therapies to treat AGA.

T12

The study of aged scalp reveals biological changes associated to the decrease of hair density

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Abstract

Hair density decreases with age in non-androgenetic alopecic individuals, both in men and women. The biological basis for these chronological changes is not clear. Hair growth is assumed to primarily rely on intrinsic controlled mechanisms. However, hair growth is also affected by factors from the hair follicle environment. To identify the origin of the decrease of hair density with age we have recruited a cohort of sixty-three Caucasian women, aged 65 to 75 y.o., with either a hair density ≥ 220 hairs/cm² (high density (HD) group) or a hair density ≤ 185 hairs/cm² (low density (LD) group). Clinical assessments, questionnaire, and RNA sequencing of scalp biopsies have been deployed to reveal the scalp characteristics in the cohort. The results show that hair diameter changes were associated to the HD and the LD groups, and also suggest the decrease of hair density with age exhibits a family history. No difference on the other demographic criteria were associated to the hair density. With other respects, mRNA sequencing identifies differentially expressed genes between HD and LD groups, which significantly highlight GO terms. Immuno histology analyses further revealed differences in Mast cells number in the scalp of LD vs. HD groups. Together our results identify modifications in the hair follicle eco system that go along with the decrease of hair density with age in women.

T13

Cryopreserved Hair Follicles as a Source of Differentiated and Stem Cells for Regenerative Medicine

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Abstract

Hair follicles obtained from routine, outpatient surgical procedures are an easily accessible source of numerous cell types, including dermal papilla cells, bulge stem cells, keratinocytes and melanocytes. Follicles can be removed quickly, with minimal scarring or complications.

The development of technologies capable of cryopreserving cells and tissue brings about the potential to preserve all the cell types found within a follicle in one place, much like an adult alternative to cryopreserving cord blood at birth for potential future regenerative therapies.

We have demonstrated that cryopreserving follicles using a proprietary method results in viable growth of numerous cell types that would be suitable for clinical application.

Follicles were thawed, washed and dissected or exposed to enzymatic digestion depending on the cell type being grown. To date, this has given rise to viable cultures of dermal papilla cells, dermal sheath cells, melanocytes and a mixed epithelial cell population from the bulge region. Many of these cell types are being used by various laboratories as starting material for potential cell therapies, including androgenetic alopecia, vitiligo, wound healing and as a source for induced pluripotent stem cells (iPS cells).

These results provide an exciting opportunity for researchers and the public to generate autologous cell banks that could be called upon as and when treatments are available and/or required. Cells can be banked when young to replenish ageing or dysfunctional tissue at a later date.

T14

Scalp and gut microbiome in Female Pattern Hair Loss – a promising therapeutic target ?

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Abstract

Background: Female pattern hair loss (FPHL) is one of the commonest forms of non-scarring hair loss in women and is characterised by follicular miniaturisation. It has a complex multifactorial hitherto unexplained pathogenesis. Cutaneous microbiome has been extensively studied as a contributing factor in various skin and hair disorders. There are studies indicating its role in alopecia areata and male androgenetic alopecia.

Objective : The objective of this study was to characterize the skin and gut microbiome of patients with FPHL, and compare microbial composition to healthy individuals.

Methods: This was a pilot, case-control study. Scalp and faecal microbiome samples were collected from 25 female patients with FPHL, and 25 age matched controls. Hair follicles were analysed from occipital and vertex scalp and characterised by 16s rRNA sequencing. The microbiome properties were compared between cases and controls.

Results: The FPHL scalp microbiome was significant for elevated Propionibacterium acnes and Malasseziomycetes in the areas affected by hair loss. The gut microbiome was significant for increased Bacilli ($p<0.05$) compared to healthy controls.

Conclusions: The composition of the scalp and gut microbiome is significantly different in FPHL compared to than healthy individuals. Future research may enable therapies for FPHL through modification of diet to regulate to disease severity and prognosis.

T15

A multi-omics approach to identifying factors involved in hair follicle growth and development

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Abstract

Mesenchymal hair follicle (HF) cells tightly control both differentiation patterns and hair cycle progression as well as possessing the ability to induce de novo HFs after transplantation into non-hair bearing skin. However, this inductivity as a structure is quickly lost when dermal papilla (DP) cells are cultured (2D). We can restore this through hanging drop culture, where spheroid (3D) formation recreates an in vivo like environment. To study this switch, we developed an in vitro model comparing DP to Papillary fibroblasts (PFi), which come from the same progenitor but are not inductive in either 2D or 3D. We hypothesize that chromatin level differences between DP and PFI exist with unique changes in 3D DP restoring an inductive mesenchymal niche. Thus, ATAC-seq & RNA-seq were used to investigate how associated changes in chromatin arrangement may regulate gene expression relating to both cell-specific and culture-specific changes underlying inductivity. By integrating differentially expressed genes with condition specific dynamic chromatin loci, we selected several transcription factors with potential roles in inductivity. Through testing various combinations of these factors using molecular techniques and the patch assay we continue to investigate if cultured cells can be reprogrammed to (re)gain HF inductivity. If successful, this would be an early step towards a possible cell therapy based approach to hair restoration addressing two major issues: the limited donor tissue supply and the loss of inductivity using traditionally cultured DP cells.

T16

Psychiatric side effects of finasteride: what do we need to know?

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Abstract

Introduction: Finasteride is used to treat benign prostatic hyperplasia (BPH) and androgenetic alopecia (AGA). Finasteride's potential for psychiatric side effects has long been a topic of discussion. The majority of prior research was uncontrolled and prone to bias. Several investigators suggested that the pharmacological effects of finasteride differ with age, with younger males with AGA being more vulnerable.

Objective: The aim of our population-based study was to determine whether finasteride therapy is associated with development of mental health conditions.

Materials and Methods: Current case-control study compared the data from patients with AGA who received finasteride 1mg daily and patients with BPH who received finasteride 5mg daily with age and gender matched controls. The incidence of psychological health outcomes within two years of beginning finasteride therapy was evaluated.

Results: The AGA group consisted of 23,227 patients and 39,444 controls. Mental health outcomes developed in 1.02% of patients and 0.94% of controls. The BPH group included 307 patients and 1218 controls. Mental health outcomes appeared in 2.3% of BPH patients and 1.5% of controls. Patients with AGA had higher rates of anxiety and depression compared to controls (0.6% vs. 0.4%, and 0.5% vs. 0.4%, respectively).

Conclusions: Our study found that finasteride users had a very low rate of mental outcomes. According to our findings, there is no justification to avoid using finasteride due to mental health concerns. Our findings will be discussed, and published data on finasteride mental side effects will be reviewed.

T17

Composition, distribution, abundance, viability, and functional effects of the human hair follicle microbiome

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Abstract

Human hair follicles (HFs) constitute an unique microbiome habitat that varies substantially from the skin surface and becomes dysbiotic in several HF-associated diseases. Traditional HF sampling methods fail to eliminate skin microbiome contaminants, assess the HF microbiome incompletely, and/or do not address the role of the microbiome in human HF physiology. Here, we used laser-capture microdissection, shotgun sequencing, and fluorescent in situ hybridization to map the human scalp HF microbiome in defined HF compartments. We found significant compartment-, tissue lineage- and donor age-dependent variations in microbiome composition. Staphylococcus epidermidis demonstrated the greatest abundance variations between HF compartments, while Cutibacterium acnes and Malassezia restricta were the most abundant viable HF commensals (propidium monoazide assay). Infection of scalp HFs ex vivo with an S. epidermidis-specific lytic bacteriophage induced HF dysbiosis and downregulated expression of genes that regulate HF development and cycling, apoptosis or immune status. This suggests that microbiome products may modulate HF functions. Indeed, butyrate, a key metabolite of S. epidermidis and other core HF commensals, delayed catagen and promoted HF autophagy, mitochondrial activity, gp100, and dermcidin expression ex vivo. Hence, this comprehensive characterization of the human HF microbiome reveals important spatial variations in its abundance and viability and suggests that it modulates human HF function, inviting therapeutic targeting.

T18

Transcriptomic profiling of laser captured suprabulbar outer root sheath reveals genes involved in immune privilege and inflammatory response by dandruff hair follicles

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Abstract

Dandruff is characterised by flaking and mild inflammation, occurring on the scalp where there is an abundance of hair follicles (HF). The HF has immune privilege (IP) which involves active mechanisms to inhibit inflammation and promote immune tolerance. We have recently found that there is weakening of HF IP in the suprabulbar outer root sheath (ORS) in dandruff as elucidated via in situ protein expression analyses of IP markers (in preparation for submission). However, it is unknown whether gene expression patterns within this compartment in dandruff scalp show any changes that might be similarly reflective of this weakened IP phenotype. We performed RNA-Seq using laser captured tissue obtained specifically from the suprabulbar ORS, comparing healthy versus dandruff HFs (lesional and non-lesional, N=4 patients). We conducted differential gene expression analysis to observe the expression levels between the comparison groups. We found a total of 115 differentially regulated genes in lesional versus healthy ORS, 715 in lesional versus non lesional ORS and 93 in non-lesional versus healthy ORS (p-value <0.01, fold change 1.5). Next, we undertook bioinformatics comparison using QIAGEN ingenuity pathway. In lesional and non-lesional compared to healthy ORS analysis revealed changes in genes involved in immune response and inflammatory canonical pathway, in particularly genes involved in immune privilege (p-value <0.01), while in lesional versus non-lesional ORS, genes are involved in the hair growth cycle pathway. Our data suggests that the suprabulbar ORS have changes in genes involved in immune privilege and may contribute towards the inflammatory response in dandruff.

T19

A novel topical treatment based on sodium dimethylglycinate and caffeine against male pattern hair loss.

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Abstract

N,N-Dimethylglycine is a naturally occurring compound being widely used as an oral supplement to improve growth and physical performance. Preclinical data already highlighted the positive impact of sodium dimethylglycinate (DMG) on crucial parameters for skin biology by promoting cellular proliferation, migration and inducing the synthesis and release of growth factors (i.e. VEGF) in cultured human epidermal keratinocytes. Further clinical data demonstrated an increase of skin microcirculation after single topical application of a DMG containing gel compared to placebo and untreated control in male and female subjects. Caffeine is a well-known natural ingredient for topical application since more than 2 decades, which has already been proven to be efficient, active and safe for the treatment of male and female pattern hair loss.

Here we report the results of two single-centre, double-blind, randomized, placebo-controlled studies on total 308 male subjects (age 18-65) suffering from male pattern hair loss. Subjects either used a caffeine- and DMG-containing verum product (tonic or shampoo) or the corresponding placebo. In both trials the reduction in the number of pulled hairs after application of the verum products was significantly greater compared to the application of the corresponding placebos. Subgroup Phototrichogram analysis showed a significantly greater increase in the number of hair, hair density and percentage of anagen hair after 6 months of verum product usage (tonic or shampoo) compared to the placebo groups.

These results emphasize the important role of sodium dimethylglycinate and caffeine as a novel treatment against male pattern hair loss.

T20

Treatment with Estetrol results into anagen prolongation, promotion of dermal papilla functions and expansion of stem cell progeny in female healthy hair follicles ex vivo

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Abstract

Female Pattern Hair Loss (FPHL) is a non-scarring alopecia resulting from telogen effluvium and the conversion of terminal into vellus hair follicles (HFs). Hormones imbalances are among the putative causes, including lower level of estrogens. However, contradictory results have been published on the effect of estrogens on HF functions. Here, we aimed at evaluating the impact of the natural estrogen Estetrol (E4) on hair growth promotion, which is currently in development for use as menopausal hormone therapy. Fronto-temporal, full-length microdissected HFs from 4 healthy female donors (>50 years) were exposed to E4 ex vivo and hair cycle associated parameters were analyzed by quantitative (immuno-)histomorphometry. E4 administration (300nM and 30µM tendentially, and 3µM significantly) enhanced anagen HF numbers and hair matrix keratinocyte proliferation (Ki-67+cells). Dermal papilla (DP) fibroblast emigration was reduced as demonstrated by significantly less cells in the DP stalk and dermal cup in E4 treated HFs, while DP size and cell density remained unaffected. E4 treatment also stimulated DP fibroblast inductivity, as shown by enhanced versican expression and alkaline phosphatase activity, particularly in anagen only HFs. Application of 3µM E4 significantly increased the % of HF stem cell progeny (CD34+cells) in the suprabulbar outer root sheath. Taking together, we show that E4 maintains anagen ex vivo, further supporting prevention of hair loss. Our finding also points towards a role for E4 in interfering with HF miniaturization by enhancing DP inductivity and stem cell progenitor pool. Thus, our data invite additional pre-clinical and clinical exploration of E4 in FPHL management.

T21

Metformin Attenuates the Loss of Keratin 15+ Epithelial Stem Cells an In Vitro Model of Scarring Alopecia

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Abstract

Primary cicatricial alopecia (PCA) or 'scarring alopecia' encompasses a group of hair loss disorders whereby the hair follicle (HF) is irreversibly damaged. The damage occurs from the loss of bulge epithelial stem cells (eSCs) via apoptosis and epithelial-mesenchymal transition (EMT). Thus, effective therapy should prevent or reverse EMT in eSCs, however, treatment options for PCA conditions are limited.

Metformin has demonstrated improvement in inflammation and fibrosis in a murine model of fibroproliferative disorders by activating AMPK, which we have previously shown to be upregulated within the human HF bulge. To test whether metformin could be effective in the prevention of PCAs, we treated human HFs (n=3) with metformin within a 5-day ex vivo EMT-induction scarring alopecia model.

As expected, HFs treated with the EMT-induction cocktail showed significantly decreased e-cadherin and keratin 15+ (K15+) expression, and significantly increased vimentin expression in the bulge, confirming that EMT induction was successful. Metformin treatment did not mitigate EMT cocktail-induced changes seen in the expression to e-cadherin and vimentin in the bulge. There was however a trending ($p=0.0685$, Kruskal-Wallis test with Dunn's multiple comparisons) rescue of K15+ expression in the bulge, suggesting that metformin may promote the survival of K15+ cells following massive EMT-induction within our model. Therefore, this work warrants further investigation with additional donors to determine whether metformin can effectively prevent eSC loss to help manage PCAs.

T22

Pharmacologic inhibition of TGFβ signaling improves human hair follicle growth cycle

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Abstract

Androgenic alopecia (AGA) is characterized by hair follicle (HF) miniaturization during repeated hair cycles with shortened anagen. Androgens, in particular dihydrotestosterone (DHT) generated by α5-reductase metabolization of testosterone, act via the DP in inducing hair loss. The higher levels of type II α5-reductase and of androgen receptors (AR) in DPCs from balding vs. non-balding scalp HFs, drive a gene expression program that negatively impacts hair growth, for example inhibiting the Wnt/β-catenin signaling pathway and transcriptionally activating the transforming growth factor beta (TGFβ) signaling pathway.

Here, we set out to pre-clinically validate the efficacy of a potent TGFβ receptor I (TβRI) inhibitor as a potential pharmacological intervention to treat AGA. We found that inhibition of 2D culture-driven TGFβ signaling improves DP cell molecular signatures by inhibiting pro-fibrotic gene expression, which is relevant for bioengineering approaches using DP cell expansion. TGFβ signaling inhibition in the DP of human HFs translates into improved proliferation and β-catenin levels in the hair bulb epithelial compartment and delayed catagen onset. Moreover, using depilated mice, we demonstrated that topical drug treatment prolongs the hair cycle anagen stage, enhancing hair growth without apparent side effects. Histological studies further confirmed that drug treatment improves the proliferation of murine hair germ progenitor cells.

Overall, we disclosed a small-molecule compound that improves DP fitness and the HF cycle, thus encouraging its clinical validation as a safe and effective pharmacologic treatment for human hair loss.

T23

Soluble CD83 mediates hair growth by triggering stem-cell related pathways and accelerating anagen progression

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Abstract

Introduction
Hair loss is a global issue affecting up to 70% of world's population. Current treatment strategies for androgenic hair loss only prevent or slow down further hair loss but formation of new follicles has not been achieved to date. However, this would be the ultimate aim.

Methods
To investigate, weather we can transfer the pro-regenerative capacities of sCD83, observed during wound healing, into the setting of hair regrowth, 7w old female C57BL/6 mice have been depilated and treated systemically for three consecutive days with sCD83 (100 µg/ml) or PBS as a control. Hair regrowth has been assessed for the next 15 days, using microscopic as well as histological analyses. In addition, to elucidate underlying mechanisms on a molecular level, transcriptome analyses have also been included.

Results
Subsequent to depilation, sCD83-treated mice showed a prominent pigmentation and wrinkling of dorsal skin, which indicates an accelerated onset and progression of the anagen-stage. On histological level, hair follicles of sCD83-treated mice surpassed PBS-controls in number, size and shaft length on day 7 and day 15. In addition, RNA sequencing analyses of skin biopsies unveiled the upregulation of stem-cell associated transcripts such as Wnt, Notch and SHH.

Conclusion
Herein, we report the interesting properties of sCD83 regarding hair regrowth. Thus, translation of these results into the human setting is pivotal for us, since it might provide a new therapeutic option for the treatment of hair loss, including androgenic alopecia as well as alopecia areata.

T24

Innervation patterns around the human hair follicle

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Abstract

The hair follicle (HF) plays an important role in biological processes beyond hair production including angiogenesis and wound repair. However, its influence on other tissues such as the nervous system remain underexplored. Recent studies in mice have explored the effects of the perineural niche on the HF, but to our knowledge, the HF's influence on the nervous system has not yet been examined. In our preliminary studies, we showed that the K15+ bulge and upper bulge of the human HF is innervated by a diverse network of sensory neuron subtypes and possesses significant enrichment of genes involved in neuron differentiation and development, highlighting a close connection between the HF and the nervous system. To interrogate if this connection was bidirectional, we used biochemical and voltammetry analysis, and found that bulge cells release synaptic vesicles that can directly activate sensory neurons in vitro, demonstrating that the HF signals to the nervous system. We hypothesised that in addition to signalling, the HF bulge also influences the development and maturation of sensory neuron subtypes around it. To investigate this, we used direct neuronal reprogramming of fibroblasts via ASCL1 overexpression as a model for developing neurons, observing transcriptional upregulation of neuroectodermal progenitor markers in the induced neurons post-transduction. To explore the role of the bulge on guiding innervation, we evaluated the effects of bulge cell-conditioned media on neuronal induction. Overall, our work sheds light on the developmental mechanism of HF innervation and ultimately how the HF interacts with other tissues in the body.

T25

Exploring the potential of farudodstat, a DHODH inhibitor, as an alopecia areata therapeutic in a novel ex vivo model of human hair follicle immune privilege collapse

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Abstract

Alopecia areata (AA), an inflammatory hair follicle (HF) disorder, is characterized by hair loss resulting from the collapse of immune privilege (IP) in the HF bulb and a Th1-dependent inflammatory response. Given the key role of dihydroorotate dehydrogenase (DHODH) in T-cell proliferation and pro-inflammatory cytokine production, we explored whether farudodstat, a novel DHODH inhibitor, may address key events of AA pathophysiology. To test the potential of farudodstat, we utilized an ex vivo HF organ culture and induced the HF IP collapse by activating resident intra- and peri-follicular T-cells with an anti-CD3/CD28 antibodies. Induction of T-cell receptor (TCR) activation ex vivo yielded in local enrichment of proliferative T-cells as indicated by up-regulation of CD3+ and CD3+Ki-67+ cells, and promoted key signs of HF IP collapse, i.e. an increase in of MHC class I and II expression and numbers of MHC class II+ cells in the bulb. Farudodstat tested at clinically relevant doses in this AA-HF disease model resulted in significant reduction of proliferative T-cells. Additionally, farudodstat treatment abrogated MHC I and II expression, and reduced MHC II+ presenting cells. Importantly, farudodstat treatment in healthy HFs had no effect on hair cycle, hair matrix keratinocyte production or MHC I and II expression. Our results indicate TCR activation induced by anti-CD3/CD28 in ex vivo human HF exhibits key features of AA including IP collapse. Additionally, our data suggest that farudodstat protects against IP collapse by blocking key events of AA pathophysiology and may offer a potential approach for the treatment of AA.

T26

Topical Cinnamaldehyde Exposure of Reconstructed Human Skin with Integrated Neopapillae: an Organ-on-Chip Study

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Abstract

All cosmetic ingredients registered in Europe must be evaluated for their safety using non-animal methods. Microphysiological systems (MPS) offer a more complex higher-tier model to evaluate chemicals. Skin is one of the major routes of penetration into our body after substance exposure. Our aim was to generate a robust culture for a next-generation human skin-on-chip model containing neopapillae to mimic the hair shaft penetration route and to establish proof-of-concept testing with the sensitizer, cinnamaldehyde. Reconstructed human skin consisting of a stratified and differentiated epidermis on a fibroblast populated hydrogel containing neopapillae spheroids (RhS-NP), were cultured in air-liquid interphase and under dynamic flow for 10 days. The epidermis was seen to invaginate into the hydrogel towards the neopapille spheroids. The model demonstrated high viability and stable metabolic activity throughout the culture period in three independent experiments. Topical cinnamaldehyde exposure to RhS-NP resulted in dose-dependent cytotoxicity (increased LDH release) and elevated cytokine secretion of IL-18, IL-1β, IL-23 and IFNγ, as well as IL-10 and IL-12p70. This study demonstrates the robustness and feasibility of complex next-generation skin models for investigating compound safety and toxicity.

Poster Presentations

Abstract Number	Title
	Alopecia Areata
P1	A long journey to a safe, affordable and effective injectable treatment for alopecia areata
P2	A retrospective study on the clinical characteristics and prognosis of alopecia totalis and universalis : an update on prognosis
P3	Case series of alopecia areata in inflammatory bowel disease patients
P4	Patient-Reported Burden of Severe Alopecia Areata: First Results from the Multinational Alopecia Areata Unmet Need Survey
P5	The Contribution of Hair Regrowth to Health-Related Quality of Life Improvements in Patients with Alopecia Areata Treated with Baricitinib or Placebo
P6	Efficacy of Baricitinib in Patients with Various Degrees of Alopecia Areata Severity: Results from BRAVE-AA1 and BRAVE AA-2
P7	Scalp Hair Regrowth is Associated with Improvements in Health-Related Quality of Life (HRQoL) and Psychological Symptoms in Patients with Severe Alopecia Areata: Results from Two Randomized Controlled Trials
P8	Long-term Efficacy of Baricitinib in Alopecia Areata: 104-week Results from BRAVE-AA1 and BRAVE AA-2
P9	Outcomes of Down-Titration in Patients with Severe Scalp Alopecia Areata Treated with Baricitinib 4-mg: Week 104 Data from BRAVE AA-2
P10	The role of inflammasome in alopecia areata
P11	A Clinical Investigation of Early-Onset Alopecia Areata in Children: onset earlier than 4 years of age might have a better prognosis
P12	Real-world effectiveness and safety of baricitinib in patients with alopecia areata
P13	Efficacy of calcipotriol/betamethasone ointment in management of pediatric alopecia areata
P14	Clinical efficacy and safety of baricitinib for alopecia areata in Korea: single centre experience
P15	Recurrent episodes of alopecia totalis post COVID-19 vaccination
P16	Evaluation of the early efficacy and safety of JAK inhibitors in patients with refractory severe Alopecia Areata
P17	Markers of Th2 in alopecia areata and their correlations to allergy, atopy and longer disease duration
P18	Risk of subclinical atherosclerosis in severe alopecia areata patients
P19	Efficacy of topical immunotherapy with 2,3-Diphenylcyclopropenone-1(DPCP) in patients with extensive Alopecia Areata. Twenty years of experience from the Hair Diseases Department of “Andreas Syggros” Hospital, Athens, Greece.
P20	Alopecia Areata Totalis treated with phytotherapy and intradermotherapy with results similar to JAK inhibitors
	Genetic and Acquired Alopecia
P21	Dermoscopy findings of the axilla of women with frontal fibrosing alopecia
P22	Immersive VR : an adjunctive measure to improve quality of life in chemotherapy induced alopecia
P23	The involvement of the scalp and nail apparatus in cutaneous lupus erythematosus patients: A retrospective study

Poster Presentations

Abstract Number	Title
P24	Efficacy of oral retinoids as a maintenance therapy in cicatricial alopecia: a retrospective study
P25	Minoxidil-induced trichostasis spinulosa of vellus hair?
P26	Do statins have a role in treating Frontal Fibrosing Alopecia?
P27	A case of male frontal fibrosing alopecia after COVID-19 vaccination
P28	Vibration assisted analgesia during intralesional corticosteroid therapy for alopecia
P29	3D camera imaging of Frontal Fibrosing Alopecia: a novel assessment method
P30	Lichen planopilaris in women with Afro-textured hair
P31	Frontal fibrosing alopecia in South Africa: a questionnaire study
	Hair Ageing and Hair Loss
P32	Seasonal hair loss in Northern and Southern Hemispheres: Insights from Google Trends data
P33	Interest of a Cinchona succirubra extract and its association with Caffeine in hair loss
P34	Molecular monitoring of transcriptional effects following treatment of male volunteers with commencing hair loss after treatment with an extract of Quassia Amara Wood containing serum
	Hair and Scalp Science
P35	Trichoscopic findings after hair transplant with FUE technique
P36	Scalp analysis with Multiparametric Ultrasound before and after application of cosmetic with vasoconstrictor active
P37	Pitfalls in alopecia photography.
P38	Scalp flora plays a role in the hair regrowth effect of topical minoxidil.
P39	Scalp interactome, what impact does a new treatment shampoo have on the ecosystem of the scalp with seborrheic dermatitis? Focus on flaking, inflammation and pruritus.
P40	Targeting inflammation and specialized pro-resolving mediators: a new pathway to improve scalp condition?
P41	Quantifying Particle Deposition on Hair by Streaming Potential
P42	Is the fatigue and failure resistance of hair dependent on ethnic origin?
P43	Evolution of hair measurements for clinical outcomes: Are they reliable?
P44	Effect of particulate matter on hair disease
P45	Effect of ethnicity, temperature, and humidity on the viscoelastic behaviour of human hair fibres, and the associated structural changes identified with FT-IR microscopy
	Hair Growth and Cycling
P46	Transcriptomics to uncover the role of the dermal papilla in human hair fibre pigmentation
P47	Impact of topical application of anti-dementia agents on hair growth

Poster Presentations

Abstract Number	Title
P48	Mapping HIF1a and ARNT to cell states and identities in cycling human hair follicle: the keratinocyte fate in the “adaptive signaling landscape”
P49	Unveiling the trichogenic signature of the human native dermal papilla
P50	Activation of mitochondrial aldehyde dehydrogenase 2 promotes hair growth
P51	Noncontact compression promotes hair growth through vasodilation
P52	Revealling the anagen prolonging effects of a ginger extract by means of different in vitro and ex vivo hair follicle models
P53	Wnt ligand expression diversity during mouse hair follicle development.
	Macroenvironment and Models
P54	Using in vitro and ex vivo culture models to study the ability of cooling to suppress oxidative stress-mediated, chemotherapy drug-induced alopecia
P55	The role of T-helper 17 cells and regulatory T cells in acute diffuse and total alopecia
P56	A concept for the molecular monitoring of transcriptional effects of hair growth stimulating serums
P57	High throughput screening in vitro assays for the identification of drug candidates inhibiting immune privilege collapse in alopecia areata
P58	Optimized Hidradenitis Suppurativa skin
P59	Ex vivo evaluation of the hydration capacity of a new haircare product and its active ingredient based on cactus extract by using the method of Nuclear Magnetic Resonance (NMR)
	Patterns of Hair Loss
P60	The investigation of clinical characteristics of male patients diagnosed with early-onset androgenetic alopecia: a possible association with metabolic syndrome
P61	Efficacy and safety of dutasteride 0.2mg in male androgenic alopecia patients: a multi-center, randomized, double-blinded, placebo-controlled, parallel group, phase III clinical trial
P62	Hi-C 3D Genomic Interactions confirm role of wnt in androgenetic alopecia
	Psychology
P63	Eye Movement Desensitisation and Reprocessing Therapy (EMDR) in the management of Alopecia Areata (AA)
P64	The percentage of online consultation increased from 15% to 40% after the COVID-19 pandemic.
P65	There's a sense of losing yourself and who you are”: Development of a conceptual model via literature and interviews points to large psychosocial burden and lower health-related quality of life for UK-based alopecia patients with ≥50% hair loss.
P66	The socioeconomic burden of Alopecia Areata
P67	The importance of trichoscopy in psychotrichologic disorders
P68	Successful treatment of trichotillomania with habit reversal therapy in a child.
P69	Unsupervised Self-sourced Medication for Alopecia: The Tip of the Iceberg?

P1

A long journey to a safe, affordable and effective injectable treatment for alopecia areata

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Abstract

Although the pathogenetic pathways of alopecia areata (AA) are now better understood, treatment is still a challenge and not always successful. Novel therapeutic modalities, such as JAK-inhibitors, are a new hope for effective AA treatment. However, they are not curative, they need to be used long term for continued results, and current oral administration modalities are expensive. For people on a budget, those with limited insurance, and/or those treated within state health care systems, intradermal injection may potentially be more financially viable and similarly efficacious in promoting hair growth. Low dose triamcinolone-corticosteroid injections for AA have been available for many years. However, dermatologists providing such treatments report that injecting large areas of scalp is tedious, can be painful for the patient, and results can vary depending on the consistency of injection application. To overcome these problems, we herewith describe the development of a unique, motorised injection device, to precisely and reproducibly deliver very small (µl) volumes to predefined depths of the scalp, with consistent distribution. We describe the development of prototypes, needle cushions, contact cooling plates and finally functional tests, which led to the device currently undergoing approval processes by regulators. The device will speed up intra-dermal injection procedures, reduce costs by consistently applying specific drug volumes across larger areas of skin, and its push button design will reduce the risks of repetitive strain injury for dermatologists. We believe the device will add new treatment possibilities for AA, and also for other skin and scalp diseases.

P2

A retrospective study on the clinical characteristics and prognosis of alopecia totalis and universalis : an update on prognosis

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Abstract

Alopecia totalis and universalis are the most severe forms of alopecia areata, and they are known to have a poor prognosis with high relapse rate, and treatment failure is observed in many patients, regardless of the type of treatment. Through recent advances in therapeutic modalities, the prognosis of alopecia totalis and universalis has improved over the years, however old data are routinely cited in many scientific literatures without questioning them.

We aimed to study the clinical characteristics and prognosis of alopecia totalis and universalis to update and compare the results with those of previously reported studies.

We retrospectively reviewed patients diagnosed with alopecia totalis and universalis from 2006 to 2017 in our institution.

Of the 419 patients diagnosed with alopecia totalis or universalis, the mean age of 1st episode was 22.9 years, and 24.6 % had early onset (≤13 years old). During follow-up, 53.9% had more than 50% hair growth, and 19.6% of patients showed an >90% hair growth. Among patients who showed >50% improvement, 36.7% had no recurrence during the follow-up.

In early studies conducted in the 1950s and 1960s, the chance of full hair regrowth was reported to be <10%. We provide an update on data regarding the prognoses of alopecia totalis and universalis. This study reports the largest series of patients with AT and AU describing the specific data of important value to clinicians when informing patients about their prognosis.

P3

Case series of alopecia areata in inflammatory bowel disease patients

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Abstract

Alopecia areata (AA) is common cause of non-scarring hair loss. AA may occur as a single disease entity or coexist with other autoimmunological disorders such as Hashimoto thyroiditis and vitiligo. Recently the relationship with inflammatory bowel disease (IBD) was observed, but there are few reports of AA in IBD patients.

We aimed to investigate the clinical characteristics and prognosis of AA occurring in IBD, and to confirm relationship between them. We retrospectively reviewed total 6 patients diagnosed with both AA and IBD from 2005 to 2022.

Six patients consisted of 4 men and 2 women, 3 of whom were in 10s and the rest were in their 40s to 50s. Three of 6 patients were presented as alopecia totalis, and 1 patient showed acute diffuse and total alopecia, and 1 patient presented as AA with single lesion. IBD type was mostly ulcerative colitis except for one crohn's disease. No relationship was confirmed between the diagnosis dates, but 3 patients (50%) started hair loss and diarrhea at the similar time. Just 1 patient was using anti-TNF-α agents for IBD, and the improvement and deterioration of AA were repeated for all of them.

In our series, we found that the ratio of alopecia totalis and ulcerative colitis was high. So far AA occurring in IBD was described as a side effect of anti-TNF-α agents for IBD, but our series show no relationship between them. We report these cases to emphasize the importance of careful observation for IBD symptoms in AA patients.

P4

Patient-Reported Burden of Severe Alopecia Areata: First Results from the Multinational Alopecia Areata Unmet Need Survey

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Background: Alopecia areata (AA) can have considerable psychosocial sequelae. These are first results from the large multinational cross-sectional AA Unmet Need Survey, which collected patient-reported data on disease burden associated with severe AA.

Methods: Adults from 11 countries (Asia, Europe, South America; N=747) with self-reported/dermatologist-confirmed AA were recruited via internet panels (February-April 2023) using market research methodology. Patient-reported responses to questions including those on demographics, disease characteristics, anxiety, depression, sleep problems, Dermatology Life Quality Index (DLQI; 0-30), long-term impact of AA and coping mechanisms were collected. Observed data were analysed only for the subset of respondents who, at the time of survey, had ≥50% scalp hair loss and were reported descriptively, overall and by scalp hair loss severity (50-94% and ≥95%).

Results: 653 patients were included (57.6% female; mean [SD] age of 44.1 [6.9] years, disease duration of 4.9 [6.6] years and DLQI of 17.1 [5.9]). Approximately 80% of participants reported AA-related impact on their life. Sleep problems, anxiety and depression were reported by 28.5%, 25.0% and 17.6% of participants, respectively. Impact on self-esteem (32.5%), mental health (28.2%) and day-to-day activities (26.8%) were the most reported negative long-term effects of AA. Most frequently reported coping mechanisms included talking in person with healthcare professionals (52.8%) or someone with AA (44.1%) and physical activity (45.2%).

Conclusion: The results of this large multinational survey of patients with AA highlight the substantial burden that severe AA can have on patients beyond hair loss.

P5

The Contribution of Hair Regrowth to Health-Related Quality of Life Improvement in Patients With Alopecia Areata Treated With Baricitinib or Placebo

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Abstract

Background: This post-hoc analysis investigated the evolution of health-related quality of life (HRQoL) and psychological symptoms after treatment with baricitinib 4-mg in severe alopecia areata (AA).

Methods: Patients were randomized to once-daily placebo, baricitinib 2-mg, or baricitinib 4-mg in BRAVE-AA1 and BRAVE-AA2; data from these trials were pooled. In patients treated with baricitinib 4-mg or placebo, improvements in HRQoL and psychological burden were measured using Skindex-16 for AA (Symptoms/Emotions/Functioning) and Hospital Anxiety and Depression Scales (HADS). Changes from baseline through Week 36 were analysed using analysis of covariance (ANCOVA). Mediator analysis was carried out to assess the contribution of scalp hair regrowth (measured by Severity of Alopecia Tool [SALT] change from baseline) to the improvements in HRQoL and psychological symptoms at Week 36. Modified last observation carried forward was applied to missing data.

Results: At Week 36, improvements in HRQoL and psychological symptoms were greater for baricitinib-4mg than placebo [change from baseline for baricitinib / placebo, (p-value vs placebo); Symptoms -2.53 / 0.93, (p=0.010); Emotions -24.11 / -11.72, (p<0.001); Functioning -17.14 / -9.49, (p<0.001); HADS Anxiety -1.04 / -0.41, (p=0.001); HADS Depression -0.33 / 0.15, (p=0.006)]. Mediator analysis showed that changes in SALT accounted for 57%, 62%, 67%, 47%, and 57%, of improvements in Symptoms, Emotions, Functioning, HADS-Anxiety, and HADS-Depression scores at Week 36 respectively.

Conclusion: In two large trials, improvements in HRQoL and psychological symptoms were observed after treatment with baricitinib 4-mg. These results support that hair regrowth has a positive impact on HRQoL and psychological burden in AA.

P6

Efficacy of Baricitinib in Patients with Various Degrees of Alopecia Areata Severity: Results from BRAVE-AA1 and BRAVE-AA2

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Abstract

Background: Baricitinib is an oral selective Janus kinase (JAK)1/JAK2 inhibitor with demonstrated efficacy in patients with alopecia areata (AA). This analysis evaluated the difference in response among subgroups of patients with various degree of severity based on the Severity of Alopecia Tool (SALT) score from phase 3 results of two randomized, double-blinded, placebo-controlled trials (BRAVE-AA1 and BRAVE-AA2).

Methods: Both BRAVE-AA1 (N=654) and BRAVE-AA2 (N=546) enrolled adult patients with ≥50% scalp hair loss. Severity of scalp hair loss at baseline was defined as severe AA (SALT score 50-94) or very severe AA (SALT score 95-100). In addition, investigators were asked to record patients considered as alopecia universalis (AU). The primary efficacy endpoint was the proportions of patients achieving SALT score ≤20 at week 36. Data analyses are presented for each subgroup using Fishers exact test.

Results: Overall, 1200 adult patients were enrolled with 46.8% and 53.2% of patients qualifying as severe and very severe, with 44.3% identified as AU. At week 36, both BARI 2-mg and BARI 4-mg were significantly superior to placebo for the proportion patients achieving SALT ≤20 across all subgroups: severe AA (BARI 2-mg: 32.7% $p<0.001$; BARI 4-mg: 47.6% $p<0.001$ vs placebo: 7.8%), very severe AA (9.8% $p<0.001$; 21.3% $p<0.001$ vs 0.6%) and AU (19.6% $p<0.001$; 27.7% $p<0.001$ vs 2.9%).

Conclusion: BARI 2-mg and BARI 4-mg demonstrated superiority over placebo in achieving hair regrowth (SALT ≤20) at week 36 in adult patients across the various degrees of severity of scalp hair loss.

P7

Scalp Hair Regrowth is Associated with Improvements in Health-Related Quality of Life (HRQoL) and Psychological Symptoms in Patients with Severe Alopecia Areata (AA): Results from Two Randomized Controlled Trials

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Abstract

Background: Here we report association between hair regrowth, HRQoL improvement, and psychological burden in patients with severe alopecia areata (AA).

Methods: Adult patients (Severity of Alopecia Tool [SALT] score ≥50) were randomized (once-daily placebo/baricitinib 2mg/4mg) in BRAVE-AA1/BRAVE-AA2, and categorized according to scalp hair regrowth (Week36) into 3 groups: patients achieving SALT≤20 (N=256); patients not achieving SALT≤20 but achieving ≥30% improvement from baseline (BL)(SALT30) at any post-BL visit (intermediate response; N=268); patients never achieving SALT30 (minimal/no-response; N=676). Skindex-16 for AA (Skindex-16AA) assessed effects of AA on HRQoL over 3 domains: emotions, symptoms, functioning. Hospital Anxiety and Depression Scales identified patients with borderline/abnormal-severity (B/AB) scores for anxiety/depression at BL.

Results: BL HADS and Skindex-16AA scores were similar across groups. Up to Week36, the SALT≤20-response group achieved greater improvements in all BL Skindex-16AA domain scores vs the minimal/no-response group. Among patients with B/AB anxiety/depression scores, the SALT≤20 group achieved greater improvements in HADS up to Week36, and more patients' scores shifted from B/AB to normal range vs minimal/no-response group. Improvements were observed in the intermediate-response group, but less than the SALT≤20-response group.

Conclusion: Patients with severe AA achieving scalp hair regrowth at Week36 experienced improvements in HRQoL and anxiety and depression symptoms vs those with minimal/no regrowth. Higher benefit was observed in patients achieving SALT≤20. Longer treatment duration may be needed to assess the full impact on scalp hair regrowth, HRQoL, anxiety and depression symptoms.

P8

Long-term Efficacy of Baricitinib in Alopecia Areata: 104-week Results from BRAVE-AA1 and BRAVE-AA2

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Abstract

Background: This analysis evaluates long-term efficacy with two years of continuous baricitinib therapy in severe alopecia areata (AA).
Methods: Integrated data from the BRAVE-AA1/BRAVE-AA2 phase 3 trials included patients with Severity of Alopecia Tool (SALT) scores ≥50 (≥50% scalp hair loss) randomized to and continuously treated with 2-mg or 4-mg baricitinib through Week 104 (W104). Analysis included 2-mg-treated and 4-mg-treated patients with SALT score ≤20 (≤20% scalp hair loss) at Week 52 (W52; W52 responders), and baricitinib-4-mg-treated patients who had SALT score >20 at W52 but had achieved SALT score ≤20 at prior visit(s) and/or had experienced eyebrow/eyelash regrowth at W52. W104 outcomes included the proportions of patients achieving SALT score ≤20 and Clinician-Reported Outcomes (ClinRO) for Eyebrow and Eyelash Hair LossTM scores 0/1 (full coverage/minimal gaps) and ≥2-point improvements from baseline (among those with baseline scores ≥2). Data were censored after treatment discontinuation.
Results: Among baricitinib-4-mg-treated and baricitinib-2-mg-treated W52 responders, respectively, 117/129 (90.7%) and 58/65 (89.2%) maintained SALT score ≤20 at W104; among W52 responders with baseline ClinRO scores ≥2, 67/80 (83.8%) and 25/37 (67.6%) had ClinRO Eyebrow (0,1), and 55/68 (80.9%) and 22/30 (73.3%) had ClinRO Eyelash (0,1) at W104. Among baricitinib-4-mg-treated patients with SALT score >20 at W52, 43/110 (39.1%) reached SALT score ≤20 by W104.
Conclusions: Efficacy of baricitinib for severe AA was maintained at W104 in W52 responders. Efficacy increased in patients with SALT score>20 at W52, illustrating that long-term treatment may be needed to observe maximum benefit in some patients.

P9

Outcomes of Down-Titration in Patients with Severe Scalp Alopecia Areata Treated with Baricitinib 4-mg: Week 104 Data from BRAVE-AA2

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Abstract

Background: Baricitinib (2-mg and 4-mg, once-daily), an oral, selective, Janus kinase 1/2 inhibitor, was superior to placebo at achieving hair regrowth in patients with severe alopecia areata (AA) at Week-36. Here we report Week-104 efficacy results from the down-titration portion of BRAVE-AA2 (NCT03899259), a randomized, double-blind, placebo-controlled phase 3 trial.

Methods: BRAVE-AA2 enrolled 546 adults with severe AA (Severity of Alopecia Tool [SALT] score ≥50). At Week-52, patients initially randomized to baricitinib 4-mg who were responders (SALT score ≤20) were rerandomized 1:1 to stay on 4-mg or down-titrate to 2-mg. Retreatment to initial baricitinib dose was automatically triggered by a worsening of Week 52 SALT score >20 points ("loss of treatment benefit"). Descriptive statistics are summarized using observed data and multiple imputation.

Results: At Week-52, 86/234 baricitinib 4-mg treated patients were responders. Following rerandomization, 44 patients remained on baricitinib 4-mg, and 42 down-titrated to baricitinib 2-mg. At Week-104, a SALT score ≤20 was maintained in 90.2% of responders who remained on baricitinib 4-mg. Overall, 45.2% of patients who down-titrated to baricitinib 2-mg experienced a loss of treatment benefit by Week-104. For patients who had achieved SALT score ≤20 by Week-36 and maintained it up to Week-52 (sustained response) loss of treatment benefit occurred in 39.4% (13/33) compared to 66.7% (6/9) for patients who had not. During 36 weeks of retreatment, 71.4% (5/7) recaptured SALT score ≤20.

Conclusion: These data help to inform decisions on down-titration, however, more work will be needed to better define timing and conditions for successful downtitration.

P10

The role of inflammasome in alopecia areata

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Abstract

The inflammasome, protein complex plays an role in auto-inflammatory diseases. It activates several cytokines in response to pathogens or endogenous stress. Recently, NLRP3 inflammasome has been linked to psoriasis, vitiligo, lupus, and alopecia areata (AA).

This study performed to elucidate the relationship between inflammasome and AA development and the correlation between inflammasome expression and the clinical features of AA patients.

A total of 144 patients with AA and 22 controls were included in the study. Scalp skin and serum samples were obtained from the participants. We measured NLRP3-related molecules by performing quantitative polymerase chain reaction in both groups. Serum cytokines and chemokines associated with NLRP3 inflammasome were measured using enzyme-linked immunosorbent assays. Additionally, we measured the expression of NLRP3 and caspase-1 in outer root sheath by performing immunostaining on the samples.

Lesional IL-1β was significantly increased in patients with AA at any stage compared to controls. In the progressive stage, lesional CXCL10 was significantly increased compared to control levels and levels at other stages. Serum IFN-γ levels were significantly increased in the progressive stage of AA compared with controls. NLRP3 and caspase-1 showed strong positivity in the outer root sheath in the initial and progressive stages of AA compared to the recovery stage of AA in immunostaining.

Strong staining of NLRP3 and caspase-1 in the initial and progressive stages suggests that the inflammasome is associated with the development of AA. The increased levels of lesional IL-1β and serum IFN-γ support this correlation. Moreover, CXCL10 is closely associated with disease progression.

P11

A Clinical Investigation of Early-Onset Alopecia Areata in Children: onset earlier than 4 years of age might have a better prognosis

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Abstract

Alopecia areata (AA) is a non-scarring autoimmune hair loss on the scalp or body. While early onset was considered a primary factor for poor prognosis, children with early-onset AA show varied responses to treatment.

This study was conducted to describe the clinical characteristics and assess the prognostic factors of early-onset AA in children.

We performed a retrospective study of AA patients under 10 years of age of onset who visited our dermatologic clinic from January 2013 to December 2020. A clinical review of medical records, and photographs were performed. Treatment efficacy was assessed visually depending on the degree of hair regrowth compared to the initial state at 12 months of follow-up.

Among 3,916 patients with newly diagnosed AA, 291 were under 10 years of age of onset. Among these patients, 162 were followed-up more than 12 months. 57.4% of patients showed more than 50% hair growth after these treatments. We compared the over 75% of hair regrowth group and under 25% of hair regrowth groups including patients with aggravation and relapse. There were no significant differences in the presence of known prognostic factors between the two groups except presence of personal atopic history. In addition, patients younger than 4 years of age at onset showed a significantly better response than older patients.

Early onset AA patients are not affected by factors associated with the poor prognosis of general AA. In particular, it was confirmed that the prognosis was rather good in patients under 4 years of age.

P12

Real-world effectiveness and safety of baricitinib in patients with alopecia areata

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Abstract

Janus kinase (JAK) inhibitors have demonstrated its effectiveness in reversing hair loss in alopecia areata (AA). Recently, the oral selective reversible JAK1/JAK2 inhibitor, baricitinib has been approved in the United States and South Korea for the treatment of severe AA in adults. We investigated the real-world effectiveness of baricitinib in patients diagnosed with AA.
This retrospective analysis included all patients aged ≥18 years diagnosed with AA treated with baricitinib 4 mg for a minimum of 6 months from January 2019 to January 2023 in our institution. The efficacy was evaluated using the severity of alopecia tool (SALT).
Total of 19 patients were analyzed. Mean baseline SALT score was 92.09 ± 17.89, where 9 patients were diagnosed with alopecia totalis, and 7 patients were diagnosed with alopecia universalis at the time of baricitinib treatment initiation. Mean treatment period with baricitinib was 14.37 ± 8.60 months, where any form of hair growth was observed in 16/19 (84.21%) patients. The median time for notable hair growth was 4 months after treatment. Of the 19 patients, the proportion of patients achieving SALT score ≤ 50 and/or SALT score ≤ 20 at the most recent follow-up visit after treatment was 57.89% (11/19), and 47.37 (9/19), respectively. Regarding safety of baricitinib, a single case of eczema herpeticum developed during treatment. The remaining patients presented no treatment-emergent adverse events. Baricitinib 4 mg demonstrated efficacy and safety in AA, even in the most severe forms. This is the first real-world data reporting the efficacy of baricitinib in AA.

P13

Efficacy of calcipotriol/betamethasone ointment in management of pediatric alopecia areata

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Abstract

Background: Topical corticosteroids are widely acknowledged as the first-line treatment for pediatric alopecia areata (AA). However, there still exist some cases that are recalcitrant to topical corticosteroid application. Vitamin D analogs may serve as a viable alternative treatment option for such cases.
Objective: To evaluate the effectiveness of calcipotriol/betamethasone ointment in pediatric AA
Methods: In this 12-week retrospective study, 33 patients under 18 years old with AA were included. The affected areas were treated with an 0.0001% calcipotriol/betamethasone ointment twice a day. Baseline and subsequent SALT scores were assessed at 4, 8, and 12 weeks.
Results: The 32 participants were composed of 20 females and 12 males, with a mean age of 4.25 2.51 years. Out of all the patients, 18 had a SALT score above 50 and 14 had a SALT score below 50. The mean duration of disease was 5.53 7.86 months. Patients with SALT scores higher than 50 showed hair regrowth in 7.41 4.57 weeks, whereas patients with SALT scores lower than 50 had hair regrowth in 6.77 3.00 weeks. After the 12-week trial, 71.9% of the patients showed hair regrowth, and 9.3% of patients did not respond to the treatment. It was found that 16 (69.6%) patients had a change in SALT score of less than 25%, while 7 (30.4%) patients had a change in SALT score between 25-50%. No significant adverse effects were reported.
Conclusion: Calcipotriol/betamethasone ointment can be a potentially safe and effective therapeutic approach for treating pediatric AA.

P14

Clinical efficacy and safety of baricitinib for alopecia areata in Korea: single centre experience

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Abstract

Background: Alopecia areata (AA) is a common autoimmune disease characterized by hair loss ranging from patch to complete hair loss. As the importance of the JAK/STAT pathways has recently been recognized, they have been targeted for AA treatment.

Objective: To investigate the effectiveness and safety of baricitinib in Korean AA patients

Methods: We retrospectively reviewed 52 AA patients who were treated with baricitinib once-daily dose of 4mg. The Severity of Alopecia Tool (SALT) and the Clinicial-Reported Outcome (ClinRo) were used to assess the extent of scalp-hair loss and eyebrows or eyelashes, respectively.

Results: Patients with a baseline SALT score of 50 or more were defined as the severe AA group, and patients with a baseline SALT score of 20 or more and less than 50 were defined as the moderate AA group.

In the severe AA group (n=39), the percentage of patients with a SALT score of 20 or less at week 36 was 26%. In the moderate AA group (n=13), 54% of patients showed complete remission within 24 weeks. The percentage of ClinRO measure for eyebrow and eyelash with an improvement at week 16 were 33%(4 out of 12) and 42%(3 out of 7), respectively. Acne was relatively common side effect.

Conclusion: In our study, the rate of achieving SALT 20 among severe AA group was lower than data from phase 3 trial (26% vs 37%, respectively), but still showed a better response than the placebo group (26% vs 5%, respectively).

P15

Recurrent episodes of alopecia totalis post COVID-19 vaccination

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Abstract

We present a 58 year old female with three episodes of alopecia totalis, each episode occurring shortly after receiving a COVID-19 vaccination. The patient had a medical history of rheumatoid arthritis managed with Azathioprine and Etanercept. There was no history of prior COVID-19 infection.

Within 6 weeks of receiving her first AstraZenica COVID-19 vaccination she experienced total hair loss of the scalp, axillae and pubic regions with sparing of the eyebrows and eyelashes. Her hair slowly re-grew, in full, over 4 months. 6 months later, she received the second dose of the AstraZenica COVID-19 vaccine and developed extremely rapid alopecia totalis within a few weeks. A further 6 months later she received the Pfizer COVID-19 booster vaccination. Within four weeks she developed a third episode of alopecia totals.

Trichoscopy demonstrated exclamation mark hairs, black and yellow dots and curled hairs. A diagnostic biopsy confirmed a reduction in the number of hair follicles with approximately a third demonstrating a bee-like perifollicular lymphocytic infiltrate.

Several publications have reported de-novo/flares of pre-existing alopecia areata occurring after COVID-19 vaccination. Suggested mechanisms include molecular mimicry between the vaccine-induced protein of SARS-COV-2 and human hair components, as well as a role for vaccine adjuvants.

To our knowledge this is the first reported case of recurrent episodes of alopecia totalis after each COVID-19 vaccination. This case contributes to the existing literature describing vaccination as a trigger for alopecia areata in susceptible individuals and highlights the risk of recurrent episodes with repeated doses.

P16

Evaluation of the early efficacy and safety of JAK inhibitors in patients with refractory severe Alopecia Areata

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Abstract

Background: The efficacy and consequences of JAK inhibitors for treating alopecia areata (AA) needs elucidation, particularly regarding influence factors and changes in cytokine levels. Methods: 48 patients with severe types of AA, and failure to respond to conventional steroid treatment, were treated with JAK inhibitors (JAKi); Tofacitinib or Baricitinib. Clinical data were collected and cytokine plasma levels of patients and 24 healthy individuals were detected by ELISA before, and 1,3,6,9,12 months after, treatment. Results: AA patients were 25.60±7.74 years old with a median Severity Of Alopecia Tool (SALT) score of 95, and median onset age was 19 (3-51). The treatment response rate, as judged by 50% hair regeneration, was 70.83% (34/48) at 6 months, 69.57% (16/23) at 12 months. We observed it was critical for hair regeneration to begin within 3 months, as the unresponsive rate increased if hair regrowth was delayed beyond 3 months. The hair regrowth rate was positively correlated with the age of onset and negatively correlated with the disease course. 31.25% of patients suffered mild adverse reactions. The AA relapse rate was 79.41% at 12 months, but no correlation with any clinical factors was found. Before treatment, only IL-5 was found significantly decreased in AA patients versus controls. After treatment, IFNγ and IL-4 decreased, while IL-5 and IL-13 increased ($P < 0.05$), in responsive versus unresponsive patients. Conclusion: JAKi treatment of severe AA patients was effective with mostly mild adverse reactions. Mechanisms of JAKi in recalcitrant AA may be related to modulation of the Th1/Th2 balance.

P17

Markers of Th2 in alopecia areata and their correlations to allergy, atopy and longer disease duration

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Abstract

Background: We explored the influence of clinical characteristics, especially allergic factors, in alopecia areata (AA) patients to identify biomarkers for precision medicine. Methods: A retrospective cross-sectional study of 1108 AA patients assessed epidemiological and clinical data, comorbidities and laboratory results. Plasma IL-4, IL-10, IL-13 and IL-33 were measured by ELISA in 16 patients. Results: AA patients had a median onset age of 24 years (interquartile range [IQR]:13-34), 0.5 years median disease course (IQR:0.17-3), and median Severity of Alopecia Tool (SALT) score of 30 (IQR:10-80). The most common AA subtype was multiple patches (50.4%), followed by alopecia universalis (15.4%), single patch (14.0%), diffuse AA (10.8%), alopecia totalis/universalis (5.4%, AT/AU) and ophiasis (4.0%). 28.1% of patients also had atopy, including allergic rhinitis (19.9%), atopic dermatitis (6.6%) and asthma (1.6%). Elevated total IgE (tIgE) levels were found in 33.5% of patients, higher in those with AT/AU (46.7%). Patients with elevated tIgE, more frequently exhibited younger onset, larger hair loss area, longer disease course, eosinophilia, dust mite (DM) allergy, and atopic diseases (Ps<0.05). AA comorbid with atopic dermatitis (AA-AD) correlated with younger onset age and higher SALT scores (P<0.05). Moreover, IL-4 and IL-13 levels were higher in 16 AA-AD patients compared to a control group (P<0.05). Conclusions: Elevated tIgE predicts severe, persistent AA. DM allergy has a significant influence on AA in patients with childhood onset. We suggest AA comorbidity with DM allergy and/or AD results in Th2-dominant immune responses, causing earlier, more severe AA and increasing treatment resistance.

P18

Risk of subclinical atherosclerosis in severe alopecia areata patients

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Abstract

Introduction: Alopecia areata (AA) is a chronic immune-mediated disease that causes non-scarring hair loss. Although traditionally considered an organ-specific disease, recent studies have proven the presence of systemic inflammatory changes and suggest a higher incidence of cardiovascular diseases (CVDs) among AA patients.

Objectives: To determine the prevalence and distribution of subclinical atherosclerosis in patients with AA.

Methods: We conducted a prospective observational study in patients with severe AA (SALT >75), excluding those with known CVDs. Subjects underwent bilateral femoral and carotid ultrasound examination with a Clarius Ultra-High Frequency Linear Scanner. An atherosclerosis plaque was defined as a focal structure protruding at least 0,5mm intro the lumen or a thickening >50% of the surrounding intima. Subclinical atherosclerosis was defined as the presence of any plaque in any of the studied arteries.

Results: The study population included 31 patients (12 male and 19 female), with a mean age of 45,03±11.6 years. At least 1 atherosclerotic plaque was present in 17 patients (54,8%), 13 (39,39%) in the carotid and 7 (21,21%) in the femoral arteries. Patients with AA and subclinical atherosclerosis were older ($p<0.001$), had a longer duration of the disease ($p=0,004$), higher levels of glycated hemoglobin ($p=0.029$) and higher triglyceride levels ($p=0.009$); compared to those without atherosclerotic plaques

Conclusion: Our cohort of AA patients present a high prevalence of subclinical atherosclerosis. Together with traditional cardiovascular risk factors, duration of AA disease appears to play a role in the development of atherosclerosis.

P19

Efficacy of topical immunotherapy with 2,3-Diphenylcyclopropenone-1(DPCP) in patients with extensive Alopecia Areata. Twenty years of experience from the Hair Diseases Department of "Andreas Syggros" Hospital, Athens, Greece.

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Abstract

Introduction: Alopecia Areata (AA) is a common, chronic, autoimmune, inflammatory disease that affects the hair follicles and causes non-scarring alopecia. AA is unpredictable in course and progression, and therapy is challenging for dermatologists. Topical immunotherapy with DPCP is considered an effective treatment, especially in the extended types of this condition.

Aim: The purpose of this study was to evaluate the efficacy of DPCP in patients with extensive AA treated, following a standard protocol, at the Hair Diseases Department of "Andreas Syggros" Hospital for 20 years as well as to investigate the possible factors that may affect the efficacy, as there is no such study in Greece so far.

Material and methods: We conducted a retrospective study. The medical records of all patients kept at the Laboratory were reviewed anonymously. We collected information on patients' demographics' personal and family history, and data on DPCP treatment. We analyzed the findings using IBM SPSS 22.0 (Statistical Package for Social Sciences).

Results: 326 patients were studied, 202 (62%) women and 124 men (38%). One hundred thirty-four patients continued the topical therapy, and the overall response rate for hair regrowth was 41.1%. Relapse was observed in 38 (11.7%) patients. Common side effects were itching erythema and local lymphadenopathy.

Conclusions: Topical immunotherapy with DPCP is an effective therapy for patients with extended types of AA. The study findings agree with those of relevant studies from the international literature.

P20

Alopecia Areata Totalis treated with phytotherapy and intradermotherapy with results similar to JAK inhibitors

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Abstract

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Introduction & Objectives: The treatment outcome for Alopecia Areata is widely known with the use of JAK inhibitors but the use of herbal medicines can further enhance the results safely and effectively. Some patients have viable follicles that, if nourished, can be recovered, giving a result similar to more expensive treatments like JAK inhibitors.

Material & Methods: Patient attended Éclairé Hair Research for 9 months using resveratrol 100 mg, Curcumin 200mg, vitamin D 50.000 IU per week and intradermotherapy with growth factors (Growth Factors Components:

Oligopeptide1+ Polypeptide 9 + Polypeptide 1 + Copper Peptide) every 15 days and BETAMETHASONE 2MG/ML + BETAMETHASONE DISODIUM PHOSPHATE 2MG/ML once a month. A ThricoZoom Trichoscope was used to analyze the images of the follicles. Liver and kidney examinations were collected every 3 months during therapy.

Results: in Trichoscopy, an increase in the number of hairs per follicle and thickness of the hairs can be observed. The results were photographed as pictures showing an amazing result equivalent to JAK inhibitors. There were no liver or kidney changes during treatment. Patient had no side effects during treatment.

Conclusion: JAK inhibitors treatment cost is sometimes prohibitive for some patients. By maximizing the amount of hair per follicle, we achieve an important visual improvement and avoid drug side effects.

P21

Dermoscopy findings of the axilla of women with frontal fibrosing alopecia

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Abstract

Frontal fibrosing alopecia (FFA) is characterized a banded alopecia in the frontal region and rarefaction of the eyebrows associated with the rarefaction of body hair. The axilla being the most affected site. To describe and compare the dermoscopic findings of the axillar hairs of a group of women with FFA (case) with a group of women without FFA (control), an observational case-control study was done. The control group was matched for age groups and phototypes with the cases. Thirty women with a clinical and histopathological diagnosis of FFA were included. Dermoscopy of the axilla in patients with FFA revealed the presence of axillary hair in 93.3% (28/30) of the cases and all patients had follicular openings. More than one hair shaft per follicular ostium was observed in 70% (21/30) of the patients and variability in the diameter of the hair in 83.3% (25/30) of the cases. Regarding dermoscopic inflammatory signs, peripillary brownish halo was present in 83.3% (25/30) of patients, peripillary desquamation in 56.7% (17/30), diffuse desquamation in 63.3% (19/30) and pigmented network of the epidermis in 73.3% (22/30) of the cases. When comparing these with the dermoscopic findings of the axilla of non-ill women, the chance of occurrence of brownish peripillary halos between cases was greater than the twice the chance of occurrence of these halos among controls (OR=2.7; 95%CI 1.2-6.2; p=0.029). The other dermoscopy variables were not statistically associated with the FFA. This study allow to characterize the dermoscopic findings of the axillary involvement of patients with FFA.

P22

Immersive VR : an adjunctive measure to improve quality of life in chemotherapy induced alopecia

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Abstract

Introduction:
Chemotherapy induced alopecia (CIA) is associated with profound psychosocial implications resulting in trichodynia, anxiety, depression and lowered quality of life (QOL). Effective treatment regimens are often refused due to associated hair loss. Immersive Virtual reality (IVR) may serve as a supportive measure to aid treatment-related psychological distress.

Objective:
We aimed to assess the feasibility and acceptability of IVR for managing trichodynia, anxiety and distress among women with chemotherapy induced alopecia(CIA).

Materials & Methods:
A mixed methods study involving 30 consenting female patients undergoing chemotherapy for various haematological/ solid organ malignancies,(18- 60 years of age) were recruited. They were randomly allocated to two arms (Intervention and control arm). IVR sessions were held 5 hours and 5 minutes prior , 5 minutes following chemotherapy . Control arm received standard care. The process was followed for each of the 6 sessions. The quantitative outcome measures and qualitative data were compared with baseline .

Results:
Patients in the intervention arm showed significant reduction in anxiety (Hospital anxiety and depression score) from baseline by 33% ($p < 0.03$). Anxiety was reduced from pre-session during VR sessions by 65%($p < .01$). Twelve participants (80%) reported significant improvement in the QOL measures post VR sessions. All participants (100%) reported a signficant decrease in trichodynia compared to controls.

Conclusion:
IVR is promising in alleviating the psychological effects and trichodynia in CIA. Further investigation is warranted to evaluate its adoption of such technologies in routine clinical practice.

P23

The involvement of the scalp and nail apparatus in cutaneous lupus erythematosus patients: A retrospective study

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Abstract

Discoid lupus erythematosus (DLE) is one of the LE-specific skin diseases on the scalp, and some cases induce scarring alopecia. In systemic LE (SLE), variable nail changes not specific to LE can occur, including leukonychia, longitudinal ridges, and partial onycholysis. However, there are insufficient reports that investigate the characteristics and relationship of hair and nail changes in LE patients.

This study aimed to identify the clinical features of scalp and nail involvement in Korean patients with cutaneous LE (CLE). This was a retrospective study that included 113 CLE patients who visited the Department of Dermatology at Hanyang University Seoul Hospital in Korea between October 2021 and October 2022. Patient medical records, demographic information, and clinical photographs were reviewed,.

Among the 113 CLE patients, 69 (61.1%) showed hair loss and 19 (16.8%) showed fingernail involvement. The CLE patients with hair loss exhibited earlier disease onset ($p=0.001$) and were more frequently accompanied by SLE ($p<0.001$), facial CLE lesions ($p=0.012$), and fingernail changes ($p=0.012$). Of the 69 CLE patients with hair loss, 59 (85.5%) showed DLE alopecia. In the DLE alopecia group, patients with fingernail changes showed a higher incidence rate of additional CLE lesions on extremities ($p=0.049$) and the Raynaud phenomenon than those without fingernail changes ($p=0.009$). There were significant differences in positivity for antinuclear antibody between CLE patients with DLE alopecia and other patients ($p=0.04$).

Involvement of the scalp and nails in CLE is an important disease manifestation, and proper understanding could be essential for diagnosis and efficient management.

P24

Efficacy of oral retinoids as a maintenance therapy in cicatricial alopecia: a retrospective study

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Abstract

Cicatricial alopecias (CA) comprise a diverse group of scalp disorders with unknown etiology that result in permanent hair loss. The main treatment goal is to reduce the ongoing inflammation and prevent further hair loss. We investigated the efficacy of oral retinoids as a maintenance therapy for various CA.

This retrospective analysis included all biopsy proven cicatricial alopecia patients aged ≥18 years treated with either isotretinoin, or alitretinoin as maintenance therapy from January 2015 to December 2022 in our institution.

Total of 75 patients were included in the study. Of the 75 patients, 60 patients were diagnosed with folliculitis decalvans, 5 patients with frontal fibrosing alopecia, 5 patients with pseudopelade of Brocq, 4 patients with dissecting cellulitis of scalp, and 1 patient with discoid lupus erythematosus. The mean treatment period was 17.41 months ± 19.23, and the mean time period of oral retinoid initiation was 3.47 months ± 9.04 after the diagnosis. For the initial bridging therapy, cephalexin was used in 58 patients, and systemic corticosteroid was used in 17 patients. Complete response (absence of active lesions) was seen in 54/75 patients, where partial response (persistence of some active lesions), and no response were seen in 18/75, and 3/75, respectively. Three patients exhibited disease progression, and the most common treatment emergent adverse event was xerosis.

Oral retinoids demonstrated effectiveness as a maintenance therapy in CA, and when active inflammation is halted after the use of antibiotics and/or systemic corticosteroids, retinoids can provide a reliable treatment choice for disease maintenance.

P25

Minoxidil-induced trichostasis spinulosa of vellus hair?

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Abstract

Introduction:
Trichostasis spinulosa (TS) is a hair follicle disorder in which multiple telogen vellus hairs are retained in a dilated hair follicle, along with follicular hyperkeratosis. TS commonly affects the nose, where it can be mistaken for comedones. Three case studies will be presented.

Material and methods:
Trichoscopy was conducted, and epilated TS hair bundles were examined using microscopy. All three patients (males) were using a proprietary topical formulation containing 5% minoxidil.

Results:
TS was observed at the hair margins, with affected hair bundles easily and painlessly epilated, each containing approximately 25 vellus hairs, the majority telogen. TS was not found in other areas of the scalp, and not reported on the body.

Discussion:
Malassezia yeast and topical minoxidil have previously been suggested as possible causes of TS. It is commonly seen on the nose and interscapular region, both sebaceous-gland-rich sites. In our patients, TS was observed at the hair margins and upper forehead, also areas with high sebaceous gland density. All three also had a diagnosis of seborrhoeic dermatitis (SD) of the scalp. Therefore SD and/or high sebum excretion, may be risk factors for TS, in patients applying topical minoxidil.

Conclusions:
Individuals with SD and androgenetic alopecia using topical minoxidil may be at increased risk of developing TS at the frontal hair margins. Additionally, the combination of topical minoxidil and high sebum excretion may be a predisposing factor. It is therefore suggested that clinicians use trichoscopy to check for the presence of TS in such patients.

P26

Do statins have a role in treating Frontal Fibrosing Alopecia?

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Abstract

Frontal fibrosing alopecia (FFA) is the commonest primary cicatricial alopecia. While a genetic predisposition is recognised, the reason(s) for the increased incidence is uncertain. Postulated trigger factors include exogenous hormones, sunscreens and cosmetics. Recently, increased caveolin-1 (Cav1) expression, a scaffolding protein and key component of specialised cell membrane microdomains (caveolae), has been identified in FFA hair follicles (HF). It is proposed that Cav1 may promote HF immune privilege collapse by several mechanisms. Statins such as lovestatin downregulate Cav1 in human ORS keratinocytes by cholesterol disruption of caveolae, and a potential role for statins in treating FFA has been proposed. The drug history of 200 FFA patients (188F,12M) was reviewed to identify the proportion taking a statin prior to stated FFA onset and at time of diagnosis. Mean age at onset was 55yrs and mean age at diagnosis 59yrs. Prior to stated onset, n=15 took a statin (0% 50-59y; 21.4% 60-64y; 27% 65-69y; 16.6% 70+y). At diagnosis, 28 were taking a statin (1.8% 50-59y; 8.8% 60-64y; 26.6% 65-69y; 41.4% 70+y). NICE recommend a 10% risk threshold for statin prescribing, effectively including almost all >65yrs. Based on ASSIGN 20, 32% of the Scottish population >40yrs are eligible for statins and ISD Scotland (2017-18) showed 29.8% of Scots >45yrs were prescribed a statin (33.6% NHSGGC). Our data suggest fewer FFA patients attending a tertiary Hair Clinic are prescribed statins than is recommended or generally prescribed. Further studies such as case-control studies may establish whether statins have a beneficial role in FFA.

P27

A case of male frontal fibrosing alopecia after COVID-19 vaccination

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Abstract

We present the case of a 51-year-old male with no prior medical history, who developed frontal fibrosing alopecia after COVID-19 vaccination. The patient received his first AstraZeneca COVID-19 vaccination and within 6 weeks noted itch and discomfort affecting the anterior hairline with subsequent development of associated alopecia. Two months later, he received his second AstraZeneca COVID-19 vaccination. Subsequently, he noted further retraction of his anterior hairline. 6 months later he received his booster Pfizer vaccination and due to ongoing hair loss, presented to dermatology. Of note, his son developed de-novo oral lichen planus after his first COVID-19 vaccination.

On examination our patient had retraction of his frontal hair margins with perifollicular erythema, scaling and visible scarring. Two 4mm punch biopsies demonstrated scarring alopecia with perifollicular fibroblasts surrounding degenerating hair follicles and follicles replaced with fibrotic scar tissue. Patch testing was undertaken which revealed positive reactions to Nickle, Cobalt, Fragrance series 1 and Balsam of Peru.

The patient was treated with topical corticosteroids, courses of Lymecycline and Doxycycline as well as Hydroxychloroquine which led to a degree of stabilisation. The hair loss has caused significant psychological impact for the patient. This is one of the first reported cases of male frontal fibrosing alopecia after COVID-19 vaccination and contributes to an expanding literature of trichological sequalae secondary to COVID-19 infection and vaccination.

P28

Vibration assisted analgesia during intralesional corticosteroid therapy for alopecia

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Abstract

Intralesional corticosteroid therapy (ICT) is a recommended management strategy for various inflammatory hair loss disorders, including alopecia areata. Pain from ICT can limit the use of this treatment option in some patients, particularly younger people, and those with needle phobia. However, strategies to mitigate pain during injections are rarely used in routine dermatology practice.

To investigate the efficacy and safety of vibration assisted analgesia (VAA), we audited pain-perception immediately following ICT for alopecia, from our tertiary hair clinic, between March-August 2022, using a standard proforma and questionnaire. Vibration was delivered using a commercially available vibrator, placed inside a glove and applied to the nearby skin.

Fifty-two patients were included (45 female:7 male), with an average age 47 years (range 16-85). The conditions treated included alopecia areata (n=25), frontal fibrosing alopecia (n=21), lichen planopillaris (n=4), and folliculitis decalvans (n=2).

Forty-nine / 52 patients received VAA during ICT. Of these, 39/49 had previously received, and could recall, their experiences with ICT without analgesia, allowing for comparison of pain. Of these: 85% (n=33) felt that their pain was improved, with n=23 stating this was “a lot better” and n=10 “a little better”; 13% (n=5) felt VAA “made no difference”; and one person felt it was “a little worse”. One patient felt VAA caused a headache. No other adverse events were reported.

Our data suggests that VAA is a cheap, safe, and effective analgesic during ICT in routine dermatology care and may allow the use of ICT in a wider cohort of patients.

P29

3D camera imaging of Frontal Fibrosing Alopecia: a novel assessment method

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Abstract

Frontal fibrosing alopecia (FFA) is the commonest primary cicatricial alopecia. Robust research into effective treatment is limited by lack of accurate and reproducible assessment methods. As FFA is characterized by well-delineated frontotemporal hairline recession, we hypothesized that 3D camera (3DC) image analysis could be used to accurately measure alopecia extent. We previously conducted a pilot study to assess reliability of a 3DC system in measuring forehead surface area (as substitute for alopecia area) in 9 volunteers. Results showed a high degree of inter and intra-observer concordance for the technique. Subsequently, 12 FFA patients completed a 2-year prospective observational study. Alopecia area was imaged with a 3DC (Vectra®H2, Canfield) at 6 monthly intervals over 24 months. In addition, standard clinical assessments were recorded including measurements, patient and clinician global activity assessments, FFASI and DLQI scores. 11/12 patients demonstrated an increase in 3DC-assessed alopecia area over 2 years. The increase was progressive in 10/12 but some variation in 3DC scores was noted in 2 cases. In 1/12 disease stability was demonstrated, with complete correlation between all clinical assessments and 3DC score. In 2/12, all clinical assessments suggested disease stabilisation but 3DC scores suggested alopecia progression. We wish to highlight this novel method of assessing alopecia area in FFA and its potential value in monitoring treatment efficacy, including future clinical drug trials. This method of assessing alopecia area could be used in conjunction with guidelines for FFA clinical trials proposed by the International FFA Cooperative Group (IFFACG).

P30

Lichen planopilaris in women with Afro-textured hair

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Abstract

Over the last five years we have observed a rise in the number of young women of colour with Afro-textured hair presenting with lichen planopilaris (LPP), to the extent that LPP is now more common than CCCA in this patient group. These women exhibit small to large patches of cicatricial hair loss on the scalp and experience symptoms including varying degrees of shedding, pain, and itching.

The recent increase in the frequency of LPP raises the possibility of an environmental cause. A common feature in these patients is the application of hair oils to the scalp and a tendency to infrequent hair washing. These practices are based on the belief that frequent washing may lead to loss of essential oils from hair that is characteristically already dry. Additionally, oiling the scalp is thought to have therapeutic and stimulating benefits.

As part of the treatment protocol, patients were asked to discontinue the use of all hair oils and scalp moisturisers. Additionally, hair washing was recommended three times a week, and no less than once a week. This approach has resulted in significant improvement in both symptoms and progression of hair loss within a relatively short period of time.

The Afro hair market is saturated with oils, leave-in conditioners and serums, ranging from home remedies to imported products that have not necessarily been tested to an accepted cosmetic standard. To explore the possible correlation between their use and LPP research on a larger cohort in the UK and Kenya is planned.

P31

Frontal fibrosing alopecia in South Africa: a questionnaire study

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Abstract

In the last 15-20 years, as in populations elsewhere, there has been a large increase in black South Africans presenting with frontal fibrosing alopecia (FFA). To explore the possibility of an environmental cause we conducted a questionnaire study covering a range of lifestyle factors in these patients.

100 patients with FFA were recruited. The mean age of onset was 36.5 (range 7-74). 34 subjects were postmenopausal. Loss of eyebrows occurred in 29 subjects. Over half reported skin darkening, mainly on the face, which was more common in those with eyebrow loss (81%) than in those without (40%).

51 subjects had used hormonal drugs (contraceptives, HRT). The use of hair prosthetics - wigs, weaves, extensions - was common, 88 subjects having used at least one of these. All subjects used leave on skin and/or hair cosmetics (92% daily or often, 8% sometimes). 92% reported using facial moisturiser, 90% used sunscreens and all used leave-on hair conditioners.

The study of FFA in populations with different cultural practices and environmental exposures may help in the search for its cause. Thus, as in white populations, Africans also show a high level of use of leave-on skin and hair care products, including moisturisers and sunscreens. In contrast, the use of hair prosthetics is much higher than in white populations. Nevertheless, the early age of onset of FFA in some Africans, the lower frequency of eyebrow loss, and the improvement sometimes seen when prosthetics are discontinued, suggest a contributory role.

P32

Seasonal hair loss in Northern and Southern Hemispheres: Insights from Google Trends data

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Abstract

Seasonal hair loss patterns in humans have been previously documented in the Northern Hemisphere, with the highest shedding levels observed during autumn. This study aimed to investigate whether similar trends are present in the Southern Hemisphere and countries near the equator using Google Trends data from 2010 to 2022. Google Trends, a web-based database that tracks search queries on Google worldwide, offers valuable insights into seasonality and event-driven search behaviour. However, it does have multiple limitations including normalization of data, potential geographic biases, and restricted granularity for niche topics. Never-the-less, we analysed the weekly frequencies of “hair loss”-related searches in select countries across the globe. Our findings revealed that European countries (Germany, United Kingdom, Sweden, Portugal, Spain) and Southern Hemisphere countries (Brazil, Argentina, South Africa, Australia, New Zealand) exhibited similar trends, with the highest search rates occurring during their respective autumn seasons (September, October, and March, April). Countries near the equator (Colombia, Kenya, Malaysia, Indonesia) showed no clear seasonal trends in hair loss related searches. Seasonal trends were less differentiated in some countries (USA, Canada, UK, Japan) as compared to others (Brazil, Argentina, Portugal, Spain). We conclude that humans in both hemispheres experience increased seasonal hair loss during autumn, likely due to sunlight exposure and related hormonal changes. We speculate the reduced differentiation in hair loss-related search activity over the year in some countries may be linked to increased indoor living. We further speculate the findings may suggest that light therapy could benefit individuals affected by seasonal hair shedding.

P33

Interest of a *Cinchona succirubra* extract and its association with Caffeine in hair loss

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Abstract

Natural plant extracts have been reported as potential therapy for hair loss treatments by normalizing Wnt/ß-catenin signaling. A Cinchona succirubra extract regulates Wnt/ß-catenin pathway and stimulates, in association with Caffeine, Syndecan-1 involved in anchoring. These effects were confirmed in vivo with an anti-hair loss serum combining both ingredients.

The effect of Cinchona succirubra extract and Caffeine on Dickkopf-related protein 1 (DKK1) and Syndecan-1 production by human hair follicle dermal papilla cells was first investigated. A clinical study was then conducted in 53 included subjects with acute telogen effluvium who applied the serum for 16 weeks. Hair density (telogen and anagen), anagen to telogen ratio, hair count, hair thickness/density, hair volume, hair mass and global hair were assessed at baseline, 4 and 16 weeks.

Cinchona succirubra extract significantly inhibited DKK1 production and stimulated Syndecan-1 expression in association with Caffeine. Trichogram results showed an improvement in the anagen/telogen ratio from 4 weeks with an increase of anagen hair and a reduction of telogen hair. Furthermore, the number of collected hair decreased after 4 weeks versus baseline. A significant improvement in self-evaluation of hair loss was also observed. Hair loss was also decreased after shampoo, after brush, on the clothes and subjects found their hair stronger.

These results confirm the interest of Cinchona succirubra extract to regulate hair cycle and of its association with Caffeine to reinforce hair anchoring. The good efficacy of a natural Cinchona succirubra extract-based hair care formulation was clinically assessed and displayed a good tolerance.

P34

Molecular monitoring of transcriptional effects following treatment of male volunteers with commencing hair loss after treatment with an extract of Quassia Amara Wood containing serum

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Abstract

Androgenetic alopecia (AGA) is the most common type of hair-loss driven by genetic predisposition and hormones. Men suffering from AGA experience an impact on their quality-of-life; technologies to prevent hair-loss are highly appreciated. To identify those technologies, reliable in vivo screening methods are essential.
Previously our group presented beneficial effects of a Quassia Amara Wood Extract (QAW) on the extracellular matrix targeting protection, synthesis, processing, and organization of essential skin-compartments. QAW further stimulates intracellular antioxidant systems. Initial lab experiments revealed promising effects on hair follicle cells, like induction of Versican, KI67, Catalase and hair-keratins.
In the present study, 91 male participants with commencing hair loss were assigned to 4 test groups to investigate the effects of a QAW treatment vs placebo and other technologies. RNA-Seq was performed on plucked hair follicle samples before, after 4-day and after 6-week-treatment.
Following QAW treatment, 1895 and 1461 genes showed differential expression ($p<0,05$) at 4-day and 6-week-treatment, respectively. Further analysis showed involvement of 11 hair-growth associated pathways, e.g. FGF- and EGF-pathways. The strongest upregulation compared to placebo was observed for GREM1, DKK3-3; KRT33A1, KAP4-4 and POSTN; while downregulation was shown for CALML5, DAPK3 and CDK2
Using different molecular-biological tools to investigate effects of QAW on the hair follicle provides a deeper understanding about active principles, helping to develop effective products against hair-loss in men with commencing hair-loss. However, further studies are needed to prove the relevance of the shown gene-modulations regarding hair-loss prevention in vivo.

P35

Trichoscopic findings after hair transplant with FUE technique

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Abstract

OBJECTIVE. We aimed to describe trichoscopic findings in donor and receptor areas in the following months after the hair surgery is performed in androgenic alopecia (AGA).

METHODS. A retrospective descriptive study was designed, based in the analysis of trichoscopic images obtained with TrichoScan (FotoFinder Systems) in patients with AGA who underwent a hair transplant using the follicular unit excision technique. We followed a total of 50 patients, with a maximum follow-up of 1,5 years after hair transplant. Trichoscopic findings were evaluated by three different dermatologists focused in trichology.

RESULTS. We evaluated a total of 34 patients in the resting period (month 0-4), 13 patients in developmental phase (months 4-8) and 29 patients in maturation period (months 9-15). Pink areas, dystrophic hairs, perifollicular white dots and accentuation of the follicular opening were the most frequent signs in receptor area. We also describe the eclipse sign and pseudo-tufting. Broken hairs, red areas and haemorrhagic crusts were more frequent in the initial phases. In donor area, most frequent signs were white dots and the arborizing vascular pattern.

CONCLUSIONS. This study is the first description of trichoscopic signs associated to the different phases of a hair transplant. Perifollicular erythema and hyperkeratosis, could be observed in some patients after the surgery. We observed that perifollicular white dots, which are described in some scarring alopecias, are very frequent, probably due to scarring process induced by the incisions. We describe for first time eclipse sign and pseudo-tufting, which could be common signs in transplanted scalps.

P36

Scalp analysis with Multiparametric Ultrasound before and after application of cosmetic with vasoconstrictor active

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Abstract

The use of dermatological ultrasound has emerged as an useful tool for dermatological and aesthetic use. Its use for the diagnosis of hair and scalp problems is an option that emerges as a non-invasive and in vivo form of evaluation.

When used in a multiparametric way, in which information on B-mode, flowmetry and elastography are used together, it is possible to perform a richer and accurate analysis.

In this study, two volunteers underwent to the application of a vasoconstrictor cosmetic active in different dosages and vehicles.

In volunteer 1, the cosmetic was used in a higher dosage with a vehicle plus a permeation accelerator for a more intense and fleeting response.

Volunteer 2 used the lower dose cosmetic without the permeation accelerator with an expected longer lasting response, however, less intense.

The equipment used was a Canon Aplio i800 Ultrasound with 24 and 33MHz transducers.

The equipment was used before and after the cosmetic. In the volunteer 1, the images were collected after 5 minutes of application and in the volunteer 2, after 30 minutes.

Significant differences were found in vascularization and tissue stiffness, identified by high-sensitivity Doppler vascular map and Strain Wave elastography, respectively. The changes perceived in volunteer 1 were more intense.

Inflammatory and cicatricial processes, evaluation of the layers of the skin and the hair follicle itself, are objects of study of multiparametric scalp ultrasound. Its application in clinical practice makes the physician's work more efficient and accurate both in diagnosis and in treatment follow-up.

P37

Pitfalls in alopecia photography.

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Abstract

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Photographic images are often the primary means by which alopecia is assessed in clinic. Although assessment scores exist for some types of alopecia such as alopecia areata (SALT score) and female pattern hair loss (Sinclair score), these are estimates of the extent and severity of disease, and alopecia is often best recorded and assessed by means of comparison with previous clinical images. Images are usually taken at baseline and updated prior to starting new treatment(s), for the purpose of assessing treatment benefit at subsequent clinic visits. There are however, a number of pitfalls in alopecia photography of which both the clinician and photographer should be aware. Unfortunately, any errors made when taking images may not become apparent until the patient is reviewed again at clinic, at which point comprehensive assessment of treatment efficacy is not possible.

Typical errors include incomplete reflection of hair from the hairline; “pseudo-hairline” caused by kinking of hair held back with a hairband or pulled across the true hairline; omission of anatomical landmarks and incomplete exposure of alopecia patches. Apparent variation in hair density and central part width due to traction, is also highlighted. The development of national photography standards will assist medical photographers in avoiding these errors, to ensure standardised comparable imaging of alopecia

P38

Scalp flora plays a role in the hair regrowth effect of topical minoxidil.

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Abstract

Minoxidil is a widely used over-the-counter topical treatment for hair loss. The response rate for topical minoxidil is relatively low. It is recognized that there are individual differences in the hair growth-promoting effects of topical minoxidil in humans. Therefore, we hypothesized that scalp flora might be involved in the hair regrowth effect of topical minoxidil in this study.

First, to clarify the involvement of scalp flora in minoxidil hair growth effects, mice treated with and without antibiotics (Vancomycin: 0.05%, Ampicillin: 0.1%, Neomycin: 0.1%) were compared. The results showed a significant delay in hair growth in the antibiotic group at 14 days after hair removal. In addition, to examine the effects of each antibiotic individually, a study was conducted in which one each of vancomycin, ampicillin, and neomycin was administered. As a result, the effect of minoxidil on hair growth was markedly suppressed in the ampicillin-treated group. Therefore, it is suggested that the flora suppressed by ampicillin is involved in the minoxidil hair-growing effect. Flora analysis showed that some butyrate-producing bacteria showed a decreasing trend. Butyrate produced by bacteria has been shown to induce regulatory T cell differentiation (Furusawa et al., 2013), and Treg cells have also been reported to promote hair follicle stem cell proliferation and differentiation and promote hair regeneration (Ali et al., 2017). Based on these findings, we are currently studying whether the inhibition of the hair-growing effect by ampicillin can be cancelled by butyric acid bacteria.

P39

Scalp interactome, what impact does a new treatment shampoo have on the ecosystem of the scalp with seborrheic dermatitis? Focus on flaking, inflammation and pruritus.

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Abstract

Seborrheic dermatitis (SD) is a chronic relapsing dermatosis characterized by scaling, pruritus and mild erythema, affecting sebum-rich areas such as scalp. A pharmaco-clinical study was conducted to monitor the evolution of clinical signs of SD, treated with a new shampoo formula containing antifungal, soothing, antioxidant and keratolytic actives. Clinical assessment was performed using Squire dandruff score. Scalp ecosystem was studied using a multi-omics approach.

The aim of this study was to understand, through an integrative and ecosystemic approach, the positive clinical course of scaling, inflammation and pruritus in scalp SD.

This two-stage study was conducted on 41 subjects, with a two-week attack phase (W0-W2) with SD shampoo three times a week, followed by an 8-week maintenance phase (W2-W10) with SD shampoo once a week and neutral shampoo twice a week (treated group) or neutral shampoo three times a week (control group). Subjects were randomly assigned to these two parallel comparison groups. Measurements and samples were taken at W0, W2, W6 and W10 depending on the assessment method used. Clinical, biochemical, metabolomic and metagenomic analyses were performed.

During the attack phase, a significant reduction in clinical signs was observed: (I) desquamation associated with a decrease in metabolites involved in cell proliferation and apoptosis; (II) pruritus and inflammation with a decrease in IL8, cathepsin S, pro-inflammatory lipids from Malassezia metabolism and metabolites involved in pruritus. Scalp microbiota was also significantly rebalanced. All these markers were maintained during the maintenance phase in the treated group, while they were regressed in the control group.

P40

Targeting inflammation and specialized pro-resolving mediators: a new pathway to improve scalp condition?

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Abstract

Under poor conditions, scalp can affect the natural hair growth and brightness but also lead to pathologic conditions such as dandruff or seborrheic dermatitis. The inflammation is one of the key elements of the unhealthy scalp. Specialized pro-resolving lipid mediators (SPMs) are endogeneous lipids that actively regulate the immune system to promote the resolution of inflammation. Although SPMs have been studied in the skin to end the inflammation process and promote tissue regeneration, no studies have been provided in the scalp.

An Anetholea anisita extract was selected based on its anti-inflammatory properties found on HFDPC. These results were confirmed with a clinical study on volunteers (n=40, 18-40 years) presenting dandruff and oily hair where the extract was tested in a rinse-off shampoo formula. For the first time, SPMs were detected in the scalp after a LC-MS/MS analysis of volunteers' sebum. Treatment with the extract increased the expression of LxB4 (+98%), RvD1 (+62%) and RvD2 (+72%) compared to placebo. Moreover, a significant decrease of pro-inflammatory markers such as PGE2, LTB4 and IL8 by 38%, 41% and 48%, respectively, was observed and confirmed the results obtained in-vitro on HFDPC. All these benefits result in an improvement of scalp barrier integrity and consequently a decrease of dandruff and an increase of hair brightness.

To conclude, these results highlighted SPMs as a promising target to improve scalp health. It also reinforces the strategy that targeting scalp disorders help to improve hair conditions such as dandruff and hair brightness.

P41

Quantifying Particle Deposition on Hair by Streaming Potential

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Abstract

It is often desirable for active hair care ingredient formulations to stay longer on hair despite repeated washing. However, it is known that the surface properties of healthy hair and damaged hair are different, impacting how nanoparticles and microparticles commonly used in hair care products adhere to the hair surface. To engineer the best particle adherence to hair, it is important to be able to objectively compare both the differences between healthy and damaged hair and to objectively analyse particle deposition data. Not only can streaming potential analysis allow quantification of the differences between healthy and damaged hair, this technique also allows quantification of particle deposition. Past research has focused on Scanning Electron Microscopy (SEM) to observe particle deposition, but this has proved tedious and inaccurate, and only serves as a visual representation. Here, we propose the use of streaming potential analysis which quantifies particle deposition between healthy and damaged hair, through in situ observation of particle deposition on bulk hair tresses. Combined with numerical modeling, we investigate the effects of particle concentration, size, hydrophobicity, zeta potential, and material composition on the transport and deposition of particles on hair. Our results find applications in consumer care, colloidal filtration and microfluidics.

P42

Is the fatigue and failure resistance of hair dependent on ethnic origin?

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Abstract

We investigate whether the resilience of the human hair fibre (in anagen) is dependent on its ethnic origin.

Chinese, Indian, and Caucasian hair fibres were crimped and cyclically fatigued at constant 5% strain for 500K cycles under standard conditions. The data are suitable for the Weibull analysis, providing characteristic lifetimes (63.2% fibre break) and slopes of the data regression in the Weibull-plot, as indicator of the failure behaviour.

We observe a significant reduction in resilience for Chinese and Indian compared to Caucasian hair. Caucasian and Indian fibres showed Weibull-behaviour with a slope lower than 1. In contrast, Chinese hair showed a period of latency up to 9k cycles followed by a sudden increase of failure (slope>1). Chinese hairs have a larger cross-sectional area (1.5x), as well as a lower mean stress. This may indicate that thicker fibres are able to withstand more cyclic insults and then rapidly start to break. This is, however not reflected by the characteristic lifetime.

Constant strain fatigue is a good method to monitor the influence of ethnicity on hair´s resilience. Caucasian fibres are more hydrated than Asian and African hair, suggesting better flexibility and hence, resilience. Interestingly, the highest Weibull-slope is found in Chinese hair, known to have the biggest melanosomes. This study lays the ground for future translational research for the influence of melanosome size on the resilience of human hair fibres in line with the weakest link theory, phenotypic/genetic variations (e.g.EDAR370A, ARG163Gln), the hair cycle (FGFR2), and the macromolecular stability.

P43

Evolution of Hair Measurements for clinical outcomes: Are they reliable?

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Abstract

Background:
Negative alterations of scalp hair result in the perception of alopecia. The naked eye perceives the global phenotype, while high magnification imaging enables the quantification of proliferation and differentiation of hair fibres from follicles. The measurements determining diagnosis and relating progression or intervention outcomes are sample surrogates for a global effect and prognosis. The fallibility of precision measurements can, on the one hand, lead to new knowledge, yet, on the other hand, can allow authoritative miscommunication.

Objective:
To review the evolution and accuracy of studied alopecic outcomes.

Methods:
Literature review of seminal and pervasive hair measurement evolution.

Results:
Uncalibrated global scoring and quality of life instruments are subjective, and subject self-perception does not correlate with changes in hair measurements. Manual counting and high magnification phototrichoscopy of unclipped or clipped hair have all known or ignored operator errors. Calibration methods of image analysis software appear reasonable yet are not easily verifiable. Averages smooth away the unidentified confounders, and selective statistical method analysis can overplay outcomes.

Conclusion:
The field of hair measurement for diagnosis and treatment outcomes has evolved to higher precision data generation. Calibration of analytical instruments and statistical methods describing an outcomes-effect require standardisation. In addition, benchmarks defining clinically relevant outcomes are also required. While research procedures require evaluation of hair follicle productivity by the rigour of fibre and time, translation into simplified surrogates for in-clinic patient evaluation is essential. Amongst these evolving measurement tools, scalp coverage scoring is an emerging discriminator.

P44

Effect of particulate matter on hair disease

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Abstract

Particulate matter (PM), a major air pollutant, is a complex mixture of solid and liquid particles of various sizes. PM has been demonstrated to cause intracellular inflammation by inducing reactive oxygen species (ROS) generation in human keratinocytes, and is associated with various skin disorders, including atopic dermatitis, eczema, and skin aging. Although PM has been known to penetrate into the hair follicles, there have been few studies on the effect of PM on hairs. A recent study demonstrated that the cycling pattern of the disease flare of alopecia areata (AA) partially corresponded to that of PM concentration. So, in the present study, we investigate the effect of PM on human outer root sheath (ORS) cells.

PM increased ROS generation in ORS cells via activation of aryl hydrocarbon receptor. PM also induced activation of p38, c-Jun, and STAT3 and increased the level of proinflammatory cytokines including IL-1, IL-6, IL-8, and MMP-1 as well as IL-15. These data suggest that penetrated PM into the hair follicle may cause inflammatory response in ORS cells by increased production of ROS which could impair hair growth.

P45

Effect of ethnicity, temperature, and humidity on the viscoelastic behaviour of human hair fibres, and the associated structural changes identified with FT-IR microscopy

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Abstract

Whilst tensile testing of hair has been well established in literature, dynamic mechanical analysis (DMA) gives a better characterisation of the viscoelastic properties, and is still underutilised.

Applying a novel test method on single hair fibres, the effects of hair type (Caucasian, Asian, and African); relative humidity; and bleaching, on viscoelasticity, are investigated across a temperature range of 40 - 210 o C. The fibres are tested in tension and the normalised storage and loss moduli indicate consistent, dramatic changes.

Limited work has been done to understand the structural changes during heating. Although there is a body of research indicating the chemical composition of hair cross sections before and after heating, there is no unified understanding of the effects on thermomechanical behaviour.

FTIR-ATR (attenuated total reflectance) microscopy is used with a heated stage on the cortex of hair fibre cross sections to identify chemical changes in the dominant structure of the hair.

P46

Transcriptomics to uncover the role of the dermal papilla in human hair fibre pigmentation.

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Abstract

As the hair follicle is growing during anagen, melanocytes release melanin, which is transferred to the follicle medulla, giving hair fibres their pigment. The contribution of eumelanin (brown/black melanin) to pheomelanin (yellow melanin) leads to variations in hair colour, while loss of melanin during ageing leads to production of white hair fibres.

During hair growth the dermal papilla (DP), a cluster of cells located at the base of the hair follicle, signals to surrounding matrix cells facilitating their incorporation into the layers of the hair fibre and follicle. More recently, mice with a knockout of Sox2 in their DP were found to have increased pheomelanin (relative to eumelanin) in their hair fibre, indicating a new role for the DP in the control of hair pigmentation. Here, we hypothesise that the DP can also influence whether or not melanocytes produce melanin in humans, and therefore have a role in human hair greying.

To address this hypothesis, we isolated patient matched DP from pigmented and non-pigmented hair follicles from 4 individuals. We then performed bulk RNA-seq on the DP, to identify specific genes associated with the presence or absence of pigmentation. To explore the role of these DP genes in pigmentation, we are using co-culture assays to look at melanin production and transfer. Our work challenges the dogma of pigmentation loss being due to the loss of melanocyte stem cells in the bulge, bringing a novel perspective to the cause of hair greying in humans.

P47

Impact of topical application of anti-dementia agents on hair growth

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Abstract

Recent study revealed that patients with alopecia areata (AA) had a higher risk of developing dementia (CY. Li et al. J Clin Psychiatry. 82, 21m13931 (2021)). However, the underlying pathophysiology between AA and dementia remains unclear. Therefore, we hypothesized that the impairment of decreased hair follicle and cerebral blood flow caused by vasoconstriction may be one of the common factors of the complex pathogenesis of AA and dementia. We speculated that anti-dementia agents may also have hair loss suppression and hair regrowth effects. Thus, we applied a 1% solution of Aricept® (donepezil hydrochloride), an anti-dementia drug, and a supplement such as bacopa extract (Foods with Functional Claims in Japan) to half of the body of shaved mice and examined changes in hair growth. To quantify hair growth, mice were skin excised for hair growth-related gene alterations. We also observed the effects of anti-dementia agents on blood vessels using real-time angiographic imaging. The results showed that the dermal application of anti-dementia agents significantly accelerated hair growth. It has been assumed that anti-dementia agents promoted blood flow improvement in the scalp and reconsidered the scalp environment suitable for hair growth. As a novel treatment method, we would like to implement an all-in-one treatment that can prevent not only AA but also male pattern baldness and the subsequent onset of dementia by using anti-dementia agents. Further studies are needed to elucidate the mechanism of hair growth and vasodilation.

P48

Mapping HIF1a and ARNT to cell states and identities in cycling human hair follicle: the keratinocyte fate in the "adaptive signaling landscape"

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Abstract

Hair follicle (HF) cyclic transformations are accompanied by changes in cell behavior and metabolism. Nevertheless, it is not clear how self-renewal, proliferation and differentiation are related to activity of adaptive machinery such as HIF1 (HIF1a/ARNT heterodimer). By mapping nuclear localization of HIF1a/ARNT to distinct cell identities during HF cycle, we delineate a follicle cell fate scenario in which state transitions are determined by a "landscape" of HIF1a/ARNT expression.

Telogen is characterized by a lack of HIF1a in the bulge and in papilla-adjacent epithelial cells. ARNT is high in the later, but low in bulge. Anagen entry is marked by increase of HIF1a and ARNT in germinative zone, while bulge remains negative. Wave-like HF cell activation/growth (Ki67+) shadows the upward propagation of HIF1a/ARNT in lower HF. In stationary anagen, the upper ORS remains HIF1a-negative but ARNT-positive. The acquisition of IRS and hair shaft cell fates is associated with retention of ARNT-positivity and downregulation of HIF1a. In catagen, HIF1a in lower ORS and in the matrix declines, while some cells of germinative layer (which are likely to acquire germ cell fate in telogen) retain ARNT.

We propose that life history of an ordinary follicular keratinocyte - starting from quiescent uncommitted state (HIF1alow/ARNTlow/a6-integrin+), through committed ORS or germinative cell states (HIF1alow/ARNThigh/a6-integrin+), then to proliferating cells of the matrix and lower ORS (HIF1ahigh/ARNThigh) and finally to differentiating cells of IRS and precortex (HIF1alow/ARNThigh/a6-integrin-) - is unfolded in a "landscape of HIF1a/ARNT activity", which serves as a framework for coordination between cell metabolism, behavior and identity.

P49

Unveiling the trichogenic signature of the human native dermal papilla

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Abstract

Human mesenchymal dermal papilla cells (DPCs) modulate hair follicle (HF) development and growth cycle and represent a reservoir of easily accessible adult progenitor cells, which has been largely explored for HF tissue engineering therapies against hair loss. However, hair cloning strategies resorting to human DPCs expanded in vitro remain intangible due to DPCs' loss of trichogenic properties upon cell culturing. This represents the major bottleneck in HF bioengineering for replacement therapy: our knowledge of the human native DP and the molecular mechanisms controlling human hair growth is still very limited. Hence, the step forward will require the understanding of mechanistic cues behind DPCs' loss of trichogenic properties in order to come up with counteracting strategies.

In this study, we performed chromatin accessibility and transcriptional profiling of human DPCs in native (freshly isolated DPs) vs. in vitro (conventional 2D culturing) conditions. The study enrolled a total of 15 Caucasian male patients aged between 18-55 years under informed consent. Only occipital anagenic HFs from the scalp of AGA patients undergoing FUE hair transplant were included.

Overall, our work identified several transcription factors and fundamental pathways regulating human hair trichogenicity that could be targeted to prevent or revert hair loss. By combining ATAC-seq and RNA-seq it was possible to determine specific changes in chromatin accessibility associated with loss of trichogenicity in human DP. We foresee that this analysis will bring valuable insight to human hair growth regulation by disclosing key master regulators of trichogenicity and, thus, novel molecular targets for hair loss treatment.

P50

Activation of mitochondrial aldehyde dehydrogenase 2 promotes hair growth

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Abstract

Hair loss is a prevalent condition influenced by multiple factors, including genetics, hormones, and environmental factors. Mitochondrial dysfunction-induced oxidative stress has been reported as a significant contributor to hair loss, resulting from an imbalance between the production of reactive oxygen species (ROS) and cellular antioxidant defense. ROS accumulation causes damage to cellular components, including DNA, proteins, and lipids. Moreover, a previous study reported that oxidative stress suppresses hair growth by downregulating β-catenin, leading to hair follicle miniaturization and hair loss.

In this study, we investigated the impact of activating mitochondrial aldehyde dehydrogenase 2 (ALDH2) on hair follicles (HFs) to promote hair growth. ALDH2 is an enzyme that reduces oxidative stress by targeting cytotoxic aldehydes, including 4-hydroxynonenal (4-HNE) and malondialdehyde (MDA). Through a series of in vitro, ex vivo, and in vivo experiments, our findings demonstrate that ALDH2 activation promotes hair growth by mitigating ROS levels and increasing the clearance of aldehyde adducts in outer root sheath cells. Furthermore, we found that ALDH2 activation upregulated Akt/GSK 3β/β-catenin signaling, which plays a crucial role in hair growth.

Overall, our results suggest that ALDH2 activation on HFs could be a promising therapeutic strategy for promoting hair growth. This study provides novel insights into the impact of ALDH2 modulation as a viable approach for promoting hair growth, potentially leading to the development of new treatment options for hair loss.

P51

Noncontact compression promotes hair growth through vasodilation

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Abstract

Noncontact ultrasonic phased-array device accelerated hair growth by locally stimulated cyclic compression (10 Hz, >20 min/day for three consecutive days). It has been installed in multiple clinics across Japan as the most promising device for hair growth. When shaved mice were rotated to a left lateral decubitus position, and 5% minoxidil topical reagent or cyclic compression was applied at the right cranial spot, reagent and mechanical stimulation promoted hair growth only on the right lateral side. Therefore, we examined the acute effects on vascular function when minoxidil topical reagent or cyclic compression was applied at the right cranial spot. After an intravenous injection of angiography reagent, shaved backs of C57BL/6 mice were stimulated by 5% minoxidil topical reagent or cyclic compression (10 Hz, 20 min), respectively. Then, angiography with a real-time fluoroscopic imaging technique was used to visualize the inside of blood vessels. Angiographic images appear to be hyperpermeability associated with local vasodilation, which may presumably accelerate the hair growth cycle. U-37883A, a potent inhibitor of KATP channel (especially composed of Kir6.1/SUR2B) showed the delay of hair growth under mechanical compression and the suppression of local vasodilation. Cyclic compression-induced Kir6.1/SUR2B activation of endothelial cells and blood vessels may be an essential and effective strategy for androgenic alopecia. Clinics around Japan are planning to install more and more sets of devices. We will also report some of the results of clinical trials.

P52

Revealling the anagen prolonging effects of a ginger extract by means of different in vitro and ex vivo hair follicle models

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Abstract

Premature catagen development is the primary event leading to excessive hair shedding. Given the negative impact on quality-of-life, new anti-hair loss cosmeceutical technologies are highly demanded. Although ginger extracts are used in hair care products, its main component, 6-Gingerol is described to inhibit hair shaft production in hair follicle (HF) organ culture and hair growth in mouse. Thus, to clarify whether a ginger extract possesses anagen prolonging effects, this was administered into the culture medium of 1) dermal papilla fibroblasts (DP) spheroids arranged within matrix (Cultispheres), 2) 3D reconstructed HFs in which Cultispheres are embedded together with ORS keratinocytes within a horizontal matrix, 3) DP spheroids prepared using the hanging-drop method, and 4) human microdissected HFs, and performed RNAseq. Comparative transcriptome analysis of experimental groups receiving the ginger extracts versus vehicle deriving from the different in vitro models used and organ cultured HFs revealed common differentially expressed genes. Transcriptomic responses to the ginger extract in treated microdissected HFs and hanging-drop DP spheroids was particularly similar and revealed modulation of Wnt and BMP pathways, suggesting the potential of this plant extract to promote anagen. Although hair shaft production impediment was observed, macroscopic hair cycle analysis indeed revealed inhibition of premature catagen induction in HFs treated ex vivo with the ginger extract in comparison to vehicle. Thus, our data encourage the use of different models to unravel the complex response to novel compounds, and propose the tested ginger extract as cosmeceutical option to promote anagen and maintain hair health.

P53

Wnt ligand expression diversity during mouse hair follicle development.

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Abstract

Introduction and Objectives:
Wnt signalling has recognised importance for cell fate specification in developing skin and hair follicles. However the Wnt pathway family includes multiple components, whose individual roles are less well understood and which have been mainly characterised at the gene level. This study aimed to define the spatio-temporal relationship between individual Wnt ligands and early follicle development in mice at the translational level.

Methods:
Wnt activity was characterised in mouse back skin, between E12.5 and E14.5, using Lef-1 immunofluorescence labelling or Wnt reporter embryos [TCF/Lef:H2B-GFP]. Locality and expression of 11 Wnt ligand members [canonical: Wnt1, Wnt2, Wnt3, Wnt10a and non-canonical: Wnt4, Wnt5a, Wnt5b, Wnt7a/b, Wnt11 and Wnt16 and indeterminate: Wnt2b] was also investigated by immunofluorescence staining. Developing pelage [back skin] and vibrissa follicles [whisker pad skin, E13.5] were doubled-labelled with selected ligands and laminin and visualised by confocal microscopy.

Results:
Dynamic changes in Wnt activity was observed in all skin compartments between E12.5 and E14.5, including a progressively restricted gradient of dermal Wnt expression leaving only cells immediately below the epidermis labelled at E14.5. Immunostaining revealed diversity of epidermal and dermal Wnt ligand expression, most strikingly at the dermal-epidermal junction, where Wnt1 and Wnt2b antibodies revealed discontinuous labelling at the site of follicle initiation in back skin but not vibrissae.

Conclusions:
The role of specific Wnt ligands in the crosstalk between proto-hair follicle dermal and epidermis cells may be highly specific, perhaps reflecting localised exchange via basement membrane.

P54

Using in vitro and ex vivo culture models to study the ability of cooling to suppress oxidative stress-mediated, chemotherapy drug-induced alopecia

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Abstract

Chemotherapy drugs cause cytotoxicity to the highly-proliferative hair follicle (HF) matrix keratinocytes leading to HF regression. Currently, scalp cooling represents the only available intervention to combat hair loss. We previously reported that cooling reduces cytotoxicity via direct temperature-dependent mechanisms, including reduction in drug cellular uptake. Here, we investigated whether chemotherapy induces keratinocyte apoptosis and HF damage via induction of oxidative stress. Anthracyclines triggered reactive oxygen species (ROS) generation in keratinocytes at 37°C, which was partially-attenuated by sub-optimal (26°C) and prevented by optimal (18°C) cooling. Notably, treatment with several antioxidants (AOs) could curtail (but not prevent) cytotoxicity, yet cooling in the presence of AO was more efficacious than cooling alone, whilst combination of sub-optimal cooling and AO efficiently suppressed cytotoxicity. Our in vitro observations were confirmed using an ex vivo organ culture system involving treatment with 4HC and assessing HF viability using Ki-67/TUNEL labelling and Masson-Fontana histochemistry. Optimal (18°C) cooling during 4HC treatment a) rescued matrix keratinocyte proliferation , b) maintained hair growth, c) suppressed induction of catagen and preserved the viability of anagen-phase HFs, and d) maintained the pattern/intensity of melanin expression equivalent to that observed in untreated HFs. Importantly, although sub-optimal (26°C) cooling or AO (N-acetyl cysteine/NAC) alone partially-attenuated drug-mediated toxicity, combination of sub-optimal cooling with NAC fully-rescued HFs from drug toxicity. Collectively, our findings have provided an improved understanding of the mechanisms of cooling-mediated cytoprotection and conceptualised the development a highly-promising combinatorial approach to potentiate the clinical efficacy of scalp cooling.

P55

The role of T-helper 17 cells and regulatory T cells in acute diffuse and total alopecia

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Abstract

Acute diffuse and total alopecia (ADTA) is a variant of alopecia areata (AA) that lacks the typical patchy hair loss seen in classical AA and presents with an acute onset of diffuse hair loss. It has a favorable prognosis.

This study was performed to assess the role of T-helper (Th) 17 cells and regulatory T cells (Tregs) in the pathogenesis of ADTA.

Twenty-four patients with ADTA and 12 healthy controls were included. Scalp skin samples were obtained for measuring lesional mRNA levels of Th17 cells and Tregs related cytokines using qPCR. Serum cytokines associated with Th17 cells and Tregs were measured using ELISA. Additionally, we measured the ratio of Th17 and Treg cells around hair follicles by immunostaining for Th17 cells and Tregs.

IL-2, IL-10, and IL-23A levels were significantly higher in patients with ADTA than in controls. In the progressive stage, lesional IL-2, IL-13, and IL-23A levels were significantly increased compared to those in controls. Serum IL-15 levels was significantly lower in patients than in controls in the progressive stage. In the recovery stage, lesional IL-13 and IL-23A levels were significantly increased compared to those in controls. The ratios of Th17/CD4+ cells and Tregs/CD4+ cells surrounding hair follicles of the patients were 40.73% and 8.50% respectively, according to immunostaining results.

The increased activity of Treg cells identified through IL-10 and IL-15 is a characteristic of ADTA that is distinct from AA. The increased function of Tregs may explain the favorable prognosis of ADTA.

P56

A concept for the molecular monitoring of transcriptional effects of hair growth stimulating serums

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Abstract

Male-pattern hair loss is a prevalent condition with limited treatment options. The development of effective, low-risk hair growth-stimulating agents (HGSA) is therefore of great interest. Currently, the efficacy of HGSA is mainly evaluated by hair comb tests and trichograms, which do not provide early insights into treatment response.

We propose a concept for the molecular monitoring of HGSA treatment response in vivo, based on RNA and microRNA expression profiling before and during treatment that can be extended by individual genotype information to assess the impact of genetic constitution on treatment response.

In this exemplary study, 91 male participants with commencing hair loss were assigned to 4 test groups to investigate the effects of three HGSA versus placebo. RNA-Seq was performed on plucked hair follicle samples before, after 4-day and after 6-week-treatment. Genotyping was performed on DNA extracted from blood or saliva samples.

Differential expression analyses identified 52 differentially expressed genes and 47 modulated pathways. The majority of effects were detectable after 6-week-treatment, ~20% of genes however showed early regulation (after 4-day-treatment). Integration with genetic data through pathway-based polygenic risk score analyses identified 6 associations between genetic background and HGSA-mediated effects, pointing to a potential value of companion diagnostics for HGSA treatment.

We suggest that this molecular monitoring approach can provide insights into HGSA treatment response as early as days within commencing treatment and may be suitable to monitor long-term compliance. In combination with genetic analyses, our approach has the potential to enable personalized prediction of treatment efficacy and adverse effects.

P57

High throughput screening in vitro assays for the identification of drug candidates inhibiting immune privilege collapse in alopecia areata

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Abstract

The inflammatory hair loss disorder alopecia areata (AA) is characterized by immune privilege (IP) collapse of the hair follicle (HF) bulb. While testing IP protective or restorative drugs for AA management can be performed in HF organ culture, this model is insufficient for high-throughput screenings. Here, we aimed at establishing in vitro models for this purpose. We mimicked IP-collapse-like responses (i.e. upregulation of MHC class Ia and II (MHCI/II)) by applying IFNγ, the main cytokine driving AA, to outer root sheath keratinocytes (ORSKs) and normal human epidermal keratinocytes (NHEK), despite the latter lack IP in vivo. For model validation, we employed the IP guardian α-melanocyte stimulating hormone (αMSH), the immunosuppressive drug Tacrolimus, which protects and restores HF IP ex vivo, and the JAK-inhibitor and AA therapeutic Tofacitinib. Confirming activation of IFNγ signaling in NHEK and ORSK, IFNγ treatment promoted CXCL10 release into the medium (ELISA) and led to enhanced mRNA and protein expression of MHCI/MHCII assessed by qRT-PCR and quantitative immunofluorescence. Up-regulation of MHCI/II and CXCL10 release were prevented by Tofacitinib in NHEK and ORSK, whereas application of Tacrolimus and αMSH prevented MHCI/II up-regulation exclusively in ORSK. When used in a therapeutic setting, Tofacitinib and Tacrolimus could rescue the enhanced expression of MHCI/MHCII in ORSK. Thus, NHEK and ORSK can both be used as in vitro models for the screening of drugs interfering with IFNγ signaling, while only ORSK are appropriate for analysing IP protective/restorative candidate drugs targeting other pathways involved in IP maintenance.

P58

Optimized Hidradenitis Suppurativa skin organ culture as preclinical research platform

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Abstract

The inflammatory disorder Hidradenitis suppurativa (HS) manifests in chronic abscesses, resulting from occlusion and disruption of hair follicles. Currently available therapeutic strategies are unsatisfactory and research models lack characterization. We sought to standardize the lesional HS skin organ culture as preclinical research platform for the analysis of candidate HS therapeutics. Full-thickness lesional (nodule- or fistula-containing) and peri-lesional skin samples from HS patients were cultured for 24h, 48h or 72h in serum-free medium. Treatment of fistula-containing lesions with adalimumab, an anti-TNFα antibody, resulted into reduced expression of HS-relevant genes, i.e. S100A7A/A9, CAMP, DEFB4A, LCN2 and IL17C (RNAseq). Since tissue integrity was lost after 48h in standard culture medium ex vivo, we sought to extend and optimize the culture period while preserving the disease phenotype. Analysis of disease activity markers (Krt15, Krt17, LCN2), and immune cell markers (CD3, CD66b, CD19) by immunostaining and CCL20 secretion by ELISA confirmed the preservation of the pro-inflammatory phenotype after 72h culture in a defined, serum-supplemented proprietary medium. Short periods of serum starvation did neither affect HS phenotype nor skin integrity, providing a window where biologics/drugs can be applied. Our optimized HS organ-culture assay provides an ideal platform to assess candidate HS therapeutics, to identify biomarkers and responders ex vivo, and to mechanistically assess HS pathogenesis.

P59

Ex vivo evaluation of the hydration capacity of a new haircare product and its active ingredient based on cactus extract by using the method of Nuclear Magnetic Resonance (NMR)

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Abstract

Introduction: Water amount is important in the chemical composition of hair. Water absorption gives the hair its required moisture content which is important for healthy hair appearance. It can be modified by external stress on the hair cuticle leading to structural alteration of the hair shaft. A new haircare product containing cactus extract was developed to promote hair hydration.

Objective: The hair care product and its active ingredient were evaluated ex vivo on hair using NMR, a non invasive and quantitative method to investigate on their ability to hydrate damaged hair shaft.

Materials & Method: this study was carried out on bleached hair strand. Damaged hair was soaked in a solution containing the active ingredient or treated by direct application of the haircare product, the third part remaining untreated (control group). Measures and dosage of the humidity of hair samples were made using the low field NMR (20 MHz). Total quantity of proton on sample, proton mobility, compartmentation of proton in hair (proton more or less tied) were analyzed.

Results: After a single standardized application, the quantity of protons and the binding force of protons (water) were higher for the damaged hair treated with the cactus extract or with the haircare product than for damaged untreated hair.

Conclusion: Results show that the cactus extract alone or incorporated in a new haircare product demonstrates interesting moisturizing properties to the hair shaft and helps the fixation of water to the hair keratin, helping damaged hair to restore its appearance and physical properties.

P60

The investigation of clinical characteristics of male patients diagnosed with early-onset androgenetic alopecia: a possible association with metabolic syndrome

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Abstract

Association between Androgenetic alopecia (AGA) and hypertension, diabetes mellitus, dyslipidemia, and coronary heart disease has been suggested in several studies. Especially in early-onset AGA, the predisposition to metabolic syndrome has been highlighted, but the exact relationship and pathophysiology linking the two diseases has not been fully elucidated.

We analyzed the clinical characteristics of male patients diagnosed with AGA at 2nd to 3rd decades, and assessed their glycemic, lipid, hormonal laboratory profiles to investigate the possible association with metabolic syndrome.

This prospective study included all male AGA patients aged 10-29 years old at the time of diagnosis. Basic demographic factors, physical examination, and baseline laboratory evaluation were performed.

Total of 89 patients were included in the study. The mean age at diagnosis was 21.54 ± 4.27 years, with 95.51% recalling a positive family history of AGA. At baseline, 17.98% (16/89) of patients met the diagnostic criteria for metabolic syndrome. In terms of insulin resistance calculated with HOMA-IR index, only 6.74% showed optimal insulin sensitivity, where 43.8% (39/89) showed significant insulin resistance. Sex hormone levels were all within normal limits, showing no signs of gonadal dysfunction.

Early-onset AGA may predispose male patients in developing metabolic syndrome, as considerable number of patients exhibited insulin resistance. Close surveillance of patients diagnosed with AGA in the early ages should be implemented with regards to the development of hypertension, dyslipidemia, diabetes mellitus, and cardiovascular diseases.

P61

Efficacy and safety of dutasteride 0.2mg in male androgenic alopecia patients: a multi-center, randomized, double-blinded, placebo-controlled, parallel group, phase III clinical trial

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Abstract

Background: Dutasteride prevents converting testosterone into dihydrotestosterone (DHT), the primary androgen involved in androgenic alopecia.

Objective: To investigate the efficacy and safety of 0.2mg dutasteride in men with androgenic alopecia.

Methods: Eleven center, randomized, double-blinded, placebo-controlled parallel-group study was done. Men with androgenic alopecia (18 - 50 years of age) were randomized to receive 0.2mg, 0.5mg dutasteride or placebo once daily for 24 weeks. The primary outcome is change from baseline in target area hair count within target area circle (1cm2) at vertex at week 24. The secondary outcomes include change from baseline in target area hair count within target area circle (1cm2) at vertex at week 12, change from baseline in the average thickness of the thickest five hairs within target area circle (1cm2) at vertex, global photography evaluation by investigators and independent review panels, subjective assessments on hair growth.

Results: 137 men with androgenic alopecia were included. Of the 137 patients, 55 were allocated to dutasteride 0.2mg, 54 to placebo, and 28 to conventional dose (dutasteride 0.5mg). Change from baseline in target area hair count within target area circle at vertex was significantly higher in dutasteride 0.2mg group, compared to placebo, at week 24 ($p<0.05$). In addition, dutasteride 0.2mg treated patients showed greater improvement in hair growth change measured by independent photographic assessment ($p<0.05$). Overall incidence of adverse events (AEs) during the study period were not statistically different between treatment and placebo groups.

Conclusions: Dutasteride 0.2mg is an effective treatment for androgenic alopecia with a safety profile.

P62

Hi-C 3D Genomic interactions confirm role of wnt in androgenetic alopecia

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Abstract

Background:
Androgenetic alopecia (AGA) is a polygenic, heritable, age-dependent process that results in a progressive decline in scalp hair density in a sex-dependent pattern. Previous genome-wide association studies (GWAS) reported various alterations associated with protein-coding genes responsible for the onset and progression of AGA. Notably, the expressions of Wnt genes are significantly reduced in AGA subjects compared to controls, among other gene expression differences. In addition, prior research considered a linear approach to link mutations to the nearest genes. However, a 3D approach provides insight into the spatial organisation of chromosomes and how SNPs interact with distal genes.

Objective:
Reanalyse mutations' impacts on AGA using a 3D genomic approach to Hi-C.

Methods:
Topologically associating domains (TADs) of human embryonic stem cells (H1-hESC) were obtained using the Hi-C technique to identify 3D interactions of SNPs in AGA risk loci and beyond.

Results:
SNPs located within the Wnt family domains were found to have strong interactions within their associating domains. All SNPs had highest interactions with the closest genes, confirming prior linear analysis. However, in the case of rs7648585, a weak downstream interaction was seen in the MED12L gene. MED12L involves in the Wnt/b-catenin pathway, further confirming that Wnt plays a role in AGA.

Conclusion:
Hi-C identified interactions in TADs in human stem cells, suggesting many proximal SNP gene relations. Hi-C analysis supported findings from GWAS and linear studies while suggesting MED12L for further research. Sample data of AGA and unaffected populations will be required for complete analysis.

P63

Eye Movement Desensitisation and Reprocessing Therapy (EMDR) in the management of Alopecia Areata (AA)

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Abstract

Alopecia Areata (AA) is a condition that can have a chronic, relapsing, and unpredictable clinical course often associated with significant psychological impact. AA can be associated with reduced quality of life, increased anxiety, depression and even suicide. Non-pharmacological therapies such as psychotherapy and hypnotherapy are increasingly recognised in AA management. Eye Movement Desensitization and Reprocessing Therapy (EMDR) is a form of psychotherapy that combines therapeutic techniques with eye movements or other rhythmic stimulation to activate the brain's information processing system, allowing it to reprocess a difficult situation.

We present two AA patients who successfully developed improved coping mechanisms and quality of life after undergoing EMDR therapy. Patient A, a 21-year-old gentleman with chronic patchy AA, underwent 6-8 weeks of EMDR therapy delivered face to face and virtually by clinical psychology. Pharmacological treatment included: serial intralesional triamcinolone injections, ezetimibe and simvastatin, topical steroid and topical minoxidil. At 3 months, there was self-reported reduction in mood, an 11-point reduction in CORE-10 score and 2% reduction in the SALT score. Patient B, a 47-year-old female with rapid-onset alopecia universalis and associated post-traumatic stress disorder, received 68 sessions of EMDR therapy both face to face and virtually alongside topical immunotherapy. She self-reported an improvement in coping mechanisms and overall quality of life.

EMDR therapy has shown promising results in improving the psychological well-being and overall quality of life of patients. EMDR facilitated via clinical psychology can complement conventional pharmacological therapies to improve our holistic approach in the management of AA patients.

P64

The percentage of online consultation increased from 15% to 40% after the COVID-19 pandemic.

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Abstract

[Background] We have been providing medical care especially for male pattern hair loss since 1999 in Japan. In recent years, we started online consultations to respond to demand from distant patients. In January 2020, the first COVID-19 infection was confirmed in Japan, and since then, a state of emergency has been declared multiple times. Along with this, changes in lifestyle progressed, and affected the medical examination system at our clinics.

[Purpose] We report on changes in the percentage of online consultations at our clinics after the COVID-19 pandemic.

[Results] In 2019, before the COVID-19 pandemic, online consultations at our clinics accounted for about 15% of all consultations, but after 2020, they accounted for 30% to 40%. In addition, the proportion of online consultations increased in line with the 2nd, 3rd, 4th, and 5th waves when the number of people infected with COVID-19 surged.

P65

“There's a sense of losing yourself and who you are”: Development of a conceptual model via literature and interviews points to large psychosocial burden and lower health-related quality of life for UK-based alopecia patients with ≥50% hair loss.

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Abstract

Background: Alopecia areata (AA) is an autoimmune disease characterised by non-scarring hair loss, which almost always involves the scalp and sometimes other areas of hair growth (eyebrows, eyelashes, facial and body hair). AA is associated with poor health-related quality of life (hrQoL) for many patients, due to serious psychological and emotional consequences. This study aimed to qualitatively explore the adult, caregiver and adolescent experience of AA.

Methods: A targeted literature review (searching Medline and PsycInfo) and qualitative semi-structured concept elicitation interviews with ten representatives from six UK Patient Advocacy Groups were conducted to elicit AA signs/symptoms and hrQoL impacts experienced. Verbatim transcripts were analysed using thematic analysis. The literature search and the interviews focused on patients with ≥50% hair loss.

Results: Sixteen symptoms of AA were reported including pain, itching or tenderness of the scalp. Two mediating factors were reported: disease management and coping. Eight domains of psychosocial impact were reported, including emotional, functional and activities of daily living. Emotional and psychological impacts were reported to substantially influence hrQoL, ahead of physical impacts and symptoms. A conceptual model was developed to summarize the findings.

Conclusion: This comprehensive conceptual model documents the broad range of symptoms and impacts that are relevant from the patient perspective. It can be used to aid understanding the psychosocial burden and impact of AA. It has potential as a tool for trialists, regulators and payers in evaluating the suitability of patient-reported outcome and utility measures and assessing the true efficacy and value of relevant interventions.

P66

The socioeconomic burden of Alopecia Areata

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Abstract

Alopecia areata (AA) can have a significant impact on psychosocial wellbeing and daily functioning. Individuals with AA often seek treatments or products to promote hair regrowth or use strategies to conceal their hair loss, resulting in direct financial cost to the individual. The presented study aimed to examine the socioeconomic burden of AA to understand the wider impact of the condition.

To address the question, we conducted an online mixed-methods survey of 829 adults with AA. In a predominantly white female sample, individuals reported spending a significant amount of money on AA-related products and services, with wigs incurring the greatest cost (median = £700 over the previous year). Private dermatology and mental health services were also found to be costly when used. Over 50% also reported that the products and services they used made their quality of life a little or much better. Individuals with lower disposable incomes spent proportionately more on AA-related products and services, suggesting such spending is seen as essential. Furthermore, female gender and greater AA symptomology predicted higher financial burden from AA-related products and services. A fifth of participants also reported being signed off work due to AA since their diagnosis, and out of these individuals, those more recently diagnosed reported lower work productivity.

The findings highlight the need for health providers, commissioners, and policy makers to consider the financial and psychosocial impact of AA, and associated demographic risk factors, when designing services to support the wellbeing of individuals living with the condition in the UK.

P67

The importance of trichoscopy in psychotrichologic disorders

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Abstract

Self- inflicted hair loss is type of compulsive skin picking disorder (SPD), representing deliberate and repetitive picking, scratching and rubbing of hair and scalp.

While self -inflicted hair loss is formally classified as a mental health disorder, it is mostly diagnosed by dermatologists, because self-induced skin lesions are usually obvious on dermatologic examination.

Among pathological skin-picking syndrome of all the compulsive skin picking syndromes, the most common is Trichotillomania - compulsive recurrent pulling out of one's hair resulting in hair loss. Less common are: Trichoteiromania- compulsive rubbing of hair, which can cause hair loss, Trichotemnomania - compulsive habit of cutting or shaving the hair, Trichophagia - eating the hair that has been pulled out and the consequent Trichobezoar (a wad of swallowed hair that sometimes can cause blockage of the digestive system, often at the exit of the stomach).

The differential diagnosis between self-inflicted hair loss can be complicated for dermatologists. To handle the complexity of investigation, trichoscopy is used as a valuable tool in differential diagnosis of self -inflicted hair loss and various hair and scalp diseases.

The benefit of trichoscopy is that, there are some characteristic trichoscopic features in all diseases that facilitates differentiation between them.

Given the psychotrichological profile of the disease, the management of patients with pathological destruction of the hair and scalp requires great effort, experience and knowledge, patience and a multidisciplinary diagnostic approach.

P68

Successful treatment of trichotillomania with habit reversal therapy in a child.

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Abstract

We present a case of a 12 year-old girl with a background of onychotillomania who was referred to the hair clinic with a patch of hair loss, noted a few weeks after moving to a new secondary school. Her parents noted that she would manipulate her hair episodically1.

On examination, there was patchy alopecia with hairs of uneven length. Dermoscopy revealed decreased hair density, broken hairs, irregular coiled hairs and trichoptilosis. The diagnosis of trichotillomania was explained and she was referred for habit reversal therapy (HRT), led by a clinical nurse specialist.

Techniques employed included increasing awareness of times where she is particularly at risk of hair manipulation, for example when watching TV after school; using a tally counter to record episodes of hair manipulation and devising techniques to minimise manipulation, such as clenching her fists and slowly counting to 30 when she is about to touch her hair. At her follow up appointment a few months later, her hair had fully re-grown and there were no further areas of hair loss.

Trichotillomania is included in the DSM-5 under 'obsessive-compulsive and related disorders', and defined as 'recurrent pulling out of one's hair, resulting in hair loss'2. Pharmacological management is complicated, given the lack of approved drugs for its treatment. HRT is considered first line treatment for trichotillomania for people of all ages; meta-analysis demonstrates superiority over treatment with clomipramine and selective serotonin reuptake inhibitors3. This case corroborates the use of HRT in the treatment of trichotillomania in children.

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Unsupervised Self-sourced Medication for Alopecia: The Tip of the Iceberg?

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Abstract

There is a growing and concerning trend of a large number of alopecia patients sourcing prescription medications from online abroad pharmacies despite advice from patient support groups against this. There are several contributing factors including: difficulties in getting to see a General Practitioner, long waiting times for dermatology appointments and greater awareness of new, effective and high-cost alopecia treatments not currently available on the NHS.

We present five examples of unsupervised therapy in patients presenting to our specialist hair clinic in the last three months. These cases include: 3 female, 1 transfemale and 1 male patient with their ages ranging from 25 to 54 with either alopecia universalis (n=4) or androgenetic alopecia (n=1). The following medications were bought online without supervision: oral minoxidil, bicalutamide, cyproterone acetate, tofacitinib and baricitinib. One patient self-administered their parent's methotrexate injections.

Alarmingly, all patients were unaware of some of these medications having black box warnings with serious potentially life-threatening side effects. They had no medical pre-screening or monitoring until seen in our clinic. One patient developed deranged liver function tests due to methotrexate which was found incidentally. Several patients also had significant co-morbidities including biliary cirrhosis, hypercholesterolaemia and psychiatric conditions. Majority of our patients were taking inappropriate doses of these medications including higher than recommended; therefore, increasing their complication risk.

We fear that these examples are only the "tip of the iceberg" and support the efforts of Alopecia UK in raising the awareness of the safety implications of taking therapies without medical supervision.