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Practical Approach for Treatment lines of Alopecia Areata: Review Article

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ABSTRACT

Background: Those with the autoimmune disease alopecia areata (AA) may experience temporary hair loss on the scalp or in other regions where hair typically grows. Hair loss can occur in discrete areas on the scalp or all over the body, but AA can also express itself in more diffuse forms. Most people with AA go through unpredictable cycles of relapse and remission. Some individuals, especially those with significant hair loss, may experience chronicity.
Objective: Review of literature about practical approach for treatment lines of alopecia areata.
Methods: We searched Science Direct, Google Scholar as well as PubMed for relevant articles on Alopecia Areata and its Treatment. However, only the most recent or thorough study was taken into account between September 2001 and April 2021. The authors also evaluated the value of resources culled from other works in the same genre. Documents written in languages other than English have been ignored due to a lack of translation funds. Unpublished works, oral presentations, conference abstracts, and dissertations were generally agreed upon not to qualify as scientific research.
Conclusion: Care for patients with alopecia areata include providing emotional support and making treatment options available to those who want them. Response to treatment for alopecia areata varies greatly, and few well-designed clinical trials have examined the methods that have been used. Methods such as topical, intralesional, and systemic medications and devices are used in these treatments. Due to the limited but promising evidence supporting the effectiveness of other treatments, individuals with patchy alopecia areata typically begin treatment with intralesional or topical corticosteroids.
Keywords: Alopecia areata, Approach, Treatment.

INTRODUCTION

Alopecia areata (AA) is an autoimmune disorder that causes temporary hair loss on the scalp and other hair-bearing regions. Loss of hair might affect only certain sections of the scalp or spread throughout the entire body, but AA can also express itself in more diffuse forms. Most people with AA go through unpredictable cycles of relapse and remission. Some individuals, especially those with significant hair loss, may experience chronicity. The effects of AA on patients' lives are substantial, and the disease itself may lead to the development of mental health problems (e.g., anxiety as well as depression) [(1)].

There is an estimated 1-2% prevalence of alopecia areata in the general population, with a 1.7% lifetime risk. However, depending on the community under study, the true prevalence can range from 0.1% to 6.9% [(2)]. It is unknown if alopecia areata outbreaks occur more frequently throughout certain times of the year. A retrospective study of about 450 children with alopecia areata found that outbreaks of the condition tend to occur in the winter. This finding has to be confirmed in a separate investigation [(3)]. Alopecia areata is an autoimmune illness that causes the premature transition of hair follicles in the growth phase (anagen) into the non-proliferative involution (catagen) and resting (telogen) phases, resulting in the loss of existing hair and the suppression of new hair growth. In alopecia areata, unlike cicatricial alopecia, the hair follicle is not irreversibly destroyed by the inflammatory process [(4)].

It is still unclear what causes alopecia areata. Breakdown of follicular immune privilege and the subsequent formation of a T cell-mediated immunological onslaught on cells within the hair bulb are both potential critical events. Some people are just more likely to experience alopecia areata than others [(5)].

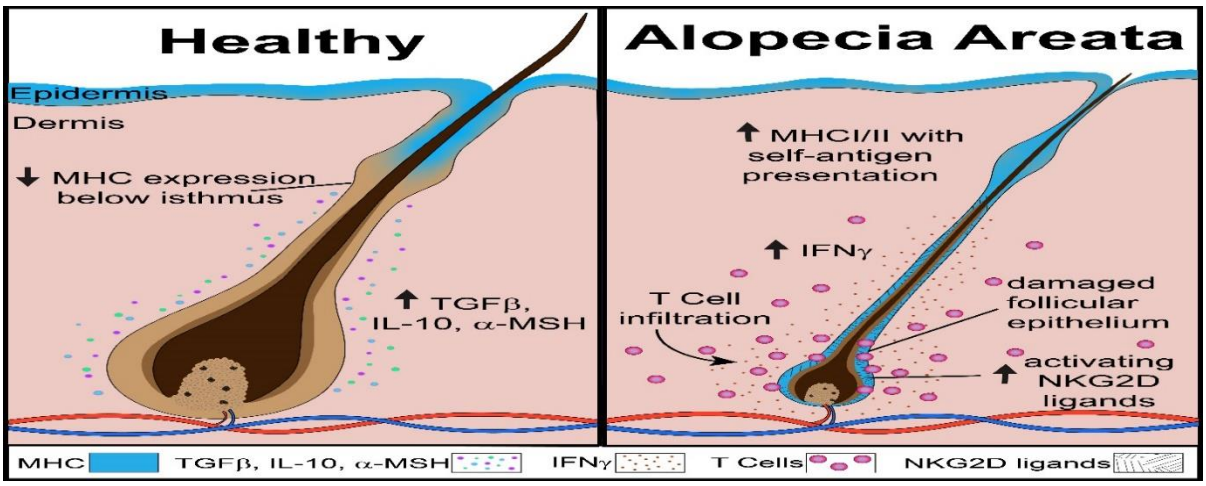

Figure (1): Alopecia areata is characterized by a breakdown of immunological privilege in the anagen hair follicle [(6)].

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Alopecia areata is best managed by providing emotional support for the patient as well as treatment options for those who are interested. Response to treatment for alopecia areata varies greatly, and few well-designed clinical trials have examined the methods that have been used. A wide variety of topical, intralesional, and systemic medications and devices fall within this category [6].

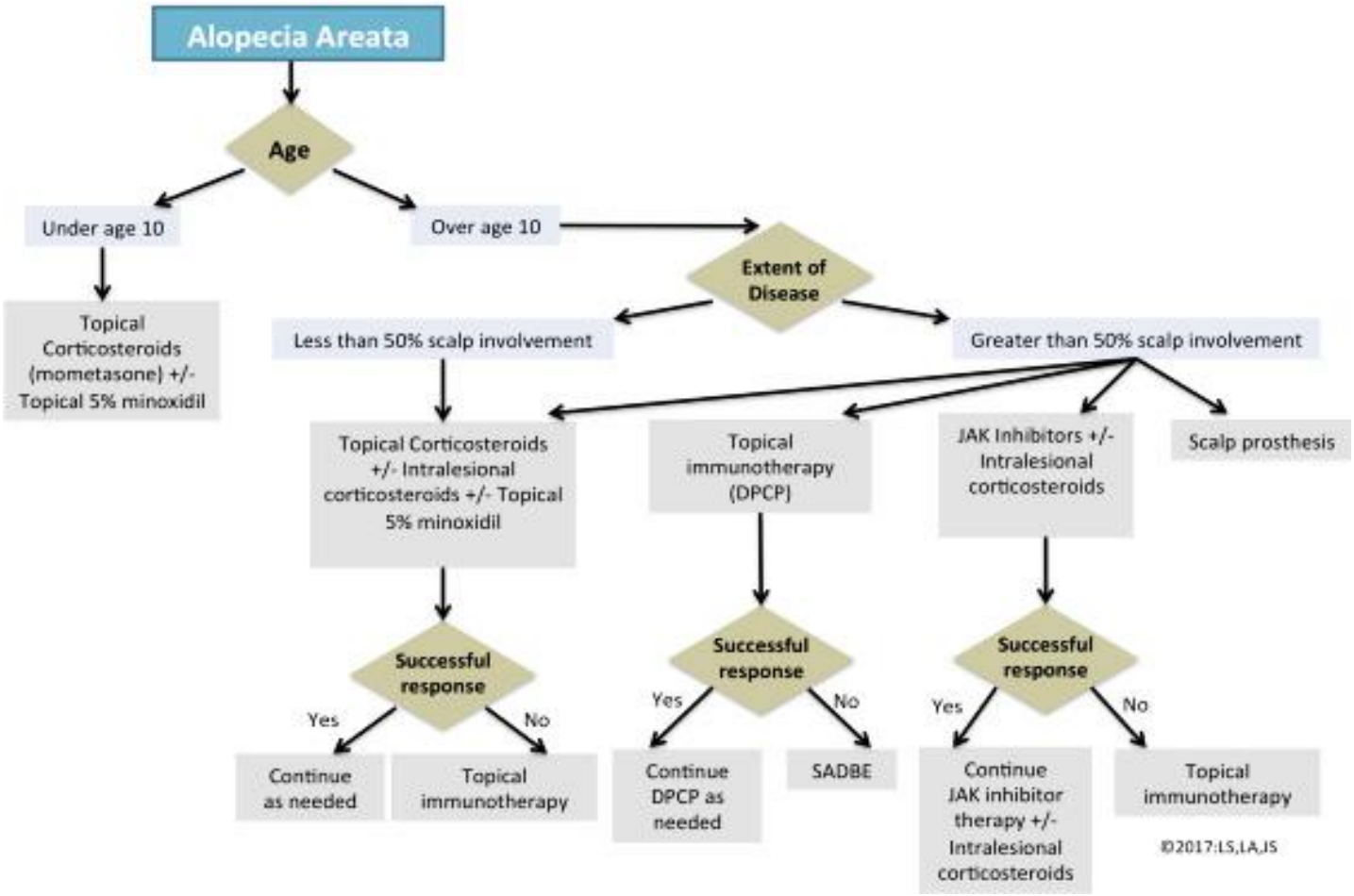

Figure (2): Evidence-based approach to treatment of alopecia areata [6].

First-Line Therapies:

Most patients with patchy alopecia areata begin treatment with intralesional or topical corticosteroids because of their low risk and some proof of their effectiveness [7].

A. Topical corticosteroids:

In both adults and children, restricted patches are typically treated with topical corticosteroids (TCs), which work by decreasing inflammation surrounding hair follicles [8].

In the treatment of AA, topical corticosteroids (e.g., clobetasol propionate ointment/foam or halometasone cream) have been shown to be effective. For ophiasis, AT, or AU, they did not seem to work very well. At least three months of treatment is recommended. If after 6 months there is no response, however, medication should be discontinued. Transient folliculitis and skin shrinkage are the most common adverse reactions to TCs [9].

B. Intralesional corticosteroids:

ICs are the therapy of choice for adults with a couple of small patches, and even bigger regions (less than 50% scalp involvement) can be treated with them if the patient can handle the discomfort of the injections. One of the most common approaches to treat AA is with intradermal injections of triamcinolone (TA-ILI). In a randomized controlled study, TA-ILI was found to be more efficacious than both topical betamethasone valerate and topical betamethasone valerate foam. There was no significant difference in efficacy between 2.5, 5, and 10 mg/dL of triamcinolone. In addition, TA-ILI was found to be effective in reducing the severity of the hair pull test and the presence of exclamation point hairs in patients. However, TA-use ILI's is restricted due to pain, making it unsuitable for use as a primary treatment for youngsters or patients who cannot tolerate pain [9].

C. Minoxidil:

Minoxidil, a vasodilator typically used for hypertension, has been extensively used to treat several forms of hair loss, including alopecia areata. Even though it was

discovered that 5% topical minoxidil is beneficial in treating patchy AA in the adult and children, it may not be enough to treat AA by itself if used alone. Therefore, topical minoxidil for AA therapy is typically used in conjunction with other medications like corticosteroids. Oral administration of minoxidil at a modest dose (0.25-5 mg) twice a day improves clinical results in 18-82.4% of patients (including those with severe and treatment-resistant AA), with few major side effects, according to a recent systematic review [(10)].

D. Contact Immunotherapy (CI):

Numerous studies showed that CI helps people of all ages who had either mild or severe long-term AA. However, it is not appropriate for patients with severe, quickly worsening conditions. Based on the pooled data, 65.5% of CI grows back after treatment, with 74.6% of CI growing back in patchy AA and 54.5% of CI growing back in the AT/AU (mean rate, 65.5%) **[(11)].**

Second-Line Therapies:

A) Anthralin:

It is hypothesized that anthralin's irritating contact dermatitis affects hair regrowth. Twenty-five percent of participants in uncontrolled research experienced cosmetically satisfactory hair growth, however eleven cases of AT did not exhibit any therapeutic advantages. Anthralin had a more positive therapeutic impact on the treated side than the untreated side in a recent half-head investigation of pediatric patients. The results of a randomised controlled trial (RCT) comparing anthralin with azelaic acid were similar. Although, Anthralin is a common treatment for AA, there is a lack of proof that it is effective when administered alone **[(11)].**

B) Prostaglandin analogues:

Prostaglandin analogues like latanoprost and bimatoprost are used to treat open angle glaucoma, however they have the unwanted side effect of causing hypertrichosis of the eyelashes and hair on the malar area. The use of them in eyelash AA was ultimately unsuccessful due to this impact. While prior studies failed to generate hair growth, a recent experiment found that 45% of the latanoprost-treated group experienced cosmetically acceptable hair growth **[(12)].**

C) Systemic corticosteroids (SC):

In cases of severe AA or during the acute stage of the disease, systemic corticosteroids may be used. Several methods, including injections into the muscle, the veins, or the mouth have been proposed. Pulse corticosteroid therapy was found to be superior than oral daily steroid treatment in terms of clinical benefit and side-effect profile, although no expert consensus exists on the best way to utilise SCs (OD). A meta-analysis of 41 trials with a total of 1078 cases found that 43% of patients experienced full regrowth. In the lone R-PCT research done to far, the treatment group showed considerable improvement. Eighty-one percent of patients with AT/AU reacted positively to a combination of pulse corticosteroid therapy and OD, and seventy-one percent showed complete regrowth, according to a recent study. 32% of patients experienced side effects, most commonly from using multiple medications at once. Systemic corticosteroids should be used therapeutically only after physicians have carefully considered the patient's unique comorbidities and the possibility of undesirable effects. Short-term use is recommended, and prolonged exposure is not recommended **[(13)].**

D) Superficial Cryotherapy:

Liquid nitrogen cryotherapy is used to treat inflammatory and neoplastic diseases of the skin. Results showed no statistically significant difference between the response rates of superficial cryotherapy (80%) and clobetasol lotion (91.5%). There were five great responses and three satisfactory responses among the eleven AA patients who underwent jet cryotherapy but had not responded to standard treatments. When administered every 2 weeks or fewer, the therapy showed the greatest improvement. The thickness and density of eyebrow hair were shown to be greatly increased in a recent half-head research after superficial cryotherapy was used. It is expected that this treatment will have similar effects to those already described without causing as many serious side effects [(14)].

E) Excimer laser:

High-dose, monochromatic, long-wave UVB radiation is available from the 308-nm Excimer laser. T-cell apoptosis stimulation leads to hair regeneration in areas affected by alopecia areata. Children with mild patchy AA of the scalp may benefit from therapy with the 308-nm Excimer laser system. The problem of relapse following therapy termination is, however, a major worry for this and other AA programs **[(15)].**

F) Fractional photothermolysis laser:

Complete hair regrowth was described in a 35-year-old male patient with AA who had not responded to minoxidil, topical corticosteroids, or ILCSs, but who underwent several treatments with fractional Er:Glass laser. T-cell apoptosis induction and direct stimulation of hair growth are hypothesized to be the underlying mechanisms at work here **[(16)].**

G) Platelet-rich plasma (PRP)

Platelet-rich plasma is a type of plasma that had additional platelets added to it (PRP). Platelet-rich plasma (PRP) contains many growth agents and cytokines, which aid in tissue healing and HF regeneration. By stimulating the Akt signaling pathways as well as extracellular signal-regulated kinase (ERK) with boosting synthesis of -catenin and fibroblast growth factor 7, PRP increases dermal papilla cell proliferation and survival (FGF-7). Successful treatment of AA with PRP may be due in part to the drug's anti-inflammatory properties, which work by

decreasing MCP-1 expression and raising TGF- expression. Half of 45 AA patients took part in a randomised, double-blind, placebo- and active-controlled research. In compared to placebo or baseline, three PRP treatments spaced one month apart dramatically improved hair regeneration [16].

H) Tretinoin:

Treatment with topical tretinoin and intralesional triamcinolone (ILI) was compared in research involving 28 patients and 30 controls. After 4 months, the combo group responded better than the control group. Eighty AA patients were randomly assigned to receive either topical steroids (50% success rate), topical tretinoin (55% success rate), Anthralin (35% success rate), or a placebo (20% success rate). This medication's effect needs to be better understood, and more treatment data is required [17].

I) Statins:

In addition to decreasing cholesterol levels, it also has anti-inflammatory and immunomodulatory properties. Simvastatin, which has numerous postulated anti-inflammatory characteristics, is demonstrated to have a greater immunomodulatory effect when combined with ezetimibe, including inhibition of the nuclear factor-kappa B (NF-kB) and JAK/STAT pathways, reduction of reactive oxygen species (ROS) production, and activation of the Wnt/beta-catenin pathway [18]. Amongst 19 AA patients, a study was conducted. Twelve out of nineteen AA patients with scalp involvement of 40-70% had hair regeneration of more than 50% without complications [19].

J) Capsaicin:

Capsaicin's effectiveness in AA is attributed to its ability to deplete substance P and stimulate the generation of calcitonin gene-related peptides. Capsaicin, unlike other topical medicines, is both cheap and simple to use, although it can result in significant irritation [20].

K) Antidepressants:

Because AA is often accompanied by other mental health difficulties, it's important to address these concerns throughout treatment. Furthermore, these issues may aid in the progression of AA [21].

L) Calcipotriol:

Since AA tend to have low vitamin D levels and vitamin D receptor expression, recent research has focused on topical calcipotriol [22].

M) Psoralen plus ultraviolet A therapy (PUVA):

Photochemotherapy has been widely used to treat AA. Response rates to PUVA phototherapy administered orally or topically vary widely, from over 70% to less than 15% [23]. Forty percent of AA patients show full regrowth after receiving psoralen and ultraviolet (UV)-A therapy, and seventeen percent showed partial regrowth. There was 9.4% great response and 9.4% good response in patients with severe AA who were given PUVA with topical cyclosporin [23].

3rd line:

A) Janus kinase (JAK)/signal transducer and activator of transcription (STAT) inhibitors:

(JAKi) has showed promise as a potential AA therapy in recent research. There are four members of the Janus kinase (JAK) family in humans, and they're all linked to various cytokine receptors. When a ligand attaches to its specific cytokine receptor, JAKs can phosphorylate STATs to activate transcription. Several human clinical trials have investigated the effectiveness and safety of oral or topical JAKi treatment for AA. In an open-label study, tofacitinib (5 mg twice daily) was given to 66 patients with severe AA (> 50% scalp hair loss), AT, and AU. After 3 months of treatment, 64% of patients experienced hair regrowth, and 32% of patients observed a 50% improvement in their SALT score [24].

B) Cyclosporin:

There has been a lot of research into the effectiveness of combining cyclosporin with systemic steroids for treatment. The success percentages of this combo are all over the map (25-67%). However, there have been relatively few high-quality investigations using cyclosporin as a monotherapy [25].

C) Methotrexate (MTX):

Patients with severe AA who were treated with MTX + prednisolone showed a greater rate of complete recovery compared to patients treated with MTX alone. Care needs to be taken when choosing on this method of treatment [26].

DAzathioprine:

This is an alternative systemic treatment option for persistent AA. However, it is important to think about the possibility of systemic side effects [27].

E) Interleukin (IL)-12/IL-23p40 blocker:

It was hypothesized to selectively stimulate the proliferation and activity of T-regulatory cells, low-dose IL-2 was thought to reduce inflammation and modulate the immune response (Tregs) [28]. The failure of IP in AA may be aided by a lack of Tregs, making its usage in the treatment of AA less effective [29].

CONCLUSION

Care for patients with alopecia areata include providing emotional support and making treatment options available to those who want them. Response to treatment for alopecia areata varies greatly, and few well-designed clinical trials have examined the methods that have been used. Methods such as topical, intralesional, and systemic medications and devices are used in these treatments. Due to the limited but

promising evidence supporting the effectiveness of other treatments, individuals with patchy alopecia areata typically begin treatment with intralesional or topical corticosteroids.

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REFERENCES

1. **Toussi A, Barton V, Le S *et al.* (2021):** Psycho- social and psychiatric comorbidities and health-related quality of life in alopecia areata: a systematic review. J Am Acad Dermatol., 85 (1): 162-175.
2. **Salinas-Santander M, Sánchez-Domínguez C, Cantú-Salinas C *et al.* (2015):** Association between PTPN22 C1858T polymorphism and alopecia areata risk. Experimental and Therapeutic Medicine, 10 (5): 1953-1958.
3. **Putterman E, Castelo-Soccio L, Senna M *et al.* (2018):** Seasonal patterns in alopecia areata, totalis, and universalis. JAAD., 15 (79): 970-974.
4. **Rajabi F, Drake L, Senna M *et al.* (2018):** Alopecia areata: a review of disease pathogenesis. Br J Dermatol., 4 (179): 1031-1033.
5. **Bertolini M, McElwee K, Gilhar A *et al.* (2020):** Hair follicle immune privilege and its collapse in alope- cia areata. Exp Dermatol., 29 (8): 703–725.
6. **Delamere F, Sladden M, Dobbins H *et al.* (2018):** Interventions for alopecia areata. Cochrane Database Syst Rev., 3 (5): 29-40.
7. **Messenger A, McKillop J, Farrant P *et al.* (2012):** British Association of Dermatologists' guidelines for the management of alopecia areata. Br J Dermatol., 12 (2): 166-916.
8. **Lenane P, Macarthur C, Parkin P *et al.* (2014):** Clobetasol propionate, 0.05%, vs hydrocortisone, 1%, for alopecia areata in children: a randomized clinical trial. JAMA Dermatol., 150 (1): 47–50.
9. **Miteva M, Tosti A (2012):** Hair and scalp dermatoscopy. J Am Acad Dermatol., 67 (5): 1040–1048.
10. **Sharma A, Michelle L, Juhasz M *et al.* (2020):** Low-dose oral minoxidil as treatment for non-scarring alopecia: a systematic review. Int J Dermatol., 59 (8): 1013–1019.
11. **Lee S, Kim B, Lee Y *et al.* (2018):** Hair regrowth out-comes of contact immunotherapy for patients with alopecia areata: a systematic review and meta-analysis. JAMA Dermatol., 154 (10): 1145–1151.
12. **Coronel-Pérez I, Rodríguez-Rey E, Camacho Martínez F (2010):** Latanoprost in the treatment of eyelash alopecia in alopecia areata universalis. Journal of the European Academy of Dermatology and Venereology, 24 (4): 481-485.
13. **Shreberk-Hassidim R, Ramot Y, Gilula Z *et al.* (2016):** A systematic review of pulse steroid therapy for alopecia areata. JAAD., 74 (2): 372–374.
14. **Jun M, Lee N, Lee W *et al.* (2017):** Efficacy and safety of superficial cryotherapy for alopecia areata: a retrospective, comprehensive review of 353 cases over 22 years. J Dermatol., 44 (4): 386–393.
15. **Arakawa Y, Nomiyama T, Katoh N (2016):** Three hundred and eight nanometer excimer light therapy for alopecia universalis that is resistant to other treatments: a clinical study of 11 patients. J Dermatol., 43 (12): 1412–1416.
16. **Yoo K, Kim M, Kim B *et al.* (2010):** Treatment of alopecia areata with fractional photothermolysis laser. Int J Dermatol., 49 (7): 845–847.
17. **Kubeyinje E, C'Mathur M, Tosti A *et al.* (2010):** Topical tretinoin as an adjunctive therapy with intralesional triamcinolone acetonide for alopecia areata. Clinical experience in northern Saudi Arabia. Int J Dermatol., 36 (4): 320-27.
18. **Cervantes J, Jimenez J, DelCanto G *et al.* (2018):** Treat- ment of alopecia areata with simvastatin/ezetimibe. J Investig Dermatol Symp Proc., 19 (1): 25–31.
19. **Lattouf C, Jimenez J, Tosti A *et al.* (2015):** Treatment of alopecia areata with simvastatin/ezetimibe. J Am Acad Dermatol., 72 (2): 359–361.
20. **Ehsani A, Toosi S, Seirafi H *et al.* (2009):** Capsaicin vs. clobetasol for the treatment of localized alopecia areata. JEADV., 23 (12): 1451–1453.
21. **Cipriani R, Perini G, Rampinelli S *et al.* (2001):** Paroxetine in alopecia areata. Int J Dermatol., 40 (9): 600–601.
22. **Cerman A, Solak S, Altunay İ *et al.* (2015):** Topical calcipotriol therapy for mild-to-moderate alopecia areata: a retrospective study. Journal of Drugs in Dermatology, 14 (6): 616–620.
23. **Ito T, Kageyama R, Nakazawa S *et al.* (2020):** Understanding the significance of cytokines and chemokines in the pathogenesis of alopecia areata. Exp Dermatol., 29 (8): 726–732.
24. **Kennedy Crispin M, Ko J, Craiglow B *et al.* (2016):** Safety and efficacy of the JAK inhibitor tofacitinib citrate in patients with alopecia areata. JCI Insight., 1 (15): e89776. doi: 10.1172/jci.insight.89776.
25. **Rallis E, Nasiopoulou A, Senna M *et al.* (2005):** Oral administration of cyclosporine A in patients with severe alopecia areata. Int J Tissue React., 27 (3): 107–110.
26. **Royer M, Bodemer C, Vabres P *et al.* (2011):** Efficacy and tolerability of methotrexate in severe childhood alopecia areata. Br Dermatol., 165 (2): 407–410.
27. **Vañó-Galván S, Hermosa-Gelbard Á, Sánchez-Neila N *et al.* (2016):** Treatment of recalcitrant adult alopecia areata universalis with oral azathioprine. JAAD., 74 (5): 1007–1008.
28. **Sharabi A, Tsokos M, Ding Y *et al.* (2018):** Regulatory T cells in the treatment of disease. Nat Rev Drug Discovery, 17 (11): 823–844.
29. **Le Duff F, Bouaziz J, Fontas E *et al.* (2021):** Low-dose IL-2 for treating moderate to severe alopecia areata: a 52-week multicenter prospective placebo- controlled study assessing its impact on T regulatory cell and NK cell populations. J Invest Dermatol., 141 (4): 933-936.