Alopecia areata: targeted review of adverse events associated with clinical studies of treatments

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Background & Objectives

Alopecia areata (AA) is a common autoimmune disease characterized by sudden patchy hair loss in the scalp, eyebrows, and eyelashes[1]. AA may present at any age and can lead to emotional distress and reduced quality of life (QoL)[2]. A range of treatments are available for the management of AA, however the evidence for their efficacy is variable[3]. Additionally, assessment of adverse events (AEs) in some clinically controlled studies remains insufficiently established, thereby potentially compromising the safety profiles of treatments[4]. This targeted review aimed to quantify the most frequently reported AEs in clinical studies, including randomized controlled trials (RCTs) and other prospective randomized studies for the treatment of AA.

Methods

Study publications from the last 15 years (January 1, 2008 to December 31, 2022) were identified through targeted searches of the PubMed database and Google Scholar. Inclusion criteria included clinical studies in the English language that evaluated adverse events associated with AA treatment.

Study titles and abstracts were screened, then study design details and data on AEs by type of treatment were extracted and checked for accuracy by two independent reviewers. Both systemic and topical treatments were considered. The five most frequently reported AEs by participants receiving treatment were recorded for analysis.

Results

Sixteen clinical studies reporting AEs associated with four topical and 12 systemic therapies used in the treatment of AA were included (see **Table 1**). Of the 16 clinical studies included, 15 were RCTs, and one was a prospective randomized study.

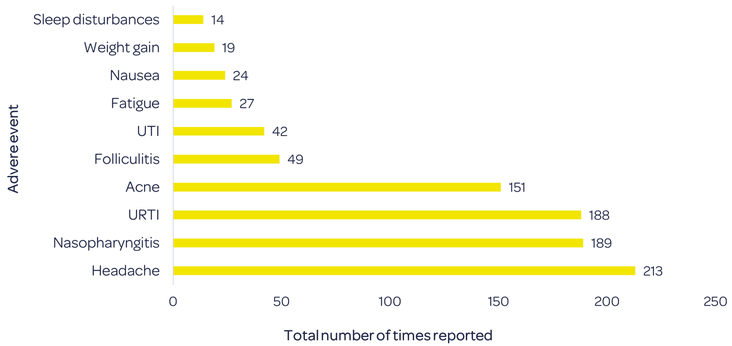

Figure 1: Total number of top ten adverse events (AEs) reported across the studies reviewed

URTI: upper respiratory tract infection

Table 1: Overview of studies included in the review

No.	Author(s)	Treatment name	Administration route	Study design/ phase	No. of participants receiving treatment
1	Guttman-Yassky et al., 2022	Dupilumab	Systemic	2a	60
2	Jabbari et al., 2018	Tofacitinib	Systemic	2	12
3	King et al., 2021 (a)	Baricitinib	Systemic	2	54
4	King et al., 2021 (b)	Ritlecitinib Brepocitinib	Systemic	2a	48 47
5	King et al., 2022 (a)	IBaricitinib	Systemic	3	851
6	King et al., 2022 (b)	CTP-543 (JAK1 & JAK2 inhibitor)	Systemic	2	105
7	Lai et al., 2019	Cyclosporine	Systemic	Not specified	18
8	Mackay-Wiggan et al., 2016	Ruxolitinib	Systemic	2	12
9	Mikhaylov et al., 2022	Delgocitinib	Topical	2a	20
10	Olsen et al., 2020	Ruxolitinib	Topical	2	83[1]
11	Pfizer, 2021	Ritlecitinib	Systemic	2b/3	718[2]
12	Price et al., 2008	Efalizumab	Topical (localized injection)	2	33
13	Rinaldi et al., 2019	UTR-M-PRP plus	Topical	Not specified	30
14	Saif et al., 2012	Methylprednisolone	Systemic	Prospective randomized study	42
15	Strober et al., 2009	Alefacept	Systemic	Not specified	23
16	Yang et al., 2012	Total glucosides of paeony capsule (TGPC)	Systemic	Not specified	44

[1]Inclusive of 12 participants from an initial open-label phase as the reported AEs were not separated by phase.

[2]Inclusive of 15 participants who received a placebo before switching to treatment as the reported AEs were not separated by subgroups.

A total of 35 AEs were recorded. As shown in **Figure 1**, the most frequently reported AEs overall were headaches (n=213), nasopharyngitis (n=189), upper respiratory tract infections (URTIs; n=188), acne (n=151), and folliculitis (n=49). Two of the five most frequently reported AEs were dermatological and two were respiratory. The most frequently reported AEs associated with systemic treatments were headaches, URTIs, and nasopharyngitis, while for topical treatments they were headaches, nasopharyngitis, and pruritus, in order of frequency.

Discussion & Conclusions

Presently, systemic and topical AA treatment options are limited and associated with high rates of AEs - particularly of a dermatological or respiratory nature - which have the potential to compromise their long-term efficacy and overall safety profile.

The findings of this targeted review highlight the following key points:

- Treatments for AA are associated with high rates of AEs, and there is an evident need for therapies with improved safety profiles. To this effect, conducting both RCTs and real-world studies to assess the efficacy and safety profiles of therapies in a controlled environment and in routine clinical practice is of paramount importance. These studies should focus on the complete and transparent reporting of AE data, particularly as detailed published literature in this area remains scarce[5].
- Few publications commented on the impact of AEs on health-related QoL (HRQol), an important factor for patients with AA[2], nor focused on the collection of patient-reported adverse events, both of which should be considered when building a full picture of treatment safety.
- Future reviews could focus on publications relating to the patient experience of AEs as well as their impact on HRQoL to shed light on the AEs of greatest importance to patients, their treatment preferences, and to identify further gaps in knowledge or unmet needs in AA management. Findings could be used to inform future clinical study design involving the collection of AE data.

References

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