




CONSENSUS ARTICLE

Treatment of alopecia areata: An Australian expert consensus statement

William C Cranwell¹  | Vivien WY Lai^{1,2}  | Louise Photiou¹  | Nekma Meah¹ | Dmitri Wall¹ | Deepani Rathnayake¹ | Shobha Joseph¹ | Vijaya Chitreddy¹ | Shyamalar Gunatheesan¹ | Kamaldeep Sindhu⁵ | Pooja Sharma¹ | Jack Green^{4,5,6} | Samantha Eisman¹ | Leona Yip⁷ | Leslie Jones^{1,8,9} | Rodney Sinclair^{1,7,8}

¹Sinclair Dermatology, East Melbourne, ²Department of Medicine, Nursing and Health Sciences, Monash University, ³North Western Dermatology, ⁴Department of Dermatology, St Vincent's Hospital, ⁵Skin and Cancer Foundation Inc, ⁶Western Dermatology, Melbourne, Victoria, ⁷Barton Specialist Centre, Barton, Australian Capital Territory, ⁸Epworth Dermatology, Richmond, and ⁹Department of Medicine, University of Melbourne, Melbourne, Victoria, Australia

ABSTRACT

Alopecia areata (AA) severity varies from a single small patch to complete loss of scalp hair, body hair, eyelashes and eyebrows. While 40% of all affected individuals only ever get one patch and will achieve a spontaneous complete durable remission within 6 months, 27% will develop additional patches but still achieve complete durable remission within 12 months and 55% will develop chronic AA. Without systemic treatment, 55% of individuals with chronic AA will have persistent multifocal relapsing and remitting disease, 30% will ultimately develop alopecia totalis and 15% will develop alopecia universalis. The unpredictable course and psychological distress attributable to AA contributes to the illness associated with AA. Numerous topical, intralesional and systemic agents are currently used to treat AA; however, there is a paucity of data evaluating their use, effectiveness and tolerability. Topical therapy, including topical glucocorticosteroids, topical minoxidil and topical immunotherapy, can be used in

cases of limited disease. There are no universally agreed indications for initiating systemic treatment for AA. Possible indications for systemic treatment include rapid hair loss, extensive disease ($\geq 50\%$ hair loss), chronic disease, severe distress or a combination of these factors. Currently available systemic treatments include glucocorticosteroids, methotrexate, ciclosporin, azathioprine, dapsone, mycophenolate mofetil, tacrolimus and sulfasalazine. The optimal treatment algorithm has not yet been described. The purpose of this consensus statement is to outline a treatment algorithm for AA, including the indications for systemic treatment, appropriate choice of systemic treatment, satisfactory outcome measures and when to discontinue successful or unsuccessful treatment.

Key words: azathioprine, cyclosporine, methotrexate, totalis, universalis.

WHAT THIS RESEARCH ADDS

- No systemic agents are currently approved for use by the Food and Drugs Administration or Therapeutic Goods Administration. There are no evidence-based Australian or International treatment guidelines for systemic therapy of AA.
- This consensus statement addresses the rationale for systemic treatment, the choice of systemic treatment, requirements for monitoring of systemic treatment, assessment of response to treatment and appropriate cessation of therapy in AA.

Correspondence: Rodney Sinclair, University of Melbourne and Sinclair Dermatology, 2 Wellington Parade, East Melbourne, Vic. 3002, Australia. Email: Rodney.sinclair@sinclairdermatology.com.au

William C Cranwell, MPH&TM. Vivien Wai Yun Lai. Louise Photiou, MBBS. Nekma Meah, MRCP. Dmitri Wall, MRCP. Deepani Rathnayake, FACD. Shobha Joseph, FACD. Vijaya Chitreddy, FACD. Shyamalar Gunatheesan, FACD. Kamaldeep Sindhu, FACD. Pooja Sharma, FACD. Jack Green, FACD. Samantha Eisman, FACD. Leona Yip, PhD, FACD. Leslie Jones, PhD. Rod Sinclair, MBBS, MD, FACD.

Conflict of interest: None.

Submitted 5 July 2018; accepted 11 September 2018.

INTRODUCTION

Alopecia areata (AA) is an immune-mediated disease that produces non-scarring hair loss. AA may occur as an acute self-limiting disorder with one to five patches that resolve within 6–12 months, as a chronic disorder with multiple patches relapsing and remitting over many years, or as total hair loss of the scalp or universal loss of every terminal hair on the body. The estimated prevalence is 1 in 1000 people, with a lifetime risk of approximately 2%.^{1,2} The onset of AA typically occurs before age 40; however, late onset is well described.^{2,5} Men and women appear to be equally affected, and there is no known racial predisposition.

Some patients regrow spontaneously without medical intervention within 12 months.⁵ Many can be managed with topical or intralesional treatments alone. No systemic agents are currently approved for use by the Food and Drugs Administration or Therapeutic Goods Administration. There are no evidence-based Australian or International treatment guidelines for systemic therapy of AA.

The response of AA to treatment is unpredictable. Even during a course of successful treatment, minor relapses can occur. It is not uncommon for a patient to develop a new lesion of AA on one part of the scalp while simultaneously experiencing regrowth in a recently treated patch of AA on another part of the scalp.

Neither a 2008 Cochrane review nor a 2018 systematic review identified any systemic therapy for AA supported by level A evidence.^{4,5} In the absence of level A evidence, an expert consensus statement can help guide management. This consensus statement will address the rationale for initiating topical and systemic treatment, the choice of systemic treatment, requirements for monitoring of systemic treatment, assessment of response to treatment and appropriate cessation of therapy in AA.

METHODS

A meeting of members of the Australasian Hair and Wool Research Society was convened at the 10th World Congress for Hair Research in Kyoto in November 2017. Members of this meeting included Australian dermatologists with a subspecialist expertise in alopecia, a research scientist with extensive experience in hair biology and disease and a dermatology clinical research fellow. Following a literature review, the discussion was conducted at the Kyoto meeting and subsequently via correspondence. A consensus statement for the systemic treatment of AA was developed from these discussions and distributed to senior Australian Dermatologists for comment.

RATIONALE FOR TREATMENT

In her landmark 1965 paper (Table 1), Ikeda described the natural history of AA among 1989 patients in Kyoto, Japan, between 1947 and 1965.³ Most patients did not receive active treatment. Only 302 patients received oral

Table 1 Prognosis alopecia areata based on study of 1989 patients seen in Kyoto, Japan, between 1947 and 1965³

Clinical presentation	Proportion with spontaneous regrowth	Risk of developing chronic AA	Risk of developing AT or AU
Solitary stable patch of AA ≤6 months duration	87%	15%	6%
Solitary stable patch of AA ≥6 months but ≤12 months	35%	65%	30%
Solitary stable patch of AA ≥12 months duration	0	100%	45%
Multiple patches within 6 months of initial presentation	65%	35%	15%
Aged 0–6 years at initial presentation	0	100%	45%
Aged 6–12 years at initial presentation	60%	40%	18%

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis.

corticosteroids up to a maximum dose of prednisolone 5 mg daily (or equivalent dose of dexamethasone). She showed that 40% of patients only ever develop a solitary patch of AA that regrows spontaneously within 6 months.⁵ Another 27% develop additional patches, but still achieve a complete and persistent remission at 1 year.^{5,6} Patients with chronic AA, defined as AA that continues beyond 1 year, tend to develop additional areas of AA and have persistent hair loss for many years. Many never achieve complete remission. Among those with chronic AA, 45% ultimately develop either alopecia totalis (AT) or universalis (AU; 30% and 15%, respectively).⁵ A longitudinal study in South Korea of 70 patients with AT or AU showed only 17% complete regrowth overall (20% and 15%, respectively).⁷ No hair regrowth was seen in 65% and 21% of cases of AU or AT, respectively.⁷

Possible indicators of poor prognosis at the time of initial presentation include AA onset before the age of 12 and in particular before the age of 6 years, disease duration of more than 1 year, development of multiple discrete patches, extensive hair loss involving >50% of the scalp, ophiasis pattern of alopecia, progression to AT or AU, associated nail disease, associated Trisomy 21, associated atopy, and a positive family history for AA or other organ-specific autoimmune disease.^{6,8}

An increased prevalence of psychiatric comorbidity, particularly mood and anxiety disorders, is well established in patients with AA.^{9,10} Significant psychological distress is particularly prevalent in those with severe or recalcitrant disease. Children and adolescents with AA experience high rates of depression and anxiety disorders.¹¹ Parents of children affected by AA may also experience anxiety and mood disturbance. In view of the unpredictable course of disease and significant morbidity and distress, many patients seek treatment for AA.

The aim of treatment of AA is to arrest disease progression and to reverse hair loss. While there is no current evidence that active treatment alters the natural history of AA, patients with multilocal AA generally develop lesions serially over a number of months. Patients rarely develop multiple discrete patches at the same time. There appears to be an accentuation of AA severity with the risk of developing each new lesion of AA increasing with disease severity.

While some patients who have recovered from an episode of acute AA, and many who are in complete remission following chronic AA, may experience a relapse of their AA at some point in future,^{12,15} it is not known whether active treatment of acute AA prevents the development of chronic AA. An analysis of 68 patients with chronic AA who received systemic treatment at a single large Melbourne alopecia clinic and who were followed for between 2 and 7 years found the rate of AT/AU was reduced to 17.6% (Table 2). The anticipated rate of AT/AU based on the Ikeda paper was 45%.³ These results require further investigation, but suggest there is a logical rationale to treat chronic AA to reduce the risk of AT/AU. However, long-term maintenance therapy to prevent relapse is currently not encouraged as the interval between episodes is unpredictable and may be years or even decades. Therefore, the potential side effects of systemic therapy have thus far outweighed the potential benefit of treatment.

Possible indications for initiation of treatment

Solitary stable patch of AA

For many patients, the presence of a single patch is cause for concern. Patients who experience significant mood change or anxiety that may impair social function (e.g. school avoidance) should be treated. Topical high-potency corticosteroid in a child and intralesional corticosteroid injection repeated every 4–6 weeks in an adult are appropriate first-line therapies.

Thirty-five percent of individual solitary lesions that have persisted beyond 6 months will still resolve spontaneously by 12 months, while 65% will persist and evolve into chronic AA.⁵ All solitary lesions present longer than

6 months should be considered for topical or intralesional therapy and all lesions that have persisted for 12 months and which have failed a 6-month trial of topical or serial intralesional corticosteroid should be considered for topical immunotherapy or systemic treatment. Likewise, patients with a large lesion of AA, who cannot be easily managed with intralesional therapy due to the discomfort associated with the number of injections required, and patients who experience dermal atrophy following intralesional corticosteroid or side effects following topical steroid use, should also be considered for topical immunotherapy or systemic therapy.

The surface area of the average male scalp is approximately 630 cm². AA affecting more than 15–20% of the scalp (95–130 cm²) generally require systemic therapy.

Solitary active patch of AA

An active patch of AA is characterised by a history of enlargement, a positive hair pull test at the border, and the presence of exclamation mark hairs or black dots within the patch. Activity within a patch of AA is an indication for active treatment.

Topical high-potency corticosteroid in a child and intralesional corticosteroid injection repeated every 4–6 weeks in an adult are appropriate first-line therapies in the presence of active disease.

Multiple patches

All patients with more than one patch should be considered for active treatment. Fifty-three percent of patients with AA develop additional patches over a number of months.⁵ Some may be unaware of the initial patch and only notice it when a second area appears. Among patients with multiple patches of AA, 65% will achieve complete remission within 12 months while 35% will progress to chronic disease.⁵

Topical high-potency corticosteroid in a child and intralesional corticosteroid injection repeated every 4–6 weeks in an adult are appropriate first-line therapies. Topical immunotherapy is an alternative first-line therapy in children. AA that fails to respond to a 6-month trial of topical or serial intralesional corticosteroid should be considered for topical immunotherapy or systemic therapy.

Patients with stable extensive disease (e.g. adults with > 95–130 cm² involvement), who cannot be easily managed with intralesional therapy, and patients who experience cutaneous side effects following topical or intralesional steroid use, should be considered for topical immunotherapy or systemic therapy.

Ophiasis alopecia

There are no available data on the rate of spontaneous regrowth among patients who present with AA in an ophiasis pattern; however, there is an expert consensus that hair loss with an ophiasis pattern indicates a poorer prognosis and merits active treatment.

Table 2 Proportion of 68 patients with chronic AA in 2012 who had subsequently developed AT or AU by 2018

Male-to-female ratio	1:2.6
Number of children aged 6 or under at onset of AA	5 (4.4%)
Number of children aged 6 or under at onset of AA who progressed to AT/AU	1 (1.5%)
Number of patients with chronic AA who progressed to AT/AU while on treatment	12 (17.6%)
Number of patients who continue to have chronic multifocal patchy AA but who have not progressed to AT or AU	56 (82.5%)
Number of patients who developed AT/AU while on treatment and who subsequently regrew either spontaneously or with subsequent systemic treatment	0

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis.

Topical high-potency corticosteroid in a child and intralesional corticosteroid injection repeated every 4–6 weeks in an adult are appropriate first-line therapies. Topical immunotherapy is considered an alternate first-line therapy in children. Due to large surface area of involvement, as described previously, these treatments may be intolerable or ineffective. Therefore, AA that fails to respond to a 6-month trial of topical or serial intralesional corticosteroid should be considered for topical immunotherapy or systemic therapy.

Topical immunotherapy or systemic therapy should be considered in patients with stable extensive disease (e.g. adults with > 95–150 cm² involvement), who cannot be easily managed with intralesional therapy, or in patients who experience dermal atrophy following intralesional corticosteroid or cutaneous side effects following topical or intralesional steroid use.

Rapid progressive hair loss/diffuse AA/extensive AA/AT or AU

Seventy percentage of patients who develop AT/AU do so rapidly and within 4 months of disease onset, while 30% take longer than 30 months to develop AT/AU.⁵ Rapid progression of hair loss that is likely to result in ≥50% hair loss, AT or AU is an indication for systemic therapy as topical and intralesional therapy are unlikely to arrest hair loss in these circumstances.

In a placebo-controlled trial evaluating patients with >50% hair loss due to AA, significant regrowth among patients in the placebo group was only seen in 7%.¹⁴

Systemic therapy in children

Children who develop AA before the age of 6 have a very high risk of developing chronic, persistent and extensive AA. In Ikeda's study (Table 1), there were 53 children below the age of 6 and no child regrew their hair spontaneously or was disease free at 12 months.⁵ All 53 children developed chronic AA.

Ikeda identified 85 children aged between 7 and 12 years at the time of initial presentation of their AA. Forty-seven had complete recovery of their hair within 3 years, while 36 went on to chronic persistent extensive disease. Half of these children then progressed rapidly to chronic persistent extensive disease, while the other 18 recovered initially but then relapsed and then developed chronic persistent extensive disease.⁵

All children with AA should be considered for active treatment. Intralesional corticosteroid injection is generally not feasible without sedation, and we believe the risks associated with sedation are not justified in the treatment of AA. Topical corticosteroid is therefore considered the most appropriate first-line therapy in children with AA. Topical minoxidil and topical immunotherapy are alternate first-line therapies in children. A combination of two or all three of these treatments is considered second-line management. Systemic therapy is considered a third-line option in children. In the absence of data confirming that

systemic therapy reduces the risk of subsequent development of AT or AU, there is no consensus opinion on the use of systemic therapy in children.

Other associations with AA

The presence of associated nail pits is seen in up to 30% of patients with AA and nail pits may precede hair loss by many years.^{15,16} Nail pitting does not correlate with hair loss severity. Trachyonychia is an uncommon nail manifestation of AA, present in approximately 4% of patients with AA in a review of 1095 patients.^{15,17}

Ikeda identified a past or family history of atopy as an indicator of poor prognosis in AA. This has not been confirmed in subsequent studies.^{18,19}

Ikeda identified 'endocrine–autonomic' disease as an indicator of poor prognosis in AA. She defined endocrine–autonomic disease as a personal history of diabetes mellitus, peptic ulcer, bilateral oophorectomy, hypertension, atherosclerosis, Grave's disease and myxoedema, but without a personal history of atopy. This has not been confirmed in subsequent studies.^{19–21}

Alopecia areata is known to be associated with other organ-specific autoimmune diseases such as Graves disease, vitiligo, pernicious anaemia, coeliac disease and type 1 diabetes mellitus.²² Genome-wide association studies in AA have identified a number of candidate genes common to these organ-specific autoimmune diseases, suggesting common molecular pathways in their pathogenesis.^{25,24}

Trisomy 21 (Down syndrome) is associated with an increased prevalence (9%) and severity of AA.²⁵ It is estimated that 40% of patients with trisomy 21 will develop AT/AU.^{25,26} Topical corticosteroids are considered the appropriate first-line therapy with topical minoxidil and topical immunotherapy as alternate first-line therapies. In our experience, intralesional corticosteroids tend to be poorly tolerated due to pain and distress. Systemic corticosteroids may increase appetite. Patients with Trisomy 21 have an increased risk of developing acute lymphoblastic leukaemia and acute myeloid leukaemia,²⁷ making systemic therapy a relative contraindication.

Diagnosis and baseline investigation

Alopecia areata is a clinical diagnosis based on visual inspection and dermoscopy. In atypical cases, a scalp biopsy may be helpful. While there are a number of known disease associations, there are insufficient data to recommend routine screening for concomitant autoimmune disease at the time of diagnosis of AA. Investigations for comorbidities should be based on history and examination, taking into account any intended use of systemic therapy.

MANAGEMENT

Conservative management

For patients with limited stable disease that is inconspicuous or easily camouflaged, reassurance alone may be appropriate. Camouflage options include colour-matched

wool fibres ground into a powder that is dusted onto the hair and dyes that are applied to the skin as a cream or aerosol spray to conceal the scalp. Wigs, top pieces and hair extensions can also be used.

Topical therapy

Patients with limited disease may seek active treatment in order to accelerate regrowth. Options include topical glucocorticosteroids, topical minoxidil and topical immunotherapy. Agents used for topical immunotherapy include diphenylcyclopropenone, dinitrochlorobenzene, squaric acid dibutyl ester and dithranol.

Intralesional glucocorticosteroids

Intradermal or upper subcutaneous injection of long-acting triamcinolone or betamethasone has been widely used to treat AA. Dilute concentration should be as effective as undiluted triamcinolone in some patients.^{28,29} Individual patches of AA generally respond well to serial intralesional injection of corticosteroid repeated every 4–6 weeks. In a study that evaluated response to intralesional triamcinolone through dermoscopy, 60 of 70 patches of AA in 70 patients demonstrated regrowth of new vellus hair at 4 weeks.³⁰ Possible side effects include pain, dermal atrophy at the injection site and systemic absorption.

Intramuscular and intravenous glucocorticosteroids

Long-acting glucocorticosteroids can be administered intramuscularly or intravenously as an alternative to oral ingestion. While there has been some suggestion in the literature that intramuscular or intravenous injection has a superior side-effect profile compared to oral ingestion,⁵¹ there is no uniform consensus on this,⁵² and unless there is a contraindication to oral ingestion, we favour oral corticosteroid.

Systemic glucocorticosteroids

Up to 89 of patients respond to oral corticosteroids, while at least 11% are refractory to treatment even with high doses.⁵³ Among those who respond, 50% will relapse with dose reduction or soon after discontinuation of treatment. Long-term use of systemic glucocorticoids is not recommended due to associated side effects. For patients who are corticosteroid responsive, but also corticosteroid dependent, a switch to an appropriate steroid-sparing agent should be considered.

The initial dose of systemic glucocorticoid selected by the treating physician may vary depending on severity of AA and treatment history. Dosing strategies include commencing with a higher dose of oral prednisolone (0.5–0.75 mg/kg) with subsequent tapering from 6 to 12 weeks; maintaining a static dose of prednisolone (0.25 mg/kg) for 6–12 weeks; or commencing a lower dose (0.1–0.2 mg/kg) and increasing the dose over time according to response

and tolerance. While most of us commence treatment with an initial dose of oral prednisolone of 0.5 mg/kg, to be tapered down over 6–12 weeks, there is no expert consensus on the optimal use of oral prednisolone in AA. While a number of dermatologists favour pulsed oral corticosteroids, there is little evidence that this offers superior efficacy or safety.²⁸ A cross-sectional study of children with severe AA found that pulsed systemic corticosteroid therapy modified the initial course but did not generally influence the long-term outcome.⁵⁴

While we suspect that failure to achieve satisfactory hair regrowth with systemic corticosteroids predicts a lower response rate to systemic steroid-sparing anti-inflammatory agents, there are no randomised controlled trials (RCTs) that address this question specifically. Repeat courses of systemic glucocorticosteroids may be indicated for relapse following initial regrowth; however, long-term maintenance therapy is not recommended. Subsequent courses should be initiated at a lower dose in patients known to respond to prednisolone.

Steroid-sparing agents – azathioprine, methotrexate and ciclosporin

There are no RCTs supporting the use of any second-line systemic agents in the treatment of AA. Agents used in open-label retrospective case series or small prospective studies include azathioprine, methotrexate and ciclosporin. These agents can be used alone or in combination with prednisolone. They appear to be most effective when used as steroid-sparing agents to prevent relapse of AA, rather than as monotherapy to initiate regrowth in AA.

There is no expert consensus regarding the choice of a certain steroid-sparing agent over another. There is also no uniformly accepted way to judge the relative efficacy of these agents either. In order to retrospectively assess the efficacy of these steroid-sparing anti-inflammatory agents in our clinic, we evaluated the number of patients who continued taking the medication continuously for 12 months (Table 5). This was predicated on the basis that only patients who tolerated the medication and in whom both the patient and the treating doctor were satisfied it was working would continue to take the medication. Patients who ceased the medication due to complete remission prior to 12 months were considered to be responders.

Azathioprine is commonly started at a low dose (0.5–1 mg/kg daily) to minimise the risk of GI upset and gradually titrated every 4–6 weeks up to 2–3 mg/kg according to patient response and tolerance. About one-third of patients continue to take concomitant prednisolone, and most have serial injections of triamcinolone into areas of residual hair loss and disease activity (Table 5). It is recommended that serum TPMT be measured prior to commencing therapy.

Methotrexate is commonly initiated at 5–10 mg once weekly, and the dose gradually titrated every 4–6 weeks up to 20–30 mg according to patient response and tolerance. More than half the patients continue to take concomitant prednisolone, and most have serial injections of

triamcinolone into areas of residual hair loss and disease activity (Fig. 1).

Ciclosporin A is commonly initiated at 2 mg/kg daily in three divided doses, and the dose gradually titrated every 4–6 weeks up to a maximum of 5 mg/kg according to patient response and tolerance. Only a third of patients are able to cease prednisolone, but most continue to have serial injections of triamcinolone into areas of residual hair loss and disease activity (Table 5).

Minor relapses while on steroid-sparing therapy tend to be treated with the addition of intralesional triamcinolone or short-term glucocorticoids. Major relapses are generally managed by cessation of the steroid-sparing agent and substitution with an alternate steroid-sparing agent.

Other systemic therapies

Regrowth of hair during treatment with tofacitinib, a small-molecule Janus kinase 1/3 inhibitor, has been described in numerous case series.^{35–39} In a retrospective study of 90 patients with severe AA who received tofacitinib (5–10 mg twice daily) for at least 4 months, 77% of patients with a duration of disease less than 10 years had a clinical response (at least 6% improvement in Severity of Alopecia Tool (SALT) score).³⁵ Furthermore, three patients treated with ruxolitinib for myelofibrosis and another treated with baricitinib for CANDLE syndrome experienced near-complete regrowth of hair within 3–5 months in the setting of moderate-to-severe alopecia areata.^{39,40} The positive results of topical ruxolitinib and tofacitinib in mouse models⁴¹ and a human randomised placebo-controlled case series further support for a potential role for Janus kinase inhibitors in AA.⁴² No topical formulation is currently available. The expert consensus group recommends involving a dermatologist with experience prescribing Janus kinase inhibitors in these cases.

A number of other systemic agents have also been reported in case reports or small uncontrolled retrospective case series. These include simvastatin/ezetimibe,⁴⁵ dapsone, mycophenolate mofetil, tacrolimus, sulfasalazine and psoralen photochemotherapy. Apart from the combination of simvastatin/ezetimibe, which may work through inhibition of the JAK/STAT pathway, the evidence for these agents is weak.⁴⁴ While we are aware that many dermatologists have trialled these agents in AA for 3–6 months in patients who fail to respond to other systemic treatments,

the expert consensus group does not recommend their use.

FOLLOW-UP

Evaluating treatment response

Clinical response should ideally be measured through history, assessment of hair shedding severity, serial photography, SALT score and quality-of-life measures including Dermatology Life Quality Index (DLQI) and Alopecia Areata Symptom Impact Scale (AASIS), comparing response at the most recent visit to baseline. A SALT50 denotes achieving 50% improvement in SALT and is an acceptable goal for treatment success. Disease activity is commonly associated with increased hair shedding (stages 4–6) and a positive hair pull test, especially at the edge of existing patches of alopecia. The presence of exclamation mark hairs and black dots on dermoscopy is also an indicator of active disease.

Cessation of treatment

For systemic glucocorticoids, treatment should be weaned over 3 months to reduce the risk of side effects known to be associated with long-term use.

For patients who have responded to steroid-sparing agents, the treatment should ideally be continued for 3–6 months after complete remission to minimise the risk of relapse. The dose can be gradually tapered during this time.

Minor relapses may occur as the dose is weaned. Options to treat minor relapses include dose escalation, the use of intralesional triamcinolone or short-term use of systemic glucocorticoids.

Patients who develop a major relapse (i.e. multiple additional new patches) while on adequate doses of systemic therapy should stop the current treatment and consider whether to commence an alternate steroid-sparing agent. Additional treatment for a major relapse may include the use of intralesional triamcinolone and/or short-term use of systemic glucocorticoids.

Treatment may also need to be ceased in patients who develop significant toxicity secondary to these systemic agents.

Progression to steroid-sparing agents is not mandatory, and many patients will elect to discontinue treatment and let the AA take its course. These patients can access expert

Table 3 Systemic therapy continuation rates at 12 months

Agent	Responders (<i>n/n</i>) (%) [†]	Proportion of responders also using concurrent prednisolone (<i>n/n</i>) (%)	Average daily dose of concurrent prednisolone (mg)
Ciclosporin	11/20 (55)	7/11 (64)	6.4
Methotrexate	9/20 (45)	5/9 (56)	4.8
Azathioprine	15/20 (65)	5/15 (58)	5.6

[†]Responders are defined as patients who have either continued to take the medication for 12 months or longer or who have stopped the medication due to complete remission. Non-responders are defined as patients who stopped the medication prior to 12 months either due to side effects or lack of efficacy (including relapse while on treatment).

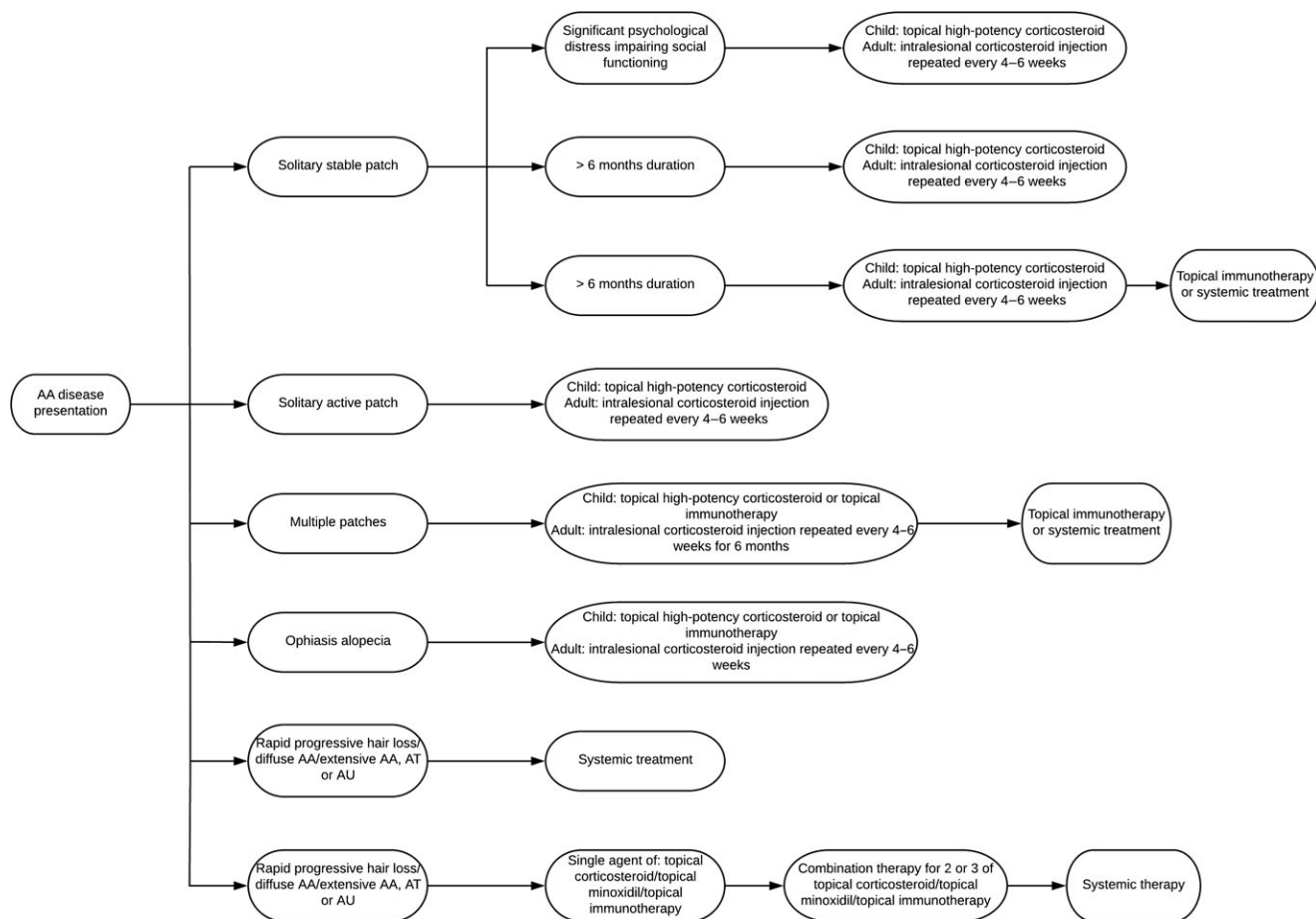


Figure 1 Treatment algorithm for systemic treatment of alopecia areata (AA, alopecia areata; AT alopecia totalis; AU, alopecia universalis).

advice on wigs through specialist centres and the Australia Alopecia Areata Foundation (www.aaaf.com.au).

CONCLUSION

This consensus statement draws upon the clinical expertise of dermatologists experienced in the treatment of AA. The advice is supported by hair biologists familiar with the aetiology, pathogenesis and current scientific literature on the biology of hair growth in general and AA in particular. These guidelines, summarised in Figure 1, provide an Australian framework for assessment and treatment of AA.

REFERENCES

- Safavi KHMS, Suman VJ, Moshell AN *et al*. Incidence of alopecia areata in Olmsted County, Minnesota, 1975 through 1989. *Mayo Clin. Proc.* 1995; **70**: 628–35.
- Madani SSJ. Alopecia areata update. *J. Am. Acad. Dermatol.* 2000; **42**: 549–66.
- Ikeda T. A new classification of alopecia areata. *Dermatology* 1965; **131**: 421–45.
- Delamere FM, Sladden MM, Dobbins HM *et al*. Interventions for alopecia areata. *Cochrane Database Syst. Rev.* 2008; **16**: CD004413.
- Lai VW, Chen G, Gin D, Sinclair R. Systemic treatments for alopecia areata: a systematic review. *Australas. J. Dermatol.* 2018. <https://doi.org/10.1111/ajd.12915>.
- Alkhalifah AAA, Wang E, McElwee KJ *et al*. Alopecia areata update: part I. Clinical picture, histopathology, and pathogenesis. *J. Am. Acad. Dermatol.* 2010; **62**: 177–88.
- Jang YH, Hong N-S, Moon SY *et al*. Long-term prognosis of alopecia totalis and alopecia universalis: a longitudinal study with more than 10 years of follow-up: better than reported. *Dermatology* 2017; **235**: 250–6.
- Tosti ABS, Iorizzo M. Alopecia areata: a long term followup study of 191 patients. *J. Am. Acad. Dermatol.* 2006; **55**: 438–41.
- Ruiz-Doblado SCA, García-Hernández MJ. Alopecia areata: psychiatric comorbidity and adjustment to illness. *Int. J. Dermatol.* 2005; **42**: 454–7.
- Koo JYSW, Hallman CP, Edwards JE. Alopecia areata and prevalence of psychiatric disorders. *Int. J. Dermatol.* 1994; **33**: 849–50.
- Ghanizadeh A. Comorbidity of psychiatric disorders in children and adolescents with alopecia areata in a child and adolescent psychiatry clinical sample. *Int. J. Dermatol.* 2008; **47**: 1118–20.

12. Shapiro JMS. Alopecia areata: diagnosis and management. *Int. J. Dermatol.* 1999; **58**: 19–24.
15. MacDonald Hull SP, Wood ML, Hutchinson PE *et al.* Guidelines for the management of alopecia areata. *Br. J. Dermatol.* 2005; **149**: 692–9.
14. Price V. Double-blind, placebo-controlled evaluation of topical minoxidil in extensive alopecia areata. *J. Am. Acad. Dermatol.* 1987; **16**(5 Pt 2): 750–6.
15. Tosti A, Morelli R, Bardazzi F *et al.* Prevalence of nail abnormalities in children with alopecia areata. *Pediatr. Dermatol.* 2008; **11**: 112–5.
16. Gandhi V, Baruah M, Bhattacharaya S. Nail changes in alopecia areata: incidence and pattern. *Indian J. Dermatol. Venereol. Leprol.* 2003; **69**: 114–5.
17. Tosti A, Fanti PA, Morelli R *et al.* Trachyonychia associated with alopecia areata: a clinical and pathologic study. *J. Am. Acad. Dermatol.* 1991; **25**: 266–70.
18. Thomas EA, Kadyan RS. Alopecia areata and autoimmunity: a clinical study. *Indian J. Dermatol.* 2008; **55**: 70–4.
19. van der Steen PHM, van Baar HMJ, Happel R *et al.* Prognostic factors in the treatment of alopecia areata with diphenylcyclopropenone. *J. Am. Acad. Dermatol.* 1991; **24**: 227–30.
20. Walker SA, Rothman S. Alopecia areata: a statistical study and consideration of endocrine influences. *J. Invest. Dermatol.* 1950; **14**: 403–13.
21. Waisman M, Kepler EJ. Alopecia areata: an appraisal of endocrine factors in its causation. *J. Am. Med. Assoc.* 1941; **116**: 2004–6.
22. Tan E, Tay YK, Goh CL *et al.* The pattern and profile of alopecia areata in Singapore—a study of 219 Asians. *Int. J. Dermatol.* 2002; **41**: 748–55.
25. Petukhova L, Duvic M, Hordinsky M *et al.* Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. *Nature* 2010; **466**: 115.
24. Betz RC, Petukhova L, Ripke S *et al.* Genome-wide meta-analysis in alopecia areata resolves HLA associations and reveals two new susceptibility loci. *Nat. Commun.* 2015; **6**: 5966.
25. Du Vivier A, Munro DD. Alopecia areata, autoimmunity, and Down's syndrome. *BMJ* 1975; **1**: 191–2.
26. Alves R, Ferrando J. Alopecia areata and Down's syndrome. *Int. Med. Rev. Down Syndr.* 2011; **15**: 54–6.
27. Xavier AC, Ge Y, Taub JW. Down syndrome and malignancies: a unique clinical relationship: a Paper from the 2008 William Beaumont Hospital Symposium on Molecular Pathology. *J. Mol. Diagn.* 2009; **11**: 571–80.
28. Ustuner P, Balevi A, Ozdemir M. Best dilution of the best corticosteroid for intralesional injection in the treatment of localized alopecia areata in adults. *J. Dermatolog. Treat.* 2017; **28**: 753–61.
29. Chu TW, AlJasser M, Alharbi A *et al.* Benefit of different concentrations of intralesional triamcinolone acetonide in alopecia areata: an intrasubject pilot study. *J. Am. Acad. Dermatol.* 2015; **75**: 358–40.
30. Ganjoo S, Thappa D. Dermoscopic evaluation of therapeutic response to an intralesional corticosteroid in the treatment of alopecia areata. *Indian J. Dermatol. Venereol. Leprol.* 2015; **79**: 408–17.
31. Kurosawa M, Nakagawa S, Mizuashi M *et al.* A comparison of the efficacy, relapse rate and side effects among three modalities of systemic corticosteroid therapy for alopecia areata. *Dermatology* 2006; **212**: 361–5.
32. Dehghan M, Alborzi A, Shahini N. Comparison of oral prednisolone pulse therapy with intravenous methylprednisolone pulse therapy in severe alopecia areata. *J. Pak. Assoc. Dermatolog.* 2015; **25**: 159–62.
35. Kar B, Handa S, Dogra S *et al.* Placebo-controlled oral pulse prednisolone therapy in alopecia areata. *J. Am. Acad. Dermatol.* 2005; **52**: 287–90.
34. Hubiche T, Léauté-Labrèze C, Taïeb A *et al.* Poor long term outcome of severe alopecia areata in children treated with high dose pulse corticosteroid therapy. *Br. J. Dermatol.* 2008; **158**: 1136–7.
35. Liu LY, Craiglow BG, Dai F *et al.* Tofacitinib for the treatment of severe alopecia areata and variants: a study of 90 patients. *J. Am. Acad. Dermatol.* 2017; **76**: 22–8.
36. Craiglow BG, Liu LY, King BA. Tofacitinib for the treatment of alopecia areata and variants in adolescents. *J. Am. Acad. Dermatol.* 2017; **76**: 29–32.
37. Gupta A, Carviel J, Abramovits W. Efficacy of tofacitinib in treatment of alopecia universalis in two patients. *J. Eur. Acad. Dermatol. Venereol.* 2016; **50**: 1373–8.
38. Ibrahim O, Bayart CB, Hogan S *et al.* Treatment of alopecia areata with tofacitinib. *JAMA Dermatol.* 2017; **155**: 600–2.
39. Messenger A, McKillop J, Farrant P *et al.* British Association of Dermatologists' guidelines for the management of alopecia areata 2012. *Br. J. Dermatol.* 2012; **166**: 916–26.
40. Jabbari A, Dai Z, Xing L *et al.* Reversal of alopecia areata following treatment with the JAK1/2 inhibitor baricitinib. *EBio-Medicine* 2015; **2**: 351–5.
41. Xing L, Dai Z, Jabbari A *et al.* Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition. *Nat. Med.* 2014; **20**: 1045.
42. Bokhari L, Sinclair R. Treatment of alopecia universalis with topical Janus Kinase inhibitors – a double blind, placebo, and active controlled pilot study. *Int. J. Dermatol.* 2018. <https://doi.org/10.1111/ijd.14192>.
45. Lattouf C, Jimenez JJ, Tosti A *et al.* Treatment of alopecia areata with simvastatin/ezetimibe. *J. Am. Acad. Dermatol.* 2015; **72**: 559–61.
44. DelCanto G, Bayer A, Kindelan CC *et al.* 081 Simvastatin reduces autoimmune alopecia through direct action on T lymphocytes. *J. Invest. Dermatol.* 2018; **158**: S14.