

Table I. Acneiform cases, their chemotherapy, retinoid, and rash improvement

Age/ sex	Chemotherapy drug	Initial reaction grade	Retinoid	Duration of retinoid therapy	Rash improvement	Concomitant tetracycline use	Reduction in chemotherapy drug dose
70/F	Erlotinib	Grade 2	Isotretinoin 20 mg daily or qod	7-8 months	Moderate	No	No
59/M	Cetuximab	Grade 3	Isotretinoin 20 mg daily	6 months	Significant	Yes	No
62/M	Cetuximab	Grade 3	Isotretinoin 60 mg daily	3 months	Significant	No	Yes
37/M	Cetuximab	Grade 3	Isotretinoin 10 mg daily	1-2 months	Significant	No	Yes
73/M	Erlotinib	Grade 3	Isotretinoin 40 mg daily	10 months	Significant	No	No
	Cetuximab and irenotecan	Grade 2	Acitretin 25 mg qod	6 months	Minimal	No	No
67/M	Afatinib	Grade 3	Acitretin 10-25 mg daily	7 months	Minimal	Yes	Yes

F, Female; M, male; qod, once every other day.

retinoid dermatitis, treated with topical corticosteroids. There were no other significant adverse effects associated with retinoid use in these patients.

In our retrospective study, treatment with both isotretinoin and acitretin led to clinical improvement in acneiform eruptions secondary to EGFR inhibitors, similar to the experience by Andrews et al¹ and others.²⁻⁴ However, isotretinoin led to greater improvement in clinical outcomes compared with acitretin, although our sample size is small. If this observation is validated by others, an explanation might be the striking difference in sebostatic activity with isotretinoin compared with other synthetic retinoids.⁵ This study further reinforces the use of oral retinoids in treating EGFR and small molecule tyrosine kinase inhibitors.

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REFERENCES

1. Andrews ED, Garg N, Patel AB. A retrospective chart review on oral retinoids as a treatment for epidermal growth factor receptor inhibitor- and mitogen-activated protein kinase kinase inhibitor-induced acneiform eruptions. *J Am Acad Dermatol.* 2020;82:998-1000.
2. Chiang HC, Anadkat MJ. Isotretinoin for high-grade or refractory epidermal growth factor receptor inhibitor-related acneiform papulopustular eruptions. *J Am Acad Dermatol.* 2013;69:657-658.
3. Gerber PA, Meller S, Eames T, et al. Management of EGFR-inhibitor associated rash: a retrospective study in 49 patients. *Eur J Med Res.* 2012;17:4.
4. Pomerantz RG, Chirinos RE, Falo LD Jr, Geskin LJ. Acitretin for treatment of EGFR inhibitor-induced cutaneous toxic effects. *Arch Dermatol.* 2008;144:949-950.
5. Hirschel-Scholz S, Siegenthaler G, Saurat JH. Isotretinoin differs from other synthetic retinoids in its modulation of human cellular retinoic acid binding protein (CRABP). *Br J Dermatol.* 1989;120:639-644.

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An open-label study evaluating the efficacy of abatacept in alopecia areata



To the Editor: Alopecia areata (AA) is a form of non-scarring autoimmune hair loss. Our previous genome-wide association study revealed strong genetic susceptibility at the cytotoxic T lymphocyte-associated protein 4 (CTLA4) locus in patients with AA.¹ CTLA4 is an immune checkpoint receptor that has emerged as a clinically important target controlling immune responses in both cancer and autoimmunity. Abatacept is a CTLA4-immunoglobulin

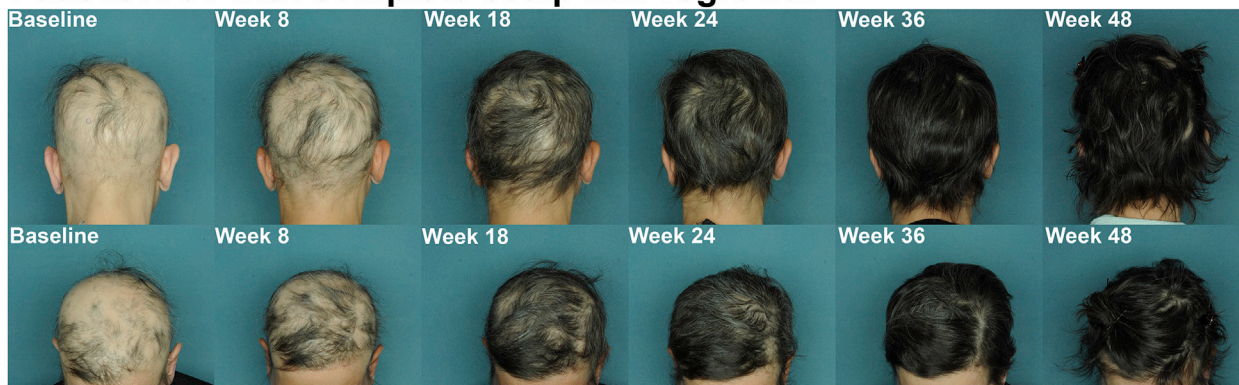
Patient A-01 with complete scalp hair regrowth**Patient A-09 with hair regrowth of the eyebrows only**

Fig 1. Hair regrowth with abatacept treatment in patients with alopecia areata (AA). *Top panel*, Clinical photographs of patient A-01 who achieved the primary endpoint of $\geq 50\%$ hair regrowth from baseline as assessed by Severity of Alopecia Tool score. *Bottom panel*, Patient A-09 who achieved increased eyebrow hair regrowth.

costimulatory modulator that attenuates the activation of T cells and is approved by the US Food and Drug Administration for the treatment of rheumatoid arthritis.² We performed an open-label, single-arm clinical trial of abatacept (125 mg subcutaneously daily for 24 weeks) in 15 patients with moderate to severe patchy type AA, alopecia totalis (AT), and alopecia universalis to assess clinical and immunopathologic responses. The [ClinicalTrials.gov](https://clinicaltrials.gov) identifier is NCT02018042, and subject demographics and treatment history can be found in Supplemental Tables SI and SVI (available via Mendeley at <https://doi.org/10.17632/39jmkdy8xz.1>).

At the end of treatment, subject A-01 experienced significant hair regrowth and achieved the primary endpoint of $>50\%$ hair regrowth from baseline by week 18, as assessed by the Severity of Alopecia Tool (SALT) score³ (Fig 1, Table I, and Supplemental Fig S1). A-01 had a SALT score of 78% at baseline compared with 7% at the end of treatment at week 24 (91% hair regrowth) and achieved complete scalp hair regrowth by week 36. Notably, the response was

lasting and durable after cessation of treatment, and hair regrowth was maintained at the posttreatment follow-up visit on week 36.

Four additional subjects (A-02, A-03, A-06, and A-11) exhibited intermediate ($\sim 15\text{--}25\%$) hair regrowth at week 24; 4 patients exhibited lower but noticeable responses ($\sim 3\text{--}10\%$; A-08, A-10, A-13, and A-15); and the remaining 4 AT/alopecia universalis subjects (A-04, A-05, A-07, and A-12) showed no response. A-12 progressed from patchy AA to AT during the study. Notably, 1 patient with AT (A-09) demonstrated hair regrowth of the eyebrows but not the scalp (Fig 1). Gene expression profiling using RNA-seq of scalp biopsy specimens obtained at baseline and weeks 4, 12, and 24 displayed significant molecular differences at 12 to 24 weeks into treatment, with normalization of AA inflammatory genes (Supplemental Fig S2). A-14 dropped out of study before week 24, and there were no safety concerns or adverse events in any subjects. Improvements of the Dermatology Life Quality Index/Scale were observed (Supplemental Tables SII and SIII).

Table I. Hair regrowth in patients during treatment and following cessation of abatacept

Subject	Time, weeks								Observation at week 24 compared with baseline	Observation during follow-up
	0	4	8	12	18	24	36	48		
A-01	0.0	1.3	25.6	39.1	64.1	91.0	98.7	74.4	High response	Continue to improve for 12 weeks
Regrowth (%)	0.0	1.3	25.6	39.1	64.1	91.0	98.7	74.4		
SALT (%)	78	77	58	47.5	28	7	1	20		
A-02	0.0	11.4	8.6	12.4	22.2	14.6			Moderate response	
Regrowth (%)	0.0	11.4	8.6	12.4	22.2	14.6				
SALT (%)	92.5	82	84.5	81	72	79				
A-03	0.0	-12.8	12.8	28.2	23.130	23.1			Moderate response	
Regrowth (%)	0.0	-12.8	12.8	28.2	23.130	23.1				
SALT (%)	39	44	34	28		30				
A-04*	0.0	0.0	0.0	0.9	0.9	1.9			No response	
Regrowth (%)	0.0	0.0	0.0	0.9	0.9	1.9				
SALT (%)	99.9	99.9	99.9	99	99	98				
A-05*	0.0	0.0	0.0	0.1	0.1	0.1	0.0		No response	No response
Regrowth (%)	0.0	0.0	0.0	0.1	0.1	0.1	0.0			
SALT (%)	100	100	100	99.9	99.9	99.9	100			
A-06*	0.0	1.7	2.9	7.5	15.6	14.5	18.5		Moderate response	Continue to improve for 12 weeks
Regrowth (%)	0.0	1.7	2.9	7.5	15.6	14.5	18.5			
SALT (%)	86.5	85	84	80	73	74	70.5			
A-07*	0.0	0.0	0.0	0.0	0.0	0.0	0.0		No response	No response
Regrowth (%)	0.0	0.0	0.0	0.0	0.0	0.0	0.0			
SALT (%)	100	100	100	100	100	100	100			
A-08	0.0	2.9	2.9	7.2	7.2	2.9	1.4		Low response	Stable for 12 weeks
Regrowth (%)	0.0	2.9	2.9	7.2	7.2	2.9	1.4			
SALT (%)	69	67	67	64	64	67	68			
A-09*	0.0	0.0	0.0	0.0	0.0	0.0			Regrowth of eyebrows but not scalp hair	
Regrowth (%)	0.0	0.0	0.0	0.0	0.0	0.0				
SALT (%)	100	100	100	100	100	100				
A-10	0.0	0.0	1.0	2.0	3.6	6.1	9.2		Low response	Continue to improve for 12 weeks
Regrowth (%)	0.0	0.0	1.0	2.0	3.6	6.1	9.2			
SALT (%)	98	98	97	96	94.5	92	89			
A-11	0.0	0.0	0.0	3.1	6.3	25.0			Moderate response	
Regrowth (%)	0.0	0.0	0.0	3.1	6.3	25.0				
SALT (%)	32	32	32	31	30	24				
A-12	0.0	-1.1	0.0	-4.3	-8.7	-8.7	-8.7		Worsening of AA; no response	No response
Regrowth (%)	0.0	-1.1	0.0	-4.3	-8.7	-8.7	-8.7			
SALT (%)	92	93	92	96	100	100	100			
A-13	0.0	1.3	0.0	0.0	6.0	8.0			Low response	
Regrowth (%)	0.0	1.3	0.0	0.0	6.0	8.0				
SALT (%)	75	74	75	75	70.5	69				
A-14	0.0	3.6	8.4	8.4	10.8	—			Dropped out at week 24	
Regrowth (%)	0.0	3.6	8.4	8.4	10.8	—				
SALT (%)	83	80	76	76	74					

Continued

Table I. Cont'd

	Time, weeks					Follow-up	Observation at week 24 compared with baseline	Observation during follow-up
	Active treatment (until week 24)							
A-15							Underlying AGA; low response	
Regrowth (%)	0.0	0.0	0.0	0.0	0.0	6.3		
SALT (%)	32	32	32	32	32	30		

A SALT score of 100% indicates complete hair loss.

AA, Alopecia areata; AGA, androgenetic alopecia; SALT, Severity of Alopecia Tool.

*Patient with alopecia totalis or alopecia universalis.

Among the patients whose SALT scores were available beyond 24 weeks, 3 continued to exhibit improved hair growth 12 weeks after treatment had stopped (A-01, A-06, and A-10 at week 36; Supplemental Fig S2). Although our study was limited by the small cohort size and potential for spontaneous improvement of AA, this is unlikely because of the long disease history in patient A-01. The robust and safe durable response observed in this patient in this study suggests that abatacept may be useful for a subset of patients with AA as a single agent or potentially as a part of combination regimens. Innovative approaches that potentially use Janus kinase inhibitors⁴ initially to induce remission and abatacept to maintain or deepen these responses could be envisioned as one sequential strategy.

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REFERENCES

- Petukhova L, Duvic M, Hordinsky M, et al. Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. *Nature*. 2010;466:113-117.
- Kremer JM, Westhovens R, Leon M, et al. Treatment of rheumatoid arthritis by selective inhibition of T-cell activation with fusion protein CTLA4lg. *N Engl J Med*. 2003;349:1907-1915.
- Olsen EA, Canfield D. SALT II: a new take on the Severity of Alopecia Tool (SALT) for determining percentage scalp hair loss. *J Am Acad Dermatol*. 2016;75:1268-1270.
- 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;20:1043-1049.

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Hidradenitis suppurativa and major adverse cardiac events: A systematic review and meta-analysis



To the Editor: Hidradenitis suppurativa (HS) is a chronic inflammatory disorder that results in significant morbidity. There is conflicting evidence on whether HS is associated with major adverse cardiac events (MACEs), including cerebrovascular