Table II. Distribution of melanomas according to tumor thickness and to the absence of nevus-associated melanoma versus common versus dysplastic nevus remnants, stratified by age and histologic type

			Absence		Common nevus		Dysplastic nevus		
Characteristic	Breslow thickness, mm	Total	n	%	n	%	n	%	*P**
Age ≤ 55 y		550	368	66.9	96	17.5	86	15.6	
	≤1	302	187	61.9	52	17.2	63	20.9	<.001
	1.01-2.00	137	88	64.2	31	22.6	18	13.1	
	2.01-4.00	71	59	83.1	9	12.7	3	4.2	
	>4	40	34	85.0	4	10.0	2	5.0	
Age > 55 y		537	428	79.7	48	8.9	61	11.4	
	≤1	209	149	71.3	23	11.0	37	17.7	.002
	1.01-2.00	104	82	78.8	11	10.6	11	10.6	
	2.01-4.00	117	101	86.3	7	6.0	9	7.7	
	>4	107	96	89.7	7	6.5	4	3.7	
SSM		813	561	69.0	124	15.3	128	15.7	
	≤1	497	326	65.6	73	14.7	98	19.7	.004
	1.01-2.00	194	137	70.6	34	17.5	23	11.9	
	2.01-4.00	93	74	79.6	14	15.1	5	5.4	
	>4	29	24	82.8	3	10.3	2	6.9	
NM		274	235	85.8	20	7.3	19	6.9	
	≤1	14	10	71.4	2	14.3	2	14.3	.006
	1.01-2.00	47	33	70.2	8	17.0	6	12.8	
	2.01-4.00	95	86	90.5	2	2.1	7	7.4	
	>4	118	106	89.8	8	6.8	4	3.4	

NM, Nodular melanoma; *SSM*, superficial spreading melanoma.
**P* value for the Pearson χ^2 test comparing the 3 groups: de novo, common nevus, and dysplastic nevus.

Drs Reyes, Manrique-Silva, and Folgado contributed equally to this work.

Supported in part by a Universidad Católica de Valencia "San Vicente Mártir" grant (no. 2018-109-001).

Conflicts of interest: None disclosed.

Correspondence to: Eduardo Nagore, PhD, School of Medicine, Universidad Católica de Valencia "San Vicente Mártir", c/ Quevedo, 2, 46001 València, Spain

E-mail: eduardo.nagore@ucv.es

REFERENCES

1. Martin-Gorgojo A, Nagore E. Melanoma arising in a melanocytic nevus. *Actas Dermosifiliogr*. 2018;109(2):123-132.
2. Garcia-Cruz A, Florez A, de la Torre-Fraga C, Cruces Prado M. Observational cross-sectional study comparing Breslow thickness of melanoma arising from naevi and melanoma de novo. *Br J Dermatol*. 2009;161(3):700-702.
3. Weatherhead SC, Haniffa M, Lawrence CM. Melanomas arising from naevi and de novo melanomas—does origin matter? *Br J Dermatol*. 2007;156(1):72-76.
4. Tsao H, Bevona C, Goggins W, Quinn T. The transformation rate of moles (melanocytic nevi) into cutaneous melanoma: a population-based estimate. *Arch Dermatol*. 2003;139(3):282-288.
5. Harley S, Walsh N. A new look at nevus-associated melanomas. *Am J Dermatopathol*. 1996;18(2):137-141.

https://doi.org/10.1016/j.jaad.2019.04.043

Retrospective outcome analysis of 25 alopecia areata patients treated with simvastatin/ezetimibe

To the Editor: Optimism regarding alopecia areata (AA) treatment efficacy with simvastatin/ezetimibe (Vytorin, Merck & Co, Whitehouse Station, NJ) from reports and small series inspired prospective trials with mixed results.[1-4] Its therapeutic mechanism remains unknown, but may involve cytokine reduction, Janus kinase (JAK)/signal transducer and activator of transcription (STAT) pathway inhibition, and increasing regulatory T cells.[5] We examined our experience treating AA with this agent in the context of methotrexate use or failure, or both.

After approval by the University of Pittsburgh Institutional Review Board, a retrospective clinical and treatment outcome analysis of patients with AA receiving once-daily simvastatin 40 mg/ezetimibe 10 mg (S/E) monotherapy de novo, after methotrexate failure, or combined with methotrexate after inadequate response to intralesional steroid (ILS) was performed. Clinical response was classified semi-quantitatively by estimated percentage regrowth: no response (0%), minimal (1%-25%), moderate (26%-75%), or complete (76%-100%).

There were 25 patients (92% white, 68% female; median age, 47 years; range, 13-80 years) who presented with patchy scalp (24%), ophiasis (16%),

Table I. Summary of patient demographics, pattern of hair loss, treatment, and response

Treatment	Age (y)	Sex	Pattern	Approx AA disease duration before treatment w/S/E (mo)	Outcome*	ADR	S/E treatment duration (mo)	S/E treatment status at time of record review
S/E	15	M	Patchy	27	No response	None	6	Discontinued due to no response
S/E	34	M	Totalis	18	No response	None	2	Discontinued due to no response
S/E	37	M	Patchy	24	Complete	None	13	Patient discontinued without disease relapse
S/E	45	M	Patchy	72	No response	None	9	Discontinued due to no response
S/E	49	F	Totalis	6	No response	None	6	Discontinued due to no response
S/E	55	F	Ophiasis	12	No response	None	5	Ongoing
S/E	57	F	Totalis	73	Minimal	None	7	Discontinued due to minimal response
S/E	58	M	Patchy	37	Minimal	None	17	Discontinued due to minimal response
S/E	64	F	Totalis	6	No response	None	14	Discontinued due to no response
S/E	80	F	Patchy	36	Complete	None	5	Ongoing
MTX → S/E	13	M	Totalis	14	No response	None	9	Discontinued due to no response
MTX → S/E	17	M	Universalis	12	Complete	None	39	Ongoing
MTX → S/E	27	F	Totalis	23	No response	None	4	Ongoing
MTX → S/E	34	F	Universalis	41	No response	None	14	Discontinued due to no response
MTX → S/E	36	F	Ophiasis	234	No response	None	3	Discontinued due to no response
MTX → S/E	41	F	Ophiasis	25	Complete	None	17	Patient discontinued without disease relapse
MTX → S/E	45	F	Totalis	20	Minimal	None	16	Discontinued due to minimal response
MTX → S/E	48	F	Totalis	87	Moderate	Myopathy	21	Discontinued due to ADR
MTX → S/E	63	F	Totalis	252	No response	None	6	No response
MTX → S/E	70	F	Totalis	42	No response	None	14	Ongoing
MTX → S/E	76	F	Totalis	187	N/A	Palpitations	1	Discontinued due to ADR
MTX + S/E	36	F	Patchy	100	Complete	Myopathy	2	Discontinued due to ADR
MTX + S/E	47	F	Universalis	80	Complete	None	8	Patient discontinued
MTX + S/E	53	F	Ophiasis	63	Minimal	None	10	Ongoing
MTX + S/E	68	M	Totalis	8	No response	None	11	Ongoing

AA, Alopecia areata; *ADR*, adverse drug reaction; *F*, female; *M*, male; *MTX*, methotrexate; *MTX → S/E*, methotrexate failed, switched to simvastatin/ezetimibe monotherapy; *MTX + S/E*, cotreatment with methotrexate and simvastatin/ezetimibe; *N/A*, not available; *S/E*, simvastatin/ezetimibe monotherapy after inadequate response to intralesional steroid; *w/*, with.
*No response (0%), minimal (1%-25%), moderate (26%-75%), complete (76-100%).

Table II. Methotrexate treatment history in patients who were switched to simvastatin/ezetimibe

Treatment	Age (y)	Sex	Duration of MTX therapy (mo)	Max weekly dose of MTX (mg)	Total dose of MTX (mg)	Outcome*	Adverse drug reaction
MTX → S/E	13	M	5	15	100	No response	None
MTX → S/E	17	M	10	25	805	No response	None
MTX → S/E	27	F	11	20	855	No response	None
MTX → S/E	34	F	23	15	2505	No response	GI upset
MTX → S/E	36	F	9	20	540	No response	GI upset
MTX → S/E	41	F	21	20	365	Moderate	None
MTX → S/E	45	F	9	17.5	570	No response	None
MTX → S/E	48	F	52	20	3960	No response	None
MTX → S/E	63	F	12	20	810	No response	None
MTX → S/E	70	F	6	15	232.5	No response	None
MTX → S/E	76	F	1	10	10	No response	Elevated creatinine

F, Female; *GI*, gastrointestinal; *M*, male; *MTX*, methotrexate; *MTX → S/E*, methotrexate failed, switched to simvastatin/ezetimibe.
*No response (0%), minimal (1%-25%), moderate (26%-75%), complete (76%-100%).

totalis (48%), or universalis (12%) pattern disease. Ten (40%) received S/E as first-line monotherapy for 2 to 17 months ($\overline{x} = 8.5$, $\tilde{x} = 6.5$ months), and 11 (44%) received S/E monotherapy for 1 to 39 months ($\overline{x} = 13.5$, $\tilde{x} = 14$ months) after methotrexate and ILS failure. Four (16%) underwent cotreatment with S/E-methotrexate for 2 to 11 months ($\overline{x} = 7.7$, $\tilde{x} = 9$ months). Methotrexate doses ranged from 10 to 25 mg/wk ($\overline{x} = 15.2$, $\tilde{x} = 15$ mg/wk).

Overall, clinical response after an average and median treatment duration of 10.4 and 9 months, respectively, was seen in 11 of 25 patients (44%), including 4 of 10 (40%) on S/E de novo monotherapy, 4 of 11 (36.4%) on S/E monotherapy after ILS and methotrexate failure, and 3 of 4 (75%) who received S/E-methotrexate cotreatment (Table I). Complete regrowth was most frequently seen in those who received S/E-methotrexate cotreatment (50% [2 of 4]), followed by S/E de novo monotherapy (20% [2 of 10]), and S/E after ILS and methotrexate failure (18.2% [2 of 11]) (Table II). Treatment with 1 to 2 years of methotrexate was not successful in 2 of 3 patients with universalis, but both demonstrated complete regrowth after 2 years of S/E monotherapy, although eyebrow madarosis persisted in 1 patient.

There were no evident treatment response differences by sex or ethnicity. S/E nonresponders often had ophiasis or totalis pattern disease. Patients with nail pitting (3 of 25 [12%]) showed no response. Clinical relapse occurred in 7 of 11 total responders (63.6%) while on therapy, including 2 cotreated with methotrexate and S/E. Relapse was most common with ophiasis or universalis alopecia. Observed adverse effects (myopathy in 2, presenting as severe muscle cramps after 1 to 2 weeks, and palpitations after 2 months in 1) resolved days after S/E discontinuation.

Our data indicate that S/E offers modest, gradual clinical benefit across AA subtypes after 1 to 2 years of monotherapy or as an adjunct to methotrexate. The overall response rate (44%) observed aligns with prior studies (18%-58%).[1-4] Interestingly, complete regrowth was observed in 24% and most frequently with S/E and methotrexate cotreatment. Notably, patients with ophiasis or totalis pattern disease or nail pitting were least likely to respond. Our data support the use of S/E as a first- or second-line monotherapy or as an adjunct to methotrexate. Prospective studies may consider the combined use of S/E and methotrexate.

Carlos Morillo-Hernandez, BS,[a] *Jonathan J. Lee, MD,*[b] *and Joseph C. English III, MD*[b]

From the University of Pittsburgh School of Medicine[a] *and the Department of Dermatology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.*[b]

Funding sources: None.

Conflicts of interest: None disclosed.

Presented at the 2019 American Academy of Dermatology Annual Meeting, ePoster Oral Presentation by Carlos Morillo-Hernandez, BS, Washington, DC, March 1-5, 2019.

Reprints not available from the authors.

Correspondence to: Joseph C. English III, MD, Professor of Dermatology, University of Pittsburgh, UPMC North Hills Dermatology, 9000 Brooktree Rd, Ste 200, Wexford, PA 15090

E-mail: englishjc@upmc.edu

REFERENCES

1. Choi JW, Suh DW, Lew BL, Sim WY. Simvastatin/ezetimibe therapy for recalcitrant alopecia areata: an open prospective study of 14 patients. *Ann Dermatol*. 2017;29(6):755-760.
2. Freitas Gouveia M, Trueb RM. Unsuccessful treatment of alopecia areata with simvastatin/ezetimibe: experience in 12 patients. *Skin Appendage Disord*. 2017;3(3):156-160.
3. Lattouf C, Jimenez JJ, Tosti A, et al. Treatment of alopecia areata with simvastatin/ezetimibe. *J Am Acad Dermatol*. 2015;72(2):359-361.
4. Loi C, Starace M, Piraccini BM. Alopecia areata (AA) and treatment with simvastatin/ezetimibe: experience of 20 patients. *J Am Acad Dermatol*. 2016;74(5):e99-e100.
5. Cervantes J, Jimenez JJ, DelCanto GM, Tosti A. Treatment of alopecia areata with simvastatin/ezetimibe. *J Investig Dermatol Symp Proc*. 2018;19(1):S25-S31.

https://doi.org/10.1016/j.jaad.2019.04.047

Brodalumab in the treatment of moderate to severe psoriasis in patients when previous anti-interleukin 17A therapies have failed

To the Editor: Brodalumab is an interleukin-17 (IL-17)-receptor A antagonist approved for the treatment of moderate to severe plaque psoriasis.[1] Other biologic drugs that target the IL-17 pathway include secukinumab and ixekizumab, although these inhibit IL-17A, not its receptor.

Data from the brodalumab pivotal trials showed that previous exposure to biologic drugs did not affect brodalumab's efficacy.[2] However, how patients respond to brodalumab after treatment specifically with anti—IL-17A agents has failed is unknown. This study evaluated the use of brodalumab in patients with moderate to severe plaque psoriasis in whom treatment with secukinumab or ixekizumab was unsuccessful.

The Icahn School of Medicine at Mount Sinai Institutional Review Board approved this study (10/5/2017). This open-label study was conducted on 39 patients with moderate to severe psoriasis enrolled at 3 sites. All investigators were Risk Evaluation and Mitigation certified. Patients received brodalumab, 210 mg, via subcutaneous injection at the standard dosing schedule up to week 16. All patients had previously experienced treatment failure with an IL-17A agent, defined as treatment with secukinumab or ixekizumab for at least 3 months, without achieving Psoriasis Area and Severity Index (PASI)-75 response or a 50% loss of original improvement.

The primary end point for this study was the proportion of patients achieving a score of "0, clear" or "1, almost clear" in the static Physician's Global Assessment (sPGA) score after 16 weeks of treatment. Secondary end points included improvement in PASI scores. Patients were assessed monthly. Statistical analysis was performed using Stata 15.1 software (StataCorp LLC, College Station, TX).

Table I. Baseline demographics and clinical characteristics of included patients

Baseline characteristic	No. (%) or mean ± SD (95% CI) (N = 39)
Age, y	50.74 ± 2.64 (45.57-55.91)
Sex	
Male	25 (64.10)
Female	14 (34.90)
Baseline PASI	20.36 ± 2.24 (15.97-24.75)
Baseline sPGA	3.41 ± 0.08 (3.25-3.57)
Previous treatment failed	
Secukinumab	16 (41.03)
Ixekizumab	19 (48.72)
Secukinumab and ixekizumab	4 (10.26)
Previously failed biologic drugs, No.	2.23 ± 0.29 (1.66-2.80)

CI, Confidence interval; *PASI*, Psoriasis Area and Severity Index; *SD*, standard deviation; *sPGA*, static Physician's Global Assessment.

Of 41 screened patients, 39 met eligibility requirements and were enrolled in the trial, with 34 patients completing all visits through week 16. The most common reason for early discontinuation was lack of efficacy. The demographics and baseline characteristics of the enrolled patients are detailed in Table I.

As-observed results at week 16 showed PASI-75, PASI-90, and PASI-100 scores in 76%, 50%, and 32% of patients who completed the trial, respectively, and 71% of these patients achieved an sPGA of 0 or 1. The data for the 39 patients, using the last observation carried forward, showed that PASI-75, PASI-90, and PASI-100 scores were achieved in 69%, 44%, and 28% of patients, respectively, with 62% achieving sPGA 0 or 1. Using a nonresponder imputation, PASI-75, PASI-90, and PASI-100 scores were seen in 67%, 44%, and 28% of patients, respectively, with 62% achieving sPGA of 0 or 1 (Fig 1) There were 6 adverse events, none of which were thought to be related to the study drug. There were no serious adverse events during the trial.

These results indicate that most patients whose previous treatment with an anti—IL-17A agent was unsuccessful had significant disease improvement with brodalumab. This may be due to the unique action of brodalumab, which inhibits the IL-17 receptor rather than the IL-17A ligand. Overall, these findings suggest that brodalumab may be a good treatment option for psoriasis patients when treatment with other biologic drugs has failed,