$I^2 = 69.16\%$; $P = .001$) compared to nail 2 (ER, 5%; 95% CI, 3-8; $I^2 = 65.22\%$; $P = .002$), nail 3 (ER, 5%; 95% CI, 3-8; $I^2 = 0.00\%$; $P = .83$), nail 4 (ER, 5%; 95% CI, 3-8; $I^2 = 0.00\%$; $P = .74$), and nail 5 (ER, 7%; 95% CI, 3-17; $I^2 = 73.02\%$; $P = .001$) (Supplemental Fig 4; available via Mendeley at https://doi.org/10.17632/y6kxmmz9x9.1). Regarding melanomas of individual toes, the distributions were as follows: hallux: ER, 40%; 95% CI, 25-57; $I^2 = 0.00\%$; $P = .53$); second toe: ER, 17%; 95% CI, 8-33; $I^2 = .00\%$; $P = .83$); third toe: ER, 24%; 95% CI, 13-38; $I^2 = 0.00\%$; $P = .91$); fourth toe: ER, 16%; 95% CI, 7-33; $I^2 = 0.00\%$; $P = .65$); and fifth toe: ER, 21%; 95% CI, 9-41; $I^2 = 9.39\%$; $P = .36$). Egger's regression analysis showed no evidence of publication bias.

Studies suggest that inflammation is a contributing factor to the development of several malignancies.[3] A 2020 meta-analysis exclusively in the Asian population found that areas of plantar pressure were associated with a higher number of melanomas.[4] Previous research suggests that the first toe, including the subungual surface, also has a greater tendency for trauma and repetitive sheer force.[5] Our systematic review and meta-analysis included study populations from all ethnic background and supports the hypothesis of repetitive mechanical stress as a risk factor for plantar melanoma carcinogenesis, with melanoma locations correlating with pressure areas of the feet. Future research exploring distributions of plantar melanoma and biomechanical stress patterns within the same patient population may provide further evidence for this hypothesis.

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Long-term treatment with apremilast in hidradenitis suppurativa: A 2-year follow-up of initial responders

To the Editor: In a previously published randomized controlled trial (RCT) among hidradenitis suppurativa (HS) patients with Hurley stage 1 and 2, we showed that the Hidradenitis Suppurativa Clinical Response (HiSCR) was met in 53.3% (8/15) of patients receiving apremilast 30 mg twice daily for 16 weeks compared with 0% (0/5) in the control group.[1] Responders continued treatment through a compassionate use program, and after 2 years of follow-up, we aimed to assess the longer-term clinical efficacy of apremilast in HiSCR responders from the initial RCT.

After study completion, 100% (8/8) of the responders, all female, chose to continue treatment. Apremilast became available through a compassionate use program 3 to 4 months after the end of the RCT, and patients were assessed approximately every 3 months during routine clinical visits. Three patients reported an increase in symptoms while waiting for the compassionate use program.

Table I. Overview of patients with moderate HS receiving apremilast in the 2-year follow-up

	Characteristics									Adverse effects	HiSCR during follow-up				Reason for discontinuation
Patient number	Age,* y	Sex, F/M	Smoker	BMI, kg/m^2	Hurley stage (1-3)	HS-PGA (1-5)	Comorbidities	Previous medical therapy†	Concomitant HS therapy‡		6 months	12 months	18 months	24 months	
1	25	F	Yes	36.3	1	3	AVSD, AD	Oral clindamycin + rifampicin, adalimumab, infliximab	—	Nausea Diarrhea	—	—	—	—	Pregnancy wish
2	30	F	Quit	24.7	1	3	Hypercholesterolemia	—	Clindamycin 1% lotion Resorcinol 15% cream	Diarrhea	UNK	Yes	Yes	Yes	
3	27	F	Quit	31.1	1	3	—	Alitretinoin, oral minocycline, oral clindamycin	—	Nausea Headache	—	—	—	—	Pregnancy wish
4	48	F	Yes	35.3	2	3	DM type 2, hypercholesterolemia	Clindamycin 1% lotion, resorcinol 15% cream, oral clindamycin + rifampicin	—		No	Yes	Yes	Yes	
5	27	F	No	35.0	1	3	—	Clindamycin 1% lotion, resorcinol 15% cream, oral doxycycline, alitretinoin, isotretinoin, oral clindamycin + rifampicin	Clindamycin 1% lotion	Headache	Yes	Yes	No	Yes	
6	51	F	Yes	30.3	1	3	Migraine	Resorcinol 15% cream, isotretinoin, oral doxycycline, oral clindamycin + rifampicin	Clindamycin 1% lotion Resorcinol 15% cream	Nausea Weight loss	Yes	Yes	Yes	Yes	
7	24	F	Yes	47.0	2	3		Resorcinol 15% cream, oral clindamycin + rifampicin	—	Nausea Diarrhea	—	—	—	—	Nausea
8	47	F	Yes	37.3	1	3	ADD, PTSD	Clindamycin 1% lotion, resorcinol 15% cream, oral minocycline	Clindamycin 1% lotion Resorcinol 15% cream	Diarrhea	—	—	—	—	Remission of disease

AD, Atopic dermatitis; *ADD*, attention deficit disorder; *AVSD*, atrium-ventricular septum defect; *BMI*, body mass index; *DM*, diabetes mellitus; *F*, female; *HiSCR*, Hidradenitis Suppurativa Clinical Response; *HS*, hidradenitis suppurativa; *HS-PGA,* Hidradenitis Suppurativa Physician Global Assessment; *M*, male; *PTSD*, posttraumatic stress disorder; *UNK*, unknown.

*Age at initial start of apremilast treatment.

†Dosage and duration of previous medical therapy was in accordance with current guidelines.

‡Concomitant therapy was used on an as-needed basis by patients with clindamycin 1% lotion recommended up to twice daily on already active lesions, and resorcinol 15% cream recommended once daily and up to 3 times a day on already active lesions.

The 2-year follow-up data were available for 50% (4/8) of initial responders, with the other 4 discontinuing treatment within the first year. All patients (4/4) who continued treatment achieved HiSCR at both the 1-year and the 2-year follow-up visits compared with baseline (Table I). Two patients discontinued apremilast due to an active pregnancy wish at 3 and 6 months after reinitiating treatment. One patient reported intolerable nausea and discontinued after 6 months; another patient stopped treatment on her own after 6 months because she had no more HS symptoms. Manageable gastrointestinal adverse effects were reported by 2 out of 4 patients who continued treatment, 1 patient reported headaches, and 1 obese patient described weight loss of 11 kg. Overall, 75% (6/8) of the participants stated they would recommend apremilast to other patients, including the 2 participants who discontinued treatment because of an active pregnancy wish. One patient did not recommend treatment, and for 1 patient no answer was noted.

Apremilast is a potential long-term treatment option in patients with HS, and this study shows prolonged clinical efficacy in initial responders after 1 and 2 years of treatment. Similar results were seen in a previously published case report describing stable disease course during 72 weeks of treatment.[2] In addition, a case series showed that 6 out of 9 patients continued treatment for a duration of 5 to 9 months.[3] However, clinical efficacy was assessed only 2 to 3 months after the start of treatment, and the reason for treatment discontinuation was not described. In our study, 2 patients with HS stopped treatment because of an active pregnancy wish. Apremilast is currently contraindicated in pregnancy based on a dose-related risk of abortion and fetal death found in animal studies.[4] This potentially influences the long-term use of apremilast in this female-biased disease, which presents itself in women's early reproductive years. A registry (NCT02775500) assessing the outcomes of pregnancies exposed to apremilast is currently underway.[5]

In conclusion, treatment with apremilast 30 mg twice daily shows prolonged efficacy after 1 and 2 years in patients who were able to continue treatment after initially achieving HiSCR at week 16. Although our small study shows promise for apremilast in the long-term treatment of HS, its long-term efficacy will need to be verified in a larger cohort.

We thank Celgene, now Amgen, for providing our patients with HS with apremilast through a compassionate use program.

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Female pattern hair loss in men: A distinct clinical variant of androgenetic alopecia

To the Editor: Female pattern hair loss (FPHL) is characterized by a reduction in hair density over the mid-frontal aspect of the scalp and crown with retention of the frontal hairline. FPHL is known to affect a small subset of men,[1] but descriptions of this