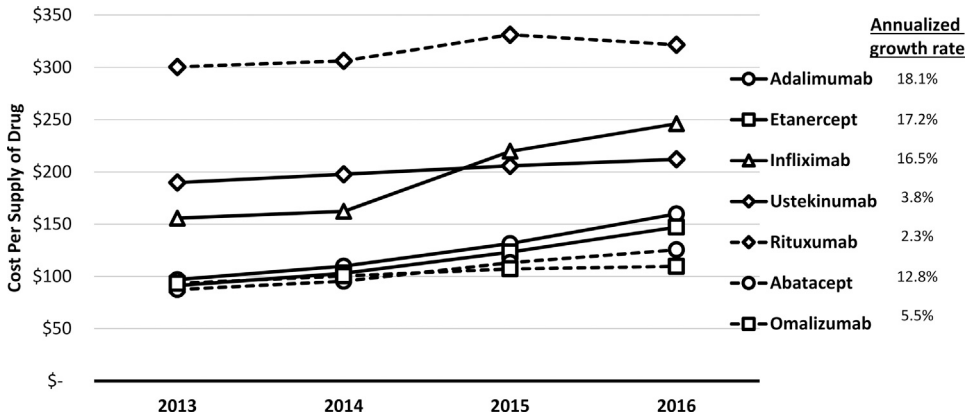

Fig 1. Trends in cost per day of biologic medication. Mean cost per day of medication per provider (95% confidence intervals) are plotted by calendar year for biologics approved for psoriasis (solid line) or only other indications (dashed line). All costs are corrected for inflation with reporting in terms of 2016 US dollars. Annualized growth of expenditure per day of medication for adalimumab, etanercept, infliximab, ustekinumab, rituximab, abatacept, and omalizumab were 18.1%, 17.2%, 16.5%, 3.8%, 2.3%, 12.8%, and 5.5%, respectively.

were most drastic for older drugs. The 4 drugs with price growth >10% were all approved by the US Food and Drug Administration between 9 and 15 years before the beginning of the claims data, while ustekinumab was only approved 4 years earlier. Moreover, drugs with the fastest growth have more indications than ustekinumab, which is only approved for plaque psoriasis. In particular, adalimumab, etanercept, infliximab, and abatacept all have rheumatologic indications, which may be driving pricing increases. These patterns may also suggest that manufacturers increased prices as Medicare and clinicians developed a higher willingness to pay and clinicians developed greater clinical experience and comfort with these drugs.

This study is limited by the lack of transparency in the true pricing of these drugs with respect to negotiated rebates and discounts. Moreover, we cannot confirm the external validity of the study with respect to commercial payers or Medicaid. Future studies are needed to better understand the reasons for cost increases of biologics in the United States.

Partik Singh, BA,[a] and Jonathan I. Silverberg, MD, MPH, PhD[b,c]

Departments of Dermatology,[a] Preventive Medicine,[b] and Medical Social Sciences,[c] Feinberg School of Medicine, Northwestern University, Chicago, Illinois

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Correspondence to: Jonathan Silverberg, MD, MPH, PhD, 676 N St Claire St, Ste 1600, Chicago, IL 60611

E-mail: JonathanISilverberg@gmail.com

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Long-term safety results from a phase 3 open-label study of a fixed combination halobetasol propionate 0.01% and tazarotene 0.045% lotion in moderate-to-severe plaque psoriasis

To the Editor: Psoriasis is a chronic immune-mediated disease with a variable natural history marked by remissions and exacerbations that is

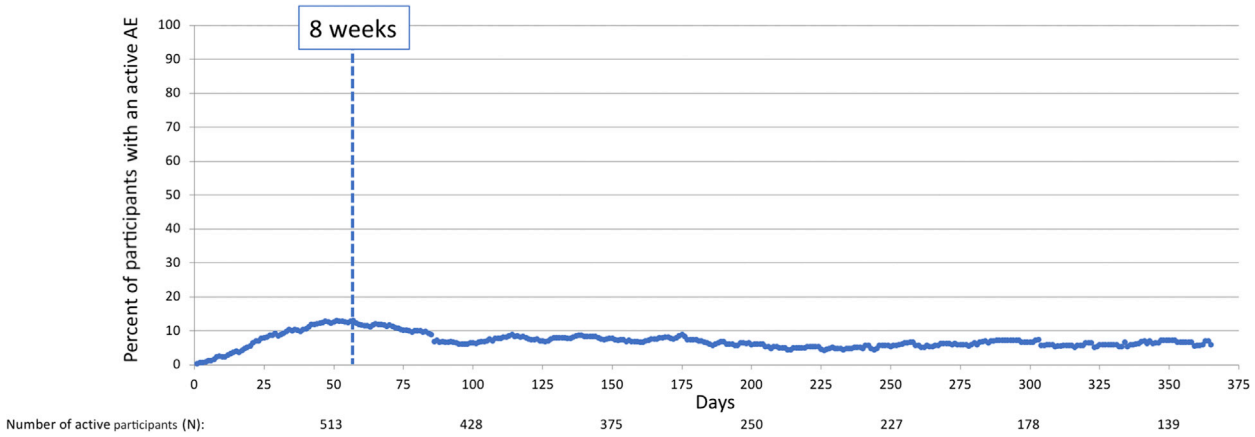

Fig 1. Percentage of participants with active dermal treatment-related AEs, by study day through day 365 (safety population, number of active participants). *AE*, Adverse event.

Table I. Summary of treatment emergent adverse events related to study drug reported by ≥2% of participants, by treatment period (safety population)

Application site reactions	0-12 weeks, N = 527	>12-24 weeks, N = 392	>24-36 weeks, N = 239	>36 weeks, EOS, N = 219
Dermatitis	38 (7.2)	20 (5.1)	6 (2.5)	2 (0.9)
Pruritus	22 (4.2)	6 (1.5)	4 (1.7)	2 (0.9)
Pain	24 (4.6)	2 (0.5)	1 (0.4)	1 (0.5)

Values given are the number of percentage of reported adverse events.
EOS, End of study.

often refractory to treatment. Topical therapy, first-line for mild disease, is often in combination with systemic agents in more severe psoriasis.[1] Approval for potent steroids is limited to 2-4 weeks.[1-3] Recent data on a novel halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ) lotion formulation were published.[4,5] This combination provided synergistic and sustained efficacy over individual active ingredients after daily use for 8 weeks and a 4-week posttreatment period with good tolerability. Treatment success (at least a 2-grade improvement from baseline Investigator's Global Assessment [IGA] score and an IGA score equating to clear or almost clear) deltas (active minus vehicle) at week 8 and week 12 were 42.8% and 31.2%, respectively, for HP/TAZ lotion compared with 32.5% and 20.0%, respectively, for the combined effect (HP+TAZ).[4] The most common treatment-related adverse events (AEs) in the subsequent phase 3 studies were contact dermatitis (6.3%), pruritus (2.2%), and application site pain (2.6%).[5] The incidence of these AEs was much lower than that reported with TAZ alone in the phase 2 study (where the most common treatment-related AEs were application site pain [8.6%], pruritis [6.9%], and erythema [3.4%]).[4]

We report results of a phase 3, long-term multicenter, open-label study in 555 participants (aged 19-87 [mean 51.9] years of age) with moderate-to-severe plaque psoriasis treated with HP/TAZ lotion followed for up to 1 year, with a focus on safety and tolerability. Baseline IGA was 3 (moderate) in 86.5% of participants and 4 (severe) in the remainder. Study participants were treated with HP/TAZ lotion once daily for 8 weeks and then as needed. Only investigator-approved nonmedicated cleansers, moisturizers, and sunscreens were allowed in the treatment areas; no other skin care product use was permitted in the study. Evaluations were carried out at baseline, weeks 2 and 4, and every 4 weeks thereafter.

Treatment success was defined as an IGA score of 0 or 1 (clear or almost clear). Participants without treatment success at week 8 were to be treated for a further 4 weeks; otherwise, they received no further HP/TAZ lotion treatment. All participants were evaluated at week 12; those who demonstrated ≥1-grade improvement in IGA from baseline continued in the study. Only 26 (4.7%) discontinued at week 12 due to lack of efficacy. Treatment continued in 4-week cycles. Participants were treated with HP/TAZ lotion once daily for 4 weeks if they had not achieved treatment success or received no treatment until the next evaluation if they had achieved treatment success, with a maximum continuous exposure of 24 weeks. Participants who did not achieve treatment success after 24 weeks of continuous treatment were discontinued. Consistent with findings in other long-term psoriasis trials of patients with moderate-to-severe disease treated with biologics,[6] one fifth (20.9%) of participants stopped treatment at

24 weeks because of lack of efficacy. Data on adherence to topical treatment suggest these data are better than what would be expected.[7,8]

AE incidence was similar to that reported in the pivotal studies and peaked around day 60, remaining stable from day 90 until study end (Fig 1). Treatment-related AEs reported by ≥2% of participants within any designated treatment period included application site reactions of dermatitis, pruritus, and pain (Table I). Overall, 7.5% of participants discontinued due to treatment-emergent AEs: dermatitis and pruritus (7 persons each) and pain (6 persons) were the most frequent. Treatment-emergent serious AEs (SAEs) were noted in 3.3% of participants; none were considered treatment-related. Three participants discontinued due to SAEs (cellulitis gangrenous, pericardial effusion, small intestine adenocarcinoma). No deaths were reported, and no clinically noticeable trends identified with regard to other local skin AEs (eg, skin atrophy, folliculitis, telangiectasia, and striae). AEs were not correlated with the timing or duration of treatment applications, frequency, and duration of use. Marked improvements in baseline severity of itching, dryness, and burning/stinging occurred within 2 weeks and were sustained over the course of the study.

In summary, we report the long-term safety profile of HP/TAZ lotion in participants with moderate-to-severe psoriasis when used as monotherapy over a period of 1 year. Though infrequent, AEs reported were consistent with a product containing TCS and retinoid.[9,10] Study limitations include the open-label design and lack of follow-up beyond 1 year.

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Mark G. Lebwohl, MD,[a] Jeffrey L. Sugarman, MD, PhD,[b] Linda Stein Gold, MD,[c] David M. Pariser, MD,[d] Tina Lin, PharmD,[e] Radhakrishnan Pillai, PhD,[f] Gina Martin, MOT,[f] Susan Harris, MS,[g] and Robert Israel, MD[g]

From the Icahn School of Medicine at Mount Sinai, New York, New York[a]; University of California, San Francisco, California[b]; Henry Ford Hospital, Detroit, Michigan[c]; Virginia Clinical Research Inc, Norfolk, Virginia[d]; Ortho Dermatologics, Bridgewater, New Jersey[e]; Dow Pharmaceutical Sciences Inc (division of Valeant Pharmaceuticals, North America LLC), Petaluma, California[f]; and Valeant Pharmaceuticals, Bridgewater, New Jersey[g]

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Correspondence to: Mark G. Lebwohl, MD, Icahn School of Medicine at Mount Sinai, New York, NY 10029

E-mail: lebwohl@aol.com

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Assessment of clinician accuracy for diagnosing melanoma on the basis of electrical impedance spectroscopy score plus morphology versus lesion morphology alone

To the Editor: Early detection and excision are important for optimizing melanoma patients' outcomes.[1] Making diagnoses on the basis of morphologic characteristics is challenging and can result in potentially unneeded biopsies or, worse, missed melanomas.[2] There is increasing interest in developing adjunctive tools that improve diagnostic accuracy.[3] Electrical impedance spectroscopy (EIS) has been shown to be highly sensitive in melanoma diagnosis.[4] The process of malignant transformation alters the electrical properties of cutaneous tissue—changes that are sensed by EIS. A low-voltage electrode is applied to the lesion; the resultant painless current propagates through the skin and is sensed by a receiving electrode on the same probe. The device generates a score of 0-10, corresponding to the different predictive values[4] for melanoma. Although an EIS device is Food and Drug Administration–approved and available (Nevisense, Scibase-AB, Stockholm, Sweden), little is known regarding how it affects clinicians' management of pigmented lesions. The goals of this study were to assess the impact of EIS results on clinicians' diagnostic accuracy and biopsy decisions.

In total, 164 dermatology trainees completed an online survey presenting clinical images of 45 pigmented lesions (28 benign, 17 melanoma). For each image, respondents were asked if they would recommend biopsy on the basis of morphologic assessment alone, and then asked again once presented with the corresponding EIS score (along with positive and negative predictive values[4]). The proportion of clinical decisions for which the addition of EIS score altered the decision to biopsy was calculated. In addition, the sensitivity, specificity, and proportion of missed melanomas and benign biopsies were determined for morphologic assessment alone and for morphologic assessment plus EIS score. Significance testing was performed using McNemar test for categorical variables and paired *t* tests for continuous variables.

Overall, 7380 clinical decisions (164 respondents × 45 lesions) were made on the basis of morphology alone and 7380 were made on the basis of morphology plus EIS score. The decision to biopsy was made in 4527 of 7380 cases on the basis of morphology alone and 4553 of 7380 cases on the basis of morphology plus EIS. The EIS results altered the individual biopsy decision in 24.3% of cases (Table I). The addition of the EIS score resulted in 402 fewer missed melanomas and a net decrease of 376 benign biopsies ($P < .001$, Table II). When including the EIS score, the mean sensitivity of respondents for ruling out melanoma increased from 80.7% to 95.2% ($P < .001$) and mean specificity from 50.4% to 58.6% ($P < .001$).

A diagnostic device is only useful if it affects clinical management and improves accuracy. In this

Table I. Change in clinical management (decision to biopsy) of pigmented lesions of 164 clinicians with the addition of electrical impedance spectroscopy score versus morphologic assessment of clinical image alone

Lesion type	No change in clinical management with EIS, n (%)	EIS results altered management from biopsy to observation, n (%)	EIS results altered management from observation to biopsy, n (%)	Overall change in decision to biopsy, n (%)
Benign, N* = 4592	3242 (70.6)	863 (18.8)	487 (10.6)	1350 (29.4)
Melanoma, N† = 2788	2350 (84.3)	18 (0.6)	420 (15.1)	438 (15.7)
Overall, N‡ = 7380	5592 (75.7)	881 (11.9)	917 (12.4)	1798 (24.3)

EIS, Electrical impedance spectroscopy.
*Total number of clinical decisions made on benign lesions (obtained by multiplying number of survey respondents, 164, by the number of benign lesions in the study, 28).
†Total number of clinical decisions made on malignant lesions (obtained by multiplying number of survey respondents, 164, by the number of malignant lesions in the study, 17).
‡Total number of clinical decisions made on benign and malignant lesions (obtained by multiplying number of survey respondents, 164, by the number of lesions included the study, 45).