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Research Letter

Dear Editor,

Development and validation of a new method for potential use of Psoriasis Area and Severity Index in teledermatology

The Psoriasis Area and Severity Index (PASI) is a validated, frequently used, psoriasis severity assessment tool.¹⁻⁵ In several countries, PASI assessment is compulsory for reimbursement considerations.^{2,5} PASI calculation requires full body evaluation of the severity of erythema,

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Conflicts of interest: HP and YD are current employees and NB is a former employee of Eli Lilly and Company. YD and NB own shares in Eli Lilly and Company. JW and KG are consultants and advisory board members for AbbVie, Celgene, Eli Lilly and Company, Janssen, and Novartis. MG is a speaker/consultant and/or advisory board member for AbbVie, Akros, Amgen, Arcutis Pharmaceuticals, Inc., Boehringer Ingelheim, Celgene, Dermira, Eli Lilly and Company, Galderma, Medimmune, Merck, Novartis, Elizer, Regeneron Pharmaceuticals, Inc., Roche, Sanofi Genzyme, Sun Pharmaceuticals Industries Ltd., UCB, and Valeant Pharmaceuticals International, Inc.

thickness and scaling of psoriatic plaques in four body regions (head/neck, trunk, upper limbs and lower limbs). Some components of PASI (i.e. plaque thickness, extent of scalp involvement) are difficult to assess by teledermatology, making its incorporation into clinical practice challenging.

We sought to develop and validate a model for estimating total PASI score using only the practical PASI features suitable for assessment in teledermatology (i.e. scores for erythema, scaling and affected areas of the trunk, lower limbs and upper limbs; Tele-PASI).

MATERIALS AND METHODS

Tele-PASI model development and statistical analyses

The Tele-PASI model was developed (for full details see Supplementary Materials 1) using screening PASI data from 4215 patients enrolled in three multicentre, double-blind, randomised controlled ixekizumab trials (UNCOVER-1, NCT01474512; UNCOVER-2, NCT01597245; UNCOVER-3, NCT01646177). 4,5 Of these, 3866 randomised patients (≥ 18 years) with moderate-to-severe plaque psoriasis (≥ 6 months), defined as $\geq 10\%$ body surface area, static Physician's Global Assessment (sPGA) ≥ 3 , and PASI ≥ 12 were included in the model.

The correlation between scores of thickness and erythema and between scores of thickness and scaling were analysed within each and across the four PASI body regions (head/neck, upper limbs, trunk and lower limbs) (Supplementary Figure S1). Difficult to assess thickness scores were estimated from erythema and scaling scores, and head/neck scores from upper limb and trunk scores

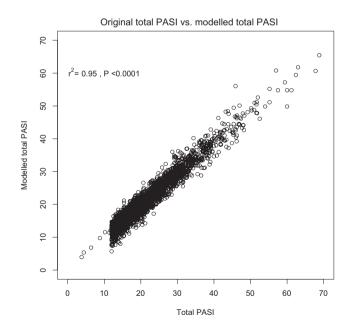


Figure 1 Correlation between original and modelled total PASI scores in the Tele-PASI model development population. Abbreviations: PASI, Psoriasis Area and Severity Index.

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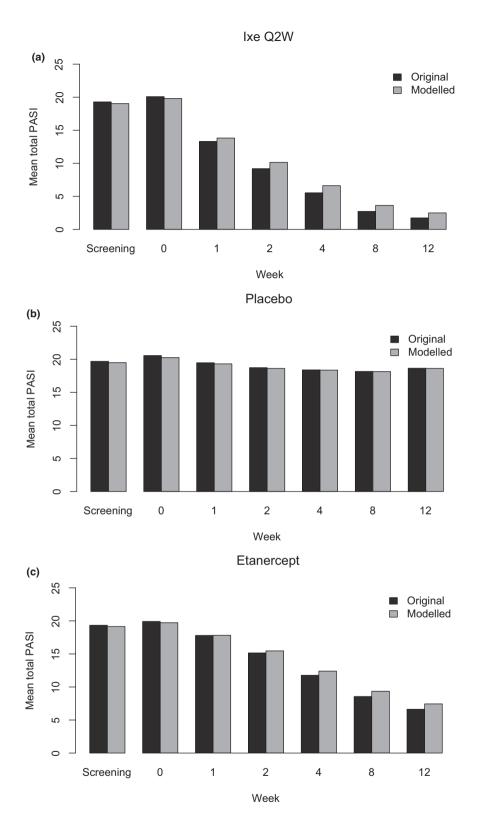


Figure 2 Original and modelled total PASI scores from screening to Week 12 in each treatment group in model development population (r^2 range for IXE [Q2W, Q4W], ETN and placebo groups were 0.945-0.9982; P < 0.0001). n range is from screening to Week 12. Only data from the first 12 weeks of treatment were used to validate the Tele-PASI model (n range for IXE Q2W: n = 1119-1169; placebo: n = 746-792; etanercept: n = 701-740). Abbreviations: ETN, etanercept; IXE Q2W, 80 mg ixekizumab every 2 weeks; n, number of patients; PASI, Psoriasis Area and Severity Index.

(using linear regression). Both were then included in the PASI calculations as surrogates for real measures (Tele-PASI model: Tables S1 and S2).

From Pearson correlation coefficients and associated r^2 -values the respective P-values were calculated. All data processing and statistical analyses were performed using R version 3.0.1.

External Tele-PASI model validation

PASI data from baseline up to 12 weeks of treatment from 1691 randomised patients from three additional multicentre, double-blind, randomised controlled ixekizumab trials (RHBP, NCT02513550; RHBS, NCT02561806; RHBZ, NCT02634801) were used to validate the Tele-PASI model. 6-8

RESULTS

At screening, thickness significantly correlated with both erythema and scaling in all four body regions. Correlation between the original total PASI score and the total PASI score excluding thickness was very high and almost unchanged when the head/neck components were excluded (Supplementary Figure S2).

In the model development population, very high correlations were observed between original and modelled total PASI scores at baseline ($r^2 = 0.95$, P < 0.0001) (Fig. 1) and at all follow-up visits, irrespective of treatment (Fig. 2 and Supplementary Figure S3).

Similarly, very high correlations between the original and modelled total PASI scores at baseline and at all follow-up visits in all treatment groups were observed in the external model validation population (Supplementary Figures S4-S6).

DISCUSSION

The Tele-PASI model described here estimates total PASI scores before and during treatment using only scores for erythema, scaling and affected areas of the trunk, lower limbs and upper limbs. During model development, very strong correlations between the original and modelled total PASI scores were observed in all treatment groups at screening, baseline and during treatment. The model performance was confirmed using data from three independent trials including various systemic treatments. The modelled total PASI scores correlated very strongly with the original total PASI scores at baseline and during treatment, suggesting that Tele-PASI may be an appropriate tool for PASI assessment in teledermatology settings.

The strengths of this study were the use of data from large scale, double-blind, placebo- and active-comparator controlled trials for model development and validation that included various systemic treatments. Because Tele-PASI was developed with data from adults with moderate-to-severe plaque psoriasis who were enrolled in clinical trials for up to 12 weeks of treatment only and because data were collected during physical examinations and not via photos/live

imaging, further real-world validation, including in patients undergoing longer-term treatment, is required.

This study has demonstrated that Tele-PASI accurately estimates total PASI for patients with moderate-to-severe psoriasis receiving various systemic treatments. The Tele-PASI may supplement PASI in clinical practice, especially when face-to-face consultations are not possible and evaluation is made in teledermatology settings (see Supplementary Materials 4 - Worksheet – an online spreadsheet that allows calculation of the Tele-PASI score).

ACKNOWLEDGEMENT

The authors thank all the dedicated patients who participated in each of the trials, as well as the investigators and site personnel for their active involvement in all trials described in this study.

ROLE OF THE SPONSOR

Eli Lilly and Company was involved in the study design, data collection, data analysis and preparation of the manuscript.

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Fig S1. Schematic explaining how the Tele-PASI model was developed and validated.

Fig S2. Correlation studies in the Tele-PASI model development population based on screening PASI.

Fig S3. Original and modelled total PASI scores from screening to Week 12 in IXE Q4W treatment group in model development population (r^2 range for IXE [Q2W, Q4W], ETN, and placebo groups was 0.945–0.9982; P < 0.0001).

Fig S4. Original and modelled total PASI scores at baseline and all follow-up visits in each treatment group in external Tele-PASI model validation population (RHBP trial).

Fig S5. Original and modelled total PASI scores from baseline to Week 12 in each treatment group in external Tele-PASI validation population (RHBS trial).

Fig S6. Original and modelled total PASI scores from baseline to Week 12 in each treatment group in external Tele-PASI validation population (RHBZ trial).

Table S1. Parameters estimate the Tele-PASI model components from the respective scores obtained at screening in the three UNCOVER trials using linear regressions

Table S2. Example of original PASI and modelled total PASI calculations

Supplementary Material

Method S1. Model Development Methods.

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Research Letter

Dear Editor,

Web Analytics: What dermatologists need to know

Online dermatology resources for patients and healthcare providers include a growing number of websites, social media accounts and mobile applications, making it challenging for resources to retain an audience.

Funding: No funding to declare.

Conflict of interest: AO is the founder and editor-in-chief of DermNet NZ.

DermNet NZ (www.dermnetnz.org) is an authoritative dermatology website founded in 1996.² DermNet initially published patient information; articles targeting health professionals were introduced later. In May 2020, DermNet had 2449 topic pages and >40 000 images.²

Google Analytics is a tool that gives an overview of user behaviour. Researchers have evaluated cardiology, genetics and sexual health websites using Google Analytics.³⁻⁵ We have not found any similar published dermatological studies.

A basic version of Google Analytics, free for Google account holders, can determine

- •When users visited (*Home* report);
- •Who was interested (Audience report);
- •What they looked for (Behaviour report); and
- •How they arrived (Acquisition report).
- •Google Trends can highlight search interest trends, surveys can define user roles and 'Contact Us' form data can show *why* users visited.
- •We analysed Google Analytics and Google Trends data from 1 May 2018 to 30 April 2020 for DermNet NZ.

Each page requires a Google tracking code.⁶ Google Analytics collects cookies containing anonymous user information.⁶ DermNet displays a privacy policy to comply with European data protection regulations about such cookies (GDPR).⁷⁻⁸

The Google Analytics *Home* page uses a heat map to signal user numbers at different times. Data are displayed in the owner's time zone, which is GMT+ 12/+13 for DermNet. Traffic was highest between 2 am and 4 pm on weekdays due to DermNet's global audience.

The *Audience* section contains user numbers, geographical and device information.

A user is a unique browser. A hit is a user action that sends data to Google Analytics. Actions that trigger hits include loading a page and viewing an image. A session is generally recorded when a user produces hits within 30 min.⁹

In two years, 22.2 million users had 34.5 million sessions on DermNet. The top five countries of origin were the United States (44%), the United Kingdom (13%), Australia (8%), Canada (5%) and India (5%). More than 90% of users set English as their preferred browser language.

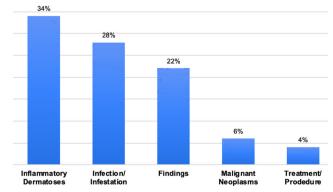


Figure 1 Top 50 DermNet NZ pages: Content breakdown.