Network meta-analysis of biologic treatments for psoriasis using absolute Psoriasis Area and Severity Index values ≤1, 2, 3 or 5 derived from a statistical conversion method

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Abstract
Background In practice, the goal of treatment for patients with psoriasis is to achieve almost clear or clear skin and maintain disease control, regardless of baseline disease severity. However, identifying absolute Psoriasis Area and Severity Index (PASI) values for new treatment goals is challenging, as most clinical trials report relative PASI 50, 75, 90 or 100 improvements but rarely absolute PASI values achieved.

Objective Our objective was to illustrate a statistical conversion method that was developed to derive absolute PASI values from available clinical trial data on relative PASI improvements. The results of network meta-analyses (NMAs) based on these derived data were then compared with those of NMAs based on the corresponding relative PASI improvement data for selected biologics for moderate-to-severe psoriasis.

Methods The PASI statistical conversion method was applied to relative PASI improvement data for 11 biologic treatment regimens and placebo at 12 weeks using data from 50 published studies. The respective proportions of patients reaching absolute PASI values ≤1, 2, 3 or 5 were then calculated. Frequentist NMAs (Rücker method) were subsequently used to compare efficacy results across relative and absolute PASI data.

Results The ranking of included treatment regimens for patients achieving absolute PASI 0 to 8 was aligned with results for relative PASI scores (from 100 to 60) at end of induction therapy. Across the range of PASI scores considered, the most effective treatment regimens based on both absolute and relative PASI NMAs were brodalumab 210 mg every 2 weeks and ixekizumab 80 mg every 2 weeks, followed by guselkumab 100 mg every 8 weeks and risankizumab 150 mg every 12 weeks.

Conclusion Data generated using this mathematical model will be useful to inform ongoing scientific discussions on treatment goals in the absence of primary absolute PASI data for all available treatments for moderate-to-severe plaque psoriasis.

Conflict of interest
UM has been an advisor and/or received speaker’s honoraria and/or received grants and/or participated in clinical trials of the following companies: AbbVie, Almirall, Amgen, Arista, Boehringer-Ingelheim, Bristol-Myers Squibb, Celgene, Dr. Reddy’s, Eli Lilly, Foamicon, Formycon, Forward Pharma, Janssen, LEO Pharma, Medac, Novartis, Phi-Stone, Pierre Fabre, Sanofi-Aventis, UCB. RBW has received consulting fees from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Celgene, Janssen, LEO Pharma, Eli Lilly, Novartis, Pfizer, Sanofi, Xenpor & UCB; and has received research grants from AbbVie, Almirall, Amgen, Celgene, Janssen, Lilly, LEO Pharma, Novartis, Pfizer & UCB. CLL has received funding from AbbVie, Actavis, Amgen, Celgene, Coherus, Dermira, Eli Lilly, Galderma, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Sandoz, Stiefel, UCB, and Wyeth. DS, HP, SH and MD are all full-time employees of Eli Lilly and Company. KR has served as an advisor and/or paid speaker for and/or participated in clinical trials sponsored by: AbbVie, Affibody, Almirall, Amgen,
Psoriasis is a chronic, often life-long inflammatory skin disease without a cure. The disease burden is high, particularly in moderate-to-severe psoriasis, and the associated quality of life impairment is considerable.

During treatment for psoriasis, the success of therapy should be regularly assessed. In practice, the goal of treatment for patients with psoriasis is not only to achieve almost clear or clear skin but also to ensure maintenance of disease control. Therefore, treatment goals should enable physicians to assess primary non-response after induction of a new treatment and secondary non-response during maintenance therapy thereafter. In 2011, a European consensus defined maintenance therapy as successful when a $\geq 75\%$ reduction from baseline Psoriasis Area and Severity Index (PASI 75) is achieved and a failure when a $\geq 50\%$ reduction from baseline PASI (PASI 50) is not achieved. In patients with a PASI 50 but not PASI 75, the Dermatology Life Quality Index (DLQI) should be used as a treatment decision-making tool. More recently, improvement of 90% or better with respect to baseline PASI (PASI90) is considered as treatment success by the European Medicines Agency and the latest guidelines are shifting away from percentage reduction and towards a target outcome. Any relative (percentage) improvement measure will relate to a baseline value. For different baseline severities, the same relative improvement may therefore indicate very different outcomes. Defining appropriate targets for absolute PASI values emphasizes the goals of clear or almost clear skin but also to ensure maintenance of disease control.

Since publication of the European consensus, there has been major progress in drug development, leading to the registration of new biologic agents. Clear or almost clear skin (PASI 100 or absolute PASI 0) can now be achieved by many patients, prompting ongoing discussion as to whether treatment goals should be adapted based on these new efficacy levels.

The objective of this analysis was to illustrate a statistical conversion method that was developed to derive absolute PASI values from available clinical trial data on relative PASI improvements. The results of network meta-analyses (NMAs) based on these derived absolute PASI data were then compared with the results of NMAs based on the corresponding relative PASI improvement data for selected biologic treatments for moderate-to-severe psoriasis. Should the results of these NMAs be aligned, our analysis will demonstrate the value of this mathematical model in filling an important data gap to inform evolving treatment goals.

Methods

Systematic literature review

A systematic literature review (SLR), conducted to evaluate systemic treatments for moderate-to-severe plaque psoriasis, provided data for the statistical conversion method. The literature review consisted of an original SLR and three updates that analysed data from January 1990 to October 2018, inclusive. Clinical efficacy data on systemic treatments for psoriasis were systematically identified through searches of databases (including Embase, Medline, Medline Daily Update, Medline In-Process and Cochrane databases), and grey literature (including selected conference proceedings, trial registries and Health Technology Assessment (HTA) websites). Further detail on the methodology used in the original and updated SLRs is provided in Appendix S1.

Suitable studies for extraction of PASI data for the statistical model, i.e., Phase 2 or 3, comparator-controlled trials of biologic treatments for moderate-to-severe psoriasis with double-blind induction phases, were selected from the SLR. All systemic biologics licensed for the treatment of chronic plaque psoriasis available globally at the time of the SLR were included: pivotal studies of risankizumab were also included. A single-dose regimen was selected for each biologic based on the registered product label for each treatment. Studies, treatments and doses included in this analysis were selected to illustrate the statistical conversion method, not to undertake an NMA in line with HTA guidance aimed at determining the comparative efficacy of included therapies.

Extracted data for each study treatment group included sample size, the time at which the efficacy of induction therapy was assessed (assessment time), baseline PASI (both the minimum PASI allowed for entry into the study and the mean [standard
Table 1  Studies and data selected for analysis. Data presented in bold type are imputed.

| Study         | Treatment regimen                                                                 | Sample size | Assessment time (week) | Baseline PASI | Mean (SD) Baseline PASI | PASI 50 | PASI 75 | PASI 90 | PASI 100 |
|---------------|-----------------------------------------------------------------------------------|-------------|------------------------|---------------|-------------------------|-------|--------|--------|---------|
| AMAGINE-1     | Brodalumab 210 mg week 0, 1, 2, Q2W                                                | 222         | 12                     | 20.4 (3.8)    | 92.31                   | 75.8  | 69.0   | 59.7   | 53.6    |
|               | Placebo                                                                           | 220         | 12                     | 19.7 (7.5)    | 17.24                   | 2.7   | 0.9    | 0.5    | 0.0     |
| AMAGINE-2     | Brodalumab 210 mg week 0, 1, 2, Q2W                                                | 612         | 12                     | 20.3 (3.8)    | 93.66                   | 86.0  | 70.0   | 44.0   |         |
|               | Placebo                                                                           | 309         | 12                     | 20.4 (8.2)    | 23.43                   | 8.0   | 3.0    | 1.0    |         |
|               | Ustekinumab 45 mg ≤ 100 kg/90 mg > 100 kg† weeks 0 and 4                           | 300         | 12                     | 20.0 (8.4)    | 84.99                   | 70.0  | 47.0   | 22.0   |         |
| AMAGINE-3     | Brodalumab 210 mg week 0, 1, 2, Q2W                                                | 624         | 12                     | 20.4 (3.8)    | 92.31                   | 86.0  | 70.0   | 44.0   |         |
|               | Placebo                                                                           | 315         | 12                     | 20.1 (8.7)    | 20.27                   | 6.0   | 2.0    | 0.3    |         |
|               | Ustekinumab 45 mg ≤ 100 kg/90 mg > 100 kg† weeks 0 and 4                           | 313         | 12                     | 20.1 (8.4)    | 85.17                   | 69.0  | 48.0   | 19.0   |         |
| Bachelez et al. 2015 | Etanercept 50 mg BIW                                                                 | 335         | 12                     | 19.4 (7.9)    | 80.3                    | 58.8  | 32.2   | 15.73  |         |
|               | Placebo                                                                           | 107         | 12                     | 19.5 (7.5)    | 20.6                    | 5.6   | 0.9    | 0.44   |         |
| Bagel et al. 2012 | Etanercept 50 mg BIW                                                                | 62          | 12                     | 19.5 (7.3)    | 85.0                    | 59.0  | 25.0   | 10.50  |         |
|               | Placebo                                                                           | 62          | 12                     | 20.1 (7.8)    | 7.0                     | 5.0   | 2.0    | 0.06   |         |
| Cai et al. 2017 | Adalimumab 80 mg then 40 mg Q2W                                                   | 338         | 12                     | 28.2 (12.0)   | 92.59                   | 77.8  | 55.6   | 13.3   |         |
|               | Placebo                                                                           | 87          | 12                     | 25.6 (11.0)   | 28.93                   | 11.5  | 3.4    | 1.1    |         |
| CHAMPION      | Adalimumab 80 mg then 40 mg Q2W                                                   | 108         | 12                     | 20.2 (7.5)    | 90.7                    | 76.9  | 48.1   | 11.1   |         |
| Saurat et al. 2008 | Adalimumab 80 mg then 40 mg Q2W                                                   | 53          | 12                     | 19.2 (6.9)    | 26.4                    | 15.1  | 7.5    | 0.0    |         |
| CIMPACT       | Certolizumab pegol 400 mg week 0, 2, 4, Q2W                                        | 167         | 12                     | 20.8 (7.7)    | 87.78                   | 66.7  | 34.0   | 12.77  |         |
| Lebwohl et al. 2018 | Certolizumab pegol 400 mg week 0, 2, 4, Q2W                                        | 170         | 12                     | 21.0 (8.2)    | 75.36                   | 53.3  | 27.1   | 8.91   |         |
|               | Etanercept 50 mg BIW                                                               | 57          | 12                     | 19.1 (7.1)    | 12.59                   | 5.0   | 0.2    | 0.01   |         |
| Chaudhari et al. 2001 | Infliximab 5 mg/kg week 0, 2, 6, Q8W                                              | 11          | 10                     | 22.1 (11.5)   | 90.46                   | 82.0  | 59.72  | 31.89  |         |
|               | Placebo                                                                           | 11          | 10                     | 20.3 (5.5)    | 34.74                   | 18.0  | 6.70   | 0.37   |         |
| CIMPASI-1     | Certolizumab pegol 400 mg week 0, 2, 4, Q2W                                        | 88          | 16                     | 19.6 (7.9)    | 90.40                   | 75.8  | 43.6   | 18.51  |         |
| Gottlieb et al. 2018a | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM                                         | 51          | 16                     | 19.8 (7.5)    | 17.78                   | 6.5   | 0.4    | 0.24   |         |
| CIMPASI-2     | Certolizumab pegol 400 mg week 0, 2, 4, Q2W                                        | 87          | 16                     | 19.5 (6.7)    | 91.41                   | 82.6  | 55.4   | 24.21  |         |
| Gottlieb et al. 2018b | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM                                         | 49          | 16                     | 17.3 (5.3)    | 33.54                   | 11.6  | 4.5    | 0.36   |         |
| CLARITY       | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM                                          | 550         | 12                     | 20.7 (8.1)    | 96.92                   | 88.0  | 66.5   | 38.1   |         |
| Bagel et al. 2018c | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM                                         | 552         | 12                     | 20.8 (8.0)    | 90.16                   | 74.2  | 47.9   | 20.1   |         |
| CLEAR         | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM                                          | 337         | 12                     | 21.7 (8.5)    | 96.89                   | 91.0  | 72.8   | 38.9   |         |
| Thaci et al. 2015 | Ustekinumab 45 mg ≤ 100 kg/90 mg > 100 kg† weeks 0 and 4                           | 339         | 12                     | 21.5 (8.1)    | 88.10                   | 79.1  | 53.4   | 25.7   |         |
| Study                  | Treatment regimen                      | Sample size | Assessment time (week) | Baseline PASI cut-off | Mean (SD) baseline PASI | PASI 50 | PASI 75 | PASI 90 | PASI 100 |
|-----------------------|----------------------------------------|-------------|------------------------|------------------------|-------------------------|---------|---------|---------|----------|
| de Vries et al. 2017  | Etanercept 50 mg BIW                   | 23          | 12                     | 10                     | 15.9 (5.1)              | 60.9    | 21.7    | 0.0     | 0.0      |
|                       | Infliximab 5 mg/kg week 0, 2, 6, Q8W   | 25          | 12                     | 10                     | 17.8 (9.7)              | 96.0    | 76.0    | 20.0    | 4.0      |
| ERASURE               | Placebo                                | 248         | 12                     | 12                     | 21.4 (9.1)              | 18.70   | 4.5     | 1.2     | 0.8      |
| Langley et al. 2014   | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM | 245         | 12                     | 12                     | 22.5 (9.2)              | 91.39   | 81.6    | 59.2    | 28.6     |
| EXPRESS                | Infliximab 5 mg/kg week 0, 2, 6, Q8W   | 77          | 10                     | 12                     | 22.8 (8.7)              | 8.0     | 3.0     | 1.0     | 0.07     |
| Reich et al. 2005     | Placebo                                | 301         | 10                     | 12                     | 22.9 (9.3)              | 91.0    | 80.0    | 57.0    | 27.63    |
| EXPRESS II             | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM | 245         | 12                     | 12                     | 20.4 (7.5)              | 90.24   | 75.5    | 45.2    | 18.80    |
| Menter et al. 2007    | Placebo                                | 208         | 10                     | 12                     | 19.8 (7.7)              | 11.40   | 1.9     | 0.5     | 0.04     |
| FEATURE               | Placebo                                | 59          | 12                     | 12                     | 21.1 (8.5)              | 9.47    | 0.0     | 0.0     | 0.0      |
| Blauvelt et al. 2015  | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM | 59          | 12                     | 12                     | 20.7 (8.0)              | 90.12   | 75.9    | 50.3    | 24.1     |
| FIXTURE               | Etanercept 50 mg BIW                   | 326         | 12                     | 12                     | 23.2 (9.8)              | 65.89   | 44.0    | 20.7    | 4.3      |
| Langley et al. 2014   | Placebo                                | 326         | 12                     | 12                     | 24.1 (10.5)             | 14.25   | 4.9     | 1.5     | 0.0      |
| EXPRESS II             | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM | 327         | 12                     | 12                     | 23.9 (9.9)              | 89.06   | 77.1    | 54.2    | 24.1     |
| IXORA-S                | Ixekizumab 160 mg then 80 mg Q2W       | 136         | 12                     | 10                     | 19.9 (8.2)              | 96.10   | 88.2    | 72.8    | 36.0     |
| Paul et al. 2019      | Ustekinumab                            | 166         | 12                     | 10                     | 19.8 (9.0)              | 86.20   | 68.7    | 42.2    | 14.5     |
| JUNCTURE              | Placebo                                | 61          | 12                     | 12                     | 19.4 (6.7)              | 11.29   | 3.3     | 0.0     | 0.0      |
| Paul et al. 2015      | Secukinumab 300 mg week 0, 1, 2, 3, 4, QM | 60          | 12                     | 12                     | 18.9 (6.4)              | 96.06   | 86.7    | 55.0    | 26.7     |
| Leonardi et al. 2003  | Etanercept 50 mg BIW                   | 164         | 12                     | 10                     | 18.4 (9.0)              | 74.0    | 49.0    | 22.0    | 4.84     |
| M02-528               | Placebo                                | 166         | 12                     | 10                     | 18.3 (7.7)              | 14.0    | 4.0     | 1.0     | 0.06     |
| Gordon et al. 2006    | Adalimumab 80 mg then 40 mg Q2W        | 45          | 12                     | 12                     | 16.7 (7.1)              | 76.0    | 53.0    | 24.0    | 11.0     |
| M04-688               | Placebo                                | 52          | 12                     | 12                     | 16.0 (7.5)              | 15.24   | 4.0     | 0.63    | 0.0      |
| Asahina et al. 2010   | Adalimumab 80 mg then 40 mg Q2W        | 43          | 12                     | 12                     | 30.2 (10.9)             | 75.48   | 53.5    | 30.2    | 11.85    |
| M10-114               | Placebo                                | 46          | 12                     | 12                     | 29.1 (11.8)             | 12.33   | 2.2     | 0.0     | 0.00     |
| Gottlieb et al. 2011  | Etanercept 50 mg BIW                   | 141         | 12                     | 12                     | 19.4 (8.0)              | 80.62   | 56.0    | 32.64   | 15.29    |
| M10-315               | Placebo                                | 68          | 12                     | 12                     | 18.5 (6.9)              | 22.46   | 7.4     | 2.45    | 0.78     |
| Strober et al. 2011   | Etanercept 50 mg BIW                   | 139         | 12                     | 12                     | 18.5 (6.0)              | 66.27   | 39.8    | 13.7    | 5.8      |
| Nakagawa et al. 2015  | Brodalumab 210 mg week 0, 1, 2, Q2W    | 37          | 12                     | 12                     | 28.0 (14.3)             | 95.72   | 94.6    | 91.9    | 59.5     |
| Ohtsuki et al. 2018   | Gusekumab 100 mg week 0, 1, 2, Q8W     | 63          | 16                     | 12                     | 26.7 (12.2)             | 95.2    | 84.1    | 69.8    | 27.0     |
| ORION                 | Placebo                                | 64          | 16                     | 12                     | 25.9 (12.3)             | 14.1    | 6.3     | 0.0     | 0.0      |
| Ferris et al. 2018    | Gusekumab 100 mg week 0, 1, 2, Q8W     | 62          | 12                     | 12                     | 20.8 (7.8)              | 90.3    | 77.4    | 54.8    | 30.6     |
| Papp et al. 2005      | Placebo                                | 194         | 12                     | 10                     | 19.5 (8.8)              | 77.0    | 49.0    | 21.0    | 5.05     |
|                      | Placebo                                | 193         | 12                     | 10                     | 18.6 (8.6)              | 9.0     | 3.0     | 1.0     | 0.07     |
| Study | Treatment regimen | Sample size | Assessment time (week) | Baseline PASI cut-off | Mean (SD) baseline PASI | PASI 50 | PASI 75 | PASI 90 | PASI 100 |
|-------|-------------------|-------------|------------------------|----------------------|--------------------------|--------|--------|--------|---------|
| Papp et al. 2012<sup>46</sup> | Brodalumab 210 mg week 0, 1, 2, Q2W | 40 | 12 | 12 | 20.6 (7.8) | 90.0 | 82.0 | 75.0 | 62.0 |
| Placebo | 38 | 12 | 12 | 18.9 (5.9) | 16.0 | 0.0 | 0.0 | 0.0 |
| Papp et al. 2015<sup>47</sup> | Placebo | 46 | 12 | 12 | 19.5 (7.8) | 17.67 | 4.0 | 1.66 | 0.50 |
| Tildrakizumab 100 mg week 0, 4, Q12W | 89 | 12 | 12 | 19.8 (7.6) | 81.95 | 61 | 35.21 | 15.04 |
| Reich et al. 2012<sup>48</sup> | Certolizumab pegol 400 mg week 0, 2, 4, Q2W | 58 | 12 | 12 | 22.0 (8.1) | 93.0 | 82.8 | 46.6 | 18.69 |
| Placebo | 59 | 12 | 12 | 22.6 (8.8) | 12.0 | 6.8 | 1.7 | 0.06 |
| reSURFACE 1 | Placebo | 155 | 12 | 12 | 19.3 (7.1) | 21.69 | 5.8 | 2.6 | 1.3 |
| Tildrakizumab 100 mg week 0, 4, Q12W | 309 | 12 | 12 | 20.0 (7.9) | 85.52 | 63.6 | 15.04 |
| Reich et al. 2017<sup>b49</sup> | Placebo | 156 | 12 | 12 | 20.0 (7.6) | 80.78 | 61.2 | 38.8 | 12.4 |
| Etanercept 50 mg BIW | 313 | 12 | 12 | 20.7 (7.4) | 85.52 | 61.2 | 38.8 | 12.4 |
| Placebo | 312 | 12 | 12 | 20.5 (7.6) | 80.78 | 61.2 | 38.8 | 12.4 |
| REVEAL | Adalimumab 80 mg then 40 mg Q2W | 814 | 12 | 12 | 19.0 (7.1) | 86.22 | 68.0 | 37.0 | 14.0 |
| Placebo | 398 | 12 | 12 | 18.8 (7.1) | 8.75 | 5.0 | 2.0 | 0.06 |
| SPIRIT | Infliximab 5 mg/kg week 0, 2, 6, Q8W | 99 | 10 | 12 | 20.0 (7.8) | 97.0 | 87.9 | 57.6 | 25.54 |
| Placebo | 51 | 10 | 12 | 18.0 (7.4) | 21.6 | 5.9 | 1.3 | 0.0 |
| Torii et al. 2010<sup>18</sup> | Infliximab 5 mg/kg week 0, 2, 6, Q8W | 35 | 10 | 12 | 31.9 (12.8) | 85.17 | 68.6 | 39.77 | 14.28 |
| Placebo | 19 | 10 | 12 | 33.1 (15.6) | 17.56 | 5.0 | 2.0 | 0.0 |
| Ultimate-1 | Placebo | 102 | 12 | 12 | 20.5 (6.7) | 22.90 | 9.8 | 3.0 | 0.59 |
| Tildrakizumab 150 mg week 0, 4, Q12W | 294 | 12 | 12 | 20.6 (7.7) | 95.70 | 86.8 | 68.0 | 32.02 |
| Ustekinumab 45 mg ≤ 100 kg/90 mg > 100 kg<sup>†</sup> weeks 0 and 4 | 100 | 12 | 12 | 20.1 (6.8) | 84.34 | 70.0 | 45.0 | 21.12 |
| Ultimate-2 | Placebo | 98 | 12 | 12 | 18.9 (7.3) | 23.36 | 8.2 | 3.0 | 0.80 |
| Tildrakizumab 150 mg week 0, 4, Q12W | 294 | 12 | 12 | 20.5 (7.8) | 96.68 | 89.7 | 30.90 |
| Ustekinumab 45 mg ≤ 100 kg/90 mg > 100 kg<sup>†</sup> weeks 0 and 4 | 99 | 12 | 12 | 18.2 (5.9) | 85.25 | 69.7 | 47.0 | 18.81 |
| UNCOVER-1 | Placebo | 433 | 12 | 12 | 20.0 (8.0) | 96.06 | 89.1 | 70.9 | 35.3 |
| Ixekizumab 160 mg then 80 mg Q2W | 431 | 12 | 12 | 20.0 (9.0) | 12.40 | 3.9 | 0.5 | 0.0 |
| UNCOVER-2 | Placebo | 358 | 12 | 12 | 19.0 (7.0) | 64.94 | 41.6 | 18.7 | 5.3 |
| Ixekizumab 160 mg then 80 mg Q2W | 351 | 12 | 12 | 19.0 (7.0) | 96.68 | 89.7 | 70.7 | 40.5 |
| UNCOVER-3 | Placebo | 168 | 12 | 12 | 21.0 (8.0) | 17.81 | 2.4 | 0.6 | 0.6 |
| Etanercept 50 mg BIW | 382 | 12 | 12 | 21.0 (8.0) | 77.16 | 53.4 | 25.7 | 7.3 |
| Ixekizumab 160 mg then 80 mg Q2W | 385 | 12 | 12 | 21.0 (8.0) | 96.80 | 87.3 | 68.1 | 37.7 |
| Placebo | 193 | 12 | 12 | 21.0 (8.0) | 18.40 | 7.3 | 3.1 | 0.0 |
deviation (SD)] baseline PASI) and any relative PASI findings at the assessment time (PASI 50, PASI 75, PASI 90 and PASI 100, as reported).

When available, 12-week data were selected because this was the most common primary assessment time-point. For treatments with different induction periods (adalimumab, certolizumab pegol and guselkumab, 16 weeks; infliximab, 10 weeks), data for these assessment times were used and were analysed as per the available 12-week data.

The current version of the PASI conversion method needed complete sets of baseline PASI values and response rates for all four PASI thresholds (PASI 50, 75, 90 and 100) at the assessment time for all study treatments. Therefore, where required data could not be extracted from the literature, missing values [baseline PASI cut-offs (inclusion criteria), mean (SD) baseline PASI values, and PASI 50, PASI 75, PASI 90 and PASI 100 response rates at the assessment time-point] were imputed using a random forest algorithm trained on all non-missing values from the complete SLR (see Appendix S2 for details). Study treatments and data included in this analysis are summarized in Table 1.

### Statistical conversion method

The PASI statistical conversion method used in this analysis has been described in detail elsewhere. In brief, the method uses available relative PASI data to estimate the proportion of patients with absolute PASI less than or equal to a given bound. In this manuscript, the focus is on absolute PASI ≤ 1, 2, 3 or 5 at a given assessment time (i.e. 12 weeks). It is based on a statistical model describing the relationship between absolute mean (SD) baseline and assessment time-point PASI values (ranging from 0 to 72), baseline PASI study inclusion criteria and relative PASI improvements (PASI 50, PASI 75, PASI 90 and PASI 100) achieved at the assessment time-point. The proportion of patients reaching PASI ≤ 1, 2, 3 or 5 (or any other PASI cut-off point), as well as other statistics such as mean (SD) assessment time-point PASI values, can be derived based on this model. In this analysis, the PASI conversion method was applied to the full set of relative PASI results.

### Table 1

| Study | Treatment regimen | Sample size | Assessment time (week) | Baseline PASI cut-off | Mean (SD) baseline PASI | PASI 50 | PASI 75 | PASI 90 | PASI 100 |
|-------|-------------------|-------------|------------------------|-----------------------|-------------------------|---------|---------|---------|----------|
| VIP Mehta et al. 2018 | Adalimumab 80 mg then 40 mg Q2W | 33 | 12 | 19.0 (6.0) | 72.81 | 47.0 | 20.9 | 4.60 |
| | Placebo | 31 | 12 | 18.0 (8.0) | 22.50 | 7.0 | 2.49 | 0.86 |
| VIP-U Gelfand et al. 2018 | Placebo | 175 | 12 | 20.3 (7.9) | 23.65 | 11.0 | 3.35 | 0.69 |
| | Ustekinumab 45 mg ≤ 100 kg/90 mg > 100 kg† weeks 0 and 4 | 271 | 12 | 20.9 (8.0) | 90.07 | 77.0 | 50.10 | 17.82 |
| VOYAGE 1 Blauvelt et al. 2017 | Adalimumab 80 mg then 40 mg Q2W | 334 | 16 | 22.4 (9.0) | 90.14 | 73.1 | 49.7 | 20.6 |
| | Guselkumab 100 mg week 0, 4, Q8W | 329 | 16 | 22.1 (9.5) | 97.41 | 91.2 | 73.3 | 37.4 |
| | Placebo | 174 | 16 | 20.4 (8.7) | 21.39 | 5.7 | 2.9 | 0.6 |
| VOYAGE 2 Reich et al. 2017a | Adalimumab 80 mg then 40 mg Q2W | 248 | 16 | 21.7 (9.0) | 85.20 | 68.5 | 46.8 | 20.6 |
| | Guselkumab 100 mg week 0, 4, Q8W | 496 | 16 | 21.9 (8.8) | 94.99 | 86.3 | 70.0 | 34.1 |
| | Placebo | 248 | 16 | 21.5 (8.0) | 22.62 | 8.1 | 2.4 | 0.8 |
| X-PLORE Gordon et al. 2015 | Adalimumab 80 mg then 40 mg Q2W | 43 | 12 | 20.2 (7.6) | 85.24 | 67.5 | 39.84 | 13.69 |
| | Guselkumab 100 mg week 0, 4, Q8W | 42 | 12 | 20.4 (7.7) | 90.34 | 75.0 | 47.37 | 19.47 |
| | Placebo | 42 | 12 | 21.8 (10.0) | 17.53 | 0.0 | 0.0 | 0.0 |
| Yang et al. 2012 | Infliximab 5 mg/kg week 0, 2, 6, Q8W | 84 | 12 | 23.9 (10.7) | 96.36 | 87.3 | 65.03 | 30.65 |
| | Placebo | 45 | 12 | 25.3 (12.7) | 50.76 | 20.9 | 4.93 | 0.31 |

Missing values imputed using the random forest algorithm (see Appendix S2) are highlighted in bold. BiW, twice weekly; PASI 50/75/90/100, the percentage of patients achieving PASI improvement of ≥50%/75%/90%/100%; PASI, Psoriasis Area and Severity Index; Q12W, every 12 weeks; Q2W, every 2 weeks; Q8W, every 8 weeks; QM, every month.† The dose of ustekinumab was based on patients’ body weight: 45 mg for patients with a body weight ≤100 kg and 90 mg for patients >100 kg.
(summarized in Table 1; missing values imputed). For all treatment regimens and studies in the network, the resulting parameter estimates were used to derive the proportion of patients achieving absolute PASI values in the range from 0 to 8 (at steps of 0.2) to show the efficacy across cut-offs. The parameter estimates from the PASI conversion method were also used to derive respective relative PASI values in the range from PASI 100 to PASI 60 (at steps of 1%) to compare the cumulative distributions for the absolute as well as the relative PASI values at the assumed assessment time-point of 12 weeks.

**Network meta-analyses**

Frequentist fixed-effect NMA (Rücker method) was applied to each of the calculated absolute PASI values in the range from 0 to 8 (at steps of 0.2) and to each of the relative PASI values in the range from PASI 100 to PASI 60 (at steps of 1%), using placebo as reference. Placebo profiles were obtained by pooling the placebo results obtained from using the PASI conversion method on all placebo-controlled studies (weighted means). Risk difference (RD) was selected as the effect measure for this analysis, as it is generally well understood and consistent with other effect measures. The RDs of each treatment from placebo (parameter estimates from the NMA) were added to these basic pooled placebo profiles, allowing a respective PASI profile to be obtained for each treatment. These profiles were then plotted as network diagrams and forest plots of RD from placebo for the NMA (including placebo) identified in the network, the resulting parameter estimates were used to derive the proportion of patients achieving absolute PASI values at assumed baseline PASI cut-off value (lowest PASI value at study entry) of 12, although eight studies specified a cut-off value of 10. For five studies that did not specify the baseline PASI cut-off, a value of 12 was assigned.

The 95% confidence intervals (CIs) for RD presented are only indicative, as variability resulting from the estimation process of the PASI conversion method was not incorporated. No formal testing of the precision of the values or the significance of the relative rankings was undertaken.

To contrast the findings of the absolute PASI NMA with the results of the relative PASI NMA, graphs are also presented for PASI 75, PASI 90 and PASI 100.

All calculations were performed in R version 3.0.1, and R package netmeta was used for performing the Rücker NMAs.

**Results**

**Description of selected study data**

Overall, data were extracted from 50 studies involving 12 treatment regimens (including placebo) identified in the SLR for inclusion in these analyses (Table 1). The dosage regimens evaluated are summarized in Table 1. Inclusion criteria for most studies specified a baseline PASI cut-off value (lowest PASI allowed at study entry) of 12, although eight studies specified a cut-off value of 10. For five studies that did not specify the baseline PASI cut-off, a value of 12 was assigned.

The treatment groups included from each study ranged in size from 11 to 814 patients (Table 1). The smallest study sample size was that of a placebo-controlled evaluation of infliximab and the largest was in a placebo-controlled evaluation of adalimumab. The observed mean baseline PASI values ranged from 15.9 (etanercept) to 33.1 (placebo), although most mean baseline PASI values were between 18 and 23. The greatest variability was in a study evaluating infliximab (SD of 15.6 for placebo), and the lowest was in a study comparing etanercept and infliximab (SD of 5.1 for etanercept). Mean baseline PASI values were not reported and were imputed in 10 instances counting individual treatment arms within studies; 14 SD values were

| Table 2 | PASI conversion method-estimated proportion of patients with absolute PASI ≤ 1, 2, 3 and 5 and derived relative PASI 75, 90 and 100 after approximately 12 weeks of treatment |
| --- | --- | --- |
| **Treatment regimen** | **Proportion of patients achieving absolute PASI (%)** | **Proportion of patients achieving relative PASI (%)** |
| | PASI ≤ 1 | PASI ≤ 2 | PASI ≤ 3 | PASI ≤ 5 | PASI 100 | PASI 90 | PASI 75 |
| Adalimumab 80 mg then 40 mg Q2W | 23.94 | 40.41 | 54.03 | 72.23 | 14.16 | 40.97 | 70.41 |
| Brodalumab 210 mg week 0, 1, 2, Q2W | 56.07 | 71.83 | 81.34 | 89.88 | 41.28 | 71.77 | 88.06 |
| Certolizumab pegol 400 mg week 0, 2, 4, Q2W | 27.44 | 44.78 | 58.00 | 74.43 | 16.69 | 44.15 | 72.74 |
| Etanercept 50 mg BIW | 10.53 | 21.18 | 32.62 | 51.79 | 6.48 | 21.29 | 49.64 |
| Guselkumab 100 mg week 0, 4, Q8W | 49.77 | 67.39 | 78.01 | 88.66 | 33.02 | 68.09 | 87.59 |
| Infliximab 5 mg/kg week 0, 2, 6, Q8W | 34.47 | 51.89 | 64.85 | 80.97 | 21.66 | 52.84 | 80.32 |
| Ixekizumab 160 mg then 80 mg Q2W | 55.10 | 71.85 | 81.93 | 88.66 | 33.02 | 68.09 | 87.59 |
| Placebo | 0.37 | 0.64 | 1.30 | 3.81 | 0.34 | 0.73 | 4.32 |
| Risankizumab 150 mg week 0, 4, Q12W | 48.37 | 66.12 | 76.47 | 86.02 | 31.05 | 64.99 | 85.12 |
| Secukinumab 300 mg week 0, 1, 2, 3, 4, QM | 41.68 | 57.56 | 69.14 | 83.08 | 29.84 | 58.54 | 82.11 |
| Tildrakizumab 100 mg week 0, 4, Q12W | 20.00 | 33.97 | 46.50 | 64.13 | 13.06 | 33.70 | 62.08 |
| Ustekinumab 45 mg ≤ 100 kg/90 mg > 100 kg | 26.76 | 42.54 | 55.59 | 72.59 | 17.82 | 42.59 | 70.56 |

*BIW, twice weekly; PASI 75/90/100, the percentage of patients achieving PASI improvement of ≥75%/90%/100%; PASI, Psoriasis Area and Severity Index; Q12W, every 12 weeks; Q2W, every 2 weeks; Q8W, every 8 weeks; QM, every month.*

†The dose of ustekinumab was based on patients’ body weight: 45mg for patients with a body weight ≤100 kg and 90 mg for patients >100 kg.
imputed. Missing values imputed using the random forest algorithm are highlighted in bold in Table 1. PASI score was reported after 12 weeks in 40 studies. The closest available values to the 12 weeks were reported after 10 weeks in five studies and after 16 weeks in five studies.

**Application of the PASI conversion method to the study data**

Table 2 shows the PASI conversion method-estimated proportions of patients with absolute PASI $\leq 1$, $\leq 2$, $\leq 3$ and $\leq 5$ after 12 weeks of treatment. The biologics brodalumab (210 mg at weeks 0, 1, 2 and then every 2 weeks) and ixekizumab (at a loading dose of 160 mg followed by 80 mg every 2 weeks) had the highest proportions of patients achieving absolute PASI scores of $\leq 1$, $\leq 2$, $\leq 3$ or $\leq 5$; guselkumab (100 mg at weeks 0, 4 and then every 8 weeks), risankizumab (150 mg at weeks 0, 4 and then every 12 weeks) and secukinumab (300 mg at weeks 0, 1, 2, 3, 4 and then every month) had the next highest proportions of patients achieving these absolute PASI scores.

**Figure 1** Scatter plots for derived and reported Psoriasis Area and Severity Index (PASI) 75 and PASI 90 values; derived values were estimated using the PASI conversion method.

**Figure 2** Fixed-effect model forest plots (RD and 95% CI) for absolute PASI NMAs. RD 95% CIs are only indicative and should be interpreted cautiously, as the variability coming from the estimation process of the PASI method was not incorporated. *The dose of ustekinumab was based on patients’ body weight: 45 mg for patients with a body weight $\leq 100$ kg and 90 mg for patients $>100$ kg. BIW, twice weekly; CI, confidence interval; PASI, Psoriasis Area and Severity Index; Q2W, every 2 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; QM, every month; RD, risk difference.*
(a) PASI 100

Contrast with placebo

- Brodalumab 210 mg week 0, 1, 2, Q2W
- Ixekizumab 160 mg then 80 mg Q2W
- Guselkumab 100 mg week 0, 4, Q8W
- Risankizumab 150 mg week 0, 4, Q12W
- Secukinumab 300 mg week 0, 1, 2, 3, 4, QM
- Infliximab 5 mg/kg week 0, 2, 6, Q8W
- Ustekinumab 45 mg ≤100 kg/90 mg >100 kg weeks 0 and 4
- Certolizumab pegol 400 mg week 0, 2, 4, Q2W
- Adalimumab 80 mg then 40 mg Q2W
- Tildrakizumab 200 mg week 0, 4, Q12W
- Etanercept 50 mg BIW

Fixed-effect model

RD 95% CI

- 0.41 [0.38; 0.43]
- 0.38 [0.35; 0.40]
- 0.33 [0.30; 0.36]
- 0.31 [0.27; 0.35]
- 0.30 [0.27; 0.32]
- 0.21 [0.19; 0.24]
- 0.17 [0.15; 0.20]
- 0.16 [0.13; 0.20]
- 0.14 [0.12; 0.15]
- 0.13 [0.10; 0.15]
- 0.06 [0.05; 0.07]

(b) PASI 90

Contrast with placebo

- Brodalumab 210 mg week 0, 1, 2, Q2W
- Ixekizumab 160 mg then 80 mg Q2W
- Guselkumab 100 mg week 0, 4, Q8W
- Risankizumab 150 mg week 0, 4, Q12W
- Secukinumab 300 mg week 0, 1, 2, 3, 4, QM
- Infliximab 5 mg/kg week 0, 2, 6, Q8W
- Ustekinumab 45 mg ≤100 kg/90 mg >100 kg weeks 0 and 4
- Adalimumab 80 mg then 40 mg Q2W
- Tildrakizumab 200 mg week 0, 4, Q12W
- Etanercept 50 mg BIW

Fixed-effect model

RD 95% CI

- 0.71 [0.69; 0.73]
- 0.70 [0.67; 0.72]
- 0.67 [0.64; 0.70]
- 0.64 [0.60; 0.68]
- 0.58 [0.55; 0.61]
- 0.52 [0.49; 0.55]
- 0.43 [0.39; 0.48]
- 0.42 [0.39; 0.44]
- 0.40 [0.38; 0.42]
- 0.33 [0.29; 0.37]
- 0.21 [0.19; 0.22]

(c) PASI 75

Contrast with placebo

- Ixekizumab 160 mg then 80 mg Q2W
- Brodalumab 210 mg week 0, 1, 2, Q2W
- Guselkumab 100 mg week 0, 4, Q8W
- Risankizumab 150 mg week 0, 4, Q12W
- Secukinumab 300 mg week 0, 1, 2, 3, 4, QM
- Infliximab 5 mg/kg week 0, 2, 6, Q8W
- Ustekinumab 45 mg ≤100 kg/90 mg >100 kg weeks 0 and 4
- Adalimumab 80 mg then 40 mg Q2W
- Tildrakizumab 200 mg week 0, 4, Q12W
- Etanercept 50 mg BIW

Fixed-effect model

RD 95% CI

- 0.86 [0.84; 0.88]
- 0.84 [0.82; 0.86]
- 0.83 [0.81; 0.86]
- 0.81 [0.77; 0.85]
- 0.78 [0.75; 0.80]
- 0.76 [0.73; 0.79]
- 0.68 [0.63; 0.73]
- 0.66 [0.64; 0.69]
- 0.66 [0.64; 0.68]
- 0.58 [0.54; 0.62]
- 0.45 [0.43; 0.47]
Table 2 also summarizes the derived PASI 75, 90 and 100 values. The same pattern of results with respect to treatments with the highest proportions of patients achieving relative PASI 75, 90 and 100 improvements was observed. Close to perfect correlations \((r = 0.998, r = 0.996)\) between derived and reported PASI 75 and PASI 90 values, respectively, were observed (Fig. 1). PASI 100 rates for derived and reported values are completely identical because the observed values were directly incorporated into the PASI conversion method estimation.

Network meta-analyses of absolute and relative PASI

Fixed-effect model forest plots for absolute PASI \(\leq 1, 2, 3\) and 5, illustrating RDs with 95% CIs for each treatment comparative to placebo, and corresponding full network diagrams are shown in Fig. 2 and Fig. S2 (Supporting Information), respectively. When fixed-effect model forest plots (versus placebo) and corresponding full network diagrams for relative PASI 75, 90 and 100 were considered (Fig. 3 and Fig. S3, Supporting Information, respectively), findings were similar to the respective values for absolute PASI \(\leq 5\), \(\leq 2\) and \(\leq 1\).

Compared with placebo, treatment with brodalumab showed the greatest difference in the proportion of patients achieving PASI \(\leq 1\) (RD 56%), followed by ixekizumab (RD 55%), guselkumab (RD 49%), risankizumab (RD 48%) and secukinumab 300 mg (RD 41%; Fig. 2a). The treatments with the smallest difference from placebo were etanercept 50 mg twice weekly (RD 10%), tildrakizumab 100 mg at weeks 0, 4 and then every 12 weeks (RD 20%) and adalimumab at a loading dose of 80 mg followed by 40 mg every 2 weeks (RD 24%). Confidence intervals are indicative of the precision of the RD estimates. The same general ranking of treatments was observed in the results of the relative PASI NMA: treatment with brodalumab showed the greatest difference in the proportion of patients achieving PASI 100 (RD 41%) versus placebo, followed by ixekizumab (RD 38%), guselkumab (RD 33%), risankizumab (RD 31%) and secukinumab (RD 30%; Fig. 3a). Similarly, treatments with the smallest difference from placebo were the same as in the absolute PASI \(\leq 1\) analysis.

Results for PASI \(\leq 2\) showed the same general ranking of treatments (Fig. 2b), with brodalumab and ixekizumab (both RD 71%), followed by guselkumab (RD 67%), risankizumab (RD 65%), and secukinumab (RD 57%) showing the greatest differences compared with placebo. Again, the smallest differences versus placebo were observed for etanercept (RD 21%), tildrakizumab (RD 33%) and adalimumab (RD 40%). Very similar results were observed for PASI 90 analyses, with brodalumab (RD 71%) followed by ixekizumab (RD 70%), guselkumab (RD 67%), risankizumab (RD 64%) and secukinumab (RD 58%) showing the greatest differences compared with placebo (Fig. 3b). Etanercept, tildrakizumab and adalimumab were the treatments with the smallest difference from placebo.

When PASI \(\leq 3\) and PASI \(\leq 5\) were considered (Fig. 2c,d), ixekizumab (RDs 81% and 89%, respectively), followed by brodalumab (RDs 80% and 86%, respectively), guselkumab (RDs 77% and 85%, respectively), risankizumab (RDs 75% and 82%, respectively) and secukinumab (RDs 68% and 79%, respectively) showed the greatest differences compared with placebo. The smallest differences versus placebo were seen with etanercept (PASI \(\leq 3\) RD 31% and PASI \(\leq 5\) RD 48%), tildrakizumab (RDs 45% and 60%, respectively) and adalimumab (RDs 53% and 68%, respectively). The same general ranking of treatments was observed for PASI 75 analysis: treatment with ixekizumab showed the greatest difference in the proportion of patients achieving PASI 75 (RD 86%) versus placebo, followed by brodalumab (RD 84%), guselkumab (RD 83%), risankizumab (RD 81%) and secukinumab (RD 78%; Fig. 3c). Once again, the treatments with the smallest difference from placebo were also the same as in the absolute PASI \(\leq 5\) analysis.

Details of the cumulative proportions of patients achieving absolute PASI 0 to 8 at week 12 (derived from the PASI conversion method) with each of the included treatment regimens are presented in Fig. 4a. More than 80% of patients achieved PASI \(\leq 8\) with all biologic treatment regimens except those of etanercept and tildrakizumab. However, the consistently most effective treatment regimens at each absolute PASI cut-off (PASI \(\leq 1, 2, 3\) and 5) were ixekizumab and brodalumab, followed by guselkumab and risankizumab, and then infliximab 5 mg/kg at weeks 0, 2, 6 and then every 8 weeks and secukinumab. The consistently least effective biologic regimens were those containing etanercept and tildrakizumab. This was again in line with results for relative PASI scores at week 12 (from 100 to 60; Fig. 4b).

Discussion

Descriptions of drug efficacy and, subsequently, definitions of treatment goals for chronic plaque psoriasis have been based on the proportions of patients achieving 50%, 75%, 90% or 100% relative improvements from baseline in PASI. However, relative PASI data have major shortcomings, as any relative improvement relates to a baseline value, resulting in the same relative improvement indicating very different outcomes for different patients. In clinical practice, the aim of any moderate-to-severe psoriasis treatment is to obtain clear or almost clear skin. This goal is relevant from both the patient’s and the physician’s
perspective to ensure ongoing control of the disease and related inflammation. However, in cases where examination of the entire body to confirm PASI 100 might be challenging in clinical practice, establishing absolute PASI values may serve as a useful and relevant alternative. Unfortunately, the definition of treatment goals using absolute PASI thresholds has been hindered by a lack of data, since absolute PASI values have only been assessed and published in few studies until very recently.6,19

Using this statistical conversion method, it was possible to calculate absolute PASI data from clinical trials of recommended agents.
and new biologic therapies in which baseline PASI values and relative improvement rates were reported. The data generated with this method provide a sound basis for the reassessment of treatment goals using absolute PASI. In the clinical trial programme for ixekizumab, both relative and absolute PASI values were assessed. Using these trial results for the analyses demonstrated that a comparable number of patients (about 80% for ixekizumab 160 mg then 80 mg every 2 weeks) reached PASI 90 and PASI ≤2 and a similar proportion (approximately 90%) reached PASI 75 and PASI ≤5. Similarly, another recent study used data from a UK real-world population-based cohort to evaluate treatment targets in psoriasis. Based on data from 13,422 patients, this study found that both an absolute PASI ≤2 and Physician Global Assessment (PGA) clear/almost clear were concordant with PASI 90 in 90% of cases. These findings were robust to subgroups based on timing of assessment, baseline disease severity and treatment modality, suggesting an absolute PASI ≤2 and PGA clear/almost clear represent relevant disease endpoints to inform future treatment goals in psoriasis.

This study has some inherent limitations. For the majority of the included therapies, absolute PASI levels are not published, so the statistical conversion method could only be assessed using the large dataset of patient-level data for ixekizumab and etanercept from the UNCOVER studies. In the absence of head-to-head trials, NMAs offer the best possible approach to comparing treatments. However, the selection of studies for an NMA is always subject to debate, and the ongoing publication of new studies with new therapies will require updates to this analysis in the future if used to determine the comparative efficacy of included therapies (e.g. for HTA or clinical decision-making), rather than as an illustration of the value of the statistical method, as per this analysis. Additionally, the NMA statistical method used could be questioned. Random effects NMA or Bayesian NMA (with non-informative priors because we had no prior information) could have been used as an alternative to the fixed-effect frequentist approach; however, the Rücker method chosen is an established scientific method. RD was chosen as the effect measure for this analysis, but other effect measures could of course be analysed based on the available data. The RD CIs presented have only indicative character, as variability resulting from the PASI conversion method estimation process was not incorporated. The imputation of missing PASI information also added further uncertainty to the findings (see Appendix S2 for details). Finally, NMAs, in general, are based on various assumptions that are very hard to verify (i.e. homogeneity of the included studies with respect to e.g., assessment time-points, dose selection, definitions of endpoints), although statistical methods were applied in this analysis to address heterogeneity wherever possible. Thus, results and, in particular, the presented rank order of drug effects (resulting from the tool) should be interpreted with care. Furthermore, psoriasis requires long-term treatment and some systemic treatments are faster acting than others. The current analysis considered only treatment efficacy at 10–16 weeks; therefore, it would also be preferable to be able to make a comparative assessment of therapies over several years rather than only over the first few months of treatment. However, long-term, randomized, active comparator studies to inform this type of analysis are unfortunately sparse at best.

In conclusion, the short-term data generated using this mathematical model will be useful to inform the scientific discussion on evolving treatment goals for plaque psoriasis in the absence of absolute PASI data on all available treatments and support treatment decision-making in clinical practice. Although illustrative, results support the use of brodalumab, ixekizumab, guselkumab, risankizumab and secukinumab in patients with moderate-to-severe psoriasis to achieve absolute PASI as well as traditional relative PASI improvement treatment goals.

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Author contributions

All authors have contributed to the conception, design, analysis and interpretation of the data, and have approved the presented findings. All authors have revised the manuscript critically for intellectual content and have given final approval for publication. All authors agree to be accountable for all aspects of the work.

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Supporting information
Additional Supporting Information may be found in the online version of this article:
Appendix S1. Systematic literature review methodology.
Appendix S2. Imputation of missing study information.
Figure S1. Combined Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for original systematic literature review and all updates.
Figure S2. Full network diagrams for absolute PASI network meta-analyses.
Figure S3. Full network diagrams for relative PASI network meta-analyses.
Table S1. Systematic literature review search terms.
Table S2. List of systematic literature review criteria for the studies.