Efficacy of Systemic Treatments of Psoriasis on Pruritus: A Systemic Literature Review and Meta-Analysis

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In the course of the last 30 years, several studies have clearly documented that pruritus is a very frequent symptom of psoriasis and its impact on the patients’ quality of life. The variety of available systemic treatments for psoriasis is increasing rapidly. Our objective was to assess their efficacy on pruritus based on a systematic literature review. A systematic literature search was performed using PubMed and Trip Database (from January 1990 to September 2016) to find published clinical trials for the treatments of psoriasis, and then a meta-analysis was performed. Among 516 articles identified, 35 studies were retained in the systematic review. At baseline, the high prevalence of pruritus (80–100%) was confirmed. The meta-analysis included 13 trials using a 0 to 10 itch scale and highlighted that all treatments evaluated reduced pruritus. Anti-IL-17, JAK inhibitors, adalimumab, and apremilast were all shown to be effective in reducing pruritus in psoriasis with variable effect size magnitudes. Our systematic review highlights that systemic treatments, including UVB phototherapy, improve pruritus in psoriasis but that it is not necessarily correlated with lesion recovering. Nonetheless, these results must be displayed carefully because there are so many variable endpoints in different studies.


INTRODUCTION

For a long time, psoriasis was considered as a nonpruritic dermatosis. Yet within the last 30 years, a number of studies have clearly documented that pruritus is a very frequent symptom of psoriasis (Yosipovitch et al., 2000). Newbold (1977) seems to be the first to describe pruritus as a common phenomenon in psoriasis because it was present in 92% of 200 hospitalized patients with psoriasis. Several studies have confirmed the prevalence of pruritus in 60–90% of patients with psoriasis, with a reported mean severity of 5.2–6.4 points on the itch visual analog scale (VAS, 0–10) (Amatya et al., 2008; Reich et al., 2010; Yosipovitch et al., 2000). Most patients with psoriasis consider pruritus as the most bothersome symptom of their disease (Lebwohl et al., 2014; Reich et al., 2014). Many patients also rank their pruritus as annoying or unbearable (Amatya et al., 2008). Patients with pruritus report a greater reduction in their health-related quality of life (QoL), including the ability to sleep, compared with those without pruritus (Gowda et al., 2010). The intensity of pruritus correlates with the degree of QoL impairment (Reich et al., 2010).

The efficacy of treatments of psoriasis is commonly judged on the Psoriasis Area and Severity Index (PASI), but it is also important to consider the resolution of pruritus, because it is the first preoccupation of the patients (Lebwohl et al., 2014; Reich et al., 2014) and because there is no specific antipruritic therapy to treat itch in psoriasis.

The aim of this study was to conduct a systematic review of the literature and a meta-analysis to evaluate the effect of systemic psoriasis treatments on psoriatic itch.

RESULTS

Among the 516 identified articles, 438 were excluded after reading the title or abstract, 45 were excluded after reading the article, and 33 were selected. Figure 1 represents the flowchart. In two articles, the results of two different studies were presented, so there were a total of 35 studies, evaluating the effects of UVB phototherapy, calcineurin inhibitors (ciclosporin and voclosporin), bioterapies (efaluzimab, etanercept, infliximab, adalimumab, secukinumab, ixekizumab, and brodalumab), and small molecules (apremilast, tofacitinib, and baricitinib).

UVB phototherapy (four trials)

In Narbutt et al.’s (2013) study on 59 patients, the mean itch score on a 0- to 20-point scale decreased from 7 at baseline to 1.05 at the end of treatment (P < 0.05) and 68% of patients experienced resolution of itch after phototherapy. In Gupta et al.’s (1999) study on 98 patients, 70% of patients described pruritus improvement or disappearance. During the treatment, 18% of patients complained of adverse effects, mainly burning and itching. Evers et al.’s (2009) study on 109 patients who received UVB phototherapy correlated the levels of itching and scratching at study with the number of irradiation sessions needed to achieve clearance: higher levels of itch and scratching predicting more sessions. In a
randomized, left-right comparison of localized UVB phototherapy versus visible light on 21 patients, Levin et al. (2014) underlined an improvement of itch VAS at week 12 in 62% of patients for the UVB-treated lesions and 27% of patients for the visible light-treated lesions, but it was not significant.

Cyclosporine (five trials)
One of the five trials tested cyclosporine versus etretinate (Schopf et al., 1998) on 31 patients. All patients suffered from itching. The mean four-point itch scale (from 0 to 3) decreased from 1.1 at baseline to 0.1 at week 10 ($P = 0.001$) for cyclosporine versus 1.8 to 1.0 (not significant) for etretinate. Although patients treated with etretinate did not experience a significant change in their pruritus, cyclosporine treatment was highly antipruritic after only 1 week. Three noncontrolled studies tested cyclosporine using a four-point itch scale to evaluate pruritus. Laburte et al. (1994) described a mean score improvement at week 12 of 30% for cyclosporine at dosage 2.5 mg/kg/d and 35% at dosage 5 mg/kg/d in severe chronic psoriasis; Christopfers et al. (1992) tested cyclosporine on 285 patients. The mean improvement in the itch scale was of 27.8% at week 36 in the 1.25 mg/kg/d group, 61% in the 2.5 mg/kg/d group, and 42.8% in the 5 mg/kg/d group (dose reached by 60% of patients in case of insufficiency response). Youn et al. (1993) described that cyclosporine was significantly effective in reducing pruritus (data not shown). Touw et al. (2001) reported that intermittent short courses of cyclosporine provide effective and reproducible control of pruritus in psoriasis (improvement of 40.78 points in a 0-95 mm VAS at the end of treatment).

Voclosporin (one trial)
Bissonnette et al. (2006), on 210 patients, compared voclosporin with placebo during 12 weeks. Treatment with voclosporin resulted in significantly better itch scores than placebo ($P = 0.022$), as early as week 4. The dose-dependent nature of success rates was confirmed with 1.5 mg/kg/d, demonstrating significantly better itch scores ($P = 0.0001$) than the 0.5 mg/kg/d dosage.

Infliximab (two trials)
Schopf et al. (2002) evaluated infliximab on eight patients. Pruritus, assessed using a four-point itch severity scale (ISS, 0-3), decreased from 2.5 at baseline to 0.43 at week 10. In the study by Cassano et al. (2004) (29 patients), there was a decrease in the itch scale (0-3) from 2.2 at baseline to 0.7 at week 10.

Etanercept (five trials)
Krueger et al. (2005) used etanercept versus placebo on 583 patients. All patients reported a pruritus, and 79% of patients assessed their itching in the range of 3-5 (six-point scale from 0 to 5). The mean improvement of pruritus from baseline to week 12 was 49% in the etanercept 50 mg/wk group, 72% in the etanercept 100 mg/wk group, and 1% in the placebo group ($P < 0.0001$). Feldman et al. (2005) included 652 patients treated by etanercept versus placebo and assessed the ISS, using a six-point scale (0-5). Patients treated with etanercept experienced significantly less itching as early as week 2 compared with those receiving placebo ($P < 0.05$). Mrowietz et al. (2015) achieved a post hoc analysis from the PRISTINE study on 270 patients treated with etanercept.
Pruritus was measured on a six-point scale. At baseline, 96% of patients reported pruritus. At week 12, the improvement in pruritus levels in the etanercept 100 mg/wk group was greater than that in the 50 mg/wk group (2.4 vs. 1.6, \( P < 0.001 \)). Patients with the most severe itching at baseline (score of 5) had a mean score of 1.7 at week 24. Cassano et al. (2006) compared etanercept 50 mg biweekly versus etanercept 100 mg weekly in a randomized noncontrolled study on 108 patients. The mean pruritus score at baseline was 49 and 46.5, respectively (assessed with a 0–100 VAS), and at week 12, the mean improvement was 69% and 72%, respectively. The etanercept effects were also evaluated in a comparative study with secukinumab (Langley et al., 2014) (see further).

### Adalimumab (three trials)

In a placebo-controlled study on 1,205 patients, Revicki et al. (2007) assessed the impact of adalimumab on patient-reported outcomes. The mean itch VAS (0–10) decreased from 6.9 at baseline to 3.1 at week 4 (mean change 3.8) and 2 at week 16 (mean change 4.9) versus mean improvements by 0.8 and 1.3 points at weeks 4 and 16 in the placebo group (\( P < 0.001 \)). Revicki et al. (2008) compared adalimumab with methotrexate (7.5–25 mg/wk) or placebo on 264 patients. Pruritus was assessed by itch VAS (0–10). At week 16, adalimumab resulted in a mean five-point decrease compared with a mean 2.5 decrease for methotrexate and 1.8 for placebo (\( P < 0.001 \)). Thaci et al. (2010) evaluated adalimumab with and without topical calcipotriol/betamethasone on 730 patients. In the total population, the mean itch VAS (0–10) at baseline was 6.6 and decreased by 4.7 at week 16 (no significant difference between groups).

### Efalizumab (three trials)

The different studies compared efalizumab with placebo, using an itch VAS scale (0–10). Menter et al. (2004) pooled data from three placebo-controlled studies (total of 1,242 patients), and reported a mean itch score of 3.9 at baseline in both treatment groups. At week 12, the mean improvement was 2.8 points in the efalizumab group and 0.6 points in the placebo group (\( P < 0.001 \)). In another study (Menter et al., 2005) that included 556 patients, the authors highlighted a mean improvement in the itch score of 2.8 points (39.6%) at

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**Table 1. Summary of studies included in the meta-analysis**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Treatment</th>
<th>Patients</th>
<th>Design</th>
<th>Outcome measure of itch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revicki et al., 2007</td>
<td>Adalimumab 40 mg/wk</td>
<td>1,212 patients Adalimumab (814) Placebo (298)</td>
<td>Parallel groups 16 wk</td>
<td>Itch VAS (0–10)</td>
</tr>
<tr>
<td>Revicki et al., 2008</td>
<td>Adalimumab 40 mg/wk</td>
<td>264 patients Adalimumab (101) Placebo (53)</td>
<td>Parallel groups 16 wk</td>
<td>Itch VAS (0–10)</td>
</tr>
<tr>
<td>Griffiths et al., 2015 UNCOVER 2</td>
<td>Ixekizumab 160 mg week 0, then 80 mg/2 wk</td>
<td>1,224 patients Ixekizumab (351) Placebo (168)</td>
<td>Parallel groups 12 wk</td>
<td>Itch VAS (0–10)</td>
</tr>
<tr>
<td>Griffiths et al., 2015 UNCOVER 3</td>
<td>Ixekizumab 160 mg week 0, then 80 mg/2 wk</td>
<td>1,346 patients Ixekizumab (385) Placebo (193)</td>
<td>Parallel groups 12 wk</td>
<td>Itch VAS (0–10)</td>
</tr>
<tr>
<td>Langley et al., 2014 ERASURE</td>
<td>Secukinumab 300 mg wk 0, 1, 2, 3, 4, 8, 12</td>
<td>738 patients Secukinumab (245) Placebo (248)</td>
<td>Parallel groups 12 wk</td>
<td>Itch VAS (0–10)</td>
</tr>
<tr>
<td>Langley et al., 2014 FIXTURE</td>
<td>Secukinumab 300 mg wk 0, 1, 2, 3, 4, 8, 12</td>
<td>1,306 patients Secukinumab (327) Placebo (326)</td>
<td>Parallel groups 12 wk</td>
<td>Itch VAS (0–10)</td>
</tr>
<tr>
<td>Papp et al., 2015</td>
<td>Apremilast 60 mg/d</td>
<td>844 patients Apremilast (562) Placebo (282)</td>
<td>Parallel groups 16 wk</td>
<td>Itch VAS (0–100)</td>
</tr>
<tr>
<td>Paul et al., 2015</td>
<td>Apremilast 60 mg/d</td>
<td>411 patients Apremilast (274) Placebo (137)</td>
<td>Parallel groups 16 wk</td>
<td>Itch VAS (0–100)</td>
</tr>
<tr>
<td>Strand et al., 2013</td>
<td>Apremilast 30 mg 2/d</td>
<td>352 patients Apremilast (88) Placebo (88)</td>
<td>Parallel groups 16 wk</td>
<td>Itch VAS (0–100)</td>
</tr>
<tr>
<td>Papp et al., 2016</td>
<td>Baricitinib 10 mg</td>
<td>271 patients Baricitinib (69) Placebo (34)</td>
<td>Parallel groups 12 wk</td>
<td>Itch NRS (0–10)</td>
</tr>
<tr>
<td>Mamolo et al., 2014</td>
<td>Tofacitinib 15 mg 2/d</td>
<td>197 patients Tofacitinib (49) Placebo (50)</td>
<td>Parallel groups 12 wk</td>
<td>ISS (0–10)</td>
</tr>
<tr>
<td>Bachelez et al., 2015</td>
<td>Tofacitinib 10 mg 2/d</td>
<td>1,106 patients Tofacitinib (132) Placebo (108)</td>
<td>Parallel groups 12 wk</td>
<td>ISS (0–10)</td>
</tr>
<tr>
<td>Menter et al., 2004</td>
<td>Efalizumab 1 mg/kg/wk</td>
<td>1,242 patients Efalizumab (763) Placebo (479)</td>
<td>Parallel groups 12 wk</td>
<td>Itch VAS (0–10)</td>
</tr>
</tbody>
</table>

Abbreviations: ISS, itch severity scale; NRS, numeric rating scale; VAS, visual analog scale.
week 12 for the efalizumab-treated group, and it was maintained at 3 (42.2% improvement) at week 24. Ortonne et al. (2005) included 793 patients and reported a mean improvement by 2.5 points from baseline in the itch score (significant difference vs. placebo, \( P < 0.001 \)).

**Secukinumab (two trials)**

Thac¸i et al. (2015) compared secukinumab with ustekinumab on 676 patients. Pruritus was assessed by an itch numeric scale (0–10). Mean scores at baseline were 6.3 and 6.2 in the secukinumab and ustekinumab groups and improved by 5 and 4.6 points, respectively. The ERASURE study (Langley et al., 2014) compared secukinumab (300 and 150 mg) with placebo on 738 patients. Mean improvements in itch VAS (0–10) were 5.45, 4.86, and 0.22 points, respectively \( (P < 0.001) \). The FIXTURE study (Langley et al., 2014) compared the same two doses of secukinumab with etanercept (100 mg/wk) and placebo on 1306 patients. Mean changes from baseline in itch VAS at week 12 were equivalent in the secukinumab 300 and 150 mg groups (4.93 and 4.92, respectively), significantly more than in the etanercept group (3.8 points) and in the placebo group (0.54 points) \( (P < 0.001) \).

**Ixekizumab (three trials)**

Leonardi et al. (2012) compared ixekizumab with placebo on 142 patients. They demonstrated a significant reduction of pruritus assessed by itch VAS (0 to 10) in the ixekizumab group versus placebo at week 8 \( (P < 0.001) \). In the UNCOVER 2 study (Griffiths et al., 2015), on 1,224 patients, a significant improvement was found in the itch numeric rating scale (NRS, 0–10) with a decrease from baseline by 5.2 points in the ixekizumab/2 wk group and 4.9 points in the ixekizumab/4 wk group versus 3.6 points in the etanercept group and 0.4 points in the placebo group \( (P < 0.001) \). In the UNCOVER 3 study (Griffiths et al., 2015), on 1,346 patients, there was a decrease from baseline in the itch NRS by 5.1 points in the ixekizumab/2 wk, 4.9 in the ixekizumab/4 wk, 3.9 in the etanercept, and 0.6 in the placebo groups at week 12 \( (P < 0.0001) \) for both ixekizumab dosages vs. etanercept and placebo.

**Brodalumab (one trial)**

Gordon et al. (2014) compared brodalumab with placebo on 198 patients. Using the 10-point VAS, itch scores at baseline were homogeneous, ranging from 2.4 to 2.8. They significantly decreased in the brodalumab group as early as week 2 compared with the placebo group, with mean improvements by 1 point at the dose of 70 mg, 2 points at the dose of 140 mg, 2.2 points at the dose of 210 mg, and 1.6 points at the dose of 280 mg, compared with 0.7 points for placebo \( (P < 0.002) \) at week 12.

**Apremilast (three trials)**

Strand et al. (2013) compared apremilast with placebo on 351 patients. At week 16, significantly greater reductions from baseline in mean pruritus scores were reported with apremilast 20 mg (improvement by 23.1 points [35.5%], \( P = 0.005 \)) and 30 mg (improvement by 23.7 points [43.7%], \( P < 0.001 \)). ESTEEM 1 (Papp et al., 2015) included 844 patients and highlighted improvement in the itch score from 66.2 at baseline to 34.7 (decrease of 31.5 points) at week 16 in the apremilast-treated group versus an improvement by 7.3 points in the placebo group. ESTEEM 2 (Paul et al., 2015) included 411 patients and reported similar results with improvement in the itch score by 33.5 points at week 16 for the apremilast-treated group. In both studies, an improvement in the itch VAS score was correlated with the Dermatology Life Quality Index at week 16 and week 32 \( (P < 0.001) \). A reduction in pruritus of approximately 70% in VAS scores achieved with apremilast was observed as early as week 2. This significant improvement was sustained through week 32.

**Tofacitinib (two trials)**

The first trial compared tofacitinib with placebo on 197 patients (Mamolo et al., 2014). At baseline, 195 patients (99%)...
presented a pruritus and mean itch score ranging from 6.8 to 7 across treatment groups. A mean improvement from baseline in the itch score was significant for all doses of tofacitinib versus placebo as early as day 3 ($P < 0.05$). At week 12, a mean improvement from baseline was 3.3, 3.2, and 4.2 points for tofacitinib 2, 5, and 15 mg, respectively, versus 0.7 for placebo. Bachelez et al. (2015) compared tofacitinib with etanercept or placebo on 1,106 patients. Mean itch scores at baseline ranged from 5.2 to 5.3 across treatment groups. At week 12, mean improvements from baseline were 3.2, 4, and 3.5 points for tofacitinib 5 mg, 10 mg, and etanercept respectively versus 0.4 for placebo.

Baricitinib (one trial)
Papp et al. (2016) compared baricitinib with placebo on 271 patients. A mean improvement at week 12 in the itch NRS (0–10 or 0–100) was significant in all baricitinib groups (2.8, 3.3, 3.8, and 4.7 points for baricitinib 2, 4, 8, and 10 mg, respectively) versus placebo (1.1 points).

In the meta-analysis, we included placebo-controlled clinical trials that fulfilled different methodological criteria. The primary outcome measure retained was the improvement in itch score between baseline and the end of the study, assessed by an ISS, filled by patients. Itch scales used were VAS, NRS, and ISS assessing the degree of pruritus from 0 to 10 or 0 to 100 (values were divided by 10 to allow aggregation of the scores across the trials).

Among the 35 clinical trials retained for the systematic review, 13 met the criteria to be included in the meta-analysis and are summarized in Table 1. The evaluation of the ISS was performed at baseline then at week 12 in nine trials and week 16 in four trials.

A global analysis (presented in Supplementary Figure S1 online) combining results from all treatments led to a significant reduction in mean itch score compared with placebo by 3.41 points (95% CI [−3.82, −3]; $P < 0.00001$), but also highlighting a tremendous level of heterogeneity ($I^2 = 98\%$) between studies.

Consequently, we undertook an analysis by subgroups of treatment to handle this bias: Figure 2 for anti-tumor necrosis factor-α (Langley et al., 2014; Revicki et al., 2007, 2008, Figure 3 for anti-IL-17 (Griffiths et al., 2015; Langley et al., 2014), Figure 4 for apremilast (Papp et al., 2015; Paul et al., 2015; Strand et al., 2013), and Figure 5 for JAK inhibitors (Bachelez et al., 2015; Mamolo et al., 2014; Papp et al., 2016).

**DISCUSSION**

Pruritus is a subjective feeling and the objective measurement of its intensity remains a challenge. All clinical trials use quantitative evaluations of itch as VAS (0–10 or 0–100), NRS, ISS, 4- to 6-point or 20-point scales. The most frequently employed instrument was the VAS, filled by patients. Reich et al. (2012) performed a study to validate this scale as an instrument for the measurement of itch intensity, providing its easy, rapid, and reproducible estimation. It was shown that data from VAS, NRS, and VRS provided a high degree of reliability and correlation among each other. Nonetheless, they only explore the quantitative aspect. The qualitative aspect can be explored with a specific questionnaire, in particular the validated 5D itch scale (Elman et al., 2010). One skin-specific instrument to assess QoL in dermatological diseases is the Dermatology Life Quality Index (Finlay and Khan, 1994), which is well known and frequently used in clinical trials. ItchyQoL is the first pruritic-specific instrument for data collection on QoL (Desai et al., 2008). The use of these quantitative itch-specific scales in further clinical trials would enable us to better understand the specific impact of pruritus on QoL and the level of improvement induced by treatments.

Our meta-analysis, including 13 studies, highlighted that all evaluated treatments had a beneficial impact on pruritus. The ISS was judged as the most relevant criterion, and we retained it in the meta-analysis because it has been shown to
be a valid and reliable method for pruritus assessment in patients with psoriasis (Reich et al., 2012).

Anti-IL-17 showed the most important magnitude of effect size in reducing pruritus in psoriasis (~ 4.52 points). The other antipruritic therapies also showed significant results: JAK inhibitors (baricitinib and tofacitinib, ~3.56 points), adalimumab (~3.52 points), and apremilast (~2.18 points). Nevertheless, this meta-analysis was only performed to provide a quantitative estimation of each therapeutic effect size, and does not permit us to conclude precisely on a presumed hierarchy between treatments. Furthermore, these results must be displayed carefully because there are so many variable endpoints in different studies.

The other studies included in the systematic review used various methodological criteria for the evaluation of itch and that did not allow comparisons in a meta-analysis. Nevertheless, we noted that UVB phototherapy would be an effective and durable treatment of pruritus (70% of patient remained improved after 3 months), but pruritus was often mentioned as a side effect of UVB phototherapy in studies that we excluded of the systematic review. No studies reporting the effect of UVA phototherapy, methotrexate, or fumaric acid derivatives on pruritus were indexed from 1990 to 2016. Although methotrexate and retinoids have a long history as systemic psoriasis treatments (methotrexate is used since 1958; Dogra and Mahajan, 2013), the available evidence of their efficacy in clinical trials is scarce and none showed results on pruritus. It could be explained by the fact that these are old studies, published at a time when pruritus was not unanimously recognized as a symptom of psoriasis and not considered as important. Moreover, no study assessing the impact of ustekinumab on pruritus was indexed, although it is a recent treatment.

In our systematic review, three studies (Krueger et al., 2005; Mrowietz et al., 2015; Narbutt et al., 2013) highlighted an absence of correlation between the score of psoriasis (measured by the PASI) and pruritus severity. In accordance with these observations, several authors (Reich et al., 2010; Roblin et al., 2014) have highlighted that no significant correlation was found between disease severity and the presence and intensity of pruritus. However, conflicting reports exist in the literature as to whether pruritus is strictly correlated to those on PASI. Specific effects on itch can be expected due to probable effects on neurons, in addition to effects on skin and immune cells.

Several studies showed correlations between the improvement of itch scores and changes in QoL scores (Dermatology Life Quality Index [Krueger et al., 2005; Sobell et al., 2016; Touw et al., 2001] or 36-Item Short Form Survey [Strand et al., 2013]). Zhu et al. (2014) showed significant correlations between the PASI and Dermatology Life Quality Index with itch scores.

Studied populations were homogeneous because all studies included patients with moderate-to-severe chronic psoriasis (with involvement of ≥10–15% of total body surface area and minimum PASI of 10–13 depending on the studies) and one included only severe psoriasis (Laburte et al., 1994) (PASI ≥ 18). However, pruritus intensity at baseline was variable across studies. In general, pruritus was measured at baseline between 5 and 7/10.

The most important limitation of our meta-analysis is that we could not include all the clinical trials retained in the systematic review because not all of them have specifically measured the changes in pruritus score from baseline to the end of the study. In our systematic review, 72% of studies were published in or after 2005. The majority of trials studied biotherapies and recent molecules available in psoriasis treatment, confirming that pruritus in psoriasis and its impact on QoL were recently taken into account. This also highlights that available treatments for psoriasis have been multiplied in the last few years, and even if PASI remains the primary outcome in most studies, pruritus increasingly appears to be one of the main patient-reported outcomes to relieve.

Another limitation is that some of the studies had relatively small sample sizes. Moreover, a number of studies included in the systematic review were uncontrolled and so had a risk of bias. Indeed, the placebo effect contributes to the effects of treatment for various symptoms and conditions, especially pruritus. In a meta-analysis, van Laarhoven et al. (2015) investigated the magnitude of the placebo effect on itch in clinical trials. They highlighted that placebo treatment significantly decreased itch (overall reduction of 24%), indicating that itch can be considerably reduced by placebo effects. This confirms the need to carry out controlled studies to assess the impact of treatments on pruritus.

Our systematic review highlights that available treatments for psoriasis are efficient on pruritus, although it is sometimes poorly evaluated. As pruritus has a major impact on QoL, measurable and verifiable itch improvement should be included systematically as a primary or secondary endpoint in future randomized clinical trials of systemic treatments of psoriasis. It may be interesting to diversify assessment of pruritus by adding qualitative scales such as the 5D itch scale.

**MATERIALS AND METHODS**

A systematic literature search was performed in September 2016 using PubMed and Trip Database to find clinical trials evaluating the treatment of psoriasis published from 1990 to 2016. The following algorithm was used: “Psoriasis” (tw) AND “Pruritus”(tw) AND “Itch”(tw). The search was limited to English and French languages, and human studies. We selected only systemic treatments, and topical treatments of psoriasis were excluded. After removing duplicates, two independent authors (CT and EB) reviewed all titles and abstracts, and then full text of the potentially relevant articles. Disagreements were resolved by consensus or by a third party (LM). The final set of articles was assessed independently by two authors (CT and EB) using a standardized file. The reviewers were blinded to publication details, and differences were resolved by consensus.

In a second stage, a meta-analysis was performed. The primary outcome measure was the improvement in itch score between baseline and the end of the study. Pruritus was assessed by several scores. The most frequent was an ISS, completed by patients, from 0 to 10 or 0 to 100, where 0 indicated “no pruritus” and 10 or 100 indicated “the worst pruritus imaginable.” The change in pruritus between baseline and time of evaluation was recorded for each treatment arm in each study. The mean variation, with associated standard deviation, was estimated in each group (studied treatment vs. placebo).
A meta-analysis comparing the evolution of ISS in patients treated by active treatments versus placebo controls was performed using the Revman program with an inverse variance model. Heterogeneity was evaluated with Cochran’s Q-test and I² value. In case of the I² value higher than 20%, a random-effect model was used. P-values less than 0.05 were considered as significant. This systematic review conforms to the PRISMA guidelines.

**CONFLICT OF INTEREST**

Dr. Brenaut reports non-financial support from Janssen, Abbvie, and Lilly, as well as grant support from Novartis and Ameen and support from AstraZeneca that is outside the scope of this work. Dr. Misery reports personal fees and non-financial support from Abbvie, grants from Ameen and AstraZeneca, grants and personal fees from Celgene, personal fees and non-financial support from Janssen, personal fees from Leo Pharma and Lilly, personal fees and non-financial support from MSD, grants, personal fees and non-financial support from Novartis, personal fees and non-financial support from Pfizer, and grants and personal fees from Pierre Fabre, outside the scope of this work. Drs. Therene and Barnetche state no conflicts of interest.

**SUPPLEMENTARY MATERIAL**

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at https://doi.org/10.1016/j.jid.2017.05.039.
Reich A, Hrehoro´w E, Szepietowski JC. Pruritus is an important factor negatively influencing the well-being of psoriatic patients. Acta Derm Venereol 2010;90:257–63.