

Table 1. Enthesitis measures used in randomized controlled trials in psoriatic arthritis.

Enthesis Measure	Method (score range)	Trials in PsA	Validation in PsA
Modified Mander Enthesitis Index <sup>25,25a</sup>	Tenderness at 21 sites, scored at each site on 4-point scale: 0 = no pain; 1 = mild tenderness; 2 = moderate tenderness; 3 = wince or withdrawal. 1st cervical spinous process; 2nd cervical spinous process; 7th cervical spinous process; 1st thoracic spinous process; 12th thoracic spinous process; 1st lumbar spinous process; 5th lumbar spinous process; 1st sacral spinal process; symphysis pubis; greater trochanters, left, right (L,R); pelvic abductor origin (L,R); anterior superior border of the iliac crest (L,R); ischial tuberosity (L,R); Achilles tendon insertion (L,R); plantar fascia insertion (L,R)	Clegg 1996 <sup>15</sup>	No
IMPACT Index <sup>9</sup>	Tenderness (yes/no) at 4 sites (0–4); Achilles tendon insertion (L,R); Plantar fascia insertion (L,R)	Antoni 2005 <sup>8,9</sup> ; Mease 2005 <sup>10</sup> ; Genovese 2007 <sup>11</sup> ; Gottlieb 2009 <sup>13</sup> ; Sterry 2010 <sup>14</sup>	No
Maastricht AS Enthesitis Score (MASES) <sup>26</sup>	Tenderness (yes/no) at 13 sites (0–13). 1st Costochondral joint (L,R); 7th Costochondral joint (L,R); Posterior superior iliac spine (L,R); Anterior superior iliac spine (L,R); Iliac crest (L,R); 5th Lumbar spinous process; Proximal insertion of Achilles tendon (L,R)	Kavanaugh 2014 <sup>18</sup> ; Ritchlin 2014 <sup>19</sup>	No
PsA Modified MASES <sup>12</sup>	Tenderness (yes/no) at 15 sites (0–15). 1st Costochondral joint (L,R); 7th Costochondral joint (L,R); Posterior superior iliac spine (L,R); Anterior superior iliac spine (L,R); Iliac crest (L,R); 5th Lumbar spinous process; Proximal insertion of Achilles tendon (L,R); Plantar fascia insertion (L,R)	Kavanaugh 2009 <sup>7,12</sup> ; McInnes 2013 <sup>16</sup>	No
Leeds Enthesitis Index (LEI) <sup>5</sup>	Tenderness (yes/no) at 6 sites (0–6); lateral epicondyle (L,R); medial femoral condyle (L,R); Achilles tendon insertion (L,R)	Mease 2014 <sup>17</sup>	Yes <sup>27</sup> , clinical LEI, odds ratio: 2.16 (0.81–5.70) for PsA vs RA

and assessment technique; mean (SD) scores at baseline and followup; mean (SD) change scores; and percentage with enthesitis at baseline and followup. Two independent reviewers extracted data (AO, JW). Where applicable, effect size calculations were based on mean score change and baseline standard deviation in the treatment and placebo groups, respectively. We used Stata statistical software (Stata 13, StataCorp LP) for Cohen's d effect size calculations<sup>20</sup>.

## RESULTS

Enthesitis measures used across PsA RCT are summarized in Table 1. Effects of various agents on enthesitis in PsA RCT are summarized in Table 2.

**Sulfasalazine.** In this study, which used the most complex enthesitis index, the modified Mander Enthesitis Index, the change in score was not statistically significant between treatment and placebo<sup>15</sup>.

**Infliximab.** In 2 infliximab trials (IMPACT 1 and 2), the IMPACT Index was used to assess enthesitis. Post-treatment percentages of patients with enthesopathy were statistically significantly smaller for infliximab versus placebo (14% vs 31%,  $p = 0.021$ ; and 20% vs 37%,  $p = 0.002$ , respectively)<sup>8,9</sup>. Mean change scores, required for effect size calculation, were not reported.

**Adalimumab.** The adalimumab trials assessed the IMPACT Index. Mean scores were not reported in the ADEPT trial (exploratory endpoint)<sup>10</sup>, and in the second trial, mean change scores were not statistically different between adalimumab and placebo at 16 weeks (–0.5 vs –0.2,  $p > 0.05$ )<sup>11</sup>.

**Golimumab.** The PsA modified Maastricht Ankylosing

Spondylitis Enthesitis Score (PsA-modified MASES) was used in the GO-REVEAL trial<sup>7,12</sup>. Differences in mean percentage change scores at 24 weeks were significant between each golimumab group (50 mg, 100 mg, and overall) and placebo (not tested between the active arms). Effect sizes were –0.49 (95% CI –0.7, –0.2) for golimumab 50 mg and –0.62 (95% CI –0.9, –0.4) for golimumab 100 mg. Posthoc analysis of MASES change scores similarly favored golimumab (no baseline MASES scores were given to allow effect size calculations)<sup>7</sup>.

**Etanercept.** Enthesitis was not an outcome in the initial etanercept trial in PsA<sup>21</sup>. In the observational PRESTA trial<sup>14</sup>, where 2 active arms of etanercept were compared, no differences were observed between the groups in percentages with enthesitis (IMPACT Index); 70% and 80% of patients had improved IMPACT enthesitis scores at 12 and 24 weeks, respectively (no placebo comparison arm).

**Certolizumab.** In the RAPID-PsA trial<sup>17</sup>, differences in the LEI at 24 weeks were statistically significant in favor of certolizumab versus placebo. Participants in this trial included patients previously treated with an anti-tumor necrosis factor (TNF) agent (20%). Effect sizes were –0.4 (95% CI –0.7, –0.2) for certolizumab 400 mg monthly and –0.6 (95% CI –0.8, –0.3) for certolizumab 200 mg every 2 weeks.

**Ustekinumab.** In the initial ustekinumab trial<sup>13</sup>, percentages of patients with enthesitis (IMPACT Index) at 12 weeks were statistically significantly smaller for ustekinumab