Network meta-analysis to evaluate the efficacy of ixekizumab in the treatment of moderate-to-severe psoriasis

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INTRODUCTION
- Chronic plaque psoriasis (hereafter, psoriasis) is a persistent, chronic inflammatory skin disease. Characterized by well-defined erythematous plaques: it affects 2–4% of the global population.
- Celestevery A is commonly measured using the Psoriasis Area and Severity Index (PASI), which assesses four body regions for redness, thickness, and scaling of the skin, on a scale ranging from 0 to 72. Efficacy is reported as percentage improvement e.g. PASI 75 indicates a 75% improvement in PASI score.
- Symptoms and comorbidities associated with psoriasis result in impaired patient quality of life.
- Clinical studies have demonstrated a link between the degree of skin clearance, health-related quality of life (HRQoL), and productivity outcomes. Patients who achieve PASI 90 and 100 have substantially greater improvements in HRQoL.
- A wide range of treatments are available for moderate-to-severe psoriasis, including several biologics; nonetheless, many patients do not achieve their treatment goals.
- Less than half of patients (45%) receiving biologic treatments report feeling very satisfied, 83% of patients feel there is a need for better therapies.
- Ustekinumab (Taber) is a new monoclonal antibody that binds with high affinity to interleukin 17A (IL-17A), which plays a key role in psoriatic plaque formation.
- Ustekinumab has shown significantly greater efficacy in comparison to placebo and etanercept 50 mg twice a week (Q2W) in pivotal UNCOVER trials.
- However, data on the efficacy of biologic agents used in moderate-to-severe psoriasis, was used in an economic model to quantify the benefit of ustekinumab in a NICE submission.

OBJECTIVE
- The aim of this study was to determine the relative clinical efficacy of ustekinumab 80 mg every two weeks (Q2W) versus other biologic treatments approved for moderate-to-severe psoriasis in Europe.

METHODS
- Input data for the NMA were identified through a systematic literature review (2007-2015) of published and grey literature (1990 to Nov 2015). This review included phase II, III, and IV randomized controlled trials (RCTs) on relevant conventional and biologic therapies in moderate-to-severe psoriasis.
- Only RCTs approved by the CERG (Common Assessment Methodology). The NMA was conducted using Review Manager 5.3 software.
- The NMA was weighted by the number of studies included in each treatment arm, and the size of each study was determined using a random-effects model.
- Given the scarcity of head-to-head trials, network meta-analysis (NMA) was widely accepted by decision makers for generating comparative efficacy data for health technology assessment. For example, a previous NMA conducted by Reid et al. was comparing the efficacy of biologic agents used in moderate-to-severe psoriasis, and was used in an economic model to quantify the benefit of ustekinumab in a NICE submission.

RESULTS
- The following results reflect the base case NMA network diagram (see Figure 1): lines are weighted by the number and size of the studies.

Figure 1. Full network diagram for the PASI base case NMA

- (ixekizumab 80 mg Q2W had the highest likelihood [95%, being the best therapy in the base case followed by ustekinumab 80 Q2W with a probability of 74% of being the second best therapy (see Figure 2).
- Finally, none of the diagnostic tests, outlined in the methodology section, detected any significant heterogeneity, inconsistencies or autocorrelation issues. Cochrane’s Q to assess heterogeneity was not significant for the base case NMA (Table 2), and the NMA plot did not highlight any inconsistencies (Figure 3).

Table 3. Cochrane’s Q as a heterogeneity test for the base case NMA

- The results of the base case and the sensitivity analyses consistently demonstrated that ixekizumab 80 mg Q2W was superior to other biologic treatments currently available for moderate-to-severe psoriasis in Europe.
- The MTD results demonstrated the robustness of the analyses and further corroborated ustekinumab 80 mg Q2W being the best treatment among comparators included.
- The network, ustekinumab 80 mg Q2W had the highest probability of achieving a PASI response across all thresholds; this included PASI 90 and 100, which have been linked to significant improvements in patient HRQoL.
- One limitation of the NMA was that it was based on induction dosing period data only. A lack of long-term placebo-controlled RCT data meant that the relative efficacy of ustekinumab 80 mg Q2W could not be analysed over prolonged time-frames.

REFERENCES