EFFECTIVENESS OF INFLUENZA VACCINE IN TNF INHIBITORS TREATED PATIENTS

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Background: Tumor Necrosis Factor-α inhibitors (TNFi) are immunosuppressive therapies that are known to increase infectious risk. Indeed, patients affected by TNFi requiring conditions are at higher risk of influenza compared with healthy controls. Furthermore, mildly reduced seroconversion rate after influenza vaccination had been reported in TNFi-treated patients. Nonetheless the immune response is considered large enough to recommend influenza vaccination in all patients affected by rheumatoid arthritis, regardless of treatment. However, there are data showing that patients are not being vaccinated as recommended. In addition, given that subjects with autoimmune conditions treated with TNFi are at higher risk for influenza, the exact number needed to vaccinate (NNV) for this condition is still unknown.

Objectives: We sought to determine the NNV for influenza in TNFi treated patients and the cost for preventing one case of influenza compared with general population.

Methods: The present analysis included data from cohorts of healthy subjects [1] and TNFi treated patients [2]. We calculated NNV for preventing one case of influenza in each cohort. NNV is the required number of patients receiving vaccination to prevent one case of a given infectious disease. NNV is the inverse of the absolute risk reduction (ARR), which is calculated as following: Control Event Rate (CER) – Experimental Event Rate (EER). In addition, the NNV gives us the opportunity to calculate the cost for preventing one case of influenza, assuming a cost per vaccine from 20 to 40 $.

Results: In total 1290 abstracts were screened of which 133 were regarded as potentially relevant, with 44 trials (19 agents, 48 regimens, 17476 patients) finally included in the analysis. Summary estimates revealed that outcomes of P2 trials were systematically overestimating the subsequent P3 results for ACR20 (OR: 1.40; 95% CI: 1.15–1.77; p<0.001), ACR50 (OR: 1.36; 95% CI: 1.21–1.54; p<0.001) and ACR70 (OR: 1.39; 95% CI: 1.02–1.90; p=0.037). Exploration of determinants of this systematic bias revealed that inclusion criteria for minimum number of required swollen (IC-SJC) and tender joints (IC-TJC) as well as the joint count used for inclusion (28 vs. 66/68 joint count) were significant determinants of P2/P3 efficacy differences. Figure 2 shows scatter plots of efficacy differences (shown as OR), revealing that higher IC-SJC and IC-TJC, as well as using the 66-JC instead of the 28-JC for study inclusion lead to a significantly lower chance of efficacy overestimation.

Conclusion: Our results reveal that Phase 2 clinical trials overestimate the treatment effects when compared with subsequent Phase 3 trials in RA. The identification of this systematic bias towards overestimation of efficacy by Phase 2 studies has implications for clinical investigations, sponsors, and regulatory agencies during the development and licencing process of new compounds, as well as potential ethical implications.

Acknowledgement: We want to thank Dr. Eva Chwala for her assistance with the literature search and Bruno Bierbaumer, MSc for his important contribution to the database infrastructure.

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Figure 1. Number Needed to Vaccinate (NNT) for influenza in the general population and in patients treated with Tumor Necrosis Factor-α inhibitors (TNFi)
How to treat SpA? From physiotherapy to new IL-17 blocking drugs

DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB WAS ASSOCIATED WITH IMPROVEMENTS IN PATIENT-REPORTED AND QUALITY-OF-LIFE OUTCOMES IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

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Background: Ankylosing spondylitis (AS) is a chronic immune-mediated inflammatory disease primarily affecting the sacroiliac joints and spine, causing pain, stiffness and loss of mobility and function. These manifestations can severely impair patients’ quality of life (QoL). Dual neutralisation of IL-17 in addition to IL-17A has been shown to reduce inflammation to a greater extent than inhibition of IL-17A alone in disease–relevant cell models. Results previously reported from this Phase 2b study (NCT02963506) demonstrated that, during the 12-week double-blind treatment period, bimekizumab provided substantial clinical improvements in disease outcome measures, including Assessment of SpondyloArthritis international Society 40% (ASAS40), in patients with active AS.

Objectives: To assess the impact of bimekizumab on patient-reported and QoL outcomes at Week 12 in patients with active AS.

Methods: In this 48-week Phase 2b study (double blind to Week 12 then dose blind to Week 48), 303 patients with active AS (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] > 4; spinal pain > 0–10 numerical rating scale]), fulfilling the modified New York criteria, were randomised 1:1:1:1:1 to receive subcutaneous bimekizumab 16mg, 64mg, 160mg, 320mg or placebo Q4W for 12 weeks. Prior exposure to one anti-TNF therapy was permitted. Secondary and exploratory endpoints included: BASDAI >50% improvement in BASDAI (BASDAI 50), ASAS40, ASAS5/6, ASAS66, ASAS70, ASAS90, ASQoL, PGA, HRQoL (EQ-5D-3L and SF-36v2) and global assessments. Safety was also assessed.

Results: Overall, 297 (98.0%) patients completed the 12-week double-blind period. Baseline scores on patient-reported and QoL outcomes were similar across treatment groups (Table). At Week 12, BASDAI 50 was achieved by 23.7% of netakimab-treated patients versus 23/60 (38.3%) for placebo; the majority were of greater magnitude compared to placebo: ASQoL (−2.3 to −4.6 vs −1.3) and PGA (−1.9 to −3.3 vs −1.0). The overall incidence of treatment-emergent adverse events was 89/243 (36.6%) for bimekizumab-treated patients versus 23/60 (38.3%) for placebo; the majority were of mild or moderate intensity. No unexpected safety findings were observed.

Conclusion: Dual neutralisation of IL-17A and IL-17F with bimekizumab was associated with improvements in patient-reported and QoL outcomes including pain, fatigue and tenderness in patients with active AS after 12 weeks of treatment. No new safety findings were observed versus previous studies of bimekizumab.

NETINGAKIMAB REDUCES THE DISEASE ACTIVITY OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS. RESULTS OF ASTERA STUDY

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Background: Efficacy and safety of netakimab (NTK), a humanized anti-IL17A antibody, was established in phase 2 clinical trials in patients (pts) with radiographic axial spondyloarthritis (r-axSpA) and psoriasis.

Objectives: The abstract presents 16-week data from ongoing ASTERA study (NCT0347704) in pts with active r-axSpA.

Methods: ASTERA is a phase 3 international double-blind placebo (PBO)-controlled study. 228 adult pts with r-axSpA (active BASDAI ≥ 4) despite the standard NSAIDs, were randomly assigned (1:1) to receive 120 mg NTK or PBO SC at Week (Wk) 0,1.2 and then q2w through Wk 16. After Wk 16 all pts will start to receive NTK up to Wk 52. Primary endpoint was ASAS40 rate at Wk 16.

REFERENCE: