EFFECTIVENESS OF INFLUENZA VACCINE IN TNFα INHIBITORS TREATED PATIENTS

Giovanni Adami, Angelo Fassio, Giovanni Orsolini, Alessandro Giolo, Davide Gatti, Maurizio Rossini. University of Verona, Rheumatology Unit, Verona, Italy

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 might be misleading. The difference in NNV for influenza between healthy individuals and TNFi treated patients is due to a greater absolute risk for influenza in this population, 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.

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).

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 the interpretation of clinical investigations, sponsors, and regulatory agencies during the development and licensing 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.

Disclosure of Interests: Andreas Kerschbaumer Speakers bureau: Bristol-Myers-Squibb, Celgene, Pfizer, Harold Herkner: None declared, Josef S. Smolen: Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers-Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB


REFERENCES:


Figure 1. Number Needed to Vaccinate (NTV) for influenza in the general population and in patients treated with Tumor Necrosis Factor-α inhibitors (TNFi)
DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH NETAKIMAB REDUCED THE DISEASE ACTIVITY OF ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

Désirée van der Heijde1, Lianne S. Genstler2, Atul Deodhar3, Xenophon Baraliakos4, Denis Poddubnyy4, Mary Katherine Farmer5, Dominique Baeten6, Jason Coarse7, Marga Oortgiesen8, Maxime Dougados9.

1Leiden University Medical Center, Leiden, Netherlands; 2UCSF, San Francisco, United States of America; 3C HMS, Portland, United States of America; 4Ruhr-University Bochum, Herne, Germany; 5Charité – Universitätsmedizin Berlin, German Rheumatism Research Centre, Berlin, Germany; 6UCB Pharma, Raleigh, United States of America; 7UCB Pharma, Brussels, Belgium; 8Cochin Hospital, Paris, France

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).1 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.2 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.3

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 SpondyloArthritis Disease Activity Index [BASDAI] ≥ 4; spinal pain ≥ 0–10 numerical rating scale), fulfilling the modified New York criteria, were randomised 1:1:1:1:1:1 to receive subcutaneous bimekizumab 16mg, 64mg, 160mg, 320mg or placebo QW for 12 weeks. Prior exposure to one anti-TNF therapy was permitted. Secondary and exploratory endpoints included: BASDAI ≥ 50% improvement in BASDAI (BASDAI 50), 50% improvement in BASDAI 40% (ASAS40), in patients with active AS.3

Results: Overall, 297 (98.0%) patients completed the 12-week double-blind treatment 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 bimekizumab-treated patients versus 23/60 (38.3%) for placebo; the majority were of medium or mild/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.3,4

REFERENCE:

Disclosure of Interests: Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Lianna S. Genstler Grant/research support from: AbbVie, Amgen, UCB Pharma, Consultant for: Novartis, Lilly, Jansen, Atul Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB. Consultant for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Xenonol Baraliakos Grant/research support from: AbbVie, Roheringe Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Pfizer, Novartis, Pfizer, UCB Pharma, Denis Poddubnyy Grant/research support from: AbbVie, Merck Sharp & Dohme, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, Mary Katherine Farmer Employee of: UCB Pharma, Consultant for: UCB Pharma, Dominique Baeten Shareholder of: UCB Pharma, Employee of: UCB Pharma, Jason Coarse Employee of: UCB Pharma, Marga Oortgiesen Shareholder of: UCB Pharma, Employee of: UCB Pharma, Maxime Dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma


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

Inna Gavdyukova1, V Mazurov1, Shandor Erdes2, Tatiana Dubinina3, Olga Nesmeyanova4, Elena Illivanoa5, Elena Kunderza6, Nikolaj Soroka6, Aleksander Kastanayan7, Tatyanap8, Elena Zhugrova9, Tatyanap Ackina10, Pavel Shesternya11, Tatyanap Kropotina12, Olga Antipova13, Elena Smolyarchuk14, Oksana Tolup15, Diana Budagianeva16, Diana Kretkovich17, Ivan Gordeev18, Vadim Tverenko19, Aleksandra Strelkova20, Anna Ermeeva21, Ekaterina Chemyayeva22, Roman Ivanov23, Mchnikov North-Western State Medical University, St-Petersburg, Russian Federation; 2Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; 3Regional Clinical Hospital, Chelyabinsk, Russian Federation; 4Leningrad Region Clinical Hospital, St-Petersburg, Russian Federation; 5Healthcare Institution Municipal Clinical Hospital No. 1, Minsk, Belarus; 6Scientific and Practical Center of Surgery, Transplantology and Minos, Minsk, Belarus; 7Rostov State Medical University, Rostov-on-Don, Russian Federation; 8Road Clinical Hospital, Saratov, Russian Federation; 9Municipal Inpatient Facility No 38, St-Petersburg, Russian Federation; 10Nizhny Novgrod Regional Clinical Hospital, Nizhny Novgrod, Russian Federation; 11Krasnoyarsk State Medical University, Krasnoyarsk, Russian Federation; 12Municipal Clinical Hospital, Omsk, Russian Federation; 13Municipal Clinical Hospital, Irkutsk, Russian Federation; 14Sechenov First Moscow State Medical University, Moscow, Russian Federation; 15Municipal Clinical Hospital No 4, Barnaul, Russian Federation; 16Kazan State Medical University, Kazan, Russian Federation; 17Regional Clinical Hospital, Smolensk, Russian Federation; 18City Clinical Hospital No 15, Moscow, Russian Federation; 19Kirov Military Medical Academy, St-Petersburg, Russian Federation; 20Voloschev First Clinical Hospital, Smolensk, Russian Federation; 21JSC BIOCAD, St-Petersburg, Russian Federation

Background: Efficacy and safety of netakimab (NTK), a humanized anti-IL17 antibody, was established in phase 2 clinical trials in patients (pts) with radiographic axial spondyloarthritis (r-axSpA) and psoriasis.1

Objectives: The abstract presents 16-week data from ongoing ASTERA study (NCT03447704) 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 treated with NTK (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 r-axSpA up to Wk 52. Primary endpoint was ASAS40 rate at Wk 16.