Cochrane Library to identify all randomized controlled double-blind trials investigating biological (b) and targeted synthetic DMARDs in RA. The criteria for inclusion in the analyses were defined as follows: (i) treatment arms in P2 and P3 used the same treatment regimen; (ii) the same RA population was studied (DMARD naïve; conventional DMARD insufficient responders (IR); bDMARD IR). The treatment regimen was regarded the same when a DMARD was used at the same dose, interval and route in P2 and P3. Multilevel mixed model logistic regression was used to determine a summary estimate for comparison of P2 versus P3 results on the outcomes of American College of Rheumatology (ACR)20, ACR50, and ACR70 responses (in separate models). Results are expressed as Odds Ratio (OR) and 95% confidence intervals (95% CI). Possible determinants of systematic overestimation were explored using the same statistical technique, investigating study and baseline characteristics of the individual trials and study arms, respectively.

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: 1.15-1.57; $p \leq 0.001$), ACR50 (OR: 1.36; 95% CI: 1.21-1.54; $p \leq 0.001$) 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 considerations of clinical investigators, sponsors, and regulatory agencies during the development and licencing process of new compounds, as well as potential ethical implications.

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OP0230

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 71,221 healthy individuals influenza vaccination reduced influenza rate from 2.3% in individuals without vaccination (CER = 0.023) to 0.9% in vaccinated individuals (EER = 0.009). The calculated NNV is 71 (NNV = 1/ARR, ARR = 0.023 – 0.009), namely 71 healthy adults need to be vaccinated to prevent one of them experiencing influenza. The costs to prevent a case of clinical influenza in healthy controls would range from 1,420 to 2,840 \$. On 15,132 patients exposed to adalimumab, influenza-related adverse events have been reported in 55 of 382 not-vaccinated patients (CER = 0.14) and in 8 of 179 vaccinated patients (EER = 0.04). In this population (mean age 53.5 years, predominantly white women) the NNV of influenza vaccines is 10 (NNV = 1/ARR, ARR = 0.144 – 0.045) and preventing a case of influenza would cost approximately from 200 to 400 \$, which is largely lower when compared to healthy controls' costs. The relative risk of influenza vaccination in healthy individuals (2.3% to 0.9%, RR 0.41, 95% confidence interval (CI) 0.36 to 0.47) and rheumatoid arthritis patients treated with TNFi (14.4% to 4.5%, RR 0.31, 95% CI 0.15 to 0.64) are similar, while there is a large difference between NNVs (71 vs 10) (Figure 1).

Conclusion: When estimating the effectiveness of vaccinations, clinicians should always include the calculation of the NNV and not only the calculation of relative risk, 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 the latter group. The present analysis provides further evidences on the effectiveness of influenza vaccination in patients affected by rheumatoid arthritis receiving treatment with TNFi and should represent a call-to-action for all rheumatologists to consider vaccination in such patients.

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Figure 1. Number Needed to Vaccinate (NNV) for influenza in the general population and in patients treated with Tumor Necrosis Factor- α inhibitors (TNFi)

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How to treat SpA? From physiotherapy to new IL-17 blocking drugs

OP0231

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).¹ Dual neutralisation of IL-17F 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 Ankylosing Spondylitis Disease Activity Index [BASDAI] ≥ 4 ; spinal pain ≥ 4 [0–10 numerical rating scale]), fulfilling the modified New York criteria, were randomised 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 other endpoints included: BASDAI, $\geq 50\%$ improvement in BASDAI (BASDAI 50), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Quality of Life (ASQoL) and Patient's Global Assessment of Disease Activity (PGADA) at Week 12. 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 23.7–47.5% of bimekizumab-treated patients versus 11.9% receiving placebo. All bimekizumab doses were associated with greater reductions in individual BASDAI components, including: fatigue (range: -1.6 to -2.5 vs -0.8); neck, back or hip pain (-2.0 to -3.3 vs -1.2); discomfort due to tenderness to touch or pressure (-1.6 to -3.0 vs -1.1); level of morning stiffness (-2.5 to -3.5 vs -1.2) and duration of morning stiffness (-1.7 to -3.3 vs -1.4) (Table). Compared with placebo, greater reductions from baseline were also achieved with bimekizumab for BASFI (-1.4 to -2.2 vs -0.6), ASQoL (-2.3 to -4.6 vs -1.3) and PGADA (-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.

Measure (SD)	Placebo (n=60)	16mg (n=61)	64mg (n=61)	160mg (n=61)	320mg (n=60)
BASDAI: fatigue					
Baseline	6.7 (1.6)	7.1 (1.6)	6.8 (1.3)	6.5 (1.6)	6.4 (1.9)
Week 12	5.8 (2.3)	5.5 (2.2)	4.9 (2.3)	4.9 (2.3)	4.4 (2.4)
BASDAI: neck/back/hip pain					
Baseline	7.4 (1.8)	7.7 (2.2)	7.7 (2.2)	7.6 (2.1)	7.5 (1.8)
Week 12	6.3 (2.5)	5.8 (2.4)	4.9 (2.4)	4.4 (2.5)	4.2 (2.4)
BASDAI: discomfort due to tenderness to touch/pressure					
Baseline	5.9 (2.1)	6.2 (2.4)	6.2 (2.0)	5.8 (2.3)	6.2 (2.0)
Week 12	4.9 (2.8)	4.8 (2.5)	3.8 (2.4)	3.2 (2.5)	3.2 (2.5)
BASDAI: level of morning stiffness					
Baseline	7.3 (1.8)	7.3 (2.2)	7.3 (1.9)	6.9 (2.0)	7.1 (2.1)
Week 12	6.2 (2.4)	4.8 (2.5)	4.0 (2.5)	4.1 (2.4)	3.6 (2.4)
BASDAI: duration of morning stiffness					
Baseline	6.3 (2.4)	6.8 (2.5)	6.4 (2.0)	6.0 (2.3)	6.1 (2.6)
Week 12	5.0 (2.8)	4.1 (2.8)	3.4 (2.4)	3.3 (2.3)	2.8 (2.5)
BASFI: overall score					
Baseline	5.8 (2.0)	5.9 (1.7)	6.0 (1.8)	5.8 (2.2)	5.9 (2.0)
Week 12	5.3 (2.4)	4.5 (2.4)	4.1 (2.4)	3.8 (2.3)	3.7 (2.5)
ASQoL					
Baseline	8.9 (4.7)	8.9 (4.2)	8.8 (4.1)	8.5 (4.3)	8.7 (4.3)
Week 12	7.8 (5.2)	6.8 (5.0)	4.9 (5.3)	4.9 (4.5)	4.1 (4.1)
PGADA					
Baseline	7.0 (1.7)	7.1 (1.5)	7.0 (1.6)	6.5 (1.8)	7.1 (1.9)
Week 12	6.0 (2.4)	5.3 (2.3)	4.9 (2.2)	4.3 (2.2)	3.9 (2.2)

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}

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Disclosure of Interests:

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OP0232

NETAKIMAB 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)¹ and psoriasis².

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, 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.