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[OP0228] GSK3196165 AN INVESTIGATIONAL ANTI-GM-CSF MONOCLONAL ANTIBODY, IMPROVES PATIENT REPORTED OUTCOMES IN A PHASE IBB STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: GSK3196165 is a human mAb that inhibits GM-CSF, a key driver in a broad range of immune-mediated conditions (Hamilton, 2016). In trials of anti-inflammatory and autoimmune diseases. Nat Rev Drug Discov 2016; 16:53-70

Conclusion: The results of this Phase Ib study showed that GSK3196165 substantially improved the scores of a range of PRO measures among RA patients. In particular, there was a highly significant improvement in pain; a key symptom of RA. These effects were observed despite achieving much lower drug exposure than predicted. Further studies are required to confirm the additional patient relevant benefits that are expected to arise from increased exposure to GSK3196165.

REFERENCES:


[OP0229] PHASEII CLINICAL TRIALS SYSTEMATICALLY OVERESTIMATE TREATMENT EFFECTS OF SUBSEQUENT PHASE III TRIALS IN RHEUMATOID ARTHRITIS

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Background: Phase 3 (P3) clinical trials are the mainstay of drug development in all areas of medicine, including rheumatology, allowing to determine safety and efficacy of new drugs on their way to approval. Historically, efficacy results of P3 trials have often been disappointing with respect to the expectations set by phase 2 (P2) trials. It is unclear whether these observations are reflection of a true bias or merely a play of chance.

Objectives: To systematically compare efficacy results of P2 versus P3 trials in RA and investigate potential determinants of efficacy differences.

Methods: We performed a systematic review of disease modifying anti-rheumatic drugs (DMARDs) tested in P2 trials in rheumatoid arthritis (RA) over the last 20 years for which also P3 trials exist. We searched Medline, EMBASE, and the
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 2,940 $. 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.

REFERENCES:

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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)

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