Effectiveness of influenza vaccine in TNF inhibitors treated patients: comment on the article by Burmester *et al*

Tumour 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.¹ Furthermore, mildly reduced seroconversion rate after influenza vaccination had been reported in TNFi-treated patients.² Nonetheless, the immune response is considered large enough to recommend influenza vaccination in all patients affected by rheumatoid arthritis, regardless of treatment.³ However, there are data showing that patients are not being vaccinated as recommended.⁴ In addition, given that subjects with autoimmune conditions treated with TNFi are at higher risk for influenza,¹ the exact number needed to vaccinate (NNV) for this condition is still unknown.

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). For example, influenza vaccination reduced influenza rate in 71 221 healthy adults from 2.3% in individuals without vaccination (CER=0.023) to 0.9% in vaccinated individuals (EER=0.009).⁵ The NNV in this scenario 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. 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, the costs to prevent a case of clinical influenza in healthy controls would range from \$1420 to \$2840.

In this recent analysis on 15 132 patients exposed to adalimumab, Burmester and colleagues reported influenza-related adverse

events in 55 of 382 not-vaccinated patients (CER=0.14) and in 8 of 179 vaccinated patients (EER=0.04).⁶ In this population (mean age 53.5 years, predominantly white women), the NNV of influenza vaccines was 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 with healthy controls' costs. Thus, when estimating the effectiveness of vaccinations, clinicians should always include the calculation of the NNV and not only the calculation of risk ratio (RR), which might be misleading. For example, the RRs of influenza vaccination in healthy individuals (2.3% to 0.9%, RR 0.41, 95% CI 0.36 to 0.47) and patients with rheumatoid arthritis 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). This difference 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 NNV for influenza in the general population and in patients treated with TNFi. NNV, number needed to vaccinate; TNFi, tumour necrosis factor- α inhibitors.