Background: Patients with IMID, and notably patients with rheumatoid arthritis RA, are at increased risk of cancer compared with the general population [1,2]. It is hence paramount to assess the impact of biological or targeted DMARD (e.g., tofacitinib and TNFi) on the risk of cancer outcome in patients already at-risk, particularly in the context of ORAL Surveillance which showed a higher risk for malignancies (excluding nonmelanoma skin cancer, NMSC) with tofacitinib, in comparison with TNFi, in RA patients [3].

Objectives: To assess the impact of tofacitinib and TNFi on the risk of malignancies in patients with RA treated in real-world clinical practice.

Methods: The RELATION study is a retrospective observational cohort study using the French nationwide healthcare database (SNDS). Patients aged 18 years or older, affiliated to the national health insurance with a diagnosis of RA and initiating tofacitinib after November 1, 2017 or TNFi after January 1, 2010 (including adalimumab, etanercept, or other TNFi, without previous exposure to tofacitinib) were followed from treatment initiation to December 31, 2020. Patients with a previous history of a malignancy (excluding NMSC) in the 4 years preceding cohort entry were excluded. All malignancies events were defined by the first hospitalization for malignancy during follow-up. Comorbidities and traditional cardiovascular (CV) risk factors were identified using hospitalizations, procedures, or medication dispensing in the 4 years prior cohort entry. The unadjusted incidence rate (IR) of malignancies (excluding NMSC) was assessed in patients initiating either tofacitinib or a TNFi (with associated 95% confidence intervals [95% CI]). A 1:3 PS matching was conducted to balance the baseline characteristics of patients initiating tofacitinib and TNFi. Cox proportional hazards regression models were used to compare the risk of malignancy with tofacitinib vs TNFi during the follow-up period.

Results: Between 2010 and 2020, a total of 39,578 patients with RA were included in the study. Among these, 2,811 initiated tofacitinib and 36,767 initiated a TNFi (adalimumab: 10,621, etanercept: 16,512, other TNFi: 9,634). Patients had a mean age of 53 years at cohort entry, and 72% to 81% were women. Around 61% of the cohort had at least one CV risk factor (66.3% for tofacitinib and 50.8% for TNFi). After PS matching, the tofacitinib cohort included 2,628 patients, and the TNFi cohort included 7,884 patients. Over a median follow-up period of 11.31 months (tobafacinib: 8.56 months, TNFi: 12.52 months), 15 incident malignancy events occurred in the tofacitinib cohort (IR: 5.89 (3.55–9.77) per 1,000 patient-year (PY)) and 135 occurred in the TNFi cohort (8.03 (6.78–9.50)). The risk of malignancies was similar with tofacitinib vs TNFi (adjusted HR 0.76 [95%CI 0.44, 1.32]; p=0.3347). Similar results were found for other (other than breast, melanoma, colorectal, lung cancer or lymphoma) active cancers (HR 0.97 [95% CI 0.50, 1.89]; p=0.9382). For other specific cancer types (cited above), the number of events was too low to perform these analyses.

Conclusion: In this large population-based study, tofacitinib was not associated with an increased risk of malignancies (excluding NMSC) in comparison with TNFi in patients with RA treated in real-world settings. Studies with longer follow-up durations may be necessary to understand the long-term implications of TNFi in patients with RA treated in real-world settings.

REFERENCES:

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POS0834 LONG-TERM EXTENSION STUDY OF THE SAFETY AND EFFICACY OF IMMUNO MODULATION USING A VAGUS NERVE STIMULATION DEVICE IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Non-pharmacological interventions, Rheumatoid arthritis, Randomized control trial


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Background: The inflammatory reflex is a centrally integrated physiological mechanism whereby vagus nerve signaling regulates the production of proinflammatory cytokines that mediate systemic inflammation. The safety and efficacy of a neuroimmune modulation device were assessed in a first-in-human, double-blind pilot study in subjects with multi-drug refractory rheumatoid arthritis (RA). Previously reported data showed that vagus nerve stimulation (VNS) for 12 weeks using the neuroimmune modulation device, a miniature, leadless neurostimulator that is surgically implanted in the neck on the left vagus nerve, improved clinical outcomes, was safe and well-tolerated.[1] We now report 36-month long-term data from this pilot study.

Objectives: Determine the long-term safety and efficacy of neuroimmune modulation using a novel neuroimmune modulation device.

Methods: Subjects (N=14) with active RA and prior insufficient response to ≥2 biological or targeted synthetic (b/ts)DMARDs with ≥2 modes of action were implanted with the neuroimmune modulation device.[1] All subjects who completed Week 12 (N=14) were enrolled in an open-label, long-term extension study where subjects continued or if assigned to the sham group, began to receive treatment. Of these subjects, 11 completed 36 months of treatment as follows: VNS for 1 minute either once per day (QD, N=4) or four times per day (QID, N=3); subjects randomized to sham treatment during the first 12 weeks were crossed over to active VNS for 1 minute, randomized to either QD (N=3) or QID (N=1). The addition of a concomitant b/tsDMARD to study treatment was allowed at the discretion of the investigator and the subject. The safety and clinical effectiveness of VNS using the Clinical Disease Activity Index (CDAI) were evaluated.

Results: The 11 subjects completing the Month 36 visit had previously failed, on average, five different agents, with 73% (8/11) having failed a tsDMARD. The average CDAI change from baseline (i.e., initiation of stimulation) for the 11 subjects completing Month 36 was −17.8 (SD 16.3). At Month 36, 64% (7/11) of subjects achieved a CDAI MCID response from baseline (by the 20/60/40/10 criteria[1]), of whom two (2) were treated with VNS monotherapy and five (5) were on continuous VNS with concomitant b/tsDMARD. The number of subjects in low disease activity (LDA) increased from 9% (1/11) at baseline to 45% (5/11) at Month 36, while the number of subjects in high disease activity (HDA) decreased from 64% (7/11) at baseline to 36% (4/11) at Month 36. Through Month 36, 81% (9/11) subjects elected to combine VNS with a b/tsDMARD, with 8/11 continuing concomitant b/tsDMARD at Month 36. Two adverse events related to VNS therapy occurred during the long-term follow-up period. These events were non-serious, anticipated, and reported by the same subject. One event was a mild sore throat, and the other was moderate tenderness near the implant site. Both events resolved without sequelae following a reduction in stimulation strength. There were no related infections, surgical revisions, or device explantations.

Conclusion: Despite small numbers, data demonstrate long term use of VNS was safe and effective treatment for RA to maintain or lower disease activity including when added to a b/tsDMARD.


Acknowledgements: NIL.

Disclosure of Interests: None declared.

POS0835 EFFECTIVENESS AND SAFETY OF JAK INHIBITORS IN RHEUMATOID ARTHRITIS-INTERSTITIAL LUNG DISEASE. NATIONAL MULTICENTER STUDY OF 57 PATIENTS

Keywords: Rheumatoid arthritis, Lungs, Disease-modifying drugs (DMARDs)