EVALUATION OF LIVE ZOSTER VACCINE IN A SUBSET OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB WITH OR WITHOUT METHOTREXATE, AND ADALIMUMAB WITH METHOTREXATE: RESULTS FROM A PHASE 3B/4 RANDOMISED TRIAL


Cleveland Clinic Foundation, Cleveland, OH, United States, 2Hospital Central, San Luis Potosí, Mexico, 3Outsourcemedical Center, Baton Rouge, LA, United States, 4Konyuk University School of Medicine, Seoul, Korea, 5Pfizer Inc, Collegeville, PA, 6Pfizer Inc, New York, NY, 7Pfizer Inc, Groton, CT, United States, 8Pfizer Inc, Shanghai, China, 9Metropolix Clinical Research Center and University of Texas Southwestern Medical Center, Dallas, TX, United States

Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Patients (pts) with RA are at increased risk for herpes zoster (HZ) and this risk is further increased with tofacitinib treatment. Objectives: To evaluate the effect of live zoster vaccination (LZV) on HZ rates in a subset of methotrexate inadequate responder (MTX-IR) pts with RA who received tofacitinib with or without MTX, or adalimumab (ADA) with MTX in the ORAL Strategy randomised controlled trial (RCT).

Methods: ORAL Strategy (NCT02187055) was a Phase 3b/4, 1-year, triple-blind, dummy active-comparator-controlled RCT. Pts were randomised 1:1:1 to receive tofacitinib 5 mg twice daily (BID; tofa mono), tofacitinib 5 mg BID+MTX (tofa+MTX) or tofacitinib 5 mg BID+MTX (ADA+MTX); target MTX dose was 15–25 mg/week. In countries where LZV was available, pts aged ≥50 years received LZV at the investigator’s discretion, 28 days before the first dose of study drug. HZ incidence rates (IR; pts with events per 100 pt-years) and 95% confidence intervals (CI) were calculated for each treatment arm and for vaccinated vs non-vaccinated pts.

Table 1. IRs and 95% CIs of HZ (serious and non-serious), and demographic characteristics among patients vaccinated and not vaccinated against HZ in the ORAL Strategy RCT

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vaccinated vs non-vaccinated</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>75.0 (73.0–77.0) vs 76.0 (74.0–78.0)</td>
<td>0.12</td>
</tr>
<tr>
<td>Gender</td>
<td>Male: 74.9% (72.9–76.9%) vs 75.2% (73.2–77.2%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Race</td>
<td>Caucasian: 74.5% (72.5–76.5%) vs 75.1% (73.1–77.1%)</td>
<td>0.46</td>
</tr>
<tr>
<td>HZ IR</td>
<td>19.9% (17.7–22.2%) vs 20.2% (18.0–22.6%)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Results: Of 1146 pts who received study drug (mean age: 50.1 years), 216 received LZV (proportion of pts who received LZV by treatment group: tofa mono: 18.0%; tofa+MTX: 19.9%; ADA+MTX: 18.7%) 28 days before randomisation in this RCT; 30 pts self-reported prior vaccination (Table). No pts had zoster-like events – during study drug. HZ incidence rates (IR; pts with events per 100 pt-years) and 95% confidence intervals (CI) were calculated for each treatment arm and for vaccinated vs non-vaccinated pts.

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EFFECT OF TOFACITINIB ON REDUCING PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS

A. Codi6, K. de Vlam7, I. B. McNie6, P. J. Mease4, P. Bae6, T. Lukic6, K. Kwock6, C. Wang7, M.-A. Hue2, A. Maniccia6, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, United States, 2Leuven, Leuven, Belgium, 3University of Glasgow, Glasgow, United Kingdom, 4Swedish Medical Center and University of Washington, Seattle, WA, United States, 5Baer Weinberg MPC, Scarborough, ON, Canada, 6Pfizer Inc, New York, NY, 7Pfizer Inc, Groton, CT, United States

Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA) and psoriatic arthritis (PsA), which has also been evaluated in other inflammatory rheumatic diseases (IRD) including ankylosing spondylitis (AS). Pain contributes substantial morbidity in patients (pts) with IRD and directly impacts treatment adherence, assessment of disease improvement and health-related quality of life.

Objectives: To evaluate the effectiveness of tofacitinib in reducing pain in randomised controlled clinical trials in pts with RA, PsA and AS.

Methods: Five pt populations treated with tofacitinib 5 mg twice daily (BID), 10 mg BID or placebo (PBO) were evaluated: [1] conventional synthetic disease-modifying antirheumatic drug (csDMARD)-inadequate response (IR) RA pts pooled from ORAL Scan (NCT00847613), ORAL Sync (NCT00855644) and ORAL Standard (NCT00853385), [2] tumour necrosis factor inhibitor (TNFi) RA pts from ORAL Step (NCT00960440), [3] csDMARD-IR PsA pts from OPAL Broaden (NCT01777668), [4] TNFi-IR PsA pts from OPAL Beyond (NCT01882439) and [5] AS pts from a Phase 2 study (NCT01786668). Pain outcomes evaluated from baseline to Month (M)6 (Week [W]12 in the AS population) included Pt’s Assessment of Rheumatism Pain (PAAR) (RA and PsA pts only), Short-Form Health Survey (SF)-36v2 Q7 (bodily pain in the past week), SF-36v2 Bodily Pain Domain (BP), EQ-5D PD and BASDAI Q2 were reported at W12 and were numerically greater vs PBO.

Results: The csDMARD-IR RA, TNFi-IR RA, csDMARD-IR PsA, TNFi-IR PsA and AS pts and AS populations comprised a total of 2066, 399, 316, 394 and 155 pts in the FRAS, respectively. In each RA or PsA csDMARD-IR and TNFi-IR population treated with tofacitinib, mean PAAP at baseline (5 mg BID, range 5.5–6.75 mm; 10 mg BID, 5.4–6.01 mm) decreased as early as W2 (1st post-baseline assessment: 45.8–49.8 mm; 38.9–44.8 mm) and continued to decrease through M6 (30.9–34.4 mm; 28.2–36.7 mm); decreases were numerically greater vs PBO and the magnitude of change in RA and PsA populations was similar (Table). Improvements in SF-36v2 Q7 (Table), SF-36v2 BP (Table) and EQ-5D PD were observed in all 4 RA and PsA csDMARD-IR and TNFi-IR populations, and in BASDAI Q2 and Q3 in the csDMARD-IR PsA and TNFi-IR PsA populations. In the AS population, improvements from baseline in mean SF-36v2 Q7 (Table), SF-36v2 BP (Table), EQ-5D PD and BASDAI Q2 were reported at W12 and were numerically greater vs PBO.

REFERENCES: