lack the capacity to form MTX-PGs. Mechanistically, the low FPGS activity in spermatozoa is likely associated with a higher ratio of mRNA expression of an alternatively spliced form of the FPGS gene (8PR) over the WT transcript. These results support and clarify our previous findings that treatment with MTX does not affect sperm quality parameters and provides further evidence that MTX can be safely used in men with a wish to become a father.

REFERENCES:

Figure 1. MTX-PG accumulation in spermatozoa (A) compared to RBCs and PBMCs (B).

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OP0225
EVALUATION OF RESPONSE TO ADJUVANTED RECOMBINANT ZOSTER VACCINATION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING UPADACITINIB: RESULTS FROM A RANDOMIZED TRIAL SUB-STUDY

Keywords: Vaccination/imunization, Rheumatoid arthritis, Targeted synthetic drugs

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Background: Upadacitinib (UPA) is an oral JAK inhibitor (JAKi) approved for the treatment of RA. JAKi have been associated with an elevated risk of herpes zoster (HZ) in patients (pts) with RA. The adjuvanted recombinant zoster vaccine (RZV, Shingrix) was shown to be well-tolerated and effective in preventing HZ in adults aged ≥ 50 years.[1] The efficacy and safety of RZV have not been studied in pts with RA while on UPA in combination with MTX.

Objectives: To assess the immunogenicity of RZV in pts with RA receiving UPA 15 mg once daily (QD) with background MTX.

Methods: Eligible adults aged ≥ 50 years with RA enrolled in the ongoing SELECT-COMPARE phase 3 trial (NCT02629159) received two RZV doses, administered at the baseline and week (wk) 12 visits. Pts should have been on stable doses of UPA 15 mg QD and background MTX for ≥ 8 wks before the first vaccination and ≥ 4 wks after the second vaccination. Antibody titers were collected pre-vaccination (baseline), 4 wks post-dose 1 vaccination (wk 4), and 4 wks post-dose 2 vaccination (wk 16). The primary endpoint was the proportion of pts with a humoral response to RZV defined as ≥ 4-fold increase in pre-vaccination concentration of anti-glycoprotein E [ge] titer levels at wk 16. Secondary endpoints included humoral response to RZV at wk 4 and the geometric mean fold rise (GMFR) in anti-ge titer levels at wks 4 and 16. Cell-mediated immunogenicity to RZV was an exploratory endpoint evaluated by the frequencies of ge-specific CD4+ [2+] T cells (CD4+ T cells expressing ≥ 2 of 4 activation markers: IFN-γ, IL-2, TNF-α, and CD40 ligand) measured by flow cytometry at wks 4 and 16 in a sub-cohort of pts.

Results: Of the 95 pts who received ≥ 1 RZV dose, 93 (98%) received both RZV doses. Pts had a mean (standard deviation) age of 62.4 (7.5) years. The median (range) disease duration was 117.4 (4.9–416.5) years and duration of UPA exposure was 3.9 (2.9–5.8) years. At baseline, all but 2 pts were receiving concomitant MTX and half (50%) were taking an oral corticosteroid (CS) at a median daily dose of 5.0 mg. One pt discontinued UPA by wk 16. Blood samples were available from 90/93 pts. Satisfactory humoral responses to RZV occurred in 64% (95% confidence interval [CI]: 55–74%) of pts at wk 4 and 88% (81–95%) at wk 16 (Figure 1). Age (50–<65 years: 85% [95% CI: 75–94]; ≥ 65 years: 94% [85–100]) and concomitant CS (yes: 87% [77–97]; no: 89% [80–98]) use at baseline did not affect humoral responses at wk 16. GMFR in anti-ge antibody levels compared with baseline values were observed at wks 4 (10 [2.5 CI: 7.3–14.3]) and 16 (22 [15.9–32.2]). Among the sub-cohort of pts, nearly two-thirds achieved a cell-mediated immune response to RZV (wk 4: n = 21/34, 62% [95% CI: 45–78; wk 16: n = 25/38; 66% [51–81]). Within 30 days post-vaccination of either RZV dose, no serious adverse events (AEs) (Table 1) or HZ were reported. AEs that were possibly related to RZV were reported in 17% of pts. One death occurred more than 30 days after wk 16 due to COVID-19 pneumonia.

Conclusion: More than three-quarters (88%) of pts with RA receiving UPA 15 mg QD on background MTX achieved a satisfactory humoral response to RZV at wk 16. In a subgroup of pts, two-thirds (66%) achieved a cell-mediated immune response to RZV at wk 16. Age and concomitant CS use did not negatively affect RZV response.

REFERENCE:

Table 1. Safety Results Through 30-Days Post-RZV Vaccination in UPA-Treated Patients

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>UPA 15 mg QD (N=95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>38 (40%)</td>
</tr>
<tr>
<td>AE with reasonable possibility of being related to UPA</td>
<td>13 (14%)</td>
</tr>
<tr>
<td>5 AE with reasonable possibility of being related to RZV</td>
<td>16 (17%)</td>
</tr>
<tr>
<td>Severe AE</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>0</td>
</tr>
<tr>
<td>AE leading to discontinuation of UPA</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
</tr>
</tbody>
</table>

AE, adverse event; QD, once daily; RZV, adjuvanted recombinant zoster vaccine; UPA, upadacitinib. ‘As assessed by the investigator’ Hypersensitivity.

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