

SAT0220

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

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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.¹

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).²

Methods: ORAL Strategy (NCT02187055) was a Phase 3b/4, 1-year, triple-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 subcutaneous ADA 40 mg every other week + 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

	Tofacitinib 5 mg BID monotherapy N=384		Tofacitinib 5 mg BID+MTX N=376		ADA 40 mg EQW+MTX N=386	
	Vaccinated N=1	Not vaccinated N=3	Vaccinated N=2	Not vaccinated N=6	Vaccinated N=0	Not vaccinated N=6
Vaccinated at study screening, n (%)	69 (18.0%)		75 (19.9%)		72 (18.7%)	
Vaccinated prior to study, n (%)	11 (2.9%)		9 (2.4%)		10 (2.6%)	
IR, n/N (%)	4/384 (1.0%)		8/376 (2.1%)		6/386 (1.6%)	
HZ, n/N (%)	1.13 (0.31, 2.89)		2.33 (1.00, 4.58)		1.69 (0.62, 3.67)	
IR (95% CI)	1.69 (1.49)		2.75 (2.75)		0.72 (0.05)	
Vaccinated at screening	1.59 (0.04, 8.33)		3.00 (0.56, 10.84)		0.00 (0.00, 5.79)	
Not vaccinated at screening	3/315 (1.0%)		6/301 (2.0%)		6/314 (1.9%)	
Adjusted OP	1.04 (0.21, 3.04)		2.16 (0.79, 4.71)		2.06 (0.75, 4.48)	
Characteristics of patients who had HZ						
Mean age, years	75.0	40.7	58.0	58.8	-	52.2
Gender, M/F	0/1	0/3	1/1	0/6	-	2/4
Geographic region ^a in						
North America ^b	0	1	1	3	-	2
Latin America ^c	0	1	0	1	-	0
Eastern Europe ^d	0	1	0	2	-	4
Western Europe ^e	0	0	1	0	-	0
Asia ^f	1	0	0	0	-	0
Serious HZ infection ^g	0	0	0	1	-	0
Adjusted OP	1	1	0	0	-	2

^aRegions LZV was not available in Canada, Israel or Thailand at the beginning of ORAL Strategy. In some instances, the ethics committees did not allow the vaccine to be given. ^bUSA, n=7; ^cMexico, n=2; ^dLatvia, n=1; ^eBulgaria, n=1; ^fPoland, n=3; ^gRussia, n=1; Bosnia and Herzegovina, n=1; ^hUK, n=1; Taiwan, n=1; ⁱHZ cases requiring hospitalisation or parenteral HZ treatment. ^jDefined as disseminated or multidermatomal (nonadjacent or >2 adjacent dermatomes) HZ. One case of varicella adjudicated as an OI was included as an HZ case. ADA, adalimumab; BID, twice daily; CI, confidence interval; EQW, every other week; HZ, herpes zoster; IR, incidence rate; patients with events per 100 patient-years; LZV, live zoster vaccination; MTX, methotrexate; OP, opportunistic infection; RCT, randomised controlled trial.

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 lesions within 42 days of vaccination; 1 pt had vaccination site erythema. In the overall study population, HZ IR was similar between tofa mono and ADA+MTX and numerically higher (overlapping CI) with tofa+MTX. IRs were generally similar for pts who received LZV (18.8% of pts were vaccinated) vs those who did not (81.2%) (Table). Overall, 18/1146 pts had HZ. Among vaccinated pts, 3 (1.4%) had HZ: no events were serious and 1 (0.5%) event was multidermatomal (tofa mono). Among pts not vaccinated, 15 (1.6%) had HZ: there were 2 (0.2%) serious HZ events (tofa+MTX: n=1; ADA+MTX: n=1), 2 (0.2%) multidermatomal events (tofa mono: n=1; ADA+MTX: n=1) and 1 (0.1%) disseminated event (ADA+MTX).

Conclusions: In MTX-IR pts with RA, LZV was well-tolerated. HZ IR was numerically similar between tofa mono and ADA+MTX and higher with tofa+MTX. HZ rates were generally similar in pts who received LZV vs those not vaccinated. LZV has shown efficacy in prevention of HZ in 51% (pts ≥60 years old) and 70% (50–59 years old) of immunocompetent adults.³ Efficacy of LZV could not be fully evaluated as a minority (<20%) of pts received LZV and not all geographic regions studied in other tofacitinib studies were represented.

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SAT0221

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

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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 (NCT00856544) and ORAL Standard (NCT00853385), [2] tumour necrosis factor inhibitor (TNFi)-IR RA pts from ORAL Step (NCT00960440), [3] csDMARD-IR PsA pts from OPAL Broaden (NCT01877668), [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 Arthritis Pain (PAAP) (RA and PsA populations only), Short-Form Health Survey (SF)-36v2 Q7 (bodily pain in the past week), SF-36v2 Bodily Pain Domain (BP), EuroQol Five Dimensions Questionnaire Pain/Discomfort Domain (EQ-5D PD; all populations) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Q2 (level of AS neck, back or hip pain) and Q3 (other pain) score (PsA and AS populations only; PsA pts had presence of spondylitis at screening and baseline BASDAI total score >0 in the full analysis set [FAS]). Data were analysed descriptively.

Results: The csDMARD-IR RA, TNFi-IR RA, csDMARD-IR PsA, TNFi-IR PsA and AS populations comprised a total of 2066, 399, 316, 394 and 155 pts in the FAS, respectively. In each RA or PsA csDMARD-IR and TNFi-IR population treated with tofacitinib, mean PAAP at baseline (5 mg BID, range 55.7–65.7 mm; 10 mg BID, 54.4–60.1 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.