

TOCILIZUMAB IN RHEUMATOID ARTHRITIS (RA): LITHE 2-YEAR RESULTS

Burgos-Vargas R, Fleischmann R, Castelar Pinheiro G, Andrade L, Irazoque F, Kissel K, Alecock E, Kremer J
 Hosp Gen Méx, Mexico. Metroplex Clin Res Ctr, Dallas, USA. Hosp Uni Rio Pedro Ernesto, Rheumatology Div, UNIFESP, Brazil.
 Ctr Méd Nacional 20 Nov ISSSTE, Mexico. Roche. Albany Med Coll, USA. México

In 2 trials, SAMURAI and LITHE, treatment with TCZ 8 mg/kg alone or with MTX significantly inhibited joint damage and improved RA signs/symptoms vs MTX or other DMARDs at 1 y. LITHE 2-y findings are presented here.

Methodology

Pts were randomized to blinded therapy with TCZ (4 or 8 mg/kg [TCZ4, TCZ8]) or placebo (control) every 4 wks + MTX. Stepwise rescue therapy from wk 16 onward was allowed if pts had <20% improvement in swollen and tender joints (SJC, TJC). At wk 52, pts moved to open-label TCZ8 except those with <70% improvement in SJC and TJC, who could continue on blinded therapy up to wk 104. Primary end points at y 2 were change from baseline in Genant-modified Total Sharp Score (GmTSS) and area under the curve (AUC) of change from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI).

Results

The ITT population consisted of 398 TCZ8, 399 TCZ4, and 393 control pts; by wk 104, the majority in all groups was receiving TCZ8. More control pts than TCZ pts required rescue (Table). Pts randomized to TCZ8 had less radiographic progression over time than controls, showing 81% inhibition at y 2; more TCZ8 pts had no progression ($p=0.0001$; Table). AUC of change in HAQ-DI showed significant improvement with TCZ vs control (Table). In pts randomized to TCZ8, absolute numbers achieving low disease activity (LDAS; DAS28<3.2) and DAS28 remission (DAS28<2.6) increased through ~wk 72 and were then maintained; at wk 104, 76% and 65% achieved LDAS and DAS28 remission. At y 2, duration/pt-y (PY) was 1320, 522, and 285 in TCZ8, TCZ4, and control pts. Rates/100PY of adverse events (AEs) were numerically higher in TCZ8 and TCZ4 than control pts (264, 276, 251). Rates of serious AE were comparable (11.4, 12.1, 10.9), and serious infections were numerically higher in TCZ than control pts (3.18, 3.07, 2.11).

Conclusion

Treatment with TCZ + MTX over 104 wks resulted in continued inhibition of joint damage progression and improvements in physical function and clinical signs and symptoms of RA.

TOCILIZUMAB IN RHEUMATOID ARTHRITIS (RA): LITHE 2-YEAR RESULTS

Table. Disposition and Selected End Points at Week 104 in ITT Patients

	Initial Randomized Therapy		
	Placebo + MTX	TCZ4 + MTX	TCZ8 + MTX
Randomized, n	393	399	398
Disposition ^a			
Withdrawals, % (n)	27 (104)	22 (89)	22 (88)
Completed, % (n)	74 (289)	78 (310)	78 (310)
Rescue, % (n)	50 (197)	24 (96)	15 (60)
Open-label TCZ8, % (n)	63 (248)	67 (269)	65 (260)
Mean GmTSS change from baseline	1.96	0.58 ^b	0.37 ^e
No GmTSS progression, % (n/n)	66 (195/294)	75 (256/343) ^{c,d}	83 (292/353) ^{d,e}
Adjusted mean AUC of HAQ-DI change from baseline	-139.4	-287.5 ^e	-320.8 ^e

(n/n)=pts with response/evaluable pts. Mean AUC of HAQ-DI analyzed with ANOVA adjusted for region and original treatment group. Linear extrapolation (GmTSS) or standardization (HAQ-DI) was used for missing data (postrescue data set to missing).

^aPts could be in >1 category.

^b $p=0.0025$ vs placebo + MTX.

^c $p=0.0239$.

^dp value calculated by logistic regression analysis.

^e $p<0.0001$ vs placebo + MTX.