[FRI0316] THE EFFICACY AND SAFETY OF SUBCUTANEOUS TOCILIZUMAB VERSUS INTRAVENOUS TOCILIZUMAB IN COMBINATION WITH TRADITIONAL DMARDS IN PATIENTS WITH RA AT WEEK 97 (SUMMACTA)

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Background: Tocilizumab (TCZ) is approved as an intravenous (IV) formulation globally and subcutaneous (SC) formulation in the US for the treatment of adult rheumatoid arthritis (RA). In the SUMMACTA study, efficacy and safety of TCZ-SC weekly (qw) was demonstrated through week (wk) 24 in patients (pts) with RA with an inadequate response to disease-modifying antirheumatic drugs (DMARDs).[1] TCZ-SC also demonstrated sustained efficacy through wk 49.[2]
Objectives: To evaluate the efficacy and safety of TCZ-SC vs TCZ-IV, including in pts who switched from TCZ-IV to TCZ-SC and vice versa, through wk 97.
Methods: SUMMACTA is a 2-year, randomized, active-controlled, parallel-group phase 3 study comprised of a 24-wk double-blind period, followed by re-randomization for a 72-wk open-label extension period. Pts (n=1262) were randomized 1:1 to receive TCZ-SC 162 mg qw (n=631) or TCZ-IV 8 mg/kg every 4 wks (q4w; n=631) in combination with traditional DMARDs. After 24 wks, pts who initially received TCZ-SC were rerandomized 11:1 to TCZ-SC qw (n=521) or TCZ-IV q4w (n=48) and pts who initially received TCZ-IV were rerandomized 2:1 to TCZ-IV q4w (n=372) or TCZ-SC qw (n=186).
Results: A total of 76 (14.6%), 61 (16.4%), 8 (16.7%), and 26 (14.0%) patients from the TCZ-SC, TCZ-IV, TCZ-SC to TCZ-IV, and TCZ-IV to TCZ-SC groups, respectively, withdrew from the study through wk 97. The percentages of pts who achieved ACR20/50/70 responses, DAS28 remission, and an improvement from baseline in HAQ-DI ≥0.3 were sustained through wk 97 (Table) and comparable across all treatment groups. The safety profiles of switchers were similar to that of pts with continuous TCZ-SC or TCZ-IV treatment (Table) and consistent with the well-established safety profile of TCZ-IV. No anaphylaxis cases were identified. The proportions of pts who developed anti-TCZ antibodies remained low and were comparable across treatment groups through wk 97, and no association between anti-TCZ antibody development and clinical response or AEs was observed.

	TCZ-SC qw Week 24		TCZ-SC qw Week 97		TCZ-IV q4w Week 24		TCZ-IV q4w Week 97		TCZ-SC→IV Week 97		TCZ-IV→SC Week 97	
Efficacy (ITT population[a,b])												
	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
ACR20	391/518	75.5	377/451	83.6	291/372	78.2	264/317	83.3	33/40	82.5	146/165	88.5
ACR50	263/518	50.8	295/451	65.4	196/372	52.7	198/317	62.5	23/40	57.5	111/165	67.3
ACR70	143/518	27.6	202/451	44.8	114/372	30.6	133/317	42.0	15/40	37.5	78/165	47.3
DAS28 < 2.6	198/517	38.3	238/446	53.4	137/370	37.0	142/306	46.4	20/40	50.0	90/162	55.6
↓ in HAQ-DI ≥ 0.3	347/516	67.2	322/445	72.4	254/371	68.5	219/317	69.1	22/39	56.4	115/162	71.0
Safety (safety population): rate/100 patient years (95% CI) [no. events]												
N	631		631[c]		631		631[c]		48[d]		186[d]	
Adverse events	602.8 (574.9, 631.7) [1747]		415.9 (403.4, 428.6) [4214]		588.4 (560.8, 617.1) [1697]		408.6 (394.8, 422.7) [3336]		271.9 (233.7, 314.7) [180]		394.9 (370.9, 420.1) [1010]	
Serious adverse events	11.7 (8.1, 16.4) [34]		14.6 (12.4, 17.2) [148]		14.9 (10.8, 20.1) [43]		15.4 (12.9, 18.4) [126]		9.1 (3.3, 19.7) [6]		19.6 (14.5, 25.8) [50]	
Infections	120.1 (107.8, 133.4) [348]		108.7 (102.3, 115.3) [1101]		124.8 (112.3, 138.4) [360]		105.6 (98.6, 112.9) [862]		84.6 (63.9, 109.9) [56]		97.0 (85.3, 109.8) [248]	
Serious infections	3.1 (1.4, 5.9) [9]		4.0 (2.8, 5.4) [40]		3.5 (1.7, 6.4) [10]		3.9 (2.7, 5.5) [32]		1.5 (0.04, 8.4) [1]		6.7 (3.9, 10.6) [17]	
ISRs	58.0 (49.5, 67.4) [168]		26.1 (23.0, 29.4) [264]		32.6 (26.3, 39.9) [94]		--[e]		--[e]		93.5 (82.0, 106.1) [239]	
Serious hypersensitivity events[f]	0.7 (0.1, 2.5) [2]		0.5 (0.2, 1.2) [5]		1.0 (0.2, 3.0) [3]		0.2 (0.03, 0.9) [2]		0 [0]		0 [0]	
Deaths	0 [0]		0.4 (0.1, 1.0) [4]		0.4 (0.01, 1.9) [1]		0.5 (0.1, 1.3) [4]		0 [0]		0.8 (0.1, 2.8) [2]	

[a] The week 24 intent-to-treat (ITT) population comprised all patients who received a dose of TCZ, and groups are presented according to the treatment randomized at baseline. The week 97 ITT population comprised all patients who received a dose of TCZ post week 24 and groups include patients who were rerandomized to the same treatment assigned at baseline.
[b] The per-protocol population is the primary efficacy analysis for week 24.
[c] Includes all patients who received at least 1 dose of TCZ-SC or TCZ-IV from baseline to week 97. Safety data are cumulative through week 97.
[d] Patients in the switch groups were re-baselined to the visit of their first open-label dose.
[e] Injection site reaction (ISR) data were not collected in the TCZ-IV group after week 24 as no SC injections were given.
[f] Serious adverse events occurring during or within 24 hours of the injection/infusion, excluding ISRs, and that were not deemed to be unrelated to treatment by the investigator.

Conclusions: These data demonstrate that long-term efficacy and safety of TCZ-SC qw is maintained and remains comparable to TCZ-IV, with the exception of injection site reactions, which were more commonly seen with TCZ-SC but comparable to other SC RA treatments. The efficacy and safety profiles of pts who switched were comparable to those in pts who remained on TCZ-IV or TCZ-SC. Thus, TCZ-SC could provide a more convenient administration option and an opportunity of home injection in pts with RA.

References:

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