Figure 2. Percentage of progressors in inception cohort versus percentage of progressors in non-inception cohort after one year of follow-up stratified for immunosuppressive treatment (n=250 non-inception cohort, n=106 inception cohort).

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THU0328

SAFETY AND EFFICACY OF SUBCUTANEOUS TOCILIZUMAB IN SYSTEMIC SCLEROSIS: RESULTS FROM THE OPEN-LABEL PERIOD OF THE PHASE 3 FOCUSSED TRIAL

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Background: The anti-interleukin-6 (IL-6) receptor- α antibody tocilizumab (TCZ) demonstrated skin score improvement and forced vital capacity (FVC) preservation in patients with systemic sclerosis (SSc) in a phase 2 randomized controlled trial.^{1,2} Data from the 48-week, double-blind (DB), placebo (PBO)-controlled period of the focuSSced phase 3 trial were previously presented,³ and open-label (OL) data up to week 96 are presented herein.

Objectives: To assess the long-term safety and efficacy of TCZ in SSc patients.

Methods: Adult patients with active SSc (≤ 60 -month duration, modified Rodnan skin score [mRSS] 10-35, and elevated acute-phase reactants) treated with PBO or TCZ in the DB period received OL TCZ 162 mg SC weekly from weeks 48 to 96 in the OL period (PBO $\rightarrow$ OL TCZ and TCZ $\rightarrow$ OL TCZ, respectively). Exploratory analysis of data up to week 96 included no formal statistical analyses. Changes in mRSS and percent predicted FVC (ppFVC) were assessed.

Results: Overall, 92/105 TCZ (88%) and 89/107 PBO (83%) patients entered the OL TCZ treatment period at week 48, and 85/105 TCZ $\rightarrow$ OL TCZ (81%) and 82/107 PBO $\rightarrow$ OL TCZ (77%) patients completed treatment up to week 96. Continued decline in mRSS was observed in the OL period for PBO $\rightarrow$ OL TCZ and TCZ $\rightarrow$ OL TCZ patients (Table). Change in ppFVC for patients who switched from PBO to TCZ (PBO $\rightarrow$ OL TCZ) was comparable between weeks 48 and 96 (OL period) to the change in patients who received TCZ from BL to week 48 in the DB period (Table). Rates (95% CI) of serious adverse events from weeks 48 to 96 were 15.8 (8.6, 26.5) per 100 PY for TCZ $\rightarrow$ OL TCZ patients, 14.8 (7.9, 25.3) per 100 PY for PBO $\rightarrow$ OL TCZ patients, and 15.4 (11.0, 20.9) for all TCZ exposure over 96 weeks (n = 193). Rates (95% CI) of serious infections were 2.3 (0.3, 8.1) per 100 PY for TCZ $\rightarrow$ OL TCZ patients, 3.4 (0.7, 10.0) per 100 PY for PBO $\rightarrow$ OL TCZ patients, and 3.0 (1.3, 5.9) for all TCZ exposure over 96 weeks. One death occurred during the OL period in each arm.

Conclusion: Although OL data have to be interpreted with caution, results from OL TCZ treatment show numeric improvements in mRSS and FVC preservation

similar to those of the DB period, with a beneficial effect on trajectory of FVC decline in patients who switched from PBO to TCZ. Long-term safety results were consistent with the known safety profile of TCZ, and no new or unexpected events were observed.

References:

- [1] Khanna D et al. *Lancet* 2016;387:2630-40.
- [2] Khanna D et al. *Ann Rheum Dis*. 2018;77:212-20.
- [3] Khanna D et al. *Arthritis Rheumatol* 2018;70(suppl 10):abst 898.

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THU0329

SAFETY, TARGET ENGAGEMENT, AND INITIAL EFFICACY OF AVID200, A FIRST-IN-CLASS POTENT AND ISOFORM-SELECTIVE INHIBITOR OF TGF-BETA 1 AND 3, IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSSC): A PHASE 1 DOSE ESCALATION STUDY

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Background: AVID200 is a novel, potent TGF-beta receptor ectodomain-based trap designed to selectively neutralize TGF-beta 1 and 3. These two isoforms have been implicated as central mediators of the pathogenesis of systemic sclerosis (SSc). AVID200 avoids inhibition of TGF-beta 2, the isoform that supports normal cardiac function and hematopoiesis.

Objectives: This first-in-human study (AVID200-01; NCT03831438) is a Phase 1, open label, multicenter, cohort dose-escalation trial designed to evaluate safety, tolerability, pharmacokinetic (PK) profile, pharmacodynamic (PD) effects, target engagement, and preliminary efficacy in patients with diffuse cutaneous SSc (dcSSc).

Methods: Eligible patients must have dcSSc of <5 years (y) duration and a modified Rodnan Skin Score (MRSS) ≥ 15 . AVID200 at dose levels of 1, 3, 9, or 15 mg/kg IV is administered every 2 weeks (Q2W) for 6 weeks (3 doses). Patients tolerating dosing and who have not experienced disease worsening during the initial Treatment Period may receive up to 6 additional doses Q2W (Extension Period). The ability of AVID200 to selectively sequester its target is assessed in plasma by TGF-beta quantification per ELISA and a cell-based functional read-out. Expression of biomarkers of TGF-beta inhibition and genes correlating with MRSS are assessed.

Table. Change in Efficacy From Baseline

	Baseline to Week 48		Baseline to Week 96		Week 48 to Week 96	
	PBO	TCZ	PBO $\rightarrow$ OL TCZ	TCZ $\rightarrow$ OL TCZ	PBO $\rightarrow$ OL TCZ	TCZ $\rightarrow$ OL TCZ
mRSS, mean (95% CI) ^a	-5.3 (-6.9, -3.7) n = 92	-6.7 (-8.0, -5.4) n = 97	-8.4 (-10.0, -6.8) n = 83	-9.6 (-10.9, -8.4) n = 85	-2.5 (-3.3, -1.6) n = 82	-2.3 (-3.2, -1.5) n = 85
ppFVC, mean (95% CI) [median]	-4.1 (-5.8, -2.4) [-3.9] n = 92	-0.2 (-1.6, 1.2) [-0.7] n = 94	-3.3 (-5.1, -1.5) [-3.1] n = 79	-0.5 (-2.4, 1.3) [-1.4] n = 84	0.6 (-0.7, 1.9) [0.3] n = 78	-0.3 (-1.7, 1.1) [0.0] n = 82
Decline in ppFVC $\geq 10\%$, n/N (%) ^a	15/91 (16.5)	5/93 (5.4)	14/79 (17.7)	11/84 (13.1)	NA	NA
Improvement in ppFVC, n/N (%) ^a	26/91 (28.6)	43/93 (46.2)	22/79 (27.8)	35/84 (41.7)	NA	NA

^aObserved data. NA, not assessed.