Sarilumab, a Human Anti-IL-6 Receptor Monoclonal Antibody, in Posterior Segment Non-Infectious Uveitis (NIU): The SATURN study

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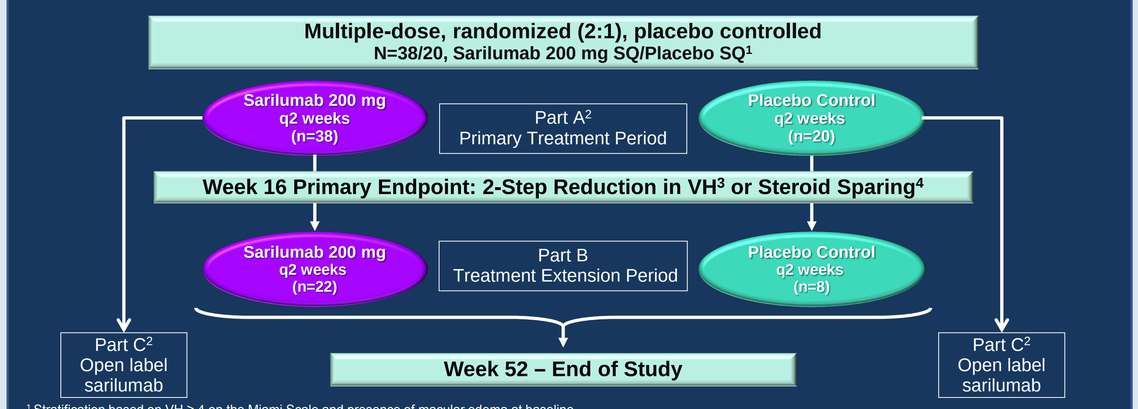
BACKGROUND

- Interleukin-6 (IL-6) and/or its soluble receptor are detected in the vitreous and aqueous humors of patients with uveitis
- Inhibition of IL-6 signaling in a murine model of experimental autoimmune uveitis suppresses the development of uveitis[1]
- SATURN was a phase 2 trial (NCT01900431) to evaluate the efficacy and safety of subcutaneous sarilumab, a human monoclonal antibody directed against the alpha subunit of the IL-6 receptor complex, in the management of posterior segment non-infectious uveitis (NIU)

[1]Mesquida et al. *Clin Exp Immunol*. 2014;176:301-309.

METHODS

Figure 1. Study Design



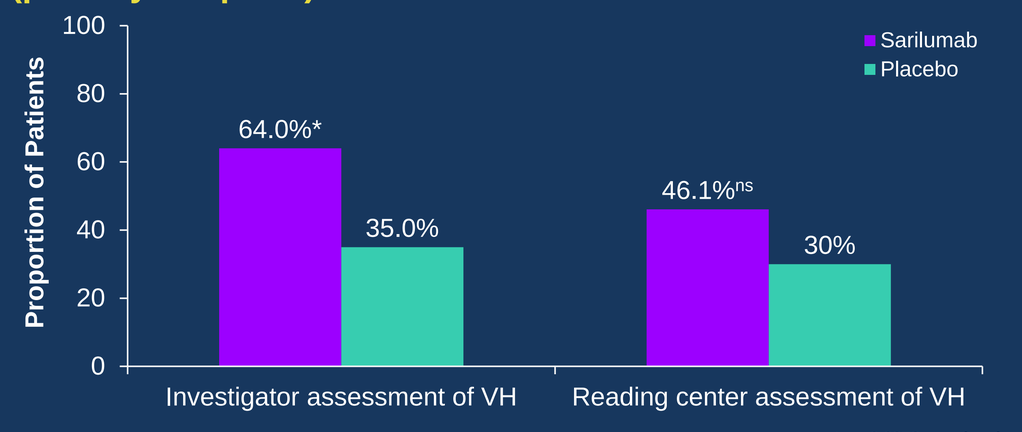
[1] Stratification based on VH ≥ 4 on the Miami Scale and presence of macular edema at baseline
[2] Patients who experienced worsening during the first 16 weeks or those who were nonresponders at week 16 could be enrolled into Part C at the investigator's discretion
[3] Based on the reading center assessment
[4] Patients were required to be on ≥15 mg/day of systemic steroids

RESULTS

Table 1. Baseline Disease Characteristics

	Placebo *(n = 20)*	Sarilumab *(n = 38)*	All Randomized *(n = 58)*
Recently active disease, n (%)	1 (5.0%)	2 (5.3%)	3 (5.2%)
Active disease, n (%)	19 (95.0%)	36 (94.7%)	55 (94.8%)
Intermediate	5 (25.0%)	7 (18.4%)	12 (20.7%)
Posterior	2 (10.0%)	12 (31.6%)	14 (24.1%)
Panuveitis	12 (60.0%)	17 (44.7%)	29 (50.0%)
Month (SD) from first diagnosis	55.5 (71.9)	39.1 (58.1)	44.7 (62.9)
VH score			
Investigator assessment			
Mean (SD)	2.2 (1.6)	2.2 (1.9)	2.2 (1.8)
VH ≥ 2, n (%)	13 (65%)	21 (55.3%)	34 (58.6%)
Reading center assessment			
Mean (SD)	1.7 (2.0)	1.4 (1.6)	1.5 (1.8)
VH ≥2, n (%)	6 (30.0)	12 (31.6)	18 (31.0)
Mean (SD) CRT, µm (Reading Center)	306 (58.9)	338 (155.5)	327 (130.8)
CRT ≥300µm, n (%)	11 (55.0%)	18 (47.4%)	29 (50.0%)
Mean (SD)	346 (42.3)	432 (181.5)	400 (149.7)
Mean (SD) BCVA, ETDRS Letters	74.5 (13.5)	70.4 (14.6)	71.8 (14.2)

Figure 2. Proportion of Patients with ≥2-Step Reduction in Vitreous Haze[a] (VH) or Steroid Dose <10 mg/day at Week 16 (primary endpoint)



p = 0.0372 vs. placebo

[a] Per Reading Center
ns = not significant (*p* = 0.2354 vs. placebo)

Figure 3. Mean Change in Best-Corrected Visual Acuity (BCVA)

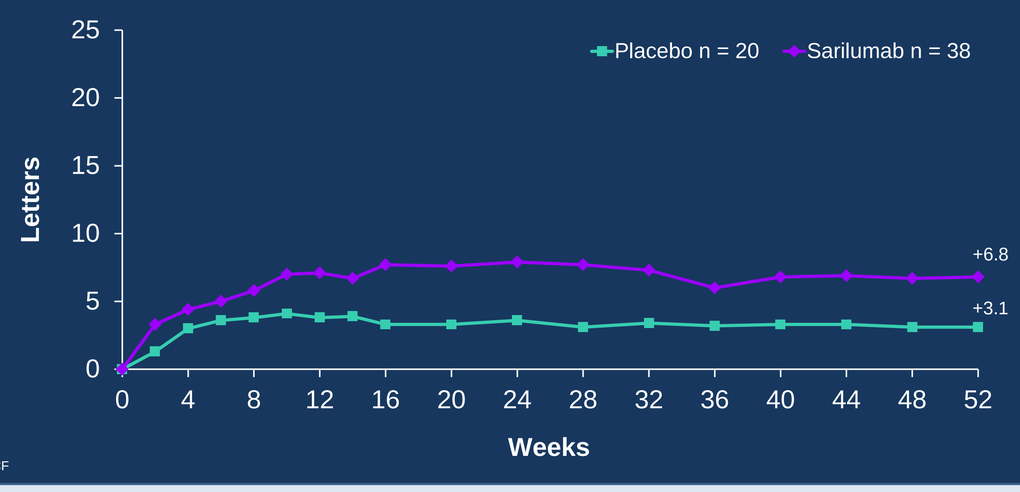


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Figure 4. Mean Change in BCVA in Subgroup of Patients with Baseline CRT ≥300

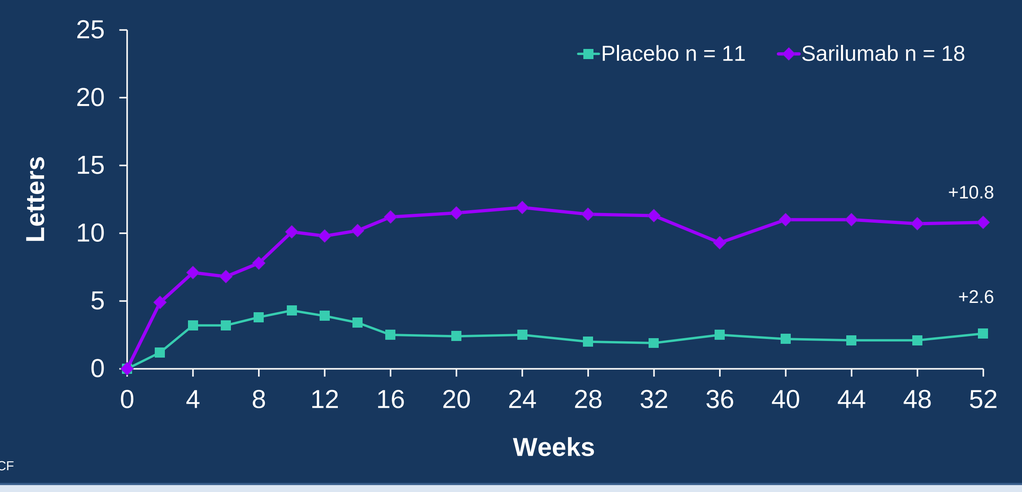

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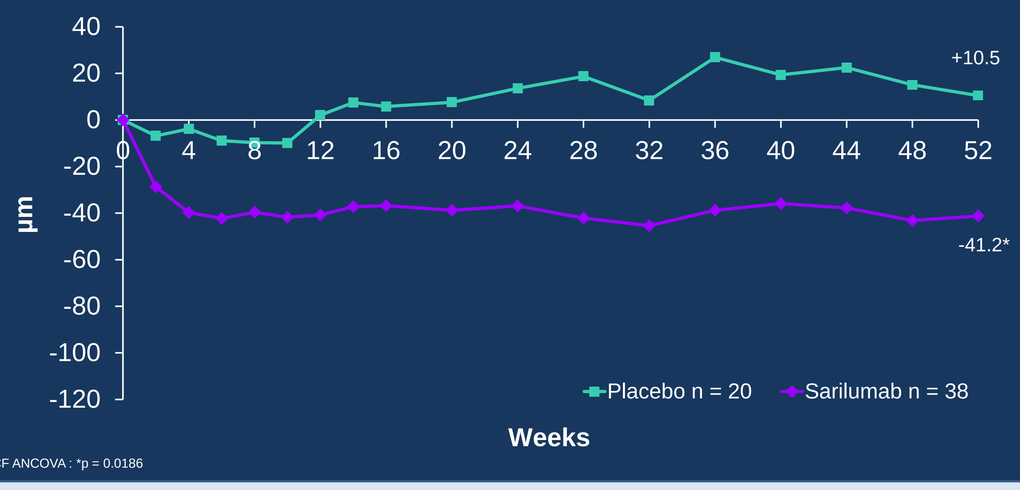
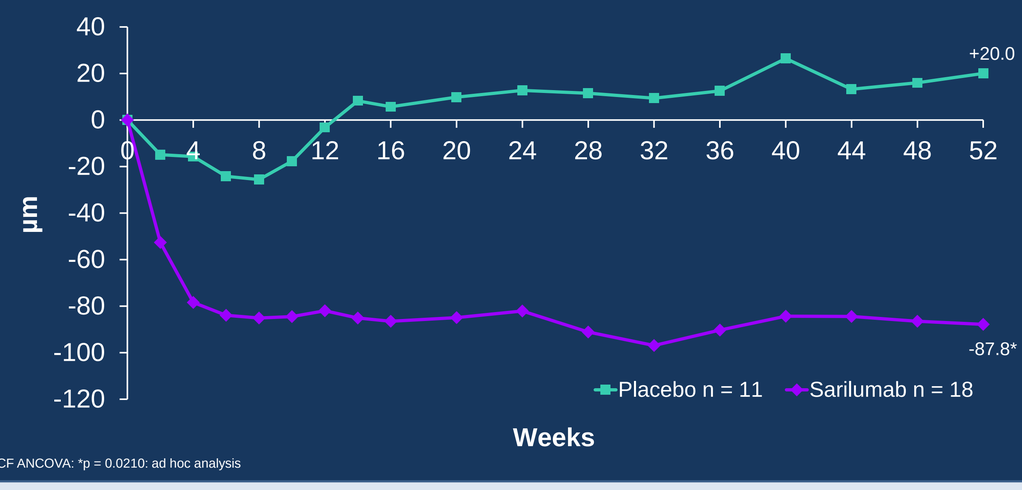
Figure 5. Mean Change in Central Retinal Thickness (CRT)



LOCF ANCOVA : *p = 0.0186

Figure 6. Mean Change in CRT in Subgroup of Patients with Baseline CRT ≥300



LOCF ANCOVA: *p = 0.0210: ad hoc analysis

Safety Through Week 52 (Parts A and B)

- Two patients (10%) in the placebo group experienced 4 serious adverse events as follow: Staphylococcal sepsis, hypoesthesia, deep vein thrombosis, and increased intraocular pressure
- Five patients (13.2%) in the sarilumab group experienced 5 serious adverse events as follow: neutropenia (led to treatment discontinuation), uveitis, increased ALT (led to treatment discontinuation), and elective abortion (let to treatment discontinuation)

CONCLUSIONS

- Patients treated with sarilumab showed an improvement in CRT through 52 weeks particularly in those with macular edema ≥300 µm at baseline
- VH, BCVA, and CRT were all numerically improved in patients treated with sarilumab through the first 16 weeks
- The results suggest that sarilumab may be effective in increasing BCVA and treating macular edema in patients with uveitis