FRI0292

A MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY TO EVALUATE THE EFFICACY AND SAFETY OF SIRKUMAB IN THE TREATMENT OF PATIENTS WITH GIANT CELL ARTERITIS

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Background: Sirukumab (SIR), a selective, high-affinity human monoclonal antibody to the interleukin-6 (IL-6) cytokine, was under development for giant-cell arteritis (GCA) and other diseases.

Objectives: To evaluate the efficacy and safety of sirukumab (SIR) in subjects with GCA.

Methods: This 2-part phase 3 study enrolled subjects with active GCA (NCT02531633). Subjects were randomized in a 3:3:2:2 ratio to one of 5 treatment arms: SIR 100 mg SC q2w + 6-mo prednisone taper (SIR100+6mo), SIR 100 mg SC q2w + 3-mo prednisone taper (SIR100+3mo), SIR 50 mg SC q4w + 6-mo prednisone taper (SIR50+6mo), placebo (PBO) SC q2w + 6-mo prednisone taper (PBO+6mo), PBO SC q2w + 12-mo prednisone taper (PBO+12mo), for 52-week treatment (Part A). Following completion of Part A, subjects could enroll into the study extension with option for open label SIR treatment (Part B). The primary endpoint was the proportion of subjects in sustained remission at Week 52. Secondary endpoints included sustained remission over time, disease flare, and safety. As a result of the early study termination due to administrative reasons, the revised primary endpoint intent-to-treat analysis (revised ITT, N=55) included only subjects who received at least 1 dose of the SC investigational product and had completed 52 weeks (N=28) or had discontinued the study prior to study termination (n=27).

Results: A total of 161 of planned 204 subjects were randomized (mean age 69.6 years, 77.0% female, 98.1% white, 55.9% with new-onset disease). Baseline prednisone dose was ≥ 30 mg/day in 50.9% of subjects. The proportions of subjects with disease flares from Week 2 (N=155) to Week 52 were lower in the SIR100+6mo (18.4%), SIR 100+3mo (28.2%) and SIR50+6mo (30.8%) arms compared to the PBO+6mo (40%) and PBO+12mo (37%) arms.

Table 1. REVISED ITT*: Summary of Sustained Remission at Week 52 – Part A

Sustained Remission Disposition	SIR100 mg SC q2w + 6 mo prednisone (N=17) n (%)	SIR 100 mg SC q2w + 3 mo prednisone (N=13) n (%)	SIR 50 mg SC q4w + 6 mo prednisone (N=9) n (%)	PBO SC q2w + 6 mo prednisone (N=9) n (%)	PBO SC q2w + 12 mo prednisone (N=7) n (%)
Sustained remission	3 (17.6)	2 (15.4)	1 (11.1)	0	0
Early study withdrawal	8 (47.1)	8 (61.5)	4 (44.4)	4 (44.4)	3 (42.9)
Not in remission at Week 12:	4 (23.5)	6 (46.2)	1 (11.1)	8 (88.9)	4 (57.1)
Reasons for not in remission					
• Presence of signs and symptoms	4 (23.5)	6 (46.2)	1 (11.1)	4 (44.4)	2 (28.6)
• CRP ≥ 1 mg/dL	4 (23.5)	6 (46.2)	1 (11.1)	7 (77.8)	4 (57.1)
• ESR ≥ 30 mm/h	4 (23.5)	6 (46.2)	1 (11.1)	7 (77.8)	4 (57.1)

*Including subjects who received at least 1 dose of the SC investigational product and had completed 52 weeks (N=28) or had discontinued the study prior to study termination (n=27).

In Part A, 152 subjects (94.4%) experienced at least 1 treatment-emergent adverse event (TEAE), with similar proportions of subjects across the treatment arms. The most common TEAE's (>10% total subjects) were headache, arthralgia, back pain, cough, upper respiratory tract infection. Treatment-emergent serious adverse events (TESAE) were reported for 31 subjects with similar incidence across all treatment arms. There were no reported deaths, GI perforations or TB activation. Infections and infestations were the most common TESAE, 6 subjects, with no clear difference between SIR and PBO. Two subjects had new onset GCA-related vision loss (SIR100+3mo, n=1; SIR50+6mo, n=1). There were 3

subjects with adjudicated major adverse cardiovascular events (SIR100+3mo, n=2; PBO+12mo, n=1). NCI CTCAE Grade 3 or 4 laboratory abnormalities of increased ALT, bilirubin, cholesterol, triglycerides and decreased leukocytes, neutrophils, and platelets occurred only in SIR treatment arms (0.6 to 2.5% of total subjects).

Conclusion: As a result of early study termination, only a few subjects, all in SIR treatment arms, achieved the primary endpoint of sustained remission at Week 52. The proportion of subjects with flares from Week 2 – 52 were higher in the PBO arms compared to SIR arms. The overall safety was consistent with the known SIR safety profile.

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FRI0293

FACTORS ASSOCIATED WITH FIRST-YEAR AND OVERALL MORTALITY IN ANCA ASSOCIATED VASCULITIS; PATIENTS WITH RENAL LIMITED VASCULITIS MAKES NO BETTER THAN MICROSCOPIC POLYANGIITIS

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Background: Overall mortality in ANCA-associated vasculitis (AAV) over the last two decades has been reported to be decreasing with the use of immunosuppressive therapies. However, mortality rates remain high and most of the deaths occur in the first year after diagnosis despite treatment.

Objectives: In this study, we aimed to determine the prevalence of mortality in our AAV patients and to investigate the factors that may be associated with first-year and overall mortality.

Methods: Patients followed up in one center with the diagnosis of AAV were included in the study. Diagnostic subgroups were; granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA), and renal-limited vasculitis (RLV). The clinical and demographic characteristics of the patients were collected retrospectively. Factors predictive of mortality were evaluated by Kaplan-Meier method and the Cox proportional hazard model.

Results: In total 104 (45 [43%] female and mean age 54.9 $\pm$ 15.4 years) AAV patients (51 GPA; 25 MPA; 27 RLV and 1 EGPA) were included in the analysis. ANCA positivity was detected in 81 (77.9%) patients with IIF and/or ELISA. ESRD had developed in 31 (32.3%) of AAV patients and in 37.8% of patients with renal involvement. Mortality rate was 14.4% in the first year after diagnosis and 27.9% during a median follow-up period of 1289 (5-5804) days. The age at diagnosis was the only significant predictor of first-year mortality (p=0.006). Univariate analysis revealed that overall mortality was associated with AAV subgroups (p = 0.035), renal (p = 0.046) (figure) and, ENT (ear-throat) involvement (p = 0.025), ESRD (p = 0.025) and hemodialysis at the time of diagnosis (p = 0.040). However Cox regression analysis showed age at diagnosis as the only significant predictor also of the overall mortality (P=0.001).

Conclusion: Our findings suggest that there could be some survival differences between AAV subgroups and patients with or without renal and ENT involvement. However, the age at diagnosis seems to be the only significant predictor of first-year and overall mortality in our AAV patients.