Sustained Remission From Weeks 16 to 52 and Weeks 24 to 52 in Patients Treated With Sarilumab: Post-hoc Analysis of SAPHYR Trial in Patients With Polymyalgia Rheumatica

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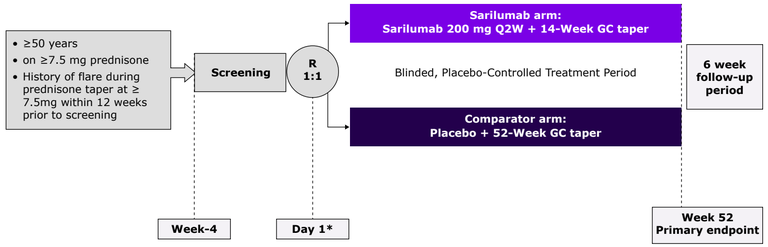
BACKGROUND

- In the SAPHYR study (NCT03600818), significantly greater proportion of patients with PMR who were treated with sarilumab, a human monoclonal antibody against the IL-6Rα,[1] achieved sustained remission versus the comparator arm[2]
- Other studies of patients with PMR treated with IL-6R blockade assessed remission/low disease activity at week 16 and/or week 24[3,4]
- This post-hoc analysis of the SAPHYR study assessed the proportion of patients achieving sustained remission and its components at weeks 16 and 24 up to week 52

METHODS

- Patients meeting the ACR/EULAR classification criteria for PMR were recruited between Oct 2018 and Jul 2020 **(Figure 1)**

Figure 1. Study design



*Prednisone dose 15 mg/day for first 2 weeks after randomization.
GC, glucocorticoid; Q2W, every 2 weeks; R, randomized.

- Sustained remission was defined as:
  - Disease remission (no PMR signs and symptoms + CRP normalization [<10 mg/L]) at 16 weeks and 24 weeks;
  - Absence of disease flare from weeks 16 to 52 and weeks 24 to 52;
  - Sustained reduction of CRP (to <10 mg/L, with no successive elevations to ≥10 mg/L) from weeks 16 to 52 and weeks 24 to 52; and
  - Successful adherence to protocol-specified GC taper dose from weeks 16 to 52 and weeks 24 to 52
- Patients who did not achieve remission, received rescue GC therapy, withdrew from the study before week 52, or had missing data that prevented assessment of the primary endpoint were considered as non-responders

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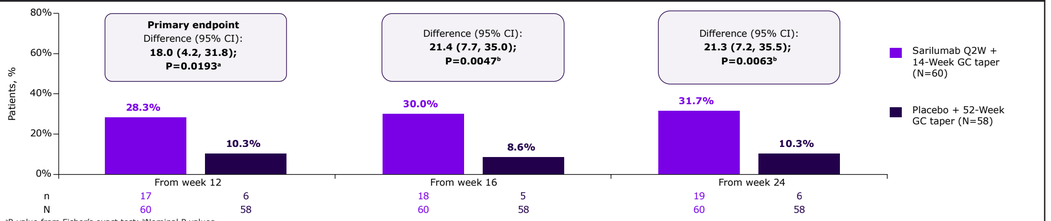
CONCLUSION

- **A higher proportion of patients in the sarilumab arm vs comparator arm achieved sustained remission and its individual components when assessed from week 16 and week 24 up to week 52**
- **Most patients who achieved sustained remission did so rapidly by week 12 with some additional responses observed between weeks 12 and 24**
- **The actual mean daily GC dose administered during the study was lower in the sarilumab arm vs comparator**

RESULTS:

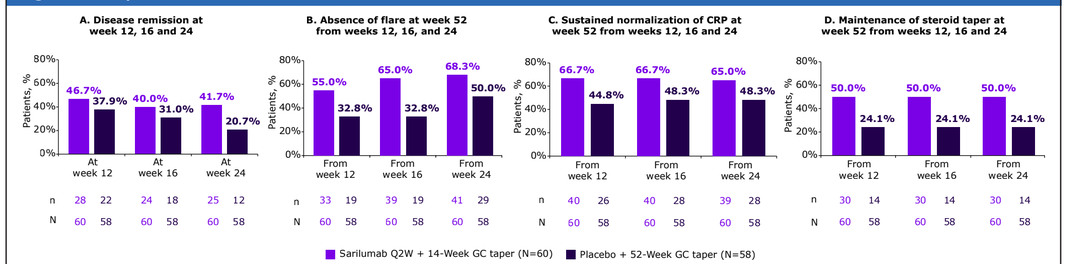
- Of 118 patients enrolled, 60 were in the sarilumab arm (median age 69.0 years [range: 51–88]), and 58 were in the comparator arm (median age 70.0 years [range: 52–88]); baseline characteristics were generally similar between sarilumab and comparator arms, with most patients being female (75.0% and 63.8%, respectively) and Caucasian (83.3% and 82.8%, respectively); the median duration of PMR (diagnosis date to baseline) was 300 days (range, 66–3992)[2]
- A higher proportion of patients in the sarilumab arm vs the comparator arm achieved sustained remission from weeks 16 to 52 and from weeks 24 to 52 **(Figure 2)**
- Components of sustained remission were achieved by a higher proportion of patients in the sarilumab arm, during each assessment period **(Figure 3)**
  - In sarilumab and comparator arms, disease remission decreased slightly over time **(Figure 3A)**; disease remission rates declined due to missing or abnormal CRP, as the proportion of patients with no PMR signs and symptoms increased over time[5]
  - In the sarilumab arm, the proportion of patients with absence of disease flare increased at week 16 and week 24 compared to weeks 12 to 52 assessments **(Figure 3B)**
  - Proportion of patients with sustained CRP normalization **(Figure 3C)** and those who adhered to protocol-defined GC taper **(Figure 3D)** remained the same during the three assessment periods
- After protocol-defined taper reached 2 mg/day, the actual mean daily GC dose including rescue was <2.5 mg for sarilumab arm and >2.5 mg for comparator arm at all time points **(Figure 4)**
- The safety data were consistent with the known safety profile of sarilumab, with no new or unexpected AEs reported in this study

Figure 2. Sustained remission at week 52 from week 12, 16, and 24



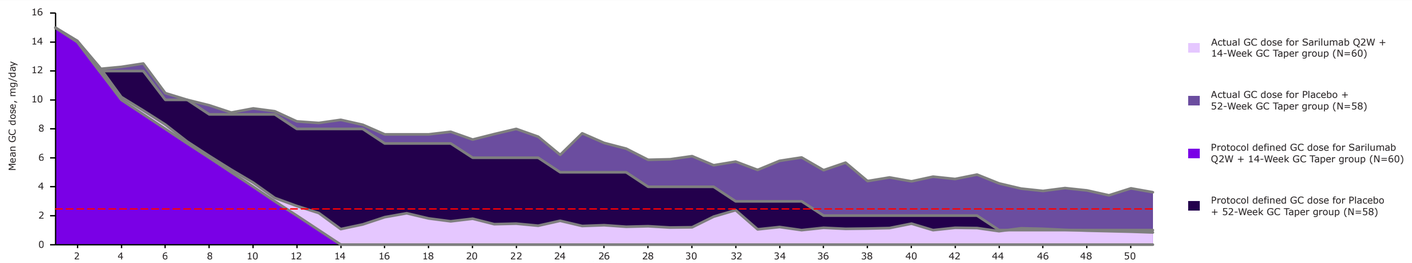
[a]P-value from Fisher's exact test; [b]Nominal P values
CI, confidence interval; GC, glucocorticoids; Q2W, every 2 weeks

Figure 3. Components of sustained remission



CRP, C-reactive protein; GC, glucocorticoids; Q2W, every 2 weeks.

Figure 4. Protocol-defined and actual mean daily GC dose administered during the study



Weeks	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50
Actual dose for sarilumab arm	14.08	10.21	8.3	6.14	4.28	2.67	1.08	1.9	1.81	1.8	1.45	1.65	1.34	1.27	1.2	2.38	1.22	1.16	1.11	1.45	1.17	0.94	1.1	0.97	0.9
Actual dose for comparator arm	14.08	12.28	10.47	9.63	9.42	8.51	8.63	7.63	7.62	7.26	8	6.2	7.03	5.86	6.11	5.74	5.79	5.14	4.39	4.37	4.54	4.24	3.71	3.75	3.89
Protocol-defined dose for sarilumab arm	14	10	8	6	4	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Protocol-defined dose for comparator arm	14	12	9	9	9	8	8	7	7	6	6	5	5	4	4	3	3	2	2	2	2	1	1	1	1

The red dashed line denotes that average GC dose for sarilumab arm was below 2.5 mg at all timepoints.
GC, glucocorticoids; Q2W, every 2 weeks

DISCLOSURES

RR (presenter) is an employee of Sanofi and may hold stock and/or stock options in the company; **Dasgupta B (presenter)**: Consultant - Roche Chugai and Sanofi. Grant/research support - AbbVie, Roche Chugai, and Sanofi. Speaker/honoraria - Cipla and Roche Chugai. **Praestgaard A, Fiore S, Ford K,** and **Sloane Lazar J** are employees of Sanofi and may hold stock and/or stock options in the company; **Dua AB**: Consultant - AbbVie, Sanofi, GSK, Chemocentryx, Novartis; **Spiera R**: Consultant - AbbVie/Abbott, Chemocentryx, GSK, Novartis, Roche, Sanofi, and Vera. Grant/research support - Boehringer-Ingelheim, Chemocentryx, Corbus Pharmaceutical, GSK, and InflaRx.

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ABBREVIATIONS

AE, adverse event; CI, confidence interval; CRP, C-reactive protein; GC, glucocorticoids; IL-6R, interleukin-6 receptor; PMR, polymyalgia rheumatica; Q2W, every 2 weeks.

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