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Real-world Effectiveness of Interleukin-6 Receptor Inhibitors Compared to Methotrexate in Steroid-refractory Frail Patients with Polymyalgia Rheumatica

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BACKGROUND

Patients with frailty have increased risk of:

- Worse health outcomes
- GC toxicity

- IL-6 implicated in both PMR and frailty pathogenesis^{1,2}
- IL-6Ri reduce GC use in PMR³

In prior analysis of frail (claims-based frailty index [CFI]≥0.2) patients with PMR⁴:

- Patients on IL-6Ri were twice as likely to discontinue GCs vs. conventional synthetic immunomodulators (csIMs) (HR: 2.32; P=0.002)
- This effect size was almost two-fold larger than the effect seen in the overall PMR cohort (HR: 1.28; P=0.031)

Current analysis:

- Compares IL-6Ri to MTX (second-line only) as a PMR treatment
- Has two additional years of data (up to 2022)
- Frailty (CFI≥0.25⁵) is an inclusion criterion
- Frailty level is a propensity score (PS) match covariate

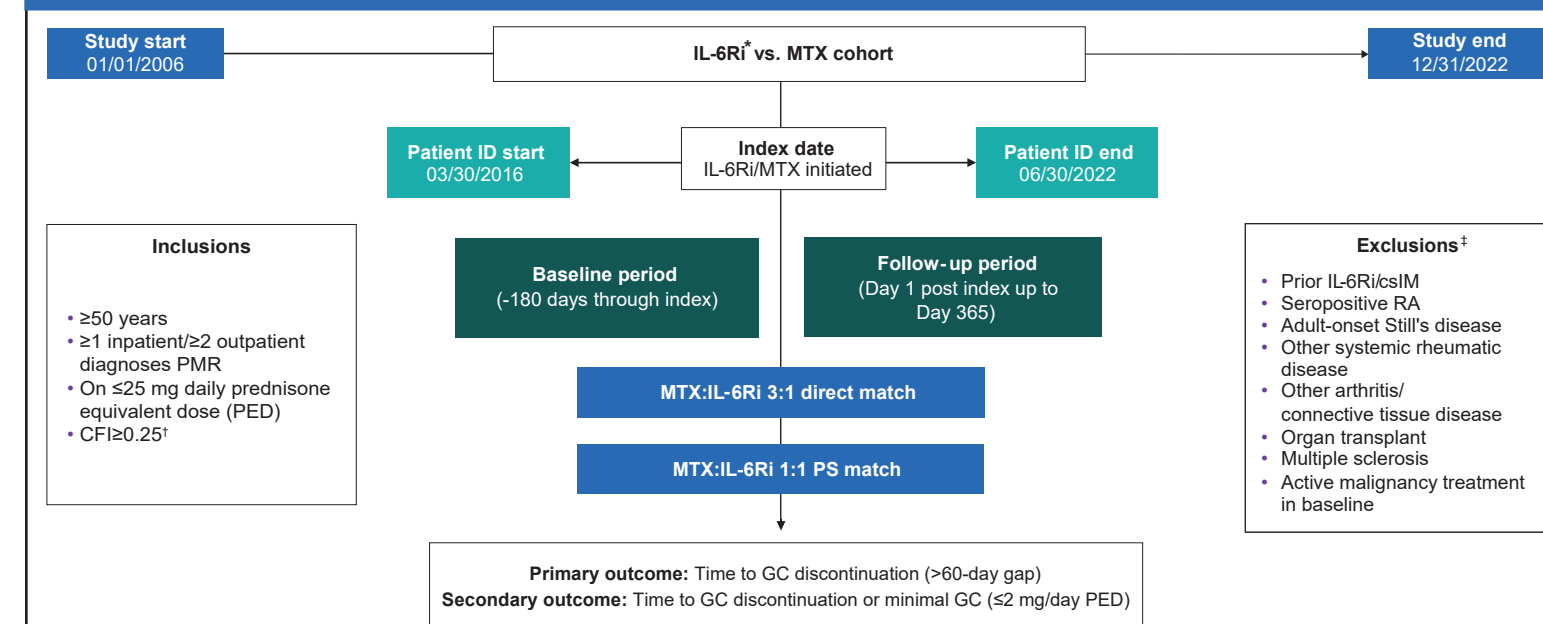
OBJECTIVE

- To compare the effectiveness of IL-6Ri to MTX in GC-refractory/intolerant frail patients with PMR

METHODS

- Observational retrospective comparative cohort study using US Medicare claims data (Figure 1)
- MTX initiators were direct matched to IL-6Ri initiators on select characteristics and then PS matched on demographics, treatment, and clinical characteristics
- Covariates were deemed to be imbalanced if both SMD>0.1 and P<0.05, and were included in the adjustment of Cox model
- In addition to the outcomes, patients were censored for 60 days prior to end of enrollment, death, 1 year, stop index drug, switching/adding another PMR drug
 - Patients were censored for 60 days prior to end of enrollment as 60 days are required to determine the outcome
 - Switching/adding another PMR drug included only the PMR drugs used in this study

Figure 1: Study design



¹Sarilumab, tocilizumab. ²Algorithm for estimation of frailty levels, based on evaluation of gait speed, grip strength, 2-year death risk, institutionalization, disability, hospitalization, and prolonged (>30 days) skilled nursing facility stay. ³Due to the difficulty in differentiating PMR from seronegative RA clinically, and given patients with GCA often develop PMR, patients with seronegative RA and GCA diagnoses codes during the baseline period were not excluded. Additionally, diagnosis of seronegative RA and GCA may also have been used to obtain reimbursement for off-label use of IL-6Ri.

CONCLUSIONS

- Frailty is common in patients with PMR and may be associated with worse outcomes and GC toxicity
- Compared to methotrexate, IL-6Ri therapy led to a more rapid discontinuation of GCs or to achieving a minimal GC dose of ≤2 mg/day in the second-line treated frail patients with PMR

RESULTS

- A total of 290/1,017 (29%) and 1,402/7,645 (18.3%) patients in the IL-6Ri and MTX groups, respectively, had a CFI≥0.25
- Of these, 86 matched pairs were identified who were receiving second-line treatment and had no prior IL-6Ri therapy
- Patient characteristics after PS match were balanced, some had SMD>0.1, though none were statistically significant (Table 1)

Table 1: Characteristics of patients receiving IL-6Ri or MTX after PS match

Characteristics	IL-6Ri* (N=86)	MTX* (N=86)	SMD	P value
Age at index, years [†]	79.0 (6.0)	78.4 (5.6)	0.10	0.395 ^a
Gender, female [†]	71 (82.6%)	67 (77.9%)	0.12	0.444 ^b
Race, white	77 (89.5%)	76 (88.4%)	0.20	0.505 ^c
Original reason for qualifying for Medicare, age ≥65 years	72 (83.7%)	72 (83.7%)	0.00	>0.999 ^b
Time from PMR diagnosis to index, median (IQR)	598.5 (231.3, 1,477.0)	531.0 (172.8, 1,118.5)	0.23	0.183 ^a
Baseline PED category, mg/day [†]				
<2.5	<11	<11	0.15	0.995 ^c
2.5–<5	14 (16.3%)	15 (17.4%)		
5–<10	35 (40.7%)	36 (41.9%)		
10–<15	19 (22.1%)	21 (24.4%)		
15–<20	<11	<11		
20–<25	<11	<11		
>25	<11	<11		
Index daily PED category, mg [†]				
<2.5	<11	<11	0.35	0.404 ^c
2.5–<5	<11	<11		
5–<10	27 (31.4%)	34 (39.5%)		
10–<15	17 (19.8%)	23 (26.7%)		
15–<20	21 (24.4%)	13 (15.1%)		
20–<25	16 (18.6%)	13 (15.1%)		
Charlson Comorbidity Index category				
0–1	16 (18.6%)	24 (27.9%)	0.24	0.307 ^b
2–3	24 (27.9%)	24 (27.9%)		
4+	46 (53.5%)	38 (44.2%)		
Level of frailty				
Mildly frail (CFI: 0.25–0.34)	68 (79.1%)	63 (73.3%)	0.14	0.371 ^b
Moderately to severely frail (CFI: ≥0.35)	18 (20.9%)	23 (26.7%)		
GCA (any history) [†]	43 (50.0%)	43 (50.0%)	0.00	>0.999 ^b
Seronegative RA	28 (32.6%)	19 (22.1%)	0.24	0.124 ^b

Index date was the date IL-6Ri or MTX was initiated. Baseline was defined as the 180 days prior to index date. Unless otherwise stated, continuous variables are reported as mean (SD) and categorical as n (%). ^aTo protect patient privacy and avoid potential identification of patients, only results with ≥11 patients are reported, and data are redacted when there are <11 patients when such results would allow derivation of the number of patients when <11 are reported; ^bCovariates used both for direct and PS match; ^cWilcoxon rank sum test; [†]Pearson's Chi-squared test; [‡]Fisher's exact test.

DISCLOSURES

Sattui SE: Research funding from Rheumatology Research Foundation Investigator Award, National Institute of Aging (grant number R03AG082983), Consulting and advisory boards for Sanofi and Amgen (all funds toward research support), Speaker Fees from Fresenius Kabi (all funds toward research support), Research support Amgen and Glaxo Smith Kline (clinical trials); Dejaco C: Consulting/speaker's fees from AbbVie, Eli Lilly, Janssen, Novartis, Pfizer, Sparrow, Roche, Boehringer, Galapagos, and Sanofi, Editorial board member of the *Annals of the Rheumatic Diseases*; Ford K: Former employee of Sanofi; Fiore S and Ackermann M (presenter): Employee of Sanofi and may hold stock and/or stock options in the company; Unizony SH: Consulting - Sanofi, IQVIA, and Harvard Pilgrim Health Care Inc.; Xie F: No conflicts of interest; Curtis JR: Consulting, research grants from AstraZeneca, Amgen, AbbVie, Bendcare, Genentech, GSK, Horizon, Janssen, Lilly, Novartis, Pfizer, Sanofi, Scipher Medicine, Setpoint, and UCB.

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ABBREVIATIONS

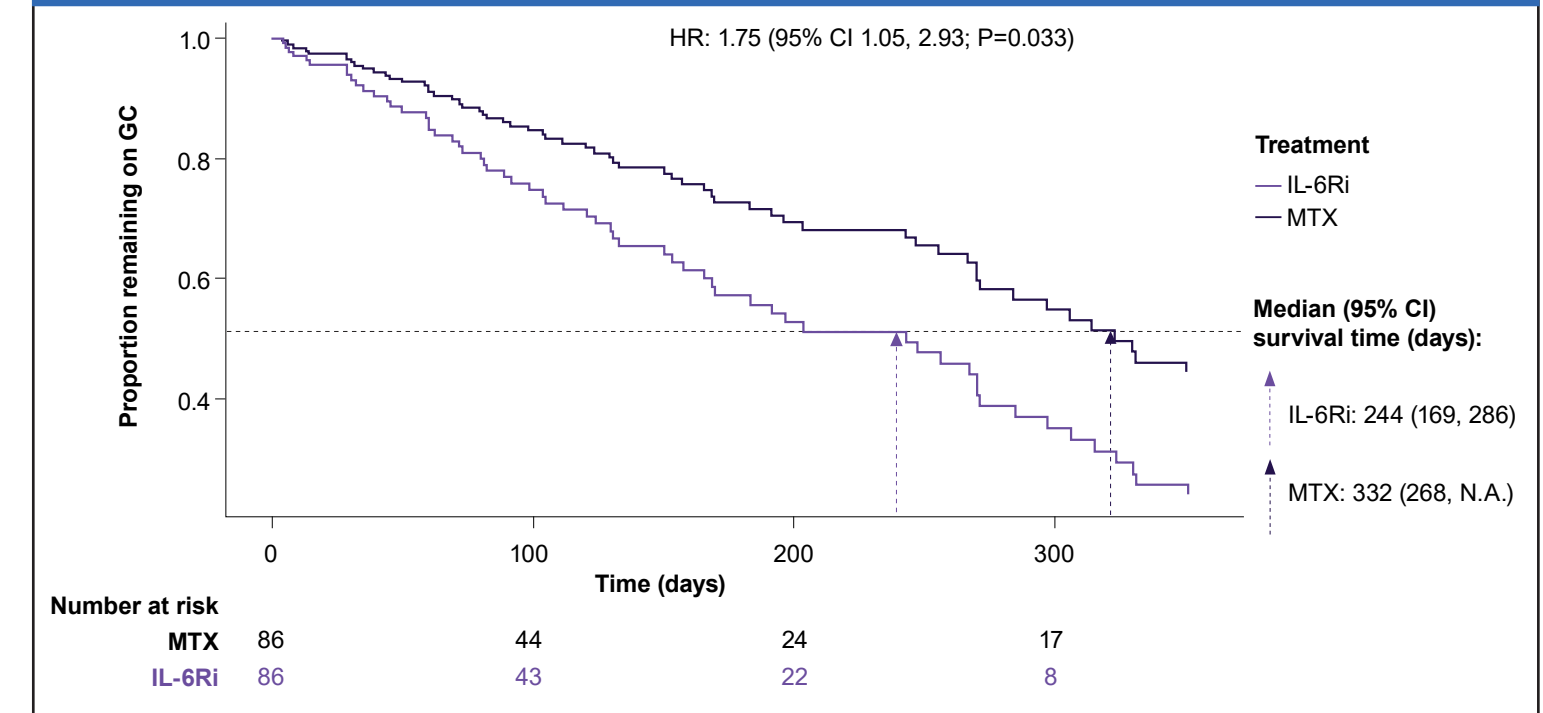
CFI, claims-based frailty index; CI, confidence interval; csIM, conventional synthetic immunomodulator; GC, glucocorticoid; GCA, giant cell arteritis; HR, hazard ratio; IL-6Ri, interleukin-6 receptor inhibitor; IQR, inter quartile range; MTX, methotrexate; PED, prednisone equivalent dose; PMR, polymyalgia rheumatica; PS, propensity score; RA, rheumatoid arthritis; SD, standard deviation; SMD, standardized mean difference.

ACKNOWLEDGEMENT

FASTER statisticians completed all the analyses. All authors contributed to the design of the analysis and interpretation of the results. Data included in this poster were originally presented at European Alliance of Associations for Rheumatology (EULAR) 2025, Barcelona, Spain (June 11–14, 2025). Medical writing support for the original poster (EULAR 2025) was provided by Kritika Dhamija, M.S. (Pharm.), of Sanofi and editorial support for this encore poster was provided by Himani Powle, Pharm D, of Sanofi.

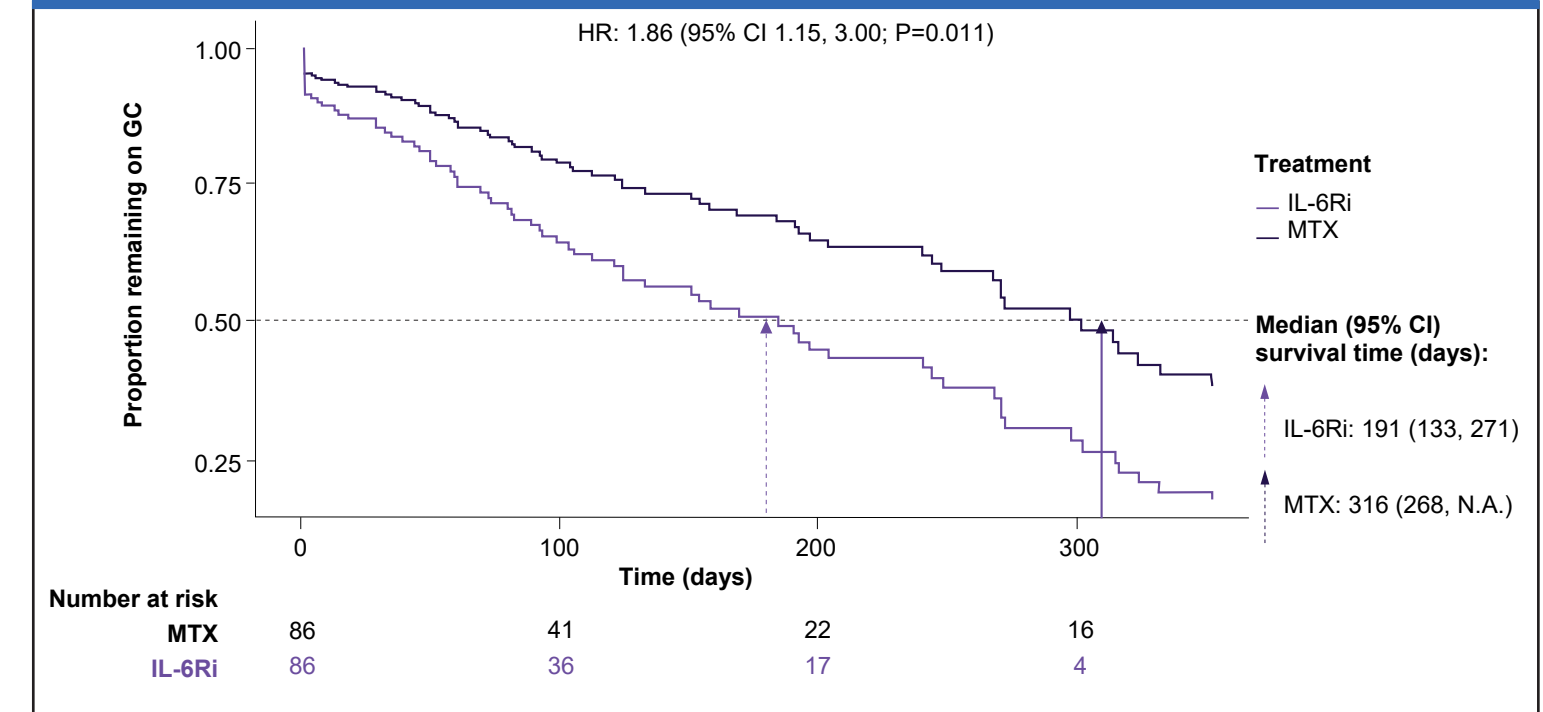
- Time to GC discontinuation up to 1 year was significantly shorter for the IL-6Ri vs. MTX-treated patients (Figure 2)

Figure 2: Kaplan-Meier survival curve of time to GC discontinuation up to 1 year



- Time to GC discontinuation or minimal GC (≤2 mg/day PED) up to 1 year was significantly shorter for the IL-6Ri vs. MTX-treated patients (Figure 3)

Figure 3: Kaplan-Meier survival curve of time to GC discontinuation or minimal GC up to 1 year



LIMITATION

- The number of patients with frailty may have been underestimated due to the exclusion of comorbidities that would have contributed to the frailty score, particularly malignancies which are common in this elderly population

REFERENCES

- Sattui SE, et al. *Rheumatology (Oxford)*. 2022;61(11):4455–6.
- Motta F, et al. *Front Immunol*. 2020;11:576134.
- Iorio L, et al. *Rheumatology (Oxford)*. 2025;64(Supplement_1):i48–54.
- Sattui SE, et al. EULAR 2024. Poster POS1427.
- Kim DH, et al. *J Gerontol A Biol Sci Med Sci*. 2019;74(8):1271–6.