CANAKINUMAB PROPHYLAXIS WITHOUT CORTICOSTEROIDS, PREVENTED FLARES IN PATIENTS INITIATING PEGLOTICASE WITH METHOTREXATE FOR UNCONTROLLED GOUT: A PROSPECTIVE, MULTICENTER, OPEN LABEL, PROOF-OF-CONCEPT, PHASE IV, CLINICAL TRIAL

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Background

- Pegloticase + methotrexate (MTX), FDA approval July 2022,[1] is effective in reducing signs/symptoms of uncontrolled gout.[2]
- The pivotal trial (MIRROR RCT) confirmed pegloticase + MTX superiority in safety and efficacy (month 6 response rate: 71% vs. 39%; IR rate: 4% vs. 31%).
- Gout flare, the most common adverse event, occurred in 54% of patients in the pegloticase + MTX treatment group despite daily NSAID or colchicine prophylaxis and pre-infusion IV methylprednisone 125 mg.[3]
- Canakinumab is FDA approved for treatment of recurrent gout flares in patients who cannot be treated with NSAIDs, colchicine, or repeated courses of corticosteroids (CS)[4] and can reduce subsequent flares during allopurinol initiation, presumably through the IL-1 pathway,[5,6] but has not been studied as prophylaxis.

Objective

- To determine if canakinumab prophylaxis (without CS, NSAIDs, or colchicine) prevents gout flares associated with initiating pegloticase + MTX (MIRROR-C).

Methods

- In this multicenter, open label trial, 12 sequential adult uncontrolled gout patients scheduled to initiate pegloticase + MTX treatment were consented.
- Patients were TB negative and able to take MTX for ≥4 wks prior to pegloticase initiation.
- Key exclusion criteria (similar to MIRROR RCT) included MTX or pegloticase contraindication, previous uricase exposure, eGFR <25 mL/min/1.73 m^2 or dialysis.
- Canakinumab 150 mg was given subcutaneously 7 days prior to the first pegloticase infusion and ≥3 wks after starting MTX.
- Pegloticase every 2 wks + MTX was initiated without preinfusion CS, NSAIDs, or colchicine.
- Assessment for gout flares using validated, patient reported criteria published by Gaffo et al[7] was performed at canakinumab injection and every 2 wks at each pegloticase infusion (or appointment if pegloticase was discontinued) for 6 mos.
- The primary endpoint was monthly gout flares vs. previously published results from MIRROR RCT, with particular interest at 12 wks.
- Preinfusion serum uric acid (SUA) and pegloticase response rates (intention to observe – last observation carried forward) were also collected.

Results

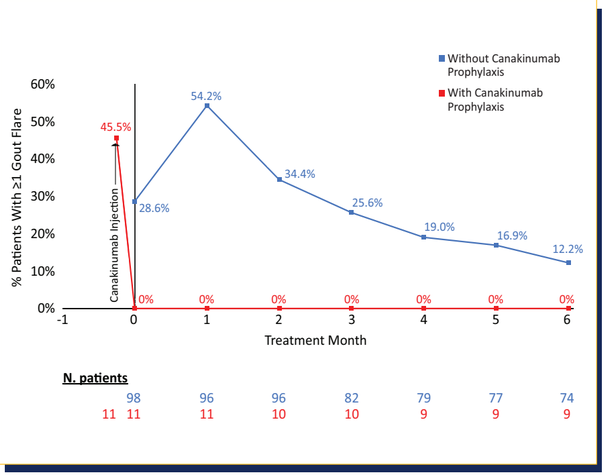
- Twelve patients met inclusion criteria from 3 separate sites and 11 received canakinumab prophylaxis and ≥1 pegloticase infusion (**Table 1**).

Table 1. Demographic and baseline characteristics in those patients that received canakinumab

Patient	Sex	Race	Age (at start)	Comorbidities	Tophi Present?	Previous Gout Treatments	Year of Gout Diagnosis	Baseline sUA
1	M	White	49	Ulcerative Colitis Morbid Obesity	N	Allopurinol Febuxostat	1992	9.7
2	M	Hispanic/ Latino	46	HTN	Y	Allopurinol	2017	8.5
3	M	White	56	HTN Hyperlipidemia Asthma	Y	Allopurinol Febuxostat	2018	10.8
4	M	White	69	CKD HTN	N	Allopurinol	2015	9.3
5	M	White	49	T1DM Hyperlipidemia	Y	Allopurinol	1998	7.2
6	M	White	72	HTN Hyperlipidemia Prediabetes Hypothyroidism	N	Allopurinol	1992	9.0
7	M	White	82	T2DM DVT Bradycardia Hyperlipidemia GERD Glaucoma	Y	None	2023	7.3
8	M	White	43	Kidney Stones	N	Allopurinol Febuxostat	2002	7.8
9	M	Asian	57	CKD HTN Hyperlipidemia Atrial Fibrillation	Y	Allopurinol Febuxostat	2003	9.0
10	M	Native Hawaiian/ Pacific Islander	38	HTN	Y	Allopurinol Febuxostat Probenecid	2003	10.4
11	M	Native Hawaiian/ Pacific Islander	38	CKD HTN Hyperlipidemia	Y	Allopurinol Febuxostat	2015	6.9

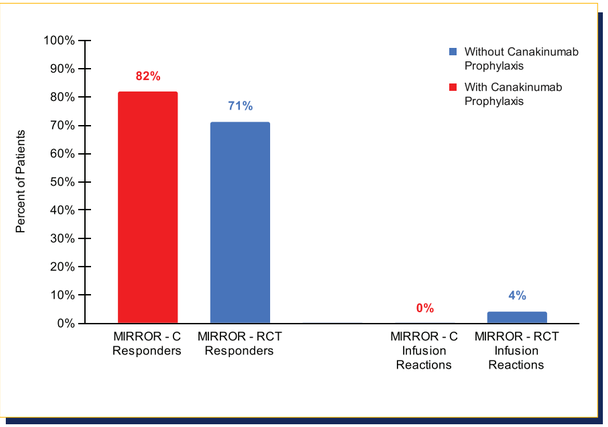
- One patient was lost to follow up after infusion 1.
- Two patients discontinued pegloticase, 1 due to a rise in SUA and 1 by patient choice.
- One patient experienced a rise in SUA but continued pegloticase.
- No new gout flares were reported in any patient receiving canakinumab prophylaxis (**Figure 1**).
- All active gout flares resolved within 48 hours of administration (**Figure 1**).
- Pegloticase + MTX response rate of 82% and infusion reaction rate of 0% were comparable to previous MIRROR RCT results (**Figure 2**).
- No new safety signals.

Figure 1. Percentage of patients experiencing ≥1 acute gout flare by month



Flares required ≥3 of 4 criteria (patient-defined gout flare, pain at rest score >3 on 0-10 scale, ≥1 swollen joint, ≥1 tender joint). Canakinumab injection administered at day -7 ± 2. Canakinumab flare data represents the prior 3-week MTX run-in period before injection. Month 0 flares are from canakinumab administration to first pegloticase infusion. Data from MIRROR RCT (active arm) provided for non-statistical comparison only.[3] Month 0 represents the 4-week MTX run-in period.

Figure 2. Percentage of MIRROR-C (with canakinumab prophylaxis) responders and percentage of patients with an infusion reaction as compared with published results from MIRROR RCT[3]



Conclusions

- Prophylaxis using a single dose of canakinumab 150 mg prevented gout flares in all patients initiating pegloticase + MTX for uncontrolled gout without CS and did not compromise efficacy or safety.
- Although additional studies are needed to corroborate these results, this data supports prophylaxis with canakinumab instead of CS when initiating pegloticase + MTX treatment.

References

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Disclosure of Interest

John Botson Speaker bureau: Abbvie, Amgen, and Horizon Therapeutics (now Amgen, Inc.)., Consultant: Horizon Therapeutics (now Amgen, Inc.) and Novartis., Grant/research support: Study site and principal investigator: Horizon Therapeutics (now Amgen, Inc.) and Olatec., Jeff Peterson Speaker bureau: Eli Lilly, Horizon Therapeutics (now Amgen, Inc.), and Janssen., Consultant: GlaxoSmithKline, Horizon Therapeutics (now Amgen, Inc.), Novartis, and Union Chimique Belge., Grant/research support: Study site and principal investigator Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Horizon Therapeutics (now Amgen, Inc.), Olatec, and SetPoint Medical.

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