Evaluation of Proposed Criteria for Remission and Evidence-Based Development of Criteria for Complete Response in Patients With Chronic Refractory Gout

Naomi Schlesinger, N. Lawrence Edwards, Puja P. Khanna, Anthony E. Yeo, and Peter E. Lipsky

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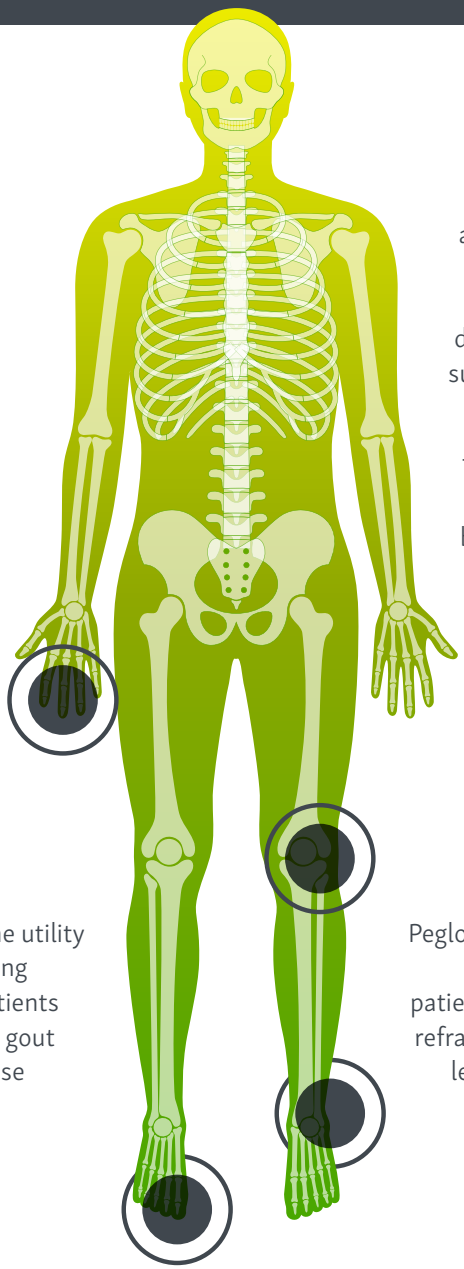
Background:

Treating to target is an approach to disease management that considers physiologic targets for controlling disease activity

A treat-to-target approach has become the standard of care in many chronic diseases and has been suggested for Gout[1,2,3,4]



However, treatment goals for patients with gout have not been fully defined[5,6,7]

Treatment goals have typically focused on biochemical response to treatment, for instance, lowering serum urate levels to < 6 mg/dl. However, reaching these levels does not guarantee an achievement of clinical goals

8 mg EVERY 2 WEEKS

This study evaluated the utility of proposed criteria using clinical results from patients with chronic refractory gout who received pegloticase

Pegloticase is an approved treatment for adult patients with chronic gout refractory as an oral urate level-lowering therapy

Methods:

Results from two identical randomized controlled trials (RCTs) of pegloticase and their open label extension (OLE) were analysed

18+

Patient were 18 years of age or older

Each patient had chronic refractory gout – defined as a baseline serum urate acid [sUA] of 8 mg/dl or more

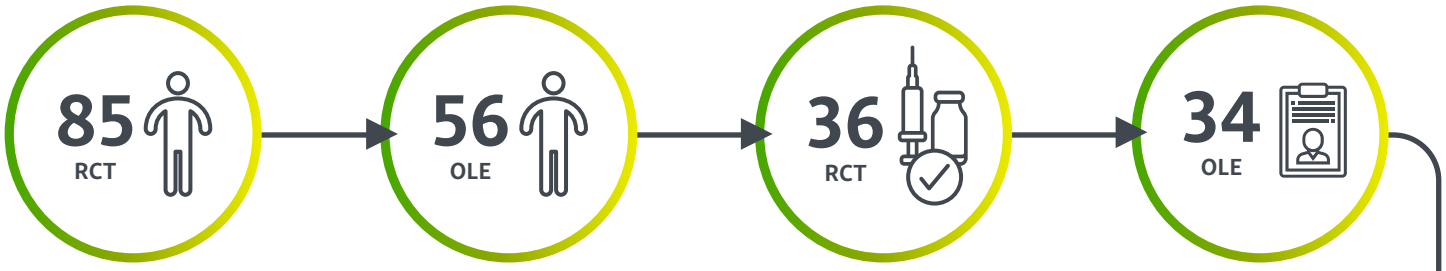
Patients were randomly assigned to 6 months of treatment with intravenous infusions of either:

- pegloticase 8 mg at each infusion
- pegloticase 8 mg alternating with a placebo
- or a placebo

The **primary endpoint** for the RCTs was a patient with a serum urate level less than 6 mg/dl for greater than or equal to 80% of the time during months 3 and 6

Secondary end points included:

- tophus resolution
- reductions in the proportion of patients with gout flares and in the number of flares per patient during months 1-3 and 4-6 of the trial
- eduction in tender joint counts (TJCs) and swollen joint counts (SJCs)
- patient-reported changes in pain, physical function, and quality of life, as measured by the Health Assessment Questionnaire (HAQ) pain scale, the HAQ–Disability Index, and the 36-item Short Form Health Survey (SF-36)[8]



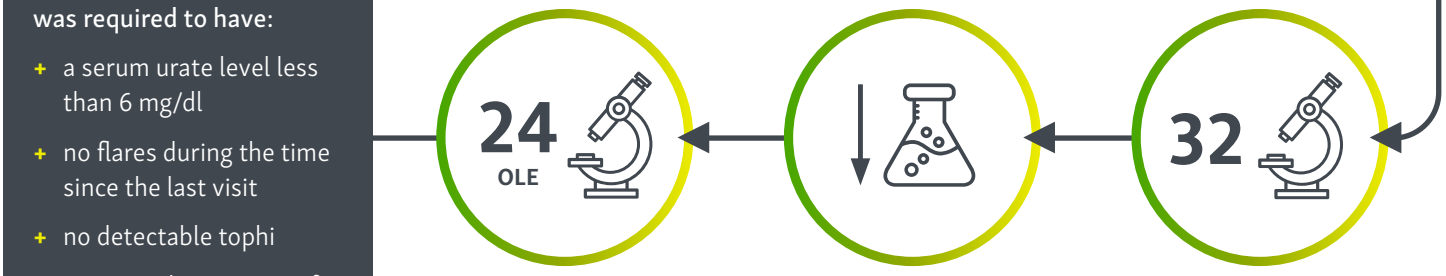
Of the 85 patients who entered the RCTs a total of 56 proceeded to the OLE with data collected to assess if they met the criteria of remission

Of these patients, 36 responded to treatment in the RCTs

34 entered the OLE[9]

To be classified as meeting remission criteria, a subject was required to have:

- a serum urate level less than 6 mg/dl
- no flares during the time since the last visit
- no detectable tophi
- a pain and PGA score of less than 2 on a 10-cm visual analog scale (VAS)



Of those without persistent lowering of urate levels in the RCT (nonresponders), 24 proceeded to the OLE and had sufficient data collected to be analyzed

32 had adequate data collected to assess

A repeated-measures mixed-effects model that controlled for repeated observations was used to relate the time when a response was noted in:

- PGA scores
- SF-36 bodily pain scores
- VAS pain levels
- TJC
- SJC
- the number of flare episodes
- the degree of tophus resolution

Results:

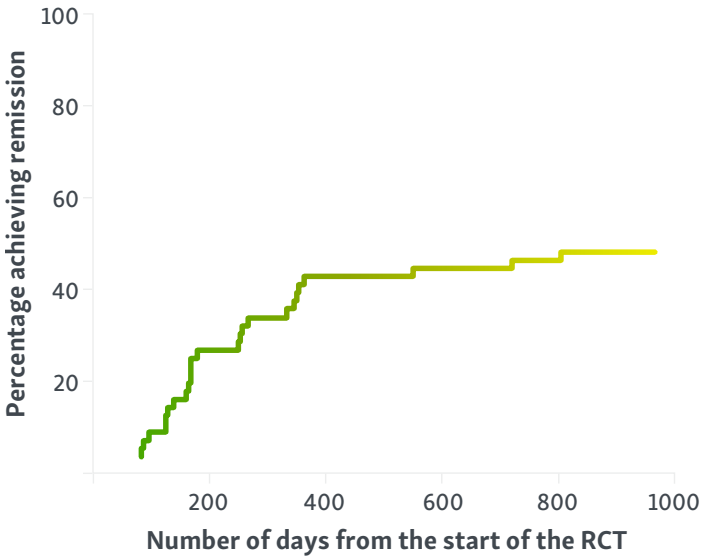
Achievement of remission

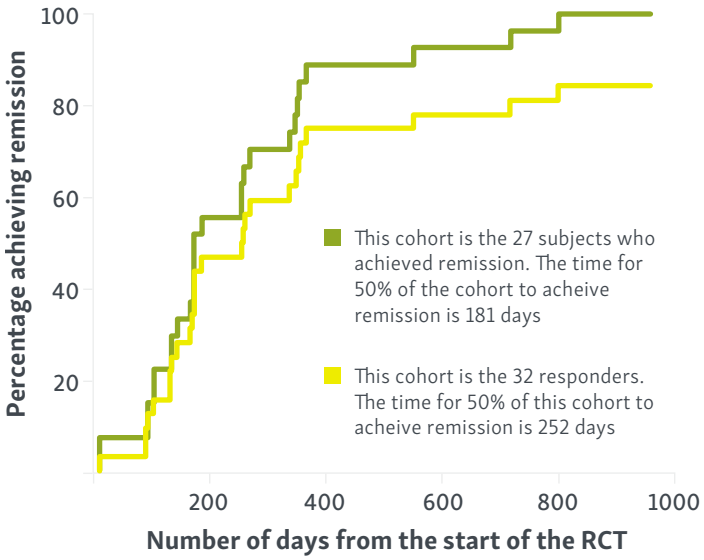
48.2% REMISSION

Of the **56 evaluable patients** treated with bi-weekly pegloticase, 27 or 48.2% met criteria for remission

84.4% REMISSION

Of the **32 responders** to pegloticase in the RCTs who entered the OLE, 27 (84.4%) met the criteria for remission





252 The length of time required for 50% of patients to achieve remission was 252 days (8.4 months) for all responders

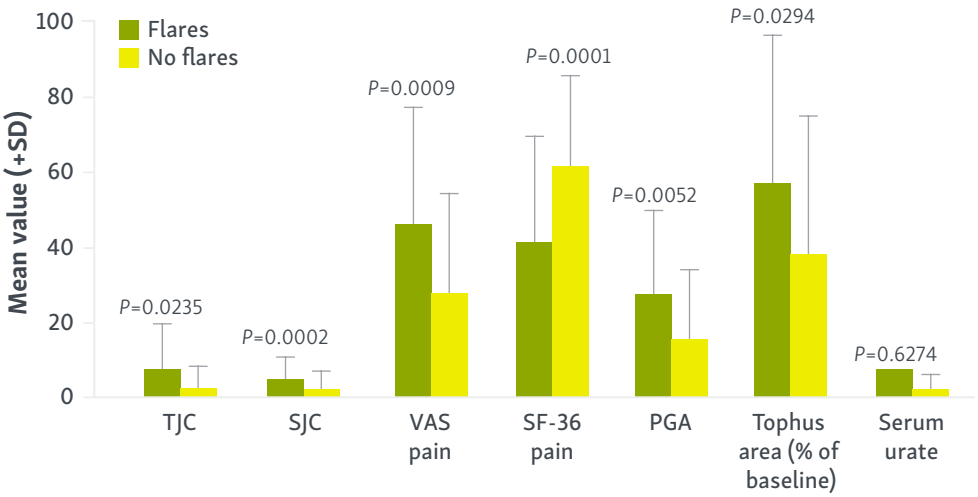
181 It took 181 days (6.0 months) for responders who achieved remission

When the requirement of a serum urate level less than 6 mg/dl was waived, only 2 of 24 (8.3%) nonresponders and 0 of 43 (0.0%) subjects receiving a placebo met clinical criteria for remission

Relationships between flares, serum urate levels, and patient clinical characteristics.

The relationships between gout flares and other variables were assessed

- All clinical variables were significantly worse at the time of a flare compared with assessments when there was no flare
- There was no significant difference between the serum urate level at the time of a flare and the serum urate level at other times



Results of mixed modelling

To develop new composite criteria for a complete response (CR) from this data set, repeated-measures mixed-effects modelling with backward elimination of components with the least statistical significance was conducted

The final criteria for CR were a serum urate level less than 6 mg/dl, resolution of all measured tophi, a PGA score of 1 or more, a SJC of 1 or more, and a TJC of 1 or more

Achievement and maintenance of CR

71.9%
MET CRITERIA OF CR

Of the 32 responders, 23 (71.9%) met the criteria of CR

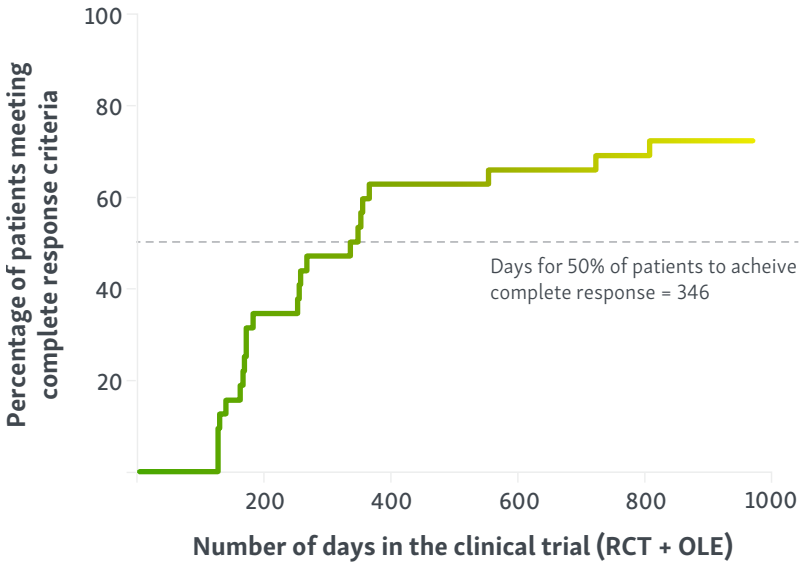
346

+ The time it took for 50% of patients to achieve a CR was **346 days**

+ All patients who achieved a CR maintained it until the end of the follow-up

507

+ The mean duration of a CR was **507.4 days**



Analysis of results for patients who responded to administration of monthly pegloticase.

Of the 25 patients who responded to administration of pegloticase every 4 weeks and completed the RCTs indicated that:

64%
(16 PEOPLE) MET THE CRITERIA FOR A CR

50%
OF THIS SUBGROUP ACHIEVED THIS RESPONSE IN 424 DAYS

Conclusions:

85.3%
REMISSION

85.3% of responders to biweekly pegloticase met the criteria for remission, which included:

+ a serum urate level less than 6 mg/dl
+ no tophi
+ no flares
+ a pain score of less than 2 on a 10-cm VAS
+ a PGA score of less than 2 on a 10-cm VAS

Therefore, the proposed remission criteria clearly appeared to be effective in distinguishing the quality of the response in subjects with chronic refractory gout treated with pegloticase

The composite CR measure can serve as an evidence-based target to inform the design and end points of future clinical trials in chronic gout

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