Recurrence pericarditis (RP) is characterized by the recurrence of pericarditis signs and symptoms after a presumed non-recurrent episode of RP. The incidence of RP recurrence varies, but it is estimated to occur in 10-20% of patients. The recurrence period is defined as 100% of patients who experience recurrence within 100 days of the initial episode. Approximately 16.7% of patients experience recurrence in the first 3 months after the initial episode.

In terms of tissue damage caused by IL-1, IL-1α and IL-1β, thus preventing interaction with IL-1β, the pericardium stimulates additional IL-1α to amplify the inflammatory response. This amplification leads to the release of additional pro-inflammatory cytokines, which contribute to the chronic inflammation of the pericardium.

Safety data from this study are consistent with the known safety profile of rilonacept (rilonacept, Regeneron, Tarrytown, NY). No serious adverse events (SAEs) were reported in the study. The most common adverse events (AEs) reported during the study were nasopharyngitis and upper respiratory tract infection.

Neutrophils in patients with corticosteroid (CS) dependency allowed for discontinuation of corticosteroids without pericarditis recurrences, including patients who had previously required corticosteroid treatment. All patients on CS at baseline who completed the Extension Period reduced their prednisone dosing by over 50% from baseline.

Corticosteroid-dependent patients who entered the study without an active pericarditis episode maintained low prednisone dosing and CRP levels without disease recurrences despite tapering off the corticosteroids while rilonacept treatment continued.

The clinical response for patients who were on CS during the extension period showed that 87.5% of patients who entered the extension period with CS had a decrease in CS dose and 55.6% of patients had complete withdrawal of CS by the end of the extension period.

All patients on CS at baseline who completed the Extension Period reduced their prednisone dosing by over 50% from baseline and none of these patients experienced a pericarditis recurrence while on an rilonacept treatment.

Rilonacept was generally well tolerated and no new safety signals were identified. The most common adverse events were nasopharyngitis and upper respiratory tract infection. There were no serious adverse events reported in the study.

CONCLUSIONS

- Rilonacept treatment in both patient groups (CS and non-CS) and other clinical characteristics of pericarditis (age, sex, and sex) were well balanced. Rilonacept was well tolerated and no new safety signals were identified.

- Clinically meaningful reductions in pain severity and CRP tests were seen as early as the first rilonacept administration and maintained throughout the 6-month period.

- Minor rilonacept CRP normalization was seen as early as the first rilonacept administration.

- Treatment with rilonacept reduced CRP, IL-1α, and IL-1β levels in patients with corticosteroid dependence, indicating a potential role for rilonacept in the treatment of patients with corticosteroid-dependent RP.

- All patients who entered the extension period with CS had a decrease in CS dose and none of these patients experienced a pericarditis recurrence while on an rilonacept treatment.

- Rilonacept was generally well tolerated and no new safety signals were identified. The most common adverse events were nasopharyngitis and upper respiratory tract infection. There were no serious adverse events reported in the study.
Supplemental Information

Supplementary Figure 3. Study Design of RHAPSODY (NCT03737110)

Supplementary Table 2. Baseline Demographics and Clinical Characteristics

Supplementary Table 3. Changes in pain NRS and inflammation (n=11 patients)

Supplementary Table 4. Summary of Adverse Events by System Organ Class

Supplementary Table 5. Summary of Local Changes

Changes in joint NRS and inflammation (n=11 patients)

Case Study: Treatment/Withdrawal of RP with Rilonacept

Pain: Patient’s pain levels with placebo and celecoxib were 6 and 7, respectively, at baseline. After 2 weeks, pain decreased to levels of 2 and 3, respectively, with celecoxib.

CRP: CRP decreased from baseline levels of 8.85 mg/dL to 0.90 mg/dL with celecoxib.

Addition of rilonacept to colchicine background rapidly reduced pain (week 2 pain NRS 0/10; week 24 pain NRS 0/10), decreased CRP (week 2 CRP 0.66 mg/dL; week 24 CRP 0.09 mg/dL), and resolved pericardial effusion (week 24 CRP 0.09 mg/dL; absence of pericardial effusion).

Results from this study support the design of RHAPSODY, an ongoing, double-blind, placebo-controlled randomized withdrawal trial (NCT03737110) Phase 1 placebo trial with an open-label extension, intended to evaluate the efficacy and safety of rilonacept treatment in patients with pericarditis.

Supplementary Figure 4. Study Design of RHAPSODY (NCT03737110)

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