Tapering and discontinuation of background therapies during the transition to rilonacept monotherapy in RHAPSODY, a phase 3 clinical trial of rilonacept in patients with recurrent pericarditis

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BACKGROUND

Recurrent Pericarditis (RP)

- Debilitating autoinflammatory disease often requiring months to years of treatment[1-3]
- ~15 to 30% of patients will experience additional episodes, or recurrent pericarditis (RP).[1, 4]

Role of IL-1

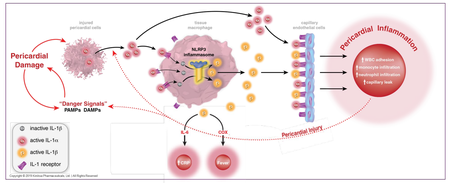
- Interleukin 1 (IL-1) has been implicated as a key mediator of recurrent pericarditis.[5-9]

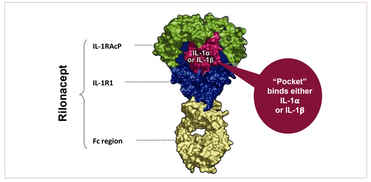
Rilonacept

- Once-weekly IL-1α and IL-1β cytokine trap
- Phase 3 clinical trial RHAPSODY (NCT03737110) demonstrated efficacy and safety of rilonacept in patients with RP.[10]
  - RHAPSODY data helped support FDA approval of the first therapy for RP.[11]

Tapering of Therapies

- Non-specific immunosuppressants commonly used: NSAIDs/colchicine/corticosteroids
  - Many patients require long-term use of corticosteroids, which are associated with significant morbidity.[1-2]
  - NSAIDs and colchicine are associated with gastrointestinal side effects.[12]
- Treatment with CS with fast tapering may be associated with an increased risk of pericarditis recurrences.[13]
- Following an episode of recurrent pericarditis, physician approach to medication tapering is variable.
- ESC guidelines recommend gradual tapering of corticosteroids.[1]
  - Decrease by 1-2.5 mg/day every 2-6 weeks over 1-2 years





HYPOTHESIS

- Rilonacept allows faster tapering of therapies while reducing risk of recurrence

METHODS

RHAPSODY[10]: Global, Double-blind, Placebo-controlled, Randomized Withdrawal Phase 3

Inclusion Criteria:

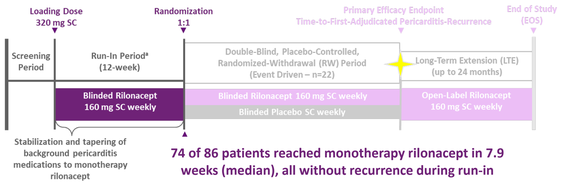
- Presenting with at least 2nd pericarditis recurrence; pain NRS ≥4, CRP≥1 mg/dL
- NSAIDs/Colchicine/Corticosteroids in any combination
- Multiple etiologies

Definition of Clinical Response

- Weekly average of daily pericarditis pain of ≤2.0 on the 11-point NRS
- CRP level ≤0.5 mg/dL
- On monotherapy study drug without a recurrence

Post Hoc Analysis

- Analysis of approaches to tapering of therapies during treatment with rilonacept



74 of 86 patients reached monotherapy rilonacept in 7.9 weeks (median), all without recurrence during run-in

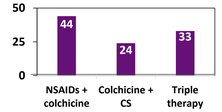
- In this retrospective analysis, in the group of patients (n=79) who reached rilonacept monotherapy, we evaluated therapies at baseline
- Patients were divided into groups based on their use of NSAIDs, colchicine, and corticosteroids (CS) at baseline
  - NSAIDs + colchicine
  - Colchicine + CS
  - Triple therapy (NSAIDs + colchicine + CS)
- In patients being treated with both colchicine and CS, patients were divided into subgroups depending on tapering approach
  - Sequential tapering: colchicine taper initiated only after CS taper completed
  - Concurrent tapering: colchicine taper initiated during CS taper

RESULTS

Baseline Demographic and Clinical Characteristics

- A majority of patients entered the trial on multiple commonly used therapies; 19% were being treated with a single therapy
- About half (48%) of patients were treated with CS at baseline

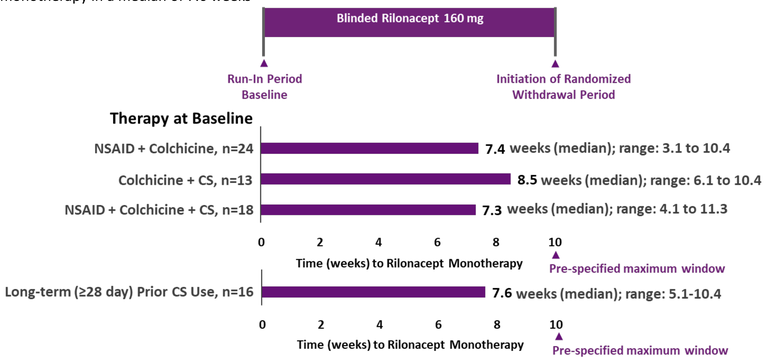
Proportion of Patients Treated at Baseline with Combinations of NSAIDs, colchicine, and CS n=55*



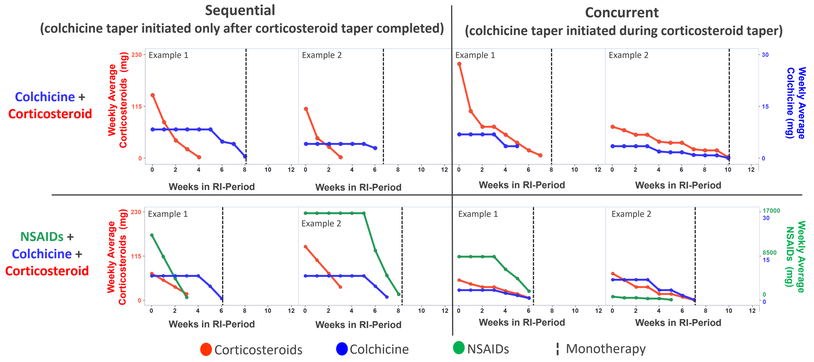
*Patients receiving only one therapy alone or one therapy in combination with therapies besides NSAIDs, colchicine, and CS (i.e. analgesics) are not included (n=17); also not included are 2 patients treated with the combination of NSAIDs and CS.

Time to Monotherapy by Therapy Combination at Baseline

- In RHAPSODY, 74 of 86 patients reached rilonacept monotherapy in 7.9 weeks (median), without recurrence
- Patients on multiple therapies reached monotherapy rilonacept with medians ranging from 7.3 to 8.5 weeks
- The subset of patients whose recurrent pericarditis had been treated with long-term (≥28 day) CS reached rilonacept monotherapy in a median of 7.6 weeks

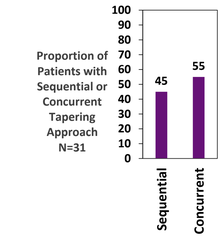


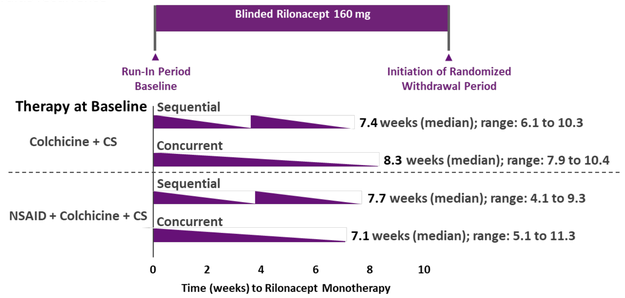
Representative Approaches to Tapering of Colchicine and Corticosteroids



Colchicine and CS Tapering Approach During Run-In Period

- Similar numbers of patients were tapered sequentially (colchicine taper initiated only after CS taper completed) as were tapered concurrently (colchicine taper initiated during CS taper)
- Patients who were tapered sequentially or concurrently all successfully reached rilonacept monotherapy within a median of 7.4- 8.3 weeks without pericarditis recurrence





CONCLUSIONS

- In RHAPSODY, initiation of rilonacept in patients presenting with an acute recurrence despite standard therapy resulted in rapid resolution of pericarditis, with an average time to treatment response of 5 days
- In RHAPSODY, patients on rilonacept rapidly and successfully tapered off commonly used therapies, including long-term CS, in a median of 7.9 weeks or less, which is faster than recommended by ESC guidelines
  - ESC guidelines recommend gradual tapering of CS, decreasing by 1-2.5 mg/day every 2-6 weeks over 1-2 years
  - ESC guidelines also recommend stopping a single class of drugs at a time
  - Patients in RHAPSODY were tapered faster than the 10-week period allowed by the study protocol
- The clinical trial design provided a 10-week structure for tapering
  - While this could be seen as a limitation of interpretation of this data, the observed result of successful tapering in 7.9 weeks (median) suggests instead that the observed rapid treatment response may have increased in investigator confidence to taper more rapidly than in clinical practice
- These findings suggest rapid tapering of commonly used therapies to achieve rilonacept monotherapy could be feasible without recurrence. This may help lessen the side effects of prolonged CS exposure compared to ESC guidelines.

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Disclosures

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