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RHAPSODY: a pivotal phase 3 trial to assess efficacy and safety of rilonacept, an interleukin 1 alpha and beta blocker, in patients with recurrent pericarditis

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Topic(s): Trial Design

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Background: Recurrent pericarditis (RP) is managed with nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids (CS), and colchicine; up to 15% of pericarditis patients experience multiple recurrences. Interleukin 1 (IL-1) is an important cytokine in the pathophysiology of RP. Rilonacept (KPL-914) is a recombinant fusion protein which binds IL-1α and IL-1β. An ongoing Phase 2 study of rilonacept demonstrated improvements in RP symptoms and inflammation.

Purpose: To evaluate the efficacy and safety of subcutaneous (SC) rilonacept in patients with RP in a Phase 3, randomized, placebo-controlled trial.

Methods: RHAPSODY is a double-blind, placebo-controlled, randomized-withdrawal trial; ~50 patients will be enrolled (Figure). Patients (≥12 y) must present with at least a third pericarditis episode (all etiologies except infectious and malignant) characterized by a pain score ≥4 on the 11-point Numeric Rating Scale (NRS) and C-reactive protein (CRP) ≥1 mg/dL at screening. Patients may be receiving stable doses of analgesics, NSAIDs, colchicine, and/or CS. After a loading dose (320 mg SC in adults and 4.4 mg/kg SC in children), all patients will receive weekly rilonacept (160 mg SC in adults and 2.2 mg/kg SC in children) during the run-in period. Patients able to taper and discontinue concomitant pericarditis medications and achieve clinical response (mean daily NRS score ≤2.0 during the 7 days before randomization and CRP level ≤0.5 mg/dL) will be randomized 1:1 in a blinded fashion to continued rilonacept or matching placebo weekly SC injections. Investigators may choose different treatments for pericarditis recurrences based on patient clinical status, including bailout rilonacept, while maintaining the blind to prior treatment assignment. The primary efficacy endpoint is time to pericarditis recurrence (adjudicated by an independent committee) in the randomized-withdrawal portion of the study. Secondary efficacy endpoints are the proportion of patients maintaining a clinical response, percentage of days with NRS pain score ≤1, and percentage of patients with no-to-minimal pericarditis symptoms based on patient global assessment. Safety evaluations include adverse events monitoring, physical examinations, and laboratory tests.

Conclusions: RHAPSODY is a pivotal Phase 3 trial evaluating the efficacy and safety of rilonacept in patients with RP using a double-blind, placebo-controlled, randomized-withdrawal design. The results of this study may inform the management of RP.
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*Duration of the run-in period is not disclosed to maintain patient blinding to the start of the randomized-withdrawal period.

Figure 1