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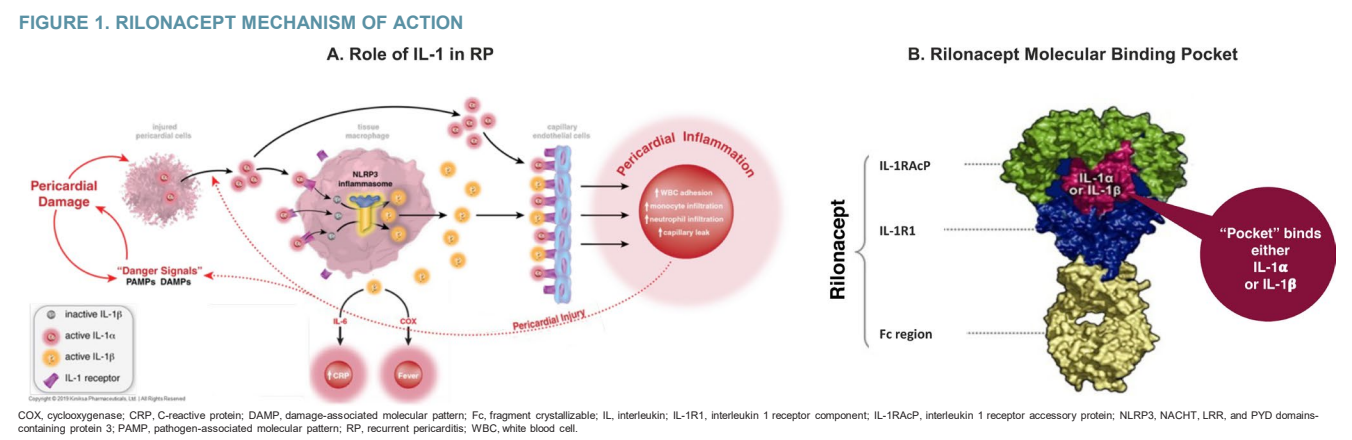
BACKGROUND

Recurrent Pericarditis (RP)

- RP is a chronic, debilitating autoinflammatory disease mediated in part by interleukin-1 (IL-1)^{1,2} (Figure 1)
- Among patients with multiple recurrences, epidemiologic data describe a median disease duration of 2.84 years³
- More recently, a chart review study showed that, for patients (n = 106) presenting with an active flare (median 3 prior recurrences) and hs-CRP level > 10 mg/L (n = 92), only 31% of these patients achieved clinical remission (no longer requiring anti-inflammatory therapy) during the median 21-month observation period (IQR, 12–38 months)⁴
- Treatment for RP commonly consists of nonspecific oral therapies (e.g., NSAIDs, colchicine, or corticosteroids). However, NSAIDs and colchicine have incomplete efficacy and dose-limiting side effects, and corticosteroids have serious safety risks when used long-term^{2,5,6}

Riloncept

- Riloncept is a once-weekly interleukin-1α (IL-1α) and interleukin-1β (IL-1β) cytokine trap that prevents engagement of IL-1 with its cell-surface receptor, thus inhibiting IL-1α and IL-1β activity (Figure 1)⁷
- Riloncept is approved in the United States for the treatment of recurrent pericarditis and reduction in risk of recurrence in adults and children 12 years and older. It is also approved for cryopyrin-associated periodic syndromes (CAPS) in adults and children 12 years and older and for the maintenance of remission of deficiency of interleukin-1 receptor antagonist (DIRA) in adults and pediatric patients weighing 10 kg or more⁸

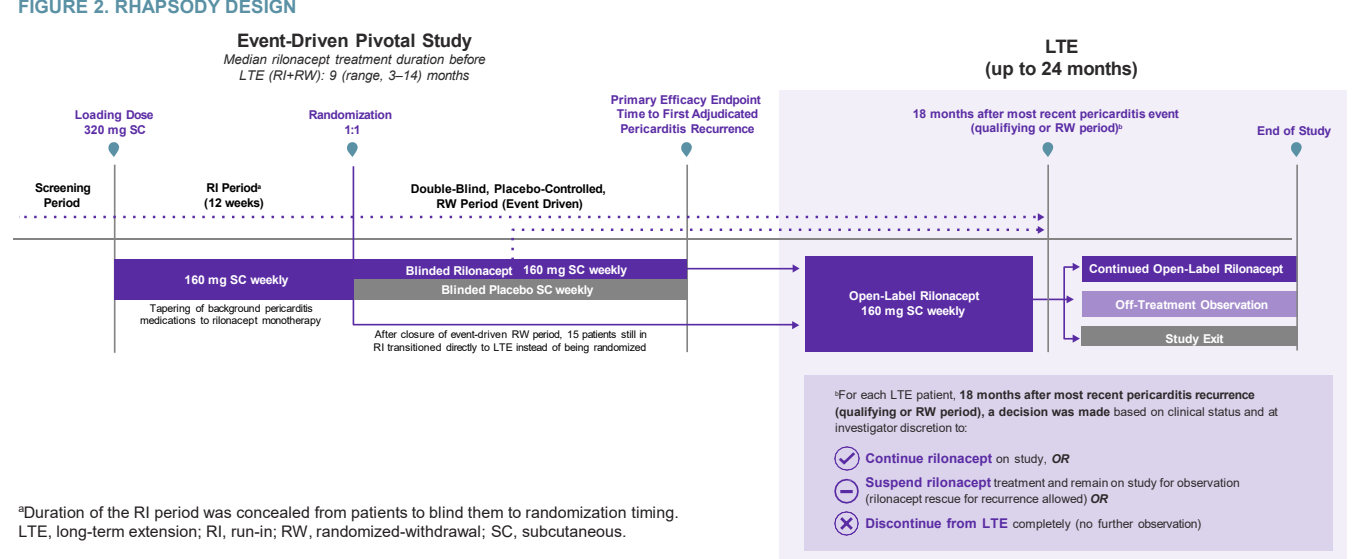


RHAPSODY

- RHAPSODY was a phase 3, double-blind, placebo-controlled, event-driven, randomized-withdrawal (RW) trial of riloncept in patients with RP, which also included a long-term extension (LTE) phase, allowing up to 24 months of additional open-label riloncept treatment (Figure 2)
- Population: Patients enrolling in the pivotal study had a mean disease duration of 2.4 years and presented with an acute pericarditis recurrence (qualifying episode) despite use of NSAIDs (67%), colchicine (80%), or corticosteroids (49%)
 - Mean CRP level was 6.2 mg/dL
 - The cause of pericarditis was idiopathic in 85%, post-pericardiotomy syndrome in 14%, and Dressler syndrome in 1% of the cohort
- All suspected pericarditis recurrence events in the event-driven RW period were formally adjudicated by the Clinical Endpoint Committee (CEC)
- Results of the pivotal study
 - During the run-in period, the median (95% CI) time to pain response was 5 (4–6) days, and the median (95% CI) time to normalization of the CRP level was 7 (5–8) days. The median (95% CI) time to the prespecified treatment response was 5 (4–7) days
 - During the RW period, patients receiving riloncept experienced a 96% reduction in the risk of recurrence (hazard ratio in a Cox proportional-hazards model, 0.04; 95% CI, 0.01–0.18; P<0.0001 by log-rank test)
 - There were too few recurrence events in the riloncept group to allow for the median time to the first adjudicated recurrence to be calculated
 - The median (95% CI) time to the first adjudicated recurrence in the placebo group was 8.6 (4.0–11.7) weeks
 - In the period until the event-driven RW portion of the study was closed, 2 of 30 patients (7%) in the riloncept group experienced a pericarditis recurrence, as compared with 23 of 31 patients (74%) in the placebo group
 - The 2 recurrence events in the riloncept group were associated with temporary interruptions of the trial-drug regimen of 1 to 3 weekly doses
 - The most common adverse events were injection-site reactions and upper respiratory tract infections

PURPOSE

- The LTE phase of RHAPSODY was designed to provide further insights into the efficacy and safety of riloncept in patients with RP and to help inform future clinical decision-making in this disease

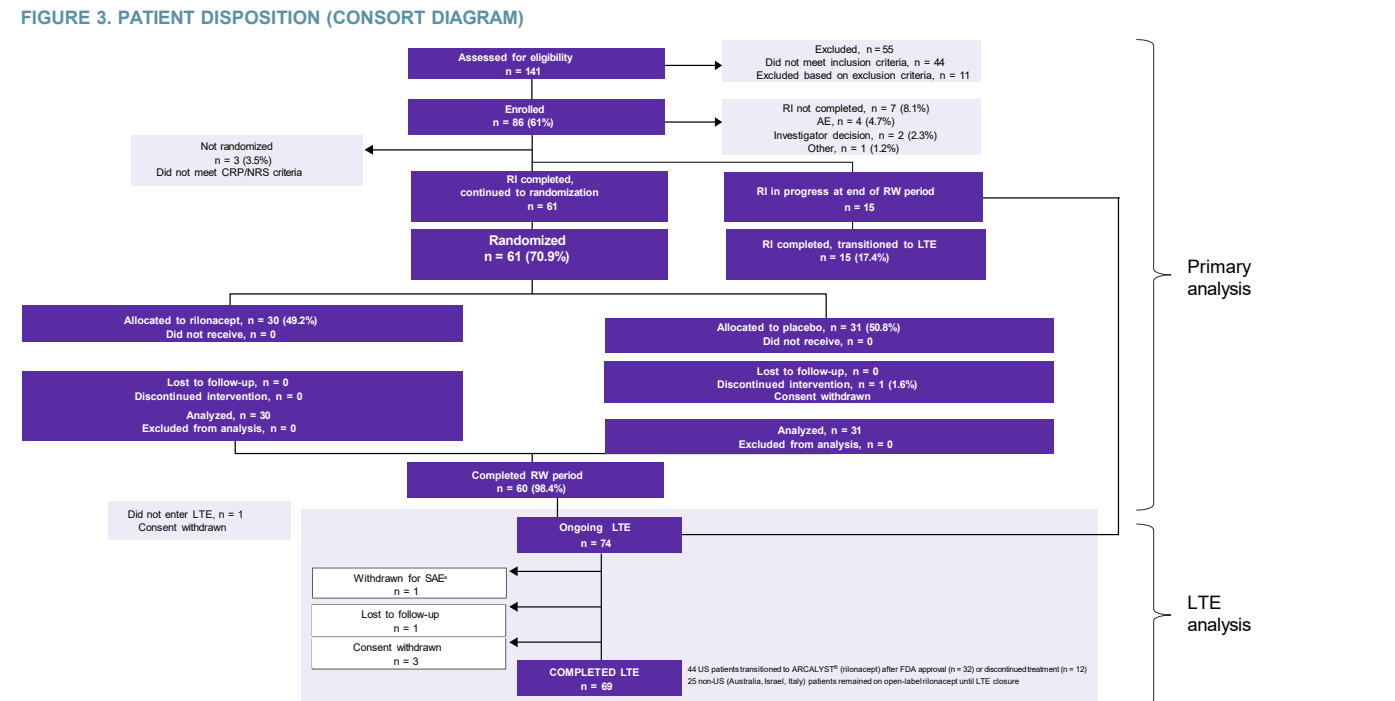


*Duration of the RI period was concealed from patients to blind them to randomization timing. LTE, long-term extension; RI, run-in; RW, randomized-withdrawal; SC, subcutaneous.

RESULTS

Patient Disposition

- Patients entering the LTE already had a history of 2.5 years of disease duration (mean 3.8 pericarditis recurrences) before entering RHAPSODY
- At the end of the event-driven RW study, the median duration of riloncept therapy had reached 9 months (maximum 14 months)
- In May 2020, 74 of 75 eligible patients continued into the RHAPSODY open-label LTE (Figure 3)
- Baseline demographics and prior pericarditis history at run-in baseline for participants in the LTE (n = 74) are summarized in Figure 4
- At the 1-year anniversary of the LTE (April 2021), the median duration of continuous riloncept treatment had reached 20 months
- All patients were followed in the LTE until geography-specific study closure
 - Total LTE—all geographies (n = 74)
 - Median riloncept treatment duration from run-in baseline was 23 months (maximum 35 months)
 - US patients (n = 45)
 - In April 2021, the LTE was concluded in the United States, and all US patients either switched to commercial ARCALYST® (riloncept) therapy (n = 32) or discontinued riloncept (n = 12)
 - Median continuous riloncept treatment duration from run-in baseline was 18 months (maximum 27 months)
 - Non-US (Italy, Israel, Australia) patients (n = 29)
 - In June 2022, the non-US LTE was concluded, and all patients discontinued riloncept
 - Median riloncept treatment duration from run-in baseline was 29 months (maximum 35 months)



*Acute endocarditis. AE, adverse event; CRP, C-reactive protein; FDA, US Food and Drug Administration; LTE, long-term extension; NRS, numerical rating scale; RI, run-in; RW, randomized-withdrawal; SAE, serious adverse event.

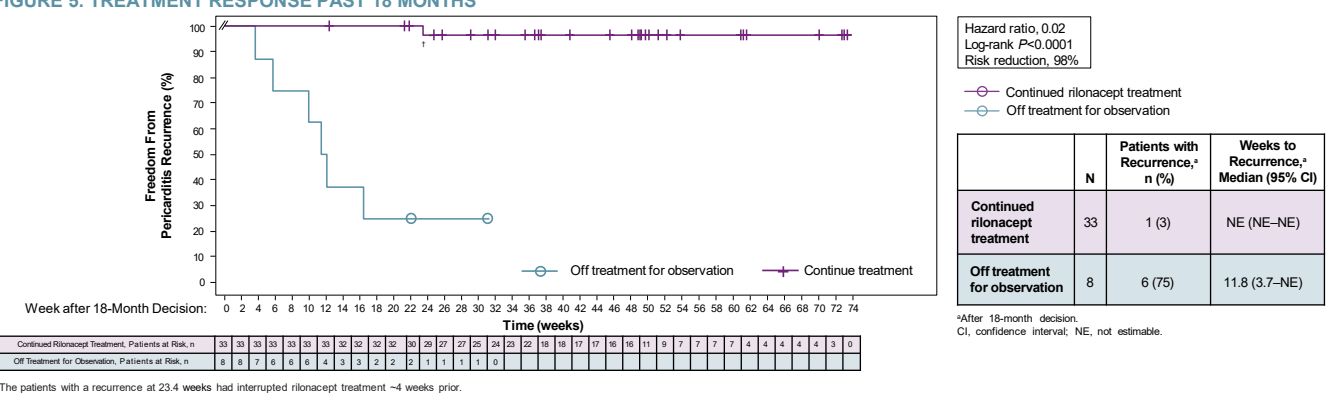
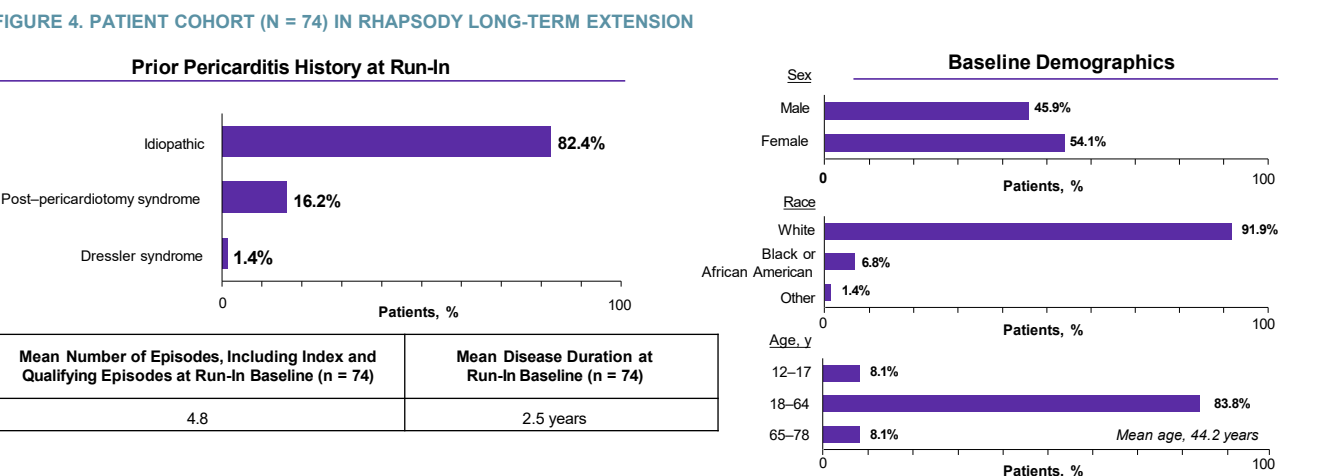
Efficacy Up to 18-Month Decision Point

- During treatment with open-label riloncept in the LTE (before 18-month decision point), continued riloncept treatment resulted in continued treatment response
 - Pericarditis recurrences, inflammation signs (CRP levels), and severity of RP symptoms (Patient Global Impression of Pericarditis Severity [PGIPS]) remained low
 - At each study visit:
 - >95% of patients had CRP levels ≤1 mg/dL
 - >86% of patients reported absent or minimal pericarditis symptoms (PGIPS)
 - Only 3 investigator-assessed recurrences were reported
 - Annualized incidence: 0.04 events per patient-year

Efficacy After 18-Month Decision Point

- A total of 52 patients reached the 18-month decision point while on riloncept (i.e., 18 months since most recent recurrence, whether qualifying episode or in the RW period)
 - 33 patients continued treatment with open-label riloncept
 - 8 patients suspended riloncept treatment and remained on study for observation (riloncept rescue for recurrence was allowed)
 - 11 patients discontinued study participation
- Continued treatment with riloncept past 18 months resulted in continued treatment response
 - There was a 98% reduction in risk of recurrence (hazard ratio, 0.02; P<0.0001) (Figure 5)
 - Recurrence (investigator-assessed) rate was 3.0% (1/33) in the patients who continued riloncept treatment. This recurrence occurred at 23.4 weeks into the LTE and was associated with a treatment interruption of 4 weeks
 - Recurrence (investigator-assessed) rate was 75.0% (6/8) in the patients who suspended riloncept treatment for observation
 - The median (IQR) time to recurrence after suspending riloncept treatment was 11.8 (3.7–not estimable [NE]) weeks
 - Reinitiation of riloncept resulted in resolution of acute pericarditis recurrence
 - Annualized recurrence rate^b (95% CI) was 0.18 (0.06–0.41) events per patient-year for the patients who remained on riloncept and 2.18 (0.80–4.75) events per patient-year for the patients who interrupted riloncept
- At the end of the LTE treatment period, patients stopped riloncept treatment and were returned to standard of care for recurrent pericarditis. Patients were monitored in a posttreatment safety follow-up period (6 weeks post-last dose) for adverse events
 - 4 additional pericarditis recurrences occurred during the posttreatment follow-up period, at ~6 weeks post-riloncept treatment (3 patients) and ~3 weeks post-riloncept treatment (1 patient)

*Two-sided P value, log-rank test. ^bNumber of recurrences in LTE periods for all patients/sum of patient-years in LTE periods for all patients. For patients who continued in study off treatment for observation, patient-years calculated as treatment, minimum (end-of-study date, cutoff date, first-dose date, after observation -1) - LTE 18-month disposition date +1; for patients who continued treatment, patient-years calculated as minimum (end-of-study date, cutoff date) - LTE 18-month disposition date +1; 95% CI calculated using an exact method with Poisson distribution.



Safety (Table 1)

- During the LTE period, treatment-emergent adverse events (TEAEs) were experienced by 83.8% of patients (n = 62)
- In most patients, the maximum severity of TEAEs was mild (37.8%) or moderate (37.8%)
- 2 patients experienced serious TEAEs (acute endocarditis, viral pneumonia) considered "related" to the study drug

TEAE Category,* n (%)	LTE Period (n = 74)
Any TEAE ^b	62 (83.8)
TEAE by maximum severity ^c	
Mild	28 (37.8)
Moderate	28 (37.8)
Severe	6 (8.1)
TEAE related to study drug ^d	21 (28.4)
Patients with serious TEAEs ^e	5 (6.8)
Serious TEAE related to study drug	2 (2.7)
Leading to dose interruption	2 (2.7)
Leading to study drug discontinuation	3 (4.1)
Leading to death	0
Infection or infestation	31 (41.9)
TEAE of upper respiratory tract infection	12 (16.2)
TEAE of injection-site reaction	4 (5.4)

*Patients with multiple events were counted once in same category. ^bAdverse event that starts or increases in severity from first study-drug dose to 6 weeks after last dose. ^cEach patient represented according to maximum severity. ^dEvent was related, possibly related, or missing, as assessed by investigator. ^ePatients experienced serious TEAEs: 1. Pneumothorax; 2. Acute endocarditis, aortic valve disease, acute myocardial infarction, pericarditis; 3. Transient ischemic attack, coronavirus infection; 4. Pneumonia, pneumonia viral (COVID-19); 5. Left ventricular failure, hip fracture, bile duct stone, cardiac-device malfunction. LTE, long-term extension; TEAE, treatment-emergent adverse event.

Limitations

- A relatively small number of patients participated in RHAPSODY
 - Despite the small cohort, the findings were robust and significant
- The randomized-withdrawal trial design limited the study population to patients who had a positive response to riloncept in the run-in period
 - >90% of patients entering RHAPSODY demonstrated a treatment response (to a prespecified level) during the run-in period and were eligible for study randomization, suggesting that the study findings are relevant to many patients with RP

DISCLOSURES

Massimo Imazio reports other fees from Kiniksa Pharmaceuticals and Sobi Pharmaceuticals outside the submitted work. Allan L. Klein reports grants and other fees from Kiniksa Pharmaceuticals during the conduct of the study and other fees from Cardiol Therapeutics, Sobi Pharmaceuticals, and Pfizer outside the current work. Antonio Abbate reports other fees from Kiniksa Pharmaceuticals. Michael Arad, Eliyazar Gaddam, Antonella Insalaco, Basil S. Lewis, Stephen J. Nicholls, Paul Sutej, and Yishay Wasserstrum report no disclosures. Antonio Brucato reports institutional funding from Kiniksa Pharmaceuticals as an investigator site, an unrestricted research grant from Sobi Pharmaceuticals and Accor, and travel and accommodation for advisory committee from Sobi and Kiniksa. Paul C. Cremer reports grants and personal fees from Sobi Pharmaceuticals. Martin M. LeWinter reports grants and advisory board, consulting, and other fees from Kiniksa Pharmaceuticals outside the submitted work and consulting fees from Sobi Pharmaceuticals outside the current work. David Lin reports personal fees from Regeneron outside the current work. Sushil A. Luis reports consultant fees from Kiniksa Pharmaceuticals, Sobi Pharmaceuticals, and Medtronic. Manoj Samant was an employee of Kiniksa Pharmaceuticals at the time of the study. JoAnn Clair, Indra Agarwal, and Sheldon Wang are employees of Kiniksa Pharmaceuticals. John F. Paolini is an employee of Kiniksa Pharmaceuticals and is an inventor on patents and pending patent applications licensed to Kiniksa Pharmaceuticals covering methods of using riloncept for treating recurrent pericarditis. This study was sponsored by Kiniksa Pharmaceuticals (UK), Ltd.

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