Rilonacept Reduces Pericarditis Recurrence Risk: Clinical Outcomes From the RESONANCE Patient Registry

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Real world data from the RESONANCE patient registry demonstrate that rilonacept reduced pericarditis recurrence rates by 99.5% (p=0.002) over long-term treatment

BACKGROUND

Recurrent Pericarditis (RP)

- Recurrent pericarditis (RP) is an IL-1-mediated chronic autoinflammatory disease[1,2]
- Emerging evidence implicating IL-1 in RP pathophysiology informed the development of rilonacept (IL-1α and IL-1β cytokine trap) to address the well-known concerns of prolonged corticosteroid use[3-5]
- The phase 3 trial RHAPSODY demonstrated that rilonacept was effective in treating RP not only as a third-line agent (after glucocorticoids) but also as a second-line agent (instead of glucocorticoids) and in reducing recurrence risk, supporting authorization by the FDA as the only approved treatment for RP[3,4]
- Recent international expert position statements present treatment algorithms positioning IL-1 pathway inhibition use earlier in the disease course (2nd-line) as an evidence-based steroid-sparing strategy[6,7]
- Building on the demonstrated efficacy of rilonacept in the controlled clinical trial setting of RHAPSODY, further characterization of real-world outcomes is warranted to inform implementation science and assess adoption of trial evidence and expert consensus recommendations into actual clinical practice

RESONANCE Patient Registry

- REgiStry Of the NAtural history of recurrent periCarditis in pEdiatric and adult patients (RESONANCE) (NCT04687358) was developed to quantify trends in contemporary real-world clinical practice in RP to inform treatment selection and optimize care
- RESONANCE, the largest multi-center US-based observational registry, has been collecting long-term data from US-based pericardial-disease-dedicated programs since 2020[8]
- Patients with RP diagnosis were enrolled into 2 cohorts:
  - Active (recurrence within 3 years of enrollment, and on treatment at enrollment)
  - Inactive (prior RP diagnosis but no episodes and not on treatment within 3 years prior to enrollment)
- Since the start of RESONANCE (March 2021), data have been captured from 493 patients

METHODS

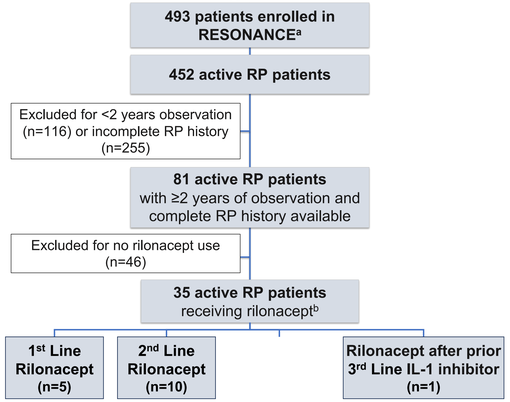
- RESONANCE employs a hybrid data collection approach: up to 1-year retrospective data (the year prior to enrollment) are combined with prospective data into a single seamless observation period
- This interval analysis was designed to evaluate the efficacy of rilonacept in RP in a real-world setting, extending the findings of the phase 3 trial RHAPSODY
  - Investigator-assessed pericarditis recurrences from only the retrospective and prospective observation periods were included (i.e., not historical events prior to the retrospective period)
- Data were collected and analyzed from pts with ≥2 years of RESONANCE observation who received rilonacept for >30 days, from March 2020 until the data cutoff date (DCO) Feb 5, 2025

Data Analysis

- Data analyzed include general RP disease data (e.g., date of RP diagnosis), medication history (e.g., medications prescribed prior to rilonacept and reasons for rilonacept initiation), and pericarditis recurrence data (i.e., number of recurrences prior to rilonacept initiation and while receiving rilonacept)
- Investigator-assessed pericarditis recurrences were collated and reviewed in the context of standardized pericarditis recurrence event adjudication criteria used by the Clinical Endpoint Committee (CEC) in the RHAPSODY program, based on available contemporaneous objective clinical indicators of recurrence (e.g., patient-reported chest pain, serum C-reactive protein [CRP], and/or cardiac imaging)[3,4,9]
- Annualized recurrence rates were calculated per RP treatment regimen (e.g., NSAIDs ± colchicine, corticosteroid-containing RP treatment regimens) as total number of investigator-assessed pericarditis recurrences divided by total patient-years (PY) while receiving that treatment
  - Annualized recurrence rates prior to rilonacept initiation were compared with those after rilonacept initiation for each patient and pooled per line of treatment
- Normally distributed data are presented as mean ± standard deviation (SD); all other data are presented as median [Q1, Q3] and n (%)
  - Wilcoxon signed-rank test was utilized to analyze the significance in change of annualized recurrence rates before and after rilonacept initiation

RESULTS

FIGURE 1. Interval Analysis Patient Flow Chart



[a]Number of patients as of the data cutoff date (Feb 5, 2025).
[b]Receiving rilonacept for >30 days.
First-line therapy (1L), i.e., after diagnosis of RP; Second-line (2L), i.e., after NSAIDs ± colchicine; Third-line (3L), i.e., after corticosteroid-containing regimen.

TABLE 1. Demographics and Patient Characteristics

Characteristic	RESONANCE n=35
Age at time of rilonacept initiation, years; median [Q1,Q3]	44 [33, 65]
Idiopathic / viral pericarditis etiology*, n [%]	88.6%
Female, n [%]	54.3%
Pericarditis disease duration at DCO†, years; median [Q1, Q3]	3.2 [2.6, 4.0]
Time from RP diagnosis to rilonacept initiation, months; median [Q1,Q3]	
All RP lines of therapy (n=35)	4.9 [2.8, 8.5]
1st Line Rilonacept (n=5)	0.9 [0, 1.6]
2nd Line Rilonacept (n=10)	7.1 [4.4, 10.2]
3rd Line Rilonacept (n=19)	5.6 [2.8, 8.2]
3rd Line Rilonacept (after prior IL-1 inhibition) (n=1)	9.0
Rilonacept treatment duration‡, years; median [Q1, Q3]	2.3 [1.8, 2.9]
Observation period, years, median [Q1,Q3]; total patient-years	3.0 [2.6, 3.4]; 106.6 PY

*Remaining etiologies include post cardiac injury/post-pericardial injury syndrome (2.9%) and other (8.6%).
†Pericarditis disease duration calculated as time from incident episode until DCO.
‡Duration of rilonacept treatment in the RESONANCE observation period or until DCO.

TABLE 2. Annualized Recurrence Rates Before and After Rilonacept Initiation

Line of Therapy (Rilonacept Initiation)	Prior Regimen	Annualized Recurrence Rate Prior to Rilonacept*[a]	Reasons for Rilonacept Initiation[b]	Annualized Recurrence Rate while on Rilonacept*[c]	% Reduction in Recurrence Rate while on Rilonacept	P-value
1st line	**N/A** (n=5)	N/A	1st treatment for RP	0	N/A	N/A
2nd line	**NSAID ± Colchicine** (n=10)	3.73	• Inadequate response to prior therapy[d] (n=8) • Unknown (n=2)[e]	0.06[f]	98.4%	0.02
3rd line	**Corticosteroid-Containing Regimen** (n=19)	4.14	• Inadequate response to prior therapy[g] (n=19) • Intolerance to prior therapy (n=3)	0	100%	<0.001
3rd line (after prior IL-1 inhibitor)	**NSAID + Colchicine + Steroid → Anakinra** (n=1)	4.04	• Inadequate response to prior therapy[h] (n=1) • Intolerance to prior therapy (n=1)	0	100%	>0.05
Total Rilonacept (n=35)	**4.00**			**0.02**	**99.5%**	**0.002**

*Annualized recurrence rate was calculated by dividing the total number of investigator-assessed pericarditis recurrences (may include patient-reported chest pain and/or elevated markers of inflammation and/or EKG changes and/or pericardial friction/rub) by the total patient-years of follow-up.
[a]Incident episode was managed with NSAIDs and/or colchicine and/or corticosteroids.
[b]More than one reason for treatment transition could be captured.
[c]Annualized recurrence rate as of the data cutoff date (Feb 5, 2025).
[d]32% (6/19) of the investigator-assessed pericarditis recurrence events were confirmed based on a CRP ≥1 mg/dL, 5% (1/19) of events had a CRP < 1 mg/dL, and 63% (12/19) of events did not have a corresponding CRP value recorded within 30 days of each event.
[e]Reason unknown.
[f]One investigator-assessed recurrence event reported in 1 patient; this event included chest pain only, as CRP (0.8 mg/dL) was not above the RHAPSODY event adjudication criterion of 1 mg/dL. This patient continued on rilonacept with no additional events reported by DCO.
[g]52% (24/46) of the investigator-assessed pericarditis recurrence events were confirmed based on a CRP ≥1 mg/dL, 7% (3/46) of events had a CRP < 1 mg/dL, and 41% (19/46) of events did not have a corresponding CRP value recorded within 30 days of each event.
[h]This patient experienced three investigator-assessed recurrences events (included patient reported chest pain; no CRP data available within 30 days of each event for all 3 events) while on NSAID + colchicine + steroid and one investigator-assessed recurrence event (included patient reported chest pain; no CRP/imaging data available) on anakinra.
PY, patient year.

RESULTS/DISCUSSION

- Regardless of line of therapy (e.g., 2nd line [29%; 10/35]; 3rd line [57%; 20/35]), the most common reason for rilonacept initiation was inadequate response to prior therapy before rilonacept
  - Rilonacept was frequently utilized as an escalation/rescue therapy in patients with inadequate disease control on prior treatment regimens, including inflammasome inhibition (i.e., NSAIDs/colchicine) and/or broad immunosuppression (i.e., corticosteroids). IL-1 pathway inhibition achieved disease control
- Patients who initiated rilonacept during RESONANCE experienced a 99.5% reduction in the annualized pericarditis recurrence rate while receiving rilonacept (**Table 2**)
  - The one investigator-assessed recurrence on rilonacept included only chest pain: CRP (0.8 mg/dL) was not above the RHAPSODY event adjudication criterion of 1 mg/dL. This patient continued on rilonacept with no additional events reported by DCO
- Reduction in annualized recurrence rate was consistent across the range of RP lines of therapy (2nd line: 98.4% [p=0.02]; 3rd line: 100% [p<0.001])
  - The consistent reduction in recurrence rates across lines of therapy suggests that rilonacept may be utilized across a broad spectrum of RP treatment settings; benefits are independent of prior treatment

Limitations

- All data were derived from an interval analysis of an unlocked database from an ongoing registry; as such, data may be missing, incomplete, and/or may change with future data cleaning
- Pericarditis recurrences and medication history which occurred prior to the retrospective observation period were not entered into the registry database and were not evaluated
- RESONANCE pericarditis recurrences were investigator-assessed, versus the formal adjudication of suspected pericarditis recurrences by the CEC in RHAPSODY. Only events confirmed based on clinical outcomes measures (i.e., pain, CRP ≥1 mg/dL, ECG, pericardial effusion, and pericardial friction rub) were used in the Primary Efficacy Endpoint analysis of RHAPSODY[3]
  - Investigator-assessed pericarditis recurrences in this analysis were based patient-reported chest pain and could not always be uniformly confirmed with objective recurrence indicators (e.g., CRP, imaging)
  - Pericarditis recurrence rates in this analysis may therefore overestimate actual event rates based on standardized adjudication criteria in controlled trials (e.g., RHAPSODY)
  - Missing/absent confirmatory data (e.g., CRP, imaging) due to variability in assessments in clinical practice may limit quantitative comparisons to rigorous clinical trial endpoints
- The inclusion of established pericardial-disease-dedicated programs, with principal investigators experienced in the management of RP, may limit generalizability
  - Findings derived from these institutions with pericardial-disease-dedicated centers set the benchmark for best practices and inform clinical guidance within RP. However, further education or resourcing may be needed for implementation in community practice centers in following the example of these established pericardial-disease-dedicated centers

CONCLUSIONS

- This first report of real-world outcomes from RESONANCE demonstrates that rilonacept treatment provided a statistically significant 99.5% reduction in pericarditis recurrence rates over long-term (>2 year) treatment, affirming sustained treatment throughout the disease duration
- These data from RESONANCE build upon the published findings of the pivotal phase 3 trial RHAPSODY, reinforcing the effectiveness of rilonacept in the management of RP and further informing the implementation science of new treatment paradigms

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