

Rilonacept Reduces Pericarditis Recurrence Risk, Hospitalizations, and ED Visits: Outcomes From the RESONANCE Patient Registry

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Real-world data from RESONANCE demonstrate that 2nd-line rilonacept provides superior clinical outcomes and reduced hospitalizations/ED visits versus 2nd-line glucocorticoid-based management strategies

BACKGROUND

Recurrent Pericarditis (RP)

- Recurrent pericarditis (RP) is an IL-1-mediated chronic autoinflammatory disease^{1,2}

- The rilonacept development program (IL-1 α and IL-1 β cytokine trap) was designed to address the well-known concerns of prolonged glucocorticoid use and was informed by contemporaneous evidence implicating IL-1 in RP pathophysiology³⁻⁵

- The Phase 3 trial RHAPSODY demonstrated that rilonacept was effective in treating RP and in reducing recurrence risk not only as a third-line agent (after glucocorticoids) but also as a second-line agent (instead of glucocorticoids), supporting authorization by the FDA as the only approved treatment for RP^{3,4}

- Based on clinical trial evidence, the 2025 ACC Concise Clinical Guidance (CCG) on the Diagnosis and Management of Pericarditis recently elevated IL-1 pathway inhibition to 2nd-line (glucocorticoid-sparing) therapy after 1st-line NSAIDs/colchicine⁶

RESONANCE Patient Registry

- The RegiSty 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 disease understanding and management strategies

- RESONANCE, the largest multi-center US-based observational registry, has been collecting long-term data from US-based pericardial-disease-dedicated programs since 2021⁷

- 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 real-world observation period

- Patients with RP diagnosis were enrolled into either
 - Active (recurrence \leq 3 years of enrollment, and on treatment at enrollment)
 - Inactive (prior RP diagnosis but with no episodes and not on treatment within 3 years prior to enrollment)

Hypothesis

- 2nd-line rilonacept reduces recurrence rates, hospitalizations, ED visits, and escalation to next line therapy versus 2nd-line glucocorticoids

METHODS

- This interval analysis compared the efficacy of 2nd-line RP therapies (IL-1 pathway inhibition versus glucocorticoids [GC]) versus prior 1st-line NSAIDs \pm colchicine therapy

Data Analysis

- Data for this interval analysis were collected from pts with \geq 2 years of RESONANCE observation between March 2020 until the data cutoff date (Jan 15, 2026)

- Data analyzed include general RP disease data (e.g., date of RP diagnosis, disease duration at DCO), medication history (e.g., medications prescribed prior to rilonacept and reasons for rilonacept initiation), pericarditis recurrence data (e.g., number of recurrences on 1st-line NSAIDs \pm Colchicine and on 2nd-line regimens), and hospitalization/ED data (e.g., instances and reasons for hospitalizations/ED visits while on treatment)

- Investigator-assessed pericarditis recurrences were reviewed in the context of standardized pericarditis recurrence event adjudication criteria used by the Clinical Endpoint Committee (CEC) in the RHAPSODY program, including available contemporaneous objective clinical indicators such as patient-reported chest pain, serum C-reactive protein [CRP], and/or cardiac imaging³
 - Annualized recurrence rate (ARR) was calculated per RP treatment regimen (e.g., NSAIDs \pm colchicine, rilonacept, and glucocorticoids) as total number of investigator-assessed pericarditis recurrences divided by total patient-years (PY) while receiving that treatment

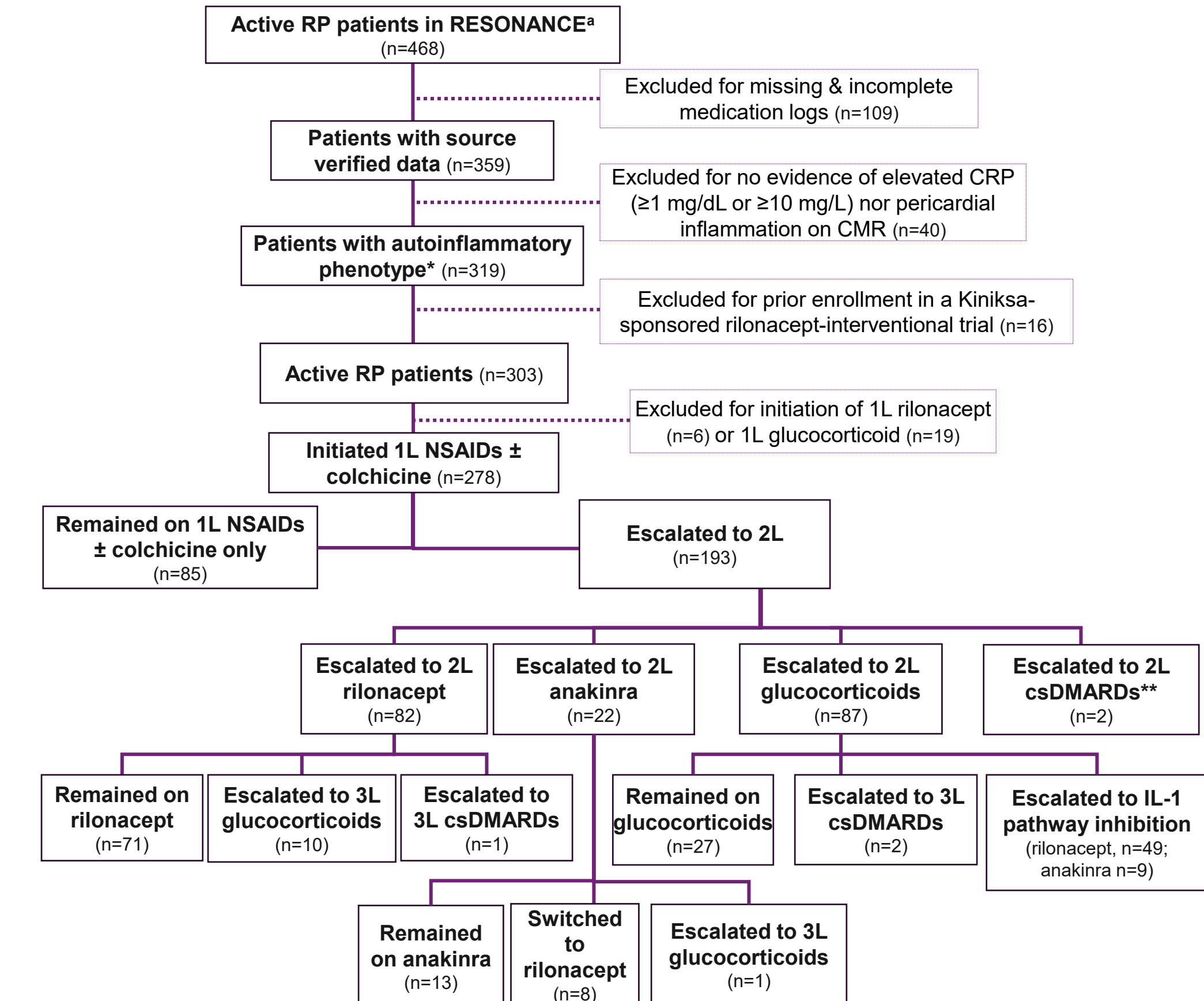
- Hospitalization and ED visit data were extracted by chart review, and event frequencies were calculated per RP treatment regimen as total number of hospitalizations or ED visits normalized to 100 PY while receiving that treatment

- Reasons for RP-related hospitalizations include > 24 hours for chest pain, pericarditis recurrence, shortness of breath, pericardial effusion, tamponade, constriction, friction rub, pericardiectomy, and pericardiocentesis
- Reasons for RP-related ED visits include chest pain, chest palpitations, pericarditis recurrence, shortness of breath, pericardial effusion, tamponade, and friction rub

- Normally distributed data are presented as mean \pm standard deviation (SD); all other data are presented as median [Q1, Q3] and n (%)
 - Separate generalized estimating equations negative binomial regression models with a log link were fitted to evaluate within-patient changes in rates of pericarditis recurrences, pericarditis-related hospitalizations, and pericarditis-related ED visits
 - Follow-up time was included as an offset to model incidence rates, and results were reported as % changes in incidence rates comparing post-treatment and pre-treatment periods

RESULTS

FIGURE 1. Interval Analysis Patient Flow Chart



^aNumber of patients as of Jan 15, 2026.

^{*}Patients with elevated CRP (\geq 1 mg/dL or \geq 10 mg/L) and/or evidence of pericardial inflammation on CMR.

^{**}Methotrexate, n=1; azathioprine, n=1.

1L, first-line therapy (i.e., after diagnosis of RP); 2L, second-line therapy (i.e., after NSAIDs \pm colchicine); 3L, third-line therapy.

TABLE 1. Demographics and Patient Characteristics

Characteristics	Continued 1L NSAIDs \pm Colchicine (n=85)	Escalated to 2L IL-1 Pathway Inhibition (n=104)	Escalated to 2L Rilonacept (n=82)	Escalated to 2L Anakinra (n=22)	Escalated to 2L Glucocorticoids (n=87)	Escalated to 2L csDMARD (n=2)	P-value
Age at DCO, years; median [Q1,Q3]	47 [35, 65]	48 [38, 62]	50 [39, 62]	45 [36, 59]	54 [40, 65]	37 [36.5, 37]	0.7
Time to RP diagnosis, years; median [Q1,Q3]	0.6 [0.2, 1]	0.3 [0.1, 0.8]	0.3 [0.1, 1]	0.3 [0.2, 0.7]	0.2 [0.08, 0.3]	0.2 [0.1, 0.3]	0.2
Time from RP diagnosis to 2L treatment, years; median [Q1,Q3]	N/A	2.1 [0.4, 4.5]	1.4 [0.3, 3.8]	2.8 [0.1, 3.9]	0.1 [0.08, 0.8]	0.5 [0.4, 0.5]	<0.0001
Disease duration at DCO, years; median [Q1,Q3]	4.1 [2.4, 6.3]	4.5 [3.4, 7]	4.4 [3.2, 7.8]	5.8 [4.5, 9]	3.9 [2.7, 5.8]	4.4 [4, 4.8]	0.1
Length of RESONANCE observation, years; median [Q1,Q3]	2.5 [1.8, 3.8]	3.2 [2.7, 4]	3.5 [2.5, 4.1]	2.9 [2, 3.9]	3.2 [2.2, 4.2]	4.3 [4.1, 4.5]	0.4
Etiology, % (n)							
Idiopathic/ viral	80.0% (68)	78.8% (82)	78.0% (64)	81.8% (18)	86.2% (75)	100% (2)	0.97
PPS	12.9% (11)	11.5% (12)	12.2% (10)	9.1% (2)	6.9% (6)	0	
Other	7.1% (6)	9.6% (10)	9.8% (8)	9.1% (2)	6.9% (6)	0	
Female, % (n)	60% (51)	61.5% (64)	64.6% (53)	50.0% (11)	60.9% (53)	100% (2)	0.4

^{*}Patients remaining on NSAIDs \pm Colchicine who did not escalate therapy to 2nd-line treatment.

^aAge at DCO (Jan 15, 2026).

^{*}Pericarditis disease duration calculated as time from incident acute episode to last follow-up (ongoing disease) or to disease resolution (no flares while off all RP therapy \geq 6 months)

DCO, data cutoff date; PPS, post-pericardiectomy syndrome; PY, patient-years; RP, recurrent pericarditis.

TABLE 2. Clinical Outcomes and Healthcare Resource Utilization in Patients With RP

Therapy (n)	Median [SD] duration on 1L NSAIDs \pm Colchicine, years	Median [SD] duration on 2L regimen, years	Annualized Recurrence Rate (per PY)			Hospitalizations (per 100 PY)			ED visits (per 100 PY)			
			While on 1L NSAIDs \pm Colchicine ^a	While on 2L regimen	Relative risk difference [P-value]	While on 1L NSAIDs \pm Colchicine	While on 2L regimen	Relative risk difference [P-value]	While on 1L NSAIDs \pm Colchicine	While on 2L regimen	Relative risk difference [P-value]	
1st Line												
NSAIDs \pm Colchicine^a (n=85)	1.5 [0.6, 2.8]	N/A	0.74 ^b	N/A	N/A	11.2	N/A	N/A	39.2	N/A	N/A	
2nd Line												
IL-1 Pathway Inhibition (n=104)	2.1 [0.4, 4.5]	1.8 [0.8, 2.6]	1.41 ^c	0.043 ^d	- 97% [$<$ 0.001]	11.9	0	- 100% [0.02]	34.1	0.009	- 99.9% [0.01]	
Rilonacept (n=82)	1.4 [0.3, 3.8]	1.9 [0.9, 2.7]	1.52 ^e	0.032 ^f	- 97.9% [$<$ 0.001]	11.8	0	- 100% [0.018]	42.2	0	- 100% [0.008]	
Anakinra (n=22)	2.8 [0.1, 3.9]	1.7 [1.1, 2.4]	1.12 ^g	0.18 ^h	- 83.9% [$<$ 0.001]	12.2	0	- 100% [0.02]	21.4	0.021	- 99.9% [0.01]	
Glucocorticoids (n=87)	0.1 [0.08, 0.8]	0.6 [0.12, 0.9]	2.13 ⁱ	3.3 ^j	+ 54.9% [0.034]	16.4	22.7	+ 38.4% [$<$ 0.001]	65.5	153.4	+ 134.2% [0.006]	
csDMARD^{**} (n=2)	0.5 [0.4, 0.5]	0.5 [0.4, 0.6]	3.33 ^k	2 ^l	- 39.9% [0.8]	0	0	N/A	0	0	N/A	

^{*}Patients remaining on NSAIDs \pm Colchicine who did not escalate therapy to 2nd-line treatment.

^{**}2L csDMARDs included patients on azathioprine (n=1) and methotrexate (n=1).

^aIncident episode was managed with NSAIDs and/or colchicine and/or glucocorticoids.

^b11% of events confirmed by chest pain + RHAPSODY adjudication criteria; 7% did not meet RHAPSODY adjudication criteria; 81% had no CRP value \leq 30 days of each event.

^c19% of events confirmed by chest pain + RHAPSODY adjudication criteria;12% did not meet RHAPSODY adjudication criteria; 70% had no CRP value \leq 30 days of each event.

^d20% of events confirmed by chest pain + RHAPSODY adjudication criteria; 30% of events did not meet RHAPSODY adjudication criteria; 50% of events had no CRP value \leq 30 days of each event.

^e21% of events confirmed based on chest pain + RHAPSODY adjudication criteria; 12% of events did not meet RHAPSODY adjudication criteria; 67% of events had no CRP value \leq 30 days of each event.

^f17% of events confirmed by chest pain + RHAPSODY adjudication criteria; 50% of events did not meet RHAPSODY adjudication criteria; 33% of events had no CRP value \leq 30 days of each event. 67% of events on rilonacept were associated with dose interval elongation; 33% of events were breakthrough but had no CRP values that met RHAPSODY adjudication criteria \leq 30 days of chest pain.

^g15% of events confirmed by chest pain + RHAPSODY adjudication criteria; 11% of events did not meet RHAPSODY adjudication criteria; 74% of events did not have a CRP value \leq 30 days of each event.

^h22% of events confirmed by chest pain + RHAPSODY adjudication criteria; 22% of events did not meet RHAPSODY adjudication criteria; 56% of events did not have a CRP value \leq 30 days of each event. 56% of events were associated with dose interval elongation; 44% of events were breakthrough,75% of breakthrough events had CRP values that met RHAPSODY adjudication criteria \leq 30 days of chest pain.

ⁱ29% of events confirmed based on chest pain + RHAPSODY adjudication criteria; 27% of events did not meet RHAPSODY adjudication criteria; 44% of events had no CRP value \leq 30 days of each event.

^j62% of events confirmed by chest pain + RHAPSODY adjudication criteria; 7% of events did not meet RHAPSODY adjudication criteria; 31% of events had no CRP value \leq 30 days of each event. All 86% of events were associated with dose tapering; 14% of events were breakthrough, all breakthrough events had CRP values that met RHAPSODY adjudication criteria \leq 30 days of chest pain.

^k33% of events confirmed by chest pain + RHAPSODY adjudication criteria;67% of events had no CRP value \leq 30 days of each event.

^l100% of events confirmed by chest pain + RHAPSODY adjudication criteria. All events were breakthrough but had no CRP values that met RHAPSODY adjudication criteria \leq 30 days of chest pain.

RESULTS/DISCUSSION

- Of the patients initiating 1st-line NSAIDs \pm colchicine (n=278), 30.6% (n=85) remained on NSAIDs \pm colchicine, and 69.4% (n=193) advanced to 2nd-line therapy (IL-1 pathway inhibition [53.9%; n=104]; GC [45.1%; n=87]) after a mean duration on 1st-line therapy of 2.1 vs 0.1 years, respectively

- Amongst patients who escalated to 2nd-line therapy, pericarditis event rates and disease burden accrued while on 1st-line NSAIDs \pm colchicine were generally consistent between those who escalated to rilonacept versus those who escalated to glucocorticoids (ARR: 1.52 vs. 2.13; Hospitalizations: 11.8 vs. 16.4; ED visits 42.2 vs. 65.5)

- 2nd-line rilonacept significantly reduced ARR versus prior (1st-line) NSAIDs \pm colchicine (0.032 vs 1.52; 97.9% reduction; P<0.001), whereas 2nd-line GC significantly increased ARR versus prior NSAIDs \pm colchicine (3.33 vs 2.13; 54.9% increase; P=0.034; **Table 2**)

- All pericarditis recurrences during rilonacept treatment were associated with deviation from the labeled weekly dosing interval, i.e., during dose-interval elongation, affirming that consistent and continuous blockade of IL-1 signaling is necessary to maintain RP disease control

- Glucocorticoids are particularly challenging to use in RP given that the risk of adverse events with long-term use drives serial tapers to mitigate adverse events. Only 13.8% of recurrences represented breakthrough events while maintained on stable glucocorticoid therapy. Conversely, 86.2% of recurrences observed during glucocorticoid treatment occurred during tapering, which resulted in premature recurrences due to sub-therapeutic dosing and unmasking of the underlying autoinflammatory disease

- Recurrence risk and HCRU outcomes during 2nd-line rilonacept treatment were significantly superior to those during 2nd-line glucocorticoid treatment (ARR: 0.032 vs. 3.3, P<0.001; hospitalizations: 0 vs. 22.7, P=0.008; ED visits: 0 vs. 153.4, P<0.001; **Table 2**)

- The consistent reductions in recurrence risk, hospitalizations, and ED visits during rilonacept treatment suggest that IL-1 α /IL-1 β pathway inhibition enabled continued targeted immunomodulation without interruption, leading to successful long-term disease control

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, hospitalizations, ED visits, and medication history which occurred prior to the 1-year retrospective observation period were not entered into the registry database and were not evaluated

- Suspected RESONANCE pericarditis recurrences were initially identified based upon investigator assessment, but only events confirmed based on clinical outcomes measures (i.e., pain, CRP \geq 1 mg/dL, ECG, pericardial effusion, and pericardial friction rub) were used in this RESONANCE analysis; while robust, the most rigorous adjudication process has been the formal adjudication of suspected pericarditis recurrences performed by the independent CEC in RHAPSODY³
 - Investigator-assessed pericarditis recurrence rates in this analysis may be an overestimate relative to actual confirmed event rates based on standardized adjudication criteria in controlled trials (e.g., RHAPSODY)
 - Missing/absent confirmatory data (e.g., CRP, imaging) due to variations 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 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 following the example of these established pericardial-disease-dedicated centers

CONCLUSIONS

- Approximately one-third of patients who initiated 1st-line NSAIDs/Colchicine remained on that therapy after 1.5 years. Of the two-thirds of patients in this population who escalated to 2nd-line therapy, baseline disease characteristics of those who escalated to rilonacept or to glucocorticoids were generally comparable

- In patients failing NSAIDs/Colchicine, 2nd-line rilonacept was superior to 2nd-line glucocorticoids in reducing recurrence rate and disease burden (hospitalizations and ED visits), affirming the evidence-based shift to a glucocorticoid-sparing paradigm recommended by the 2025 ACC CCG and the need for prompt escalation to effective 2nd-line therapies to improve patient outcomes

- 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 in the real-world and further informing the implementation science of this new treatment paradigm

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