Sex Differences in the Management of Recurrent Pericarditis: Insights from the RESONANCE Registry

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Real world data from RESONANCE indicate that women were diagnosed with RP sooner than men but, despite similar disease severity, experienced later escalation to second-line therapy, resulting in additional recurrences while remaining on first-line therapy

BACKGROUND

Recurrent Pericarditis (RP)

- Recurrent pericarditis (RP) is an IL-1-mediated chronic autoinflammatory disease[1,2]
- Among patients with multiple RP recurrences, the majority (54.7 %) are female; although there is no known gender predisposition to developing pericarditis, women may be more prone to specific conditions (e.g., autoimmune diseases) that predispose them to more frequent recurrences and complications[3,4]
- Sex-related differences in RP management are not well described; deeper understanding could enable proactive individualized management strategies

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 disease understanding and management strategies
- RESONANCE, the largest multi-center US-based observational registry (>500 patients), has been collecting long-term data from US-based pericardial-disease-dedicated programs since 2021[5]
- 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
- Patients with a diagnosis of RP were enrolled into either
  - Active (recurrence ≤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

- Based on evidence from prior clinical trials, the 2025 ACC Concise Clinical Guidance (CCG) on the Diagnosis and Management of Pericarditis recently elevated IL-1 pathway inhibition to 2nd-line (i.e., glucocorticoid-sparing) therapy after NSAIDs/colchicine[6-8]
- Treatment paradigms in RP management are agnostic to sex; however, in real-world practice females and males may have distinct pathophysiology, diagnosis, and management patterns

METHODS

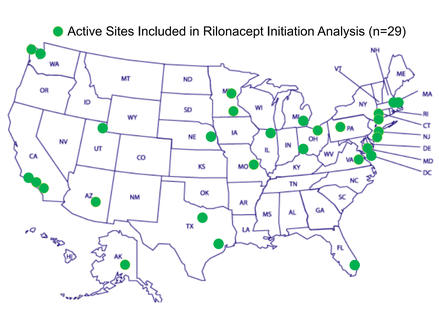
- Data were collected and analyzed from pts with ≥2 years of RESONANCE observation, from March 2020 until the data cutoff date (DCO; Jan 15, 2026; **Figure 1 + 2**)

Data Analysis

- Data analyzed include general RP disease characteristics, medication history, treatment patterns (e.g., proportion and timing of escalation to 2nd-line therapy), and number of recurrences prior to escalation to 2nd-line therapy
- 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 imaging[6]
- Normally distributed data are presented as mean ± standard deviation (SD); all other data are presented as n (%)
- Student's t-test and chi-squared test were utilized to evaluate statistical differences in demographics/clinical characteristics and observed treatment patterns between sexes

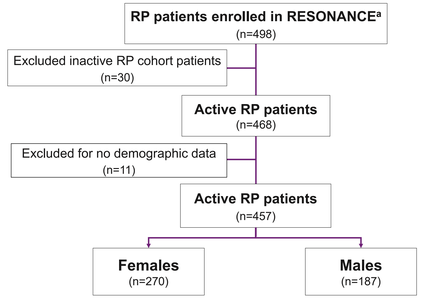
FIGURE 1. RESONANCE Sites Included in this Analysis

Principal Investigator	Site	State
Allan Klein	Cleveland Clinic Foundation	OH
S. Allen Luis	Mayo Clinic Rochester	MN
Moneal Shah	Allegheny Health Network	PA
Daniel Huck	Brigham & Women's Hospital	MA
Jonathan Salik	Massachusetts General Hospital	MA
Michael Garshick	NYU Langone health	NY
Georgia Thomas	Virginia Commonwealth University	VA
Dennis Finkelstein/ James Walter	Northwell Health/Lennox Hill Hospital	NY
Amanda Verma	Barnes Jewish/Washington University	MO
Dipan Shah	Houston Methodist	TX
Nicolas Phreaner	University of California, San Diego	CA
David Lin	Minneapolis Heart Institute Foundation	MN
Luigi Adamo	Johns Hopkins	MD
Michael Portman	Seattle Children's Hospital	WA
Austin Robinson	Scripps Health	CA
Robert Siegel	Cedars Sinai Medical Center	CA
Mohamed Al-Kazaz	Northwestern University	IL
John Ryan	University of Utah	UT
Tracey Hagerty	University of Vermont Medical Center	VT
Arif Albulushi	University of Nebraska Medical Center	NE
Suneet Purohit	Alaska Heart and Vascular Institute	AK
Thomas Waggoner	Pima Heart and Vascular	AZ
Jesson Yeh	TKL Research (decentralized site)	NJ
Craig Asher	Cleveland Clinic - Florida	FL
Alraies Chadi	DMC Harper Hospital	MI
Waqas Haider	Medstar Washington Hospital Center	DC
John Peterson	Swedish Medical Center	WA
Tim Henry	The Christ Hospital	OH
Kathleen Zhang	University of Texas Southwestern Medical Center	TX



RESULTS

FIGURE 2. Interval Analysis Patient Flow Chart



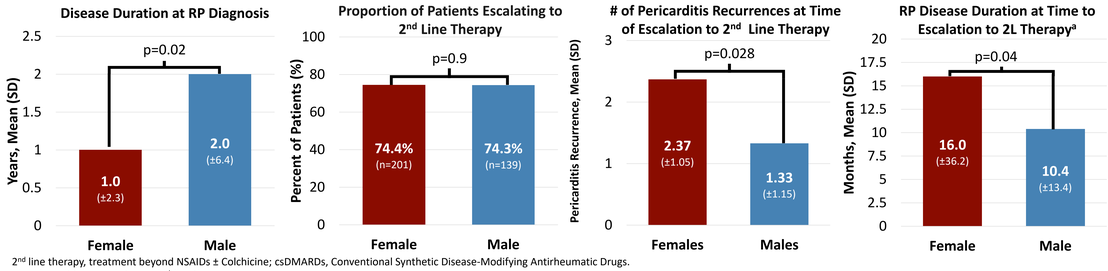
[a]Number of patients as of DCO (Jan 15, 2026).
DCO, data cutoff date.

TABLE 1. Demographics and Patient Characteristics

Characteristic	Females (n=270)	Males (n=187)	P-value
Age at incident pericarditis episode, years; mean ± SD	52 ± 15	49.8 ± 16.6	0.03
Pericarditis disease duration at DCO†, years; mean ± SD	5.5 ± 4.8	6.2 ± 7.6	0.25
Etiology, % (n)			
Idiopathic / viral pericarditis etiology	83.0% (224)	81.8% (153)	0.24
Postcardiac injury/postprocedural	8.9% (24)	11.2% (21)	
Other causes	8.1% (22)	7.0% (13)	
Inflammatory phenotype*, % (n/N)	91.2% (237/260)	92.6% (163/176)	0.7

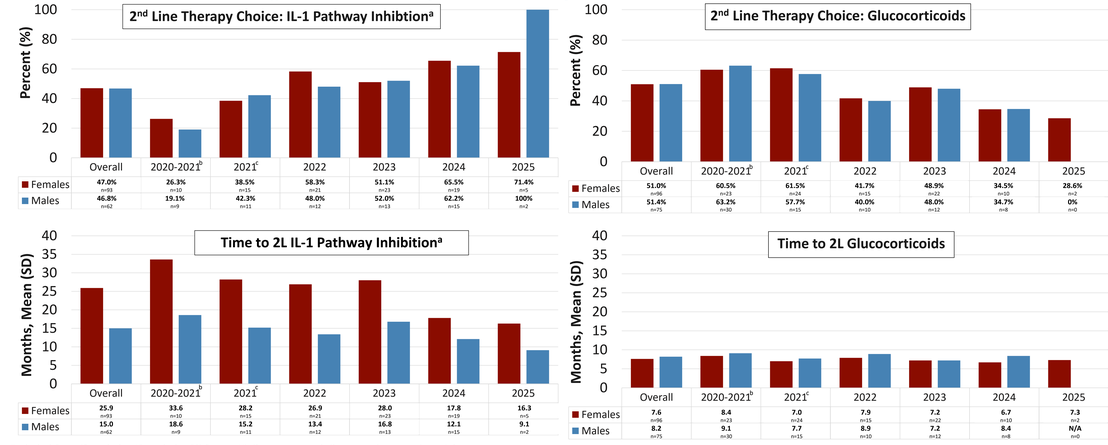
†Pericarditis disease duration was defined as time from incident acute episode to last follow-up (ongoing disease) or to disease resolution (no flares while off all RP therapy ≥6 months).
*Patients with elevated CRP (≥1 mg/dL or ≥10 mg/L) and/or evidence of pericardial inflammation on CMR. Denominator represents patients with non-missing CRP and/or non-missing CMR findings).
DCO; data cutoff date; RP, recurrent pericarditis

Figure 3: RP Disease Characteristics by Sex



2nd line therapy, treatment beyond NSAIDs ± Colchicine; csDMARDs, Conventional Synthetic Disease-Modifying Antirheumatic Drugs.
[a]Time from RP diagnosis to any 2nd-line therapy.

Figure 4: 2nd Line RP Management and Adoption of Therapies over Time by Sex



[a]Excluded 3 pts (female [n=1]; male [n=2]) from a Kiniksa-sponsored rilonacept-intervention trial.
[b]1 year prior to rilonacept approval in recurrent pericarditis.
[c]Partial year after rilonacept commercial availability in recurrent pericarditis

RESULTS

- Although women had a shorter disease duration at RP diagnosis than men (1.0 ± 2.3 vs. 2.0 ± 6.4 years, p = 0.02), they remained on 1st-line NSAIDs ± colchicine for longer (16.0 ± 36.2 months vs. 10.4 ± 13.4 months, p = 0.04; **Figure 3**) despite ultimately having a similar proportion of escalations to next line of therapy (74.4% vs. 74.3%, p=0.9)
- Consequently, women accrued more recurrences at the time of escalation to 2nd-line therapy (2.37 ± 1.05 vs. 1.33 ± 1.15, p=0.028): during the additional 5.6 months of 1st-line therapy vs men, women had experienced 1.39 (mean) more recurrences
- Once the decision to escalate to 2nd-line therapy had been made, treatment choice did not differ between sexes, with comparable rates of 2nd-line glucocorticoids (51.0 vs 51.4%; **Figure 4**) and 2nd-line IL-1 pathway inhibition (47.0 vs. 46.8%) between women versus men; however, women did have a significantly longer time to IL-1 pathway inhibition initiation than men (25.9 vs 15.0 months; p=0.04), whereas there was no difference in time to GC initiation between women and men (7.6 vs 8.2 months; p=0.21)

Discussion

- Previous analyses reported that, in the first 3 years after approval in recurrent pericarditis, rilonacept increasingly replaced corticosteroids as second-line therapy.[5] In this interval analysis, proportional adoption of the steroid sparing paradigm was consistent between women and men
- Although recurrence burden while on 1st line therapy was higher among women, differences in timing of therapy escalation may have been a factor in the observed sex-related differences in recurrence burden rather than differences in choice of therapy
- Delay in escalating to 2nd-line therapy after recurrence on 1st-line NSAIDs/colchicine could result in additional and possibly preventable recurrences which have potential downstream consequences and increased healthcare resource utilization (i.e., ED visits/hospitalizations)
- This disparity in timing of treatment escalation may reflect differences in clinical presentation, disease characteristics, and differential risk perception between the sexes, underscoring the need for prompt evidence-driven treatment decisions which are individualized to the clinical setting

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 1-year 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 Endpoint analysis of RHAPSODY[6]
  - 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 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 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 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 following the example of these established pericardial-disease-dedicated centers

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DISCLOSURES

E. Sullivan: no relationships to disclose; P.C. Cremer: grants and consultant fees from Kiniksa Pharmaceuticals, grants and personal fees from Sobi; M. Al-Kazaz: research grant support from Kiniksa Pharmaceuticals, Ventyx, and Cardiol Therapeutics; speaking honoraria from Kiniksa Pharmaceuticals, and consulting fees from Edwards Lifesciences; S.A. Luis: consultant fees from Kiniksa Pharmaceuticals, Cardiol Therapeutics, and Medtronic; A. Raisinghani: consultant fees from Kiniksa Pharmaceuticals, Novo Nordisk, Horizon Therapeutics, and BMS; V. Parameswaran and J.F. Paolini: shareholders and employees of Kiniksa Pharmaceuticals; A.L. Klein: grants and consultant fees from Kiniksa Pharmaceuticals, Cardiol Therapeutics, Ventyx, and Pfizer.

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