Baseline demographics and disease characteristics of patients enrolled in REgiStry Of the NAtural history of recurreNt periCarditis in pEdiatric and adult patients (RESONANCE)

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INTERIM ANALYSIS KEY LEARNINGS

- **Mean total prior disease duration (from incident episode until enrollment) was 3.5 years (408 patient-years)**
- **Medical management intensified with worsening disease severity; IL-1 pathway inhibition increasingly prominent in patients with ≥2 recurrences**
- **RESONANCE to examine associations between recurrent pericarditis (RP) management and patient-reported and clinical outcomes**

BACKGROUND

Recurrent Pericarditis (RP)

- RP is a chronic, painful, and debilitating autoinflammatory disease driven by interleukin-1 (IL-1).[1]
- RP negatively impacts quality of life, and refractory disease requires treatment over periods of years.[1-3]
- ARCALYST® (rilonacept), an IL-1 trap,[5] is the first FDA-approved drug for the treatment of RP and the prevention of recurrence in patients ≥12 yrs, supported by data from the pivotal trial, RHAPSODY.[4]
- Further understanding the disease natural history will better inform clinical decision-making.

RESONANCE, the first multicenter US RP Patient Registry

- The REgiStry Of the NAtural history of recurreNt periCarditis in pEdiatric and adult patients (RESONANCE) (NCT04687358) is a natural history registry of RP being conducted in the US.
- RESONANCE is designed to collect observational data from real-world clinical practice to better understand the presentation, management, and outcomes of patients with RP.
- Study Objectives:
  - Further the understanding of the natural history of RP and the variability of the RP patient's clinical course, including diagnosis, prognosis, and disease management
  - Deepen the understanding of symptoms during RP episodes and in between episodes
  - Generate real-world data on the impact and effectiveness of treatments on clinical outcomes
  - Better understand impact of RP and treatments on patients' Health Related Quality of Life (HRQoL)
- RESONANCE launched in March 2021 and is planned to continue through 2026, with an enrollment target of 500 patients in up to 50 centers across the US.

PURPOSE

RESONANCE is positioned to inform:

1. **Duration of RP Disease – and early predictors of long-term disease**
2. **Drivers of RP Disease management**
   a. **Predictors/drivers of therapeutic class selection (patient and HCP characteristics)**
   b. **Predictors/drivers of evolution of treatment paradigm over time, in particular, steroid-sparing and uptake/utilization of FDA-approved therapies**
3. **Patient outcomes (clinical and patient reported) based on RP treatment**

METHODS (ACTIVE COHORT, INTERIM ANALYSIS)

Patient Population

- Active RP Cohort: patients having a documented RP episode ≤3 years prior to enrollment and on treatment at time of enrollment were considered to have "active" disease.
- Inactive RP cohort: a prior diagnosis of RP but no episodes nor treatment within 3 years prior to enrollment.
- Patients with RP related to trauma, malignancy and connective tissue disease were excluded.
- Target enrollment ratio: **90% active RP patients** / 10% inactive RP patients.

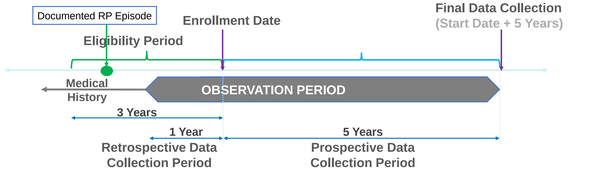
Data Collection

- Demographic characteristics are referenced to the time of enrollment.
- Duration of disease, number of recurrences, annualized incidence rate of RP recurrence, and duration of RP episodes are collected from initial acute episode to end of observation period.
- Medication use is collected from disease onset to end of observation period.
- A hybrid approach was taken in which 1 year of intensive retrospective data (the year prior to enrollment) is added to standard prospective intensive data collection (enrollment to end of observation period).

Periodic Interim Analyses (IA)

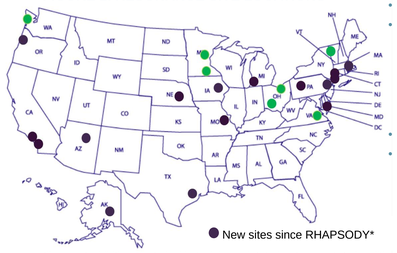
- Analyses of the enrolled population will be conducted at relevant intervals (disease characteristics and medical management since disease onset).
- The present analysis provides the data from the 1-year Retrospective Data Collection Period from those **active RP cohort patients** for whom complete and verified enrollment and 1-year retrospective data were available at the time of IA data cutoff (30 January 2023).

FIGURE 1. HYBRID STUDY DESIGN (RETROSPECTIVE/PROSPECTIVE DATA COLLECTION)



RESULTS

FIGURE 2. RESONANCE SITE LOCATIONS



* Rilonacept Inhibition of Interleukin-1 Alpha and Beta for Recurrent Pericarditis: a Pivotal Symptomatology and Outcomes Study (RHAPSODY)

- Enrollment began March 2021 and continues at 23 US sites, including 7 RHAPSODY[4] sites (FIGURE 2).
- As of 30 January 2023 (IA data cutoff), 253 patients have been enrolled (224 active cohort; 28 inactive cohort; 1 unspecified).
  - Among 184 with available data, mean total prior disease duration at time of enrollment (i.e., starting at incident pericarditis episode until enrollment) was 3.23 years (595 patient-years).
  - Complete data from the 1-year Retrospective Data Collection Period could be verified for 129 adult and 3 pediatric patients.
  - This sub-population (n=132; 118 with non-missing date information) had a mean total prior disease duration (i.e., starting at incident pericarditis episode until enrollment) of 3.5 years (408 patient-years).
- Select patient characteristics and RP disease characteristics are reported in TABLE 1 and TABLE 2, respectively.
- The proportion of medication use for the total patient population (n = 132) with use stratified by number of recurrences is shown in FIGURE 3.

TABLE 1. SELECT PATIENT CHARACTERISTICS

	Active RP Patients N = 132
Age (years)	
Mean ± SD	48.18 ± 15.62
Median [IQR]	50.00 [37.00, 60.00]
Range	10.00 - 86.00
Age Category, n (%)	
<18	3 (2.27%)
18-64	110 (83.33%)
65-78	16 (12.12%)
≥79	3 (2.27%)
Sex, n (%)	
Male	50 (37.88%)
Female	82 (62.12%)
Race, n (%)	
Race reported	125 (94.70%)
White	114 (91.20%)
Black or African American	6 (4.80%)
Native Hawaiian/Other Pacific Islander	3 (2.40%)
Asian	1 (0.80%)
American Indian or Alaska Native	0 (0.00%)
Other	1 (0.80%)
Missing (%)	7 (5.30%)
Geographic Location, n (%)	
Northeast	43 (32.58%)
Midwest	55 (41.67%)
South	17 (12.88%)
West	17 (12.88%)

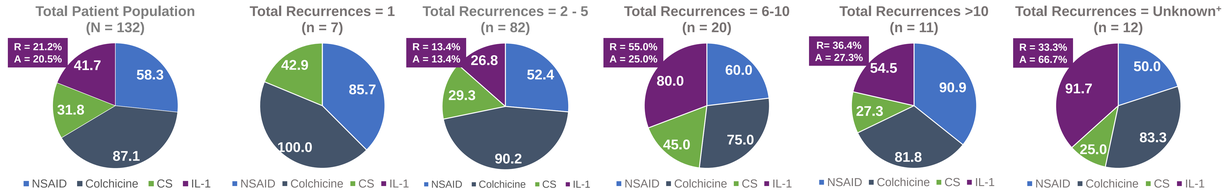
TABLE 2. SELECT RP DISEASE CHARACTERISTICS

	Active RP Patients N = 132
Etiology of Initial Acute Pericarditis Episode, n (%)	
Idiopathic	65 (49.24%)
Post-viral	18 (13.64%)
Post-pericardial injury syndrome/post-cardiac injury	10 (7.58%)
Other	15 (11.36%)
Not reported	24 (18.18%)
Total Disease Duration (years)	
Mean ± SD	3.46 ± 4.91
Median [IQR]	2.00 [0.95, 4.46]
Range	0.09 - 38.58
Missing (%)	14 (10.61%)
Number of Recurrences in 1-year Retrospective Data Collection Period	
Mean ± SD	1.08 ± 0.97
Median [IQR]	1.00 [0.00, 1.00]
Range	0.00 - 5.00
Missing (%)	1 (0.76%)
Patients with at least one recurrence in 1-year Retrospective Data Collection Period, n (%)	95 (71.97%)
Missing (%)	1 (0.76%)
Comorbidities, n (%)	
Yes	33 (25.55%)
Hypertension	11 (33.33%)
Cardiac arrhythmia	8 (24.24%)
COVID-19	6 (18.18%)
Depression	4 (12.12%)
Anxiety	3 (9.09%)
Duration of the RP episode (days)	
Mean ± SD	11.25 ± 10.79
Median [IQR]	7.50 [5.50, 14.50]
Range	2.00 - 40.00
Missing (%)	120 (90.91%)

FIGURE 3. PROPORTION* OF MEDICATION USE SINCE DISEASE ONSET

Total Patient Population (*Percentages do not sum to 100%)

Medication Use in Patient Population Subsets Stratified by Total Number of Reported Recurrences (from incident episode to enrollment) (*Percentages do not sum to 100% because of multi-drug or serial regimens)



NOTE: Medication use is overlapping and not mutually exclusive (due to multidrug and serial regimens) therefore percentages do not sum to 100%. Use of each medication at any time since disease onset was included, and patients can participate in more than one medication class grouping simultaneously.

+ "Unknown": the investigator did not know the number of recurrences, not that data are missing; Abbreviations: CS = corticosteroids; R = rilonacept; A = anakinra

DISCUSSION

- RESONANCE is an observational registry following natural history and disease management in RP over a 6-year per-patient intensive-observation period: a 5-year prospective period plus a unique 1-year retrospective period, making one year of intensive data already available at time of enrollment.
- Over twice as many sites have commenced enrollment versus the initial RHAPSODY[4] sites, indicating a growing and broader nationwide adoption of best practices since Phase 3 program completion.
- Demographic data highlight the impact of this chronic disease, given that most patients were otherwise-healthy middle-aged women.
- Low rates of anxiety and depression diagnoses, while consistent with the historically low rates of these formal diagnoses in RP patients, are inconsistent with the substantially lower mental health domain scores reported more broadly in RP patients using patient-reported outcomes (PRO) instruments,[6] suggesting an under-reporting of the impact of RP on patient Quality of Life. Analyses of RESONANCE PRO instruments could clarify the correlation.
- Conventional oral treatment (NSAIDs, colchicine, steroids) use varies with recurrence density.
- Over 40% of patients have received IL-1 pathway inhibition, a therapeutic strategy which was increasingly prominent in those patients with ≥2 recurrences.
- Future periodic interim analyses will examine the relationships between natural history and medical management using clinical events and PROs with the aim of informing future standard of care in RP.

LIMITATIONS

- Patients are not randomized to interventions.
- Data are derived from an interim download from an unlocked database; data may be missing or incomplete and/or may change with future data cleaning.
- Patients were selected for the IA due to having complete data for the Retrospective Data Collection Period (132 of 253); they may not be representative of the total RESONANCE population enrolled.
- This IA represents data from the 1-year retrospective period only.
- Future analyses should contain larger sample sizes and longer observation durations at IA cut-off.

CONCLUSIONS

- **RESONANCE: 1st US multicenter registry of RP natural history and treatment strategies.**
- **This IA assessed patient and disease characteristics for 408 patient-years of data.**
- **RP impacts a preponderance of otherwise-healthy women without major comorbidities.**
- **Medical management intensifies with increasing recurrence burden; proportional IL-1 antagonist use increases in patients with ≥2 recurrences.**
- **RESONANCE is designed to reveal important RP characteristics informing therapeutic decision-making and guiding clinical practice to improving RP patient quality of life.**

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DISCLOSURES

P. Cremer: consultant fees from Kiniksa Pharmaceuticals, grants and personal fees from Sobi; S.A. Luis: consultant fees from Kiniksa Pharmaceuticals, Sobi and Medtronic; M. Portman: consultant fees from Kiniksa Pharmaceuticals; A. Raisinghani: institution receives consultancy funding from Kiniksa Pharmaceuticals; Y. Song and Y. Wang are employed by Analysis Group; J. Clair and J. F. Paolini are employed by Kiniksa Pharmaceuticals Corp.

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