Rilonacept Utilization in a Steroid-Sparing Paradigm for Recurrent Pericarditis: Real-World Evidence Demonstrating Increased Adoption

Sushil A. Luis, MBBS, PhD[1]; Paul C. Cremer, MD[2]; Ajit Raisinghani, MD[3]; Michael A. Portman, MD[4]; Robert W. Biederman, MD[5,6,7]; Brittany Weber, MD, PhD[8]; David Lin, MD[9]; Michael S. Garshick, MD[10,11]; Yueying Chen, PhD[12]; Allison Curtis, PhD[13]; Vidhya Parameswaran, MPH[13]; JoAnn Clair, PhD, MBA[13]; Allan L. Klein, MD[14]; and John F. Paolini, MD, PhD[13], on behalf of the RESONANCE Study Group

[1]Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN; [2]Northwestern University, Chicago, IL; [3]Division of Cardiology, Department of Medicine, Sulpizio Cardiovascular Center, University of California San Diego, San Diego, CA; [4]Seattle Children's Research Institute, and Division of Cardiology, Department of Pediatrics, University of Washington, Seattle, WA; [5]Division of Cardiology, Allegheny Hospital, Pittsburgh, PA; [6]West Virginia University, Morgantown, WV; [7]Roper Hospital/Medical University of South Carolina, Charleston, SC; [8]Division of Cardiovascular Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; [9]Minneapolis Heart Institute at Abbott Northwestern Hospital, Minneapolis, MN; [10]Cardio-Rheumatology Program, Center for the Prevention of Cardiovascular Disease, NYU Langone Health, New York, NY; [11]Leon H. Charney Division of Cardiology, Department of Medicine, New York University School of Medicine, New York, NY; [12]DeltaMed Solutions, Inc, Somerset, NJ; [13]Kiniksa Pharmaceuticals, Lexington, MA; [14]Department of Cardiovascular Imaging, Center for the Diagnosis and Treatment of Pericardial Diseases, Heart and Vascular Institute, Cleveland Clinic, Cleveland, OH.

BACKGROUND

Recurrent Pericarditis (RP)

- RP is a chronic autoinflammatory disease mediated by interleukin-1 (IL-1).[1]
- RP negatively impacts quality of life, and refractory disease requires treatment over a number of years.[1-3]
- While the 2015 European Society of Cardiology Guidelines position IL-1 pathway inhibition only after corticosteroids, complications associated with long-term steroid use underscore the importance of steroid-sparing strategies.
- Rilonacept, an IL-1α and IL-1β cytokine trap, is the only FDA-approved treatment for RP (available since April 2021), supported by data from the pivotal trial, RHAPSODY.[3,4]
- RHAPSODY data showed that, while 50% of RP patients (pts) transitioned to rilonacept from steroids in the traditional paradigm, 50% of pts transitioned from NSAIDs/colchicine, in a steroid-sparing paradigm.[3]
- Further understanding RP disease natural history and treatment paradigm selection 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 pts (RESONANCE) (NCT04687358) is designed to collect observational data from real-world clinical practice to better understand the presentation, management, and outcomes of pts with RP.
- RESONANCE launched in March 2021 with plans to continue through 2026 and an enrollment target of 500 pts in up to 50 centers across the US.

Hypothesis:
Rilonacept availability for RP has enabled the corticosteroid-sparing paradigm in patients failing aspirin/NSAIDs/colchicine.

METHODS

Data Collection

- Hybrid approach: up to 1-year retrospective data (the year prior to enrollment) were combined with prospective data into a single seamless observation period (**Fig 1**).
- Data were collected from study start (March 2021) until the data cutoff date (DCO) (February 15, 2024).

Data Analysis

- **Medication Class Use:** Fractional sum of patient-years (PY) on each medication class; data censored at last check-in visit.
- **Treatment Intensification:** In pts failing aspirin/NSAIDs/colchicine, proportion who added/switched to conventional disease-modifying antirheumatic drugs (csDMARDs), corticosteroids, anakinra, or rilonacept; data censored at last check-in visit.
- Normally distributed data presented as mean ± standard deviation (SD); all other data presented as median [Q1, Q3] and n (%).

FIGURE 1. RESONANCE PATIENT REGISTRY STUDY DESIGN[5,6]

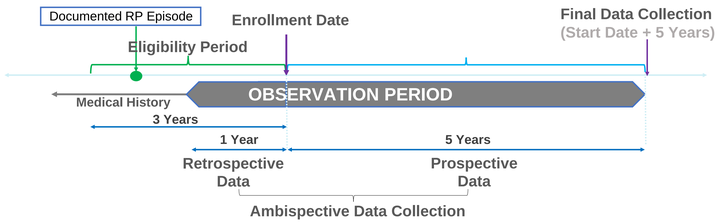
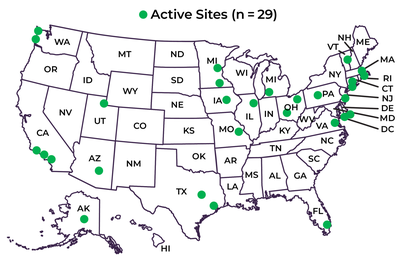


FIGURE 2. RESONANCE SITE LOCATIONS

Principal Investigator	Site	State	Pts
Allan Klein	Cleveland Clinic Foundation	OH	71
S. Allen Luis	Mayo Clinic Rochester	MN	50
Moneal Shah	Allegheny Health Network	PA	45
Brittany Weber	Brigham & Woman's Hospital	MA	25
Michael Garshick	NYU Langone Health	NY	21
Georgia Thomas	Virginia Commonwealth University	VA	20
Jesson Yeh	TKL Research (decentralized site)	NJ	17
Dennis Finkelstein/James Walter	Northwell Health/ Lennox Hill Hospital	NY	15
Jonathan Salik	Massachusetts General Hospital	MA	12
Nicolas Phreaner	University of California, San Diego	CA	12
David Lin	Minneapolis Heart Institute Foundation	MN	11
Amanda Verma	Barnes Jewish/Washington University	MO	11
Dipan Shah	Houston Methodist	TX	11
Luigi Adamo	Johns Hopkins	MD	9
Thomas Waggoner	PIMA Heart and Vascular	AZ	7
Michael Portman	Seattle Children's Hospital	WA	6
Austin Robinson	Scripps	CA	4
Tracy Hagerty	University of Vermont	VT	4
Suneet Purohit	Alaska Heart and Vascular Institute	AK	3
Nicholas Shammas	Midwest Cardiovascular Research Center	IA	2
John Peterson	Swedish Medical Center / Providence Health	WA	2
Mohamed Al-Kazaz	Northwestern University	IL	2
Chadi Alraies	Wayne State / Detroit Medical Center	MI	1
Robert Siegel	Cedars Sinai	CA	-
Kathleen Zhang	UT Southwestern	TX	-
Allan Klein (Craig Asher)	Cleveland Clinic - Florida	FL	-
Sanoh P. Bathvala	Cincinnati Children's Hospital	OH	-
John Ryan	University of Utah	UT	-
Ashraf Harahsheh	Children's National Hospital	DC	-



Note: all treatments were prescribed as part of routine clinical care. The registry did not influence the diagnosis or management of RP pts in the study.

RESULTS

FIGURE 3. PATIENT DISPOSITION

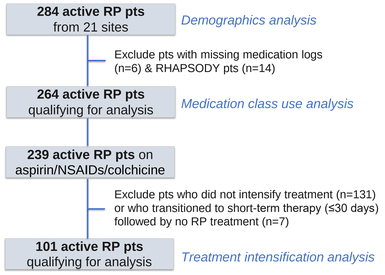
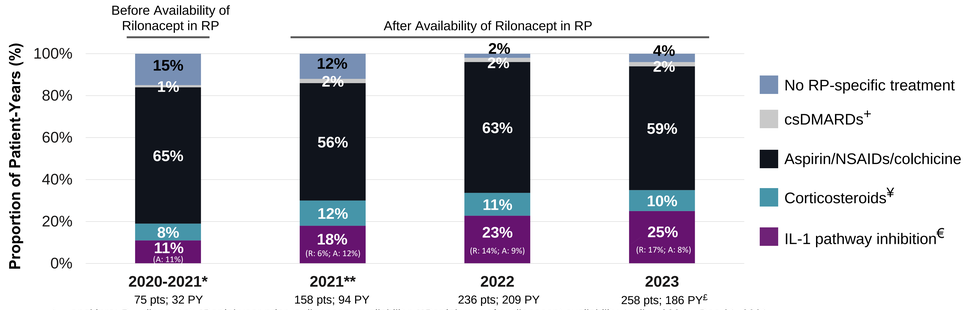


TABLE 1. SELECT PATIENT AND DISEASE CHARACTERISTICS

	All Pts (N=284)
Age*, years; mean ± SD	50.2 ± 16.6
Female, %	57.4%
White, %	83.5%
Etiology, %	
Idiopathic / viral pericarditis	67.6%
Post-cardiac injury / post-procedural	7.8%
Other causes	10.2%
Not reported / unknown / missing	14.4%
RP disease duration*, years; median [Q1, Q3]	3 [1.9, 5.2]
Number of recurrences**; median [Q1, Q3]	3 [2, 5]
Observation period, years, median [Q1,Q3]; sum	2.1 [1.5, 2.6]; 604.8 PY

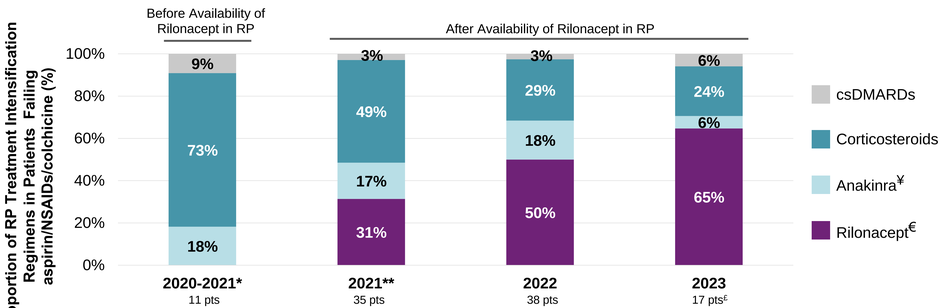
*At the end of the observation period (last check-in visit or DCO); RP disease duration calculated as time since index acute episode
**At time of enrollment

FIGURE 4. PROPORTIONAL MEDICATION CLASS USE# (IN PATIENT-YEARS) OVER TIME (n=264)



A = anakinra; R = rilonacept; *Partial year prior to rilonacept availability; **Partial year after rilonacept availability April 1, 2021 – Dec 31, 2021
# Not mutually exclusive, pts could contribute whole/fractions of PY to multiple medication classes (i.e., includes combination therapy and sequential therapy)
€ 24% of pts using anakinra went on to use rilonacept; of those, 9% used anakinra for ≤30 days (possibly as short-term bridge therapy)
¥ 16% of pts who utilized steroids did so as short-term bridge therapy (≤30 days) before transitioning to rilonacept
+ Includes azathioprine, methotrexate, hydroxychloroquine/Plaquenil®, sulfasalazine
£ Data censored at last check-in visit
Total absolute pt counts: rilonacept (n=89); anakinra (n=45), corticosteroids (n=85), aspirin/NSAIDs/colchicine (n=239), csDMARDs (n=12)
csDMARDs: conventional disease-modifying antirheumatic drugs

FIGURE 5. RP TREATMENT INTENSIFICATION CHOICE OVER TIME IN PATIENTS FAILING ASPIRIN/NSAIDS/COLCHICINE



*Partial year 2021 prior to rilonacept availability on April 1, 2021; **Partial year 2021 after rilonacept availability after April 1, 2021
€ Of 41 pts starting rilonacept after aspirin/NSAIDs/colchicine, 4 pts utilized steroids as a short-term bridge prior to starting rilonacept (1 pt in 2021, 2 pts in 2022, 1 pt in 2023); 1 pt (in 2022) utilized anakinra as a short-term bridge prior to starting rilonacept
¥ Of 16 pts starting anakinra after aspirin/NSAIDs/colchicine, 3 pts utilized steroids as a short-term bridge prior to starting anakinra (1 pt in 2021, 2 pts in 2022)
£ Data censored at last check-in visit
csDMARDs: conventional disease-modifying antirheumatic drugs

DISCUSSION

- RESONANCE pts had a median RP disease duration of 3 years, with a median of 3 prior recurrences at enrollment.
- Proportional IL-1 pathway inhibition use increased from 11% of medication PY (before rilonacept availability) to 25% of medication PY (in 2023), with rilonacept use driving this observed shift.
- For pts failing aspirin/NSAIDs/colchicine
  - Prior to rilonacept availability in RP, substantially more pts transitioned to corticosteroids (73%) instead of IL-1 pathway inhibition (18%).
  - Year-on-year after rilonacept availability in RP, more pts transitioned to rilonacept, and fewer pts transitioned to corticosteroids
    - » Transition to rilonacept: 31%, 50%, 65% of pts in 2021, 2022, and 2023, respectively
    - » Transition to corticosteroids: 49%, 29%, 24% of pts in 2021, 2022, and 2023, respectively

LIMITATIONS

- Pts were not randomized to interventions, given the observational nature of the study.
- 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.

CONCLUSIONS

- **RESONANCE data reveal a temporal shift in RP management by RP-focused cardiologists, with increased proportional IL-1 pathway inhibition use since rilonacept availability in 2021.**
- **Advancing from prior 2015 guidelines, IL-1 pathway inhibition is often being used in colchicine-resistant patients in a steroid-sparing paradigm, a trend that has increased each year since rilonacept availability.**
- **Long-term outcomes from RESONANCE may guide RP treatment strategies to improve patient quality of life and inform future contemporary RP management guidelines in the era of steroid-sparing strategies.**

ACKNOWLEDGEMENTS

The authors would like to acknowledge the RESONANCE study investigators, including their research staff, as well as the patients who agreed to participate; James Lastra, and Nichole Reed of Red Nucleus for clinical research operations and data management; and Pamela Harvey from Acumen Medical Communications for assistance with medical writing. Funding for this study, including statistical analysis performed by DeltaMed, was provided by Kiniksa Pharmaceuticals.

DISCLOSURES

S.A. Luis: consultant fees from Kiniksa Pharmaceuticals, Cardiol Therapeutics, and Medtronic; P.C. Cremer: grants and consultant fees from Kiniksa Pharmaceuticals, grants and personal fees from Sobi; A. Raisinghani: consultant fees from Kiniksa Pharmaceuticals; M. Portman: consultant fees from Kiniksa Pharmaceuticals; R. W. Biederman: consultant fees from Kiniksa Pharmaceuticals, Bristol Myers Squibb, Janssen, and Lantheus; B. Weber: consultant fees from Kiniksa Pharmaceuticals; D. Lin: advisory board for Kiniksa Pharmaceuticals; M. S. Garshick: consultant fees from Kiniksa Pharmaceuticals; Y. Chen: no relevant disclosures; S. Gibbons, A. Curtis, V. Parameswaran, J. Clair and J. F. Paolini are shareholders and employees of Kiniksa Pharmaceuticals; A.L. Klein: grants and consultant fees from Kiniksa Pharmaceuticals, Cardiol Therapeutics, and Pfizer.

REFERENCES

1. Imazio M, Lazaros G, Gattorno M, et al. Anti-interleukin-1 agents for pericarditis: a primer for cardiologists. European Heart Journal 2022;43:2946–2957.
2. Chiabrando JG, Bonaventura A, Vecchie A, et al. Management of Acute and Recurrent Pericarditis. J Am Coll Cardiol 2020;75:76-92.
3. Klein AL, Imazio M, Cremer P, et al. Phase 3 Trial of Interleukin-1 Trap Rilonacept in Recurrent Pericarditis. N Engl J Med 2021;384:31-41.
4. ARCALYST (rilonacept) [package insert]. London: Kiniksa Pharmaceuticals (UK), Ltd.; 2021. ARCALYST® is a registered trademark of Regeneron Pharmaceuticals, Inc.
5. Reid A, Klein A, Lin D, et al. RESONANCE Registry: rationale and design of the retrospective and prospective longitudinal, observational registry in pediatric and adult patients with recurrent pericarditis. Eur Heart J 2021;42: Issue Supplement 1.
6. Clair J, PC Cremer, SA Luis, et al. Baseline demographics and disease characteristics of patients enrolled in the registry of the natural history of recurrent pericarditis in pediatric and adult patients (RESONANCE). J Am Coll Cardiol 2023;81 (8_Supplement):626.

PRESENTED BY SUE GIBBONS, KINIKSA PHARMACEUTICALS AT 3RD ANNUAL WOMEN'S CARDIOVASCULAR SYMPOSIUM • OCTOBER 11, 2024 • CINCINNATI, OH USA