SUMMARY OF PIVOTAL STUDY, INCLUDING THE UP TO 24-MONTH LONG-TERM EXTENSION, ON TREATMENT AND REDUCTION IN RISK OF RECURRENCE IN PATIENTS WITH RECURRENT PERICARDITIS

Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis

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Sustained pericarditis recurrence risk reduction with long-term rilonacept

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"In patients with recurrent pericarditis, consistent treatment for the full duration of the disease without interruption may be warranted for long-term pericarditis recurrence prevention."[1]

This reprint is being disseminated for informational purposes. Some data provided in this publication are not included in the ARCALYST US Prescribing Information (USPI). ARCALYST has not been approved by the FDA to improve patient-reported quality-of-life outcomes, or improvements in findings such as ECG changes, pericardial effusion, or cardiac imaging. The safety and effectiveness of ARCALYST in these uses has not be established. This publication was supported by Kiniksa Pharmaceuticals, the manufacturer of ARCALYST. Some authors involved with this publication may have received grants or payment from Kiniksa. Author financial disclosures are included in this publication.

INDICATION

ARCALYST is indicated for the treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and pediatric patients 12 years and older.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Interleukin-1 (IL-1) blockade may interfere with the immune response to infections. Treatment with another medication that works through inhibition of IL-1 or inhibition of tumor necrosis factor (TNF) is not recommended as this may increase the risk of serious infection. Serious, life-threatening infections have been reported in patients taking ARCALYST. Do not initiate treatment with ARCALYST in patients with an active or chronic infection.
- Discontinue ARCALYST if a patient develops a serious infection.
- It is possible that taking drugs such as ARCALYST that block IL-1 may increase the risk of tuberculosis (TB) or other atypical or opportunistic infections.
- Although the impact of ARCALYST on infections and the development of malignancies is not known, treatment with immunosuppressants, including ARCALYST, may result in an increase in the risk of malignancies.

Please see Important Safety Information throughout and full Prescribing Information at ARCALYST.com/PI.

RHAPSODY pivotal trial design[1,2]

A Phase 3, multicenter, double-blind, event-driven, randomized-withdrawal trial of ARCALYST in recurrent pericarditis patients with acute symptoms of at least a second recurrence despite treatment with traditional therapies (NSAIDs, colchicine, or corticosteroids, alone or in combination). Trial began with a 4-week screening period to establish trial eligibility and was followed by 3 periods, run-in, randomized-withdrawal, and long-term extension.

12-week run-in
Initiation of ARCALYST and transition to monotherapy

- 1-week stabilization
- 9 weeks weaning from background therapies
- 2 weeks ARCALYST monotherapy

Event-driven, double-blind randomized-withdrawal
Treatment with ARCALYST or placebo*

- 1:1 randomization to weekly ARCALYST or placebo
- Continued until the prespecified number of primary efficacy end point events

Long-term extension
Eligible patients were offered open-label ARCALYST for up to 24 additional months

- 18 months after the most recent pericarditis event (qualifying or randomized-withdrawal period), a decision was made for each patient to†:
  - —Continue open-label ARCALYST
  - —Suspend treatment for observation (ARCALYST rescue for recurrence allowed)
  - —Exit the study

NSAID, nonsteroidal anti-inflammatory drug.
*For patients who met the prespecified clinical response criteria for ARCALYST.
†Based on clinical status and at investigator discretion.

All patients receiving corticosteroids at baseline were successfully transitioned off corticosteroids after starting ARCALYST during the run-in period of RHAPSODY.[2]

- No patient in the randomized-withdrawal period had a reintroduction of corticosteroid therapy

52% of patients were not on corticosteroids at baseline.[3]

- Median time to ARCALYST monotherapy was 7.9 weeks from traditional therapies‡

‡From traditional therapies, including NSAIDs, colchicine, or corticosteroids, alone or in combination.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Warnings and Precautions (continued)

- Hypersensitivity reactions associated with ARCALYST occurred in clinical trials. Discontinue ARCALYST and initiate appropriate therapy if a hypersensitivity reaction occurs.
- Increases in non-fasting lipid profile parameters occurred in patients treated with ARCALYST in clinical trials. Patients should be monitored for changes in their lipid profiles.

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RHAPSODY pivotal trial inclusion and exclusion criteria[2,3§]

KEY INCLUSION CRITERIA AT SCREENING

- Male or female
- 12 years of age or older
- Diagnosed with recurrent pericarditis
- Presenting with at least a second recurrence of pericarditis
- If using NSAIDs, colchicine, and/or corticosteroids, doses remained stable or were not increased 3 days prior to first drug administration

KEY EXCLUSION CRITERIA AT SCREENING

- Diagnosis of pericarditis secondary to specific prohibited etiologies:
  - —Tuberculosis
  - —Neoplastic, purulent, or radiation etiologies
  - —Post-thoracic blunt trauma (eg, motor vehicle accident)
  - —Myocarditis
  - —Systemic autoimmune diseases (with exception of Still's disease)
- Pregnant, breastfeeding, planning a pregnancy, or planning on fathering a child
- History of immunosuppression

SELECT CHARACTERISTICS OF CLINICAL TRIAL PARTICIPANTS

- Total population: **86**
- Mean patient age: **45 years** (range: 13-78)
  - —57% female
- Diagnosis:
  - —"Idiopathic" pericarditis: 85% (n=73)
  - —Post cardiac injury 15% (n=13)
- Medications used in the qualifying event[‖] (alone or in combination): NSAIDs **67%** (n=58), colchicine **80%** (n=69), corticosteroids **49%** (n=42)
- Mean duration of disease: **2.4 years**
- Mean pericarditis events per year: **4.4** (including the qualifying pericarditis event)[‖]
- Mean qualifying NRS pain score: **6.2**
- Mean qualifying CRP level: **6.2 mg/dL** (62 mg/L)

CRP, C-reactive protein; NRS, Numerical Rating Scale.
[§]This list is not all-inclusive.
[‖]Qualifying pericarditis event: NRS ≥4 (0-10) and CRP ≥1 mg/dL.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Warnings and Precautions (continued)

- Since no data are available, avoid administration of live vaccines while patients are receiving ARCALYST. ARCALYST may interfere with normal immune response to new antigens, so vaccines may not be effective in patients receiving ARCALYST. It is recommended that, prior to initiation of therapy with ARCALYST, patients receive all recommended vaccinations, as appropriate.

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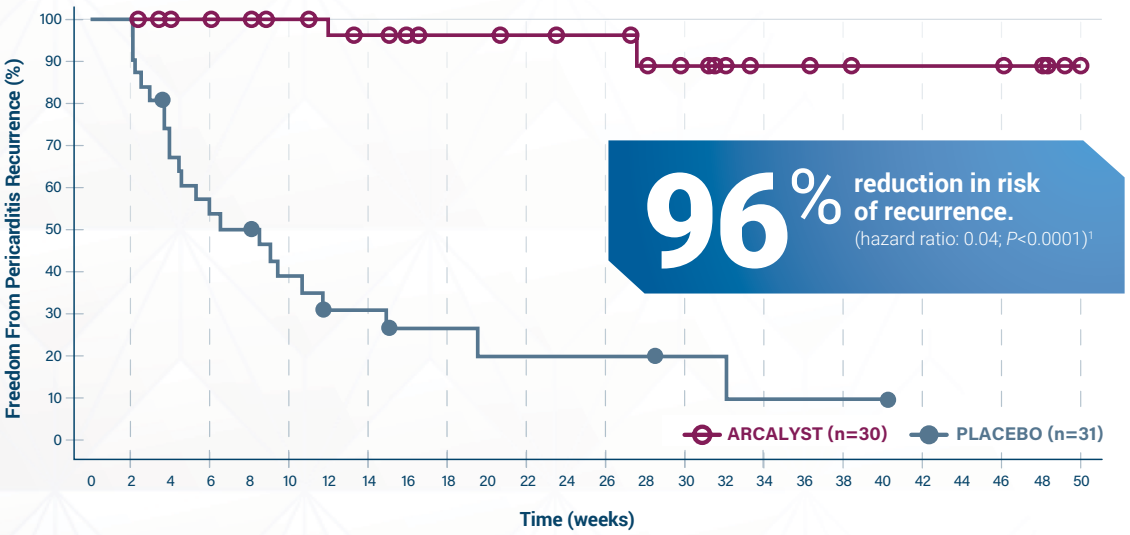
RHAPSODY RANDOMIZED-WITHDRAWAL PERIOD (PRIMARY EFFICACY END POINT):

ARCALYST significantly reduced risk of pericarditis recurrence[2,3]*



7% (2 of 30) of patients treated with ARCALYST experienced a recurrence (**both during treatment interruptions** of 1 to 3 weekly doses).

- The median time to recurrence could not be estimated due to low number of recurrences

74% (23 of 31) of patients treated with placebo experienced a recurrence at the time the event-driven randomized-withdrawal portion of the trial was closed.

- The median time to recurrence on placebo was 8.6 weeks (95% CI: 4.0, 11.7)

Primary end point results were consistent regardless of baseline corticosteroid use.[2]

SECONDARY END POINTS

In the run-in period:

97% of patients achieved treatment response, most as early as after the first dose.[2,3†]

- Median time to treatment response: 5.0 days (95% CI: 4.0, 7.0)
- Median time to pain response: 5.0 days (95% CI: 4.0, 6.0)
- Median time to CRP normalization: 7.0 days (95% CI: 5.0, 8.0)

In the randomized-withdrawal period, patients reported:

92% of trial days with minimal or no pericarditis pain (NRS ≤2) compared with 40% for patients on placebo (*P*<0.0001), assessed at week 16.[3]

*Primary efficacy end point was time to first adjudicated pericarditis recurrence in randomized-withdrawal period.
†Time to treatment response was defined as the time from the first dose to the first day when pericardial pain was NRS ≤2 and CRP ≤0.5 mg/dL (measured within 7 days before or after the pain response).

IMPORTANT SAFETY INFORMATION (CONTINUED)

Adverse Reactions

- The most common adverse reactions (≥10%) include injection-site reactions and upper respiratory tract infections.

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ARCALYST significantly reduced recurrences for up to an additional 24 months in the long-term extension

99% (74 of 75) eligible patients chose to continue treatment with ARCALYST for up to an additional 24 months in the RHAPSODY long-term extension[1‡]

‡N=74; 59 patients after completing the randomized-withdrawal period and 15 directly from the run-in period after enrollment in the randomized withdrawal period closed.

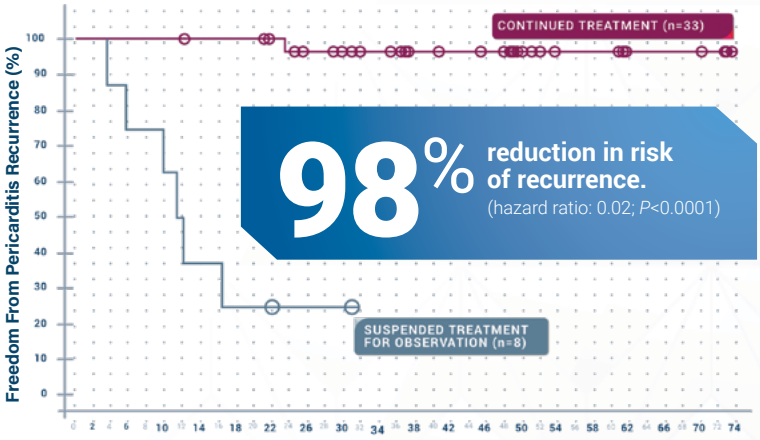
EFFICACY UP TO THE 18-MONTH DECISION MILESTONE[1§]:

- **94% (49 of 52) of patients did not experience an investigator-assessed recurrence** while on treatment with ARCALYST in the long-term extension period up to the 18-month decision milestone
  - —The 3 recurrences (3 of 52) did not meet the formal RHAPSODY event-adjudication criteria (eg, only symptoms without CRP elevation)
- Disease history during the 2.5 years (mean) prior to the entry of trial was **4.4 events per patient-year**[¶]

§N=74; 59 patients after completing the randomized-withdrawal period and 15 directly from the run-in period after enrollment in the randomized withdrawal period closed.

¶While being treated with NSAIDs, colchicine, or corticosteroids, alone or in combination.

EFFICACY PAST THE 18-MONTH DECISION MILESTONE[1]:



Week after 18-month decision milestone
(after most recent pericarditis event [qualifying or randomized-withdrawal period])

3% (1 of 33) of patients who continued ARCALYST treatment experienced a recurrence (**during a treatment interruption** of 4 weekly doses).

- The median time to recurrence could not be estimated due to low number

75% (6 of 8) of patients who suspended treatment for observation experienced a recurrence.

- The median time to recurrence after suspension of ARCALYST treatment was 11.8 weeks (95% CI: 3.7-NE weeks)

Results are consistent with the primary efficacy end point.

In the randomized-withdrawal and the long-term extension periods, ARCALYST was proven to significantly reduce risk of recurrence as long as there were no interruptions in therapy.[1,2]

REINITIATION

All patients who reinitiated ARCALYST after a flare experienced resolution[1,2‖]**:**

- In the randomized-withdrawal period, all patients who had a recurrence (25) reinitiated ARCALYST and experienced resolution of their flare
- In the long-term extension period, all patients who had a recurrence and reinitiated ARCALYST (6/7) experienced resolution of their flare[**]

NE, not estimable.

‖All recurrences experienced by patients being treated with ARCALYST occurred during temporary treatment interruptions of 1 to 4 weeks.

**1 patient experienced a recurrence but did not reinitiate ARCALYST.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Drug Interactions

- In patients being treated with CYP450 substrates with narrow therapeutic indices, therapeutic monitoring of the effect or drug concentration should be performed, and the individual dose of the medicinal product may need to be adjusted.

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ARCALYST safety profile

EVENT†*	RUN-IN PERIOD	RANDOMIZED-WITHDRAWAL PERIOD				TOTAL (N=86)
	ARCALYST (N=86)	ARCALYST, Including Bailout (N=30)	Placebo, Including Bailout (N=31)	ARCALYST, Before Bailout (N=30)	Placebo, Before Bailout (N=31)	
	Number of patients with event (percent)					
Any Adverse Event	69 (80)	24 (80)	22 (71)	24 (80)	13 (42)	74 (86)
Adverse events according to maximum severity†						
Mild	52 (60)	16 (53)	17 (55)	16 (53)	9 (29)	47 (55)
Moderate	15 (17)	8 (27)	5 (16)	8 (27)	4 (13)	25 (29)
Severe	2 (2)	0	0	0	0	2 (2)
Serious adverse event	1 (1)	1 (3)	3 (10)	1 (3)	1 (3)	5 (6)
Adverse event leading to death	0	0	0	0	0	0
Adverse event leading to dose interruption	0	1 (3)	0	1 (3)	0	1 (1)
Adverse event leading to discontinuation of ARCALYST or placebo	4 (5)	0	0	0	0	4 (5)
Cancer‡	0	1 (3)	0	1 (3)	0	1 (1)
Injection-site reaction	28 (33)	6 (20)	2 (6)	5 (17)	0	29 (34)
Infection or infestation	14 (16)	12 (40)	7 (23)	12 (40)	3 (10)	29 (34)
Upper respiratory infection	12 (14)	7 (23)	2 (6)	7 (23)	0	12 (22)

*For patients who did not discontinue the trial regimen and who transitioned to the open-label extension period, the adverse events reported here are those that occurred between the first dose of ARCALYST in the run-in period and the last visit during the randomized-withdrawal period. For patients who discontinued ARCALYST during the run-in period (10 patients) or who discontinued ARCALYST or placebo during the randomized-withdrawal period (1 patient) or at the end of the randomized-withdrawal period (1 patient) (ie, did not continue into the long-term extension period), data on adverse events continued to be collected for 6 weeks after the last dose of ARCALYST or placebo. Patients with multiple events were counted once in each appropriate category.

†Each patient was counted once, according to the maximum severity of the adverse event.

‡Cancer was an event of special interest. Basal cell carcinoma of the skin was excluded.

Long-term extension safety[1]

- During the long-term extension period, treatment-emergent adverse events (TEAEs) were experienced by 83.8% of patients (n=62)
- In most patients, the maximum severity of TEAEs was mild (36.5%) or moderate (37.8%)
- 2 patients experienced serious TEAEs (acute endocarditis, viral pneumonia) considered possibly study-drug related

Conclusions:

- ARCALYST was proven to significantly reduce risk of recurrence as long as there were no interruptions in therapy[1,2]
- Primary end point results were consistent regardless of baseline corticosteroid use[2]
- The resolution of acute episodes of recurrent pericarditis and the prevention of subsequent episodes of recurrent pericarditis with ARCALYST monotherapy support the hypothesis that interleukin-1 is an important mediator of recurrent pericarditis[1,2]

To view the *N Engl J Med* article, scan this QR code or visit ARCAYST.com/trial

To view the *J Am Heart Assoc* article, scan this QR code or visit www.ARCALYST.com/lte

References: 1. Imazio M, Klein, AL, et al. Sustained pericarditis recurrence risk reduction with long-term rilonacept. *J Am Heart Assoc*. 2024;13:e032516. doi:10.1161/JAHA.123.032516 **2.** 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(1):31-41. **3.** ARCALYST. Package insert. Kiniksa Pharmaceuticals; 2021.

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