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

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

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***N Engl J Med*. 2021;384(1):31-41.**

Prolonged rilonacept treatment in RHAPSODY long-term extension provided persistent reduction of pericarditis recurrence risk

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Poster 2223. Presented at: American Heart Association Scientific Sessions; November 5-7, 2022; Chicago, IL.

"The results of this trial suggest that patients treated with rilonacept [ARCALYST] may be able to discontinue colchicine and glucocorticoids."[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), including the assessment of pericarditis symptoms according to the patient's global impression of pericarditis severity rating scale and safety data from the RHAPSODY clinical study. There is a discrepancy between this publication and the ARCALYST USPI regarding the number of patients taking corticosteroids: 42 patients (49%) at the time of the qualifying event vs 41 patients (48%) at baseline, respectively.[1,2]

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[1,3]

A Phase 3, multicenter, double-blind, event-driven, randomized-withdrawal (RW) trial of ARCALYST in RP 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 (RI), RW, and LTE.

12-week RI
Initiation of ARCALYST and transition to monotherapy

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

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

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

LTE
Eligible patients were offered open-label ARCALYST for up to 24 additional months

- 18 months after the most recent pericarditis event (qualifying or RW 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 RI period of RHAPSODY.[1]

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

52% of patients were not on corticosteroids at baseline.[2]

- 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[1,2§]

KEY INCLUSION CRITERIA AT SCREENING

- Male or female 12 years of age or older
- Diagnosed with RP
- Presenting with at least a second recurrence of pericarditis
  - —If using NSAIDs, colchicine, corticosteroids, or any combination thereof, 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, including lupus (with exception of Still's disease)

SELECT CHARACTERISTICS OF CLINICAL TRIAL PARTICIPANTS

- Total population: **86**
- Mean patient age: **45 years** (range: 13-78)
  - —57% female
- Diagnosis of "idiopathic" pericarditis: **73 (85%)**
  - —Remainder: post-pericardiotomy syndrome and Dressler syndrome
- Mean duration of disease: **2.4 years**
- Medications used in the qualifying event (alone or in combination)[§]: NSAIDs (n=58), colchicine (n=69), corticosteroids (n=42)
- 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**

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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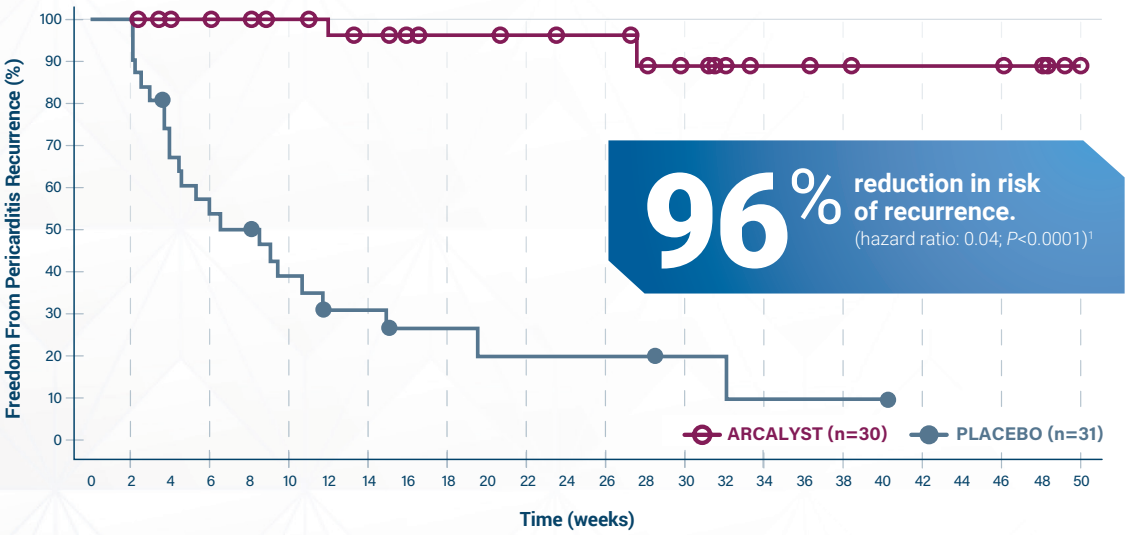
RHAPSODY RW PERIOD (PRIMARY EFFICACY END POINT):

ARCALYST significantly reduced risk of pericarditis recurrence[1,2*]



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 RW 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.[1]

SECONDARY END POINTS

In the RI period:

97% of patients achieved treatment response, most as early as after the first dose.[1,2†]

- 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 RW 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.[2]

*Primary efficacy end point was time to first adjudicated pericarditis recurrence in RW 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 LTE

99% (74 of 75) eligible patients chose to continue treatment with ARCALYST for up to an additional 24 months in the RHAPSODY LTE.[3‡]

‡N=74; 59 patients after completing the RW period and 15 directly from the RI period after enrollment in the RW period closed.

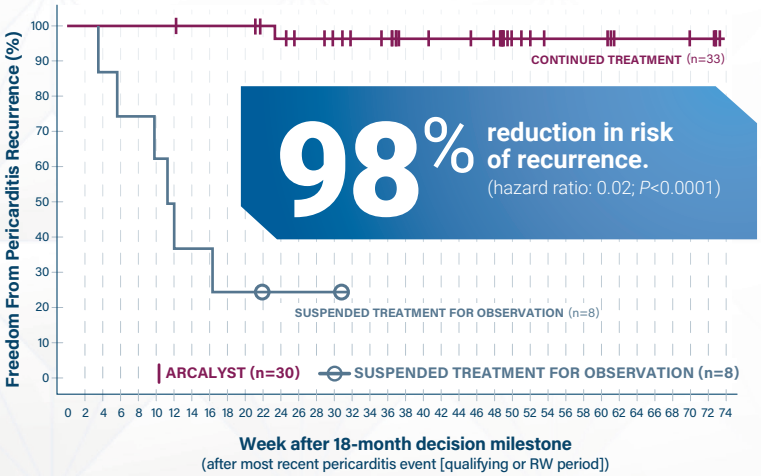
EFFICACY UP TO THE 18-MONTH DECISION MILESTONE[3§]:

3 of the 74 patients experienced an investigator-assessed recurrence while on treatment with ARCALYST in the LTE period up to the 18-month decision milestone.

- These recurrences 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 RW period and 15 directly from the RI period after enrollment in the RW period closed.
¶While being treated with NSAIDs, colchicine, or corticosteroids, alone or in combination.

EFFICACY PAST THE 18-MONTH DECISION MILESTONE[3]:



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

Results are consistent with the primary efficacy end point.

In the RW and the LTE periods, ARCALYST was proven to significantly reduce risk of recurrence as long as there were no interruptions in therapy.[1,3]

REINITIATION

All patients who reinitiated ARCALYST after a flare experienced resolution[1,3,4‖]**:**

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

‖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 RI period and the last visit during the RW period. For patients who discontinued ARCALYST during the RI period (10 patients) or who discontinued ARCALYST or placebo during the RW period (1 patient) or at the end of the RW 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.

LTE Safety[3]

- During the LTE 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 (37.8%) or moderate (37.8%)
- 2 patients experienced serious TEAEs (acute endocarditis, viral pneumonia) considered "related" to the study drug

Conclusions:

- ARCALYST was proven to significantly reduce risk of recurrence as long as there were no interruptions in therapy[1,3]
- Primary end point results were consistent regardless of baseline corticosteroid use[1]
- The resolution of acute episodes of RP and the prevention of subsequent episodes of RP with ARCALYST monotherapy support the hypothesis that interleukin-1 is an important mediator of RP[1,3]

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

View the results from the 24-month RHAPSODY LTE at ARCALYST.com/HCP

To request to speak with a Clinical Sales Specialist, visit ARCALYST.com/HCP.

References: 1. 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. **2.** ARCALYST. Package insert. Kiniksa Pharmaceuticals (UK), Ltd; 2021. **3.** Imazio M, Klein AL, et al. Prolonged rilonacept treatment in RHAPSODY long-term extension provided persistent reduction of pericarditis recurrence risk. Poster 2223. Presented at: American Heart Association Scientific Sessions; November 5-7, 2022; Chicago, IL. **4.** Data on file. Kiniksa Pharmaceuticals (UK), Ltd.

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