Arcalyst® (rilonacept) For Injection

RHAPSODY PIVOTAL STUDY ON TREATMENT AND REDUCTION IN RISK OF RECURRENCE

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

Allan L. Klein, Massimo Imazio, Paul Cremer, Antonio Brucato, Antonio Abbate, Fang Fang, Antonella Insalaco, Martin LeWinter, Basil S. Lewis, David Lin, Sushil A. Luis, Stephen J. Nicholls, Arian Pano, Alistair Wheeler, and John F. Paolini, for the RHAPSODY Investigators*

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

*A complete list of the RHAPSODY investigators is provided in the Supplementary Appendix of this article, available at NEJM.org.

"The **resolution of acute episodes** *and the* **prevention of subsequent episodes** *during rilonacept monotherapy support the hypotheses that interleukin-1 is an important mediator of recurrent pericarditis..."*[1]

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

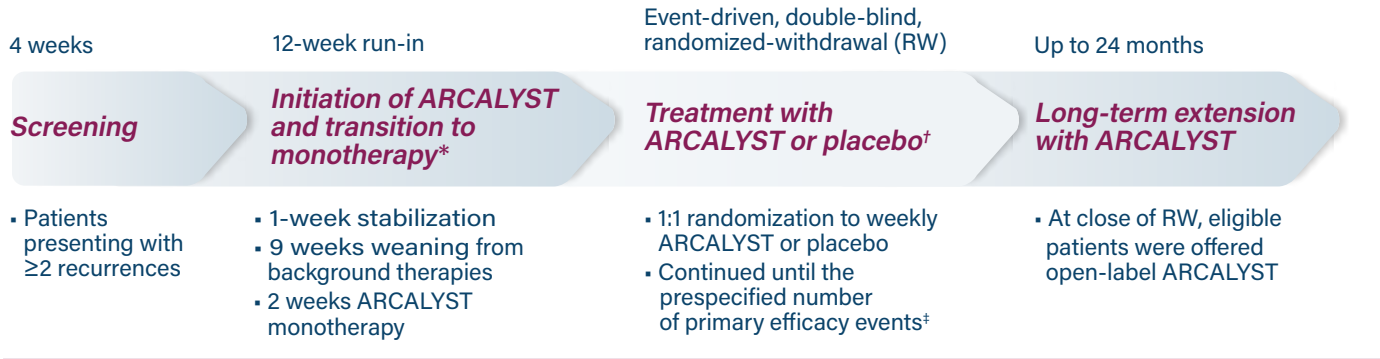
- Interleukin-1 (IL-1) blockade may interfere with the immune response to infections. Treatment with another medication that works through inhibition of IL-1 or inhibition of tumor necrosis factor (TNF) is not recommended as this may increase the risk of serious infection. Serious, life-threatening infections 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.

The RHAPSODY trial tested the primary hypothesis that ARCALYST would lead to a lower risk of pericarditis recurrence than placebo.[1]

RHAPSODY CLINICAL TRIAL DESIGN

A Phase 3, multicenter, double-blind, event-driven, randomized-withdrawal trial of ARCALYST in patients (≥12 years of age) with acute symptoms of recurrent pericarditis and systemic inflammation despite treatment with NSAIDs, colchicine, or corticosteroids, alone or in any combination (N=86).[1]



During the run-in period, patients receiving corticosteroids were effectively transitioned to ARCALYST monotherapy[1]

- **48%** (41 of 86) of patients were receiving corticosteroids at baseline[2]

Median time to ARCALYST monotherapy was **7.9 weeks**.*

> *"The results of this trial suggest that* ***patients treated with rilonacept may be able to discontinue…glucocorticoids."***[1]

*From traditional therapies, including NSAIDs (58 patients), colchicine (69 patients), or corticosteroids (41 patients), alone or in combination.[1,2]
†For patients who met the prespecified clinical response criteria for ARCALYST.
‡Primary efficacy end point was time to first recurrence in patients receiving ARCALYST compared with placebo during the randomized-withdrawal period.

NSAIDs, nonsteroidal anti-inflammatory drugs.

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.
- 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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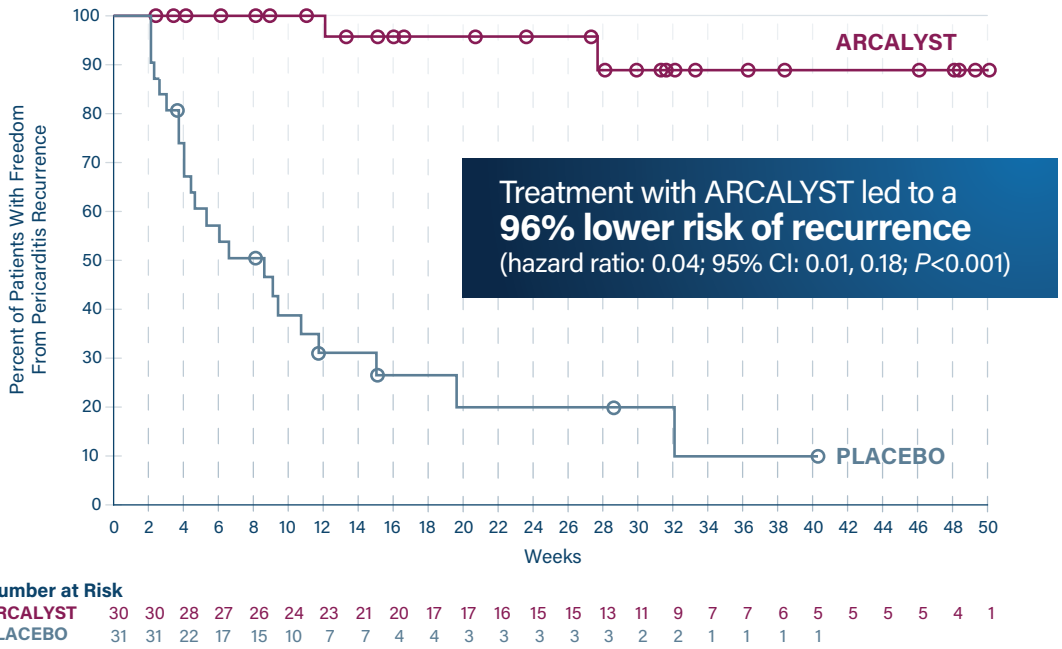
PRIMARY END POINT

Proven to reduce risk of recurrence[1,2]*



- 2 of 30 patients (7%) in the ARCALYST group had a pericarditis recurrence compared with 23 of 31 patients (74%) in the placebo group: **the 2 pericarditis recurrences in the ARCALYST group occurred during temporary treatment interruptions**[1]
- 1 of 2 patients in the ARCALYST group and all 23 patients in the placebo group who had a recurrence event received bailout ARCALYST: **no patient who received bailout ARCALYST had a recurrence event during the remainder of the RW period**[1]

SECONDARY END POINTS

During the run-in period, 97% of patients taking ARCALYST experienced rapid treatment response[1,2]:

- 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)
- Median time to treatment response=**5.0 days** (95% CI: 4.0, 7.0)

Secondary end points measured at Week 16 of the RW period showed the benefit of ARCALYST monotherapy[1,2]:

- **Persistent clinical response:** **81%** of patients who received ARCALYST vs 20% who received placebo, *P*<0.001
- **Days with no or minimal pericarditis pain:** **92%** with ARCALYST vs 40% with placebo, *P*<0.0001

99% (74 of 75) of eligible patients chose to continue treatment with ARCALYST in the open-label, long-term extension period.[1]

CI, confidence interval; CRP, C-reactive protein.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Adverse Reactions

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

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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ADVERSE EVENTS[1]*

EVENT	RUN-IN PERIOD	RANDOMIZED-WITHDRAWAL PERIOD				TOTAL (N=86)
		Including Bailout		Before Bailout		
	ARCALYST (N=86)	ARCALYST (N=30)	Placebo (N=31)	ARCALYST (N=30)	Placebo (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 tract infection	12 (14)	7 (23)	2 (6)	7 (23)	0	19 (22)

Injection-site reactions and upper respiratory tract infections were the most common adverse events associated with the use of ARCALYST.[1§]

CONCLUSIONS

Among patients with recurrent pericarditis, ARCALYST led to rapid resolution[‖] of recurrent pericarditis episodes and was proven to reduce the risk of recurrence[1]

To view the full study, visit ARCALYST.com/trial.

Request to speak to a Clinical Sales Specialist at ARCALYST.com/HCP

*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.
§Injection-site reactions included erythema, swelling, pruritus, mass, bruising, inflammation, pain, edema, dermatitis, discomfort, urticaria, vesicles, warmth, and hemorrhage.[2]
‖ 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). Median time to treatment response=5.0 days (95% CI: 4.0, 7.0).

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.

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RHAPSODY pivotal trial inclusion and exclusion criteria

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Key inclusion criteria at screening[1]*

- Male or female aged 12 years or older
- Diagnosed with recurrent pericarditis
- Presenting with at least a second recurrence of pericarditis
- If using NSAIDs, colchicine, or corticosteroids, alone or in any combination, doses were stable or not increased for ≥3 days prior to study drug administration

Key exclusion criteria at screening[1]*

- Pericarditis secondary to tuberculosis, post-thoracic blunt trauma, myocarditis, systemic autoimmune diseases (excluding Still's disease), or neoplastic, purulent, or radiation etiologies
- Pregnant, breastfeeding, or planning a pregnancy, or fathering a child during study or ≤3 months after receiving last study drug
- History of immunosuppression

Baseline characteristics of clinical trial participants[2]

- Total population: **86**
- Mean patient age: **45 years** (range 13-78)
  - 57% female
- Diagnosis of "idiopathic" pericarditis: **73 (85%)**
  - Remainder: post-cardiac injury pericarditis
- 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**

*This list is not all-inclusive.
†Qualifying pericarditis event: 0-10 point Numerical Rating Scale (NRS) ≥4 and C-reactive protein (CRP) ≥1 mg/dL.

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