Arcalyst® (rilonacept) For Injection

PIVOTAL STUDY ON TREATMENT AND REDUCTION OF RISK

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

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*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…during rilonacept monotherapy support[s] the hypothes[is] that interleukin-1 is an important mediator of recurrent pericarditis in patients who have evidence of systemic inflammation…."*

INDICATION

ARCALYST® (rilonacept) 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 has been associated with an increased risk of serious infections, and serious infections have been reported in patients taking ARCALYST. ARCALYST is not recommended for use with tumor necrosis factor (TNF) inhibitors because this may increase risk of serious infections. ARCALYST should be discontinued if a patient develops a serious infection. Treatment with ARCALYST should not be initiated in patients with an active or chronic infection.
- It is possible that taking drugs that block IL-1 increase the risk of tuberculosis (TB) or other atypical or opportunistic infections. Refer to current practice guidelines to evaluate and to treat possible latent TB infections before initiating therapy.
- The impact of ARCALYST on infections and the development of malignancies is not known. However, treatment with immunosuppressants may result in an increase in the risk of malignancies.
- Hypersensitivity reactions occurred in clinical trials. If a hypersensitivity reaction occurs, discontinue ARCALYST and initiate appropriate therapy.

Please see Important Safety Information throughout and full Prescribing Information.

RHAPSODY CLINICAL TRIAL DESIGN

Arcalyst® (rilonacept) For Injection

A Phase 3, multicenter, double-blind, event-driven, randomized withdrawal trial of rilonacept 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]

1 Screening Period

(4 weeks)

- Presenting with at least a second recurrence of pericarditis

2 Initial Taper to Rilonacept Monotherapy

Single-Blind, Run-In Period

(12 weeks)

- 1-week stabilization period
- 9-week period to wean from background therapy for pericarditis
- 2-week period of rilonacept monotherapy

3 Treatment With Rilonacept or Placebo

Double-Blind, Randomized Withdrawal (RW) Period

(n=22 recurrence events)

- For patients who met the prespecified clinical response criteria for rilonacept
- 1:1 randomization to weekly rilonacept or placebo

4 Long-Term Treatment With Rilonacept

Extension Period

(Up to 24 months)

- When the event-driven portion of the trial closed, eligible patients were offered open-label rilonacept

View inclusion and exclusion criteria

SECONDARY ENDPOINT

During the run-in period, patients experienced rapid treatment response[1]:

- 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)

CI=confidence interval; CRP=C-reactive protein; NSAIDs=nonsteroidal anti-inflammatory drugs.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- Patients should be monitored for changes in their lipid profiles and provided with medical treatment if warranted.
- Since no data are available, avoid administration of live vaccines while patients are receiving ARCALYST. Because IL-1 blockade may interfere with immune response to infections, it is recommended that, prior to initiation of therapy with ARCALYST, patients receive all recommended vaccinations, as appropriate.

Adverse Reactions

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

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PRIMARY ENDPOINT

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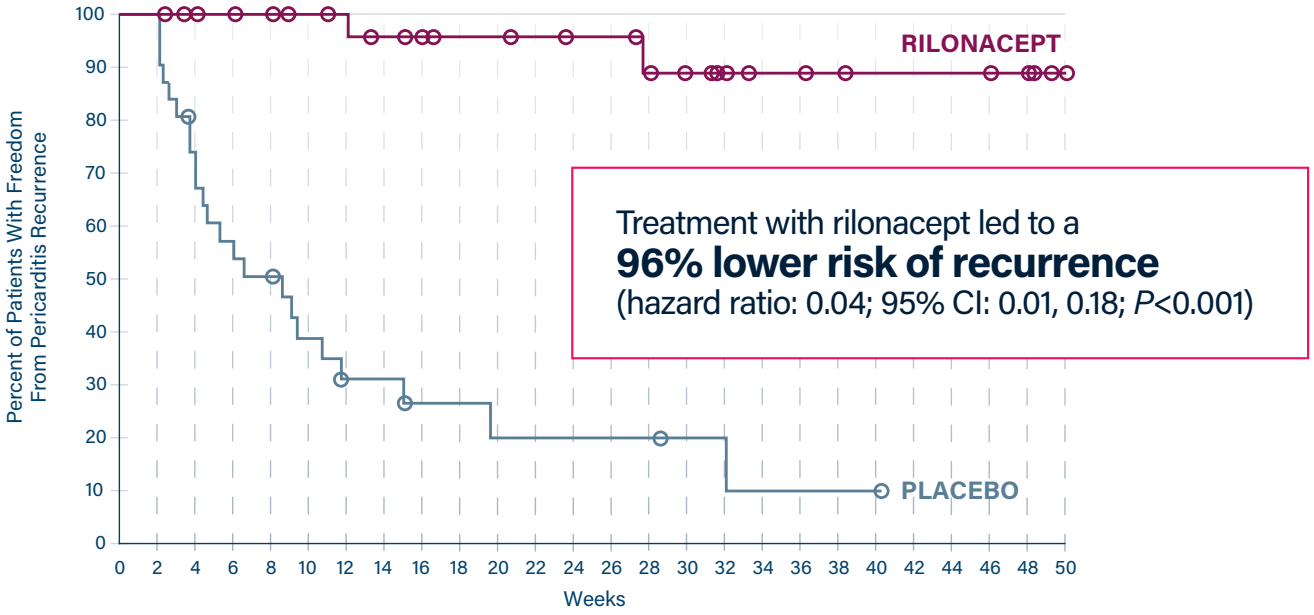
Time to the first adjudicated pericarditis recurrence[1,2]



Number at Risk

RILONACEPT	30	30	28	27	26	24	23	21	20	17	17	16	15	15	13	11	9	7	7	6	5	5	5	4	1
PLACEBO	31	31	22	17	15	10	7	7	4	4	3	3	3	3	3	2	2	1	1	1	1				

- 2 of 30 patients (7%) in the rilonacept group had a pericarditis recurrence compared with 23 of 31 patients (74%) in the placebo group
- The 2 recurrence events in the rilonacept group happened in association with temporary interruptions of the trial-drug regimen of 1 to 3 weekly doses
- 1 of 2 patients in the rilonacept group and all 23 patients in the placebo group who had a recurrence event received bailout rilonacept
- No patient who received bailout rilonacept had a recurrence event during the remainder of the RW period

SECONDARY ENDPOINTS

Secondary endpoints measured at Week 16 of the RW period showed a benefit of rilonacept monotherapy[1,2]

- **Persistent clinical response:** **81%** of patients who received rilonacept vs 20% who received placebo, *P*<0.0002
- **Days with no or minimal pericarditis pain:** **92%** with rilonacept vs 40% with placebo, *P*<0.0001

IMPORTANT SAFETY INFORMATION

Drug Interactions

- Concomitant administration of ARCALYST with TNF-blocking agents or other agents that block IL-1 or its receptor is not recommended, as this may increase the risk of serious infections.
- 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 as needed.

Use in Specific Populations

- Pregnancy outcomes reported post marketing and during clinical trials were rare, therefore, the effect of using ARCALYST during pregnancy is not known.
- There is no information on the presence of ARCALYST in either human or animal milk, the effects on the breastfed infant, or the effects on milk production.

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ADVERSE EVENTS*[1]

EVENT	RUN-IN PERIOD	RANDOMIZED-WITHDRAWAL PERIOD				TOTAL (N=86)
	Rilonacept (N=86)	Rilonacept, Including Bailout (N=30)	Placebo, Including Bailout (N=31)	Rilonacept, 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 rilonacept 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)

*Patients with multiple events were counted once in each appropriate category.
†Counted once, according to the maximum severity of the adverse event.
‡Cancer was an event of special interest.

Injection-site reactions and upper respiratory tract infections were the most common adverse events associated with the use of ARCALYST, which were mild to moderate in severity.

DURATION OF TREATMENT

- 86 patients received at least 1 dose of ARCALYST with a median treatment duration of **9 months**[1]
- The mean adherence to the trial regimen was **98.7%** ± 4.6 throughout the entire trial (run-in and randomized withdrawal periods)[1]

"The results of this trial suggest that patients treated with rilonacept may be able to discontinue colchicine and glucocorticoids."

CONCLUSIONS

Among patients with recurrent pericarditis, rilonacept led to rapid resolution of recurrent pericarditis episodes and to a significantly lower risk of pericarditis recurrence than placebo.[1]

To request a copy of the RHAPSODY Phase 3 trial, visit ARCALYST.com/HCP and select: REQUEST TO SPEAK TO A CLINICAL SALES SPECIALIST

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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