

First-in-human study of CD123 NK cell engager SAR443579 in R/R AML



KEY TAKEAWAYS

- CD123 is frequently overexpressed on leukemic blasts and **high levels are associated with poor outcomes** in several blood cancers
- **SAR443579 is a NK cell engager** that targets CD123 and facilitates the activation of NK cells leading to death of cancer cells
- The first human trial of SAR443579 showed that the treatment was **well tolerated up to doses of 6 mg/kg** with observed clinical benefit in patients with R/R AML

In a Phase I/II study, the CD123 natural killer (NK) cell engager SAR443579 was **well tolerated with initial clinical benefit observed**. The Phase I part of the study investigated the safety and the optimal dose of SAR443579 and explored a range of dose levels from 0.01 to 6 mg/kg to check for any dose-limiting toxicities (DLT).

The aim of the study was to characterize the overall safety and tolerability profile of SAR443579 and to assess preliminary anti-leukemic activity in patients with relapsed/refractory (R/R) acute myeloid leukemia (AML; n=58), or high-risk myelodysplastic syndrome (MDS; n=1).

SAR443579 has received a fast-track designation by the US Food and Drug Administration.



Summary of adverse events

All dose levels (N=59)

DLT*	1 (1.7%)
Grade 5 adverse events (AEs)†	6 (10.2%)
Treatment-related AEs (TRAEs)	39 (66.1%)
Treatment-related serious AEs (Grade ≥3)	3 (5.1%)
Cytokine release syndrome (CRS)	4 (6.8%)
CRS Grade 1	3 (5.1%)
CRS Grade 3	1 (1.7%)
Immune effector cell-associated neurotoxicity syndrome (ICANS)	0
Most common AE: infusion-related reaction	
Any grade	34 (57.6%)
Grade ≥3	1 (1.7%)

* One patient experienced a DLT (Grade 3 CRS) at 0.75 mg/kg dose of SAR443579.

† Grade 5 treatment-emergent AEs were reported as unrelated to treatment with SAR443579 and included cholestasis, hemorrhage intracranial, cerebellar hemorrhage, pneumonia, pulmonary sepsis, and urosepsis.

Responses in patients with R/R AML treated at the target dose of 1 mg/kg of SAR443579

Among 15 patients with R/R AML treated at a target dose of 1 mg/kg:
• 5 patients (33.3%) achieved CR/Cri

- Durable remission >10 months in 3 of 5 responders
- One responder proceeded to stem cell transplant
- Two remain on maintenance therapy



CR (complete remission); Cri (complete remission with incomplete hematological recovery).



WHAT DOES THIS MEAN FOR PATIENTS?

The new treatment, SAR443579, has shown **promising results in early human trials** for patients with R/R AML. It was generally well-tolerated, with most side effects being manageable. The most common side effect related to the treatment was a mild reaction to the infusion. Mild CRS occurred in three patients, while one experienced severe CRS. **Importantly, no patients experienced ICANS.** SAR443579 showed preliminary effectiveness with a third of patients with R/R AML achieving CR/Cri.

The U.S. Food and Drug Administration (FDA) has granted SAR443579 fast-track status, meaning the development and review of this treatment are being accelerated. Currently, the trial is ongoing to determine the optimal dose of SAR443579.