



For your adult patients with relapsed or refractory multiple myeloma

SARCLISA IN COMBINATION WITH Kd OR Pd¹

IKEMA Trial

SARCLISA + carfilzomib and dexamethasone (Kd) after 1 to 3 prior lines of therapy

- Evaluated in **302 patients** in a **phase 3**, multicenter, multinational, randomized, open-label study^{1,2}
- Patients received either **SARCLISA 10 mg/kg IV in combination with Kd** (n=179) or **Kd alone** (n=123), administered in 28-day cycles until disease progression or unacceptable toxicity. SARCLISA was given weekly in the first cycle and every 2 weeks thereafter¹
- **PFS** was the primary endpoint; **ORR, ≥VGPR, CR, MRD negativity**, and **OS** were key secondary endpoints^{1,2}
- Patients who permanently discontinued treatment due to adverse reactions: 8% vs 14% with SARCLISA + Kd vs Kd alone, respectively^{1,2}

mPFS
Not yet reached (NR) with SARCLISA + Kd
 vs 20.27 months with Kd alone¹
HR=0.548
 (95% CI: 0.37, 0.82; P=0.0032)^{1,a}

PFS results are based on a prespecified interim analysis, with a median follow-up time of 20.7 months. PFS results were assessed by an IRC, based on central laboratory data for M-protein, and central radiologic imaging review using the IMWG criteria.¹

^aStratified by the number of previous lines of therapy (1 vs >1) and R-ISS stage (I or II vs III vs not classified) according to IRT.¹

Indication

SARCLISA (isatuximab-irfc) is indicated:

- In combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor
- In combination with carfilzomib and dexamethasone, for the treatment of adult patients with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy

Important Safety Information

CONTRAINDICATIONS

SARCLISA is contraindicated in patients with severe hypersensitivity to isatuximab-irfc or to any of its excipients.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

NCCN

**CATEGORY 1
PREFERRED**

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Multiple Myeloma Recommend isatuximab-irfc (SARCLISA) as a Category 1 Preferred Option for Early Relapses^{3*}

- In combination with pomalidomide and dexamethasone
- In combination with carfilzomib and dexamethasone

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*1-3 prior therapies.³

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WARNINGS AND PRECAUTIONS

Infusion-Related Reactions

Serious infusion-related reactions (IRRs), including life-threatening anaphylactic reactions, have occurred with SARCLISA treatment. Severe signs and symptoms include cardiac arrest, hypertension, hypotension, bronchospasm, dyspnea, angioedema, and swelling.

Based on ICARIA-MM, IRRs occurred in 38% of patients treated with SARCLISA, pomalidomide, and dexamethasone (Isa-Pd). All IRRs started during the first SARCLISA infusion and resolved on the same day in 98% of the cases.

In IKEMA, infusion-related reactions occurred in 46% of patients treated with SARCLISA, carfilzomib, and dexamethasone (Isa-Kd).



For your adult patients with relapsed or refractory multiple myeloma

SARCLISA IN COMBINATION WITH Kd OR Pd¹

ICARIA-MM Trial

SARCLISA + pomalidomide and dexamethasone (Pd) after at least 2 prior therapies, including lenalidomide and a PI

- Evaluated in **307 patients** in a **phase 3**, multicenter, multinational, randomized, open-label study¹
- Patients received either **SARCLISA 10 mg/kg IV** in combination with Pd (n=154) or **Pd alone** (n=153), administered in 28-day cycles until disease progression or unacceptable toxicity. SARCLISA was given weekly in the first cycle and every 2 weeks thereafter¹
- **PFS*** was the primary endpoint; **ORR⁺** and **OS** were key secondary endpoints¹
- Patients who permanently discontinued treatment due to adverse reactions: 7% vs 12% with SARCLISA + Pd vs Pd alone, respectively^{1,2}

mPFS
11.53 months with SARCLISA + Pd
 vs 6.47 months with Pd alone¹
HR=0.596
 (95% CI: 0.44, 0.81; P=0.0010)¹

*PFS results were assessed by an IRC, based on central laboratory data for M-protein, and central radiologic imaging review using the IMWG criteria. Median time to follow-up was 11.6 months.

⁺sCR, CR, VGPR, and PR were evaluated by the IRC using the IMWG response criteria.

NCCN

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Multiple Myeloma Recommend isatuximab-irfc (SARCLISA) as a Category 1 Preferred Option for Early Relapses^{3†}

- In combination with pomalidomide and dexamethasone
- In combination with carfilzomib and dexamethasone

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CATEGORY 1
PREFERRED

[†]1-3 prior therapies.³

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Important Safety Information (cont'd)

Infusion-Related Reactions (cont'd)

In the Isa-Kd arm, the infusion-related reactions occurred on the infusion day in 99% of episodes. In patients treated with Isa-Kd, 95% of those experiencing an infusion-related reaction experienced it during the first cycle of treatment. All infusion-related reactions resolved: within the same day in 74% of episodes, and the day after in 24% of episodes.

The most common symptoms (≥5%) of an infusion-related reaction in ICARIA-MM and IKEMA (N=329) included dyspnea, cough, nasal congestion, and nausea. Anaphylactic reactions occurred in less than 1% of patients. To decrease the risk and severity of IRRs, premedicate patients prior to SARCLISA infusion with acetaminophen, H₂ antagonists, diphenhydramine or equivalent, and dexamethasone.

Monitor vital signs frequently during the entire SARCLISA infusion. For patients with grade ≥2 reactions, interrupt SARCLISA infusion and provide appropriate medical management. For patients with grade 2 or grade 3 reactions, if symptoms improve to grade ≤1, restart SARCLISA infusion at half of the initial infusion rate, with supportive care as needed, and closely monitor patients. If symptoms do not recur after 30 minutes, the infusion rate may be increased to the initial rate, and then increased incrementally. In case symptoms do not improve to grade ≤1 after interruption of SARCLISA infusion, persist or worsen despite appropriate medications, or require hospitalization, permanently discontinue SARCLISA and institute appropriate management. Permanently discontinue SARCLISA if an anaphylactic reaction or life-threatening (grade 4) IRR occurs and institute appropriate management.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

Important Safety Information (cont'd)

Neutropenia

SARCLISA may cause neutropenia.

In patients treated with Isa-Pd, neutropenia occurred in 96% of patients and grade 3-4 neutropenia occurred in 85% of patients. Neutropenic complications occurred in 30% of patients, including febrile neutropenia (12%) and neutropenic infections (25%), defined as infection with concurrent grade ≥ 3 neutropenia. The most frequent neutropenic infections included infections of the upper respiratory tract (10%), lower respiratory tract (9%), and urinary tract (3%).

In patients treated with Isa-Kd, neutropenia occurred in 55% of patients, with grade 3-4 neutropenia in 19% of patients (grade 3 in 18% and grade 4 in 1.7%). Neutropenic complications occurred in 2.8% of patients, including febrile neutropenia (1.1%) and neutropenic infections (1.7%).

Monitor complete blood cell counts periodically during treatment. Consider the use of antibiotics and antiviral prophylaxis during treatment. Monitor patients with neutropenia for signs of infection. In case of grade 4 neutropenia, delay SARCLISA dose until neutrophil count recovery to at least $1.0 \times 10^9/L$, and provide supportive care with growth factors, according to institutional guidelines. No dose reductions of SARCLISA are recommended.

Second Primary Malignancies

The incidence of second primary malignancies is increased in patients treated with SARCLISA-containing regimens. The overall incidence of second primary malignancies in all the SARCLISA-exposed patients was 3.6%.

In ICARIA-MM, second primary malignancies occurred in 3.9% of patients in the Isa-Pd arm and in 0.7% of patients in the Pd arm.

In IKEMA, second primary malignancies occurred in 7% of patients in the Isa-Kd arm and in 4.9% of patients in the Kd arm.

The most common ($\geq 1\%$) second primary malignancies in ICARIA-MM and IKEMA (N=329) included skin cancers (4% with SARCLISA-containing regimens and 1.5% with comparative regimens) and solid tumors other than skin cancer (1.8% with SARCLISA-containing regimens and 1.5% with comparative regimens). All patients with skin cancer continued treatment after resection of the skin cancer.

Monitor patients for the development of second primary malignancies.

Laboratory Test Interference Interference with Serological Testing (Indirect Antiglobulin Test)

SARCLISA binds to CD38 on red blood cells (RBCs) and may result in a false-positive indirect antiglobulin test (indirect Coombs test). The indirect antiglobulin test was positive during Isa-Pd treatment in 68% of the tested patients, and during Isa-Kd treatment in 63% of patients. In patients with a positive indirect antiglobulin test, blood transfusions were administered without evidence of hemolysis. ABO/RhD typing was not affected by SARCLISA treatment.

Before the first SARCLISA infusion, conduct blood type and screen tests on SARCLISA-treated patients. Consider phenotyping prior to starting SARCLISA treatment. If treatment with SARCLISA has already started, inform the blood bank that the patient is receiving SARCLISA and that SARCLISA interference with blood compatibility testing can be resolved using dithiothreitol-treated RBCs. If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given as per local blood bank practices.

Interference with Serum Protein Electrophoresis and Immunofixation Tests

SARCLISA is an IgG kappa monoclonal antibody that can be incidentally detected

on both serum protein electrophoresis and immunofixation assays used for the clinical monitoring of endogenous M-protein. This interference can impact the accuracy of the determination of complete response in some patients with IgG kappa myeloma protein.

Embryo-Fetal Toxicity

Based on the mechanism of action, SARCLISA can cause fetal harm when administered to a pregnant woman. SARCLISA may cause fetal immune cell depletion and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use an effective method of contraception during treatment with SARCLISA and for at least 5 months after the last dose. The combination of SARCLISA with pomalidomide is contraindicated in pregnant women because pomalidomide may cause birth defects and death of the unborn child. Refer to the pomalidomide prescribing information on use during pregnancy.

ADVERSE REACTIONS

In combination with pomalidomide and dexamethasone: The most common adverse reactions ($\geq 20\%$) were upper respiratory tract infection, infusion-related reactions, pneumonia, and diarrhea. The most common hematology laboratory abnormalities ($\geq 80\%$) were decreased hemoglobin, decreased neutrophils, decreased lymphocytes, and decreased platelets.

In combination with carfilzomib and dexamethasone: The most common adverse reactions ($\geq 20\%$) were upper respiratory tract infection, infusion-related reactions, fatigue, hypertension, diarrhea, pneumonia, dyspnea, insomnia, bronchitis, cough, and back pain. The most common hematology laboratory abnormalities ($\geq 80\%$) were decreased hemoglobin, decreased lymphocytes, and decreased platelets.

Serious adverse reactions occurred in 62% of patients receiving Isa-Pd. Serious adverse reactions in $>5\%$ of patients who received Isa-Pd included pneumonia (26%), upper respiratory tract infections (7%), and febrile neutropenia (7%). Fatal adverse reactions occurred in 11% of patients (those that occurred in more than 1% of patients were pneumonia and other infections [3%]).

Serious adverse reactions occurred in 59% of patients receiving Isa-Kd. The most frequent serious adverse reactions in $>5\%$ of patients who received Isa-Kd were pneumonia (25%) and upper respiratory tract infections (9%). Adverse reactions with a fatal outcome during treatment were reported in 3.4% of patients in the Isa-Kd group (those occurring in more than 1% of patients were pneumonia occurring in 1.7% and cardiac failure in 1.1% of patients).

USE IN SPECIAL POPULATIONS

Because of the potential for serious adverse reactions in the breastfed child from isatuximab-irfc administered in combination with Pd, advise lactating women not to breastfeed during treatment with SARCLISA.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

CR=complete response; IMWG=International Myeloma Working Group; IRC=independent response committee; IRT=interactive response technology; IV=intravenous; M-protein=monoclonal protein; mPFS=median progression-free survival; MRD=minimal (or measured) residual disease; NCCN=National Comprehensive Cancer Network; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; PI=protease inhibitor; PR=partial response; sCR=stringent complete response; VGPR=very good partial response.

References: 1. SARCLISA [prescribing information]. Bridgewater, NJ: sanofi-aventis U.S. LLC. 2. Data on file. sanofi-aventis U.S. LLC. 3. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V1.2022. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed August 18, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org.

SANOI GENZYME 

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SARCLISA
(isatuximab-irfc)
Injection for IV use | 500 mg/25 mL, 100 mg/5 mL