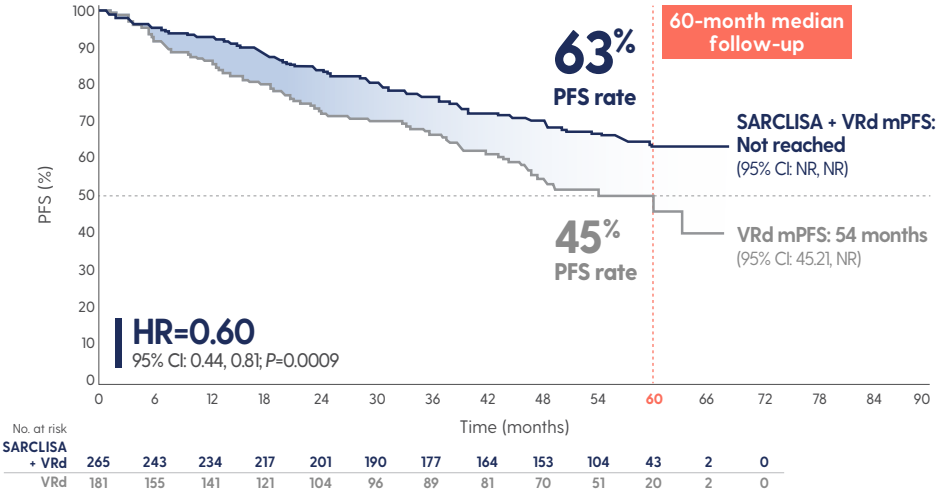
The ***first and only*** FDA-approved anti-CD38 + VRd therapy in patients with NDMM not eligible for transplant[2,3]

IMROZ Regimen: A Benchmark for mPFS vs VRd Alone

Higher 5-year PFS rate with SARCLISA + VRd vs VRd alone: 63% of patients remained alive and progression free at a median follow-up of 60 months[1,2,4,5]



SARCLISA + VRd mPFS: Not reached at 60 months[2]

PFS results were assessed by an IRC based on central laboratory data for M-protein and central radiologic imaging review using the IMWG criteria.[2]

FDA=Food and Drug Administration; IMWG=International Myeloma Working Group; IRC=independent response committee; M-protein=monoclonal protein; mPFS=median progression-free survival; NDMM=newly diagnosed multiple myeloma; NR=not reached; PFS=progression-free survival; VRd=bortezomib, lenalidomide, dexamethasone.

Indication

SARCLISA (isatuximab-irfc) is indicated:

- In combination with bortezomib, lenalidomide, and dexamethasone, for the treatment of adult patients with newly diagnosed multiple myeloma who are not eligible for autologous stem cell transplant (ASCT)

Important Safety Information

CONTRAINDICATIONS

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

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.

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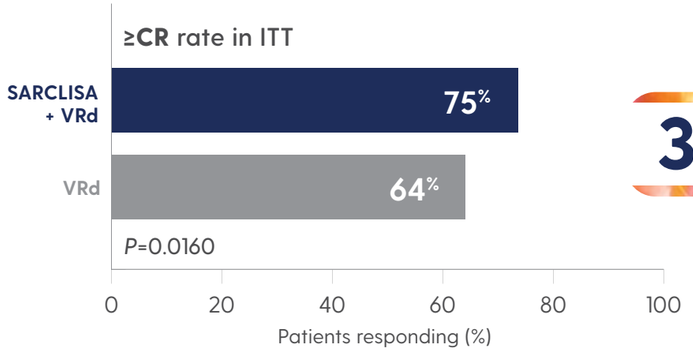
SARCLISA® (isatuximab-irfc)
Injection for IV use | 500 mg/25 mL, 100 mg/5 mL

Challenge your anti-CD38 expectations

For patients with **non-transplant NDMM**

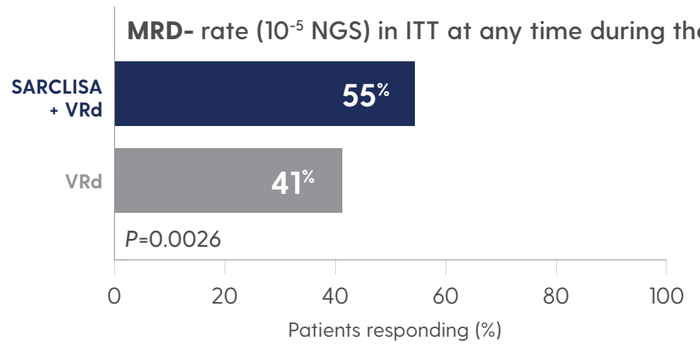
Deep and Durable Responses to Extend Frontline Remissions for Your Patients[6]

Superior rate of complete response with SARCLISA + VRd vs VRd alone[2]



3 OUT OF **4** patients achieved ≥CR with SARCLISA + VRd

Deeper rate of MRD- with SARCLISA + VRd vs VRd alone[2]



*Patients achieved both MRD- and a response of ≥CR.

MRD- and sustained MRD- in ≥VGPR (ITT)[1,2,7]

- 58% of patients receiving SARCLISA + VRd (n=265) achieved MRD- in ≥VGPR (ITT) vs 44% with VRd alone (n=181)
- **81% of patients receiving SARCLISA + VRd who achieved MRD- in ≥VGPR sustained it for ≥1 year** at a median follow-up of 60 months (46.8% with SARCLISA + VRd vs 24.3% with VRd [ITT])

Limitations: Data for MRD- and sustained MRD- in ≥VGPR (ITT) ≥1 year were not multiplicity controlled and results are descriptive. Definitive conclusions cannot be made.

CR=complete response; ITT=intent to treat; MRD-=minimal (or measurable) residual disease negative/negativity; NGS=next-generation sequencing; VGPR=very good partial response.

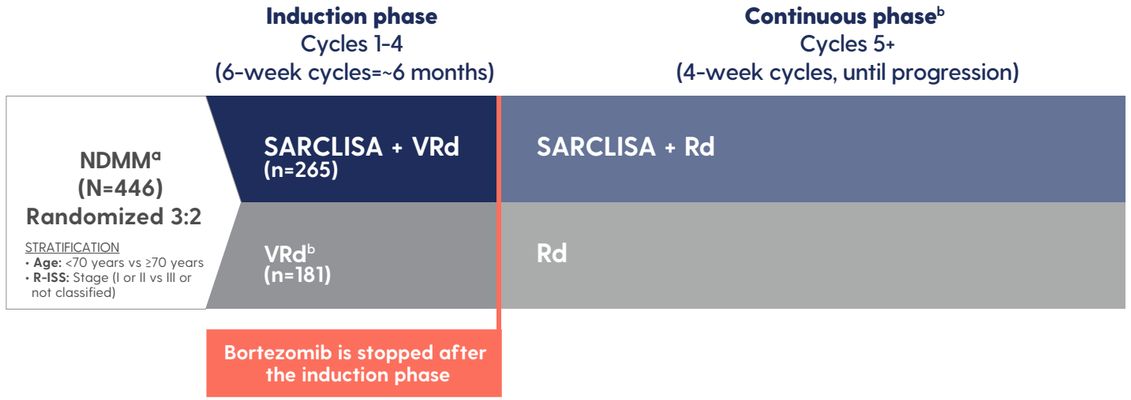
Important Safety Information (cont'd)

Infusion-Related Reactions (cont'd)

In 3 clinical trials, in patients treated with SARCLISA (N=592), infusion-related reactions occurred in 206 patients (35%). Among these 206 patients, 92% experienced infusion-related reactions during the first infusion and 12% after the first cycle.

SARCLISA: The *First and Only* FDA-Approved Anti-CD38 + VRd Therapy in Patients With NDMM Not Eligible for Transplant[2,3]

IMROZ is a large, randomized, open-label, multicenter, phase 3 trial that compared SARCLISA + VRd to VRd alone[1,2]



IMROZ was conducted in 2 phases: an induction phase and a continuous phase. Patients received either SARCLISA 10 mg/kg administered as an IV infusion in combination with VRd or VRd alone in four 42-day cycles. Following the induction phase, bortezomib was discontinued for both treatment arms. SARCLISA was given weekly in the first cycle and every 2 weeks during cycles 2 to 17, and monthly for cycle 18+.[2]

During the induction phase, bortezomib was administered subcutaneously at the dose of 1.3 mg/m^2 on days 1, 4, 8, 11, 22, 25, 29, and 32 of each cycle. Lenalidomide was administered orally at the dose of 25 mg/day from day 1 to 14 and from day 22 to 35 of each cycle. Dexamethasone (IV on the days of SARCLISA infusions, and orally on the other days) 20 mg/day was given on days 1, 2, 4, 5, 8, 9, 11, 12, 15, 22, 23, 25, 26, 29, 30, 32, and 33 of each cycle. In the continuous phase, lenalidomide was administered orally at the dose of 25 mg/day from day 1 to 21 of each cycle. Dexamethasone (IV on the days of SARCLISA infusions, and orally on the other days) 20 mg/day was given on days 1, 8, 15, and 22 of each cycle.[2]

Primary endpoint: PFS[2+]

Key secondary endpoints: ≥CR, MRD- in ≥CR, ≥VGPR, and OS.[1]

Key patient characteristics in the IMROZ trial

In the IMROZ trial (N=446), the median age was 72 years. 4% of patients were <65 years, 68% were between 65 and 74 years, and 28% were ≥75 years. ECOG PS was 0 or 1 for 89% of patients, and >1 for 11% of patients. At study start, patient breakdown by R-ISS was as follows: I in 23%, II in 64%, and III in 10% of patients. Overall, 17% of patients had high-risk chromosomal abnormalities at study entry; del(17p), t(4;14), and t(14;16) were present in 5%, 9%, and 2% of patients, respectively. In addition, 1q21+ was present in 37% of patients.[1,2]

Patient characteristics were similar between the 2 treatment arms.[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.[2]
[a]The interim analysis of PFS was performed after 162 events of disease progression or death had occurred (73% of the planned 222 events for the final analysis).[1]
[b]In the continuous phase, patients randomized to the VRd arm who experienced progressive disease during the Rd treatment period could cross over to receive SARCLISA + Rd.[1]

ECOG PS=Eastern Cooperative Oncology Group performance status; IV=intravenous; OS=overall survival; Rd=lenalidomide and dexamethasone; R-ISS=Revised International Staging System.

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Adverse Reactions for SARCLISA + VRd

Adverse reactions (≥20%) in patients receiving SARCLISA + VRd[2]

	SARCLISA + VRd (n=263)		**VRd** (n=181)	
Adverse reactions	**All grades**	**Grade 3 or 4**	**All grades**	**Grade 3 or 4**
Infections and infestations				
Upper respiratory tract infection[a]	**65%**	**4.6%**	57%[b]	6%
Pneumonia[c]	**45%**[d]	**26%**	31%[e]	19%
COVID-19[f]	**22%**	**0.8%**	17%[g]	1.7%
General disorders and administration site conditions				
Fatigue[h]	**55%**	**11%**	50%	9%
Peripheral edema	**33%**	**0%**	33%	1.1%
IRR	**24%**	**0.4%**	1.1%	0%
Gastrointestinal disorders				
Diarrhea	**55%**	**8%**	49%	8%
Constipation	**36%**	**2.3%**	41%	1.7%
Nervous system disorders				
Peripheral sensory neuropathy	**54%**	**7%**	61%	6%
Eye disorders				
Cataract	**38%**	**16%**	25%	11%
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain[a]	**38%**	**4.2%**	33%	3.3%
Skin and subcutaneous tissue disorders				
Rash[i]	**32%**	**5%**	34%	5%
Psychiatric disorders				
Insomnia	**22%**	**3.8%**	24%	2.2%

- SARCLISA + VRd demonstrated lower rates of peripheral neuropathy than VRd alone: 54% vs 61% (all grades), and comparable rates of grade ≥3 peripheral neuropathy vs VRd alone (7% vs 6%)

The IMROZ trial was conducted from December 2017 to September 26, 2023 (date of the interim analysis), during the COVID-19 pandemic.[1]

[a]Includes other related terms.[2]
[b]Includes 1 patient (0.6%) with fatal upper respiratory tract infection.[2]
[c]Pneumonia includes atypical pneumonia, bronchopulmonary aspergillosis, COVID-19 pneumonia, lower respiratory tract infection, *Pneumocystis jirovecii* pneumonia, pneumonia, pneumonia aspiration, pneumonia bacterial, pneumonia influenzal, pneumonia klebsiella, pneumonia legionella, pneumonia parainfluenzae viral, pneumonia pneumococcal, pneumonia pseudomonal, pneumonia respiratory syncytial viral, pneumonia viral, pulmonary sepsis.[2]
[d]Includes 14 patients (5%) with fatal pneumonia.[2]
[e]Includes 4 patients (2.2%) with fatal pneumonia.[2]
[f]COVID-19 includes COVID-19 infections other than COVID-19 pneumonia.[2]
[g]Includes 2 patients (1.1%) with fatal COVID-19.[2]
[h]Fatigue includes fatigue, asthenia, or malaise.[2]
[i]Rash includes dermatitis, dermatitis acneiform, dermatitis allergic, dermatitis atopic, dermatitis exfoliative generalized, drug eruption, rash, rash erythematous, rash macular, rash maculopapular, rash pruritic, rash pustular, skin exfoliation, skin hyperpigmentation, skin lesion, skin reaction, and toxic skin eruption.[2]

Serious adverse reactions[1,2]

- Serious adverse reactions occurred in 71% of patients receiving SARCLISA + VRd
  - The serious adverse reaction in >5% of patients who received SARCLISA + VRd was pneumonia (30%)
- Fatal adverse reactions (grade 5 TEAEs) were reported in 11% of patients with SARCLISA + VRd (that occurring in more than 1% of patients was pneumonia [5%]) vs 5.5% of patients with VRd alone

Additional Safety Data for SARCLISA + VRd

Hematology laboratory abnormalities in patients receiving SARCLISA + VRd vs VRd alone[2]

	SARCLISA + VRd (n=263)		**VRd** (n=181)	
Laboratory parameter	**All grades**	**Grade 3-4**	**All grades**	**Grade 3-4**
Decreased hemoglobin	**99%**	**17%**	98%	16%
Decreased leukocytes	**97%**	**32%**	88%	17%
Decreased lymphocytes	**95%**	**60%**	92%	53%
Decreased platelets	**95%**	**30%**	85%	28%
Decreased neutrophils	**87%**	**54%**	80%	37%

The denominator used to calculate the rate is based on the number of patients with a baseline value and at least one post-baseline value.

Monitor patients for signs and symptoms of infection prior to and during treatment with SARCLISA and treat appropriately. Administer prophylactic antimicrobials according to guidelines.

Permanent discontinuations due to adverse events were similar across arms: 23% for SARCLISA + VRd and 26% for VRd alone.[1,2]

IRRs[2]

- Across 3 clinical trials, IRRs occurred in 35% of patients receiving SARCLISA (n=206/592). Among these patients, 92% experienced IRRs during the first infusion and 12% experienced them after the first cycle
- Grade 1 IRRs were reported in 6% of patients receiving SARCLISA, grade 2 in 28%, and grade 3 or 4 in 1.2% across the 3 clinical trials
- IRRs may require interruption, management, and/or discontinuation of the infusion

Second primary malignancies[2]

- Monitor patients for the development of second primary malignancies
- In the IMROZ trial, at a median follow-up time of 60 months, second primary malignancies occurred in 16% of patients in the SARCLISA + VRd arm and in 9% of patients in the VRd arm

Median treatment duration[2]

The median treatment duration was 53 months (range: 0.5 to 69) with SARCLISA + VRd (n=263) vs 31 months (range: 0.6 to 67) with VRd alone (n=181).

IRR=infusion-related reaction; TEAE=treatment-emergent adverse event.

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CONTRAINDICATIONS

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

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.

In 3 clinical trials, in patients treated with SARCLISA (N=592), infusion-related reactions occurred in 206 patients (35%). Among these 206 patients, 92% experienced infusion-related reactions during the first infusion and 12% after the first cycle.

The most common symptoms (≥5%) of an infusion-related reaction included dyspnea and cough. Grade 1 infusion-related reactions were reported in 6% of patients, grade 2 in 28%, and grade 3 or 4 in 1.2%. Anaphylactic reactions occurred in less than 1% of patients. The total incidence of SARCLISA infusion interruptions was less than 1% and the incidence of patients with at least one SARCLISA infusion interruption due to infusion-related reactions was 26%. The median time to first SARCLISA infusion interruption was 61 minutes (range 4 to 240 minutes). SARCLISA was discontinued in 1% of patients due to infusion-related reactions. To decrease the risk and severity of IRRs, premedicate patients prior to SARCLISA infusion with acetaminophen, H_2 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.

Infections

SARCLISA can cause severe, life-threatening, or fatal infections. In patients who received SARCLISA at the recommended dose in 3 clinical trials (N=592), serious infections, including opportunistic infections, occurred in 46%, grade 3 or 4 infections occurred in 43%, and fatal infections occurred in 4.7%. The most common serious infection reported was pneumonia (32%).

Monitor patients for signs and symptoms of infection prior to and during treatment with SARCLISA and treat appropriately. Administer prophylactic antimicrobials according to guidelines.

Neutropenia

SARCLISA may cause neutropenia.

In 3 clinical trials, in patients treated with SARCLISA (N=592), neutropenia based on laboratory values occurred in 81%, with grade 3 or 4 occurring in 52%. Neutropenic infections occurred in 12% of patients, with grade 3 or 4 in 4.9%, and febrile neutropenia in 4%.

Monitor complete blood cell counts periodically during treatment. If needed, use antibacterial 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 x 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, during treatment and post-treatment, is increased in patients treated with SARCLISA-containing regimens. In 3 clinical trials, in patients treated with SARCLISA (N=592), second primary malignancies occurred in 71 patients (12%).

In IMROZ study, at a median follow-up time of 60 months, second primary malignancies occurred in 16% of patients treated with SARCLISA, bortezomib, lenalidomide, and dexamethasone (Isa-VRd) and in 9% of patients treated with VRd.

The most common (≥1%) second primary malignancies in 3 clinical trials (N=592) included skin cancers (7% with SARCLISA-containing regimens and 3.1% with comparative regimens) and solid tumors other than skin cancer (4.6% with SARCLISA-containing regimens and 2.9% with comparative regimens). Patients with non-melanoma skin cancer continued treatment after resection of the skin cancer, except 2 patients in the Isa-VRd arm and 1 patient in the VRd arm of the IMROZ study. 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). This interference with the indirect Coombs test may persist for approximately 6 months after the last infusion of SARCLISA. 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 5 months after the last dose. The combination of SARCLISA with lenalidomide is contraindicated in pregnant women because lenalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide prescribing information on use during pregnancy.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) in patients receiving Isa-VRd were upper respiratory tract infections, diarrhea, fatigue, peripheral sensory neuropathy, pneumonia, musculoskeletal pain, cataract, constipation, peripheral edema, rash, infusion-related reaction, insomnia, and COVID-19. The most common hematologic laboratory abnormalities (≥80%) in patients receiving Isa-VRd were decreased hemoglobin, decreased leukocytes, decreased lymphocytes, decreased platelets, and decreased neutrophils.

Serious adverse reactions occurred in 71% of patients receiving Isa-VRd. The serious adverse reaction in >5% of patients who received Isa-VRd was pneumonia (30%). Fatal adverse reactions occurred in 11% of patients with Isa-VRd (those occurring in more than 1% of patients were pneumonia [5%]).

USE IN SPECIAL POPULATIONS

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

Please see accompanying full Prescribing Information.

References: 1. Facon T, Dimopoulos MA, Leleu XP, et al; IMROZ Study Group. Isatuximab, bortezomib, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*. Published online June 3, 2024. doi:10.1056/NEJMoa2400712 **2.** SARCLISA. Prescribing information. sanofi-aventis U.S. LLC; 2024. **3.** Darzalex. Prescribing information. Janssen Pharmaceutical Companies; 2024. **4.** Kumar SK, Jacobus SJ, Cohen AD, et al. Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intent for immediate autologous stem-cell transplant (E1A11): a multicenter, open label, phase 3, randomized, controlled trial. *Lancet Oncol*. 2020;21(10):1317-1330. **5.** Durie BGM, Hoering A, Abidi MH, et al. Bortezomib with lenalidomide and dexamethasone versus lenalidomide and dexamethasone alone in patients with newly diagnosed myeloma without intent for immediate autologous stem-cell transplant (SWOG S0777): a randomized, open-label, phase 3 trial. *Lancet*. 2017;389(10068):519-527. **6.** Phases of the disease. International Myeloma Foundation. Updated July 20, 2021. Accessed August 5, 2024. https://www.myeloma.org/phases-disease **7.** Protocol to: Facon T, Dimopoulos MA, Leleu XP, et al; IMROZ Study Group. Isatuximab, bortezomib, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*. Published online June 3, 2024. doi:10.1056/NEJMoa2400712 **8.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.1.2025. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed September 24, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org.

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SARCLISA + VRd demonstrated superior PFS vs VRd alone

*At a median follow-up of 60 months, estimated PFS rate with SARCLISA + VRd was 63% vs 45% with VRd alone. mPFS NR with SARCLISA + VRd (n=265) vs 54 months with VRd alone (n=181); HR=0.60 (95% CI: 0.44, 0.81; *P*=0.0009).[1,2]

NCCN

CATEGORY 1 PREFERRED

National Comprehensive Cancer Network® (NCCN®) recommends isatuximab-irfc (SARCLISA), bortezomib, lenalidomide, and dexamethasone as a NCCN Category 1, Preferred Regimen for the treatment of patients with newly diagnosed multiple myeloma who are non-transplant candidates (<80 years old who are not frail)[8]

Scan to learn more about SARCLISA

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

NCCN=National Comprehensive Cancer Network® (NCCN®).

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