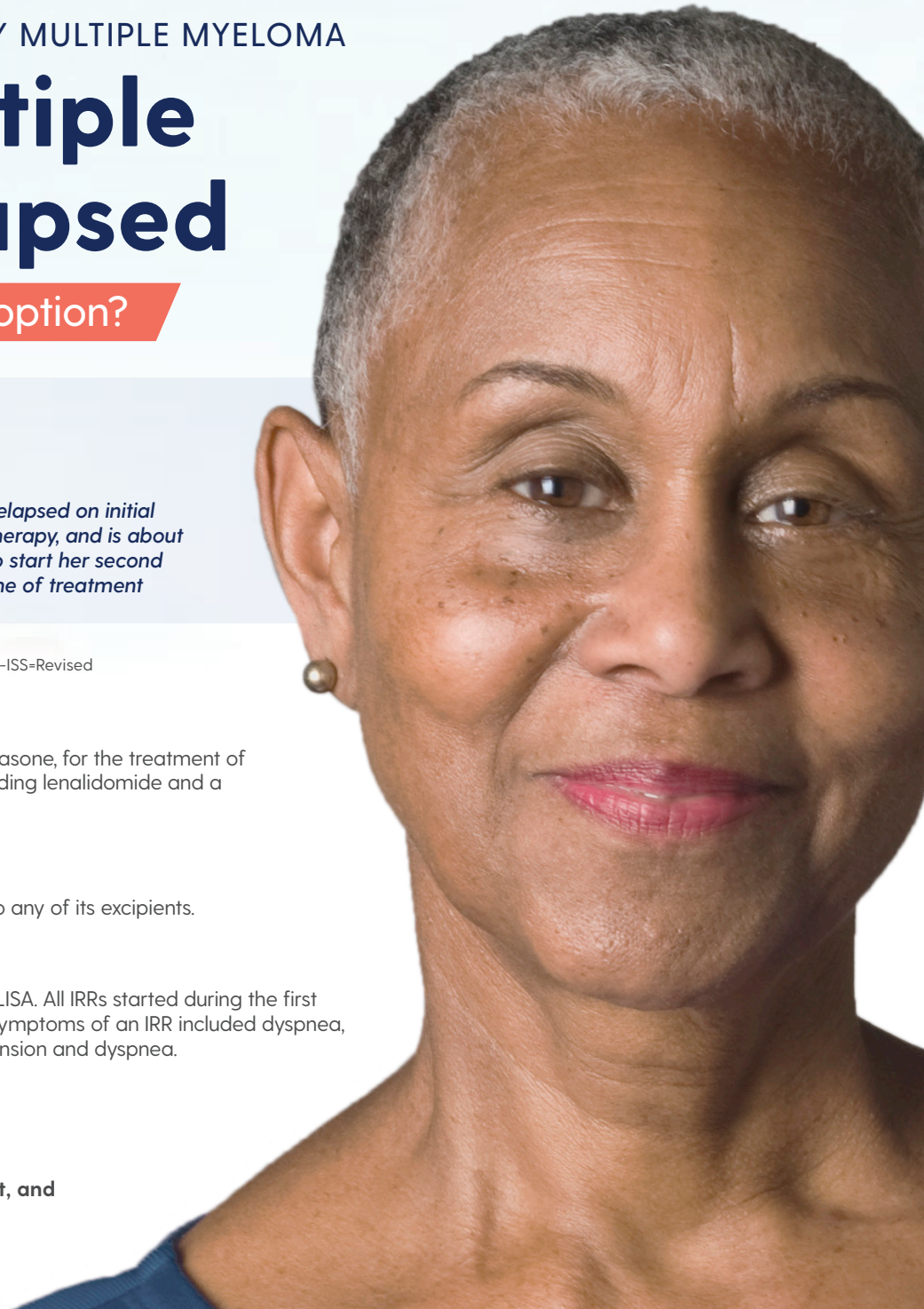
A PATIENT CASE STUDY FOR RELAPSED REFRACTORY MULTIPLE MYELOMA

Your Patient's Multiple Myeloma Has Relapsed

Could SARCLISA + Pd be the right treatment option?



Meet Lynn, a 68-year-old black female

Retired, takes care of her grandchildren during the day

- *Diagnosed with multiple myeloma 3 years ago*
- *R-ISS stage I at diagnosis*
- *ECOG PS 0*
- *Relapsed on initial therapy, and is about to start her second line of treatment*

Not an actual patient.
ECOG PS=Eastern Cooperative Oncology Group performance status; Pd=pomalidomide and dexamethasone; R-ISS=Revised International Staging System.

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 two prior therapies including lenalidomide and a proteasome inhibitor.

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
Infusion-related reactions (IRRs) have been observed in 39% of patients treated with SARCLISA. All IRRs started during the first SARCLISA infusion and resolved on the same day in 98% of the cases. The most common symptoms of an IRR included dyspnea, cough, chills, and nausea. The most common severe signs and symptoms included hypertension and dyspnea.

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

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

Lynn's Treatment History

Age

68 years old

Ethnicity

Black

Comorbidities

Asthma (moderate) · Hypertension (uncontrolled) · Osteoarthritis in knees

Initial presentation/diagnosis

- Presented to PCP for fatigue and routine blood work
- High-risk cytogenetics: t(4;14)
- Transplant eligible
- R-ISS stage I

1st line of treatment

- **4 cycles of VRd followed by ASCT and lenalidomide maintenance**
- Demonstrated CR for 3 years

Relapse

- **Relapsed while on lenalidomide maintenance**
- New lesion in humerus
- Post-MI

Time since first line of treatment

3 years

ASCT=autologous stem cell transplant; CR=complete response; MI=myocardial infarction; PCP=primary care provider; VRd=bortezomib, lenalidomide, dexamethasone.

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SARCLISA + Pd Was Studied in Patients Like Lynn

The phase 3 ICARIA-MM trial included these select patient characteristics[1,2]

	SARCLISA + Pd (n=154)	Pd (n=153)
Age		
<65 y	35%	46%
✓ **65-74 y**	**44%**	35%
≥75 y	21%	19%
R-ISS stage at study entry		
✓ **I**	**25%**	20%
II	64%	64%
III	10%	16%
Cytogenetic risk		
✓ **High[a]**	**16%**	24%
Standard	67%	51%
Missing	18%	26%
History of COPD or asthma at study entry		
✓ **Yes**	**10%**	11%
ECOG PS		
✓ **0 or 1**	**90%**	90%
2	10%	11%
Patient refractory to		
✓ **Lenalidomide**	**94%**	92%
Prior ASCT		
✓ **Yes**	**54%**	59%

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Category 1 recommendation for isatuximab-irfc (SARCLISA)

Isatuximab-irfc (SARCLISA) is the only mAb in combination with pomalidomide and dexamethasone included as an NCCN Guidelines® Category 1 recommended regimen for previously treated multiple myeloma.[3]

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.

Lynn would be eligible for treatment with SARCLISA + Pd[1,2]

PATIENT CHARACTERISTICS: The median patient age was 67 years (range, 36 to 86), and 20% of patients were ≥75 years of age. Ten percent of patients entered the study with a history of COPD or asthma. The proportion of patients with renal impairment (creatinine clearance <60 mL/min/1.73 m^2) was 34%. The ISS stage at study entry was I in 37%, II in 36%, and III in 25% of patients. The median number of prior lines of therapy was 3 (range, 2 to 11). All patients received a prior PI, all patients received prior lenalidomide, and 56% of patients received prior stem cell transplantation; the majority of patients (93%) were refractory to lenalidomide, 76% to a PI, and 73% to both an immunomodulator and a PI.[4]

[a]Of the patients who had high-risk chromosomal abnormalities at study entry, del(17p), t(4;14), and t(14;16) were present in 12.1%, 8.5%, and 1.6% of patients, respectively.[2]

COPD=chronic obstructive pulmonary disease; ISS=International Staging System; mAb=monoclonal antibody; NCCN=National Comprehensive Cancer Network; PI=proteasome inhibitor.

Important Safety Information (cont'd)

Infusion-Related Reactions (cont'd)

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 1 or 2 reactions, interrupt SARCLISA infusion and provide appropriate medical support. If symptoms improve, restart SARCLISA infusion at half of the initial rate, with supportive care as needed, and closely monitor patients. If symptoms do not recur after 30 minutes, the infusion rate may be increased

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Important Safety Information (cont'd)

Infusion-Related Reactions (cont'd)
to the initial rate, and then increased incrementally. In case symptoms do not improve or recur after interruption, permanently discontinue SARCLISA and institute appropriate management. Permanently discontinue SARCLISA if a grade 3 or higher IRR occurs and institute appropriate emergency medical management.

Neutropenia
SARCLISA may cause neutropenia. Neutropenia (reported as laboratory abnormality) occurred in 96% of patients and grade 3-4 neutropenia occurred in 85% of patients treated with SARCLISA, pomalidomide, and dexamethasone (Isa-Pd). Febrile neutropenia occurred in 12% of patients and neutropenic infections, defined as infection with concurrent grade ≥3 neutropenia, occurred in 25% of patients treated with Isa-Pd. The most frequent neutropenic infections included those of upper respiratory tract (10%), lower respiratory tract (9%), and urinary tract (3%).

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 1.0×10^9/L, and provide supportive care with growth factors, according to institutional guidelines. No dose reductions of SARCLISA are recommended.

Second Primary Malignancies
Second primary malignancies were reported in 3.9% of patients in the SARCLISA, pomalidomide, and dexamethasone (Isa-Pd) arm and in 0.7% of patients in the pomalidomide and dexamethasone (Pd) arm, and consisted of skin squamous cell carcinoma (2.6% of patients in the Isa-Pd arm and in 0.7% of patients in the Pd arm), breast angiosarcoma (0.7% of patients in the Isa-Pd arm), and myelodysplastic syndrome (0.7% of patients in the Isa-Pd arm). With the exception of the patient with myelodysplastic syndrome, patients were able to continue SARCLISA treatment. 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). In ICARIA-multiple myeloma (MM), the indirect antiglobulin test was positive during SARCLISA treatment in 67.7% of the tested 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 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
The most common adverse reactions (≥20%) were neutropenia (laboratory abnormality, 96% Isa-Pd vs 92% Pd), infusion-related reactions (38% Isa-Pd vs 0% Pd), pneumonia (31% Isa-Pd vs 23% Pd), upper respiratory tract infection (57% Isa-Pd vs 42% Pd), and diarrhea (26% with Isa-Pd vs 19% Pd). Serious adverse reactions occurred in 62% of patients receiving SARCLISA. 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%]).

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 Important Safety Information throughout, and accompanying full Prescribing Information.

References: 1. Attal M, Richardson PG, Rajkumar SV, et al; on behalf of the ICARIA-MM study group. Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study. *Lancet*. 2019;394(10214):2096-2107. **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 V.4.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed June 16, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. **4.** SARCLISA [prescribing information]. Bridgewater, NJ: sanofi-aventis U.S. LLC.

SANOFI GENZYME

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