In the treatment of relapsed and/or refractory multiple myeloma

THIS IS WHAT ***EFFICACY LOOKS LIKE***

The addition of SARCLISA to Kd or Pd extended mPFS compared with Kd or Pd (HR=0.531 and 0.596, respectively)[1]

At a median follow-up of 44 months, SARCLISA + Kd demonstrated[2]:

UNPRECEDENTED mPFS OF 3 YEARS

in a pivotal trial that includes lenalidomide-refractory patients[1-23]

IKEMA: SARCLISA + Kd vs Kd[2]

mPFS 35.7 mo
vs 19.2 mo with Kd

HR=0.58
(95.4% CI: 0.42, 0.79)

86.6% ORR
vs 83.7% with Kd

33.5% MRD-
vs 15.4% with Kd

44.1% CR
vs 28.5% with Kd

26.3% MRD- and CR
vs 12.2% with Kd

- Prespecified analysis at median follow-up of 44 months: 27.4% of patients in the SARCLISA + Kd arm vs 8.9% of patients in the Kd arm were still on treatment[2]
- Safety profiles in both arms remain consistent with prior IKEMA findings; serious TEAEs were reported in 70.1% of patients on SARCLISA + Kd vs 59.8% on Kd[2]
- The most common, non-haematologic TEAEs in the SARCLISA + Kd arm were: infusion reactions (45.8%), diarrhoea (39.5%), hypertension (37.9%), upper respiratory tract infection (37.3%), and fatigue (31.6%)[2]
- At an interim analysis follow-up of 21 months, mPFS was NR with SARCLISA + Kd vs 19.2 months with Kd (HR=0.531 [99% CI: 0.318, 0.889; *P*=0.0013])[1]

IKEMA trial: a randomised, open-label, phase 3 study evaluating the efficacy and safety of SARCLISA + Kd vs Kd in 302 patients with relapsed or refractory multiple myeloma who had received 1 to 3 prior lines of therapy. PFS was the primary endpoint; secondary endpoints included ORR, ≥VGPR, CR, MRD-, and OS. MRD- rates at 10^{-5} sensitivity shown.[1-2,24]

As the ORR (major secondary endpoint) demonstrated a nominal *P* value, the *P* values of subsequent key secondary endpoints are provided for descriptive purposes only.[24]

CR=complete response; Kd=carfilzomib and dexamethasone; mPFS=median progression-free survival; MRD-=minimal residual disease negative/negativity; NR=not reached; ORR=overall response rate; OS=overall survival; Pd=pomalidomide and dexamethasone; PFS=progression-free survival; TEAE=treatment-emergent adverse event; VGPR=very good partial response.

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▼ SARCLISA® (isatuximab)

SARCLISA® (isatuximab) – Abbreviated Prescribing Information

Name and Presentation: SARCLISA 20 mg/mL concentrate for solution for infusion. Each vial contains 100 mg of isatuximab in 5 mL of concentrate (100 mg/5 mL) or 500 mg of isatuximab in 25 mL of concentrate (500 mg/25 mL). Isatuximab is an immunoglobulin G1 (IgG1) monoclonal antibody (mAb).

Therapeutic indications: In combination with pomalidomide and dexamethasone, for the treatment of adult patients with relapsed and refractory multiple myeloma (MM) who have received at least two prior therapies including lenalidomide and a proteasome inhibitor (PI) and have demonstrated disease progression on the last therapy. In combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Dosage and administration: SARCLISA should be administered by a healthcare professional, in an environment where resuscitation facilities are available. Premedication should be used 15-60 minutes prior to SARCLISA infusion with the following medicinal products to reduce the risk and severity of infusion reactions: Dexamethasone 40 mg (when administered in combination with isatuximab and pomalidomide) or 20 mg (when administered in combination with isatuximab and carfilzomib) oral or intravenous, 20 mg for patients ≥75 years of age, Acetaminophen, Diphenhydramine. The recommended dose of SARCLISA is 10 mg/kg body weight administered as an intravenous infusion in combination with pomalidomide and dexamethasone or in combination with carfilzomib and dexamethasone (isatuximab regimen). Dosing schedule: cycle 1: days 1, 8, 15 and 22 (weekly), cycle 2 and beyond: days 1, 15 (every 2 weeks). Each treatment cycle consists of a 28-day period.

Method of administration: SARCLISA is for intravenous use. For details on preparation and infusion rate see full SmPC.

Contraindications: Hypersensitivity to the active substance or to any of the excipients. See full SmPC for full list of excipients.

Warnings and precautions: Infusion reactions, mostly mild or moderate, were observed in 38.2% of patients treated with SARCLISA in ICARIA, and in 45.8% in IKEMA but resolved on the same day in 98% of infusions. Vital signs should be frequently monitored during the entire infusion and when required infusion should be interrupted or permanently discontinued in case symptoms that do not improve to grade ≤1 after infusion interruption. Serious infusion reactions including severe anaphylactic reactions have also been observed after SARCLISA administration. Most of the grade 3-4 neutropenia have been reported as laboratory abnormalities. Neutropenic complications have been observed in 1/3 of patients treated with SARCLISA. A higher incidence of infections including grade ≥3 infections occurred with SARCLISA. Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) can be considered during treatment. Patients receiving SARCLISA should be closely monitored for signs of infection. Physicians should carefully evaluate patients before and during treatment as per International Myeloma Working Group (IMWG) guidelines for occurrence of second primary malignancies (SPM) and treatment should be initiated as indicated. Patients should be monitored closely and appropriate precautions taken for tumor lysis syndrome. Isatuximab binds to CD38 on red blood cells (RBCs) and may result in a false positive indirect antiglobulin test (indirect Coombs test). There is currently no available information with regards to how long the interference may persist. Based on the half-life of isatuximab, it may persist for approximately 6 months after the last infusion of SARCLISA. Patient should have blood type and screen tests performed prior to the first infusion of Isatuximab and should be monitored for theoretical risk of haemolysis. For details in tests interference see full SmPC.

Drug interactions: Isatuximab has no impact on the pharmacokinetics of pomalidomide and vice versa. Isatuximab may interfere with serological testing and with Serum Protein Electrophoresis and Immunofixation assays. In patients with persistent very good partial response, where isatuximab interference is suspected, consider using a validated isatuximab-specific IFE assay to distinguish isatuximab from any remaining endogenous M-protein in the patient's serum, to facilitate determination of complete response.

Fertility, pregnancy and lactation: Women of childbearing potential treated with isatuximab should use effective contraception during treatment and for 5 months after cessation of treatment. The use of isatuximab in pregnant women is not recommended since there are no available data.

Undesirable effects: Observed in ICARIA: *Infections/infestations:* very common: pneumonia, upper respiratory tract infection, bronchitis: common: Herpes zoster. *Neoplasms benign, malignant and unspecified:* common: skin cancer, solid tumour (non-skin cancer): uncommon: haematology malignancy. Blood/lymphatic system disorders: very common: neutropenia, febrile neutropenia. *Metabolism and nutrition disorders:* common: decreased appetite. *Cardiac disorders:* common: atrial fibrillation. *Respiratory, thoracic and mediastinal disorders:* very common: dyspnoea. *Gastrointestinal disorders:* very common: diarrhoea, nausea, vomiting. *Investigations:* common: weight decreased. *Injury, poisoning and procedural complications:* very common: infusion reaction. *Immune system disorders:* uncommon: anaphylactic reaction. Observed in IKEMA: *Infections/infestations:* very common: pneumonia, upper respiratory tract infection, bronchitis: common: Herpes Zoster. *Vascular disorder:* very common: hypertension. *Neoplasms benign, malignant and unspecified:* common: Skin cancers and solid tumors other than skin cancers. *Blood/lymphatic system disorders:* common: neutropenia. *Respiratory, thoracic and mediastinal disorders:* very common: dyspnoea and cough. *Gastrointestinal disorders:* very common: diarrhoea and vomiting. *General disorders and administration site conditions:* very common: Fatigue. *Injury, poisoning and procedural complications:* very common: infusion reaction. *Immune system disorders:* uncommon: anaphylactic reaction.

Pharmacotherapeutic group: Antineoplastic agents, monoclonal antibodies, ATC code: L01FC02.

List of excipients: Sucrose, Histidine hydrochloride monohydrate, Histidine, Polysorbate 80 and Water for injections.

Legal classification: Prescription Only Medicine.

Marketing authorization holder: Sanofi Winthrop Industrie, 82, avenue Raspail, 94250 Gentilly, France.

Date of last revised: April 2023.

Abbreviated Prescribing Information based on the EU SmPC as of March 2023.

Before prescribing always refer to your full local prescribing information as this information may vary from country to country

Review the Summary of Product Characteristics.

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References: 1. SARCLISA [summary of product characteristics]. sanofi-aventis groupe: Paris, France; 2023. **2.** Martin T, Dimopoulos MA, Mikhael J, et al. Isatuximab, carfilzomib, and dexamethasone in patients with relapsed multiple myeloma: updated results from IKEMA, a randomized phase 3 study. *Blood Cancer J*. 2023;13(1):72. doi:10.1038/s41408-023-00797-8 **3.** Hernández-Rivas JÁ, Ríos-Tamayo R, Encinas C, Alonso R, Lahuerta JJ. The changing landscape of relapsed and/or refractory multiple myeloma (MM): fundamentals and controversies. *Biomark Res*. 2022;10(1):1-23. **4.** Spicka I, Ocio EM, Oakervee HE, et al. Randomized phase III study (ADMYRE) of plitidepsin in combination with dexamethasone vs. dexamethasone alone in patients with relapsed/refractory multiple myeloma. *Ann Hematol*. 2019;98(9):2139-2150. **5.** Usmani SZ, Quach H, Mateos MV, et al. Carfilzomib, dexamethasone, and daratumumab versus carfilzomib and dexamethasone for patients with relapsed or refractory multiple myeloma (CANDOR): updated outcomes from a randomised, multicentre, open-label, phase 3 study. *Lancet Oncol*. 2022;23(1):65-76. **6.** Schjesvold FH, Dimopoulos MA, Delimpasi S, et al. Melflufen or pomalidomide plus dexamethasone for patients with multiple myeloma refractory to lenalidomide (OCEAN): a randomised, head-to-head, open-label, phase 3 study. *Lancet Haematol*. 2022;9(2):e98-e110. doi:10.1016/S2352-3026(21)00381-1 **7.** Du J, Fang B, Li J, et al. A study of carfilzomib and dexamethasone in patients with relapsed and refractory multiple myeloma in China. *Int J Hematol*. 2021;113(3):422-429. **8.** Terpos E, Gobbi M, Potamianou A, Lahaye M, Couturier C, Cavo M. Retreatment and prolonged therapy with subcutaneous bortezomib in patients with relapsed multiple myeloma: a randomized, controlled, phase III study. *Eur J Haematol*. 2018;100(1):10-19. **9.** Dimopoulos M, Siegel DS, Lonial S, et al. Vorinostat or placebo in combination with bortezomib in patients with multiple myeloma (VANTAGE 088): a multicentre, randomised, double-blind study. *Lancet Oncol*. 2013;14(11):1129-1140. **10.** Dimopoulos MA, Palumbo A, Corradini P, et al. Safety and efficacy of pomalidomide plus low-dose dexamethasone in STRATUS (MM-010): a phase 3b study in refractory multiple myeloma. *Blood*. 2016;128(4):497-503. **11.** Usmani SZ, Nahi H, Legiec W, et al. Final analysis of the phase III non-inferiority COLUMBA study of subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma. *Haematologica*. 2022;107(10):2408-2417. **12.** Study to evaluate the safety and efficacy of pomalidomide monotherapy in subjects with refractory or relapsed refractory multiple myeloma. ClinicalTrials.gov identifier: NCT01324947. Updated November 19, 2019. Accessed June 16, 2022. https://clinicaltrials.gov/ct2/show/NCT01324947 **13.** Janssen Research & Development. *Final synoptic clinical study report: report of long-term extension. A phase 3, randomized, open-label study of subcutaneous and intravenous VELCADE® in combination with dexamethasone in Chinese subjects with relapsed or refractory multiple myeloma*. Protocol 26866138MMY3037; Phase 3 JNJ-26866138-AAA (bortezomib). Published April 23, 2019. Accessed June 6, 2022. **14.** Hájek R, Masszi T, Petrucci MT, et al. A randomized phase III study of carfilzomib vs low-dose corticosteroids with optional cyclophosphamide in relapsed and refractory multiple myeloma (FOCUS). *Leukemia*. 2017;31(1):107-114. **15.** Kropff M, Baylon HG, Hillengass J, et al. Thalidomide versus dexamethasone for the treatment of relapsed and/or refractory multiple myeloma: results from OPTIMUM, a randomized trial. *Haematologica*. 2012;97(5):784-791. **16.** Hjorth M, Hjertner Ø, Knudsen LM, et al. Thalidomide and dexamethasone vs. bortezomib and dexamethasone for melphalan refractory myeloma: a randomized study. *Eur J Haematol*. 2012;88(6):485-496. **17.** Usmani SZ, Nahi H, Plesner T, et al. Daratumumab monotherapy in patients with heavily pretreated relapsed or refractory multiple myeloma: final results from the phase 2 GEN501 and SIRIUS trials. *Lancet Haematol*. 2020;7(6):e447-e455. doi:10.1016/S2352-3026(20)30081-8 **18.** Lonial S, Lee HC, Badros A, et al. Belantamab mafodotin for relapsed or refractory multiple myeloma (DREAMM-2): a two-arm, randomised, open-label, phase 2 study. *Lancet Oncol*. 2020;21(2):207-221. **19.** Bahlis NJ, Dimopoulos MA, White DJ, et al. Daratumumab plus lenalidomide and dexamethasone in relapsed/refractory multiple myeloma: extended follow-up of POLLUX, a randomized, open-label, phase 3 study. *Leukemia*. 2020;34(7):1875-1884. **20.** GSK provides update on DREAMM-3 phase III trial for Blenrep in relapsed/refractory multiple myeloma. Press release. London, United Kingdom: GSK; November 7, 2022. https://www.gsk.com/en-gb/media/press-releases/gsk-provides-update-on-dreamm-3-phase-iii-trial-for-blenrep/ **21.** Fu W, Li W, Hu J, et al. Daratumumab, bortezomib, and dexamethasone versus bortezomib and dexamethasone in Chinese patients with relapsed or refractory multiple myeloma: updated analysis of LEPUS. *Clin Lymphoma Myeloma Leuk*. 2023;23(1):e51-e58. doi:10.1016/j.clml.2022.10.007 **22.** Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in relapsed or refractory multiple myeloma. *N Engl J Med*. 2022;387(6):495-505. **23.** Rodriguez-Otero P, Ailawadhi S, Arnulf B, et al. Ide-cel or standard regimens in relapsed and refractory multiple myeloma. *N Engl J Med*. 2023;388(11):1002-1014. **24.** Moreau P, Dimopoulos MA, Mikhael J, et al; IKEMA study group. Isatuximab, carfilzomib, and dexamethasone in relapsed multiple myeloma (IKEMA): a multicentre, open-label, randomised phase 3 trial. *Lancet*. 2021;397(10292):2361-2371.

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