

Sarclisa[®] (isatuximab) combination therapy demonstrated superior progression free survival and clinically meaningful depth of response in patients with relapsed multiple myeloma

- * Sarclisa added to carfilzomib and dexamethasone (Sarclisa combination) reduced risk of disease progression or death by 47% versus standard of care carfilzomib and dexamethasone (Kd) alone
- * Sarclisa combination therapy delivered considerable depth of response, with undetectable levels of multiple myeloma (MM) in nearly 30% of patients with relapsed MM (MRD-negative 10⁻⁵ sensitivity)
- * Results from first planned interim analysis of the Phase 3 IKEMA trial selected as late-breaking presentation at EHA25 Virtual Congress

PARIS – June 2, 2020 – Sarclisa[®] (isatuximab) added to carfilzomib and dexamethasone (Sarclisa combination therapy) reduced the risk of disease progression or death by 47% (hazard ratio 0.531, 99% CI 0.318-0.889, p=0.0007, n=179) compared to standard of care carfilzomib and dexamethasone (Kd) in patients (n=123) with relapsed multiple myeloma (MM). Sarclisa combination therapy compared to Kd alone showed a treatment benefit consistent across multiple subgroups.

These results from the Phase 3 IKEMA trial follow the topline announcement on May 12, 2020 that Sarclisa combination therapy met the trial primary endpoint at the pre-planned interim analysis. Interim results will be presented during the late-breaking session of the European Hematology Association (EHA) Virtual Congress (EHA25) on June 14, 2020 and will form the basis for global regulatory submissions later this year.

“In the Phase 3 IKEMA trial, the addition of Sarclisa to carfilzomib and dexamethasone reduced the risk of disease progression or death by 47 percent compared to treatment with carfilzomib and dexamethasone alone,” said Philippe Moreau, M.D., Department of Hematology, University Hospital of Nantes, France. *“These results suggest the potential of Sarclisa to become a new standard of care in the relapsed multiple myeloma setting.”*

While median progression free survival (PFS), defined as time to disease progression or death, for Kd was 19.15 months, the median PFS for patients receiving Sarclisa combination therapy had not been reached at the time of the pre-planned interim analysis. The safety and tolerability of Sarclisa observed in this trial was consistent with the observed safety profile of Sarclisa in other clinical trials, with no new safety signals observed.

“This is the second Phase 3 trial to demonstrate superior results with Sarclisa combination therapy over a standard of care regimen, adding to the growing body of evidence that our anti-CD38 monoclonal antibody has the potential to make a meaningful difference for patients,” said John Reed, M.D., Ph.D., Global Head of Research and Development at Sanofi. *“We believe Sarclisa has the potential to become the anti-CD38 of choice for the treatment of multiple myeloma. We look forward to seeing the results from future clinical trials to understand the impact of Sarclisa in earlier stages of disease.”*

Depth of Disease Response with Sarclisa Combination Therapy

Secondary endpoints of the IKEMA trial examined the consistency and depth of response for Sarclisa combination therapy compared to Kd, including overall response rate (ORR), complete response (CR), very good partial response (VGPR) and minimal residual disease (MRD)-negative response. There was no statistically significant difference in ORR, which remained similar for each arm at 86.6% for the Sarclisa combination versus 82.9% for Kd ($p=0.1930$). The rate of CR was 39.7% in the Sarclisa combination arm and 27.6% in the Kd arm. The rate of VGPR was 72.6% for patients receiving Sarclisa combination therapy and 56.1% for patients receiving Kd. MRD-negative complete response was observed in 29.6% of patients in the Sarclisa combination arm versus 13% of patients in the Kd arm, indicating that nearly 30% of patients treated with Sarclisa combination therapy achieved undetectable levels of MM at 10^{-5} sensitivity as measured by next generation sequencing (NGS). At the time of the interim analysis, overall survival (OS) data were still immature.

In this trial, treatment emergent adverse events (TEAEs) of Grade ≥ 3 were observed in 76.8% of patients treated with Sarclisa combination therapy versus 67.2% of patients treated with Kd. Treatment-emergent serious adverse events (SAEs) and fatal TEAEs were similar in the Sarclisa combination therapy arm versus the Kd arm, reporting 59.3% versus 57.4% and 3.4% versus 3.3%, respectively. Infusion reactions were reported in 45.8% (0.6% Grade 3-4) of patients treated with Sarclisa combination therapy versus 3.3% (0% Grade 3-4) of patients treated with Kd. Respiratory infections of Grade ≥ 3 were seen in 32.2% of patients in the Sarclisa combination therapy arm versus 23.8% of patients in the Kd arm, and cardiac failure Grade ≥ 3 was reported in 4.0% for Sarclisa combination therapy versus 4.1% for Kd. Grade 3-4 thrombocytopenia and neutropenia were 29.9% for Sarclisa combination therapy versus 23.8% for Kd, and 19.2% for Sarclisa combination therapy versus 7.4% for Kd. Main reasons for treatment discontinuation were disease progression (29.1% for Sarclisa combination therapy versus 39.8% for Kd) and AEs (8.4% for Sarclisa combination therapy versus 13.8% for Kd).

About the trial

The randomized, multi-center, open label Phase 3 IKEMA clinical trial enrolled 302 patients with relapsed MM across 69 centers spanning 16 countries. All study participants had received one to three prior anti-myeloma therapies. During the trial, Sarclisa was administered through an intravenous infusion at a dose of 10mg/kg once weekly for four weeks, then every other week for 28-day cycles in combination with carfilzomib twice

weekly at the 20/56mg/m² dose and dexamethasone at the standard dose for the duration of treatment. The primary endpoint of IKEMA was PFS. Secondary endpoints included ORR, the rate of CR or better, the rate of VGPR or better, rate of MRD-negativity, OS and safety.¹

The results from IKEMA are anticipated to form the basis of regulatory submissions planned for later this year. The use of Sarclisa in combination with carfilzomib and dexamethasone in relapsed MM is investigational and has not been evaluated by any regulatory authority.

About Sarclisa

Sarclisa is a monoclonal antibody that binds to a specific epitope on the CD38 receptor on MM cells. It is designed to work through multiple mechanisms of action including programmed tumor cell death (apoptosis) and immunomodulatory activity. CD38 is highly and uniformly expressed on the surface of MM cells, making it a potential target for antibody-based therapeutics such as Sarclisa.

Sarclisa is approved in the EU, U.S., Switzerland, Canada and Australia in combination with pom-dex for the treatment of certain adults with relapsed refractory MM. In the U.S., the generic name for Sarclisa is isatuximab-irfc, with irfc as the suffix designated in accordance with Nonproprietary Naming of Biological Products Guidance for Industry issued by the U.S. Food and Drug Administration.

Sarclisa continues to be evaluated in multiple ongoing Phase 3 clinical trials in combination with current standard treatments across the MM treatment continuum. It is also under investigation for the treatment of other hematologic malignancies and solid tumors. The safety and efficacy of these additional uses have not been reviewed by any regulatory authority worldwide.

For more information on Sarclisa clinical trials please visit www.clinicaltrials.gov.

About Multiple Myeloma (MM)

MM is the second most common hematologic malignancy, with more than 138,000 new diagnoses of MM worldwide yearly.^{2,3} Despite available treatments, MM remains an incurable malignancy and is associated with significant patient burden. Since MM does not have a cure, most patients will relapse. Relapsed MM is the term for when the cancer returns after treatment or a period of remission. Refractory MM refers to when the cancer does not respond or no longer responds to therapy.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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¹ ClinicalTrials.gov. Identifier # NCT03275285.

<https://www.clinicaltrials.gov/ct2/show/NCT03275285?cond=NCT03275285&draw=2&rank=1>. Accessed June 2020.

² Kazandjian. Multiple myeloma epidemiology and survival: A unique malignancy. *Semin Oncol.* 2016;43(6):676-681. doi:10.1053/j.seminoncol.2016.11.004.

³ International Myeloma Foundation. Myeloma Action Month. <https://mam.myeloma.org/learn-more-about-multiple-myeloma/>. Accessed June 2020.