

Sarclisa® (isatuximab) plus KRd significantly improved rate of minimal residual disease negativity in transplant-eligible patients with newly diagnosed multiple myeloma versus KRd alone

- Phase 3 data showed Sarclisa added to carfilzomib, lenalidomide and dexamethasone (KRd) in patients with newly diagnosed, transplant-eligible multiple myeloma resulted in 77% of patients achieving minimal residual disease (MRD) negativity after consolidation therapy, detected with a sensitivity of 10^{-5}
- MRD negativity rate measured at a sensitivity of 10^{-6} was 67% for Sarclisa combination therapy
- Results shared during oral presentation at ASH 2023 plenary scientific session

PARIS, December 10, 2023. The Phase 3 trial investigating Sarclisa® (isatuximab) in combination with carfilzomib, lenalidomide and dexamethasone (KRd) showed a statistically significant improvement in the rate of minimal residual disease (MRD) negativity, compared with KRd alone, after autologous stem cell transplant (ASCT) consolidation in transplant-eligible patients with newly diagnosed multiple myeloma (MM). These results from the IsKia trial conducted by the European Myeloma Network (EMN) were presented during the oral plenary session (#4) at the American Society of Hematology (ASH) Annual Meeting by Francesca Gay, Associate Professor at the University Division of Hematology, AOU Città della Salute e della Scienza di Torino, University of Torino and Department of Molecular Biotechnology and Health Sciences - member of the Young EMN board of directors.

MRD negativity is defined as the absence of myeloma cells in the bone marrow after treatment, as measured by diagnostic techniques that must have a sensitivity of at least 1 in 100,000 cells. In this trial, MRD negativity was detected with a sensitivity of 10^{-5} (no cancer cells detected within 100,000 bone marrow cells) and 10^{-6} (no cancer cells detected within 1,000,000 bone marrow cells).

In an intent-to-treat (ITT) analysis, the primary endpoint of rate of MRD negativity using next generation sequencing with a sensitivity of 10^{-5} after consolidation for patients receiving Sarclisa combination therapy (n=151) was 77% versus 67% for those who received KRd alone (n=151) (odds ratio [OR] 1.67; p=0.049). The respective rates of MRD negativity at sensitivity of 10^{-6} were 67% versus 48% (OR 1.93; p=0.006). The MRD negativity benefit, both at 10^{-5} and 10^{-6} sensitivities, was retained in all subgroups analyzed with similar benefit in both standard-risk and high-risk patients.

There was a statistically significant difference in MRD negativity rates after induction with Sarclisa in combination with KRd versus KRd (10^{-5} : 45% versus 26%, p<0.001; 10^{-6} : 27% versus 14%, p=0.004).

The safety and tolerability of Sarclisa observed in this trial were consistent with the observed safety profile of Sarclisa in other clinical trials, with no new safety signals observed. Rates of grade 3 or higher hematologic adverse events (AEs) were 40% versus 30% and rates of non-hematologic AEs were 41% versus 37% for the Sarclisa combination versus KRd, respectively. Discontinuation rates for AEs were similar in both study arms (7% and 5%, respectively). There were three treatment-related deaths in the Sarclisa combination arm and one in the KRd arm.

Peter C. Adamson

Global Development Head, Oncology, Sanofi

“The statistically significant rates of MRD negativity observed with Sarclisa combination therapy further support our belief in Sarclisa as a potential best-in-class therapy. Effective front-line treatment is critical for newly diagnosed patients, because achieving undetectable levels of disease early in the treatment journey may lead to better long-term outcomes. We look forward to our continued collaboration with the EMN to explore the potential of this novel combination regimen for those with transplant-eligible, newly diagnosed multiple myeloma.”

The use of Sarclisa in combination with KRd in this patient population is investigational and has not been evaluated by any regulatory authority.

About the trial

The randomized, open-label Phase 3 IsKia trial enrolled 302 patients with newly diagnosed, transplant-eligible MM across eight countries and 42 sites in Europe. Patients were randomized into two arms. Patients in both arms received induction with four 28-day cycles of KRd followed by cyclophosphamide and stem cell collections, chemotherapy with Melphalan 200 mg/m² followed by ASCT (Mel200-ASCT), four 28-day cycles of KRd post ASCT consolidation and 12 cycles of KRd light consolidation. Sarclisa was added to KRd in one trial arm only. During the trial, Sarclisa was administered through an intravenous infusion at a dose of 10 mg/kg once weekly for the first four weeks of cycle one, then every other week for the rest of the induction and full consolidation periods, then every four weeks during light consolidation period.

The primary endpoint was the rate of MRD negativity by next-generation sequencing (10⁻⁵) after consolidation in the ITT population. MRD was tested in all patients who achieved at least a very good partial response. Key secondary endpoints were the rate of next-generation sequencing MRD negativity (10⁻⁵) after induction and progression free survival. MRD rates were evaluated in an ITT analysis.

High-risk patient cytogenetics per the International Myeloma Working Group (IMWG) criteria were defined as the presence of t(4;14), t(14;16), or del(17p). High-risk cytogenetic abnormality (HRCA) was defined as the presence of one of the following abnormalities: del(17p13.1), t(4;14) (p16.3;q32.3), t(14;16) (q32.3;q23), gain(1q21), or amp(1q21). Two or more HRCAs was defined as the presence of at least two high-risk cytogenetic abnormalities.

About Sarclisa

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

Based on the Phase 3 ICARIA-MM study, Sarclisa is approved in >50 countries, including the U.S. and EU, in combination with pomalidomide and dexamethasone for the treatment of certain patients with relapsed refractory MM (RRMM) who have received ≥2 prior therapies, including lenalidomide and a proteasome inhibitor and who progressed on last therapy. Based on the Phase 3 IKEMA study, Sarclisa is also approved in 50 countries in combination with carfilzomib and dexamethasone, including in the U.S. for the treatment of patients with RRMM who have received 1–3 prior lines of therapy and in the European Union for patients with MM who have received at least 1 prior therapy. 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 (FDA).

The IsKia trial marks the second positive Phase 3 trial of Sarclisa in transplant-eligible newly diagnosed multiple myeloma, and fifth positive Phase 3 readout for Sarclisa overall, demonstrating its best-in-class potential.

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 its safety and efficacy have not been evaluated by any regulatory authority outside of its approved indication.

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

About multiple myeloma

MM is the second most common hematologic malignancy.¹ 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 the European Myeloma Network (EMN) foundation

The European Myeloma Network (EMN) is a non-profit organization, created in 2005. This network is the reference organization for multiple myeloma studies in Europe: physicians can participate in cooperative projects to increase and share their experiences, and to standardize and harmonize clinical practices; pharmaceutical companies can refer to the EMN as a general interlocutor in Europe to plan and manage clinical trials with new molecules; and, most importantly, patients can be enrolled in clinical studies evaluating last-generation and promising drugs, with the ultimate goal of improving their survival and quality of life. Various national groups collaborate within the EMN, such as the Netherlands (where the headquarter is located), Italy (with the data centre of the network), Germany, Austria, France, Spain, Greece, Czech Republic, the UK, Norway, Denmark, Switzerland, Turkey, and many more countries will participate in the EMN projects in the future. For further information, please contact the EMN (President Prof. Pieter Sonneveld): <https://www.myeloma-europe.org/>

About Sanofi

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across some 100 countries, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

Sanofi is listed on Euronext: SAN and NASDAQ: SNY

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Sanofi Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to

differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that pandemics or other global crises may have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2022. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

¹ Kazandjian D. Multiple myeloma epidemiology and survival: A unique malignancy. *Semin Oncol.* 2016;43(6):676-681. doi:10.1053/j/semioncol.2016.11.004.