

Sarclisa® (isatuximab) trial is first Phase 3 study to meet primary endpoint of minimal residual disease negativity in transplant-eligible patients with newly diagnosed multiple myeloma

- * Sarclisa combination therapy is first to demonstrate superiority to standard of care lenalidomide, bortezomib and dexamethasone (RVd) in a Phase 3 trial
- * 50.1% of patients achieved undetectable levels of disease after 18 weeks of induction treatment with Sarclisa-RVd
- * GMMG will share the results as an oral presentation, and as part of the press program, at ASH 2021

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The Phase 3 HD7 trial, conducted by the German-Speaking Myeloma Multicenter Group (GMMG), met the primary endpoint, the rate of minimal residual disease (MRD) negativity after induction therapy and before transplant in patients with newly diagnosed multiple myeloma (MM) treated with Sarclisa® (isatuximab) in combination with lenalidomide, bortezomib and dexamethasone (RVd). This is the first Phase 3 trial to evaluate MRD negativity at the end of induction as a primary endpoint, and to demonstrate statistically significant improvement in rates of MRD negativity in this patient population by adding an anti-CD38 monoclonal antibody to RVd. MRD negativity is an important clinical endpoint associated with better patient outcomes, which is meaningful for MM where most patients relapse.¹

“It is unprecedented for half of patients to achieve MRD negativity this early in treatment with this regimen,” said Hartmut Goldschmidt, M.D., President of GMMG, Professor of Medicine at the Heidelberg University Hospital (UKHD), Germany and principal investigator of the study. *“We know that achieving deeper responses earlier in treatment may translate to longer periods of progression free survival and are excited about these results.”*

After an induction phase of 18 weeks, the rate of MRD negativity for patients receiving Sarclisa combination therapy (n=331) was 50.1% versus 35.6% for those who received RVd (n=329) (odds ratio [OR]=1.83; 95% confidence interval [CI]: 1.34-2.51; p<0.001). 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. Rates of all adverse events observed were 63.6% for the Sarclisa combination versus 61.3% for RVd and serious adverse effects and discontinuations were similar in

both study arms (34.8% versus 36.3%, respectively). However, the number of deaths were higher in the RVd arm (1.2% versus 2.4%) during the induction period. The trial is ongoing, following the second randomization to evaluate progression free survival (PFS) for Sarclisa and lenalidomide combination as maintenance therapy.

“The results of this trial reinforce our belief in Sarclisa’s potential to become the anti-CD38 of choice,” said Peter C. Adamson, Global Development Head, Oncology at Sanofi. *“To observe such a high proportion of patients who have MRD negative disease following a relatively brief induction period is highly encouraging. We look forward to our continued collaborative efforts with GMMG to deliver a potential treatment option to transplant-eligible patients with newly diagnosed multiple myeloma.”*

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.² This assessment is the most sensitive tool to measure the depth of response to treatment in patients with MM.³

This GMMG initiated clinical trial was conducted in close collaboration with Sanofi based on jointly defined research. Sanofi provided financial support to GMMG for this study.

The use of Sarclisa in combination with RVd is investigational and has not been evaluated by any regulatory authority.

About the trial

The pivotal, randomized, open-label, multicenter, Phase 3 GMMG-HD7 trial is a two-part study that enrolled 662 patients with newly diagnosed, transplant-eligible MM across 67 sites in Germany. In the first part of the study, all participants were equally randomized to receive three 42-day cycles of RVd in both arms of the trial, while Sarclisa was added to only one trial arm. 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 period.

MRD negativity was assessed by next-generation flow cytometry (cut off 1×10^{-5}) after induction. An odds ratio was used to measure this endpoint to determine the association between adding Sarclisa to standard of care and participants achieving MRD negativity.

The primary endpoints are MRD negativity after induction treatment for the first part of the study, and PFS following the second randomization after transplant for part two of the study, in which Sarclisa is added to lenalidomide maintenance. Secondary endpoints include rates of complete response after induction, overall survival after maintenance therapy and safety.

About Sarclisa

Sarclisa is a monoclonal antibody that targets 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.

Based on the Phase 3 ICARIA-MM study, Sarclisa is approved in a number of countries in combination with pomalidomide and dexamethasone for the treatment of patients with relapsed refractory MM (RRMM) who have received ≥ 2 prior therapies, including lenalidomide and a proteasome inhibitor. Based on the Phase 3 IKEMA study, Sarclisa is also approved in combination with carfilzomib and dexamethasone 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).

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 is the second most common hematologic malignancy,⁴ with more than 130,000 new diagnoses of MM worldwide yearly.⁵ 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 the German-Speaking Myeloma Multicenter Group (GMMG)

GMMG is the largest study group focusing on MM in Germany, with headquarters based in Heidelberg. Within the last 20 years, the GMMG study group has performed numerous trials including five randomized, multicenter Phase 3 clinical trials with 4,000 patients enrolled from about 90 participating and co-treating centers throughout Germany. The overall goal of GMMG is to generate improved therapies for myeloma patients through the development and testing of novel and personalized, genome- and signaling-driven treatment strategies.

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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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 COVID-19 will 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. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. 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, 2020. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

¹ Kostopoulos. Minimal Residual Disease in Multiple Myeloma: Current Landscape and Future Applications with Immunotherapeutic Approaches. *Front Oncol.* 2020; 10: 860. doi: 10.3389/fonc.2020.00860.

² Romano, A., Palumbo, G. A., Parrinello, N. L., Conticello, C., Martello, M., & Terragna, C. (2019). Minimal Residual Disease Assessment Within the Bone Marrow of Multiple Myeloma: A Review of Caveats, Clinical Significance and Future Perspectives. *Frontiers in oncology*, 9, 699. <https://doi.org/10.3389/fonc.2019.00699>

³ Oliva. Minimal residual disease assessment by multiparameter flow cytometry in transplant-eligible myeloma in the EMN02/HOVON 95 MM trial. *Blood Cancer Journal.* 2021; 11(106). <https://doi.org/10.1038/s41408-021-00498-0>.

⁴ Kazandjian. Multiple myeloma epidemiology and survival: A unique malignancy. *Semin Oncol.* 2016;43(6):676-681. doi:10.1053/j.seminoncol.2016.11.004.

⁵ International Myeloma Foundation. Myeloma Action Month. <https://mam.myeloma.org/learn-more-about-multiple-myeloma/>. Accessed December 2021.