Data Published in Transplantation and Cellular Therapy Suggest Antiviral Protection After Transplantation with Gamida Cell's Omisirge® (omidubicel-onlv)

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Faster immune reconstitution and decreased rate of post-transplant viral infection in patients transplanted with Omisirge versus umbilical cord blood

BOSTON--(BUSINESS WIRE)--Jul. 11, 2023-- Gamida Cell Ltd. (Nasdaq: GMDA), a cell therapy pioneer working to turn cells into powerful therapeutics, today announced the publication in press of a prospective sub-study of the Phase 3 clinical trial for Omisirge® (omidubicel-onlv), the company's allogeneic stem cell transplant therapy, characterizing immune reconstitution kinetics following hematopoietic stem cell transplantation (HCT) with Omisirge compared to umbilical cord blood (UCB). The article appears online on the *Transplantation and Cellular Therapy* journal website.

Thirty-seven patients (Omisirge: n=17, UCB: n=20) from 14 global sites were included in the sub-study and blood samples were collected from seven to 365 days post-transplantation. Omisirge was found to facilitate faster immune reconstitution, including natural killer (NK) cell and helper T (Th) cell reconstitution than UCB before day 28 post-transplantation. The early reconstitution may account for the reduced rate of viral infections observed after transplantation with Omisirge versus UCB.

"The speed of immune reconstitution is critical for patients who are vulnerable to infection immediately following transplant," said Mitchell Horwitz, M.D., senior author of the publication and stem cell transplant specialist and Professor of Medicine at Duke Cancer Institute. "These data suggest that Omisirge generates rapid functional recovery of the immune system, which may be associated with the lower rate of viral infections observed among patients who received Omisirge."

- Omisirge recipients demonstrated an up to 70-fold advantage over patients who received UCB in median cell counts across most cell populations, occurring predominantly in the short-term post-transplantation setting, including NK and T cell reconstitution in the first two weeks post-transplantation. By three weeks post-HCT, Omisirge recipients were 3 times more likely to achieve clinically relevant Th and NK cell counts of 100 cells/µL or above.
- Omisirge recipients received a 33-fold higher median dose of CD34+ stem cells than UCB recipients. The CD34+ cell content for recipients transplanted with Omisirge correlated with faster immune reconstitution by Day 7 post-HCT, which in turn coincided with earlier hematopoietic recovery.
- Omisirge recipients exhibited superior reconstitution of B cells, dendritic cells and monocytes.
- Clinical outcomes in this sub-study were consistent with those from the Phase 3 study for Omisirge. The rate of grade 2/3 infections in the first year were significantly lower with Omisirge than with UCB: 29% vs 70% for bacterial infections and 6% vs 45% for viral infections. No differences were reported in incidence of acute or chronic GVHD between the Omisirge transplanted patients and the UCB transplanted patients.

"The approval of Omisirge was based on the reduced time to neutrophil recovery and reduced risk of infection compared to standard cord blood," said Ronit Simantov, M.D., Chief Medical and Scientific Officer of Gamida Cell. "The robust recovery of multiple immune cell populations we observed provides a potential mechanism for the reduced incidence of serious bacterial, fungal and viral infections associated with Omisirge transplantation."

Stem cell graft source is a known factor influencing immune reconstitution along with other factors such as patient age, disease type, preparative chemotherapy regimen and post-transplantation supportive care.[1,2] These data support past findings that Omisirge stimulates a faster immune response than standard cord blood.[3]

The authors noted several limitations to the study, including sample size. Additionally, there is limited available literature comparing immune reconstitution by donor source. Although age variation may influence immune reconstitution outcomes, an age-adjusted analysis found no age-specific effect.

Omisirge Indication

Omisirge is a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood indicated for use in adults and pediatric patients 12 years and older with hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative conditioning to reduce the time to neutrophil recovery and the incidence of infection.

Important Safety Information for Omisirge

BOXED WARNING: INFUSION REACTIONS, GRAFT VERSUS HOST DISEASE, ENGRAFTMENT SYNDROME, AND GRAFT FAILURE

- **Infusion reactions may be fatal. Monitor patients during infusion and discontinue for severe reactions. Use is contraindicated in patients with known allergy to dimethyl sulfoxide (DMSO), Dextran 40, gentamicin, human serum albumin or bovine material.**
- **Graft-versus-Host Disease may be fatal. Administration of immunosuppressive therapy may decrease the risk of GvHD.**
- **Engraftment syndrome may be fatal. Treat engraftment syndrome promptly with corticosteroids.**

- **Graft failure may be fatal. Monitor patients for laboratory evidence of hematopoietic recovery.**

Contraindications

OMISIRGE is contraindicated in patients with known hypersensitivity to dimethyl sulfoxide (DMSO), Dextran 40, gentamicin, human serum albumin, or bovine products.

Warnings and Precautions

Hypersensitivity Reactions

Allergic reactions may occur with the infusion of OMISIRGE. Reactions include bronchospasm, wheezing, angioedema, pruritis and hives. Serious hypersensitivity reactions, including anaphylaxis, may be due to DMSO, residual gentamicin, Dextran 40, human serum albumin (HSA) and bovine material in OMISIRGE. OMISIRGE may contain residual antibiotics if the cord blood donor was exposed to antibiotics in utero. Patients with a history of allergic reactions to antibiotics should be monitored for allergic reactions following OMISIRGE administration.

Infusion Reactions

Infusion reactions occurred following OMISIRGE infusion, including hypertension, mucosal inflammation, dysphagia, dyspnea, vomiting, and gastrointestinal toxicity. Premedication with antipyretics, histamine antagonists, and corticosteroids may reduce the incidence and intensity of infusion reactions. In patients transplanted with OMISIRGE in clinical trials, 47% (55/117) patients had an infusion reaction of any severity. Grade 3-4 infusion reactions were reported in 15% (18/117) patients. Infusion reactions may begin within minutes of the start of infusion of OMISIRGE, although symptoms may continue to intensify and not peak for several hours after the completion of the infusion. Monitor patients for signs and symptoms of infusion reactions during and after OMISIRGE administration. When a reaction occurs, pause the infusion and institute supportive care as needed.

Graft-versus-Host Disease

Acute and chronic GvHD, including life-threatening and fatal cases, occurred following treatment with OMISIRGE. In patients transplanted with OMISIRGE Grade II-IV acute GvHD was reported in 58% (68/117). Grade III- IV acute GvHD was reported in 17% (20/117). Chronic GvHD occurred in 35% (41/117) of patients. Acute GvHD manifests as maculopapular rash, gastrointestinal symptoms, and elevated bilirubin. Patients treated with OMISIRGE should receive immunosuppressive drugs to decrease the risk of GvHD, be monitored for signs and symptoms of GvHD, and treated if GvHD develops.

Engraftment Syndrome

Engraftment syndrome may occur because OMISIRGE is derived from umbilical cord blood. Monitor patients for unexplained fever, rash, hypoxemia, weight gain, and pulmonary infiltrates in the peri-engraftment period. Treat with corticosteroids as soon as engraftment syndrome is recognized to ameliorate symptoms. If untreated, engraftment syndrome may progress to multiorgan failure and death.

Graft Failure

Primary graft failure occurred in 3% (4/117) of patients in OMISIRGE clinical trials. Primary graft failure, which may be fatal, is defined as failure to achieve an absolute neutrophil count greater than 500 per microliter blood by Day 42 after transplantation. Immunologic rejection is the primary cause of graft failure. Monitor patients for laboratory evidence of hematopoietic recovery.

Malignancies of Donor Origin

Two patients treated with OMISIRGE developed post-transplant lymphoproliferative disorder (PTLD) in the second-year post-transplant. PTLD manifests as a lymphoma-like disease favoring non-nodal sites. PTLD is usually fatal if not treated. The etiology is thought to be donor lymphoid cells transformed by Epstein-Barr virus (EBV). Serial monitoring of blood for EBV DNA may be warranted in patients with persistent cytopenias. One patient treated with OMISIRGE developed a donor-cell derived myelodysplastic syndrome (MDS) during the fourth-year post-transplant. The natural history is presumed to be the same as that for *de novo* MDS. Monitor life-long for secondary malignancies. If a secondary malignancy occurs, contact Gamida Cell at (844) 477-7478.

Transmission of Serious Infections

Transmission of infectious disease may occur because OMISIRGE is derived from umbilical cord blood. Disease may be caused by known or unknown infectious agents. Donors are screened for increased risk of infection, clinical evidence of sepsis, and communicable disease risks associated with xenotransplantation. Maternal and infant donor blood is tested for evidence of donor infection. See full Prescribing Information, Warnings and Precautions, Transmission of Serious Infections for list of testing performed. OMISIRGE is tested for sterility, endotoxin, and mycoplasma. There may be an effect on the reliability of the sterility test results if the cord blood donor was exposed to antibiotics in utero. Product manufacturing includes bovine-derived reagents. All animal-derived reagents are tested for animal viruses, bacteria, fungi, and mycoplasma before use. These measures do not eliminate the risk of transmitting these or other transmissible infectious diseases and disease agents**. Test results may be found on the container label and/or in accompanying records.** If final sterility results are not available at the time of use, Quality Assurance will communicate any positive results from sterility testing to the physician. Report the occurrence of transmitted infection to Gamida Cell at (844) 477-7478.

Transmission of Rare Genetic Diseases

OMISIRGE may transmit rare genetic diseases involving the hematopoietic system because it is derived from umbilical cord blood. Cord blood donors have been screened to exclude donors with sickle cell anemia, and anemias due to abnormalities in hemoglobins C, D, and E. Because of the age of the donor at the time cord blood collection takes place, the ability to exclude rare genetic diseases is severely limited.

ADVERSE REACTIONS

The most common adverse reactions (incidence > 20%) are infections, GvHD, and infusion reaction.

Please see full Prescribing Information, including Boxed Warning.

About the Omisirge Phase 3 Study

In a global, randomized Phase 3 clinical study (NCT02730299), Omisirge demonstrated a median time to neutrophil recovery of 12 days in the intent to treat population, compared to 22 days for standard cord blood ($p<0.001$).[4] Incidence of Grade 2/3 bacterial or Grade 3 fungal infections through 100 days following transplantation occurred in 39% of patients in the Omisirge arm and 60% of patients in the standard cord blood arm.[1] The full Phase 3 clinical study results are available in *Blood*, the official journal of the American Society of Hematology. The safety profile for Omisirge is consistent with the expected adverse events of allogeneic hematopoietic stem cell transplantation following myeloablative conditioning. Among 117 patients who received Omisirge for any disease, infusion reactions occurred in 47% of patients (Grade 3 or 4 in 15%), acute graft-versus-host disease (GvHD) in 58% (Grade III-IV in 17%), chronic GvHD in 35% and graft failure in 3%.[5]

About Gamida Cell

Gamida Cell is a cell therapy pioneer working to turn cells into powerful therapeutics. The company's proprietary nicotinamide (NAM) technology leverages the properties of NAM to enhance and expand cells, creating allogeneic cell therapy products and candidates that are potentially curative for patients with hematologic malignancies. These include Omisirge®, an FDA-approved nicotinamide modified allogeneic hematopoietic progenitor cell therapy, and GDA-201, an intrinsic NK cell therapy candidate being investigated for the treatment of hematologic malignancies. For additional information, please visit www.gamida-cell.com or follow Gamida Cell on LinkedIn, Facebook, Twitter and Instagram.

Cautionary Note Regarding Forward Looking Statements

This press release contains forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995, including with respect to the potentially life-saving or curative therapeutic and commercial potential of Omisirge® (omidubicel-onlv). Any statement describing Gamida Cell's goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to a number of risks, uncertainties and assumptions including those related to clinical, scientific, regulatory and technical developments and those inherent in the process of developing and commercializing product candidates that are safe and effective for use as human therapeutics. In light of these risks and uncertainties, and other risks and uncertainties that are described in the Risk Factors section and other sections of Gamida Cell's Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission (SEC) on May 15, 2023, and other filings that Gamida Cell makes with the SEC from time to time (which are available at www.sec.gov), the events and circumstances discussed in such forward-looking statements may not occur, and Gamida Cell's actual results could differ materially and adversely from those anticipated or implied thereby. Although Gamida Cell's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Gamida Cell. As a result, you are cautioned not to rely on these forward-looking statements.

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