"Prior to leukapheresis, a patient will undergo blood tests, electrolyte tests and blood coagulation tests in preparation for the procedure"

Myeloma Patients Europe has conducted a series of four written interviews on CAR-T manufacturing to better understand manufacturing processes and challenges of various myeloma CAR-T therapies. Four different stakeholders have answered our questions, including two pharmaceutical companies, which each have a myeloma CAR-T product approved by the European Medicines Agency, and two academic teams which have developed myeloma CAR-T products currently under clinical investigation. In this interview, we will learn about the manufacturing process at Bristol Myers Squibb (BMS).

What is the journey of a patient's cells?
CAR-T therapy begins with a patient visiting a hospital or cancer centre that is certified to distribute the treatment. Once admitted, the patient's T-cells, which are a type of white blood cell that function as key fighters in the immune system, are extracted by a healthcare professional trained in the treatment and removed through a process called apheresis, or leukapheresis, which takes several hours. Prior to leukapheresis, a patient will undergo blood tests, electrolyte tests and blood coagulation tests in preparation for the procedure. During the T-cell collection, blood is withdrawn via two IVs and processed in a machine where the T-cells are separated from other blood components. The remaining blood is then infused back into the patient. The collected T-cells are cryo-preserved and are shipped to a specialised cell therapy manufacturing facility where they undergo genetic 'reprogramming' to become CAR T-cells. The patient will return home while they wait for the modified T-cells.
A few days before receiving their CAR-T therapy, patients will come back to the hospital or cancer centre to receive low-dose chemotherapy, known as lymphodepleting chemotherapy, to help prepare the body to receive the reprogrammed CAR T-cells. This helps to create space in the patient's immune system to accept the CAR T-cells. The patients receive their personalised CAR T-cells with one dose, and this process usually takes about an hour. From there, the CAR T-cells may expand and travel throughout the body to attack the targeted cells.
All patients who receive a CAR-T therapy are monitored closely by their care team for possible side effects. Time at the hospital will vary based on the individual patient. Patients need to stay in proximity to the treatment centre for at least four weeks and may return home when their doctor says that it is safe to do so. However, they may need to stay nearby or return to the hospital if side effects develop after returning home. A patient's caregiver will also play a critical role in helping monitor the patient for potential side effects. The patient's care team will continue to follow up with them via phone calls and in-person appointments to assess whether the CAR-T therapy is working and to watch for side effects. Patients will see their doctor for ongoing follow-ups after treatment, though the frequency of follow-ups may vary and are determined by the doctor.

"A patient's caregiver will also play a critical role in helping monitor the patient for potential side effects"

What will happen to the cells?
The collected T-cells are shipped to a specialised cell therapy manufacturing facility where they undergo genetic 'reprogramming' to become CAR T-cells that have receptors (or hooks) added to the T-cells. These receptors help recognise and fight cells containing a specific antigen on the surface of the target cell, including normal and cancer cells. The CAR T-cells are then multiplied to create the appropriate dose consisting of millions of CAR T-cells and then washed to remove culture media. Finally, they undergo rigorous testing and quality control before being shipped back to the patient at a CAR T-cell treatment centre. The manufacturing process can take several weeks to complete."
More information, including a tour of the manufacturing facility where the cells undergo this process, is available **here.**

Bristol Myers Squibb

The Bristol-Myers Squibb (BMS) Company is an American multinational pharmaceutical company.
The European Medicines Agency authorised BMS to market Idecabtagene vicleucel (also known as ide-cel, Abecma®) in August 2021, after several years of clinical investigation to evaluate the safety and efficacy of the product. This BCMA-targeted CAR T-cell therapy is indicated for treating adults with multiple myeloma whose cancer has returned (relapsed) or has not responded to treatment (refractory).
Ide-cel is commercially used when patients' disease worsens despite receiving at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody. The product is currently under investigation to evaluate efficacy at earlier lines of therapies and benefits over other standards of care, and in combination with other treatments.

Who is involved in the process?
The cells' journey begins at the hospital, or cancer centre, with the patient's healthcare provider and are shipped to a cell therapy manufacturing facility. At the Bristol Myers Squibb cell therapy facilities, we rely on our 3,000+ employees focused on cell therapy manufacturing, development and commercialisation to help deliver cell therapies to patients globally. Our growing global manufacturing network includes three state-of-the-art cell therapy facilities in the United States and two new facilities in progress (one in the United States in 2023 and one in Leiden, the Netherlands in 2025 to support Europe).

"All patients who receive a CAR -T therapy are monitored closely by their care team for possible side effects"

How is the quality of the product ensured?
Manufacturing of autologous cell therapies requires a personalised process, with each therapy created from an individual patient's cells. Our main focus is on patient chain of identity,[1] product integrity and quality, as well as highly trained manufacturing teams. BMS uses state-of-the-art quality control labs. Testing performed here covers aspects of the manufacturing process from when the cells arrive to when the final product is given to the physician and patient. In addition, throughout this process, there are more than 500 chain of identity points that offer checks and balances to ensure continuity of the patient's cells throughout the journey.

"Our main focus is on patient chain of identity, product integrity and quality, as well as highly trained manufacturing teams. BMS uses state-of-the-art quality control labs"

What do you think needs to be improved in the near future with regards to how manufacturing is done now?
The field of cell therapy continues to evolve every day. We are investing in the future of cell therapy in many ways, including translational medicine capabilities, a robust pipeline of next-generation assets and manufacturing technologies, off-the-shelf CAR-T approaches and engineered and gene-edited T-cells for solid tumors. We continue to explore and study technologies that decrease manual manipulations – meaning the process is more automated – and decrease manufacturing footprints.

"There are more than 500 chain of identity points that offer checks and balances to ensure continuity of the patient's cells throughout the journey"

1. *A patient's identity is constantly associated to its cells and the resulting CAR T-cell product during the entire manufacturing process in order to ensure that he/she receives the correct, personalised medicine.*

CAR-T Interview Series

The CAR-T Interview Series is composed of four different interviews about CAR-T manufacturing, from cell collection to cell infusion. Click on the links below to read the interviews responded by:

- Hadassah Hebrew University Medical Centre
- Janssen Pharmaceuticals
- Dr. Halvard Bönig, Translational Development of Cellular Therapeutics, Goethe University

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 754658. Myeloma Patients Europe chose the interview questions, the stakeholders to be interviewed, and edited and published the interviews. Neither interviewee nor funders took part in this process. Interviewees sent their answers in writing and reviewed the final draft of their respective interviews before publication.

CONTACT US

info@mpeurope.org

www.mpeurope.org

@mpeurope

@MyelomaEurope

Myeloma Patients Europe

Myeloma Patients Europe