

**NHSBT Board Meeting**  
26 September 2019

**Status: Official**

**A Patient Story: CAR-T Cells**

NHS Blood & Transplant has been involved in the collection, processing and storage of cells as part of the process to treat NHS patients with Chimeric Antigen Receptor (CAR) T cells for several of the first wave of NHS treatment centres commissioned at the end of last year. CAR-T cells are genetically engineered to target CD19, a protein on the surface of lymphocytes that is present in some forms of leukaemia and lymphoma.

Nitya Raghava was diagnosed with Acute Lymphoblastic Leukaemia at the age of 16 and received standard chemotherapy at Bristol Royal Hospital for Children, achieving a good initial response. 23 months into treatment she relapsed (her leukaemia came back). Following further chemotherapy, during which she completed her A levels achieving grades to be accepted by University College London (UCL), she achieved complete remission and was referred for Allogeneic Stem Cell transplant. Following Human Leucocyte Antigen (HLA) typing (“tissue typing”) by The Histocompatibility and Immunogenetics (H&I) laboratory in NHSBT Filton, she was found to be a full match with her sister.

Her sister donated stem cells at the Therapeutic Apheresis Services (TAS) unit in Bristol, which were processed and some stored at the Cellular and Molecular Therapies (CMT) laboratory, Filton. The initial transplant proceeded without too many problems but she relapsed by day 64.

Until CAR-T cells became available, there were no curative treatment options for a patient in this position and she would have entered palliative care at this point. The Eliana trial of CAR-T cells shows an approximate 50% cure rate. She was referred to the national panel and accepted as one of the first NHS commissioned patients to receive this treatment. This provided a tight timeline for NHSBT to complete the necessary regulatory and practical agreements with the hospital and the pharmaceutical company, Novartis, to proceed.

Nitya had cells collected by TAS Bristol on 20<sup>th</sup> December 2018, they were cryopreserved at CMT Filton before shipping to USA on 27<sup>th</sup> December for manufacture. They were shipped back to Filton at the end of January and stored under our Genetically Modified Organism (GMO) licence. The patient was given preparatory chemotherapy and the cells were transferred to University Hospitals Bristol for infusion on 6<sup>th</sup> February. She developed a very common early complication of CAR-T cells called cytokine release syndrome,

but this was low grade and easily managed allowing her discharge from hospital as planned after 14 days. The CAR-T cell therapy appears to have cured her leukaemia with no detectable disease in her bone marrow within a month and this remains the case on most recent testing 4 months after cell infusion.

Unfortunately, she developed graft versus host disease (GvHD) from the CAR-T, which while predicted as a possible complication had not been reported anywhere previously. The cells have unintentionally attacked her skin, liver and gut as well as intentionally attacking the targeted leukaemia cells. She is now receiving extracorporeal phototherapy at TAS Bristol alongside 3 other treatments to control the GvHD. While skin and bowel symptoms have resolved, she has persistent liver impairment resulting in referral for potential liver transplantation.

Despite all of this she is planning to go to university in the autumn. She would not be alive today without the services she has received from NHSBT. In total she has received 18 units of red blood cells and 28 doses of platelets since her leukaemia diagnosis. She has used diagnostic services (H&I) with TAS and CMT providing therapeutic interventions. It is possible that she may also require the services of Organ Donation and Transplantation (ODT) in the near future. She was the first NHS CAR-T patient that NHSBT were involved with but many more have and continue to follow.



Photo of the cells following transport back to the hospital from NHSBT just prior to thawing

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