BSH2020 VIRTUAL 9 -14 NOVEMBER



Experiences of providing commercial Chimeric Antigen Receptor (CAR-T) cell therapy at the Northern Centre for Cancer Care

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infusion





Chimeric antigen receptor (CAR) T cell therapies are a promising new treatment option in the field of haematological malignancies. Two products - Axicabtagene ciloleucel (Yescarta) and Tisagenlecleucel (Kymriah) – have been commissioned for the treatment of diffuse large B cell lymphoma and primary mediastinal B cell lymphoma in adults. The Northern Centre for Cancer Care (NCCC) has accepted referrals for CAR-T therapy since January 2019.

AIM

The aim of this poster is to provide a summary of the experience of the first several months of providing commercial CAR-T therapy at a treating centre (the NCCC). Since submission, the data has been updated to be correct as of October 2020.

METHOD

Retrospective case note analysis for adult patients who were referred to the NCCC's MDT for consideration of CARtherapy between March 2019 and October 2020. Percentages have been rounded to the nearest whole number in this poster.

Fig. 1 Referrals to NCCC for CAR-T Patients referred to NCCC for therapy and reasons consideration of CAR-T therapy patients did not (n = 49) proceed to cell • disease progression before leukapheresis (n = 4) received other therapies (n = 4) • underwent leukapheresis but died before infusion n = 15 (n = 4) received CAR-T in another centre (n= 1) • ineligible for CAR-T for another reason (n = 2) Patients who received CAR-T infusion (n = 34)

To date, thirty-four patients have received commercial Chimeric Antigen Receptor (CAR-T) cell infusion. There have been no treatment-related deaths.

Outcomes used included:

- Number of referrals for consideration of CAR-T therapy and number of patients receiving CAR-T infusions
- Where patients did not receive CAR-T cells, the reasons why they did not
- Rates of successful product manufacture, bridging therapy use, time from leukapheresis to infusion of cells
- Features of inpatient stay, including duration, rates of cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS), medications prescribed, and treatment related deaths
- Long-term outcomes: overall response rate, overall survival and progression free survival. Some of the cohort are awaiting imminent follow-up imaging which may alter the figures significantly due to low sample size.

DISCUSSION

A national compilation and review of similar data from multiple treating centres would be valuable. This would prompt discussion around local protocols, and aid understanding of the risk profile associated with side effects of CAR-T therapy. Longer periods of follow-up will improve understanding of long-term rates of survival and remission.

Pre-infusion

Of the patients who have received CAR-T cells (n=34), twenty-two (65%) had diffuse large B cell lymphoma, six (18%) had transformed follicular lymphoma, four (12%) had primary mediastinal B cell lymphoma, one (3%) had nodular lymphocyte predominant Hodgkin's lymphoma, and one (3%) had transformed marginal zone lymphoma.

CAR-T cells were manufactured within specification at the first attempt for 95% of patients who underwent apheresis.

- Axicabtagene ciloleucel (Yescarta) was successfully manufactured at the first attempt in all cases.
- Tisagenlecleucel (Kymriah) was successfully manufactured at the first attempt in all but two cases.

Median time from leukapheresis to infusion of cells was 37 days (range 28-105). Twenty-five (74%) received bridging therapy. All were conditioned with fludarabine and cyclophosphamide.

Admission for CAR-T infusion

Twenty-six patients received axicabtagene ciloleucel (Yescarta). Eight received tisagenlecleucel (Kymriah).

Median duration of inpatient stay after CAR-T infusion was 21 days (range 13-146).

During inpatient admission, twenty-seven patients (71%) experienced cytokine release syndrome (CRS) of any grade. Six (18%) experienced CRS of grade 3 and above. Thirteen (38%) experienced immune effector cell associated neurotoxicity syndrome (ICANS) of any grade. Seven (21%) experienced ICANS of grade 3 and above.

Twenty-one (62%) received tocilizumab. Eleven (32%) received steroids. Twelve (35%) required admission to the intensive care unit: median duration of stay there was 2 days (range 1-11).

ACKNOWLEDGEMENT

Grateful thanks to Hannah Kennedy, CAR-T Therapy Clinical Nurse Specialist, Northern Centre for Cancer Care, for providing updated data.

Follow-up

Follow-up results are available for thirty-four patients. Overall response rate was 62% (twenty-one patients); of which nine achieved complete response as best overall response, and twelve achieved partial response. One (3%) had stable disease as best overall response, and twelve (35%) had progressive disease.

Overall survival rates were 94% at 28 days, 81% at 3 months, and 39% at 6 months after CAR-T infusion. Eighteen patients (53% of cohort available to follow-up) have died after CAR-T infusion.

At the time of writing, progression-free survival rates as calculated at standardised follow-up points were 62% at 28 days, 34% at 3 months, and 22% at 6 months after CAR-T infusion.

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