Chimeric antigen receptor T-cell (CART) therapy in non-Hodgkin’s lymphoma: the survival gain improves as more mature follow-up data become available

The TRANSCEND trial\(^1\) studied a cohort of more than 250 patients with relapsed/refractory non-Hodgkin’s lymphoma treated with the chimeric antigen receptor T-cell (CART) product, lisocabtagene maraleucel. This trial enrolled a high number of patients and included a relatively long follow-up (36 months).

Estimating the gain in overall survival (OS) for CART patients versus non-CART controls suffers from the lack of long-term survival information for CART. One advantage of the TRANSCEND trial is the availability of survival results at 36 months; this allows us to reliably determine the survival gain. To carry out this estimation, we kept in mind that the restricted mean survival time (RMST) is recognised to be the best outcome measure for managing long-term survival data.\(^2\)

To estimate the RMST resulting from lisocabtagene maraleucel, we analysed the OS reported in the TRANSCEND trial in comparison with long-term results observed in a large control population not given a CART (SCHOLAR-1 population).\(^3\)

We performed a first analysis with a time horizon of 36 months, and a second based on a lifetime horizon. The RMST was determined with the ‘survRM2’ R-platform package after reconstructing individual patient data as previously described.\(^4\) Extrapolation of survival to infinity (according to the Weibull function) was performed using the ‘eha’ R-platform package.\(^5\) The absolute death rate was 93.2/56 in the TRANSCEND trial\(^1\) and 505/603 for SCHOLAR-1 patients.\(^3\)

Our first analysis estimated a RMST at 36 months of 21.8 months (95% CI 19.7 to 23.9) for the CART cohort versus 12.9 months (95% CI 11.9 to 13.9) for controls; this indicates a gain of 8.9 months at 36 months. Our second analysis generated a mean lifetime survival of 54.8 months for CART versus 41.5 months for the controls; this yields an OS gain of 13.3 months.

In comparison with SCHOLAR-1 patients, tisagenlecleucel — the first CART approved for non-Hodgkin’s lymphoma — has been shown to determine a gain of 2.7 months in OS at 22 months (estimated as difference in RMST between 13.5 months for CART and 10.8 for the controls).\(^3\) In the case of axicabtagene ciloleucel — the other CART approved for non-Hodgkin’s lymphoma — the RMST for progression-free survival (PFS) at 30 months was 14.3 months,\(^5\) which is similar to the outcome found for tisagenlecleucel. The longer survival found in our analysis for lisocabtagene maraleucel (RMST around 22 months for OS compared with the results of the other two CART treatments (OS of 13.5 months for tisagenlecleucel\(^5\) and PFS of 14.3 months for axicabtagene ciloleucel\(^5\)) depends in part on the milestone at 36 months for lisocabtagene versus 22 months for tisagenlecleucel and 30 months for axicabtagene ciloleucel.\(^5\)

In our analysis, extending the time horizon to a lifetime perspective was interesting because this extrapolation showed that in comparison with no CART, the final incremental benefit of CART might go beyond 1 year of survival gain per patient.

In conclusion, the TRANSCEND trial is important because its results are more mature in terms of follow-up and more favourable than those previously reported for the other two CART treatments. This improvement in OS gain might have important pharmacoeconomic implications.

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