National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**26th May 2025 at 4.30pm**
Venue:	**Teleconference via MS Teams**
Assessment:	Brexucabtagene autoleucel Tecartus®
	Ivosidenib Tibsovo®

TEXT FOR REDACTION DUE TO DELIBERATIVE PROCESS HIGHLIGHTED IN YELLOW

TEXT FOR REDACTION DUE TO COMMERCIAL SENSITIVITY IS HIGHLIGHTED IN PINK

TEXT FOR REDACTION DUE TO CONFIDENTIALITY IS HIGHLIGHTED IN BLUE

Attendance:

Members present		
NCPE representative	National Centre for Pharmacoeconomics (NCPE)	By MS Teams
Patrick Hayden	Consultant Haematologist, St James's Hospital: IHS representative	By MS Teams
Prof Michaela Higgins	Medical Oncologist, St Vincent's University Hospital : ISMO nominee	By MS Teams
Fiona Mulligan	PCRS representative	By MS Teams
Dr Adrian Murphy	Medical Oncologist, Beaumont: ISMO nominee	By MS Teams
Ms Aishling McLoughlin	Chief I Pharmacist, NCCP (Deputy **Chair**)	By MS Teams
Dr Dearbhaile O'Donnell	Medical Oncologist, St James's Hospital: ISMO nominee	By MS Teams
Non-member invited specialists present		
Apologies (members)		
Dr Neil Barrett	Consultant Haematologist, Children's Health Ireland – Crumlin	
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	
Dr Dearbhaile Collins	Medical Oncologist, Cork University Hospital: ISMO nominee	
Dr Susan Spillane	HTA Directorate: HIQA nominee	
Observers present		
Dr Derville O'Shea	Consultant Haematologist, Cork University Hospital: IHS representative	By MS Teams
Ms Helena Desmond	Senior Pharmacist, NCCP	By MS Teams

Item	Discussion	Actions
1	**Introduction & reminder re. conflict of interest & confidentiality**	
	Members were reminded to raise any conflicts of interest that they had in relation to any drug for discussion prior to the commencement of the discussion of that item.	
2	**Notes of previous meeting and matters arising**	
	The notes of the previous meeting on May 1st 2025 were reviewed and agreed.	
3	**Drugs/Technologies for consideration**	
	Brexucabtagene autoleucel Tecartus® (Ref. TRC 174) *For the treatment of adult patients 26 years and above with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (ALL).* The clinical aspects of this indication were discussed, noting that tisagenlecleucel (Kymriah®), another CAR-T therapy is currently available for the treatment of relapsed or refractory (R/R) B-cell precursor ALL for paediatric and young adult patients up to and including 25 years of age. The supporting evidence for this indication comes from the ZUMA-3 trial, an ongoing, phase I/II, single arm, open label trial evaluating the use of brexucabtagene autoleucel for the treatment of adult patients 26 years of age and above with R/R B-cell precursor ALL. One hundred and twenty five patients were enrolled and brexucabtagene autoleucel was administered as a single once off intravenous (IV) infusion at a target dose of $1x10^6$ anti-CD19 CAR T cells/kg. The primary endpoint was overall complete remission (OCR) and after a median follow up of 2 and a half years, the trial demonstrated a clinically meaningful benefit for this patient cohort, with a OCR of 71%, minimal residual disease (MRD) negative was 76% and median OS at the 4 years analysis was 25.6 months, indicating a cure fraction or a durable long term remission. The safety profile was discussed, noting that the rate of cytokine release syndrome (CRS) and ICANS experienced with brexucabtagene autoleucel was very similar to other CAR-T products. There is a desire among the clinicians to have brexucabtagene autoleucel available for this patient cohort, while the current standard of care (SOC) options (blinatumomab and inotuzumab) are effective, in general there is a challenge in achieving remission in those with R/R disease, relapse following allogeneic stem cell transplant (SCT), and those who are ineligible for SCT, therefore representing a clinical unmet need. It is considered that brexucabtagene autoleucel would offer this cohort an effective treatment option that has the potential to induce a durable remission to facilitate allogeneic SCT. It was also noted the number of patients that would be eligible for treatment is relatively small. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The relevant comparators were outlined, and the proposed place in the treatment pathway was outlined. The supporting evidence was discussed and the NCPE Review Group highlighted a number of limitations in the trial, such as the single arm nature of the trial, small sample size and heterogeneous trial population. Indirect treatment comparisons (ITCs) were conducted to establish the relative effectiveness of brexucabtagene autoleucel versus the relevant comparators, the SCHOLAR-3 SCA-3 data set was used to inform efficacy of blinatumomab, and the INO-VATE study was used to inform efficacy of inotuzumab. The ITCs were discussed, and indicated that brexucabtagene autoleucel was associated with an improved event free survival (EFS) and OS compared to blinatumomab, and that brexucabtagene autoleucel may be associated with improved PFS and OS versus inotuzumab, however the NCPE review group highlighted concerns regarding the heterogeneity of trial populations, differences in the definition of outcomes across the studies and small sample sizes. The cost effectiveness analysis and the modelling used was outlined. In terms of cost, the price to the wholesaler for brexucabtagene autoleucel is €368,403. The total cost of brexucabtagene autoleucel including VAT is €419,979. The cost	

	of blinatumomab per treatment course, [redacted] and the cost of inotuzumab per treatment course, [redacted] In terms of the results of the cost effectiveness analysis for the Applicant's base case, the ICER versus blinatumomab is €55,992/QALY, and the ICER versus inotuzumab is €23,035/QALY. The NCPE made a number of changes, and the NCPE adjusted base case ICER versus blinatumomab is €88,787/QALY, and the ICER versus inotuzumab is €66,808/QALY. The price-ICER analysis, indicates that a 52% reduction in the price-to-wholesaler is required to meet the €45,000 per QALY threshold. In terms of the budget impact (BI), the Applicant assumed that 3 patient would be treated in year 1 increasing to 5 in year 2 onwards. However clinical opinion obtained by the review group indicated up to 10 patients would be treated per year (50 over 5 years), however there is uncertainty with regards to the BI estimates. Based on the NCPE-adjusted base case assumptions, the net BI over 5 years is estimated to be €15.83m including VAT and €12.63 excluding VAT. Overall the net BI considering the additional costs off sets, while very uncertain is estimated to be [redacted] including VAT. The NCPE recommends that brexucabtagene autoleucel not be considered for reimbursement unless the cost effectiveness can be improved relative to existing treatments. Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group subject to an improvement in cost. *(Decision: TRC 174)* **Ivosidenib Tibsovo® (Ref. TRC 175)** *As monotherapy for the treatment of adult patients with locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation who were previously treated by at least one prior line of systemic therapy.* The clinical aspects of this indication were discussed, noting that cholangiocarcinoma is a niche cancer, affecting approximately 200 patients per year in Ireland. Ivosidenib, an oral agent, is a first in class IDH1 inhibitor. The supporting evidence for this indication comes from the ClarlDHy trial, a phase III, randomised, double-blind, placebo-controlled trial, which evaluated the use of ivosidenib in patients with unresectable or metastatic cholangiocarcinoma with an IDH1 mutation following disease progression after prior therapy with at least one systemic therapy. The trial included 185 patients who were randomly assigned (2:1) in favour of ivosidenib. The trial permitted crossover from the placebo group upon disease progression, and 70% of the placebo group crossed over to receive ivosidenib. The primary endpoint was progression-free survival (PFS) by central independent radiology committee (IRC). Key secondary endpoint was overall survival (OS). The ClarlDHy trial demonstrated PFS in favour of ivosidenib 2.7 months versus 1.4 months with placebo, and numerically OS was favoured. To mitigate for bias caused by the crossover, a statistical tool, a rank-preserving structural failure time (RPSFT) was used for the analysis of OS, and the RPSFT- adjusted median OS was 5.1 months, in the placebo arm. The safety profile was discussed, ivosidenib was well tolerated, however there were concerns regarding arrhythmias due to its potential to prolongs QTc, and 3% of patients required a dose reduction due to QTc prolongation in the supporting trial. Other more serious adverse events highlighted are most likely overlying with the conditions itself such as jaundice and ascites, which are common symptoms of disease progression with this cancer. It is estimated that 200 patients per year present with cholangiocarcinoma in Ireland. In terms of IDH1 mutation, only 13% of the intrahepatic subtype harbour this mutation, and 1% of the extrahepatic subtype, usually with a 3:2	

	ratio in terms of intrahepatic vs extrahepatic in terms of presentation. Only 14% of patients are estimated to be eligible for second line treatment and there is a desire among the clinicians to have this available for this small patient cohort who harbour the IDH1 mutation. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The supporting evidence was discussed, and the NCPE Review Group highlighted a number of concerns with regards to the trial design in terms of the primary endpoint, PFS rather than OS, choice of control arm and confounding due to the crossover from the placebo arm. Indirect comparative methods were required to inform the relative effectiveness of ivosidenib versus the relevant active comparator, FOLFOX. The ABC-06 trial was used to inform the efficacy versus FOLFOX, the method was outlined and a number of limitations were highlighted by the NCPE review group such as the differences in trial design and patient demographics including cancer sites. In terms of the cost, the cost per treatment course of ivosidenib is estimated to be [redacted]. In terms of the results of the cost effectiveness analysis, for the Applicant's base case, the ICER versus FOLFOX is €170,243/QALY, with a total cost of €60,837 for FOLFOX and €135,948 for ivosidenib, and the ICER versus best supportive care (BSC) was €154,546/QALY. The incremental QALYs were 0.44 versus FOLFOX and 0.54 versus BSC. The NCPE review group made a number of adjustments which substantially increased the ICERS, and the NCPE adjusted base case ICER versus FOLFOX is €242,529/QALY and the ICER versus BSC is €228,276/QALY. In terms of the budget impact (BI), this is a very small cohort. The Applicant estimated that 42 patients would receive treatment over 5 years. In terms of the BI, the 5-year gross BI is estimated to be €3.39 million excluding VAT, and the 5-year net BI is estimated to be €3.3 million excluding VAT. The NCPE recommends that ivosidenib not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments. The price-ICER analysis, indicates that a reduction of 84.54% in the price to wholesaler of ivosidenib (versus FOLFOX), would be required to meet the €45,000/QALY threshold and a reduction of 86.46% in the price to the wholesaler of ivosidenib (versus BSC), would be required to meet the €45,000/QALY threshold. Having considered the clinical efficacy of the indication, the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group subject to an improvement in cost. *(Decision: TRC 175)*	
4	**Update on other drugs in the reimbursement process**	
	An update had been shared with the group in the documentation for the meeting	
5	**Next meeting**	
	The proposed date for the next meeting is Monday June 23rd 2025	
6	**Any other business / Next meeting**	

The meeting concluded at 17.30pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
25/05	26/05/2025	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
25/05	26/05/2025	Apply for CPD	NCCP	Complete