National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**29th January 2024 at 4.30pm**
Venue:	**Teleconference**
Assessment:	Cemiplimab (Libtayo®)
	Daratumumab (Darzalex®)

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 'phone
Dr Neil Barrett	Consultant Haematologist, Children's Health Ireland - Crumlin	By 'phone
Dr Dearbhaile Collins	Medical Oncologist, Cork University Hospital: ISMO nominee (Chair)	By 'phone
Ms Patricia Heckmann	AND NCCP	By 'phone
Dr Deirdre Kelly	Medical Oncologist, Beaumont: ISMO nominee	By 'phone
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	By 'phone
Ms Susan Spillane	HTA Directorate: HIQA nominee	By 'phone
Non-member invited specialists present		
Dr Patrick Hayden	Consultant Haematologist, St James's :IHS representative	By 'phone
Apologies (members)		
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	By 'phone
Ms Ellen McGrath	PCRS representative	By 'phone
Prof Michael O'Dwyer	Consultant Haematologist, Galway :IHS representative	By 'phone
Observers present		
Ms Helena Desmond	Senior Pharmacist, NCCP	By 'phone
Dr Derville O'Shea	Consultant Haematologist, Cork University Hospital: NCCP Clinical Lead for Haemato-Oncology	By 'phone

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 November 27th were agreed.	
3	**Drugs/Technologies for consideration**	
	Cemiplimab (Libtayo®) (Ref. TRC147) *As monotherapy for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma (CSCC) who are not candidates for curative surgery or curative radiation.* The clinical aspects of this indication were discussed. The evidence to support the use of cemiplimab for the treatment of CSCC comes from a number of phase I and II trials in which response rates were seen in 47 - 60% of patients. The supporting evidence for this indication is the phase II, open label, multicentre EMPOWER trial which evaluated the safety and efficacy of cemiplimab in patients with distant disease or locally advanced unresectable disease who were not candidates for surgery and radiation. The trial consisted of a number of groups with varying dose regimens. At a median duration of follow up of 15 months, from the data across the groups the study showed a median overall response rate (ORR) of 47%, 17% had a completed response and 30% had a partial response. Median duration of response (DOR) across the groups was 41%, median progression free survival (PFS) was 22 months and median overall survival (OS) was not reached for the total cohort, however for group 1 OS was 57 months. The safety profile of cemiplimab was discussed. In terms of toxicity seen across the trials, the grade 3 toxicities incidence is about 42% with the most common toxicity being hyperglycaemia, hypertension, myalgia, toxicities that are in keeping with the type of adverse events (AE's) seen with immunotherapies. AE's seen in the EMPOWER trial were in line with what was seen in previous studies. In terms of the current climate in Ireland, treatment for this cohort is chemotherapy with a median OS of 15 months, and the alternative, cetuxiamb (a median OS of 8 months). Overall, a rare disease in Ireland, with not a lot of good systemic therapy options with efficacy data that is seen with cemiplimab, therefore, there is a desire among clinicians to have this treatment option available for this patient cohort. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed.The supporting evidence was outlined, noting that the licensed indication recommends that cemiplimab be administered at fixed dose repeated every 3 week until disease progression, where as in the supporting trial, the EMPOWER trial, both a fixed and weight based dosing were use and a stopping rule at was implemented. The NCPE review group highlighted a number of limitations of the trial such as, small size, the single nature of the trial, lack of comparative evidence and difference in the regimens used in the trial. The review group highlighted concerns regarding the uncertainty of the treatment duration. The models for cost effectiveness used were outlined, the key limitation noted in the cost effectiveness modelling was the lack of direct comparative effectiveness estimates. In terms of the cost, with the assumption of no stopping rule the cost per treatment course for cemiplimab including [redacted]. If a treatment duration of 24 months is assumed for cemiplimab the cost per treatment course is [redacted] The cost of Cisplatin plus 5-Fluorouracil the main comparator [redacted] per treatment course	

and [redacted]. In terms of the ICERS, the ICER in the applicant's base case was €62,767 per QALY. The NCPE-adjust base case is estimated to be €105,083 per QALY, a 75% total reduction inclusive of the framework agreement rebate that is currently 8.5% is required to reduce the ICER to €45k per QALY. In terms of the budget impact (BI) it is estimated that 17 patients will be treated with cemiplimab at year-1 rising to 51 in year-5, this results in a 5-year gross BI estimated to be €39.56 million including VAT and a net BI estimated to be €39.49 million including VAT. The applicant BI assumes a much lower patient incidences with a 5-years gross and net BI estimated to be ~€9 million including VAT. The NCPE recommends that cemiplimab not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatment.

Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed by majority to recommend approval of this indication to the HSE Drugs Group.

(Decision: TRC 147)

Daratumumab (Darzalex®) **Ref. TRC 148**

In combination with lenalidomide and dexamethasone (Rd) for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant.

The clinical aspects of this indication were discussed. The supporting evidence for this indication is the open label, phase III, randomised trial, the MAIA trial, which compared the use of daratumumab in combination with lenalidomide and dexamethasone (Rd) versus Rd alone. The study showed that for daratumumab in combination with lenalidomide and dexamethasone (DRd) both a progression free survival (PFS) and overall survival (OS) advantage was seen. At a median follow up of 64 months, the median PFS in the DRd arm was 61.9 months (~>5 years) and 34 months in the Rd arm (~<2 years), giving a ≥ 2 years PFS advantage. For OS, the hazard ratio (HR) was 0.66, and at the 73 month follow up OS was not reached in the DRd arm vs 64 months in the Rd arm. There is desire among the clinicians to have this treatment available to this patient cohort given the improvement in PFS and OS.

The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The relevant comparators and comparativeness treatment analysis was outlined, the NCPE review group highlighted number of key limitations with the analysis which include the heterogeneity in terms of study design, inclusion criteria, outcome definition, patient baseline characteristics, treatment regimens and duration of follow up. In terms of the clinical safety, the safety profile of DRd was worse than that of Rd, however the additional toxicity reflects clearly the known profile of daratumumab and the majority of adverse events (AEs) are manageable and there were no new safety findings. The cost effectiveness modelling was outlined and adjustments to the model were made, the review group highlighted concerns regarding length of the treatment effect. In terms of cost, the cost per treatment course of DRd is €452,520 including VAT compared to Rd €75,000 including VAT, bortezomib/lenalidomide plus dexamethasone (RVD) is €79,000 including VAT, bortezomib/melphalan plus prednisolone (bort/Mel/pred) is €16,000 including VAT, and bortezomib, Cyclophosphamide and dexamethasone (CyBorD) is €4,500 including VAT. In terms of the ICERS in comparison to Rd the NCEP-adjusted based case ICER was €208,803 per QALY, for the comparison to RVD the NCEP-adjusted based case ICER was €290,725 per QALY, for the comparison to Bort/Mel/Pred the NCEP-adjusted based case ICER was €153,709 per QALY, and for the comparison CyBorD the NCEP-adjusted based case ICER was €152,681 per QALY. [redacted]

	[redacted]. In terms of the budget impact (BI) the cumulative 5-yr gross BI (based on the list price) is estimated to be €130.18 million including VAT, and the cumulative 5-yr net BI is estimated to be €119.78 million including VAT. [redacted]. The NCPE recommends that daratumumab not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatment. It was noted that even at €0 cost that this combination treatment could not reach the required cost effectiveness thresholds. This is a challenge for combination treatments where the combination drugs individually are high cost. Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed by majority to recommend approval of this indication to the HSE Drugs Group. One member abstained from voting, however quorum in place. *(Decision: TRC 148)*	
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 February 26th 2024	
6	**Any other business / Next meeting**	

The meeting concluded at 17.40pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
24/01	29/01/2024	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Completed
24/01	29/01/2024	Apply for CPD	NCCP	Completed