National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**26th February 2024 at 4.30pm**
Venue:	**Teleconference**
Assessment:	Pembrolizumab (Keytruda®)
	Polatuzumab vedotin (Polivy®)

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
Dr Patrick Hayden	Consultant Haematologist, St James's :IHS representative	By 'phone
Prof Michaela Higgins	Medical Oncologist, St Vincent's University Hospital: ISMO nominee	By 'phone
Ms Fiona Mulligan	PCRS representative	By 'phone
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	By 'phone
Dr Susan Spillane	HTA Directorate: HIQA nominee	By 'phone
Non-member invited specialists present		
Apologies (members)		
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	
Prof Michael O'Dwyer	Consultant Haematologist, Galway :IHS representative	
Observers present		
Ms Patricia Heckmann	AND NCCP	By 'phone
Ms Helena Desmond	Senior Pharmacist, NCCP	By 'phone
Ms Maryam Paruk	Senior Pharmacist, NCCP	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 January 29th were agreed.	
3	**Drugs/Technologies for consideration**	
	Pembrolizumab (Keytruda®) **(Ref. TRC149)** *In combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, is indicated for the treatment of adults with locally advanced, or early stage triple negative breast cancer at high risk of recurrence.* The clinical aspects of this indication were discussed. The supporting evidence for this indication is the Keynote 522 trial, an ongoing, international trial to compare standard chemotherapy alone before surgery versus pembrolizumab in combination with chemotherapy before surgery, followed by adjuvant pembrolizumab in patients with locally advanced, or early stage triple negative breast cancer (TNBC) at high risk of recurrence. The co-primary endpoints were pathological complete response (pCR) and event free survival (EFS), the secondary endpoint was overall survival (OS). At the first results read out, the study showed that the pCR in patients treated with chemotherapy alone was ~55%, while in those treated with pembrolizumab plus chemotherapy was 64%. At the second read out, EFS at 24 months had significantly increased with the addition of pembrolizumab from 81% with chemotherapy alone to 87.8% with pembrolizumab plus chemotherapy. After a median follow up of 5 years, EFS in patients who received chemotherapy alone was 72% and 81% in patients treated with pembrolizumab and chemotherapy, hazard ration (HR) 0.63. At 5 years, the absolute difference in EFS was 9%, which is considered to be a highly significant and meaningful difference in EFS, in a TNBC population EFS would be expected to correlate very completely with OS, however OS is ongoing for this study. The safety profile of pembrolizumab was discussed, the side effects were as expected with pembrolizumab, but not insignificant. Immune-mediated adverse events of grade 3 and higher were seen in almost 13% of patients in the pembrolizumab arm, such as pneumonitis, colitis, endocrinopathies and hepatitis. Non-immune-mediated adverse events were also higher among patients treated with pembrolizumab, however it was noted that clinicians have become better managing these. This is a meaningful intervention, and there is a strong desire among the clinicians to have this treatment option available to this patient cohort who unfortunately have a very poor prognosis. It was noted that pembrolizumab in this setting has been available as an expanded access programme (now closed), and therefore clinicians have experience of its use in the treatment of TNBC and would prefer to treat this patient cohort with the best curative option in the early disease setting. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The relevant compactors were discussed, and it was noted that while capecitabine is used in the adjuvant setting for patients with residual disease, it was not considered a relevant comparator. The NCPE Review Group highlight a number of limitations regarding the supporting evidence, the key limitation being that OS data was immature. The cost effectiveness modelling was outlined and a number of limitations in the Applicant's model were highlighted, such as the immaturity of the EFS	

	data, a piece wise approach to the modelling of EFS data, overestimation of the long term TNBC recurrence risk, assumption of the life lone treatment effect. In terms of the cost, in the neoadjuvant setting pembrolizumab plus chemotherapy including VAT is €58,452, and €46,782 excluding VAT. Pembrolizumab monotherapy in the adjuvant setting is €61,885 including VAT and €49,481 excluding VAT versus [redacted] In terms of the ICERS, the ICER in the applicant's base case was estimated to be €44,001 per QALY. Changes were made to the NCPE-adjust base case and was estimated to be €66,186 per QALY. When considering the PAS included, the NCPE-adjust base case falls below the 45k per QALY and the probability of cost effectiveness would increase to ~73%. In terms of the budget impact (BI), 141 patients are estimated to bel eligible for neo-adjuvant treatment with pembrolizumab plus chemotherapy in year 1, rising to 147 in year 5. For adjuvant pembrolizumab 101 patients will be eligible in year 1 rising to 105 in year 5. The 5-year gross BI was an estimated €67 million including VAT and the net BI was an estimated to be €64 million including VAT. However the review group consider the estimated BI to be underestimated. When considering the PAS, the BI estimates reduce, but are still considerable at [redacted] VAT over 5 years. The NCPE recommends that pembrolizumab 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 unanimously to recommend approval of this indication to the HSE Drugs Group. *(Decision: TRC 149)* One member absent from voting, however quorum was in place. Polatuzumab vedotin (Polivy®) **Ref. TRC 150** *In combination with riTUXimab, cyclophosphamide, DOXOrubicin, and prednisone (R-CHP) for the treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL).* The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III, randomised double blind trial, the POLARIX trial, which evaluated the use of polatuzumab vedotin (pola) in combination R-CHP (pola-R-CHP) compared with standard riTUXimab, cyclophosphamide, vincristine, DOXOrubicin, and prednisone (R-CHOP) therapy in patients with previously untreated intermediate-risk or high-risk DLBCL. The study showed that the 2 year progression free survival (PFS) improved from 70.2% in the R-CHOP arm to 76.7% in the pola-R-CHP arm, however there was no difference in overall survival (OS). The trial also demonstrated greater benefit in patients with high IPI 3-5 disease. The addition polatuzumab vedotin is a significant change in the treatment of de novo DLBCL, for the past two decades R-CHOP has been the standard of care for newly diagnosed DLBCL. pola-R-CHP is recommended by international guidelines such as NCCN, and there is desire among the clinicians to have this treatment available to this patient cohort, it was noted that salvage options for this patient cohort is now CAR-T and a 6% improvement in PFS would have a significant impact on the number of patient who would progress to CAR-T. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The place in therapy was outlined, noting that pivotal trial evaluated the use of pola-R-CHP in patients with an IPI score of 2-5, which is narrower than the licensed indication, clinical opinion obtained by the NCPE review group considered this reasonable. The supporting evidence was outlined, at the most recent data cut median PFS and OS had not reached in either arm, and the review group considered	

	immaturity of the data as a substantial limitation. The safety profile of pola-R-CHP was discussed and it is associated with a high incidence of grade 3 or higher adverse events mainly myelosuppression and infection, however it was noted that the toxicity profiles between pola-R-CHP and R-CHOP were very similar, with a higher rates of diarrhoea and neutropenia associated with pola-R-CHP. The cost effectiveness modelling was discussed, the model population was based on the POLARIX trial population, which is narrower than the licensed population but considered by the review group to be reflective of the population being treated in clinical practice. The NCPE review group identified a number of concerns and limitations regarding the modelling and changes were made to the NCPE-adjusted base case. In terms of cost, pola-R-CHP is associated with cost per treatment per course of €80,303 including VAT (€64,359 excluding VAT) compared to R-CHOP where treatment cost per course including VAT is of €12,850 including VAT (€10,459 excluding VAT). In terms of the ICERS the applicant base case was estimated to be €37,352 per QALY.A number of changes to the NCEP adjusted base case were made and the NCPE adjusted base case was estimated to be €97,744 per QALY. The probability of cost effectiveness at the €20,000 per QALY threshold is 1% using the NCPE adjusted base case, and is 11% at the €45,000 per QALY threshold. [redacted] A PAS is currently in place for polatuzumab vedotin, however further reduction is required to reach the €20,000 per QALY threshold. In terms of the budget impact (BI), it is estimated that 32 patients will be treated in year 1, increasing to 69 patients by year 5. The gross BI is estimated to be €20.8million including VAT, and net BI is estimated to be €17.5 million including VAT over 5 years. The review groups noted that drug cost are significantly underestimated. When you consider the [redacted]. The NCPE recommends that polatuzumab vedotin not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatment. It was noted that NICE and SMC have approved the use of pola-R-CHP with a restriction to patients with IPI 2-5 disease. 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, with the restriction to patients with an IPI score of 2-5 to align with supporting the POLARIX trial and BSH guidelines. One member absent from voting, however quorum was in place. *(Decision: TRC 150)*	
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 March 25th 2024	
6	**Any other business / Next meeting**	
	The Chair welcomed new member Dr Patrick Hayden to the committee, who has replaced Dr Ronan Desmond.	

The meeting concluded at 17.40pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
24/01	26/02/2024	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
24/01	26/02/2024	Apply for CPD	NCCP	Complete