National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**2nd December 2024 at 4.30pm**
Venue:	**Teleconference via MS Teams**
Assessment:	Olaparib (Lynparza®)
	Trastuzumab deruxtecan (Enhertu®)

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
Dr Neil Barrett	Consultant Haematologist, Children's Health Ireland - Crumlin	By MS Teams
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	By MS Teams
Dr Dearbhaile Collins	Consultant Medical Oncologist, Cork University Hospital: ISMO nominee **(Chair)**	By MS Teams
Prof Michaela Higgins	Consultant Medical Oncologist, St Vincent's University Hospital: ISMO nominee	By MS Teams
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	By MS Teams
Ms Fiona Mulligan	PCRS representative	By MS Teams
Non-member invited specialists present		

Apologies (members)	
Dr Patrick Hayden	Consultant Haematologist, St James's :IHS representative
Prof Michael O'Dwyer	Consultant Haematologist, Galway :IHS representative
Dr Susan Spillane	HTA Directorate: HIQA nominee
Observers present	
Ms Patricia Heckmann	AND, NCCP
Ms Aishling McLoughlin	Chief I Pharmacist, NCCP
Ms Helena Desmond	Senior Pharmacist, NCCP

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 October 21st were reviewed and agreed.	
3	**Drugs/Technologies for consideration**	
	Olaparib (Lynparza®) (**Ref. TRC 163)** *As monotherapy or in combination with endocrine therapy for the adjuvant treatment of adult patients with germline BRCA1/2-mutations who have HER2-negative, high risk early breast cancer previously treated with neoadjuvant or adjuvant chemotherapy.* The clinical aspects of this indication were discussed. It was noted that clinicians are very familiar with olaparib which is currently approved for use in some gynaecological cancer and metastatic breast cancer. The supporting evidence for this indication comes from the OlympiA study, a phase III, randomised, double-blind study which compared olaparib to placebo for the adjuvant treatment of HER-2 negative early breast cancer in patients with *BRCA1/2*-mutations at high risk of recurrence. The study demonstrated efficacy for olaparib, at the primary analysis (March 2020), invasive disease free survival (IDFS) had significantly improved in patients treated with olaparib, with a HR of 0.58. Distant disease free survival (DDFS) was also improved, as was overall survival (OS) with some maturity reported at a later analysis, showing a statistically significant improvement in OS with a HR of 0.68 and a p-value of 0.0091. It was noted, that those eligible for recruitment to the OlympiA, were patients with *BRCA* mutated early breast cancer with high risk disease that warranted treatment chemotherapy, for patients who were hormone receptor (HR) positive, high risk disease was defined as those with greater than 4 nodes positive. It is anticipated that selection of eligible patients in clinical practice will replicate the OlympiA study in selecting the patients who are at high risk. The current treatment options were discussed, noting that while this is now a crowded space, olaparib would be a suitable treatment option for *BRCA* mutated patient compared to the current standard of care such as pembrolizumab, abemaciclib or capecitabine. The safety profile was discussed, noting that clinicians are familiar with olaparib due to its used in other cancers, and therefore familiar with treatment monitoring and side effect profile. It was also noted that olaparib would offer *BRCA* mutated patients a less toxic treatment option compared to pembrolizumab which has been associated with a high risk of grade 3 toxicities when used in the treatment of breast cancer. There is a desire among the clinicians to have olaparib available for *BRCA* mutated patients with early breast cancer, at high risk of recurrence. It was also noted that the use of olaparib in this setting is recommended by international guidelines such as NCCN, and approved for use in other jurisdictions such as NICE and SMC. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The relevant comparators were outlined. The supporting evidence was outlined, noting that while, the trial initially included only patients with triple negative breast cancer (TNBC), a protocol amendment took place to allow the inclusion of patients with HR positive disease, however the number of HR positive patients enrolled in the OlympiA was low. In terms of the outcome data, at the second data cut (July 2020) at a median follow up of 3.5 years, the HR for IDSF was 0.63, 95% confidence interval (CI) 0.5- 0.7, the HR for DDFS was 0.61 and the HR for OS was 0.86, demonstrating an statistically significant and clinically meaningful benefit in both OS and IDFS. The NCPE Review Group highlighted a number of limitations, such as the immaturity of the survival data, over representation of the proportion of TNBC patients in comparison with clinical practice and imbalances in the subsequent treatment between the oplaraib arm and placebo arm. The cost effectiveness analysis was discussed and the modelling used was outlined. In terms of the results, the Applicant provided	

a separation of results based on the Intention to treat (ITT) population, the TNBC population and the HR positive HER2 negative population. Based on the ITT population, the Applicant's ICER is , an adjustment was made to the made to the NCPE-adjusted base case and the NCPE adjusted base case is . The review group highlighted a significant uncertainty in terms of the magnitude of treatment effect in the HR positive subgroup given the late protocol amendment in the OlympiA trial. In terms of reaching cost effectiveness at the willingness to pay threshold of €45,000 per QALY, a reduction of approximately 30% in the QALY would be required. In terms of the budget impact (BI) the total eligible populated is estimated that 41 patients will be treated in year 1, rising to 66 patients in year 5, however the total treated population is estimated to be 24 in year 1 increasing to 49 in year 5, which is associated with a gross BI of €10.41 million over 5 years. The NCPE recommends that olaparib be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments, it was considered to provide additional benefit, however the magnitude of long term benefit is uncertain due to the immaturity of the clinical trial data particularly for the HR positive cohort who were under represented in the trial.

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 163)

Trastuzumab deruxtecan (Enhertu®) **(Ref. TRC 164)**

As monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-low breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.

The clinical aspects of this indication were discussed, noting that trastuzumab deruxtecan is currently approved for reimbursement for HER2 positive breast cancer. The supporting evidence for this indication is the DESTINY-Breast04 trial, a phase III, randomised open-label study evaluating the use of trastuzumab deruxtecan compared to physician's choice of chemotherapy (TPC) for the treatment of adult patients with unresectable or metastatic HER2-low breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. The study included approximately 577 patients, with the vast majority of patients being hormone receptor (HR) positive. The study showed similar results for the HR positive cohort and the overall population, treatment with trastuzumab deruxtecan resulted in a doubling in median progression free survival (PFS) from approximately 5 to 10 months and this was echoed in overall survival (OS) of approximately 6 months. Median OS increased from approximately 17 to 23.5 months, demonstrating a meaningful statistically significant improvement in both PFS and a survival advantage of 6 months. The safety profile was discussed, noting that this is a quite toxic drug. However the clinicians have considerable experience with trastuzumab deruxtecan in the metastatic setting and through compassionate use programmes (CPUs), with this increased use, clinicians have become more comfortable with managing the associated side effects, such as pneumonitis/ interstitial lung disease (ILD), neutropenia, nausea, alopecia, for example and it was noted that careful patient selection is required. While there are alternative treatment options available for metastatic breast cancer, these offer efficacy rates of approximately 10%, with no meaningful response, therefore there is a desire among the clinicians to have this treatment available for this cohort of patients, which offers a small, but significant improvement in PFS and OS for this patient cohort.

The pharmacoeconomic aspects as outlined in the HTA assessment carried

	out by the NCPE were discussed. The positioning of trastuzumab deruxtecan in the treatment pathway and relevant comparators were discussed. The supporting evidence was outlined, noting this trial provided direct evidence against the comparators used in Irish clinical practice and that trastuzumab deruxtecan when compare to chemotherapy showed a statistically significant benefit. The NCPE Review Group highlighted a number of limitations regarding the supporting evidence, such as open label nature of the trial, the limited sample of the TNBC/HR negative subgroup, and the lack of comparative effectiveness against sacituzumab govitecan. The cost effectiveness analysis and the modelling used was outlined. In terms of cost, the total cost per treatment course for trastuzumab deruxtecan was €125,134 including VAT and €99,998 excluding VAT, considerably more expensive when compared TPC regimens, for example eribulin, which costs €18,000 including VAT, but cheaper that sacituzumab govitecan. However it was considered that the cost of sacituzumab govitecan was over estimated, as it was assumed that the treatment duration of trastuzumab deruxtecan is equivalent to sacituzumab govitecan. In terms of the results, the applicant's ICER is €124,741 per QALY. A number of changes were made to the NCCP base case which resulted in a NCPE-adjusted base case ICER of €153,730 per QALY. There is 0% probability of cost effectiveness in either the Applicant or the in the NCPE base case at both willingness to pay thresholds (€20,000/€45,000 per QALY) and a 68.7% reduction in the price to the wholesaler is required in order for the willingness to pay threshold of €45,000 per QALY to be reached. In terms of the budget impact (BI), the total eligible patients is estimated to be 79 in year 1, rising to 102 patients in year-5, based on the NCPE assumptions 59 patients are estimated to be treated in year 1 increasing to 87 in year 5. The cumulative net drug BI based on the list price is estimated €42.8 million include VAT, a.The NCPE recommends that trastuzumab deruxtecan be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments, it was considered to provide additional benefit, however it is associated with considerable additional costs. 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, subject to an improvement in cost. *(Decision: TRC 164)*	
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 January 27th 2025	
6	**Any other business / Next meeting**	

The meeting concluded at 17.15pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
24/01	02/12/2024	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
24/01	02/12/2024	Apply for CPD	NCCP	Complete