National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**24th April 2023 at 4.30pm**
Venue :	**Teleconference**
Assessment:	Olaparib (Lynparza®)
	Sacituzumab govitecan (Trodelvy®)

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 Dearbhaile Collins	Medical Oncologist, Cork University Hospital: ISMO nominee	
Ms AnneMarie De Frein	NCCP Chief I Pharmacist - Chair	By 'phone
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative	
Dr Michael Fay	Consultant Haematologist, Mater Hospital: IHS representative	By 'phone
Prof Michaela Higgins	Medical Oncologist, St. Vincent's University Hospital: ISMO nominee	By 'phone
Dr Helen O'Donnell	HTA Directorate: HIQA nominee	By 'phone
Prof Michael O'Dwyer	Consultant Haematologist, Galway : IHS representative	By 'phone
Ms Ellen McGrath	PCRS representative	By 'phone
Non-member invited specialists present		

Apologies (members)	
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee

Observers present		
Ms Helena Desmond	Senior Pharmacist, NCCP	By 'phone
Ms Margaret Triggs	Chief II 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 March 27th were agreed.	
3	**Drugs/Technologies for consideration**	
	Olaparib (Lynparza®) (Ref. TRC 132) *In combination with bevacizumab for the maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following first-line platinum-based chemotherapy in combination with bevacizumab and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either a BRCA1/2 mutation and/or genomic instability.* The clinical aspects of this indication were discussed, noting that both olaparib and bevacizumab are already available as single agents in the treatment of ovarian cancer for specified indications, but have not been previously used in combination. The supporting evidence for this indication is the phase III PAOLA-1 trial which evaluated the safety and efficacy of olaparib in combination with bevacizumab for the maintenance treatment of newly diagnosed patients with advanced high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer following first-line platinum-based chemotherapy and bevacizumab. The study showed that treatment with olaparib in combination with bevacizumab demonstrated a definite benefit in progression free survival (PFS), however overall survival (OS) data is immature. The median PFS was 22.1 months for the combination treatment vs 16.6 months with bevacizumab treatment alone, and a Hazard Ratio (HR) of 0.59. In the subgroup analysis, the study showed that patients with a *BRCA* mutation performed significantly better with combination therapy than with bevacizumab alone (37 vs 21 months). In the HRD-positive sub-group population with a *BRCA* mutation PFS was 37.2 months in those treated with combination therapy vs 17.7 months in those treated with bevacizumab alone, and in the HRD-positive subgroup population without a *BRCA* mutation PFS was 20.1 vs 16.6 months showing a definite benefit in PFS with combination treatment. The safety profile was discussed, noting that the side effects are consistent with the known safety profile of the drugs individually. It was discussed that the evidence in this space is still evolving, and that it will be informative clinically to learn if the benefits seen in PAOLA-1 are retained when this combination is compared to olaparib monotherapy for this patient cohort, noting that some trials are looking at this but results may be impacted by crossover. It was additionally discussed that HRD testing is not currently available and would need to be in place to support. Noting this, it was outlined that there is a desire among clinicians to have this treatment option available for this cohort of patients. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The supporting evidence was outlined and a number of concerns were highlighted by the review group, such as the immaturity of the OS data, lack of direct evidence and uncertainty with regards to the overall clinical efficacy of the combination. A number of adjustments were made for different scenarios and this was outlined. The HRQOL showed no meaningful change from baseline. The cost effectiveness model used was discussed, and the cost of olaparib is estimated to be €66,313.71 and the annual cost of bevacizumab was based on the maximum acceptable price, noting biosimiars are available. The ICER was outlined based on the applicant's base case at €18,667 per QALY for the HRD positive population and at €80,340 per QALY for the *BRCA* mutated sub-population. In the NCPE exploratory analysis for the HRD positive population the ICER was	

	estimated to be €25,221 per QALY. The budget impact (BI) was outlined, with a 5 year gross BI estimated to be €14.1 million including VAT, €13.4 million excluding VA, and 5 year net BI estimated €9.16 million including VAT and €9 million excluding VAT. The recommendation of the NCPE review group is that olaparib in combination with bevacizumab be considered for reimbursement if cost effectiveness can be improved. 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 132)* Sacituzumab govitecan (Trodelvy®) (**Ref. TRC 133)** *As monotherapy for the treatment of adult patients with unresectable or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease.* The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III, open label, randomised, ASCENT study, which evaluated the safety and efficacy of sacituzumab govitecan compared to a treatment of the physicians choice in the treatment of adult patients with unresectable or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease. The primary endpoint was progression free survival (PFS) in patients without brain metastases, the secondary endpoints were PFS in the total population and overall survival (OS). The study showed a significant improvement in PFS in the sacituzumab govitecan arm with an improvement of 4.8months in the total population, (and 5.6 months in the population without brain metastases) vs 1.7 months in the chemotherapy arm, with a hazard ratio (HR) of 0.4. In addition to a good PFS, the study showed almost a doubling in OS from approximately 6 to 12 month. Clinically, this is a cohort of very sick patients and the use of sacituzumab govitecan demonstrated a very meaningful PFS and OS advantage, with significant advantages for the patient cohort including good response rates. The safety profile was discussed nothing that sacituzumab govitecan is quite toxic and is associated with chemotherapy type side effects, notably diarrhoea, nausea and neutropenia. It was noted that while there will be a learning curve with this drug, given that the side effect profile is typical of chemotherapy drugs, the clinicians are experienced in managing these toxicities. There is a strong desire among clinicians to have this treatment option available for this cohort of patients. Currently there is a significant unmet need in the management of these very sick patients with a poor prognosis and sacituzumab govitecan would offer these patients a significant clinical benefit. The pharmacoeconomic aspects as outlined in the HTA carried out by the NCPE were discussed. The supporting evidence was outlined and the NCPE review group highlighted some limitations of the study, such as the open label nature of the study and the potential for bias in the measurement of subjective outcomes. The cost effectiveness model used was also outlined and number of limitations in the applicant's base case were identified, to which the NCPE review group made a numbers of adjustments. The review group also raised uncertainty regarding potential patient numbers as up take may be higher than estimated due to lack of other treatment options, however clinicians feel that due its safety profile this treatment will not be suited to all patients, especially, frail and elderly patients. Considering cost effectiveness sacituzumab govitecan is significantly more expensive than the current standard of care chemotherapy at a cost of €82,116 including VAT, €65,792 excluding VAT. The ICER was outlined based on the applicant's base case at €129,356 per QALY and the NCPE adjusted base case €216,138 per	

	QALY. In terms of price, a price reduction of [redacted] is required to bring the ICERS to below the €45k/QALY threshold. The budget impact (BI) was discussed, with 11 patients estimated to be treated in year 1 rising to 17 in year 5. The 5 year gross BI is estimated to be €6.05 million including VAT and the 5 year net BI is estimated to be [redacted] million including VAT. The applicant proposed a PAS in their submission, offering a reduction of [redacted], which in the applicant base case would reduce the ICER to [redacted] per QALY. In terms of BI when considering the proposed PAS offer, this would reduce the 5 year gross BI [redacted] million including VAT. The recommendation of the NCPE review group was to recommend reimbursement subject to the PAS offer being agreed. Having considered the clinical efficacy of the indication in this patient cohort the committee members agreed by a majority to recommend approval of this indication to the HSE Drugs Group. *(Decision: TRC 133)*	
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 May 22nd 2023	
6	**Any other business / Next meeting**	
	TRC Membership Changes: The Chair welcomed Dr Dearbhaile Collins to her first meeting with the committee as an ISMO nominated member. It was also announced that Ms AnneMarie De Frein will be stepping down as Chair of the committee, as she is leaving the NCCP. The NCCP National Director will appoint a replacement in the coming weeks, in the interim Ms Patricia Heckmann will act as Chair. CPD: Dr Dearbhaile Collins volunteered to complete the CPD survey for this TRC meeting	NCCP

The meeting concluded at 5.55pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
23/01	27/03/2023	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Completed
23/01	27/03/2023	Apply for CPD	NCCP	Completed