National Cancer Control Programme

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**January 24th 2022 at 4.30pm**
Venue :	**Teleconference / NCCP Offices**
Assessment:	Blinatumomab BlinCyto®
	Darolutamide Nubeqa®
	Entrectinib Rozlytrek®
	Olaparib Lynparza®

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 representatives	National Centre for Pharmacoeconomics (NCPE)	By 'phone
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	By' phone
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative	By 'phone
Dr Mark Doherty	Medical Oncologist, St. Vincent's University Hospital: ISMO nominee	By 'phone
Dr Michael Fay	Consultant Haematologist, Mater Hospital: IHS representative	By 'phone
Ms Patricia Heckmann	NCCP AND - Chair	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 Derville O'Shea	Consultant Haematologist, Cork University Hospital: IHS representative	By 'phone
Dr Susan Spillane	HTA Directorate: HIQA nominee	By 'phone
Non-member invited specialists present		

Apologies (members)	
Dr Linda Coate	Medical Oncologist, University Hospital Limerick: ISMO nominee
Dr Eve O'Toole	Research Group Lead, NCCP
Observers present	
Ms. AnneMarie De Frein	Chief 2 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. None were raised.	
2	**Notes of previous meeting and matters arising**	
	The notes of the previous meeting on November 29th 2021 were agreed.	
3	**Drugs/Technologies for consideration**	
	Blinatumomab BlinCyto® (**Ref. TRC 101)** *For the treatment of paediatric patients aged 1 year or older with high-risk first relapsed Philadelphia chromosome negative CD19 positive B-precursor acute lymphoblastic leukaemia as part of consolidation therapy.* It was noted that this is an additional indication for the use of blinatumomab as monotherapy for the treatment of paediatric patients at high-risk of relapse as part of consolidation treatment. The clinical aspects of this indication were discussed, noting that this is a rare disease and there is an unmet need in terms of availability of effective and less toxic treatment for this patient cohort. The supporting evidence was a phase III study, study 2012015, evaluating the efficacy and safety of blinatumomab as consolidation therapy versus conventional consolidation chemotherapy in paediatric patients with high-risk first relapse B-precursor ALL. The study demonstrated a statistically significant improvement in event free survival (EFS) compared to conventional consolidation chemotherapy. Clinically, it was outlined that the use of blinatumomab is understood to be more effective and less toxic than the current cytotoxic chemotherapy standard of care options (SOC). The safety profile was discussed, noting that clinicians are familiar with this drug and no new safety concerns were identified. It was highlighted that this indication is standard of care (SOC) in the UK and supported by a number of international children's cancer groups. There is a desire from clinicians to have this treatment made available to this patient cohort noting unmet need, and ensuring that these patients are treated according to best international practice and that children are not exposed to old chemotherapy regimens that add toxicity at the expense of efficacy. The pharmacoeconomic aspects as outlined in the rapid review assessment carried out by the NCPE were discussed, including that one treatment cycle is assumed per patient with a small number of patients anticipated per year, although some uncertainty was flagged in the assessment. Considering the anticipated low number of patients with high risk disease the budget impact is likely to be small. Having considered the clinical efficacy of the indication and the unmet need, the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness. *(Decision: TRC 101)*	

Darolutamide Nubeqa® (**Ref. TRC 102) FOR INFORMATION ONLY**

For the treatment of adult men with non-metastatic castration-resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease.

The group was informed by the Chair that this application for reimbursement is being progressed as a cost minimisation piece by the PCRS. All agreed that that darolutamide should be made available for reimbursement for this patient cohort.

Entrectinib Rozlytrek® (**Ref. TRC 103)**

As monotherapy for the treatment of patients with ROS1-positive advanced non-small cell lung cancer (NSCLC) not previously treated with ROS1 inhibitors

The NCPE representative summarised the rapid review assessment, noting that a full health technology assessment was not recommended. This is an orally administered agent to treat adult patients with ROS1-positive, advanced NSCLC in the first line setting. The phase II, single arm, basket trial, STARTRK-2, evaluated the efficacy and safety of entrectinib in patients with locally advanced or metastatic solid tumours that harbour NTRK 1/2/3, ROS1, or ALK gene arrangements. While the efficacy data were immature, the trial demonstrated that entrectinib had an objective response rate (ORR) of 73.4% in patients with ROS-1 positive NSCLC, with the median duration of response (DoR) of 16.5 months and median progression free survival (PFS) of 16.8 months. Entrectinib appears to have greater CNS activity than crizotinib, therefore its use is considered to be preferable in patients with brain metastases. However no direct comparator studies have been conducted and in light of this a conditional MA (marketing authorisation) was granted subject to conducting a randomised controlled trial versus crizotinib in treatment naïve ROS1-positive NSCLC patients.

The safety profile was discussed with the most frequently reported adverse events (AEs) of any grade, included fatigue, constipation, dysgeusia, dizziness diarrhoea and nausea. The CHMP concluded that the safety data is of limited extent, in terms of the disease and rarity of ROS1-positive NSCLC but the AEs are considered manageable.

From a pharmacoeconomic aspect, the cost of entrectinib is significant compared to the cost of the relevant compactors, crizotinib and chemotherapy. Commercial negotiations with the company are ongoing to consider this. There is some uncertainty regarding the budget impact due to the rarity of ROS-1 mutation. It was flagged that entrectinib is also licensed for adult and paediatric patients ≥12 with solid tumours expressing NTRK gene fusion, which the company have not yet submitted an application for reimbursement. There was a discussion on NTRK testing, noting that there is no testing pathway in place in Ireland to date. The NCPE have flagged in their rapid review assessment that a managed access programme may be required for this ROS1 indication. The group agreed that this was not for the TRC members to consider within their recommendation.

Based on the clinical effectiveness (especially in patients with CNS metastases), manageable safety profile, and small patient numbers the clinicians expressed a desire to have this treatment available, noting that there are very small numbers of patients with ROS1 mutation. It was clarified that of the subpopulation of the study patients with CNS disease, there was a high response rate which was understood to be impressive for that patient cohort.

Having considered the clinical efficacy of the indication, the committee members agreed by majority to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness.

(Decision:TRC 103)
One member was not present for the vote, quorum was in place.

Olaparib Lynparza® (**Ref. TRC 104)**

Indicated as monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and BRCA1/2-mutations (germline and/or somatic) who have progressed following prior therapy that included a new hormonal agent.

This is an orally administered agent to treat adult patients with metastatic castration-resistant prostate cancer with BRCA1/2-mutations, and is currently reimbursed for other indications in the ovarian setting. It was noted that olaparib is recommended for this cohort of patients by various international guidelines (NCCN, ESMO). BRCA testing is a requirement for this indication.

The pharmacoeconomic aspects as outlined in the rapid review assessment carried out by the NCPE were discussed, noting that a full health technology assessment was not recommended. The NCPE representative outlined the supporting evidence. The phase III randomised trial, PROfound trial, evaluated the efficacy and safety of olaparib in men with metastatic castration-resistant prostate cancer (mCRPC). Eligible patients were included in one of two cohorts depending on their qualifying gene alteration. The trial showed that olaparib demonstrated a statistically significant improvement in radiographic progression free survival (rPFS) and overall survival (OS) compared to investigators choice of New Hormonal Agents(NHAs), (rPFS 9.79 vs 2.96 months, OS 20.11 vs 14.44 months). This trend was also observed in subgroup analysis examining the subgroup of patients with a BRCA1/2 mutation. Due to the small number of patients with a BRCA1 mutation efficacy results in the BRCA1/2 mutation subgroup are likely driven by results in the BRCA2 mutation population. The safety profile was discussed, noting that no new safety concerns were identified and safety was in line with previously reported adverse events which are considered manageable.

The introduction of olaparib to the treatment pathway represents a notable increase in cost when compared to existing treatment. The total cost per treatment course is based on a median treatment duration of 7.46 months, however 20% of patients in the PROfound trial received treatment with olaparib for 12 months or more. Eligibility for treatment requires BRCA testing, currently no BRCA 1/2 mutation screening programme exists in Ireland, this is associated with a significant cost (average cost of single BRCA1/2 testing reported ~€900). The proportion of patients expected to receive treatment is uncertain, the assumption is that 10% of the patients tested will be BRCA 1/2 positive, however this is likely an underestimate.

Clinically, there is a desire from clinicians to have this treatment made available to this patient cohort, with a median OS of 19 months seen in the trial. It was noted that while the number of patients to be testing for BRCA 1/2 mutation is high, the number of patient expected to be eligible for treatment is low and the clinicians outlined that this is a well tolerated, highly effective drug which is associated with improved quality of life and is clinically meaningful for this patient cohort.

Having considered the clinical efficacy of the indication, the committee

	members agreed by majority to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness. *(Decision:TRC104)*	
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 dates is February 21st	
6	**Any other business / Next meeting**	
	There was no other business.	

The meeting concluded at 5.30pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
22/01	24.01.2022	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Completed