National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**June 27th 2022 at 4.30pm**
Venue :	**Teleconference / NCCP Offices**
Assessment:	Apalutamide Erleada®
	Encorafenib Braftovi®
	Enzalutamide Xtandi®
	Trifluridine and tipiracil hydrochloride Lonsurf®

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 Mark Doherty	Medical Oncologist, St. Vincent's University Hospital: ISMO nominee	By 'phone
Ms Ellen McGrath	PCRS representative	By 'phone
Ms Patricia Heckmann	NCCP AND - Chair	
Prof Michaela Higgins	Medical Oncologist, St. Vincent's University Hospital: ISMO nominee	By 'phone
Dr Adrian Murphy	Medical Oncologist, Beaumont: ISMO nominee	By 'phone
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	
Dr Helen O'Donnell	HTA Directorate: HIQA nominee	By 'phone
Dr Derville O'Shea	Consultant Haematologist, Cork University Hospital: IHS representative	By 'phone
Non-member invited specialists present		

Apologies (members)	
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative
Dr Michael Fay	Consultant Haematologist, Mater Hospital: IHS representative
Dr Jarushka Naidoo	Medical Oncologist, Beaumont: ISMO nominee
Observers present	
Ms Elizabeth Breen	Chief 2 Pharmacist, NCCP
Ms Helena Desmond	Senior Pharmacist, NCCP

Item	Discussion	Actions
1	**Introduction & reminder re. conflict of interest & confidentiality**	
	It was noted that there had been some changes in membership: Dr Adrian Murphy, medical oncologist has joined as an alternate ISMO member. Ms Ellen McGrath has re-joined the group as the PCRS representative. Ms Fiona Mulligan will act as an alternate for Ms McGrath. Dr Helen O'Donnell has joined as the HIQA alternate for Dr Susan Spillane. 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. One conflict of interest was raised and the member abstained from the discussion in question.	
2	**Notes of previous meeting and matters arising**	
	The notes of the previous meeting on May 30th 2022 were agreed.	
3	**Drugs/Technologies for consideration**	
	Apalutamide Erleada® (**Ref. TRC 116)** *For the treatment of patients with metastatic hormone sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy.* The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III TITAN trial, which evaluated the efficacy and safety of apalutamide versus placebo in combination with androgen deprivation therapy (ADT) in patients with mHSPC. The study showed good results with a Hazard ratio (HR) for death of 0.67 and a HR of lower for radiographic progression free survival (PFS). The safety profile was discussed, noting a risk of seizures in pre-disposed patients, therefore excluding these patients from treatment. Currently in this treatment space are ADT +/- docetaxel, with most clinicians confining docetaxel to high-risk patients and those with the highest risk of early progression. ADT alone is no longer considered standard of care for these patients and it was noted that some patients may not be fit for docetaxel. There is a desire among the clinicians to have this treatment option available to this cohort of patients to prolong and increase the depth and length of remission. The pharmacoeconomic aspects as outlined in the HTA carried out by the NCPE were discussed. While the supporting evidence, the TITAN trial, showed favourable PFS and overall survival (OS) for apalutamide, there were concerns that the trial data is immature. Network meta-analyses were carried out and in terms of OS all out puts are associated with uncertainty. Treatment with aplautamide is associated with a high ICER and a significant budget impact BI over 5 years without consideration of displacement of any other 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, subject to an improvement in cost. *(Decision:TRC116)*	

Trifluridine and tipiracil hydrochloride Lonsurf® (**Ref. TRC 117)**

As monotherapy for the treatment of adult patients with metastatic gastric cancer including adenocarcinoma of the gastro-oesophageal junction, who have been previously treated with at least two prior systemic treatment regimens for advanced disease.

The clinical aspects of this indication were discussed, noting that Lonsurf®, an oral antimetabolite has been used to treat colorectal cancer for number of years. The supporting evidence for this indication is the phase III TAGS study which evaluated the efficacy and safety of Lonsurf® or placebo versus best supportive care (BSC) in patients with previously treated metastatic gastric cancer (including adenocarcinoma of the gastro-oesophageal junction) who had been previously treated with at least two prior treatment regimens for advanced disease. Primary end point was overall survival (OS) and secondary endpoints were progression free survival (PFS), overall response rate (ORR), disease control rate (DCR) and quality of life. The study met its primary endpoint, and showed modest improvement in survival with a median OS of 5.7 months for Lonsurf® vs 3.6 month for placebo, with a HR of 0.69 and a 2-sided $_p$value 0.0006. There was also a statistically significant improvement in the HR for PFS of 0.7, although no real difference in the median 2 months vs 1.8 months. The safety profile was discussed, noting that neutropenia, thrombocytopenia and GI toxicity frequently observed with bone marrow suppression being the biggest issue in patients who have had a number of lines of treatment. It was noted that Lonsurf® is approved in other jurisdictions such as Scotland, Canada and Australia. Clinicians support the approval in the Irish context for patients who rapidly run out of treatment options. It was noted that the number of patient eligible for treatment would be small and would be a useful treatment option for this patient cohort.

The pharmacoeconomic aspects as outlined in the rapid review assessment carried out by the NCPE were discussed. While the NCPE Review Group considered that the applicants proposed comparator of BSC to be reasonable for patients who are ineligible for systemic therapy, the review group considered chemotherapy also to be an appropriate comparator for patients who are considered fit, which is actually the cohort, which are likely to receive Lonsurf®. In that context the modest increase in OS was considered that this may overestimate the relative benefit seen in clinical practice. [redacted] Cost effectiveness in the Irish setting is unknown, but unlikely to be cost effective at the proposed price. The NCPE recommended that Lonsurf® not be considered for reimbursement at the submitted price. Commercial negotiations with the company are ongoing.

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, subject to an improvement in cost.

One member abstained from voting due to conflict, quorum still in place (Decision:TRC117)

	Encorafenib Braftovi® (**Ref. TRC 118)** *In combination with cetuximab for the treatment of adult patients with metastatic colorectal cancer (mCRC) with a BRAF V600E mutation who have received prior systemic therapy.* The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III BEACON trial, which evaluated the efficacy and safety of encorafenib in combination with cetuximab in patients with BRAF V600E mutant mCRC (the most aggressive phenotype of CRC) who had progressed after 1 or 2 prior regimens. The trial was a three-arm trial consisting of a triplet arm (encorafenib in combination with binimetinib and cetuximab) versus a doublet arm (encorafenib and cetuximab) versus chemotherapy arm (FOLFIRI +cetuximab or irinotecan +cetuximab). The doublet arm vs chemotherapy arm are of interested for this indication. The study demonstrated a modest improvement in overall survival (OS) of 8.4 months in the doublet arm vs 5.4 months in the chemotherapy arm, with a HR of 0.6. The study showed an objective response rate (ORR) of 20% in the doublet arm vs 2% in the chemotherapy arm. The study also showed a median progression free survival (PFS) of 4.2 vs 1.5 months favouring the encorafenib and cetuximab arm with a HR of 0.4. There is a strong desire among the clinicians to have this treatment available. This molecular subgroup is the most aggressive type in metastatic CRC, there is an unmet need in this patient cohort who are classically younger, female, and have very poor prognostic rates compared to other molecular subtypes of CRC. The pharmacoeconomic aspects as outlined in the HTA carried out by the NCPE were discussed. Concerns identified by the NCPE's Review Group were outlined, including the applicants choice of comparator, trial design and uncertainty regarding the indirect comparator evidence. Treatment with encorafenib and cetuximab is associated with high ICERS. The NCPE's Review Group undertook an update of the budget impact (BI) analysis due to concerns in the assumptions based in the applicants submission. NCPE estimated a gross BI of €20.4 million over 5 years, and recommended that encorafenib and cetuximab not be considered for reimbursement unless cost effectiveness can be improved. Commercial negotiations with the company are ongoing. 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, subject to an improvement in cost. *(Decision:TRC118)* Enzalutamide Xtandi® *The treatment of adult men with high-risk non-metastatic castration-resistant prostate cancer (CRPC)* This indication was not discussed as it is anticipated that it will be progressed on a cost minimisation basis by the PCRS.	
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 July 25th	

6	**Any other business / Next meeting**	
	There was no other business.	

The meeting concluded at 5.40pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
22/05	27.06.2022	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete