National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**27th November 2023 at 4.30pm**
Venue :	**Teleconference**
Assessment:	Nivolumab (Opdivo®)
	Abemaciclib (Verzenio®)
	Venetoclax (Venclyxto®)

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 Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	By 'phone
Dr Neil Barrett	Consultant Haematologist, Children's Health Ireland - Crumlin	By 'phone
Ms Patricia Heckmann	AND NCCP (Chair)	By 'phone
Prof Michaela Higgins	Medical Oncologist, St Vincent's university Hospital: ISMO nominee	
Ms Ellen McGrath	PCRS representative	By 'phone
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	By 'phone
Prof Michael O'Dwyer	Consultant Haematologist, Galway :IHS representative	By 'phone
Ms Susan Spillane	HTA Directorate: HIQA nominee	By 'phone
Non-member invited specialists present **Apologies (members)**		
Dr Dearbhaile Collins	Medical Oncologist, Cork University Hospital: ISMO nominee	By 'phone
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative	By 'phone
Observers present		
Ms Helena Desmond	Senior Pharmacist, NCCP	By 'phone
Dr Derville O'Shea	Consultant Haematologist, Cork University Hospital: NCCP Clinical Lead for Haemato-Oncology	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 October 23rd 2023 were agreed.	
3	**Drugs/Technologies for consideration**	
	Nivolumab (Opdivo®) **(Ref. TRC144)** *In combination with platinum-based chemotherapy is indicated for the neoadjuvant treatment of resectable non-small cell lung cancer (NSCLC) at high risk of recurrence in adult patients whose tumours have programmed death-ligand 1 (PD-L1) expression ≥ 1%.* The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III, randomised, open label Checkmate 816 trial which evaluated the safety and efficacy of nivolumab plus platinum doublet chemotherapy compared to platinum doublet chemotherapy alone for the neo-adjuvant treatment of resectable NSCLC. The study showed an improvement in terms of event free survival (EFS) and overall survival (OS). At the most recent data at 3 years, the trial showed OS in the order of ~78% with nivolumab plus chemotherapy versus 64% with chemotherapy alone. The safety profile of nivolumab in combination with chemotherapy was discussed, it was noted that the clinicians already familiar with this combination in advanced disease, and are experienced with its use and no new safety issues were identified. There is a desire among clinicians to have this treatment option available for this patient cohort. The pharmacoeconomic aspects as outlined in the rapid review (RR) assessment carried out by the NCPE were discussed, noting that a full HTA was recommended, which has not been submitted to date. The supporting evidence was outlined, the data were immature, a concern highlighted by the NCPE review group. The median EFS data was not reached in the nivolumab plus chemotherapy arm, in the chemotherapy alone arm EFS was 26.71 months. EFS data is relatively immature, with only 27.2% of patient in the nivolumab plus chemotherapy arm had experienced an event and 45.3% in the chemotherapy alone arm. The difference in the pathological complete response (pCR) was 29.8% in favour of the nivolumab plus chemotherapy arm. Medium OS was not reached in either arm and EFS in this setting is not a validated surrogate for OS, therefore it is unclear whether the EFS will translate into OS benefit. In terms of cost, the total cost per treatment course of nivolumab in combination with chemotherapy is estimated to be [redacted] In terms of the budget impact (BI), it is estimated [redacted] patients in year 5. Based on the list price, the 5-year cumulative gross BI is estimated to [redacted] The NCPE review group recommended a full HTA based on the proposed price due to the uncertainty of the comparative effectiveness versus relevant to clinical practice in Ireland, and that the price premium maybe higher once the full cost of adjuvant therapies in the Irish clinical setting is considered. The company provided a PAS in the RR, which reduces the total comparator cost of nivolumab plus chemotherapy to [redacted] 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.	

One member abstained from voting, however quorum in place.

(Decision: TRC 144)

Abemaciclib (Verzenio®) **Ref. TRC 145**

In combination with endocrine therapy for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence.

The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III, open label, randomised trial MonarchE study, which evaluated the safety and efficacy of abemaciclib in combination with adjuvant endocrine therapy (ET) compared to ET alone in adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence. At the most recent data cut, the primary endpoint of invasive disease-free survival (IDFS) had significantly improved with the addition of abemaciclib. The IDFS at 5 years was 83.2% for abemaciclib plus ET versus 75.3% for patients treated with ET alone, an absolute benefit of 7.6% which is considered meaningful, with a highly significant HR 0.67, a 32% reduction in the risk of IDFS events. OS survival is immature and has not yet reached significance. The safety profile was discussed, noting that, while access to abemaciclib is not yet available in Ireland, this class of drug is routinely used and clinicians are experienced in monitoring and managing associated toxicities. There is desire among the clinicians to have this treatment available to the patients at high risk of recurrence, and consider that there is an unmet need in this patient cohort.

The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The supporting evidence was outlined, the NCPE review group highlighted concerns regarding the immaturity of the distant relapse free survival (DRFS) and the OS data, and the uncertainty regarding the association between IDFS and DRFS and OS. The NCPE review group also highlighted a number of limitations of the trial such as, open label design of the trial. The cost effectiveness modelling was outlined and adjustments to the model were made. In terms of cost, the cost per treatment course of abemaciclib plus ET is €59,701 and the cost per treatment course of ET alone is [redacted] The ICER in the Applicant's base case was €40,869 per QALY. The NCPE-adjusted base case ICER was €77,224 per QALY. Based on scenario analysis, the review group considered the actual true ICER probably lies between the range of €60,000 per QALY and €100,000 per QALY based on the uncertainty associated with the assumptions in the model. The probability of cost-effectiveness at the €45,000 per QALY is 1% in the NCPE adjusted base case and it is estimated [redacted] reduction in price to the wholesaler is required in order to reduce the ICER to €45,000 per QALY. In terms of the budget impact (BI), it is estimates that the eligible patient population is [redacted] The cumulative gross BI over 5 years is estimated to be €18.61 million and the net BI over 5- years is estimated to be €18.39 million The recommendation of the NCPE review group was that abemaciclib should be considered for reimbursement if the cost-effectiveness can be improved relative to existing treatments. It was noted that a PAS was not included in the HTA submission.

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.

One member was absent from voting, however quorum in place.

(Decision: TRC 145)

Venetoclax (Venclyxto®) Ref. TRC 146

In combination with a hypomethylating agent for patients with newly diagnosed AML who are ineligible for intensive chemotherapy (IC).

The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III, randomised, double-blind, placebo-controlled phase trial, VIALE-A, which evaluated the safety and efficacy of venetoclax plus azaCITIDine compared to azaCITIDine alone in patients with newly diagnosed AML who were ineligible for IC. In terms of response, the study showed a doubling of response in favour of venetoclax plus azaCITIDine with ~60% versus 40% with azaCITIDine in terms of CR+Cri rate. In terms of overall survival (OS), at a median follow up at >20 months, the median OS was 14.7 months in patients treated with ventoclax plus azaCITIDine compared to 9.6 months with azCITIDine alone, with a hazard ratio (HR) of 0.66. The safety profile was discussed, it was noted that, treatment with ventoclax plus azaCITIDine was associated with an increase in toxicity compared with azaCITIDine, such as increased neutropenia, febrile neutropenia and thrombocytopenia, which did result in dose interruptions, however, in the patient who did respond, the responses were meaningful, patients had a reduction in the transfusion requirements and patients who responded had a median durations of 17.5 months. It was also noted that clinicians have learnt a lot in terms of optimal management. There is a strong desire among the clinicians to have this treatment available for this patient cohort who are considered to have an unmet clinical need. It was also noted that that this combination is the new standard of care globally.

The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The supporting evidence was outlined, The NCPE review group highlighted a number of limitations of the trial and adjustments were made to the NCPE adjusted base case. The cost effectiveness modelling was outlined and adjustments to the model were made were noted, such as the removal of the cure assumption. In terms of cost, the total treatment course cost for ventoclax plus azaCITIDine is estimated to be €106,230 including VAT, €101,384 excluding VAT based on the assumption of 15 cycles of ventoclax plus azaCITIDine. The total treatment course cost for azaCITIDine alone is estimated to be € VAT based on the assumption of 9 treatment cycles. The Applicant's base case ICER was €130,946 per QALY and the probabilistic ICER was slightly higher. The NCPE review group made a number of changes to the NCPE-adjusted base case, and the NCPE adjusted base case ICER was €227,152 per QALY. It was noted that a PAS offer was included in the HTA submission and this reduces the ICER to

In terms of the budget impact (BI), it is estimated that the 59 patients will be treated in year-1 rising to 62 patients in year 5, which leads to a gross BI €30.74 million over 5 years and the net BI is €26.23 million over 5-years. Using the PAS . There is uncertainty with the patient population estimates, and if applying the enhanced blood cancer registry estimates this The recommendation of the NCPE review group was that ventoclax plus azaCITIDine be not considered for reimbursement if the cost-effectiveness can be improved.

The committee members highlighted their reservations with regard to voting for an indication where cost effectiveness cannot be achieved, and while acknowledging that cost effectiveness models use in the NCPE HTA assessment differed to the NICE assessment of ventoclax plus azaCITIDine for this indication, it was highlighted that the ICERS presented in the NICE assessment were significantly lower than those presented in the NCPE HTA

	assessment 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. Two member abstained from voting, however quorum in place. *(Decision: TRC 146)*	
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 22nd 2024	
6	**Any other business / Next meeting**	
	The Chair welcomed Dr Neil Barrett to his first meeting with the committee as an IHS nominated member in place of Dr Michael Fay.	

The meeting concluded at 6.05pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
23/01	27/11/2023	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Completed
23/01	27/11/2023	Apply for CPD	NCCP	Completed