National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**23rd October 2023 at 4.30pm**
Venue :	**Teleconference**
Assessment:	Atezolizumab (Tecentriq®)
	Nivolumab (Opdivo®)

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	By 'phone
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative	By 'phone
Dr Michael Fay	Consultant Haematologist, Mater Hospital: IHS representative	By 'phone
Ms Patricia Heckmann	AND NCCP (Chair)	By 'phone
Dr Deirdre Kelly	Medical Oncologist, Mater Hospital: ISMO nominee	By 'phone
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	By 'phone
Dr Helen O' Donnell	HTA Directorate: HIQA nominee	By 'phone
Non-member invited specialists present		
Dr Megan Greally	Medical Oncologist, Beaumont Hospital	By 'phone
Apologies (members)		
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	
Observers present		
Ms Helena Desmond	Senior Pharmacist, NCCP	By 'phone
Ellen Melia	Pharmacy student	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 2nd 2023 were agreed.	
3	**Drugs/Technologies for consideration**	
	Atezolizumab (Tecentriq®) **(Ref. TRC142)** *As adjuvant treatment following complete resection and platinum-based chemotherapy for adult patients with NSCLC with a high risk of recurrence whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK-positive NSCLC.* The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III, randomised, open label IMpower010 trial which evaluated the safety and efficacy of atezolizumab compared to best supportive care (BSC) for the treatment of patients with completely resected stage IB-IIIA NSCLC who received adjuvant chemotherapy with a high risk of recurrence. The median overall survival (OS) has not yet been reached and not estimable in both the atezolizumab and the BSC arms. However the study showed that OS at 48 months post randomisation in patient who received adjuvant treatment with atezolizumab at a dose of 1200mg every 3 weeks for 16 cycles was 85% versus 70.9% with BSC, a HR 0.43, showing a statistically significant improvement. The safety profile of atezolizumab was discussed, the safety of atezolizumab in the adjuvant setting was consistent with its use in other indications and no new toxicities were identified. There is a strong desire among clinicians to have this treatment option available for this patient cohort, a treatment with a potential to increase the cure rate and improve OS by 15%. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The supporting evidence was outlined and the NCPE review group highlighted concerns and limitations such as the immaturity of the data, both disease free survival (DFS) and OS. In terms of OS, at the most recent data cut (April 2023), only 14.2% of patients in the atezolizumab arm had an event versus 29% in the BSC arm. The review group highlighted concerns and uncertainties on whether atezolizumab delays disease recurrence or prevents recurrence, concerns regarding DFS in terms of relationship with OS was also highlighted and how well it correlates with OS in this treatment setting. In terms of the cost effectiveness analysis, it was assumed that atezolizumab is administered at a dose of 1680mg every 28 days for a maximum of 48 weeks. The cost effectiveness modelling was outlined, the limitations with the model were highlighted and adjustments made were noted. In terms of cost, treatment with atezolizuamab when dosed at 1680mg every 28 days, the estimated cost of treatment per patient per year is €89,224 including VAT and €71,340 excluding VAT. When dosed at 1200mg every 21 days the estimated cost of treatment per patient per year is €85,514 including VAT and €68,374 excluding VAT. The ICERS were outlined, in the Applicants base case, the ICER is €21,000 per QALY. A number of changes were made to the NCPE-adjusted base case and the NCPE-adjusted ICERS is €31,640 per QALY. In terms of budget impact (BI), it is estimated that 37 patients will be treated in year 1 rising to 38 patients in year 5. The NCPE-adjusted 5-year cumulative gross BI base on the list price for was estimated to be €16.36 million including VAT and €13.06 million excluding VAT, with the net BI is equivalent to the gross BI.	

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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 due to a conflict of interest, however quorum in place

(Decision: TRC 142)

Nivolumab (Opdivo®) **Ref. TRC 143**

In combination with fluoropyrimidine- and platinum-based combination chemotherapy for first line treatment of adult patients with HER-2 negative advanced or metastatic gastric cancer, gastroesophageal junction cancer (GEJC) or esophageal adenocarcinoma (EAC), whose tumours express PD-L1 (CPS)≥5.

The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III, open label, randomised study CheckMate 649 study, which evaluated the safety and efficacy of nivolumab in combination with chemotherapy compared to chemotherapy alone in adult patients with HER-2 negative advanced or metastatic gastric cancer, gastroesophageal junction cancer (GEJC) or oesophageal adenocarcinoma (EAC), whose tumours express PD-L1 (CPS)≥5. The primary endpoint was overall survival (OS) and progression free survival (PFS). The study showed at in the nivolumab plus chemotherapy arm the response rate was increased to 60% from 45 % in the control arm (chemotherapy alone). An improvement in both PFS and OS was seen, PFS with chemotherapy alone arm was 6 months versus 8 months with nivolumab plus chemotherapy arm with a HR 0.68. OS was 11 months with chemotherapy alone versus 14.9 months in the nivolumab plus chemotherapy arm, a HR 0.71 in the PD-L1 (CPS) ≥5 population. While a benefit was seen in all comers, it was more so in the PD-L1 (CPS) ≥5 population. An updated 3 year OS analysis showed an OS of 29% in the nivolumab plus chemotherapy arm versus 10% in the chemotherapy alone arm. The safety profile was discussed, the most common toxicities seen were nausea, diarrhoea, peripheral neuropathy and neutropenia, more chemotherapy specific side effects, with more grade 3 adverse side effects in the nivolumab plus chemotherapy arm 60% versus 45% in the chemotherapy alone arm, but it was noted that this is what the clinician would expect. There is desire among clinicians to have this treatment available for this cohort of patients, as treatment with nivolumab plus chemotherapy is the first time that an improvement in OS greater than 1 year has been seen in this setting, and is considered clinically meaningful in a disease where survival remain very poor.

The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The supporting evidence was outlined and the NCPE review group highlighted a number of limitations of the trial such as, uncertainty over the long term efficacy, open label design of the trial, patients with unknown HER2 status. The cost effectiveness modelling was outlined and adjustments to the model were made such as age of patient population and removal of the treatment stopping rule. In terms of cost effectiveness the results were based on both comparators, XELOX and FOFLOX. For the applicant's base case the ICER for nivolumab plus XELOX versus XELOX was €61,855 per QALY and for nivolumab plus FOLFOX versus FOLFOX the ICERS was €61,679 per QALY. NCPE review group made a number of changes to the model, and the NCPE-adjusted base case the ICER for nivolumab plus XELOX versus XELOX was €101,665 per QALY and for nivolumab plus FOLFOX versus FOLFOX the ICERS was €101,642 per QALY.

	[redacted] above the willingness to pay threshold of 45k per QALY. A total reduction of [redacted] is required to reduce the ICER. In terms of the budget impact (BI), the Applicant estimates that 119 patients will eligible to be treated annually, estimated the market share [redacted] for nivolumab plus chemotherapy (XELOX/FOLFOX) in year 1 increasing to [redacted] by year 5, resulting in an estimated treated population of 42 in year 1 increasing to 89 annually year 5. Considering the PAS in place, the 5-year cumulative net BI for the comparison with XELOX, assuming everyone is receiving XELOX currently [redacted] and the net BI for the comparison with FOLFOX assuming everyone is receiving FOLFOX currently is [redacted]. Considering a weighted average, the estimates would fall between the estimates presented and would be slightly lower than the impacts presented for nivolumab plus FOLFOX. The recommendation of the NCPE review group was that nivolumab plus chemotherapy not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments. 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 143)*	
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 November 27th 2023	
6	**Any other business / Next meeting**	

The meeting concluded at 5.40pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
23/01	23/10/2023	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
23/01	23/10/2023	Apply for CPD	NCCP	Complete