National Cancer Control Programme

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

NCCP Technology Review Committee (TRC)

Meeting Notes 2021.3

Date of Meeting:	**March 29th 2021 at 4.30pm**
Venue :	**Teleconference / NCCP Offices**
Assessment:	Atezolizumab (Tecentriq®)
	Pembrolizumab in combination with axitinib (Keytruda® & Inlyta®)

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. Gerard Crotty	Consultant Haematologist, MRH Tullamore: IHS representative	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. Ellen McGrath	Chief Pharmacist; HSE Corporate Pharmaceutical Unit	By 'phone
Dr. Susan Spillane	HTA Directorate: HIQA nominee	By 'phone
Non-member invited specialists present		

Apologies (members)	
Dr. Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee
Dr. Linda Coate	Medical Oncologist, University Hospital Limerick: ISMO nominee
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative
Dr. Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee
Observers present	
Ms. AnneMarie De Frein	Deputy Chief Pharmacist, NCCP

Item	Discussion	Actions
1	**Introduction & reminder re. conflict of interest & confidentiality**	
	Members were reminded of the confidentiality of documentation and discussions and reminded to submit completed conflict of interest form for 2021 which had been circulated. Members were asked 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.	COI form to be returned by all members for 2021
2	**Notes of previous meeting and matters arising**	
	The notes of the previous meeting on March 1st were approved.	
3	**Drugs/Technologies for consideration**	
	Atezolizumab (Tecentriq®) (Ref. TRC 087) *As monotherapy is indicated as treatment of locally advanced or metastatic urothelial carcinoma (LaMUC) in adult patients who are considered cisplatin-ineligible and whose tumours have PD-L1 expression ≥5%* The clinical aspect of this indication was discussed, noting that this is for adults with locally advanced of metastatic urothelial carcinoma who are ineligible for cisplatin, with PD-L1 expression ≥5%. It was noted that there is another medicine reimbursed in this indication where an alternate biomarker of CPS (combined positive score) >10%. The supporting evidence is from the phase two IMvigor study, with inclusion, exclusion and adverse events as expected from atezolizumab. It was discussed that the CHMP had some issues with this study and have requested a follow up study but did license this indication. This application for reimbursement is being progressed as a cost minimisation piece by the PCRS as an alternate immunotherapy in this indication. The committee members recommended approval for reimbursement noting that it will not be subject to a HTA and subject to cost minimisation. *(Decision:TRC 087)* **Pembrolizumab in combination with Axitinib (Keytruda® and Inlyta®) (Ref. TRC 088)** *In combination with axitinib for the first line treatment of advanced renal cell carcinoma (aRCC) in adults* The pharmacoeconomic considerations as outlined in the health technology assessment for this indication were discussed, including that that this is a license extension and there are other treatment options in this space. KEYNOTE-426 is an ongoing, phase 3, randomized, multicentre, open label study comparing the combination of pembrolizumab+axitinib with sunitinib in the first-line treatment of aRCC in adults regardless of PD-L1 tumour expression status and IMDC risk group categories. It was noted that there were two risk groups for consideration, i.e. all-risk and intermediate–poor risk. The study has a primary endpoint of overall survival and progression free survival. It was discussed that the treatment duration in the trial was 35 cycles but included an option for patients with a confirmed complete response to stop at 24 weeks (and these patients could receive an additional 17 cycles if they later relapsed). There are no final trial results to date, but the most up to date is the interim analysis 2 (IA2) which showed a hazard ratio of 0.68 for overall survival and 0.71 for progression free survival. It was	NCCP to communicate recommendations to HSE Drugs Group.

	discussed that a real-world study which compared axitinib with sunitinib in treatment-naïve patients found that axitinib significantly prolonged overall survival and therefore, there are concerns that the efficacy benefit of combination treatment could be attributed in part to higher level of activity with axitinib than sunitinib and that the lack of monotherapy experimental arms hampered assessment of the contribution each drug made to the treatment benefit It was discussed that the evidence is associated with a number of uncertainties due to the lack of longer term data as well as the stopping/ retreating considerations. In terms of cost effectiveness, the ICERs and budget impacts were outlined, which are seen to be significant and challenging for this indication. From a clinical consideration, the clinicians have outlined that this combination of medicines is internationally accepted as the best available treatment for these cancers and there is a desire to use this combination. There was a discussion about the optimal duration of treatment, including any stopping rules, and any considerations to have an option to re-treat patients in remission, who later relapse and the potential for this in practice as one means to address the uncertainties identified. This may need to be explored with the relevant NCCP clinical advisory group, should there be a need to define this in the national treatment regimen. In addition, it was noted that in the IA2, there were indications that there was no overall survival benefit seen in the intermediate-poor risk group but there was a benefit in progression free survival and the EMA approval was granted for all risks. The CHMP have requested that the final clinical study report be submitted post-approval, in particular to further characterise benefit in the subgroups. It was noted that the commercial negotiation is ongoing, and that the challenges have been recognised in this application. 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 and means to reduce the uncertainties outlined. *(Decision:TRC 088)*	
4	**Update on other drugs in the reimbursement process**	
	An update on the drugs that are in the reimbursement process was circulated to members in advance of the meeting.	
5	**Next meeting**	
	The proposed date for the next meeting dates is April 29th 2021	
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
21/03	29.3.2021	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	