National Cancer Control Programme

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**November 29th 2021 at 4.30pm**
Venue :	**Teleconference / NCCP Offices**
Assessment:	Avelumab Bavencio®
	Neratinib Neratinib®
	Pembrolizumab Keytruda®
	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 representatives	National Centre for Pharmacoeconomics (NCPE)	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
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
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
Prof Michaela Higgins	Medical Oncologist, St. Vincent's University Hospital: ISMO nominee
Dr Eve O'Toole	Research Group Lead, NCCP
Dr Susan Spillane	HTA Directorate: HIQA nominee
Observers present	
Ms. AnneMarie De Frein	Chief 2 Pharmacist
Ms Helena Desmond	Senior Pharmacist

Item	Discussion	Actions
1	**Introduction & reminder re. conflict of interest & confidentiality**	
	Dr Derville O'Shea was welcomed to the group as the new IHS representative, replacing Dr G Crotty. 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 COI had been previously notified to the Chair and that member abstained from the discussion and vote for that item.	
2	**Notes of previous meeting and matters arising**	
	The notes of the previous meeting on September 27th were agreed.	
3	**Drugs/Technologies for consideration**	
	Avelumab Bavencio® (**Ref. TRC 097**) *Avelumab in combination with axitinib for the first-line treatment of adult patients with advanced renal cell carcinoma (aRCC).* The clinical aspects of this indication were discussed, noting that there is an unmet need in the "good risk" cohort of the renal cell cancer population. It was discussed that the combination of immunotherapy and VEGF-targeted tyrosine kinase inhibitors (TKIs) is internationally accepted as the best available treatment for first line treatment of aRCC and that there is a desire to use this combination, in the absence of any available alternative treatment for the cohort. The NCPE representative outlined the supporting evidence. The phase III, JAVELIN 101 trial, evaluated the efficacy and safety of avelumab in combination with axitinib, compared to sunitinib monotherapy in first line treatment of patients with untreated advanced or metastatic RCC across all risk groups. The study showed avelumab in combination with axitinib prolonged progression-free survival (PFS) versus sunitinib. While the OS data were immature, results favour the combination over sunitinib. The pharmacoeconomic considerations for this indication were discussed. The JAVELIN 101 trial showed a slowing in progression of ~30% with avelumab in combination with axitinib over comparator and a slowing of ~20% OS over the comparator. It was highlighted that another treatment combination, pembrolizumab/axitinib, was recently assessed by the NCPE, and in terms of avelumab and axitinib was found to be less expensive, but also less effective. A number of uncertainties were highlighted as per the health technology assessment and it was noted that there is a low probability of being cost effective at the €45k/QALY threshold. There was a question and a discussion as to the duration of treatment and whether this would extend beyond two years as well as whether there would be a preferential combination of immunotherapy and VEGF for this patient cohort but this was felt to be beyond the scope of the TRC. Having considered the clinical efficacy of the indication and the unmet need, the committee members agreed by majority to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness, considering the other treatments in this space.	

(Decision:TRC 097)

One member was not present for the vote, quorum was in place.

Neratinib Nerlynx® (**Ref. TRC 098)**

For the extended adjuvant treatment of adults with early-stage hormone receptor-positive, HER2-overexpressed/amplified breast cancer and who completed adjuvant trastuzumab-based therapy less than one year ago.

This is an orally administered agent for extended adjuvant treatment following adjuvant trastuzumab-based therapy. The supporting evidence is a phase 3 randomised study, the ExeNet trial, which evaluated efficacy of neratinib vs placebo in women with early-stage HER2-positive breast cancer previously treated with adjuvant trastuzumab. The study outcomes were outlined and it was discussed that the trial showed a reduced risk of invasive disease recurrence at the 2-year follow up. The study reported a 2.5% improvement in invasive disease-free survival (iDFS) at 2 years (93.9% neratinib vs 91.6% in placebo group).

The clinical aspects of this indication were discussed, noting that there is a desire from the clinicians to have treatments available for patients with residual disease. Neratinib is one such treatment option. Breast cancer treatment is rapidly changing. There are other medicines in the assessment process, which have also recently been assessed by the NCPE in these early stages of breast cancer. It was discussed that should these be approved for reimbursement, these treatments may supplant neratinib in the treatment pathway but that ahead of that; there is a desire to have the option available for certain patients. The agreed clinical guideline includes only those patients who have not received treatment with a HER2-directed treatment other than trastuzumab in the early breast cancer setting (neo-adjuvant or adjuvant) and are less than one year from completion of trastuzumab based therapy. Treatment with neratinib will continue for one year. Considering this, it is expected that patient numbers would be small and diminishing as the newer treatments become available. The toxicity profile was outlined noting that this is associated with substantial gastrointestinal toxicity, specifically diarrhoea with 95% of patients experiencing diarrhoea.

From the pharmacoeconomic aspect, the clinical benefit of this indication is marginal and there was no improvement in quality of life reported. There were concerns regarding validity of the trial in the current breast treatment landscape, due to the evolving treatment landscape and the exclusion of patients having received prior treatment with other anti HER2 therapies such as pertuzumab (in combination with trastuzumab) for early breast cancer. The ICERs and budget impacts were outlined.

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 098)

One member was not present for the vote, quorum was in place.

Pembrolizumab Keytruda® (**Ref. TRC 99)**

Adult and paediatric patients aged three years and older with relapsed or refractory classical Hodgkin lymphoma (cHL) who have failed autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT is not a treatment option.

This application for reimbursement is a license extension for the treatment

	of classical Hodgkin Lymphoma to the paediatric patients aged three and older. This treatment option is already available to the adult population in a restriced cohort but this would extend to the full adult cohort, noting there are also alternate immunotherapy options for cHL. 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 099)* *One member was not present for the vote, quorum was in place.* Venetoclax Venclyxto® **(Ref. TRC 100)** *Venetoclax in combination with obinutuzumab for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).* The clinical aspects of this indication were discussed, noting that there is a clear unmet need for this patient cohort in the untreated CLL with an orally administered option. Current treatments in this space include fludarabine, cyclophosphamide in combination with rituximab (FCR) or bendamustine in combination with rituximab (BR). However, these treatments are associated with significant toxicities including prolonged immunosuppression and it was considered that this treatment option is a well-tolerated, effective option. The supporting evidence is a phase 3 randomised study, CLL14 trial evaluate the efficacy and safety of venetoclax and obinutuzumab (VenO) versus obinutuzumab and chlorambucil in patients with previously untreated CLL. Treatment with VenO is for a fixed duration (venetoclax for 12 cycle in combination with 6 cycles of obinutuzumab). The trial outcomes were outlined including that the VenO combination demonstrated a significantly longer PFS survival noting that a benefit in OS was not seen, as data were immature. The side effect profile was discussed, and while neutropenia is a serious toxicity associated with venetoclax, the clinicians are experienced in the management of such. From the pharmacoeconomic aspect, it was discussed that the review group identified some limitations in the modelled population and made a number of adjustments for this. The probabilistic ICERs indicate a high level of uncertainty. However, the clinical benefit of this indication showed a significant improvement in PFS and the recommendation of the review group was to recommend reimbursement. Having considered the clinical efficacy of the indication, the unmet need, and the familiarity with the treatment in avoiding toxicity and managing side effects, the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness. *(Decision:TRC100)* *One member was not present for the vote, one member abstained from the discussion and the vote (potential COI) quorum was in place.*	
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 January 22nd	
6	**Any other business / Next meeting**	
	There was no other business.	

The meeting concluded at 5.50pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
21/06	29.11.2021	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete