National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**22nd May 2023 at 4.30pm**
Venue :	**Teleconference**
Assessment:	Dostarlimab Jemperli®
	Lenvatinib Kisplyx®

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		
Dr Dearbhaile Collins	Medical Oncologist, Cork University Hospital: ISMO nominee	By 'phone
Dr Michael Fay	Consultant Haematologist, Mater Hospital: IHS representative	By 'phone
Ms Patricia Heckmann	AND NCCP (Chair)	By 'phone
Ms Ellen McGrath	PCRS representative	By 'phone
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	By 'phone
Dr Susan Spillane	HTA Directorate: HIQA nominee	By 'phone
Non-member invited specialists present		

Apologies (members)	
NCPE representative	National Centre for Pharmacoeconomics (NCPE)
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative
Prof Michael O'Dwyer	Consultant Haematologist, Galway : IHS representative
Observers present	
Ms Helena Desmond	Senior Pharmacist, NCCP

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 April 24th were agreed.	
3	**Drugs/Technologies for consideration**	
	Dostarlimab Jemperli® (Ref. TRC 134) *Monotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer (EC) that has progressed on or following prior treatment with a platinum-containing regimen.* The clinical aspects of this indication were discussed, the supporting evidence for this indication is the phase I, open label, single arm GARNET study which evaluated the safety and efficacy of dostarlimab in patients with dMMR/MSI-H recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing chemotherapy. The primary endpoints were objective response rate (ORR) and duration of response (DOR). The study showed that treatment with dostarlimab resulted in an ORR of 45.5% with 10% complete response (CR) and approximately one third of patients had a partial response. The study demonstrated good tumour responses with immune-checkpoint inhibitors in dMMR/MSI-H endometrial cancer, which is consistent with the use of immune-checkpoint inhibitors for other dMMR/MSI-H tumours such as CRC. Immune-checkpoint inhibitors are now considered an important treatment option for these patients. It was noted that other key endpoints such as DOR, overall response rate (ORR) and overall survival (OS) have not yet been reached. The safety profile was discussed, noting that the side effects were as expected of the known safety profile of immune-checkpoint inhibitors. The limitations of the study were discussed, such as the open label nature of the trial, the small size of this phase I/II, single arm study, and the immaturity of the DOR and OS data, which raise questions over the tail of the curve and the expected benefit. However, it was discussed that the introduction of an immune-check point inhibitor will be big advance in this therapeutic area. It is considered that this cohort of patients will perform better with dostartimab than compared to chemotherapy, and in practice, a lot of these limitations will resolve in time. Noting this, it was outlined that there is a desire among clinicians to have this treatment option available for this cohort of patients. There was some discussion on duration of treatment, noting this was limited to 2 years in the trial but is not limited within the licensed indication and associated summary of product characteristics. It was noted that the number of patients expected to be treated beyond 2 years would be very low. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. Treatment with dostarlimab is associated with high ICERs and had a 0% probability of cost-effectiveness at both the €20kper QALY and €45k per QALY thresholds, for the Applicant and NCPE-adjusted base case. The applicant's base case ICER was estimated to €97,812 per QALY and the NCPE adjusted base case €106,891per QALY. The annual cost of dostarlimab per patient is estimated to be ~€129K (€103k excluding VAT). The 5-year gross budget impact (BI) is estimated to be €2.23 million including VAT (€1.79 million excluding VAT), and 5-year net BI estimated €2.16 million including VAT (€1.73 million excluding VAT). The recommended of the NCPE review group was that dostarlimab 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 majority to recommend approval of this indication to the HSE Drugs Group. *(Decision: TRC 134)* Lenvatinib Kisplyx® **(Ref. TRC 135)** *In combination with pembrolizumab for the first line treatment of advanced renal cell carcinoma.* The clinical aspects of this indication were discussed. It was noted that there are other combinations of tyrosine kinase inhibitors (TKIs) and immunotherapy (I-O) in the assessment process for this indication. The supporting evidence for this indication is the phase III, open label, randomised, CLEAR trial, which evaluated the safety and efficacy of lenvatinib-plus-pembrolizumab compared to single agent sunitinib in patients with previously untreated advanced renal cell carcinoma (RCC). The trial showed a significant improvement in progression free survival (PFS) 24 months in the lenvatinib-plus-pembrolizumab arm versus 9 months in the sunitinib arm. While the median overall survival (OS) was not reached, treatment with lenvatinib-plus-pembrolizumab showed survival was significantly longer than sunitinib with a hazard ratio (HR) of 0.66, CI of 0.44 to 0.8. The safety profile was discussed and the safety prolife of the combination were consistent with the known safety profile of each drug. There is a strong desire among clinicians to have this treatment option available for first line treatment in advanced RCC in line with international guidelines. Combination therapy has become the new standard of care (SOC) for first-line treatment for advanced RCC, with international guidelines (ESMO and NCCN) recommending the use of a TKI-IO combination. While a number of TKI-IO combinations have become licensed for use in the EU, to date no TKI-IO combination has been approved for reimbursement in Ireland, therefore it is considered that there is a critical unmet need in this patient cohort. The pharmacoeconomic aspects as outlined in the rapid review assessment carried out by the NCPE were discussed, noting that a full HTA was recommended, but not completed. The NCPE review group highlighted concerns and uncertainties regarding estimated number of patient to be treated and budget impact (BI) estimates. In terms of the cost effectiveness, treatment with lenvatinib-plus-pembrolizumab is associated with high cost and budget impact (BI). The annual cost per patient per treatment course is estimated to be [redacted]. The 5-year gross budget impact (BI) is estimated to [redacted], and 5-year net BI estimated to be [redacted]. 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. *(Decision: TRC 135)*	
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 June 26th 2023	
6	**Any other business / Next meeting**	
	CPD:	NCCP

	Dr Dearbhaile Collins volunteered to complete the CPD survey for this TRC meeting	

The meeting concluded at 5.55pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
23/01	27/03/2023	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
23/01	27/03/2023	Apply for CPD	NCCP	Complete