National Cancer Control Programme

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**February 21st 2022 at 4.30pm**
Venue :	**Teleconference / NCCP Offices**
Assessment:	Brentuximab vedotin Adcetris® x 3 indications
	Durvalumab Imfinzi®
	Larotrectinib Vitrakvi®

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 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 Fiona Mulligan	PCRS representative	By 'phone
Prof Jarushka Naidoo	Medical Oncologist, Beaumont: ISMO nominee	
Dr Derville O'Shea	Consultant Haematologist, Cork University Hospital: IHS representative	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 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	Chief 2 Pharmacist, NCCP
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. None were raised.	
2	**Notes of previous meeting and matters arising**	
	The notes of the previous meeting on January 24th 2022 were agreed.	
3	**Drugs/Technologies for consideration**	
	Brentuximab vedotin Adcetris® (**Ref. TRC 105)** *Treatment of adult patients with CD30+ Hodgkins Lymphoma (HL) at increased risk of relapse or progression following an autologous haematopoietic stem cell transplant (ASCT).* The clinical aspects of this indication were discussed, noting that brentuximab vedotin is already approved for reimbursement in a number of indications and so clinicians are well experienced with this medicine. The supporting evidence for this indication is the phase III AETHERA trial, which evaluated the efficacy and safety of brentuximab vedotin versus placebo in patients with CD30+ HL at risk of relapse or progression following ASCT. The trial showed a statistically significant improvement in progression free survival (PFS) with a difference of 18.8 months between the two arms (42.9 vs 24.1 months) at the 2 year primary analysis. The trial has not shown a statistically significant difference in overall survival (OS) to date, as the OS data is still immature. The safety profile was discussed, noting that clinicians are familiar with brentuximab vedotin, it is a well-tolerated medicine, and the most common toxicities are neuropathy and neutropenia. The pharmacoeconomic aspects as outlined in the HTA carried out by the NCPE were discussed, noting that there are a number of uncertainties impacting on the cost-effectiveness considerations including the use of PFS as a surrogate for OS, the unknown long term benefits due to immaturity of data and confounding due to later treatments given to patients. There are significant costs associated with this application which were discussed as well as the difficulty in capturing meaningful benefits through the prevention of relapse in this patient cohort. The HTA assessment recommends that this indication be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments. Commercial negotiations with the company are ongoing. Having considered the clinical efficacy of the indication and the unmet need in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness being achieved. *(Decision: TRC 105)* Brentuximab vedotin Adcetris® (**Ref. TRC 106)** *Treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) after at least 1 prior systemic therapy* The clinical aspects of this indication were discussed. The supporting evidence is the phase III ALCANZA trial which evaluated the efficacy and safety of brentuximab vedotin compared to standard of care (either methotrexate or bexarotene) in the treatment of patients with CD30+	

	cutaneous T-cell lymphoma (CTCL). The study demonstrated a difference in objective response rate that lasts at least 4 months (ORR4) between the two treatment groups, after a median follow-up of 22.9 months. The difference in ORR4 between the groups was noted to be statistically significant favouring brentuximab vedotin. These is a desire among the clinicians to have this treatment option available for this niche group of patients, noting that this can be a "horrible" disease that severely impacts upon patients with currently few good treatment options. The safety profile was discussed, noting that brentuximab vedotin is well tolerated, with the most common toxicities being neuropathy and neutropenia. The pharmacoeconomic aspects as outlined in the rapid review assessment carried out by the NCPE in 2018 were discussed, noting that a full HTA was recommended, but not completed. It was noted that only some of the subtypes were included and that there were challenges to the data assessment due to confounding factors such as crossover in treatment. The budget impact (BI) was outlined, noting that brentuximab vedotin is associated with higher cost. Commercial negotiations with the company are ongoing. Having considered the clinical efficacy of the indication and the unmet need in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness being achieved. *(Decision: TRC 106)* Brentuximab vedotin Adcetris® (**Ref. TRC 107)** *In combination with cyclophosphamide, DOXOrubicin and prednisolone (CHP) for use in adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL*). The clinical aspects of this indication were discussed. The supporting evidence is a phase III trial, ECHELON-2 study evaluating the efficacy and safety of brentuximab vedotin in combination with cyclophosphamide, doxorubicin, and prednisolone (CHP) in patients with previously untreated CD30+ peripheral T-cell Lymphoma (PTCL). The trial demonstrated a clear benefit in this patient cohort. The 5 year analysis showed a 30% reduction in the risk of progression free survival (PFS) events in patients treated with brentuximab vedotin plus CHP. PFS in the sALCL population the study showed a 45% reduction in PFS events. The study also demonstrated overall survival (OS) benefit with a 34% reduction in death in the sALCL population. The safety profile was discussed, noting that clinicians are familiar with brentuximab vedotin and it is well tolerated. It was noted that as brentuximab vedotin is given for 6-8 cycles for this indication, it is unlikely for patients to experience these toxicities which are more typically associated with longer usage. 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. It was noted that there is uncertainty regarding the population of eligible patients, therefore uncertainty associated with the overall budget impact. Clinicians highlighted that the number of patients is expected to be low. The likelihood of re-treatment of patients was flagged as an uncertainty and the clinicians discussed that it may be an option in certain patients in certain scenarios. Some additional limitations were outlined, including whether PFS gain would translate to OS gain. Commercial negotiations with the company are ongoing Having considered the clinical efficacy of the indication and the unmet need	

in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness being achieved.

(Decision: TRC 107)

Durvalumab Imfinzi® (Ref. TRC 108)

In combination with etoposide and either CARBOplatin or CISplatin as first-line treatment of patients with extensive-stage small cell lung cancer (ES-SCLC).

The clinical aspects of this indication were discussed, noting that SCLC is an orphan disease with no new treatment options in the past 30 years. The supporting evidence is the phase III CASPIAN trial evaluating the efficacy and safety of durvalumab with or without tremelimumab in combination with etoposide and either CARBOplatin or CISplatin. The study showed a meaningful benefit in overall survival (OS) with durvalumab alongside standard of care chemotherapy (etoposide and either CARBOplatin or CISplatin), with a mean OS of 12.9 months in the durvalumab plus chemotherapy group vs 10.5 months in the chemotherapy arm. The safety profile was outlined, noting that there were no concerning safety signals identified, with most toxicities arising from the chemotherapy component. From a clinical perspective there is a desire to have this treatment available as there is a significant unmet need for this patient population. It was noted that an alternate immunotherapy medicine in combination with systemic anti-cancer therapy is also in the assessment process for this indication, noting that this alternate option has a three weekly maintenance requirement and was only licensed in combination with one platinum option. This may result in a desire to use this option as it has a four weekly maintenance treatment schedule which would result in patients requiring less visits.

The pharmacoeconomic aspects as outlined in the rapid review assessment carried out by the NCPE were discussed. [redacted] The group agreed that there appeared to be little difference between the available options that would warrant any price differential.

Having considered the clinical efficacy of the indication and the unmet need in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness being achieved

(Decision:TRC108)

Larotrectinib Vitrakvi® (Ref. TRC 109)

Indicated for the treatment of adult and paediatric patients with solid tumours that display a Neurotrophic Tyrosine Receptor Kinase (NTRK) gene fusion,

- *who have a disease that is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and*
- *who have no satisfactory treatment options*

Larotrectinib is an oral agent, and the first targeted option for this patient cohort of patients with NTRK gene fusions. The clinical aspects of this indication were discussed. The supporting evidence is a basket design of studies consisting of a phase I (NCT02122913 trial),a phase I/II (SCOUT trial) and a phase II (NAVIGATE trial) trial across various solid tumours expressing

	the NTRK gene (thyroid, salivary gland, GIST, soft tissue sarcoma, NSCLC, CNS, colorectal, melanoma, breast, pancreas, SCLC, bone sarcoma, prostate, cervix).The study showed a high response rate of 72%, demonstrating that for patients who identify with the NTRK gene, larotrectinib is useful and provides a meaningful benefit. Considering the evidence, there is a desire among clinicians to have this treatment option available to this patient cohort. The safety profile was outlined noting that the most common side effects were LFT changes and diarrhoea. The pharmacoeconomic aspects as outlined in the HTA carried out by the NCPE were discussed. It was noted that this was an exceptionally challenging and complex HTA to complete, as the indication is agnostic of tumour site, many of the tumour types were rare, historical data had to be utilised for comparison and the heterogeneity across the tumour sites was seen in the trials. A number of adjustments and scenarios were included in the HTA to consider this, e.g. utility values as used in the NICE considerations. It was discussed that larotrectinib requires testing for the NTRK gene. Currently there is no testing pathway in the Irish health system. The establishment of this testing is associated with significant costs, which was incorporated into the base case analysis. It was discussed that this included all negative tests, which was applied to all costs and had a significant impact. It was noted that the cost of testing should be considered separately and was beyond the scope of the TRC's considerations when making their recommendations. Larotrectinib is associated with a high ICER, which was very sensitive to a number of scenarios and the HTA assessment concluded that cost effectiveness was not demonstrated at the current willingness to pay thresholds. Having considered the clinical efficacy of the indication and the unmet need in this patient cohort the committee members agreed unanimously to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness being achieved. *(Decision:TRC109) One member had left the meeting for the vote but quorum remained*	
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 March 28th	
6	**Any other business / Next meeting**	
	There was no other business.	

The meeting concluded at 5.45pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
22/02	21.02.2022	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Completed