National Cancer Control Programme

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**April 4th 2022 at 4.30pm**
Venue :	**Teleconference / NCCP Offices**
Assessment:	Alpelisib Piqray®
	Daratumumab Darzalex®
	Pegylated Liposomal Irinotecan Onivyde®
	Zanubrutinib Brukinsa®

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 Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	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 Fiona Mulligan	PCRS representative (Substitute Chair)	By 'phone
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		
Grainne O'Kane	Medical Oncologist, St. James Hospital	By 'phone

Apologies (members)	
Dr Linda Coate	Medical Oncologist, University Hospital Limerick: ISMO nominee
Dr Ronan Desmond	Consultant Haematologist, Tallaght University Hospital: IHS representative
Ms Patricia Heckmann	NCCP AND - Chair
Prof Michaela Higgins	Medical Oncologist, St. Vincent's University Hospital: ISMO nominee
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**	
	FM stepped in as substitute Chair for this meeting. 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 February 21st 2022 were agreed.	
3	**Drugs/Technologies for consideration**	
	Alpelisib Piqray® (**Ref. TRC 110)** *In combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative, locally advanced or metastatic breast cancer with a PIK3CA mutation after disease progression following endocrine therapy as monotherapy.* The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III SOLAR -1 study, which evaluated the efficacy and safety of alpelisib in combination with fulvestrant versus fulvestrant alone in postmenopausal women, and men, with HR+, HER2- advanced breast cancer. The study enrolled patients with and without the *PIK3CA* mutation and it was discussed that patients carrying the *PIK3CA* mutation cohort performed better than those without *PIK3CA* mutation. The study showed an improvement in objective response rates with alpelisib-fulvestrant than with placebo-fulvestrant in the *PIK3CA* mutation cohort (26.6% vs 12.8%).The safety profile was discussed, noting that alpelisib is quite a toxic drug, most notably with GI and cutaneous side effects as well as hyperglycaemia which necessitated the need for pre-treatment tests e.g. HbA1c. The potential place in therapy for this medicine was discussed, noting that the trial design excluded patients who had received CDK4/6 inhibitors, which is the current standard of care. It is anticipated that most patients at this point of the pathway are offered CDK4/6 inhibitor-based therapy. There is a desire among the breast cancer clinicians to have this treatment option available for certain suitable patients with a *PIK3CA* mutation, noting that this is likely to be a small number considering the place in therapy and the toxicity profile The pharmacoeconomic aspects as outlined in the HTA carried out by the NCPE were discussed. The uncertainty of the place in therapy was highlighted here also, noting that clinical opinion indicated that the sequencing of treatment may differ to the licensed indication as there may be a desire to treat patients post CDK 4/6 inhibitor, noting that this was not licensed by the European Medicines agency, nor was it considered within the trial. Alpelisib is associated with ICERS as outlined in the HTA and it was discussed that if used beyond the licensed indication, the associated costs could be significant and this would not be supported by evidence. It was highlighted that in line with its licensed indication the number of patients eligible for treatment will be low. 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 by majority to recommend approval of this indication to the HSE Drugs Group, subject to an	

improvement in cost effectiveness being achieved.

(Decision: TRC 110)

Daratumumab Darzalex® (**Ref. TRC 111)**

In combination with bortezomib, thalidomide and dexamethasone for the treatment of adults with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant.

The clinical aspects of this indication were discussed, noting that daratumumab 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 includes the phase III MMY 3006 study, which evaluated the efficacy and safety of daratumumab in combination with bortezomib, thalidomide and dexamethasone (D-VTd) to treatment with bortezomib, thalidomide and dexamethasone (VTd) in patients with newly diagnosed multiple myeloma eligible for ASCT. At day 100 post ASCT the study showed a Stringent Complete Response (sCR) of ~29% in the D-VTd group vs ~20% in the VTd group, and a Complete Response (CR) or better of ~39% in the D-VTd group vs ~26% in the VTd group. The study demonstrated that the addition of daratumumab up front significantly improves patient outcomes. The safety profile was discussed, noting that infusion reactions are a known consideration but that there is a subcutaneous product available which has reduced this side effect significantly and there are no other significant toxicity concerns.

The pharmacoeconomic aspects as outlined in the HTA carried out by the NCPE were discussed. Limitations regarding the evidence in the CASSIOPEIA study was highlighted, noting that the patient population may be younger than what would be expected in the Irish clinical population and concerns in terms of generalisability noting that the comparator regimen is not the preferred regimen in Ireland. The ICERS were discussed and it was highlighted that they were not significantly over the willingness to pay threshold. However, the evidence suggests strong clinical benefit of this indication with clear improvement in patient outcomes. The recommendation of the review group was to recommend reimbursement subject to an improvement in price. It was noted that commercial negotiations have taken place and an offer has been put forward.

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, subject to an improvement in cost effectiveness being achieved.

(Decision: TRC 111)

Pegylated Liposomal Irinotecan Onivyde® (**Ref. TRC 112)**

Treatment of metastatic adenocarcinoma of the pancreas, in combination with 5-fluorouracil (5-FU) and leucovorin (LV), in adult patients who have progressed following gemcitabine based therapy.

The clinical aspects of this indication were discussed. The supporting evidence for this indication is the phase III NAPOLI-1 trial, which evaluated the efficacy and safety of pegylated liposomal irinotecan (peg-IRI) alone or in combination with 5-FU/LV compared to 5-FU/LV in patients with metastatic pancreatic adenocarcinoma who have progressed after gemcitabine based therapy. The study met its endpoint, both primary and secondary. The showed an increased overall survival (OS) of 6.1 months in the peg-IRI +5-FU arm vs 4.2 months in the 5FU/LV arm and progression free

	survival (PFS) of 3.1 months in the peg-IRI +5-FU arm vs 1.5 months in the 5FU/LV arm. The safety profile was discussed, noting that it was well tolerated, with most common side effects being neutropenia and diarrhoea. Overall there is a desire among the clinicians to have this treatment option available due to unmet need, noting that there has been no other study in this disease showing level 1 evidence to support. The pharmacoeconomic aspects as outlined in the HTA carried out by the NCPE were discussed. The limitations of the study were discussed and adjustment to the models were made as outlined in the HTA assessment. It was highlighted that treatment benefit was modest, and there were concerns regarding the control arm of the trial, which are likely to be inferior to clinical practice and that generalisability to the Irish population is questionable. Additionally, no benefit was seen in quality of life (HRQOL). In terms of cost effectiveness parameters were adjusted in the base case to consider a number of scenarios. This treatment is associated with high ICERS (in irinotecan naïve and pre-treated populations) and a high net budget impact, with the probability of cost effectiveness at the willing to pay threshold being near 0%. 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 by majority to recommend approval of this indication to the HSE Drugs Group, subject to an improvement in cost effectiveness being achieved. *(Decision: TRC 112)* **Zanubrutinib Brukinsa® (Ref. TRC 113)** *For the treatment of for adult patients with Waldenström's macroglobulinemia (WM) who have received at least one prior therapy, or as first-line treatment for patients unsuitable for chemo-immunotherapy.* The group was informed by the Chair that this application for reimbursement is being progressed as a cost minimisation piece by the PCRS. All agreed that that zanubrutinib should be made available for reimbursement for this patient cohort. *(Decision:TRC113)*	
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 April 25th	
6	**Any other business / Next meeting**	
	There was no other business.	

The meeting concluded at 5.20pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update
22/03	04.04.2022	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Completed