National Cancer Control Programme

NCCP Technology Review Committee (TRC)

Meeting Notes

Date of Meeting:	**24th February 2025 at 4.30pm**
Venue:	**Teleconference via MS Teams**
Assessment:	Durvalumab (Imfinzi®)
	Ribociclib (Kisqali®)

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 MS Teams
Dr Neil Barrett	Consultant Haematologist, Children's Health Ireland – Crumlin **(Chair)**	By MS Teams
Dr Patrick Hayden	Consultant Haematologist, St James's :IHS representative	By MS Teams
Ms Fiona Mulligan	PCRS representative	By MS Teams
Ms Aishling McLoughlin	Chief I Pharmacist, NCCP (Deputy Chair)	
Dr Dearbhaile O'Donnell	Medical Oncologist, St. James's Hospital: ISMO nominee	By MS Teams
Dr Susan Spillane	HTA Directorate: HIQA nominee	By MS Teams
Non-member invited specialists present		
Prof Maccon Keane	NCCP National Medical Oncology Programme Clinical Advisor	By MS Teams
Apologies (members)		
Dr Oscar Breathnach	Medical Oncologist, Beaumont: ISMO nominee	
Dr Dearbhaile Collins	Consultant Medical Oncologist, Cork University Hospital: ISMO nominee	
Prof Michael O'Dwyer	Consultant Haematologist, Galway :IHS representative	
Observers present		
Ms Helena Desmond	Senior Pharmacist, NCCP	By MS Teams

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 January 27th 2025 were reviewed and agreed.	
3	**Drugs/Technologies for consideration**	
	DurvalumAB (Imfinzi®) **(Ref. TRC 168)** *In combination with gemcitabine and cisplatin for the first-line treatment of adults with unresectable or metastatic biliary tract cancer (BTC).* The clinical aspects of this indication were discussed. The supporting evidence for this indication comes from the TOPAZ-1 trial, a phase III, double-blind, placebo-controlled trial in patients with unresectable or metastatic TBC. The trial evaluated the use of durvalumab in combination with gemcitabine and CISplatin compared to gemcitabine and CISplatin for eight cycles, then followed by durvalumab as monotherapy until disease progression. It was noted that gemcitabine in combination with CISplatin is the current standard of care (SOC) chemotherapy in Ireland for this patient cohort. The primary endpoint was overall survival (OS), and the trial showed that OS in the durvalumab plus chemotherapy arm improved to 12.8 months from 11.5 months in the chemotherapy arm. The trial also showed a progression free survival (PFS) of 7.2 months in the durvalumab plus chemotherapy arm versus 5.7 months in chemotherapy arm. The projected OS at 12 months was 54% with durvalumab plus chemotherapy versus 48% with chemotherapy alone, and 25% versus 10% at 24 months respectively. While there was not a very significant change in terms of the absolute OS gained, the tail in the survival curve is very significant with an almost doubling at 24 months, which is where the benefit of durvalumab is seen. Durvalumab in combination with chemotherapy represents new SOC in this space, and there is a desire among the clinicians to have this treatment option available to this patient cohort. It was noted that patients who don't benefit from this treatment are identified very early, and that the number of patients to reach 24 months would be very small. It is anticipated that there will be a low number of patients eligible for this treatment. The pharmacoeconomic aspects as outlined in the HTA assessment carried out by the NCPE were discussed. The relevant comparator was discussed and the supporting evidence was outlined. In terms of OS, the study met its primary objective with a median OS of 12.8 months in the durvalumab plus chemotherapy arms versus 11.5 months in the chemotherapy arm, with a hazard ratio (HR) of 0.80, and an OS maturity of 61.9% at the second internal analysis (IA2). At a further data cut of February 2022, at the 26.9 month update there was a slight improvement with a median OS of 12.9 months vs 11.3 months and a HR of 0.74. It was noted that what while the OS benefit is modest, it is considered clinically relevant in view of the poor prognosis for this patient cohort. In terms of PFS benefit, at the IA2, the median PFS was 7.2 months in the durvalumab plus chemotherapy arms versus 5.7 months in the chemotherapy arm. The NCPE Review Group highlighted a number of limitations regarding the supporting evidence, such as the high number of Asian patients, generalisability of the results and the lack of evidence in patients with ECOG performance status of ≥2. However, it was noted that a real world retrospective multicentre study conducted by Rimini et al[1], which did not include Asian population, mostly confirmed the results achieved in the TOPAZ-1 trial in terms of PFS, ORR and safety.The safety profile was	

[1] Rimini, M et al. Durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer: an early exploratory analysis of real-world data. *Liver international 2023, 43*(8), pp.1803-1812. Available here: https://pubmed.ncbi.nlm.nih.gov/37452505/

discussed, noting that no new safety concerns were identified. The cost effectiveness analysis and the modelling used was outlined. In terms of cost, the cost per treatment course of durvalumab plus gemcitabine and CISplatin based on the Applicant estimates, based on median PFS was estimated to be [redacted]. Using the NCPE estimates, based on the time to treatment discontinuation (TTD) data from the trial the estimated total cost per patient per treatment is €140,323 including VAT and €112,151 excluding VAT, and the cost of gemcitabine and CISplatin is [redacted]. In terms of the results, the applicant's ICER is €191,957 per QALY. A number of changes were made to the NCCP base case which resulted in a NCPE-adjusted base case ICER of €330,331 per QALY. A rebate of 92.9% is needed to meet the €45,000 per QALY threshold. In terms of the budget impact (BI), the total eligible patient population is estimated to be [redacted], and the market share is estimated to be [redacted] It is estimated that [redacted]. Using the NCPE adjusted base case the cumulative 5-year gross BI is estimated to be [redacted] The net BI over 5 years is estimated to be [redacted] The NCPE recommends that durvalumab 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 particularly in relation to the proportion of patients who experienced prolonged survival as evidenced by the extended tail on the survival curve, and the unmet need for this patient population, the committee members agreed by majority to recommend approval of this indication to the HSE Drugs Group subject to an improvement in cost.

(Decision: TRC 168)

Ribociclib (Kisqali ®) (**Ref. TRC 169)**

In combination with an aromatase inhibitor (AI) is indicated for the adjuvant treatment of patients with hormone receptor positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence.

The clinical aspects of this indication were discussed, noting that another CDK4/6 inhibitor, abemaciclib is currently reimbursed in the adjuvant setting, however unlike ribociclib, abemaciclib is only licensed for node positive disease, therefore, it is considered that there is an unmet need for node negative patients. The supporting evidence for this indication is the NATALEE trial, a phase III, randomised, open label trial investigating the use of ribociclib in combination with an AI for the adjuvant treatment of patients with stage II or III hormone HR+, HER2-negative early breast cancer at high risk of recurrence. The primary endpoint was invasive disease-free survival (iDFS) and trial showed a 3 year iDFS benefit of 90% in the ribociclib arm versus 87% in the placebo arm. It was noted that in terms of HR+ disease 50% of relapses occur after year 4, and it is considered a relatively early time point to achieve a 3 year disease free benefit in this group of patients. While the trial has shown a progression free survival (PFS) benefit, an overall survival (OS) benefit has not yet been demonstrated. It was noted that there is a large cohort of patient that would be eligible treatment. Based on the PFS at 3 years it is likely to reflect bigger PFS over time and that OS will reflect this. The safety profile was discussed noting that the adjuvant dose of 400mg (compared to 600mg dosing in the metastatic setting) has a low toxicity profile, and it is better tolerated than abemaciclib. There is a strong desire among the clinicians to have ribociclib available for this patient cohort.

The pharmacoeconomic aspects as outlined in the rapid review (RR)

	assessment carried out by the NCPE were discussed, noting that a full HTA was not recommended. The dosing and duration of treatment for ribociclib was discussed, along with the relevant comparator, and the positioning of ribociclib in the treatment pathway was outlined. The supporting clinical evidence was discussed, highlighting the immaturity of the data, at the final iDFS analysis in July 2023, 8.9% of the ribociclib arm experienced an event compared to 11.1% in the control arm, with a HR of 0.75 in favour of the ribociclib, demonstrating a statistical improvement in iDFS and distant disease free survival (DDFS) compared to AI alone. A 4 year landmark analysis (April 2024) also showed an improvement in iDFS and DDFS, however the OS data remains immature. The NCPE Review Group highlighted a number of limitations, such as the immaturity of the OS data, disease recurrence beyond the follow up period, uncertainty as to whether ribociclib leads to improved iDFS or delays iDSF from occurring, and the open label investigator assessed endpoints. In term of the cost, the cost of ribociclib plus an AI plus goserelin based on time on treatment (TOT) of 26.5 months (as per the NATALEE trial) is The cost of abemaciclib plus AI plus goserelin assuming TOT of 20.95 (as per the monarchE trial) is The cost of ribociclib plus an AI plus goserelin based on the maximum treatment duration of 3 years is . The cost of abemaciclib plus AI plus goserelin based on the maximum duration of 2 years is noting that cost are similar TOT is assumed. The cost of AI monotherapy plus goserelin is and the cost of tamoxifen plus goerelin is . In terms of the budget impact (BI) the applicant assumes that ribociclib will have based on the assumption that ribociclib will replace abemaciclib for patients with node negative disease, noting that the Applicant assumes that the usage in node negative population will be low and the use of CDK4/6 inhibitors in general in the adjuvant setting will increase over that timeframe. The Applicant estimates The 5-year gross BI is estimated to be including VAT and the 5-year net BI is estimated to be including VAT. Assuming the maximum duration of treatment for both ribociclib and abemaciclib the net BI for ribociclib increases to including VAT. The recommendation by the NCPE was not to recommend a full HTA and that ribociclib not be considered for reimbursement at the submitted price. Having considered the clinical efficacy and tolerability of ribociclib for this 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. *(Decision: TRC 169)*	
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 Monday March 24th 2025	
6	**Any other business / Next meeting**	

The meeting concluded at 17.50pm.

Actions arising from meeting:

Ref.	Date of meeting	Details of action	Responsible	Update

25/02	24/02/2025	NCCP to communicate recommendations to HSE Drugs Group.	NCCP	Complete
25/02	24/02/2025	Apply for CPD	NCCP	Complete