

Budget Impact of Ribociclib Plus Letrozole For The Treatment of Post-Menopausal Women With Hormone Receptor-Positive (HR+), Human Epidermal Growth Factor Receptor 2- Negative (HER2-) Advanced or Metastatic Breast Cancer in Denmark

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Introduction

Breast cancer is defined as a malignant cellular growth in the tissue(s) of the breast. Breast cancer does not generally become life-threatening until it develops the capacity to invade or metastasize to the surrounding tissues and other parts of the body¹ Breast cancer subtypes can be distinguished by the expression of hormone receptors (HRs, i.e. estrogen receptors (ERs) and progesterone receptors (PgRs)), HER2, as well as by distinct gene expression profiles (such as the proliferation marker Ki-67).² Approximately 50% and 75% of breast cancers are PgR-positive and ER-positive, respectively.^{3,4} Ribociclib is a CDK4/6 inhibitor, which in combination with letrozol (LET) has been shown to be more efficacious than LET alone in the treatment of postmenopausal women with HR-positive, HER2-negative advanced breast cancer.⁵⁻¹⁰

Objectives

The objective is to estimate cost and budget impact of establishing ribociclib+letrozole (ribociclib) as a first-line treatment option for post-menopausal women with HR+/HER2- advanced or metastatic breast cancer compared to palbociclib+letrozole (palbociclib) in Denmark

Methods

A two-year budget impact model with a Danish national payer perspective was developed to estimate the incremental cost of introducing ribociclib in patients with HR+/HER2- breast cancer eligible for treatment. Progression free survival, incidence and type of adverse events and dose distributions were all taken from the registration trial MONALEESA-2. Ribociclib has a starting dose of three times 200mg tablets (600mg) and two lower doses of 400- and 200mg (**Table 1**).⁵ Palbociclib has also three different doses with a 125 mg capsule as starting dose and two lower doses with either 100- or 75mg capsules.⁶ Acquisition costs (pharmacy purchasing price), monitoring, health state cost (progression-free and post-progression) and cost associated with relevant grade 3 and 4 adverse events, were included based on Danish tariffs (DRG) (**Table 2-6**). 270 patients were assumed eligible for treatment, based on clinical expert opinion.⁷ New patients would enter the model each year and patients could exit due to death. The budget impact was calculated based on two treatment mixes, one where ribociclib is not considered as standard treatment and one where ribociclib is considered standard treatment.

Table 1. Recommended Dose Modification for Adverse Reactions with Ribociclib

Level	Dose	Number of tablets
Starting dose	600 mg/day	three 200 mg tablets
First dose reduction	400 mg/day	two 200 mg tablets
Second dose reduction	200 mg/day	one 200 mg tablet

Source: (5)

Table 2. Drug Resource Use and Costs Used in the Cost Analysis

Drug	Daily dose (mg)	Dose per month (mg)	Pack size	Strength	Pack price (DKK)
Ribociclib	600	13697	63	200	27993
Ribociclib	400	9131	42	200	18662
Ribociclib	200	4566	21	200	9331
Palbociclib	125	2854	21	125	27993
Palbociclib	100	2283	21	100	27993
Palbociclib	75	1712	21	75	27993
Letrozole	2.5	76	100	2.5	150

Source: (5, 6 and 9)

Table 3. Resource Use Associated with the Monitoring of Treatment

Item	Ribociclib – 1 st year	Ribociclib – subsequent years	Palbociclib – 1 st year	Palbociclib – subsequent years
Electrocardiogram	3	0	0	0
Complete blood	8	0	15	13
Liver function test	8	0	0	0
Electrolytes	6	0	0	0

Source: (5 and 6)

Table 4. Monitoring Unit Costs

Item	Unit cost (DKK)	Source	Note
Electrocardiogram	171.32	(11)	Specialist
Liver status	140	(12)	Clinical and Biochemical rates
ASAT	28		
ALAT	28		
BASP	28		
BILI	28		
GGT	28		
Electrolytes	118	(12)	Clinical and Biochemical rates
P-Na	17		
P-K	17		
P-Mg	28		
P-Ca	28		
P-Fosfat	28		
Full blood	231	(13)	

Table 5. Resource Use Associated with Routine Treatment of Patients

Item	PFS, per month	PD, per month
GP visit	0.22	0.29
Oncology clinic	0.87	1.20
Nurse specialist	0.33	0.33
Nurse	0.19	0.36
Social worker	0.03	0.04
Radiographer	0.23	0.25
Hospitalization	0.47	0.70
Bone scintigraphy	0.46	0.18
Bone x-ray	0.02	0.04
Chest x-ray	0.11	0.08
CT scan	0.46	0.44
Liver ultrasound	0.10	0.23
MRI	0.07	0.33
PET	0.02	0.18

PFS: Progression free survival, PD: Progressed disease, GP: General practitioner, CT: Computer tomography, MRI: Magnet resonance imaging, PET: Positron Emission Tomography, Source (5)

Table 6. Unit Costs Associated with Routine Treatment of Patients

Item	Unit cost (DKK)	Source	Comment
GP visit	1126	(14)	Municipality physicians
Oncology clinic	1891	(15)	
Nurse specialist	686	(14)	Assumed to cost as head nurse
Nurse	522	(14)	Assumed to cost as not head nurse
Social worker	488	(14)	Assumed 1 h
Radiographer	490	(14)	Assumed 1 h
Hospitalization	4195	(15)	
Bone scintigraphy	736	See Chest x-ray	Assumption
Bone x-ray	736	See Chest x-ray	Assumption
Chest x-ray	736	DRG Takst PG14R	2017 tariff
CT scan	5063	(15)	Assumed the same as CT scan of abdomen
Liver ultrasound	521	UL-scanning, PG14K	2017 tariff
MRI	2323	DRG Takst PG14D	2017 Tariff
PET	5063		Assumed to be the same cost as for CT

PFS: Progression free survival, PD: Progressed disease, GP: General practitioner, CT: Computer tomography, MRI: Magnet resonance imaging, PET: Positron Emission Tomography, DRG: Diagnose related groups, Source (14 and 15)

Results

In a cohort of 270 patients the inclusion of ribociclib would be associated with a total saving of approximately DKK 4.3 million for a time horizon of two years (**Table 8**). Ribociclib have a lower linear acquisition cost for the lower doses of 400 and 200 mg, but palbociclib have a flat acquisition cost for all three doses. Hence, the cost-savings related to ribociclib are mostly due to reduced drug costs due to down dosing. Increased costs are noted for adverse events and monitoring, the increased costs in monitoring is due to the increased number of tests (**Table 7**).

Table 7. Results Cost per Patient (DKK) Excluding Patient Costs, Comparison Ribociclib and Palbociclib Excluding Patient Time and Travel Costs

Item	Ribociclib (DKK)	Palbociclib (DKK)	Difference (DKK)
Drug costs			
Ribociclib	369 575	0	369 575
Palbociclib	0	449 652	-449 652
Letrozole	826	826	0
Total – drug costs	370 401	450 478	-80 077
Monitoring	2 406	1759	647
Healthcare use/Imaging	174 347	174 347	0
Adverse events	3 018	2 477	541
Total	550 173	629 062	-78 889

Table 8. Results of Budget Impact Analysis Over Two Years

Item	Without ribociclib (DKK)	With ribociclib (DKK)	Difference (DKK)
Drug cost*			
Ribociclib	0	21 739 123	21,739,123
Palbociclib	199 428 161	173 301 888	-26 126 273
Total	199 428 161	195 041 012	-4 387 149
Adverse events			
Ribociclib	0	204 033	204 033
Palbociclib	1339 597	1172 148	-167 450
Total	1339 597	1376 181	36 583
Monitoring			
Ribociclib	0	162 683	162 683
Palbociclib	793 983	690 465	-103 518
Total	793 983	853 148	59 165
Healthcare			
Ribociclib	0	9 603 896	9 603 896
Palbociclib	71 999 317	62 395 421	-9 603 896
Total	71 999 317	71 999 317	0
Sum	273 561 059	269 269 658	-4 291 401

*Cost of letrozole included (the same for both arms)

Discussion

Ribociclib and palbociclib are both CDK4/6 inhibitors and have been shown to have a similar treatment profile in combination with LET (5 and 6). Thus, it was expected that the two treatment regimens included in this budget impact model, would be similar in terms of cost except for drug cost. Though one limitation of this analysis was that the model used a monthly cost for each dose and applied this to the number of patients on each dose at each month. However, typically the physician will adjust the dose in case the patients experience an adverse event (5 and 6). Thus, the model did not calculate the drug wastage in case patients would need to adjust in-between doctor visits. Ribociclib comes in packs including 200mg tablets and hence in case of dose adjustment, the patient will have to take one tablet less every day. For palbociclib the patient will have to get a new pack with a lower dose. In the pivotal trial approximately half of the patients had at least one dose adjustment (10) and hence the incremental difference in drug cost could be larger than in the base case.

Conclusion

The budget impact of introducing ribociclib in combination with LET as standard treatment in Denmark is cost-saving compared to palbociclib in combination with LET for the treatment of postmenopausal women with HR-positive, HER2-negative advanced breast cancer.

Keywords

Economic evaluation, Budget impact, Breast cancer

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