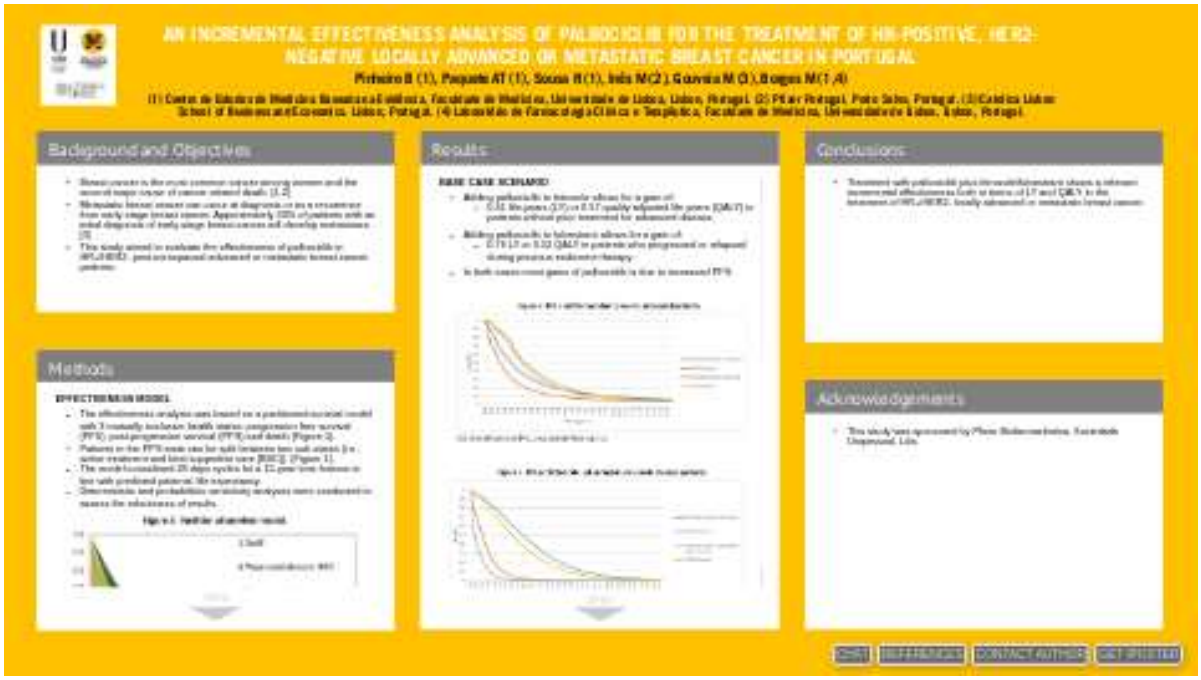
AN INCREMENTAL EFFECTIVENESS ANALYSIS OF PALBOCICLIB FOR THE TREATMENT OF HR-POSITIVE, HER2-NEGATIVE LOCALLY ADVANCED OR METASTATIC BREAST CANCER IN PORTUGAL



Pinheiro B (1), Paquete AT (1), Sousa R (1), Inês M (2), Gouveia M (3), Borges M (1,4)

(1) Centro de Estudos de Medicina Baseada na Evidência, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal. (2) Pfizer Portugal, Porto Salvo, Portugal. (3) Catolica Lisbon School of Business and Economics. Lisbon, Portugal. (4) Laboratório de Farmacologia Clínica e Terapêutica, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal.

PRESENTED AT:

Virtual ISPOR Europe 2020 | 16-19 November

BACKGROUND AND OBJECTIVES

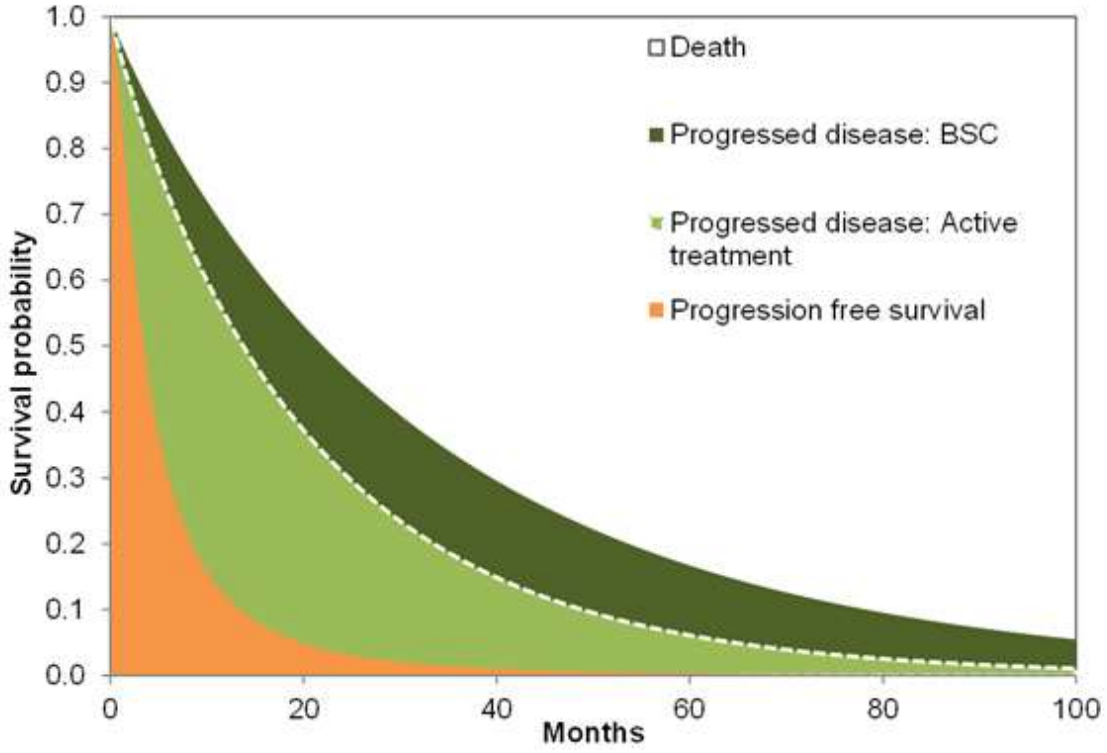
- Breast cancer is the most common cancer among women and the second major cause of cancer-related death. [1,2]
- Metastatic breast cancer can occur at diagnosis or as a recurrence from early-stage breast cancer. Approximately 30% of patients with an initial diagnosis of early-stage breast cancer will develop metastases. [3]
- This study aimed to evaluate the effectiveness of palbociclib in HR+/HER2- post-menopausal advanced or metastatic breast cancer patients:
  - Plus letrozole vs. letrozole: in women without prior treatment;
  - Plus fulvestrant vs. fulvestrant: in women with prior endocrine treatment.

METHODS

EFFECTIVENESS MODEL

- The effectiveness analysis was based on a partitioned survival model with 3 mutually exclusive health states: progression free survival (PFS), post-progression survival (PPS) and death (Figure 1).
- Patients in the PPS state can be split between two sub-states (i.e., active treatment and best supportive care [BSC]). (Figure 1).
- The model considered 28 days cycles for a 15-year time horizon in line with predicted patients' life expectancy.
- Deterministic and probabilistic sensitivity analyses were conducted to assess the robustness of results.

Figure 1. Partitioned survival model.



OS, overall survival; PFS, progression-free survival; PPS, post-progression survival

CLINICAL DATA

- A combined analysis with Kaplan-Meier (KM) data (until at least 10% of patients were still at risk of event) and parametric projections was used to estimate PFS and overall survival (OS), defining patients' distribution between the health states pre-progression, progressed disease and death (Table 1).
- Separate parametric models by arm were adjusted to PFS and OS data, based on goodness of fit criteria and clinical validity, as recommended by NICE´s Decision Support Unit [4].

Women without prior treatment

- PFS data was based on phase II trial PALOMA-2 and OS data was based on phase III trial PALOMA-1 given immature data from PALOMA-2 trial. [5,6]

Women with prior endocrine treatment

- PFS data was based on phase III trial PALOMA-3 OS data but adjusted according to Beauchemin et al. (2014). [7,8]

Table 1. Modelling summary of survival outcomes.

Outcome	Women without prior treatment		Women with prior endocrine treatment	
	Palbociclib + letrozol	Letrozol	Palbociclib plus fulvestrant	Fulvestrant
PFS	Log-logistic		Weibull	
OS	Log-logistic		Weibull (adjusted)	

OS, Overall survival; PFS, progression-free survival
Source: PALOMA-2; PALOMA-3; Beauchemin *et al* (2014).

UTILITIES

- Health related quality of life was estimated for PFS and PPS from EQ-5D-3L questionnaires from PALOMA-2 and PALOMA-3 in active treatment (Table 2). UK tariffs were used for utility calculation. [5,7,9]
- HRQL for post-progression in BSC was derived from Lloyd et al.(2006) who obtain UK-based societal preferences for distinct stages of MBC using a standard gamble method (Table 2). [10]

Table 2. Utility scores per health state.

	Women without prior treatment		Women with prior endocrine treatment	
	Palbociclib + Letrozol	Letrozol	Palbociclib + Fulvestrant	Fulvestrant
PFS	0.740	0.710	0.740	0.703
PPS, active treatment	0.643	0.643	0.590	0.590
PPS, BSC	0.448	0.448	0.448	0.448

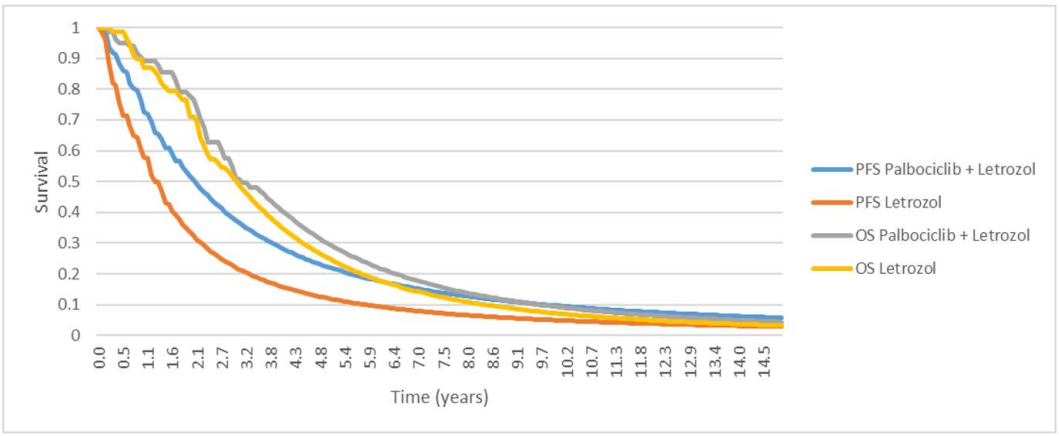
BSC, Best supportive care; PFS, progression-free survival; PPS, post-progression survival
Source: PALOMA-2; PALOMA-3; Lloyd *et al*. (2006).

RESULTS

BASE CASE SCENARIO

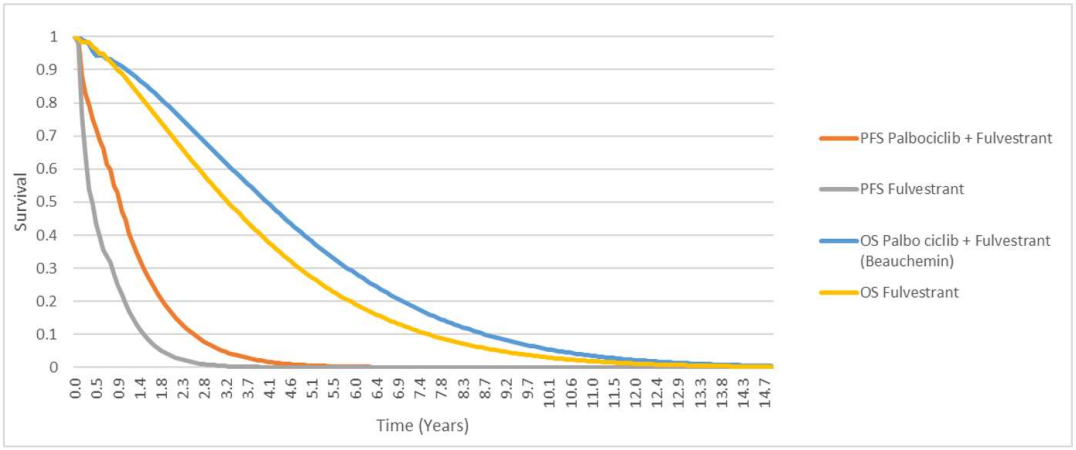
- Adding palbociclib to letrozole allows for a gain of:
  - 0.41 life-years (LY) or 0.57 quality adjusted life years (QALY) in patients without prior treatment for advanced disease.
- Adding palbociclib to fulvestrant allows for a gain of:
  - 0.76 LY or 0.52 QALY in patients who progressed or relapsed during previous endocrine therapy.
- In both cases most gains of palbociclib is due to increased PFS.

Figure 2. PFS and OS modelled curves in untreated patients.



OS, Overall survival; PFS, progression-free survival

Figure 3. PFS and OS modelled curves in previously treated patients.



OS, Overall survival; PFS, progression-free survival

Table 3. Effectiveness results: Palbociclib + letrozol *vs.* letrozol (A) and Palbociclib + fulvestrant *vs.* fulvestrant (B).

A.

	Women without prior treatment		
	Palbociclib + letrozol	**Letrozol**	**Palbociclib + letrozol *vs.* letrozol**
LY - PFS	3.59	2.42	1.18
LY – PPS	0.87	1.63	-0.76
Total LY	4.46	4.05	0.41
QALY -PFS	2.66	1.72	0.94
QALY - PPS	0.48	0.85	-0.37
Total QALY	3.14	2.57	0.57

LY, life-years; PFS, progression-free survival; PPS, post-progression survival; QALY, quality adjusted life years.

B.

	Women with prior endocrine treatment		
	Palbociclib + fulvestrant	**Fulvestrant**	**Palbociclib + fulvestrant *vs.* fulvestrant**
LY - PFS	1.22	0.66	0.52
LY - PPS	3.42	3.23	0.19
Total LY	4.65	3.89	0.76
QALY -PFS	0.91	0.46	0.44
QALY - PPS	1.61	1.52	0.08
Total QALY	2.51	1.99	0.52

LY, life-years; PFS, progression-free survival; PPS, post-progression survival; QALY, quality adjusted life years.

SENSITIVY ANALYSES

- Deterministic sensitivity analyses show that results are sensitive to parametric extrapolation of both PFS and OS and utility weights.
- In women without prior treatment, the highest and lowest incremental QALY is obtained when varying the utility values in more and less 20%
- In women with prior treatment, the highest incremental QALY is obtained when varying the utility values in more 20%. The lowest incremental QALY is obtained when OS is extrapolated through a log-logistic curve.

CONCLUSIONS

- Treatment with palbociclib plus letrozole/fulvestrant shows a relevant incremental effectiveness both in terms of LY and QALY in the treatment of HR+/HER2- locally advanced or metastatic breast cancer.

ACKNOWLEDGEMENTS

- This study was sponsored by Pfizer Biofarmacêutica, Sociedade Unipessoal, Lda.

REFERENCES

[1] Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al. Global Cancer Observatory: Cancer Today Lyon, France: International Agency for Research on Cancer; 2020 [Available from: https://gco.iarc.fr/today.

[2] Cardoso F, Harbeck N, Fallowfield L, Kyriakides S, Senkus E; ESMO Guidelines Working Group. Locally recurrent or metastatic breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2012;23 Suppl 7:vii11-9.DGS, 2012

[3] O'Shaughnessy, J. (2005) 'Extending Survival with Chemotherapy in Metastatic Breast Cancer', The Oncologist. Wiley, 10(S3), pp. 20–29. doi: 10.1634/theoncologist.10-90003-20 (http://sci-hub.tw/10.1634/theoncologist.10-90003-20).

[4] Latimer NR. Survival analysis for economic evaluations alongside clinical trials--extrapolation with patient-level data: inconsistencies, limitations, and a practical guide. Med. Decis. Making. Aug 2013;33(6):743-754.

[5] Finn R, Martin M, Rugo HS, Jones SE, Im SA, Gelmon KA, Harbeck N, Lipatov ON, Walshe JM, Moulder S, Gauthier ER, Lu D, Randolph S, Diéras V, Slamon DJ. PALOMA-2: Primary results from a phase III trial of palbociclib (P) with letrozol (L) compared with letrozol alone in postmenopausal women with ER+/HER2– advanced breast cancer (ABC). J Clin Oncol 34, 2016 (suppl; abstr 507).

[6] Finn RS, Crown JP, Lang I, Boer K, Bondarenko IM, Kulyk SO, Ettl J, Patel R, Pinter T, Schmidt M, Shparyk Y, Thummala AR, Voytko NL, Fowst C, Huang X, Kim ST, Randolph S, Slamon DJ. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozol versus letrozol alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. Lancet Oncol. 2015 Jan;16(1):25-35.

[7] Cristofanilli M, Turner NC, Bondarenko I, Ro J, Im SA, Masuda N, Colleoni M, DeMichele A, Loi S, Verma S, Iwata H, Harbeck N, Zhang K, Theall KP, Jiang Y, Bartlett CH, Koehler M, Slamon D. Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. Lancet Oncol. 2016 Apr;17(4):425-39.

[8] Beauchemin C, Cooper D, Lapierre MÈ, Yelle L, Lachaine J. Progression-free survival as a potential surrogate for overall survival in metastatic breast cancer. Onco Targets Ther [Internet]. 2014 Jun 18 [cited 2020 Oct 16];7:1101–10. Available from: https://pubmed.ncbi.nlm.nih.gov/24971020/

[9] Harbeck N, Iyer S, Turner N, Cristofanilli M, Ro J, André F, et al. Quality of life with palbociclib plus fulvestrant in previously treated hormone receptor-positive, HER2-negative metastatic breast cancer: patient-reported outcomes from the PALOMA-3 trial. Annals Oncol. 2016

[10] Lloyd A, Nafees B, Narewska J, Dewilde S, Watkins J. Health state utilities for metastatic breast cancer. BrJCancer. 2006;95(6):683-90.