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Palbociclib for mBC in real-world: a monocentric prospective study exploring efficacy (according to prior treatments), safety and subsequent therapies

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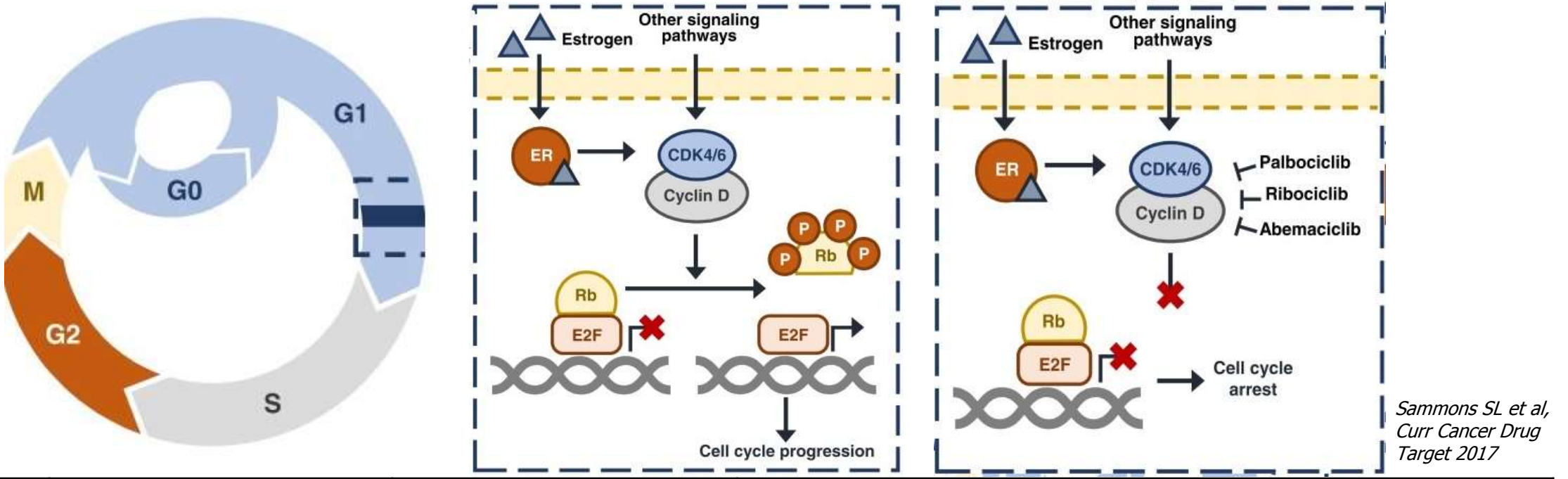
BACKGROUND: CDK 4/6 inhibitors

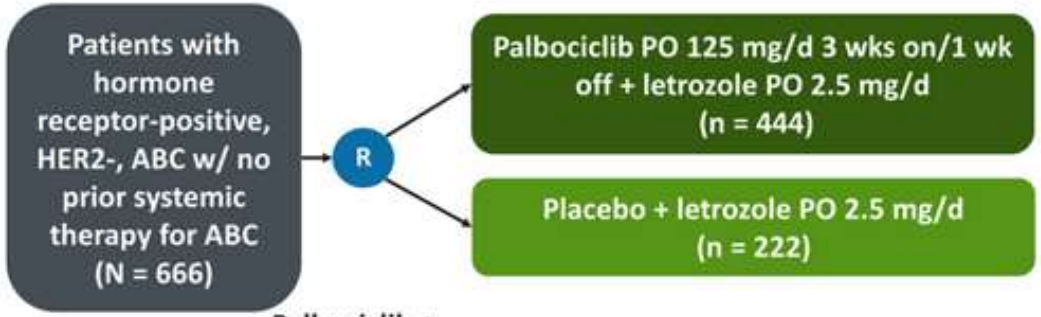


Sammons SL et al, Curr Cancer Drug Target 2017

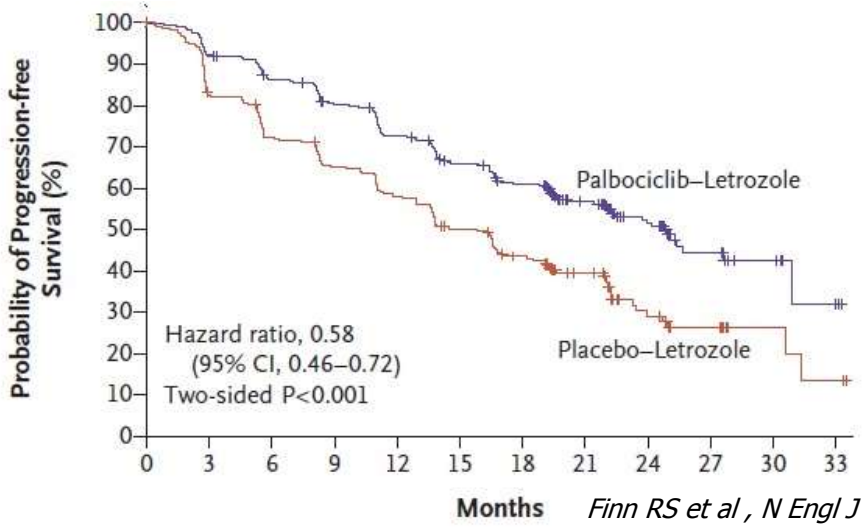
FDA-approved	Dose	Schedule	Indications
Palbociclib	125 mg daily	3 weeks on/1 week off	**First line, AI-sensitive** with AI **Progressing after ET**, with Fulvestrant
Ribociclib	600 mg daily	3 weeks on/1 week off	**First line, AI-sensitive** with AI
Abemaciclib	150 mg or 200 mg daily	Continuous	**First line, AI-sensitive** with AI **Progressing after ET** with Fulvestrant **Monotherapy after progression** on ET and CT

BACKGROUND: palbociclib

First line setting: **PALOMA 2**

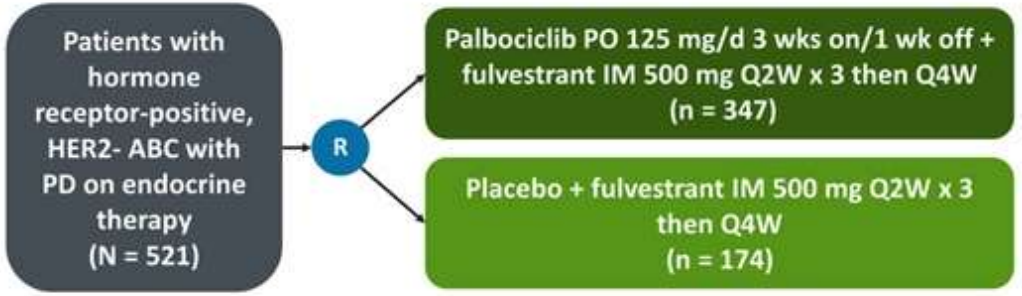


	Palbociclib + Letrozole	Letrozole	HR (95% CI)	*P* Value
Median PFS, mo	24.8	14.5	0.58 (0.46, 0.72)	<.000001

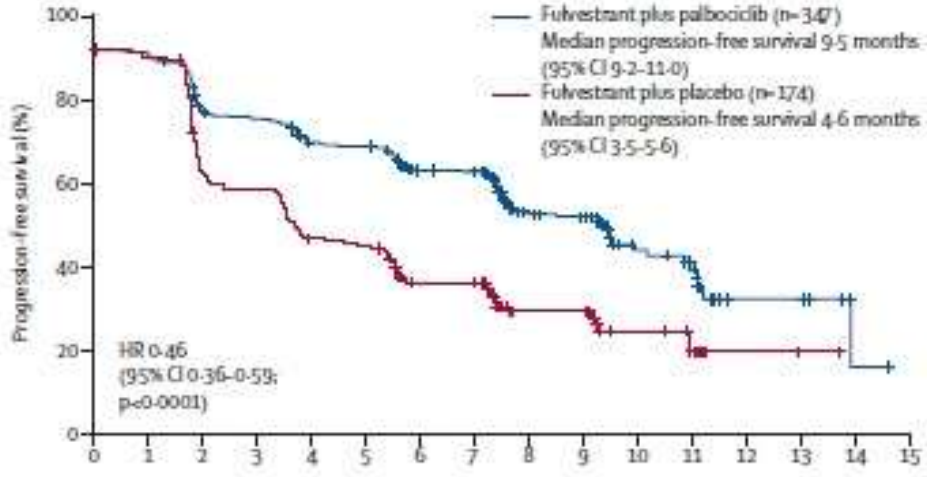


Finn RS et al , N Engl J Med, 2016

Progression after ET: **PALOMA 3**



	Palbociclib + Fulvestrant	Placebo + Fulvestrant	HR (95% CI)	*P* Value
Median PFS, mo	9.2	3.8	0.42 (0.32, 0.56)	<.001



Cristofanilli M. et al , Lancet Oncol 2016

METHODS

- Observational, single-institution, prospective study
- Approved by ethics committee
- From May 2017 to January 2018 (timeframe between AIFA palbociclib approval and price negotiation)

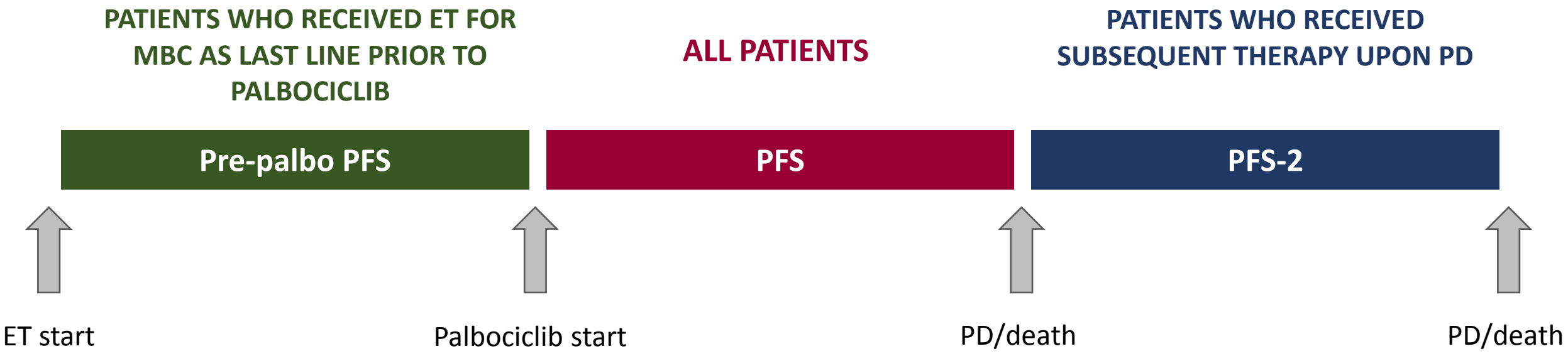
Study Population

- Pre and postmenopausal women and men with HR positive, HER2 negative MBC
- **Palbociclib + ET** (Fulvestrant or AI) in any line of treatment following specific nominal concession

Endpoints

- ORR RECIST 1.1
- PFS
- Safety (AEs NCTCAE v4.0)

METHODS: survival endpoints



RESULTS: patients' baseline characteristics

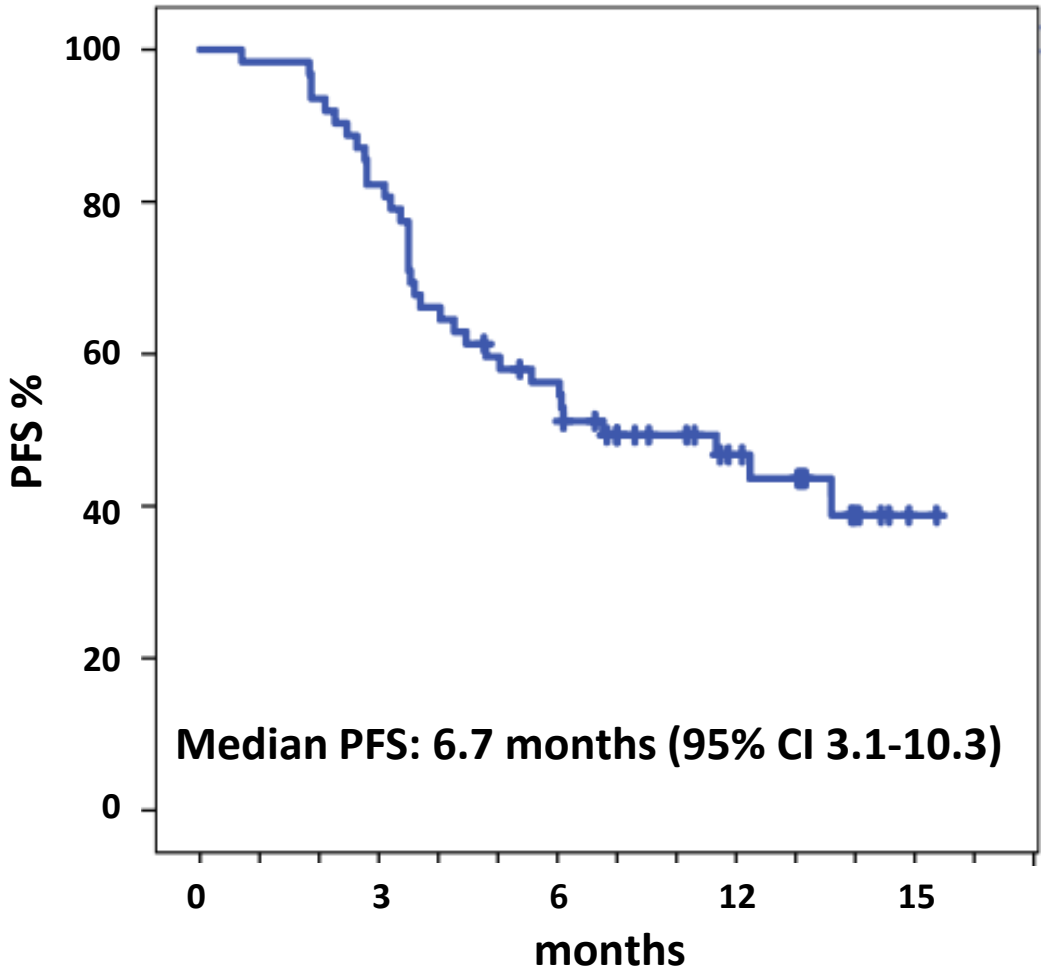
N = 62

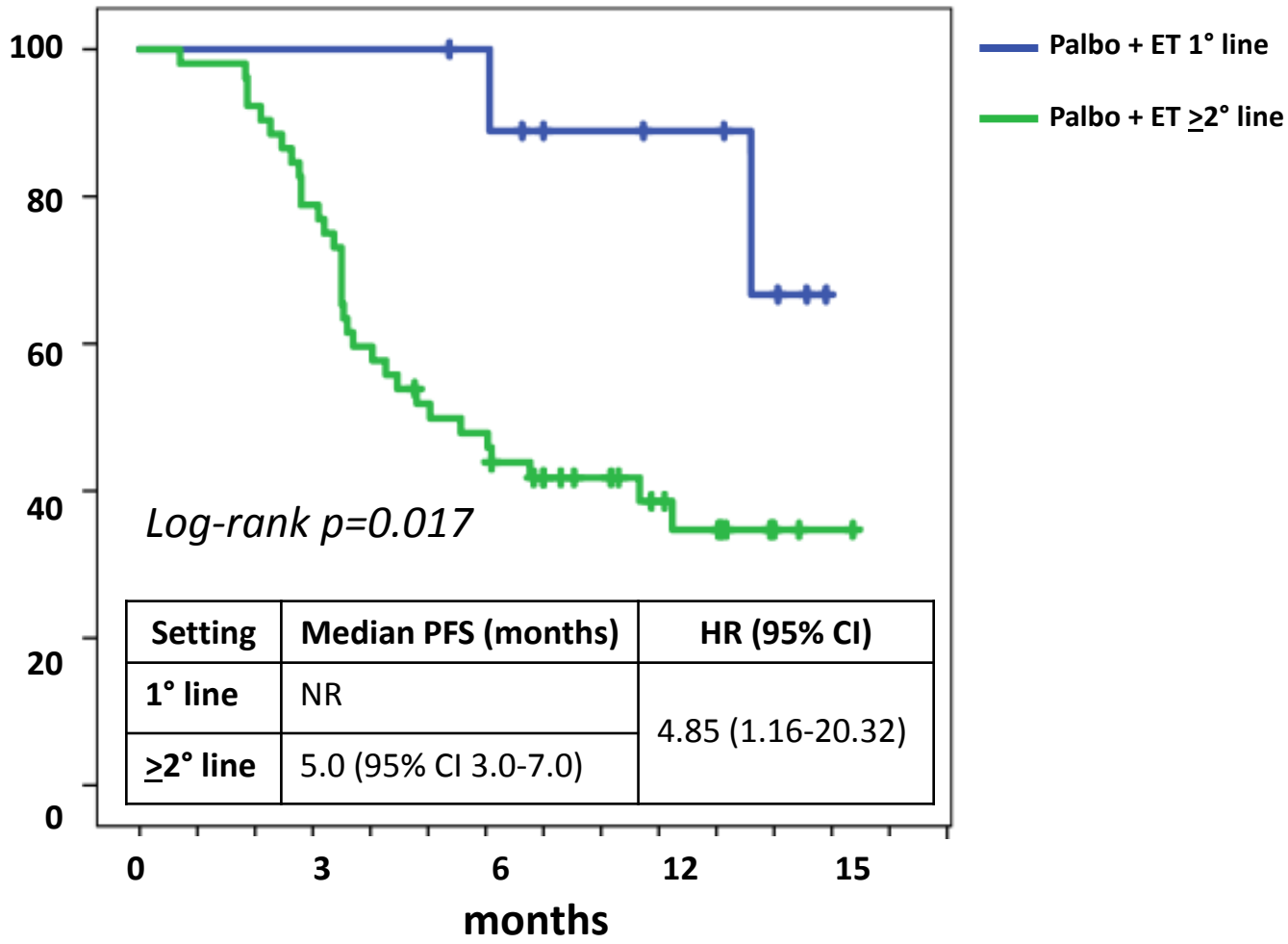
Characteristic		n (%)
Age	Median (range)	57.5 (36-78)
Sex	Female Male	61 (99) 1 (1)
Performance Status (ECOG)	0 -1 2	56 (90.3) 6 (9.7)
Menopausal Status	Premenopausal Postmenopausal	7 (11.5) 54 (88.5)
TFI from the end of adjuvant ET to first relapse	Stage IV at diagnosis No adjuvant ET ≤12 months >12 months	15 (24.2) 11 (17.7) 24 (38.7) 12 (19.4)

Characteristic		n (%)
Site of metastatic disease	Bone-only Visceral +/- bone	11 (17.7) 51 (82.3)
Previous CT lines for metastatic disease	No Yes	27 (43.5) 35 (56.5)
Previous ET for metastatic disease	No Yes	13 (21.0) 49 (79.0)
Previous everolimus + AI	No Yes	51 (82.3) 11 (17.7)
Setting of palbociclib treatment	1° line ≥ 2° line	11 (16.2) 51 (83.8)
Palbociclib association	AI Fulvestrant *Fulv-naïve* *Fulv-pretreated*	16 (25.8) 46 (74.2) *22 (47.8)* *24 (52.2)*

RESULTS: PFS

Median follow-up: 9.7 months
Tot PFS events: 34



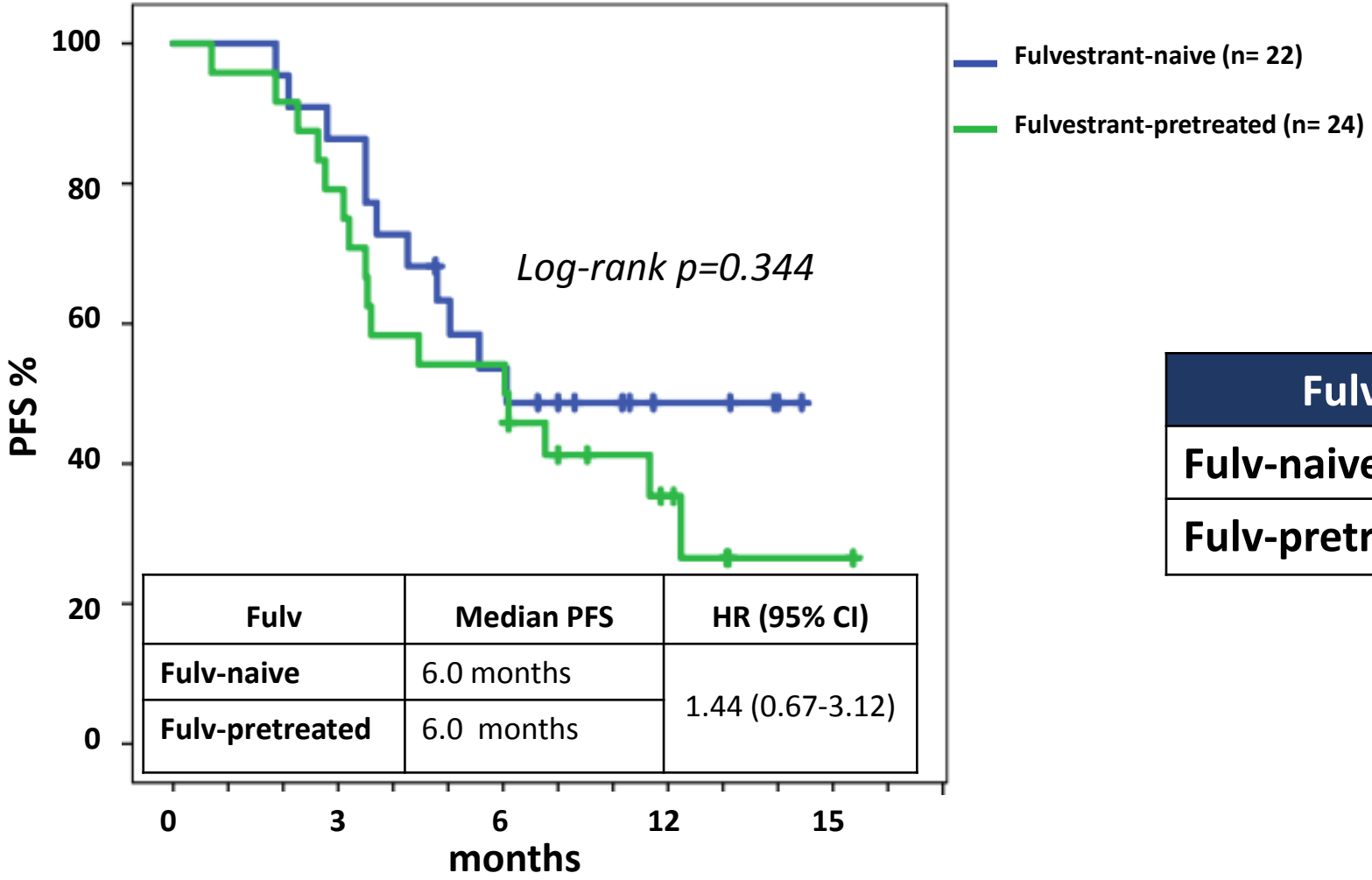


Setting	Median PFS (months)	HR (95% CI)
1° line	NR	4.85 (1.16-20.32)
≥2° line	5.0 (95% CI 3.0-7.0)	

RESULTS: ORR

Best response	Overall, n (%) n = 51	1° line, n (%) n = 7	≥2° line, n (%) n = 44
CR	0 (0.0)	0 (0.0)	0 (0.0)
PR	11 (17.8)	2 (20.0)	9 (17.3)
SD	17 (27.4)	5 (50.0)	12 (23.1)
PD	23 (37.1)	0 (0.0)	23 (44.2)

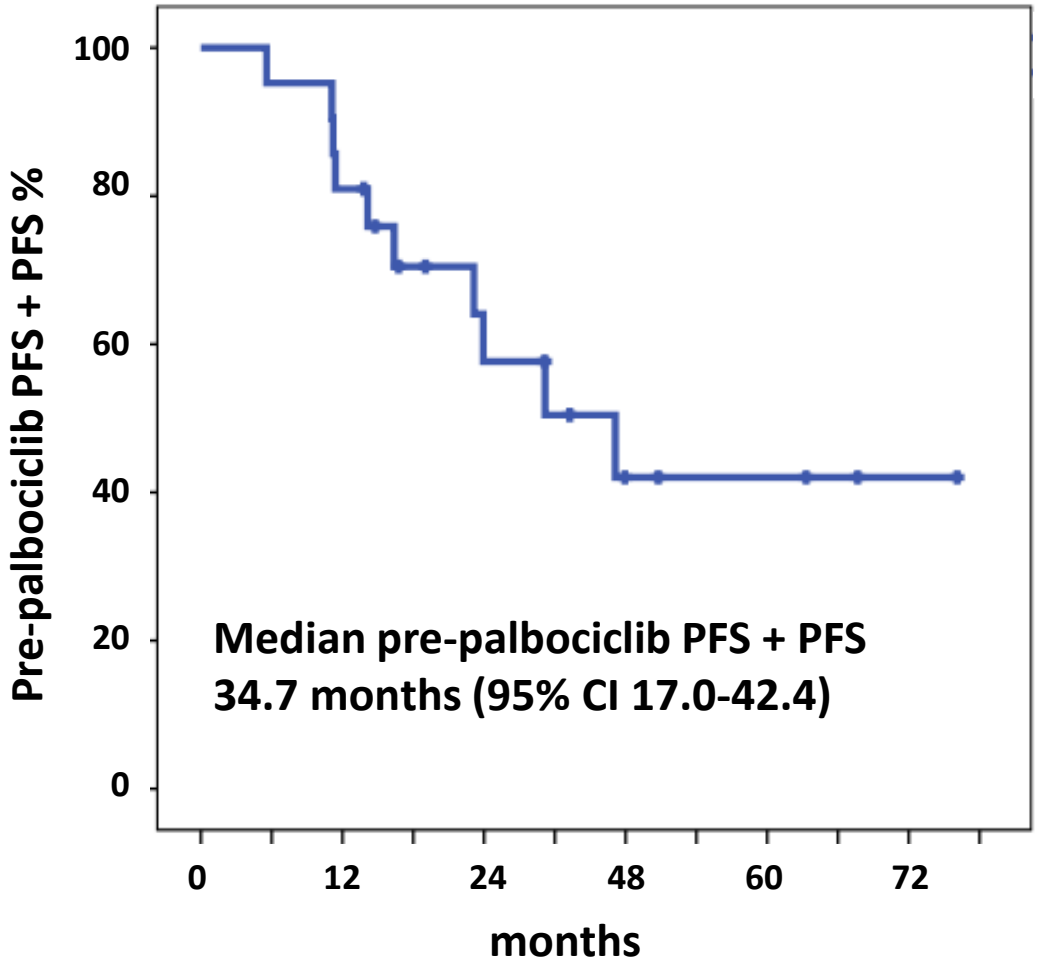
RESULTS: PFS according to prior therapy
efficacy of palbociclib + Fulv according to prior Fulv exposure



Fulv	Median PFS	HR (95% CI)
Fulv-naive	6.0 months	1.44 (0.67-3.12)
Fulv-pretreated	6.0 months	

Fulv	≥ 3° lines	
Fulv-naive	46%	**p 0.002**
Fulv-pretreated	88%	

RESULTS: pre-palbociclib PFS + PFS



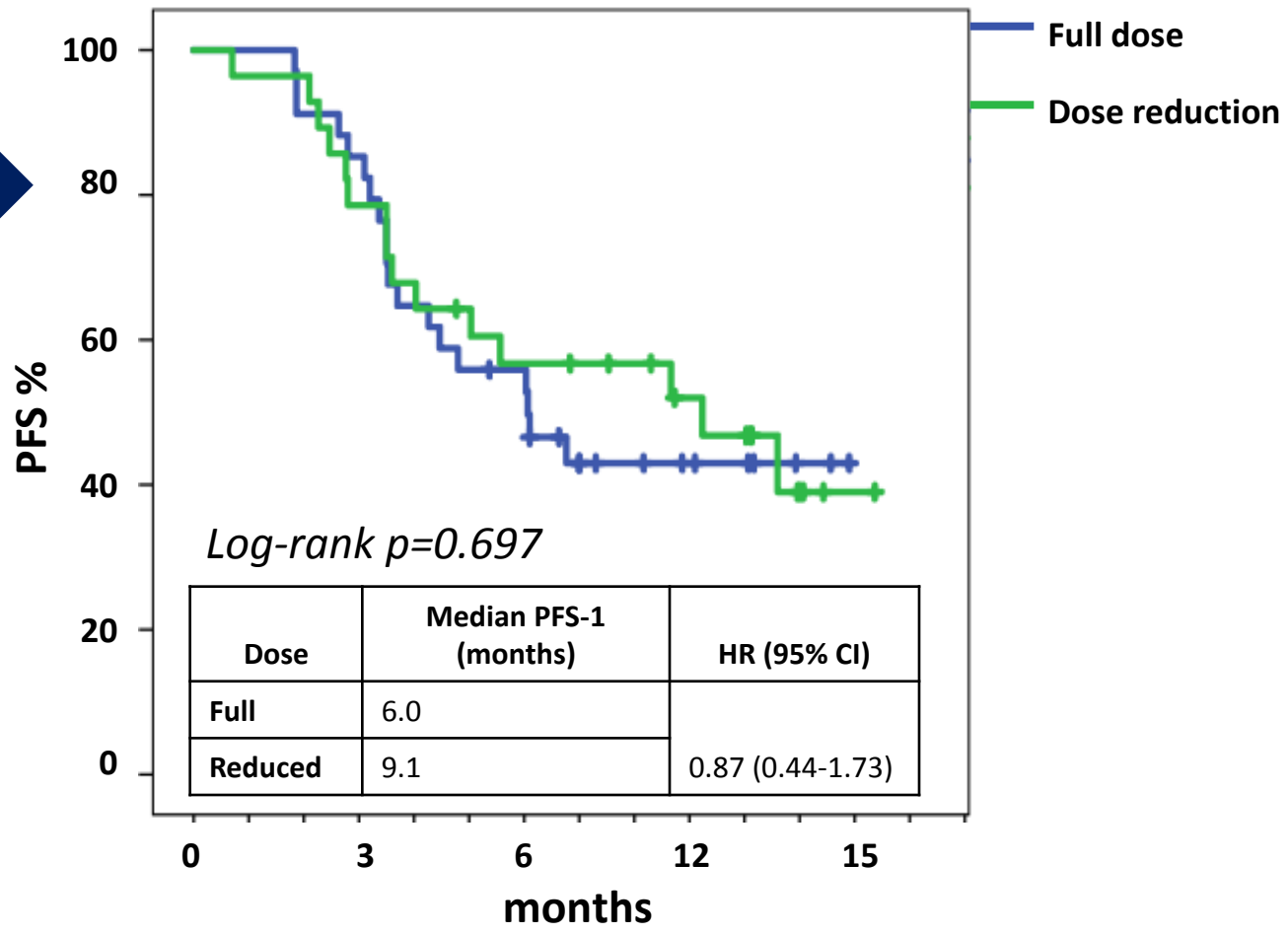
Characteristic (n = 21)		n (%)
Site of metastatic disease	Bone-only Visceral +/- bone	12 (57.1) 9 (42.9)
TFI from the end of adjuvant ET to first relapse	Stage IV at diagnosis No adjuvant ET <12 months ≥12 months	4 (19.0) 4 (19.0) 6 (28.6) 7 (33.3)

RESULTS: safety

AE	Any grade	G1-2	G3	G4
Hematologic toxicity	61 (98.4)			
Neutropenia	60 (96.8)	14 (22.6)	35 (56.5)	11 (17.7)
Febrile Neutropenia	2 (3.2)			
Thrombocytopenia	38 (61.3)	30 (48.4)	7 (11.3)	1 (1.6)
Anaemia	41 (66.1)	39 (62.9)	2 (3.2)	0 (0.0)
Non-hematologic toxicity	44 (71.0)			
Increased AST and/or ALT	33 (53.2)	27 (43.6)	5 (8.1)	1 (1.6)
Stomatitis	7 (11.3)	7 (11.3)	0 (0.0)	0 (0.0)
Nausea	5 (8.1)	4 (6.4)	1 (1.6)	0 (0.0)
Vomiting	2 (3.2)	2 (3.2)	0 (0.0)	0 (0.0)
Diarrhoea	6 (9.7)	6 (9.7)	0 (0.0)	0 (0.0)
Fatigue	14 (22.6)	13 (20.9)	1 (1.7)	0 (0.0)
Rash	1 (1.6)	1 (1.6)	0 (0.0)	0 (0.0)

RESULTS: dose reductions and interruptions

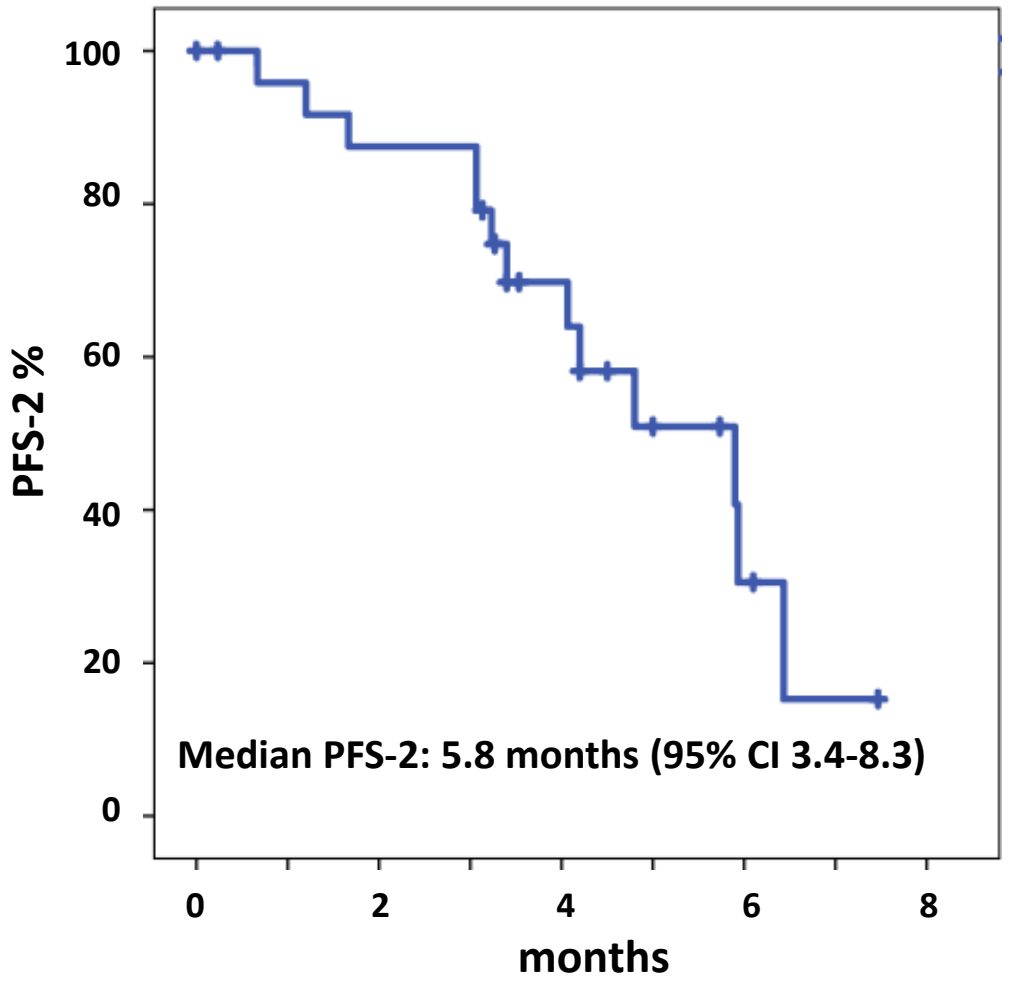
Characteristic	Frequency (%)
Dose reduction	
Yes	28 (45.2)
No	34 (54.8)
Temporary Interruption	
Yes	17 (27.4)
Hematologic toxicity	8 (47.1)
Non-hematologic toxicity	3 (17.6)
Surgical procedures	6 (35.3)
No	45 (72.6)
Definitive Interruption	
Yes	35 (56.5)
Disease progression	34 (97.1)
Toxicity	1 (2.9)
No	27 (43.5)



RESULTS: subsequent therapy and PFS-2

Treatment post-palbociclib	Frequency (%)
Systemic anticancer treatment	26 (76.5)
Chemotherapy	24 (92.3)
Caelyx	4 (15.4)
Capecitabine	7 (26.9)
Carboplatin + Gemcitabine	1 (3.8)
Eribuline	6 (23.1)
Nab-paclitaxel	5 (19.3)
MTX – Ciclofosfamide	1 (3.8)
Endocrine Therapy	2 (7.7)
Everolimus + Exemestane	2 (7.7)
Best Supportive Care	8 (23.5)

Best Response	Frequency (%)
CR	0 (0.0)
PR	1 (4.2)
SD	15 (62.5)
PD	8 (33.3)



CONCLUSIONS

- Efficacy of palbociclib + ET treatment in real-world setting.

PALOMA-3 Median PFS 9.5 months	**Our experience** Median PFS 6.7 months	**Other real-world experience** Median PFS 5.8 months
• **59%** visceral disease • **33%** CT for metastatic disease • **0%** previous everolimus + AI	• **82%** visceral disease • **43%** more than 3 lines of CT • **18%** previous everolimus + AI	• **83%** visceral disease • **53%** more than 2 lines of CT • **100%** previous everolimus

Du Rusquec P. et al, 2017

- Safety was in line with results pivotal trials.

CONCLUSION and DISCUSSION

Relevant clinical questions addressed:

- No differences in PFS between fulvestrant-naïve vs fulvestrant-pretreated patients. Is there a possibility for treatment re-challenge? (Malorni L. et al, Ann Oncol 2018)

- No differences in PFS between patients treated with full-dose vs patients who required dose reduction confirmed in a real-world setting. (Verma S et al, Oncologist 2016)

- Some patients can achieve a long benefit from ET followed by palbociclib combination. How to select these patients?

- Chemotherapy is recommended by guidelines after the exhaustion of endocrine sensitivity. Our results confirm the role of cytotoxic treatment in this setting, by showing efficacy after ET+CDK4/6 inhibitors.

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