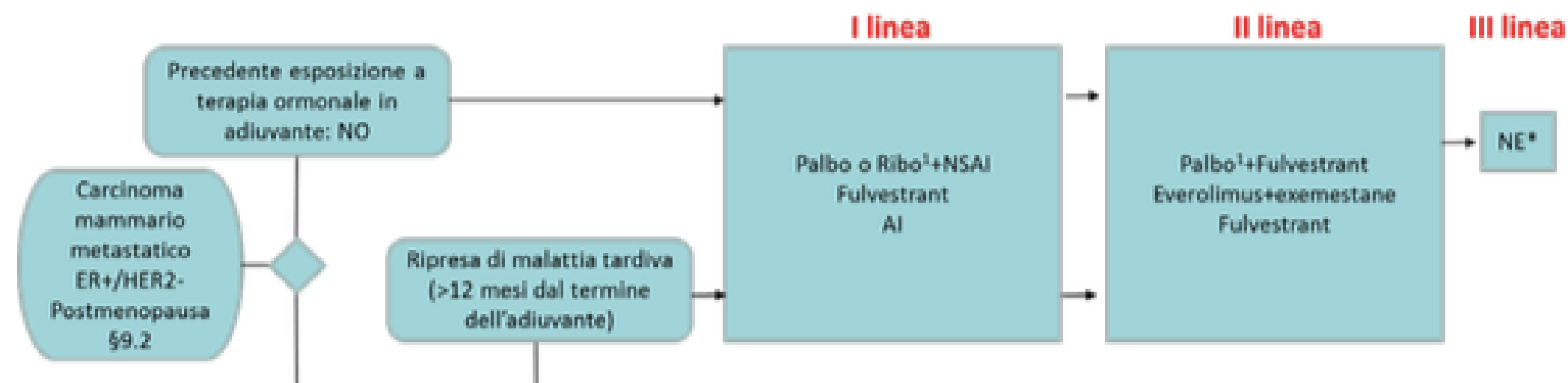




QUESITO CLINICO 3: Nelle pazienti in postmenopausa con carcinoma mammario HR positivo/HER2 negativo non candidate a chemioterapia, con lungo intervallo libero di malattia, metastasi solo ossee, è opportuno considerare la combinazione antiaromatasi+inibitore di CDK 4/6 rispetto al solo antiaromatasi?

**Quale impatto nella pratica clinica
&
Take home message**

Figura 14 – CARCINOMA MAMMARIO METASTATICO ER+/HER2-: Terapia ormonale in postmenopausa

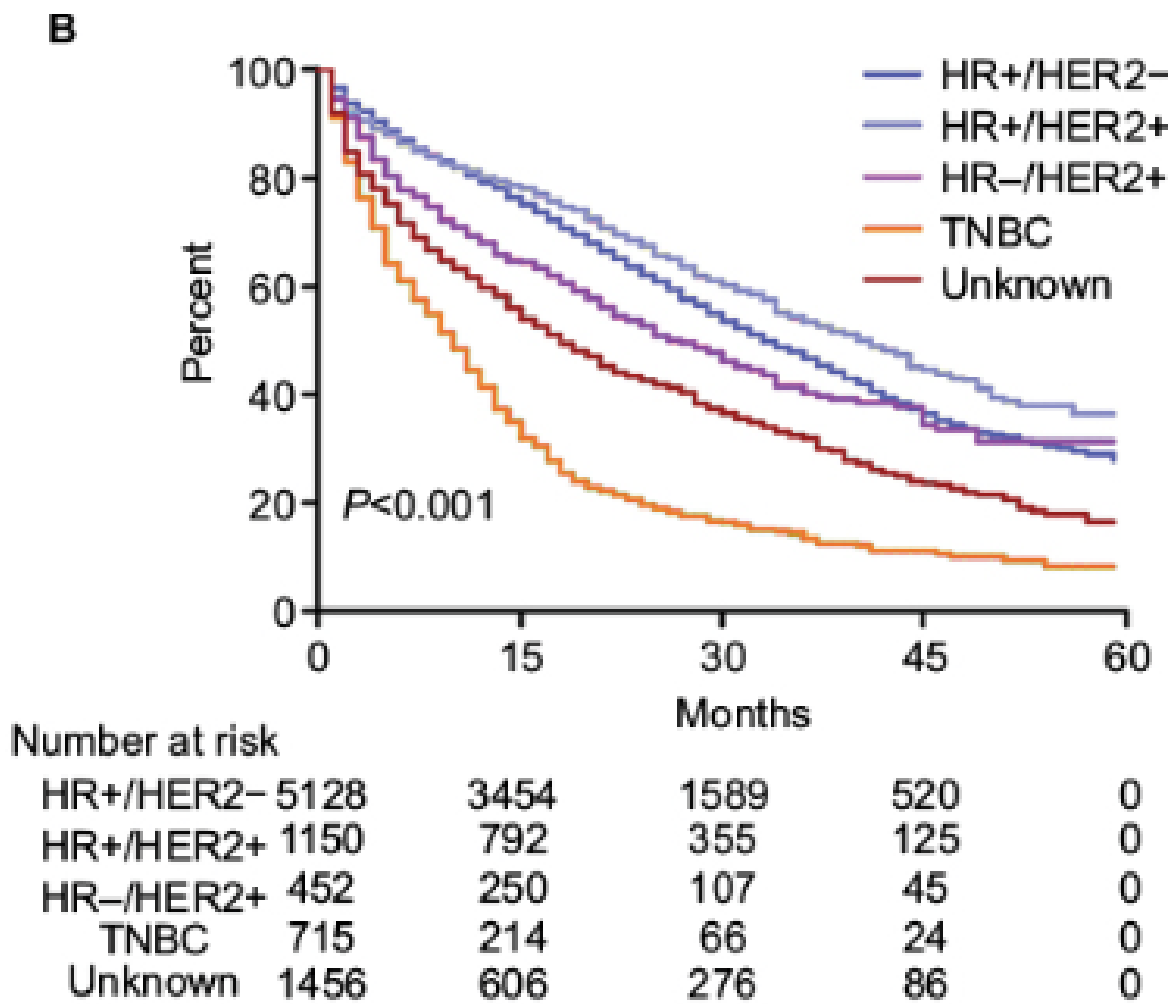


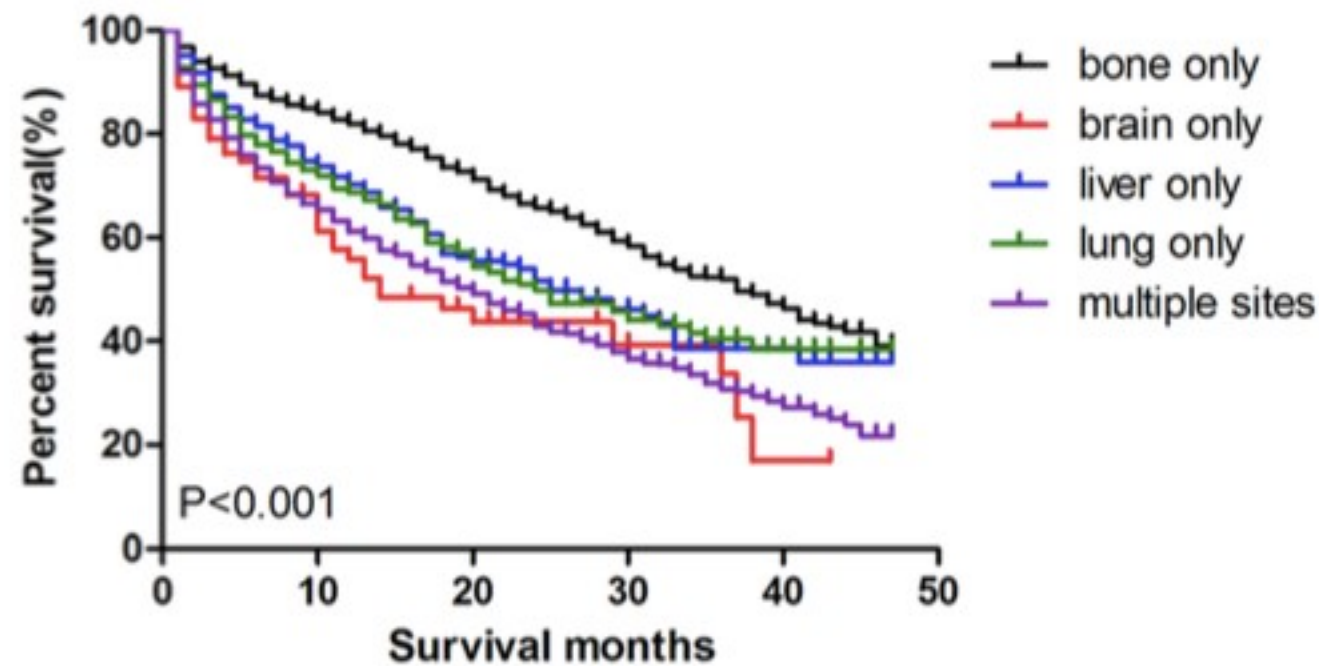


QUESITO CLINICO 3: Nelle pazienti in postmenopausa con carcinoma mammario HR positivo/HER2 negativo non candidate a chemioterapia, con [REDACTED] è opportuno considerare la combinazione antiaromatasi+inibitore di CDK 4/6 rispetto al solo antiaromatasi?

Bone Metastasis Pattern in Initial Metastatic Breast Cancer

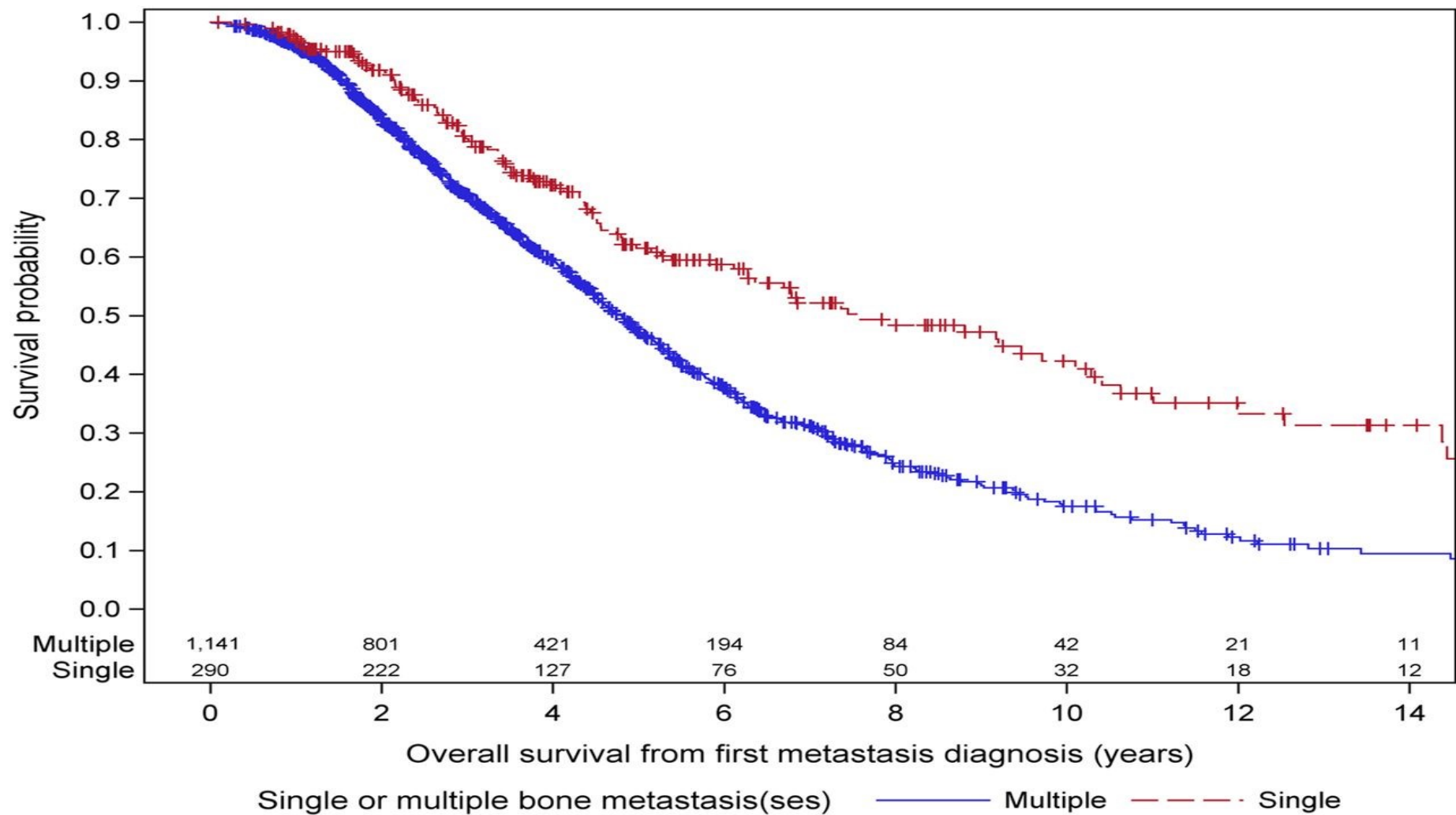
Cancer Management and Research 2018:10 287–295 | doi.org/10.2147/CMAR.S155524





	1-year	2-year	MST (months)
Bone only	81.9%	66.5%	37
Brain only	55.9%	43.7%	14
Liver only	70.3%	54.0%	25
Lung only	68.7%	51.1%	24
Multiple sites	61.1%	45.2%	20

Overall survival from first metastasis diagnosis by number of bone metastases among patients with breast cancer and bone-only metastases (n = 1,445).



Amanda Parkes et al. The Oncologist 2018;23:1282-1288

Cyclin-dependent kinase 4/6 inhibitors as first-line treatment for post-menopausal metastatic hormone receptor-positive breast cancer patients: a systematic review and meta-analysis of phase III randomized clinical trials

Allan Ramos-Esquivel^{1,2} · Hellen Hernández-Steller¹ · Marie-France Savard³ · Denis Ulises Landaverde^{2,4}

Breast Cancer (2018) 25:479–488

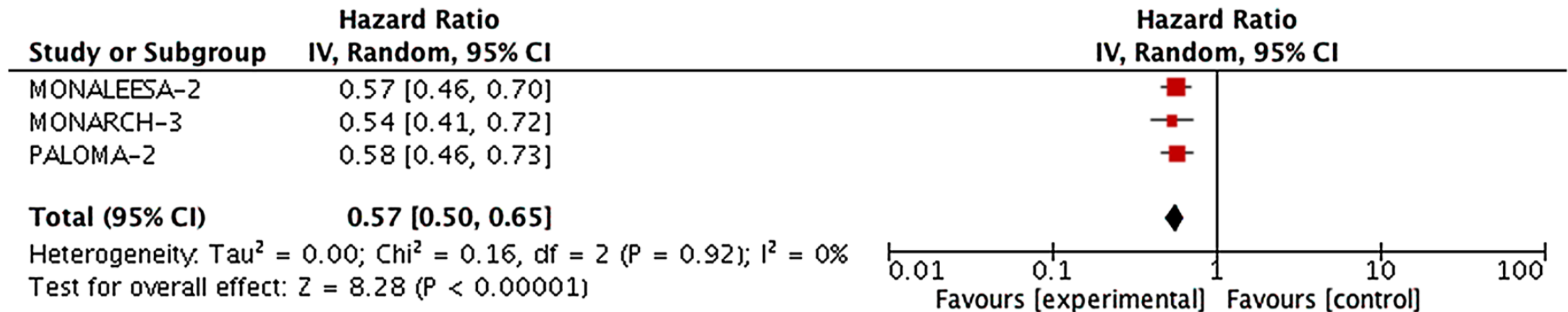
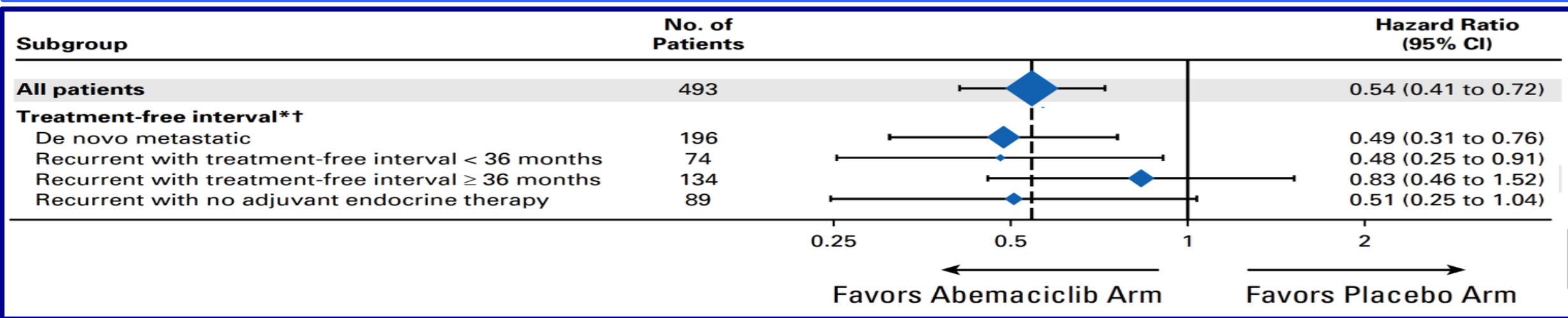
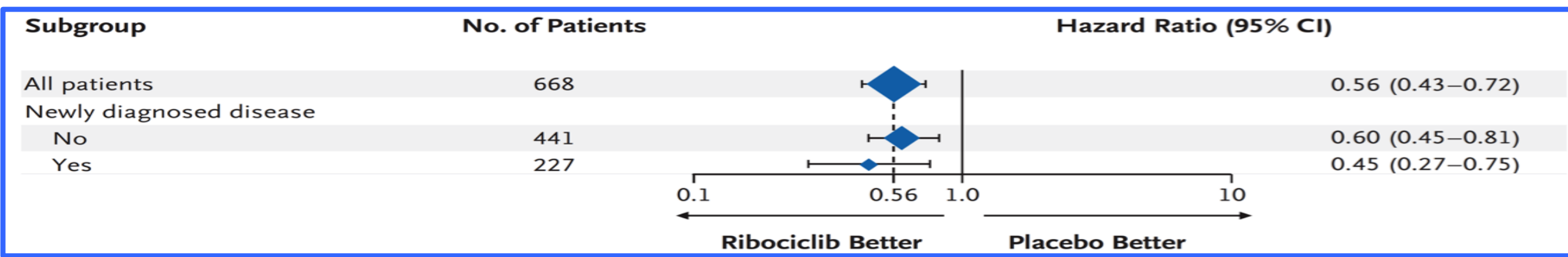
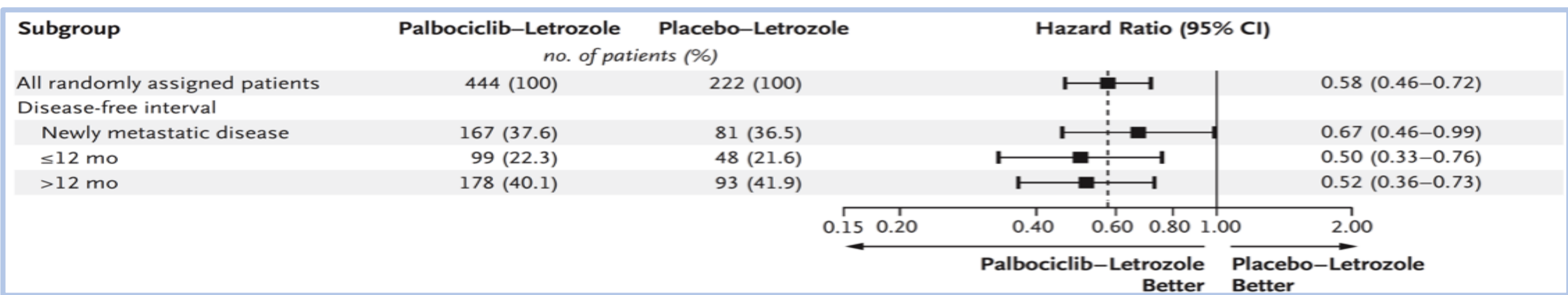
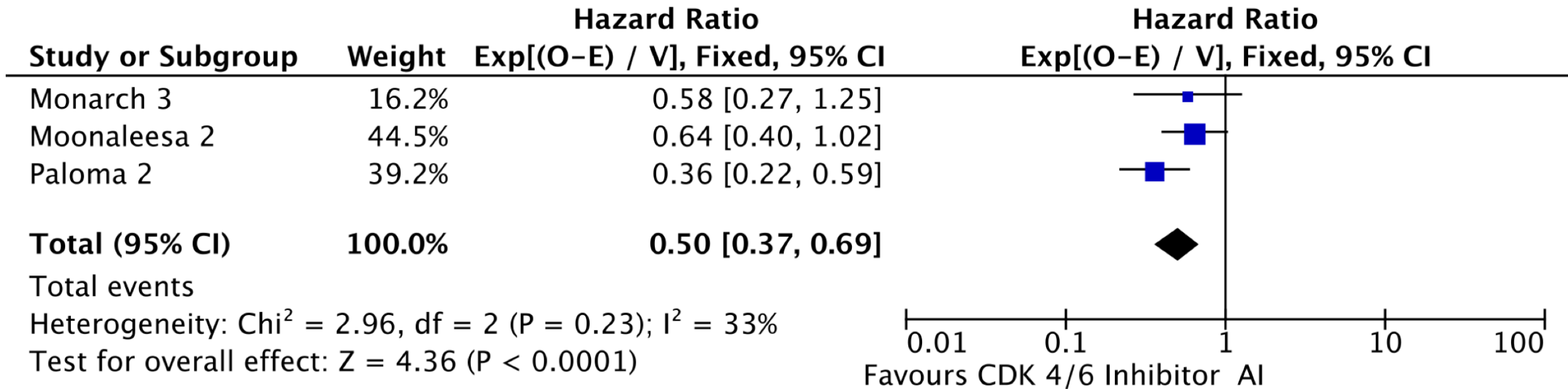


Fig. 2 Forest plot for progression-free survival



Inibitori di CDK 4/6 + AI Vs AI

Analisi combinata degli studi di 1a linea: PFS nelle pazienti con malattia solo ossea



Cyclin-dependent kinase 4/6 inhibitors as first-line treatment for post-menopausal metastatic hormone receptor-positive breast cancer patients: a systematic review and meta-analysis of phase III randomized clinical trials

Allan Ramos-Esquivel^{1,2} · Hellen Hernández-Steller¹ · Marie-France Savard³ · Denis Ulises Landaverde^{2,4}

Breast Cancer (2018) 25:479–488

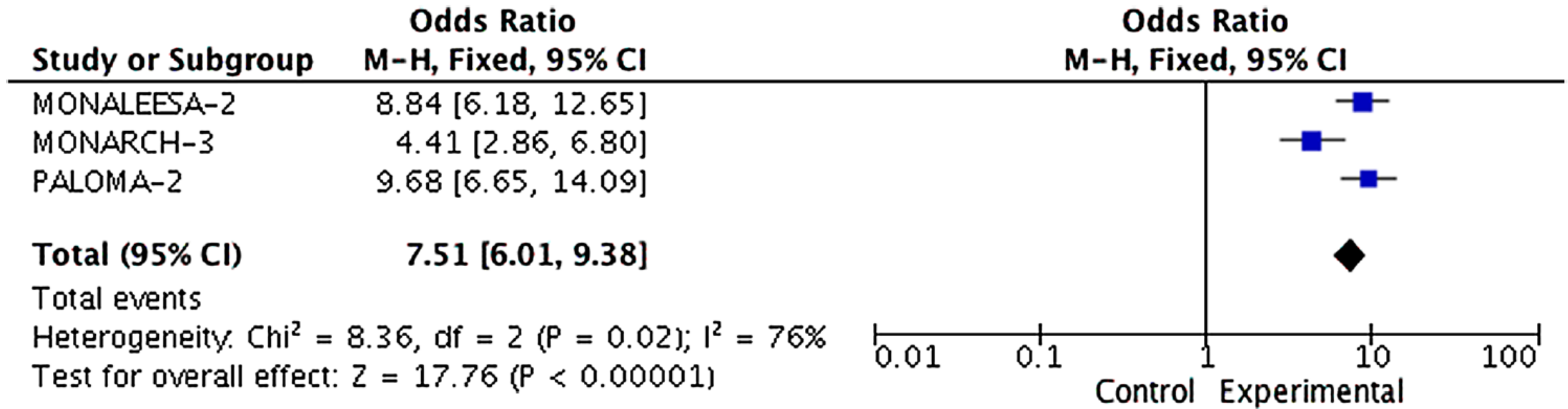


Fig. 5 Forest plot for treatment-related side effects

Comparative Toxicities of CDK4/6 Inhibitors

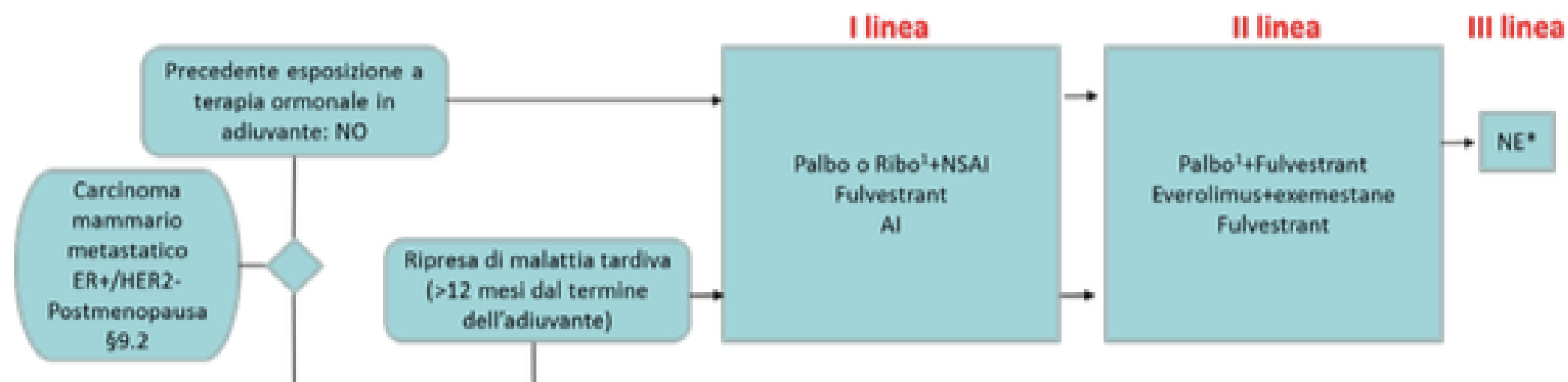
AEs,* %	PALOMA-2 ^[1,2]			MONALEESA-2 ^[3]			MONARCH 3 ^[4,5]		
	Palbociclib + Letrozole (n = 444)			Ribociclib + Letrozole (n = 334)			Abemaciclib + NSAI (n = 327)		
	Any Gr	Gr 3	Gr 4	Any Gr	Gr 3	Gr 4	Any Gr	Gr 3	Gr 4
Neutropenia	79.5	56.1	10.4	76.9	52.4	9.6	41.3	19.6	1.5
QTcF prolongation									
▪ > 60 ms vs BL	NR	NR	NR	3.0	--	--	NR	NR	NR
▪ ≥ 1 post-BL > 480 ms	NR	NR	NR	3.6	--	--	NR	NR	NR
▪ ≥ 1 post-BL > 500 ms	NR	NR	NR	0.6	--	--	NR	NR	NR
Gastrointestinal									
▪ Diarrhea	26.1	1.4	0	38.3	2.4	0	81.3	9.5	0
▪ Vomiting	15.5	0.5	0	33.5	3.6	0	28.4	1.2	0
▪ Abdominal pain	11.3	0.9	0	NR	NR	NR	29.1	1.2	--
▪ Decreased appetite	14.9	0.7	0	20.7	1.5	0	24.5	1.2	0
LFTs									
▪ Increased ALT	43	2	< 1	NR	NR	NR	15.6	5.8	< 1
▪ Increased AST	52	3	0	NR	NR	NR	15	3	0
▪ Increased ALT, AST, and/or blood bilirubin	NR	NR	NR	20.1	8.4	1.8	NR	NR	NR
Fatigue	37.4	1.8	--	41.3	2.7	0.3	40.1	1.8	--

*Any-cause AEs for PALOMA-2 and MONALEESA-2; TEAEs for MONARCH 3, except for any-cause increased ALT/AST.



Slide credit: clinicaloptions.com

Figura 14 – CARCINOMA MAMMARIO METASTATICO ER+/HER2-: Terapia ormonale in postmenopausa



Your Patient Case

What is your patient's tumor phenotype? HR positive, HER2 negative

Does your patient have a germline BRCA1/2 mutation? No

Does your patient have a history of systemic therapy for breast cancer? No

What systemic therapy do you plan to use for this patient? Palbociclib + NSAI (anastrozole or letrozole)

Recommendations

	Recommendations	Comments
Expert 1	CDK4/6 inhibitor + letrozole	Would not use ribociclib for patients with arrhythmia
Expert 2	CDK4/6 inhibitor + NSAI (anastrozole or letrozole)	Consider abemaciclib for CNS metastases or poor bone marrow function
Expert 3	CDK4/6 inhibitor + NSAI (anastrozole or letrozole)	Consider an AI or fulvestrant alone in some patients with comorbidities or long natural history
Expert 4	CDK4/6 inhibitor + NSAI (anastrozole or letrozole)	
Expert 5	CDK4/6 inhibitor + NSAI (anastrozole or letrozole)	

SPECIAL ARTICLE

4th ESO–ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4)[†]

Section IV: ER-positive/HER2-negative (luminal) ABC

Guideline statement	LoE/GoR	Consensus
The addition of a CDK 4/6 inhibitor to an AI, in patients naïve or pre-exposed to ET, provided a significant improvement in median PFS (~10 months), with an acceptable toxicity profile, and is, therefore, one of the preferred treatment options for pre- and peri-menopausal women with OFS/OFA, men (preferably with LHRH agonist) and post-menopausal women. Patients relapsing <12 months from the end of adjuvant AI were not included in the published studies and may not be suitable for this combination. OS results are still awaited. QoL was comparable to that with ET alone.	I/A	90%
ESMO-MCBS v1.1 score: 3		

ESMO-Magnitude of Clinical Benefit Scale



ESMO-MCBS
ESMO-Magnitude of Clinical Benefit Scale

Promoting clear and evidence-based communication about the benefit of cancer treatments

A tool to assist in the prioritisation of medicines in cancer care

Palbociclib



Indication details

Tumour Type	Breast Cancer
Tumour Sub-type	Breast Cancer
Tumour Sub-Group	HR+ HER2-
Tumour stage	Metastatic
Combined Agent(s)	Letrozole
Control Arm	Letrozole + placebo
Treatment Setting	1st line metastatic HR+ HER2-
Trial Name	PALOMA-2

Agent Score

3

Scorecard version: 1
ESMO-MCBS v1.1

Primary Outcome(s)

Primary Outcome(s)	PFS	Form(s)	Form 2b
--------------------	-----	---------	---------

Outcome data

PFS Control	14.5 months
PFS Gain	10.3 months
PFS HR	0.58 (0.46-0.72)

Ribociclib



Indication details

Tumour Type	Breast Cancer
Tumour Sub-type	Breast Cancer
Tumour Sub-Group	HR+ HER2-
Tumour stage	Metastatic
Combined Agent(s)	Letrozole
Control Arm	Letrozole + placebo
Treatment Setting	1st line metastatic post-menopause HR+ HER2-
Trial Name	MONALEESA-2

Agent Score

3

Scorecard version: 1
ESMO-MCBS v1.1

Primary Outcome(s)

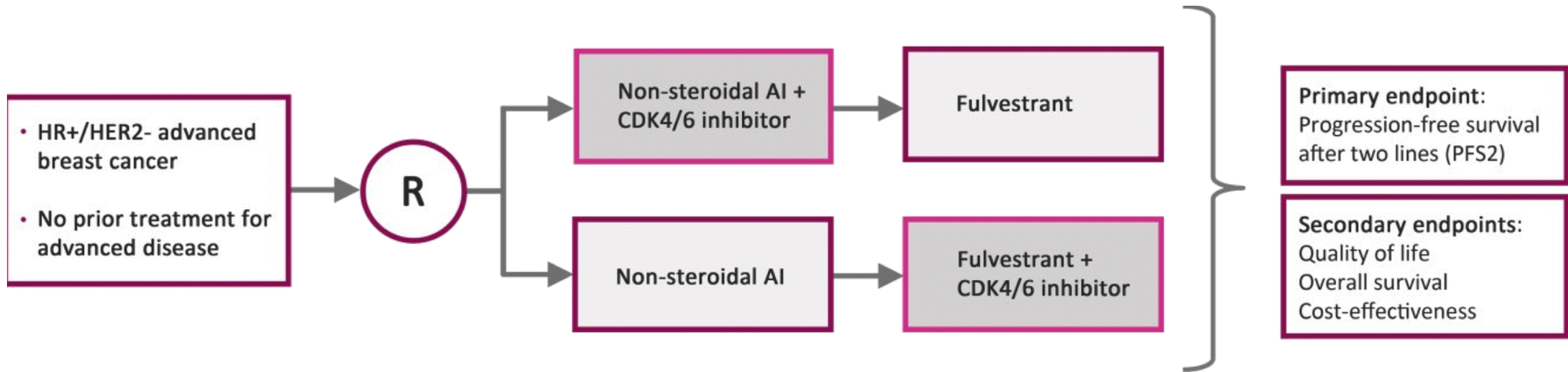
Primary Outcome(s)	PFS	Form(s)	Form 2b
--------------------	-----	---------	---------

Outcome data

PFS Control	16 months
PFS Gain	9.3 months
PFS HR	0.57 (0.46-0.70)
OS HR	Not mature data

Does each patient need a combination ET from the beginning?

Endocrine Therapy Plus CDK4/6 in First or Second Line for Hormone (SONIA) Receptor Positive Advanced Breast Cancer:
NCT03425838



Considerazioni finali

- Pazienti con MBC bone-only, asintomatiche e lungo DFI identificano pazienti comunque a miglior prognosi
- La maggioranza delle pazienti con MBC ha un'età > 60 aa: comorbidità e la conseguente polifarmacia rendono indispensabile uno stretto monitoraggio dei pazienti, non solo per gli eventi collaterali
- La tossicità finanziaria dei trattamenti deve essere presa in considerazione nel processo decisionale

Grazie per l'attenzione
angiolic@aou-careggi.toscana.it