

ESMO Clinical Practice Guidelines

Metastatic breast cancer: sequence of therapies

Clinical Case Presentation

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DISCLOSURES

no conflicts of interest to declare

Initial diagnosis

Dec 2005:

A healthy 47-year-old woman presented with a left breast lump found at clinical examination

Jan 2006:

Quadrantectomy and sentinel lymph node biopsy.

Initial stage: pT1cN0M0

Immunohistochemistry: invasive ductal carcinoma ER 90%, PR 70%, ki67 20% and HER2 negative

Feb 2006:

Whole breast irradiation

Feb 2006-Feb 2011:

Adjuvant tamoxifen

ER, oestrogen receptor; PR, progesterone receptor



First recurrence - Diagnosis

Jan 2016:

This lady presents with a new palpable left supraclavicular adenopathy



Q1: Would you perform a biopsy before starting treatment?

1. Yes

2. No

(one answer)



First recurrence - Biopsy

Jan 2016:

She undergoes a supraclavicular lymph node biopsy, which reveals metastatic adenocarcinoma consistent with breast primary, ER 95%, PR 60%, HER2-

ER, oestrogen receptor; PR, progesterone receptor



First recurrence - Staging

Feb 2016:

Bone scan: uptake in multiple ribs bilaterally, as well as throughout her cervical, thoracic, and lumbar spine and the pelvis

Feb 2016:

CT scan of the chest, abdomen, and pelvis: bone metastases, abnormal bilateral axillary, supraclavicular, and internal mammary lymph nodes, and two subcentimetric liver metastases



Clinical features

PS ECOG 0

58-year-old woman

Bone, liver and lymph node metastases

Asymptomatic

No comorbidity



Q2: Which treatment strategy would you choose as first-line therapy?

1. Endocrine therapy alone
2. Endocrine therapy plus biologic agents
3. Chemotherapy

(one answer)



Q3: Which first-line therapy would you choose? (no prior ET with AI)

1. AI
2. Fulvestrant
3. AI + CDK 4/6 inhibitor
4. Monochemotherapy
5. Polychemotherapy

(one answer)



SPECIAL ARTICLE

3rd ESO–ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 3)

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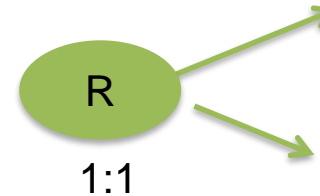
SECTION 4. ER POSITIVE/HER-2 NEGATIVE (LUMINAL) ABC

GUIDELINE STATEMENT	LoE	Consensus
Endocrine therapy (ET) is the preferred option for hormone receptor positive disease, <u>even in the presence of visceral disease</u> , unless there is visceral crisis or concern/proof of endocrine resistance.	1 A	Voters: 41 Yes: 93% (38) Abstain: 7% (3)
a second trial with a similar outcome may be offered to some patients with MBC without prior exposure to adjuvant ET.		No: 53% (23) Abstain: 14% (6)
The addition of everolimus to an AI is a valid option for some postmenopausal patients with disease progression after a non-steroidal AI, since it significantly prolongs PFS, albeit without OS benefit. The decision to treat must take into account the individual relevant toxicities associated with this combination and should be made on a case by case basis.	1 B	Voters: 40 Yes: 84% (34) Abstain: 13% (5)
Tamoxifen can also be combined with everolimus.	2 B	
The addition of the CDK4/6 inhibitor palbociclib to an aromatase inhibitor, as <u>1st line therapy</u> , for postmenopausal patients (except patients relapsing <12 months from the end of adjuvant AI), provided a significant improvement in PFS (10 months), with an acceptable toxicity profile, and is therefore one of the preferred treatment options, where available. OS results are still awaited.	1 A	Voters: 37 Yes: 92% (34) Abstain: 3% (1)

No prior AI (endocrine naïve or prior tamoxifen)

FIRST¹

MBC ER+HER2-
Postmenopausal
1st line; >1 year from end of adj. AI

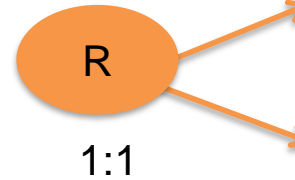


Anastrozole 1 mg

Fulvestrant 500 mg

FALCON²

MBC ER+HER2-
Postmenopausal
1st line; >1 year from end of adj. AI

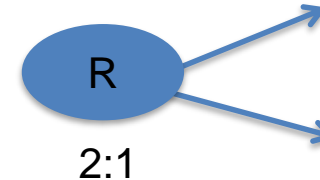


Fulvestrant 500 mg + placebo

Anastrozole 1 mg + placebo

PALOMA-2³

MBC ER+HER2-
Postmenopausal
1st line; >1 year from end of adj. AI

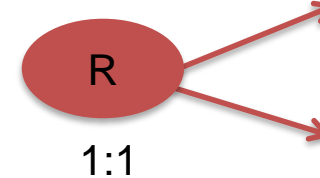


Palbociclib 125mg+ letrozole 2.5 mg

Placebo + Letrozole 2,5 mg

MONALEESA-2⁴

MBC ER+HER2-
Postmenopausal
1st line; >1 year from end of adj. AI



Ribociclib 600 mg + Letrozole 2.5 mg

Placebo + Letrozole 2.5 mg

Progression after first line

Which second-line treatment?

Feb 2016:

Patient started letrozole

July 2017:

17 months later, a new restaging CT scan shows modest liver and bone progressive disease (lymph nodes maintain response)

The patient is still asymptomatic

ECOG 0



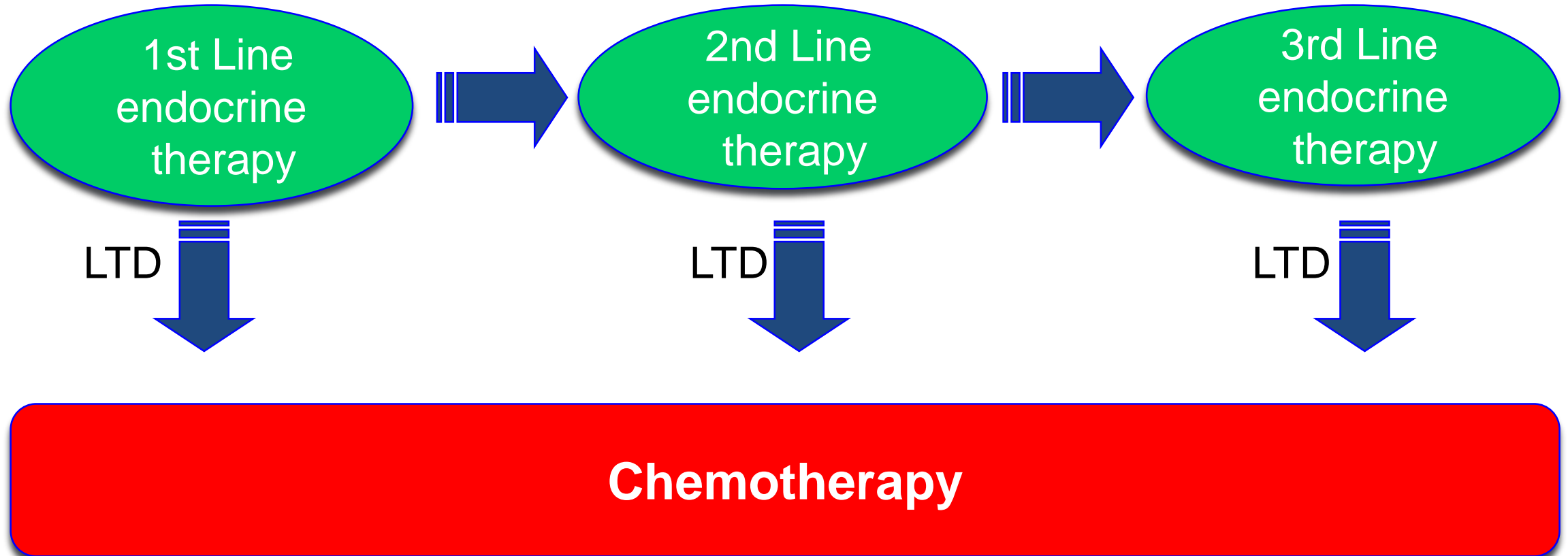
Q4: Which second-line therapy would you choose? (PD \geq 6 months after first-line ET)

1. Fulvestrant
2. Fulvestrant + CDK 4/6 inhibitor
3. Exemestane + everolimus
4. Monochemotherapy
5. Polychemotherapy

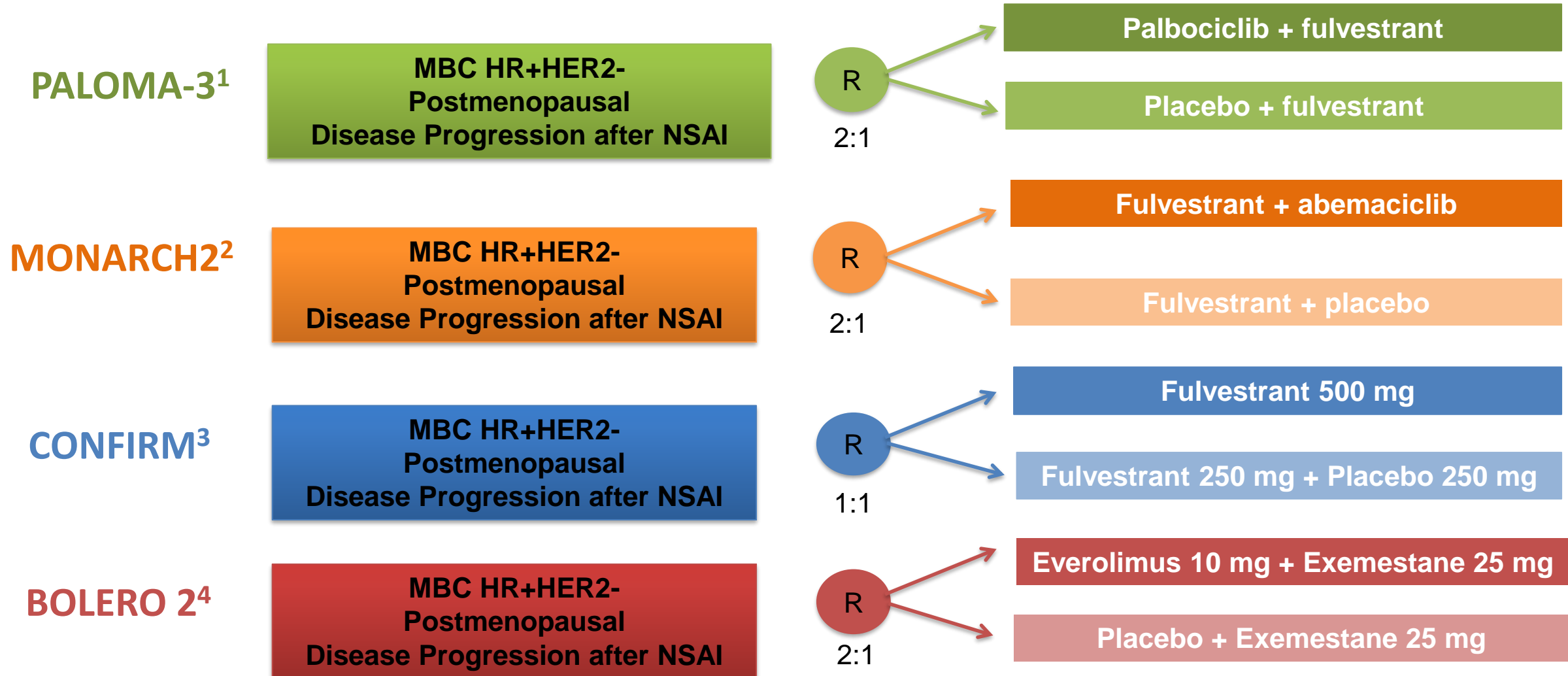
(one answer)



Advanced breast cancer



Second-line therapy (PD \geq 6 months after first line ET)



1. Turner, NEJM 2015; 2. Sledge, JCO 2017; 3. Di Leo, JCO 2010; 4. Baselga, NEJM 2012

Second-line therapy (PD \geq 6 months after first-line ET)

August 2017:

Patient started fulvestrant-palbociclib



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