

As per NCCN 2023, Ribociclib is the ONLY CDK4/6i to be a Category 1 preferred treatment in 1L setting irrespective of the ET partner²

NCCN v4 Guidelines 2022¹

HER2-Negative and Postmenopausal or Premenopausal Receiving Ovarian Ablation or Suppression^a

Preferred Regimens

First-Line Therapy

- Aromatase inhibitor + CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) (category 1)^b
- Selective ER down-regulator (fulvestrant, category 1) + non-steroidal aromatase inhibitor (anastrozole, letrozole) (category 1)^c
- Fulvestrant + CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) (category 1)^b

a. Baseline assessment of bone density recommended for patients receiving an aromatase inhibitor who are at risk of osteoporosis (eg, age >65, family history, chronic steroids).

b In phase 3 randomized controlled trials, ribociclib + endocrine therapy has shown overall survival benefit in the first-line setting.

c A single study (S0226) in patients with HR-positive breast cancer and no prior chemotherapy, biological therapy, or endocrine therapy for metastatic disease demonstrated that the addition of fulvestrant to anastrozole resulted in prolongation of time to progression and overall survival. Subset analysis suggested that patients without prior adjuvant tamoxifen and more than 10 years since diagnosis experienced the greatest benefit. Two studies with similar design (FACT and SOFEA) demonstrated no advantage in time to progression with the addition of fulvestrant to anastrozole.

NCCN v2 Guidelines 2023²

HER2-Negative and Postmenopausal or Premenopausal Receiving Ovarian Ablation or Suppression^a

Preferred Regimens

First-Line Therapy

- Aromatase inhibitor + CDK4/6 inhibitor^b
 - ▶ Aromatase inhibitor + ribociclib (category 1)^c
 - ▶ Aromatase inhibitor + abemaciclib
 - ▶ Aromatase inhibitor + palbociclib
- Fulvestrant^d + CDK4/6 inhibitor^b
 - ▶ Fulvestrant + ribociclib (category 1)^e
 - ▶ Fulvestrant + abemaciclib (category 1)^e
 - ▶ Fulvestrant + palbociclib

a Baseline assessment of bone density recommended for patients receiving an aromatase inhibitor who are at risk of osteoporosis (eg, age >65, family history, chronic steroids).

b There is controversy on the choice of CDK4/6i as there are no head to head comparisons between the agents and there are some differences in the study populations in the phase 3 randomized studies.

c In phase 3 randomized controlled trials, ribociclib + endocrine therapy has shown OS benefit in the first-line setting.

d Consider for disease progression on adjuvant ET or with early disease relapse within 12 months of adjuvant ET completion

e In phase 3 randomized controlled trials, fulvestrant + ribociclib or abemaciclib has shown OS benefit in the first-line setting

Note: All recommendations are category 2A unless otherwise indicated^{1,2}

NCCN, national comprehensive cancer network; CDK4/6i, cyclin-dependent kinase inhibitor; 1L, first line; ET, endocrine therapy; v4, version 4; v2, version 2; HER2, human epidermal growth factor receptor 2; OS, overall survival. As per NCCN Categories of Evidence and Consensus, Category 1 treatment is based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. As per NCCN Categories of Evidence and Consensus, Category 2A treatment is based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate. As per NCCN Categories of Preference, Preferred Intervention are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.

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