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Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer

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RobotReviewer report

Risk of bias table

trial	design	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Im S, 2019	RCT	+	+	+	+

Population	1. Eligible women were 18 to 59 years of age, were premenopausal or perimenopausal at the time of trial entry, and had histologically or cytologically confirmed hormone-receptor-positive, HER2-neg- ative advanced breast cancer. 2. A lthough breast cancer is known to be more aggressive and to be associ- ated with a poorer prognosis in younger women than in older women, 1,2 the recommended treatment for hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-nega- tive advanced breast cancer in premenopausal and postmenopausal patients is generally similar, [3][4][5] with the exception of the addition of ovarian sup- pression in premenopausal women.
Interventio n	1. Patients also received either a nonsteroidal aromatase inhibitor (letrozole at a dose of 2.5 mg or anastrozole at a dose of 1 mg) or tamoxifen (at a dose of 20 mg), administered orally once daily continuously. 2. METHODS We randomly assigned patients to receive either ribociclib or placebo in addition to endocrine therapy (goserelin and either a nonsteroidal aromatase inhibitor or tamoxifen). 3. Patients were randomly assigned, in a 1:1 ratio, to receive ribociclib (at a dose of 600 mg, admin- istered orally once daily for 21 consecutive days, followed by 7 days off, for a complete cycle of 28 days) or matching placebo.
Outcomes	1. 17 Overall survival, the protocol- specified key secondary end point, was defined as the time from randomization to death from any cause. 2. The results regarding the primary end point, inves- tigator-assessed progression-free survival, were re- ported previously.

3. The sample size was calculated on the basis of the primary end point of progression-free survival.

Bias	Judgement	Support for judgement
Random sequence generation	low	1. From December 17, 2014, to August 1, 2016, a total of 335 patients were randomly assigned to the ribociclib group, and 337 to the placebo group (Table S1 in (Table 1). 2. Randomization was stratified according to the presence or absence of liver or lung metasta- ses, previous chemotherapy for advanced disease (yes or no), and endocrine therapy (tamoxifen plus goserelin or an aromatase inhibitor plus gose- relin). 3. Patients were randomly assigned, in a 1:1 ratio, to receive ribociclib (at a dose of 600 mg, admin- istered orally once daily for 21 consecutive days, followed by 7 days off, for a complete cycle of 28 days) or matching placebo.
Allocation concealment	low	1. From December 17, 2014, to August 1, 2016, a total of 335 patients were randomly assigned to the ribociclib group, and 337 to the placebo group (Table S1 in (Table 1). 2. The time to subsequent chemotherapy was defined as the time from randomization to the beginning of the first chemotherapy after discontinuation of the trial regimen. 3. Randomization was stratified according to the presence or absence of liver or lung metasta- ses, previous chemotherapy for advanced disease (yes or no), and endocrine therapy (tamoxifen plus goserelin or an aromatase inhibitor plus gose- relin).
Blinding of participants and personnel	low	1. From December 17, 2014, to August 1, 2016, a total of 335 patients were randomly assigned to the ribociclib group, and 337 to the placebo group (Table S1 in (Table 1). 2. Patients were randomly assigned, in a 1:1 ratio, to receive ribociclib (at a dose of 600 mg, admin- istered orally once daily for 21 consecutive days, followed by 7 days off, for a complete cycle of 28 days) or matching placebo. 3. All patients as well as all investigators who administered treatment, assessed outcomes, and analyzed data were unaware of the group assign- ments.
Blinding of outcome assessment	low	1. All patients as well as all investigators who administered treatment, assessed outcomes, and analyzed data were unaware of the group assign- ments. 2. ,Ä° Data for patients were censored at the date the patient was last known to be alive. 3. The PALOMA-3 trial included premenopausal and post- menopausal patients who were more heavily pre- Progression-free survival during receipt of subsequent therapy was defined as the time from randomization to the first documented dis- ease progression while the patient was receiving second-line therapy (as reported by the physician) or to death from any cause, whichever occurred first.

References

1. Im S et al. Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer Vopr Onkol 2019. 381(6); 307-323 PMID: 9123900