Poster #CO164



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Ribociclib versus CDK4/6 inhibitors and endocrine therapies (ET) for first line (1L), metastatic or advanced HR+ HER2- pre- and postmenopausal breast cancer in Asia: A systematic review and network meta-analysis

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CONCLUSION

 NMA results were estimated based on data of Asia region population and suggested that RIBO was associated with significant PFS benefit versus PAL in post-menopausal patients and was comparable or numerically better versus other CDK4/6 inhibitors (ABE and DAL) among pre/post-menopausal patients.

LIMITATIONS

- Limited data were reported for Asia subgroup in pre-menopausal patients; no trial was identified for PAL and ABE, while DAL trial reported only PFS.
- OS results should be interpreted with caution. RIBO has proven OS benefits in 1L phase 3 trial in both pre/peri menopausal and post-menopausal patients. However, for Asia region in pre-menopausal population only one study of RIBO whereas for post-menopausal RIBO and ABE reports OS data and thus we are exploring more options with chemotherapy studies to conduct analysis to draw conclusion on OS results.
- These results are based on trials' subgroup analysis from which is often underpower.
- Non-steroidal aromatase inhibitors (NSAI) plus goserelin were assumed to have equal efficacy as NSAI alone in pre-menopausal population, since in China most patients receive goserelin during their treatment cycle.

BACKGROUND

- Among all subtypes of breast cancer, approximately 68% are HR+ (i.e. estrogen receptors [ERs] and progesterone receptors [PRs])/HER2-1.
- Treatments used to treat HR+/HER2– advanced breast cancer include cyclin-dependent kinase 4/6 (CDK4/6) inhibitors, endocrine therapies (ET), chemotherapies, and targeted agents².
- Studies have showed that the addition of a CDK4/6 inhibitor to ET provided a greater benefit regarding progression-free survival (PFS) than ET alone in pre/post- menopausal patients with advanced HR+/HER2– breast cancer³.
- The magnitude of PFS benefit is ethnicity-dependent and it is different between Asian and non-Asian population in first line treatment⁴
- In China four CDK 4/6 inhibitors abemaciclib (ABE), palbociclib (PAL), ribociclib (RIBO) and dalpiciclib (DAL) approved for treating breast cancer⁵.

RESULTS

Evidence identified from review

- Eight randomized controlled trials included in systematic literature review contributed to NMA for both post-menopausal (n=7) and pre-menopausal (n=2)inclusively (**Table 2**)
- In post-menopausal, PFS data was available for CDK4/6 inhibitors, but OS was reported only for ABE and RIBO in the Asia subgroup.
- For pre-menopausal only PFS data was available for RIBO and DAL among CDK 4/6 inhibitors whereas DAL have no OS data, so analysis was not conducted.

Table 2. An overview of survival outcome of available RCT studies in Asia region

Study	Treatment	Comparator	PFS (HR; 95% CI)	OS (HR; 95% CI)
Post-menopausal population				
MONALEESA-2 ^{6,7}	RIBO+AI	AI	0.26 (0.13-0.52)	0.64 (0.35-1.16)
FALCON ⁸	FUL500	AI	0.81 (0.43-1.50)	_
PALOMA-2 ⁹	PAL+AI	AI	0.49 (0.27-0.87)	_
PALOMA-4 ¹⁰	PAL+AI	AI	0.68 (0.53-0.87)	_
DAWNA-2 ¹¹	DAL+AI	AI	0.52 (0.36-0.75)	_
MONARCH plus ¹²	ABE+AI	AI	0.39 (0.26-0.59)	_
MONARCH 3 ^{13,14}	ABE+AI	AI	0.32 (0.20-0.53)	0.63 (0.37-1.07)
Pre-menopausal population				
MONALEESA-7 ^{15,16}	RIBO+ET	ET	0.42 (0.27-0.66)	0.64 (0.40–1.03)
DAWNA-2 [11]	DAL+ET	ET	0.53 (0.33-0.85)	_

ABE = abemaciclib, AI = aromatase inhibitors, DAL = dalpiciclib, ET = endocrine therapy, FUL500 = fulvestrant 500mg, HR= hazards ratio, PAL = palbociclib, PFS = progression free survival, RCT = randomized control trial, RIBO = ribociclib

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OBJECTIVE

• The objective was to compare RIBO versus CDK4/6 inhibitors and ET in patients with the first line pre/post-menopausal HR+/HER2-metastatic/advanced breast cancer patients in Asia.

METHODS

- Literature search was conducted using key words in English (Embase, MEDLINE, Cochrane, and MEDLINE in-process) and Chinese (Wanfang) language literature databases from 2007 onwards up to September 2022 (Table 1).
- Data reported on Asia population was extracted and considered for Bayesian network meta-analysis (NMA), comparing overall survival (OS) and PFS
- Both fixed and random effects models were fitted to account for different assumptions regarding heterogeneity of treatment effects for post-menopausal whereas for pre-menopausal there was only one trial per contrast thus fixed effect was feasible.



Table 1. Inclusion criteria for study selection

Criteria	Pre/peri menopausal	Post-menopausal		
<section-header></section-header>	 Disease: HR+/HER2- advanced/metastatic, pre/peri menopausal breast cancer Age: Adults (≥18 years) Line of therapy: First line Gender: Any Race: Any 	 Disease: HR+/HER2 advanced/metastatic post- menopausal breast cancer Age: Adults (≥18 years) Line of therapy: First line Gender: Any Race: Any 		
Intervention/ Comparators	 CDK4/6 inhibitors: abemaciclib, ribociclib, dalpiciclib, palbociclib Endocrine therapies:letrozole, anastrozole, exemestane, tamoxifen, fulvestrant 			
Trial design	Randomized controlled trials (RCT)			
Language restrictions	English & Chinese			

ET (HR: 0.42 [0.27, 0.66]) and numerically better compared to DAL plus ET (HR: 0.79 [0.41,1.52])

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