

Examining Real World Evidence in the Management of Breast Cancer: Pharmacist Implications



How do you know a study is valid?

Expert controls in the process convey a level of confidence in the quality of the trial.

A **statistician** as an author on the paper gives credibility to the results.

An **industry-sponsored** trial must be approved by the FDA when the intended use of the data is for marketing (with or without a change to the prescribing information).

- Due to the high cost of research, industry sponsors generally meet with the FDA to discuss the acceptability of the research.

National Cancer Institute-designated cancer centers have a protocol review and monitoring committee to vet the scientific merit of protocols prior to institutional review board approval.

Questions to consider—study design and controls:

1. **How big is the population? Does it describe most patients?** A large population can minimize random error.
NOTE: power analysis is uncommon in epidemiology
2. **What is the study design?** Interventional trial > cohort > case-control
 - a. Did they find all people with an exposure and then determine outcome?
 - b. Did they find people with the outcome and then look back for exposure?
3. **How did they measure the findings?**
 - a. Did they control for differences in patient disease severity?
 - b. How reliable are the outcome measurements?

Current FDA-Approved Drugs

	Abemaciclib	Palbociclib	Ribociclib
Approved indication	HR+, HER2-, Adv, or Met breast cancer	HR+, HER2-, Adv, or Met breast cancer	HR+, HER2-, Adv, or Met breast cancer
Regimen(s)	150 mg po bid w/ AI as first-line or w/ fulvestrant as second-line 200 mg po bid as monotherapy	125 mg po daily x 21 days followed by 1 week off w/ AI as first-line or w/ fulvestrant as second-line	600 mg po daily x 21 days followed by 1 week off w/ AI as first-line
Administration	Take regardless of food	Take w/ food	Take regardless of food
Drug-food interaction	Increases AUC by 9%	Increases AUC by 21% and decreases variability Avoid taking w/ grapefruit juice	Food has no effect
Drug-drug interaction	CYP3A4 substrate – avoid strong inhibitors/inducers	CYP3A4 substrate – avoid strong inhibitors/inducers	CYP3A4 substrate – avoid strong inhibitors/inducers

Adv, advanced; AI, aromatase inhibitors; AUC, area under the curve; bid, twice daily; CYP, cytochrome P450; Met, metastatic; po, by mouth.

FDA-Approved Indications

	Abemaciclib	Palbociclib	Ribociclib
First-line in combination with hormone therapy	X w/ an AI	X w/ an AI postmenopausal	X w/ an AI pre-/perimenopausal and postmenopausal; w/ fulvestrant postmenopausal
Second-line in combination with hormone therapy	X w/ fulvestrant	X w/ fulvestrant	X w/ fulvestrant
As monotherapy in pretreated patients	X after progression on hormone therapy and chemotherapy		

Source: Ibrance prescribing information.; Kisqali prescribing information.; Verzenio prescribing information.