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?

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**Current FDA-Approved Drugs**

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

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

**FDA-Approved Indications**

<table>
<thead>
<tr>
<th></th>
<th>Abemaciclib</th>
<th>Palbociclib</th>
<th>Ribociclib</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line in combination with hormone therapy</strong></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>w/ an AI</td>
<td>w/ an AI postmenopausal</td>
<td>w/ an AI pre-/perimenopausal and postmenopausal w/ fulvestrant postmenopausal</td>
<td></td>
</tr>
<tr>
<td><strong>Second-line in combination with hormone therapy</strong></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>w/ fulvestrant</td>
<td>w/ fulvestrant</td>
<td>w/ fulvestrant</td>
<td></td>
</tr>
<tr>
<td><strong>As monotherapy in pretreated patients</strong></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>after progression on hormone therapy and chemotherapy</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

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