- The study drug may be easier to administer. An example of this is fingolimod (98,99) which is a pill for multiple sclerosis, in contrast to natalizumab, which is injected
- The study drug may be administered by a flexible schedule, while the active control may require a strict, disciplined schedule.

b. Add-on design active control

With an add-on design, the study drug is administered in combination with a previously established drug, and the control group receives only the previously established drug (100). According to the ICH Guidelines, "[a]n add-on study is a placebo-controlled trial of a new agent conducted in people also receiving standard treatment. Such studies are particularly important when available treatment is known to decrease mortality or irreversible morbidity, and when a non-inferiority trial with standard treatment as the active control cannot be carried out or would be difficult to interpret. It is common to study anticancer, antiepileptic, and heart failure drugs this way" (101). The FDA has recognized that add-on design clinical studies are common in clinical trials in oncology, heart failure, seizure disorders, and human immunodeficiency virus (HIV) (102).

According to Roberts et al. (103) it may be easier to obtain regulatory approval for an anti-cancer drug when trial uses an add-on design, writing that, "most agents with first-line indications are approved for use in combination (eg, irinotecan plus fluorouracil and leucovorin for first-line colon cancer)."

In a clinical trial on non-small cell lung cancer, Rosell et al. (104) used an add-on design. The new drug was an antibody (cetuximab). The established therapy was the combination of two small molecules, namely, cisplatin and vinorelbine. In the words of the investigators, "[t]he main purpose of this study was to assess the add-on activity of cetuximab."

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