

- Run-in period, that determines response to chemotherapy, where chemotherapy is provided before initiation of the clinical trial (45)
- Two study arms, where one arm uses sequential dosing with two drugs, while the other arm uses concurrent administration of the same two drugs (46)
- Comparing neoadjuvant therapy with adjuvant therapy (47)
- Schema where each study arm uses both neoadjuvant therapy, followed by surgery, followed by adjuvant therapy (48)
- Two study arms, where the first arm uses a specific order of administration of two different drugs, while the second arm uses the reverse order of administration of the two drugs (49)
- Patients receiving three different drugs, each drug having its own different schedule (50).
Burstein et al. (51) provide an interesting thumbnail diagram depicting a dozen different schema for various oncology clinical trials. Chittick et al. (52) provide a particularly interesting schema from a clinical trial on infections.

b. Sequential Treatment Versus Concurrent Treatment—The Perez Schema

In a clinical trial with three arms, Perez et al. (53) disclosed the first arm as the control arm, the second arm as a sequential arm, and

⁴⁵Hanna NH, Sandier AB, Loehrer Sr PJ, et al. Maintenance daily oral etoposide versus no further therapy following induction chemotherapy with etoposide plus ifosfamide plus cisplatin in extensive small-cell lung cancer: a Hoosier Oncology Group randomized study. *Ann. Oncol.* 2002;13:95–102.

⁴⁶Perez EA, Suman VJ, Davidson NE, et al. Cardiac safety analysis of doxorubicin and cyclophosphamide followed by paclitaxel with or without trastuzumab in the North Central Cancer Treatment Group N9831 adjuvant breast cancer trial. *J. Clin. Oncol.* 2008;26:1231–8.

⁴⁷Gianni L, Baselga J, Eiermann W, et al. Phase III trial evaluating the addition of paclitaxel to doxorubicin followed by cyclophosphamide, methotrexate, and fluorouracil, as adjuvant or primary systemic therapy: European Cooperative Trial in Operable Breast Cancer. *J. Clin. Oncol.* 2009;27:2474–81.

⁴⁸Untch M, Möbus V, Kuhn W, et al. Intensive dose-dense compared with conventionally scheduled preoperative chemotherapy for high-risk primary breast cancer. *J. Clin. Oncol.* 2009;27:2938–45.

⁴⁹Puhalla S, Mrozek E, Young D, et al. Randomized phase II adjuvant trial of dose-dense docetaxel before or after doxorubicin plus cyclophosphamide in axillary node-positive breast cancer. *J. Clin. Oncol.* 2008;26:1691–7.

⁵⁰Sekine I, Nishiwaki Y, Noda K, et al. Randomized phase II study of cisplatin, irinotecan and etoposide combinations administered weekly or every 4 weeks for extensive small-cell lung cancer (JCOG9902-DI). *Ann. Oncol.* 2003;14:709–14.

⁵¹Burstein HJ, Prestrud AA, Seidenfeld J, et al. American Society of Clinical Oncology clinical practice guideline: update on adjuvant endocrine therapy for women with hormone receptor-positive breast cancer. *J. Clin. Oncol.* 2010;28:3784–96.

⁵²Chittick GE, Zong J, Blum MR, et al. Pharmacokinetics of tenofovir disoproxil fumarate and ritonavir-boosted saquinavir mesylate administered alone or in combination at steady state. *Antimicrob. Agents Chemother.* 2006;50:1304–10.

⁵³Perez EA, Suman VJ, Davidson NE, et al. Cardiac safety analysis of doxorubicin and cyclophosphamide followed by paclitaxel with or without trastuzumab in the North Central Cancer Treatment Group N9831 adjuvant breast cancer trial. *J. Clin. Oncol.* 2008;26:1231–8.