

Global Biometrics and Data Science

Short topic

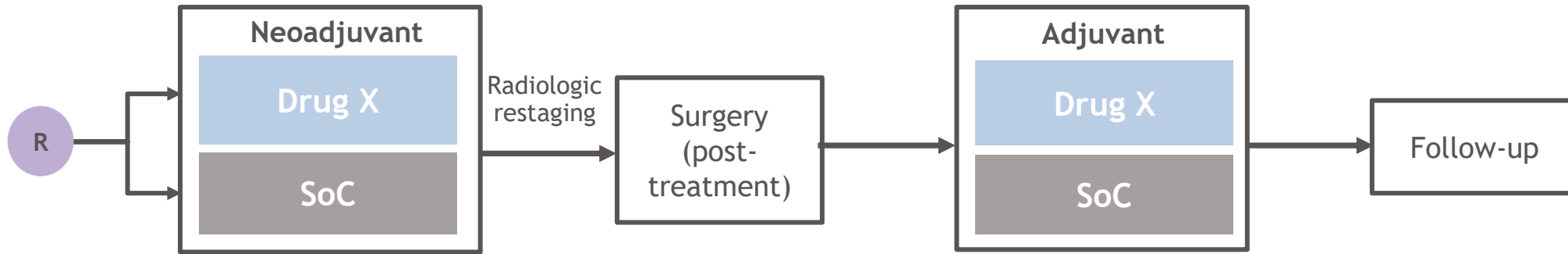
Contribution of Sequence

9th EFSPi Reg Stats Workshop, Basel, 11 Sept 2024

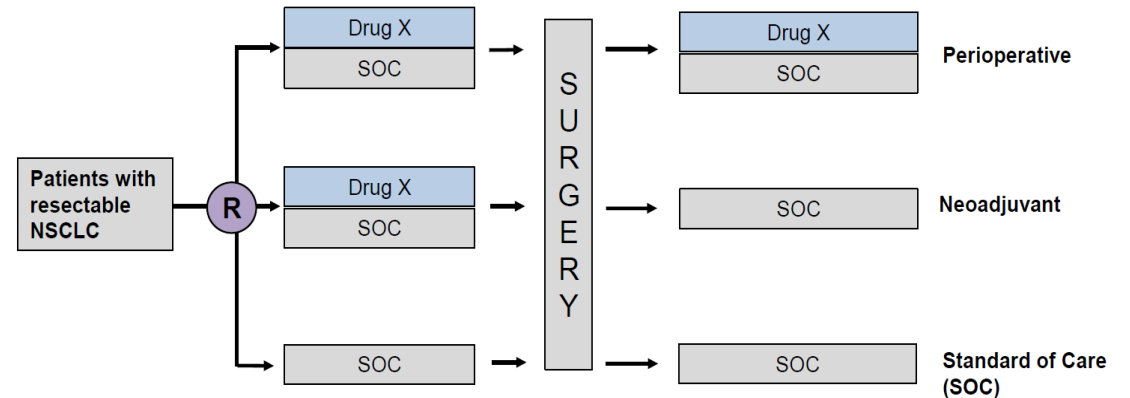
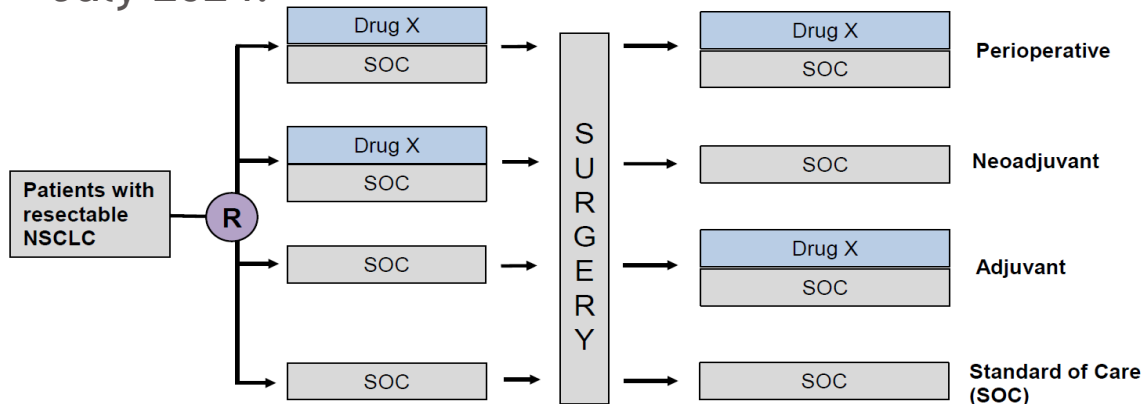
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Contribution of Sequence

- Many study designs with surgery contain different treatment periods: Neoadjuvant, Adjuvant or Peri-operative
- Peri-operative treatment period and sequence: Neoadjuvant -> Surgery -> Adjuvant -> Follow-up



- To address the contribution of additional adjuvant effect and to avoid safety concerns due to overdosing, FDA recommended to use factorial design or at least 3-arm design in a peri-operative setting in ODAC meeting on 25th July 2024.



Contribution of Sequence

- ***Our questions:***

- As shown, FDA recommended to use factorial design or at least 3-arm design in a peri-operative setting. ***What are the recommendations from other regulatory agencies?***
- Assuming that a 3-arm design approach is pursued, ***which type of treatment regimen should be compared with peri-adjuvant/peri-operative regimen***, neo-adjuvant only or adjuvant only for assessing contribution of sequence?
- ***Can a phase-2 study with 3 arms be used*** for demonstrating contribution of sequence?
- In a peri-operative setting with only 2 arms (peri vs. SoC), ***could we demonstrate the treatment effect from neoadjuvant period or adjuvant period using statistical methods?***
 - landmark analysis from surgery or other time point
 - indirect comparison (propensity score analysis) using external control or historical data
 - responder analysis or subgroup analysis
- ***Are there any draft/final guidelines*** that we can refer to for the new and existing studies involving different treatment sequences or treatment phases?

Thank you for your inputs!