CROSSOVER EFFECTS IN CLINICAL TRIALS

Crossover occurs when patients in the control arm receive the investigational treatment after disease progression.

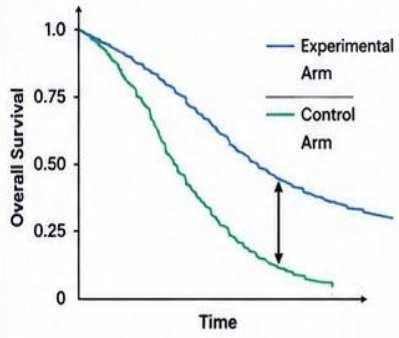
WHY IT MATTERS?

Crossover can dilute the difference in Overall Survival (OS) between the treatment arms, making it harder to detect a true survival benefit.

HOW CROSSOVER WORKS?

IMPACT ON OVERALL SURVIVAL (OS)

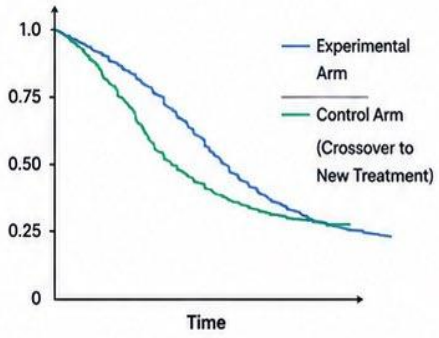
NO CROSSOVER



Clear separation between curves.

True survival benefit can be detected.

WITH CROSSOVER



Curves converge due to crossover.

Survival difference is reduced.

OS benefit may appear smaller or insignificant.

KEY POINTS

- Crossover is common in oncology trials for ethical reasons.
- It can reduce the observed OS benefit.
- Progression-Free Survival (PFS) is less affected by crossover and often used as a primary endpoint.
- Subsequent therapy data should be reported transparently.

HOW TO ADDRESS CROSSOVER EFFECTS?

- Use statistical methods to adjust for crossover (e.g., Rank Preserving Structural Failure Time – RPSFT)
- Perform sensitivity analyses
- Report both ITT and adjusted analyses
- Interpret OS results in the context of crossover and subsequent therapies

TAKE-HOME MESSAGE

Crossover protects patients and is often necessary, but it can mask the true overall survival benefit of a new treatment. Always interpret OS results with the crossover context in mind.

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