

Immunotherapy in the Peri-Operative Setting



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Neoadjuvant vs Adjuvant?

Patient Selection?

Surgical Challenges?

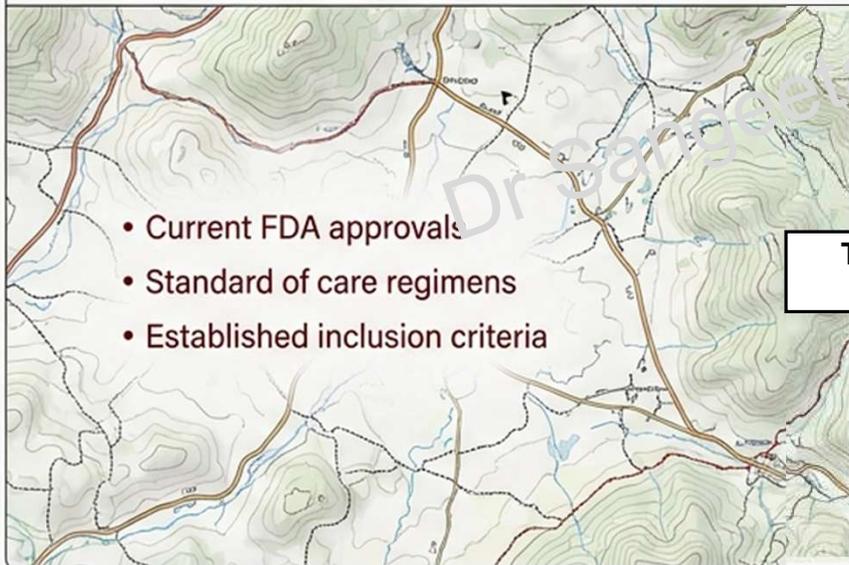
Evidence, uncertainty, and clinical judgment

A MULTI-EDITION THEMATIC SERIES

For Oncology Healthcare Professionals

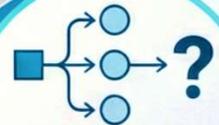
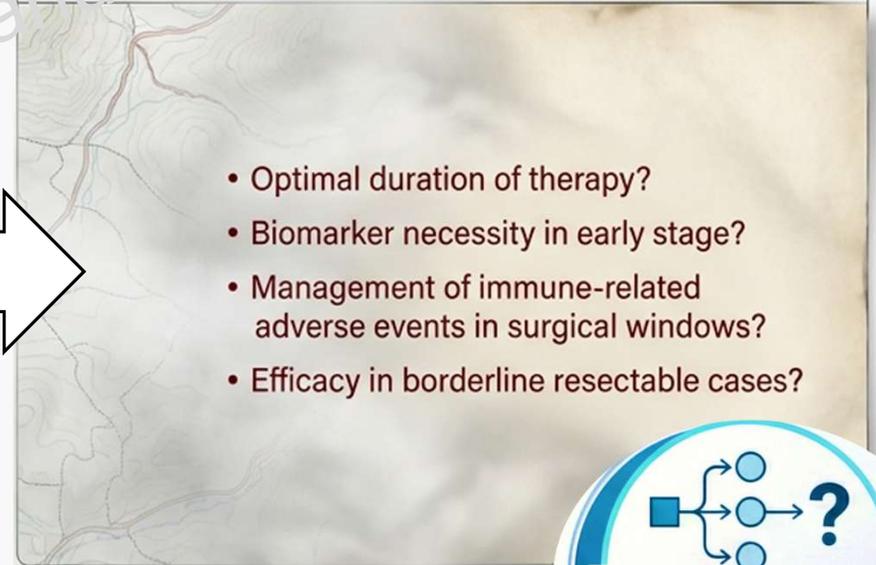
Where Guidelines End and Questions Begin

THE KNOWN (Guidelines)



The Clinical Reality

THE UNKNOWN (The Grey Zone)



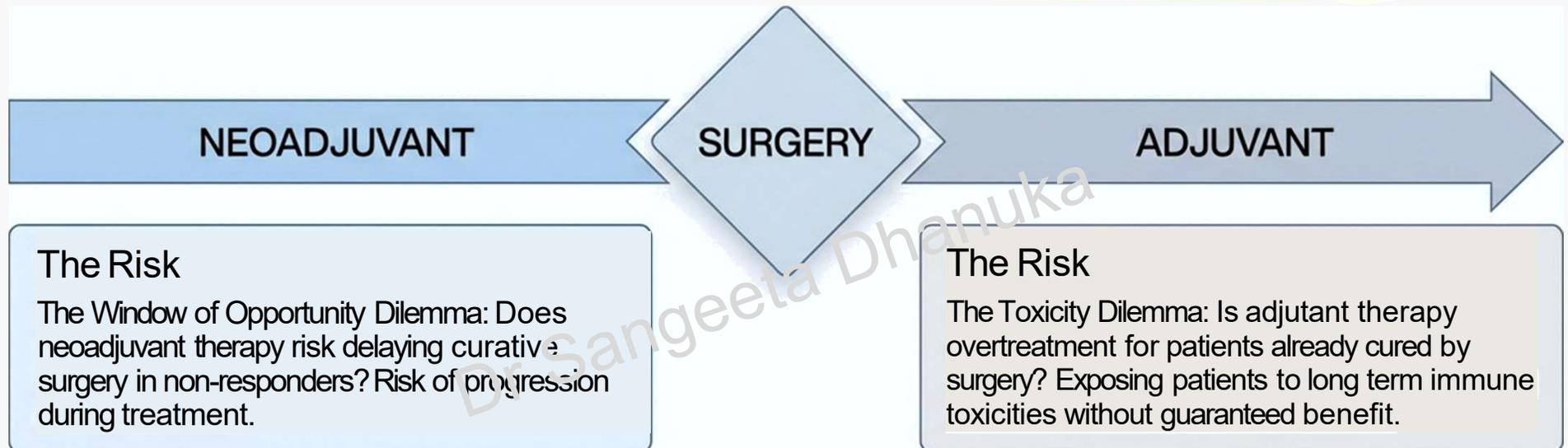
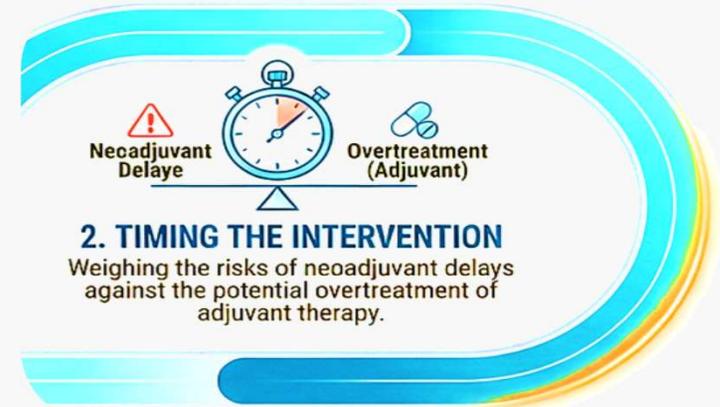
1. THE GUIDELINE GAP

Identifying where standard protocols end and clinical questions begin for immunotherapy.

EDITION 2

The Timing Controversy

Should we downstage disease or consolidate after complete resection?



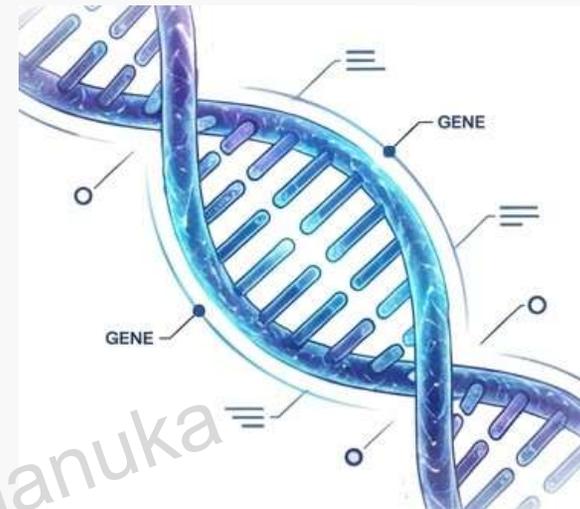
Synthesis: Evaluating the trade-offs between pre-operative systemic control and post-operative insurance.

The Patient Variable: Selection and Biology



3. THE BIOMARKER PUZZLE

Evaluating if PD-L1 status or oncogene drivers should dictate peri-operative treatment decisions.



The PD-L1 Debate

What is the role of PD-L1 expression in the peri-operative setting? While predictive in the metastatic setting, its utility here is debated. Should immunotherapy be offered regardless of status, or is it a requisite for efficacy?

The Genetic Exception

Oncogene-driven tumors (e.g., EGFR, ALK). The biology of these tumors often precludes benefit from checkpoint inhibitors. Are these patients candidates for IO, or does the risk of hyper-progression or toxicity outweigh the benefit?

The Surgical Reality: Tissue, Fibrosis, and Healing



Clinical Alert: Intra-operative Challenges

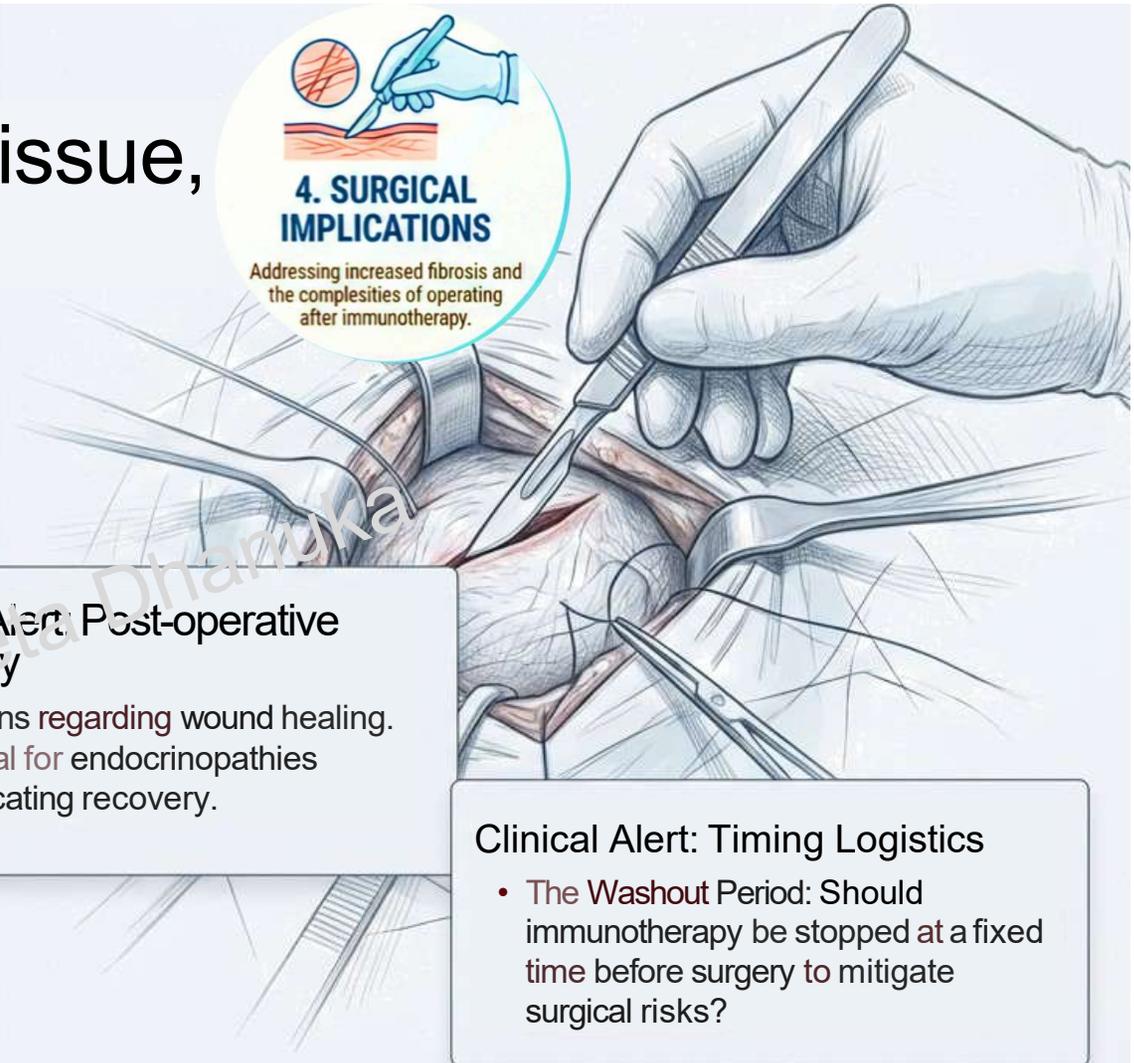
- Increased tissue fibrosis
- Increased tissue fibrosis and inflammation.
- “Sticky” hila making dissection complex.
- Higher conversion rates from minimally invasive to open surgery

Clinical Alert: Post-operative Recovery

- Concerns regarding wound healing.
- Potential for endocrinopathies complicating recovery.

Clinical Alert: Timing Logistics

- **The Washout Period:** Should immunotherapy be stopped at a fixed time before surgery to mitigate surgical risks?



The Duration Dilemma: How Much Is Enough?

The Strategy Conflict

Fixed duration protocols (often 1 year) vs. Response-adapted therapy.

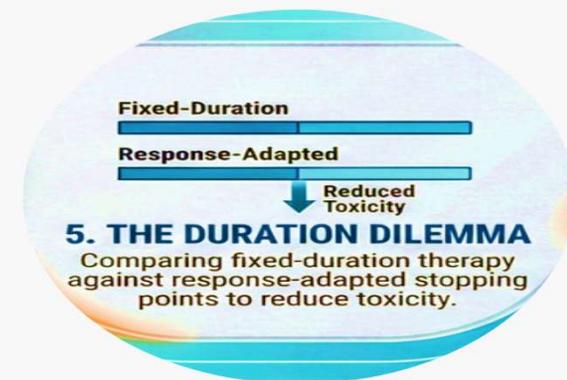
The Cost/Benefit Equation

- Financial toxicity: High cost of sustained IO
- Patient burden: Infusion visits and time off work
- Cumulative toxicity risk over time.



The De-escalation Question

Can patients with a Deep Pathological Response (pCR) safely stop therapy early? Is further treatment redundant?



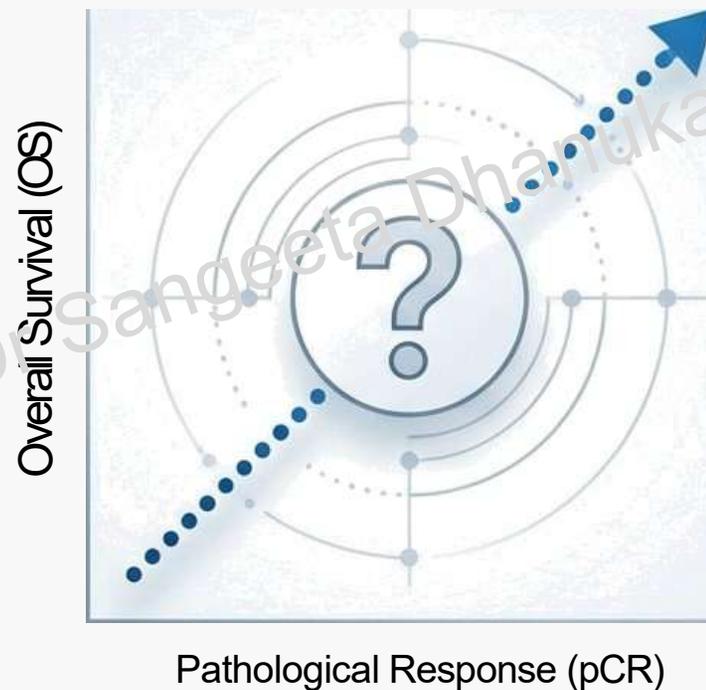
EDITION 6

The Metrics of Success: pCR, EFS, or OS?

The Surrogate Endpoint Debate

Can pathological complete response (pCR) or major pathological response (MPR) reliably predict overall survival?

Regulatory bodies accept pCR, but does it guarantee a cure?



Long-term Efficacy
Event-Free Survival (EFS) vs.
Overall Survival (OS)

Will early EFS benefits translate into durable survival advantages, or simply delay recurrence?



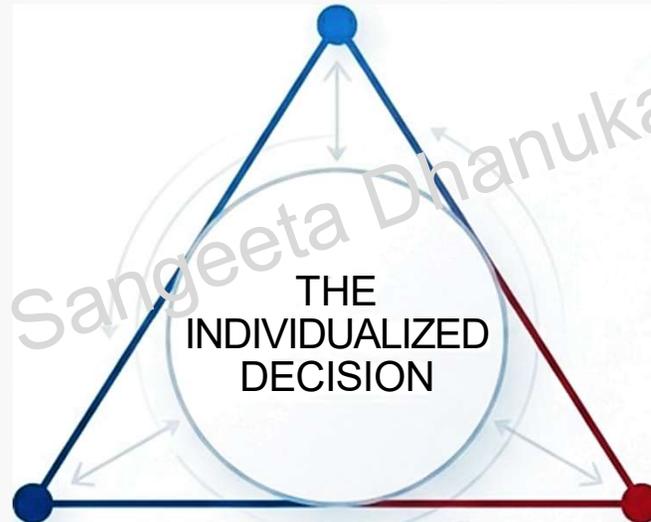
6. DEFINING SUCCESS

Debating whether surrogate endpoints like pCR reliably predict long-term overall survival.

The Clinical Synthesis: How Are Decisions Made Today?

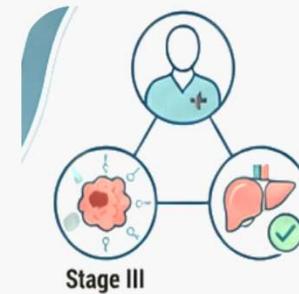
TUMOR STAGE

Extent of disease driving urgency



RESECTABILITY

Technical feasibility of upfront surgery vs. need for downstaging



7. THE FINAL DECISION

Synthesizing tumor stage, resectability, and patient fitness into a cohesive treatment plan.

PATIENT FITNESS

Ability to tolerate dual-modality (Chemo-IO) or tri-modality therapy

The Variability Factor: Highlighting significant inter-physician and inter-center variability in approach due to lack of definitive data