

Black boxes in mUC: what to do upon progression to adjuvant CPI?

The biology of sequential immunotherapy

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Conflicts of interest

- Advisory: Numab, Pieris, BMS
- Speaker's bureau: MSD, Replimune
- Grant travel: Roche, BMS, AZ
- Research grant: Roche, BMS

A New Black Box

Adjuvant CPI exposure → relapse → ???

CM 274

(Neoadj CT)→

Surgery→**Adjuvant nivolumab**

NIAGARA

Neoadj CT+durvalumab-->

Surgery→**Adjuvant durvalumab**

Key question: Does it make sense to re-treat with PD-1 or PD-L1 blockade strategies?

Aspects to consider

Time to relapse

Type of (neo)adjuvant treatment

Immune TME at the time of recurrence

A black box shared by different tumor types

MELANOMA

Pembrolizumab (**KN 054** and **KN 716**) and Nivolumab (**CM76K** and **CM238**)

NSCLC

Pembrolizumab (**PEARL**), Atezolizumab (**IMpower 010**) and Perioperative trials

RCC

Pembrolizumab (**KN 564**)

Esophageal/GEC

Nivolumab (**CM 577**)

cSCC

Cemiplimab (**C-POST**)

TNBC

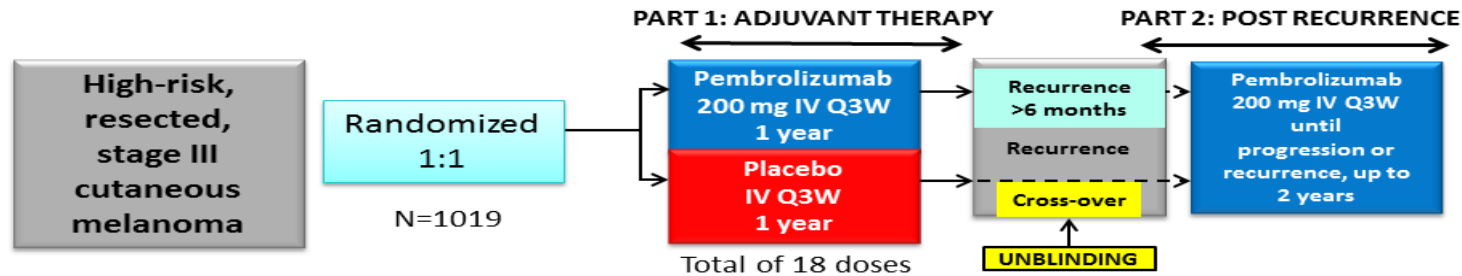
Pembrolizumab (**KN 522**)

Melanoma previous experience

Eggermont AM, Cancer Research 2018

L. Eggermont AACR 2018

EORTC 1325/KEYNOTE-54: Study Design

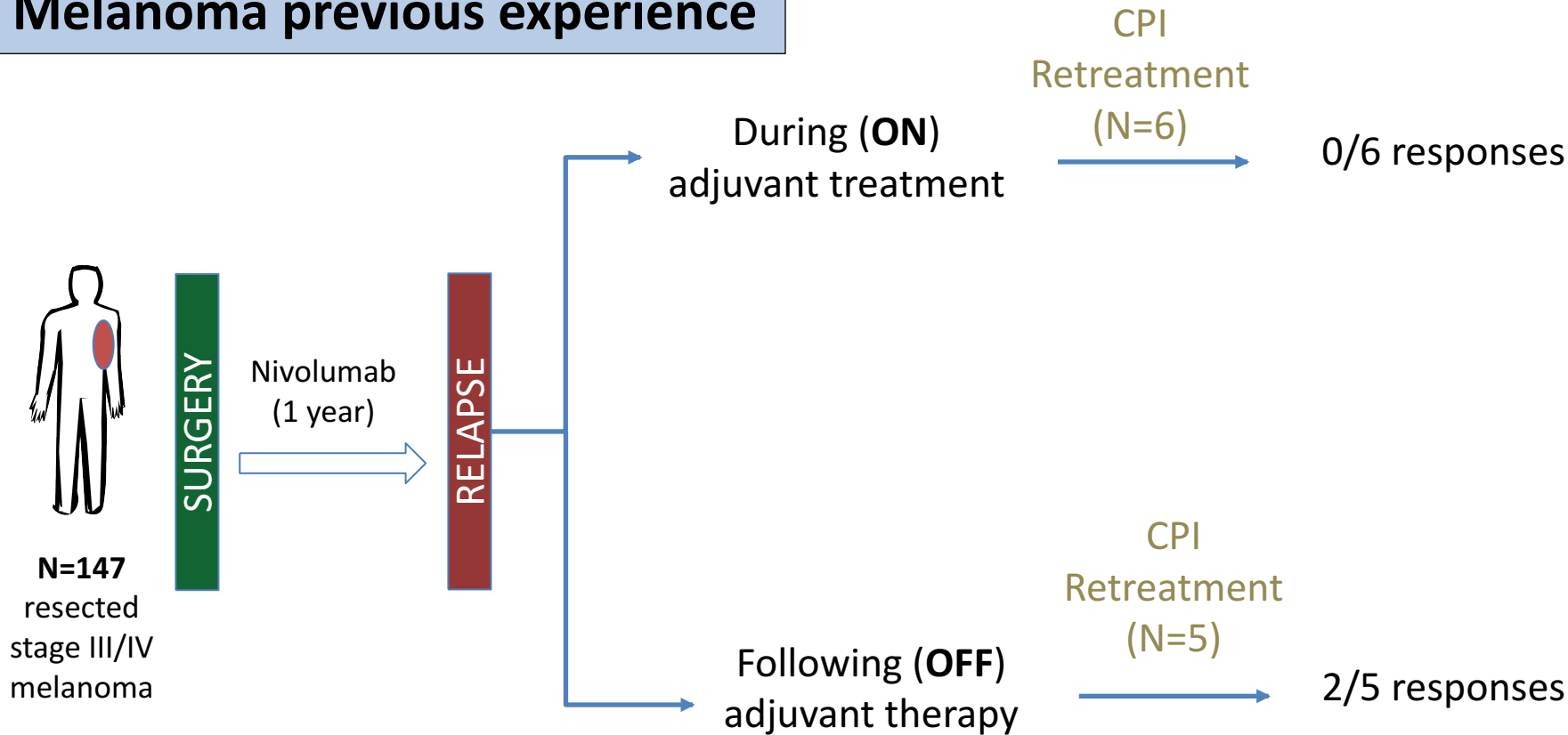


From 9 patients (1 CR, 3 SD, 5 PD)

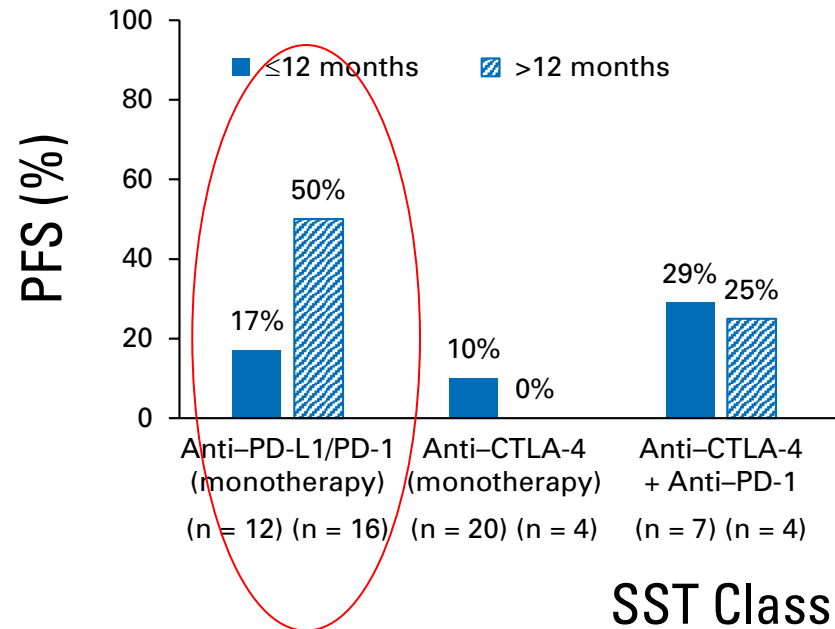
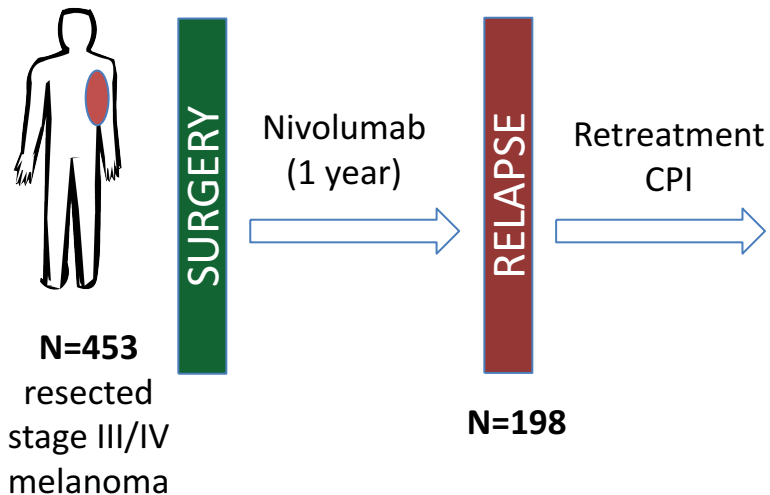
Median PFS: 4.1 months (Expected naive-CPI treated mPFS: 12 months)

CPI retreatment in adjuvant CPI-experienced patients is less active than in CPI-naïve patients

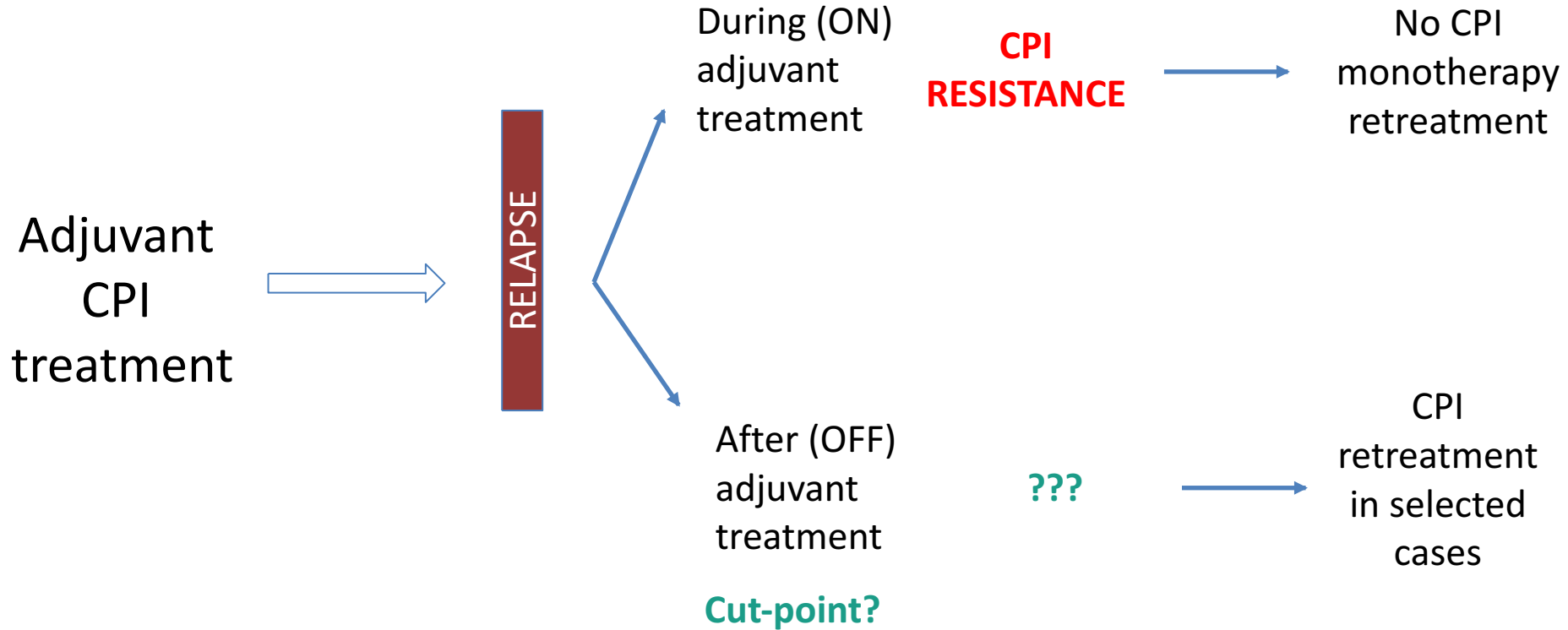
Melanoma previous experience



Melanoma previous experience



Time to relapse



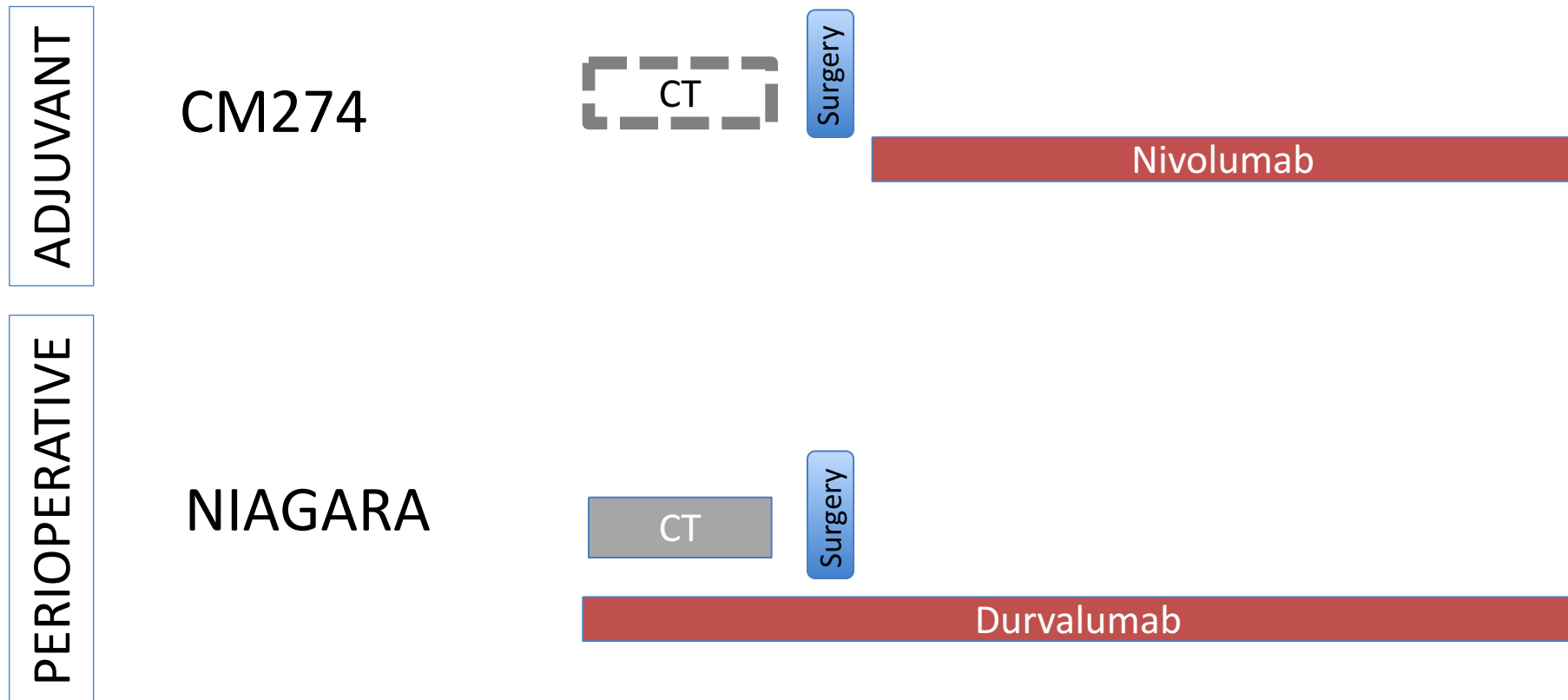
Aspects to consider

Time to relapse

Type of (neo)adjuvant treatment

Immune TME at the time of recurrence

Emerging landscape of immunotherapy in early stage UC



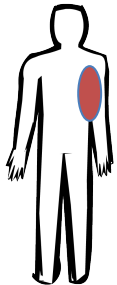
Melanoma previous experience: Benefit of neoadjuvant vs adjuvant

SWOG S1801

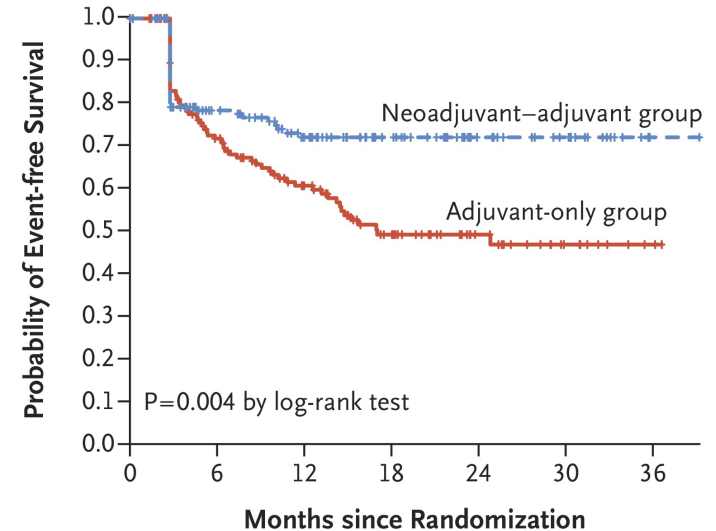
ADJUVANT



NeoADJUVANT



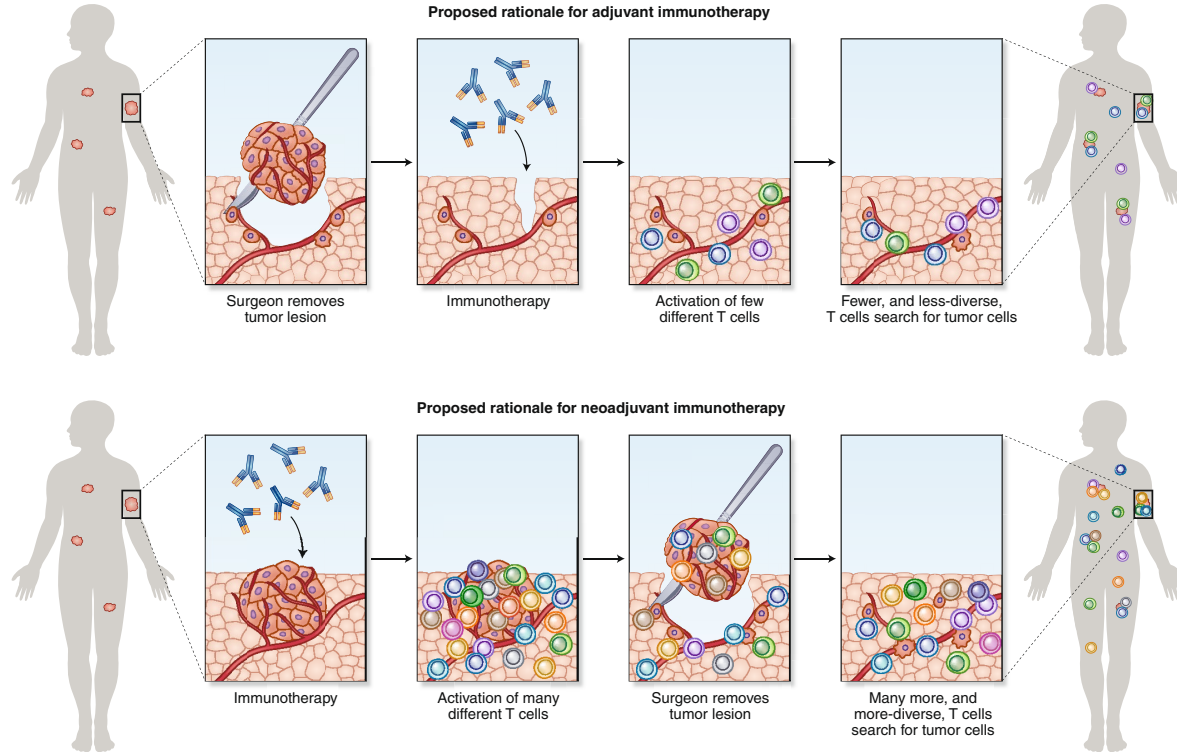
N=198
resected
stage III/IV
melanoma



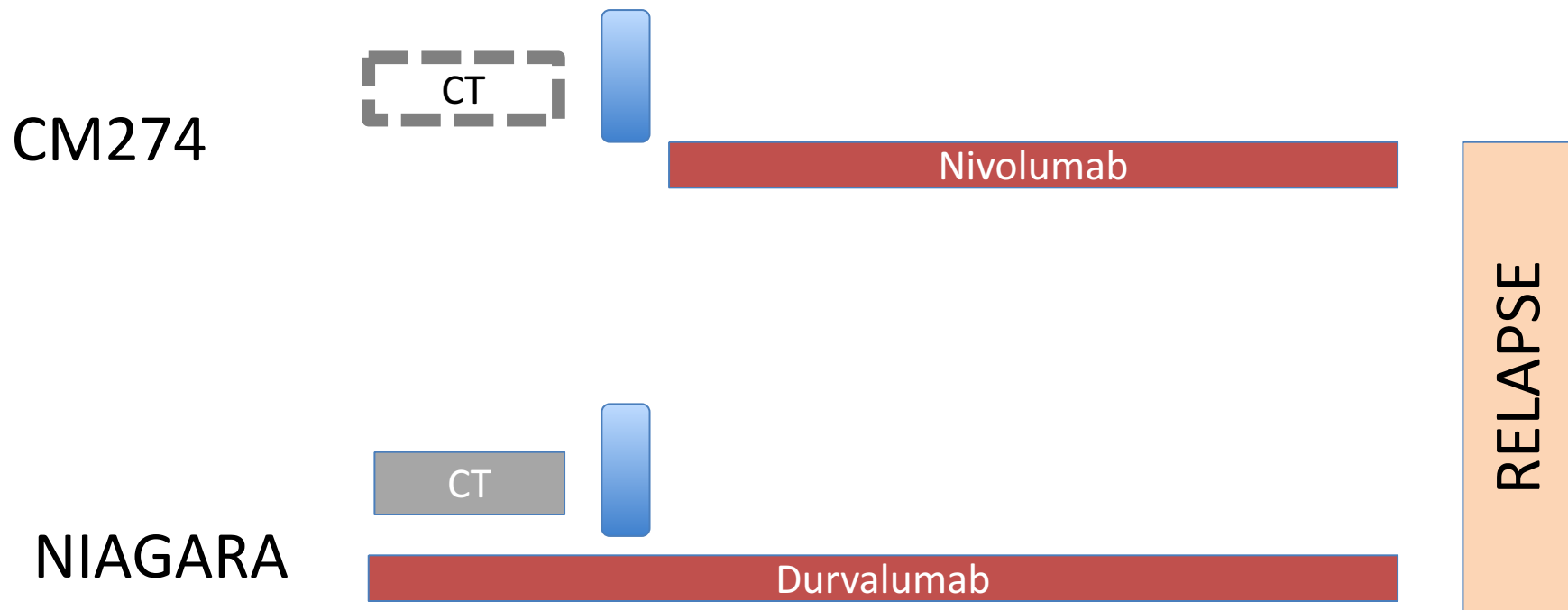
No. at Risk

Neoadjuvant–adjuvant group	154	96	69	46	25	17	1
Adjuvant-only group	159	98	67	40	22	10	2

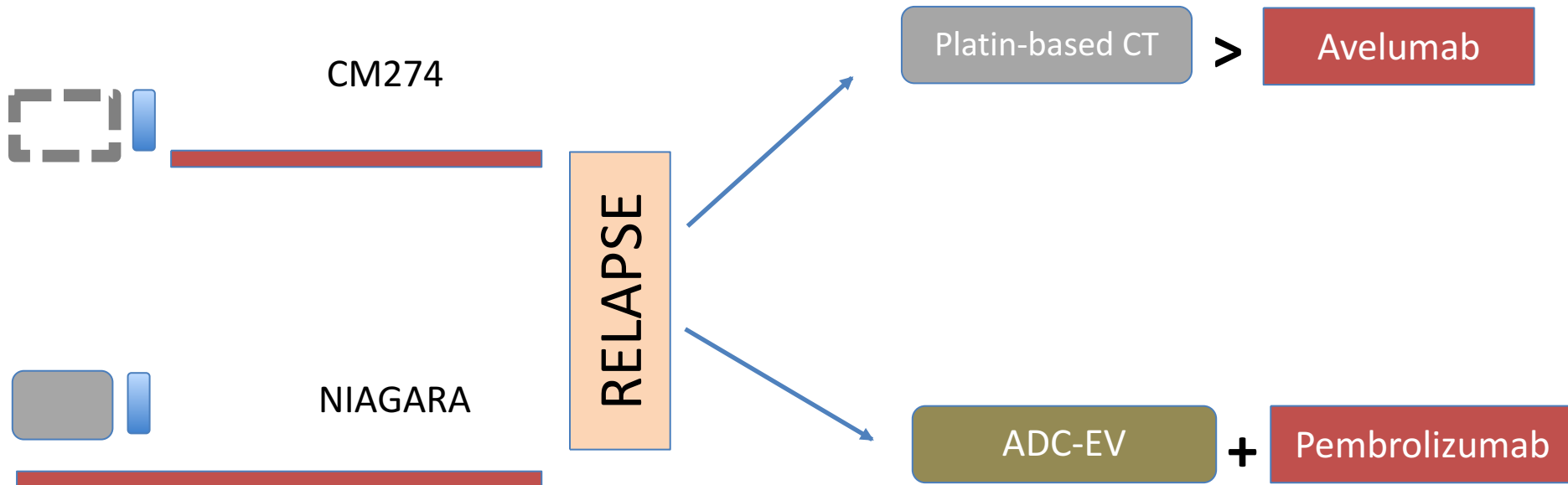
Rationale for prioritizing neoadjuvant treatment over adjuvant



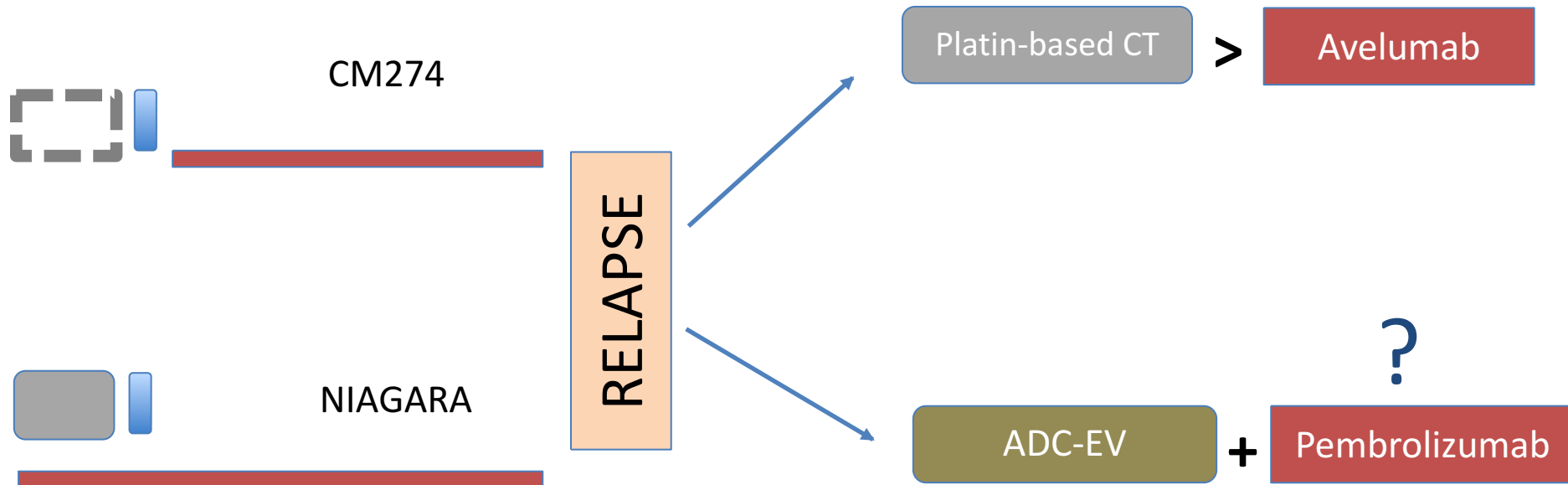
CPI failure may be biologically different in adjuvant vs perioperative



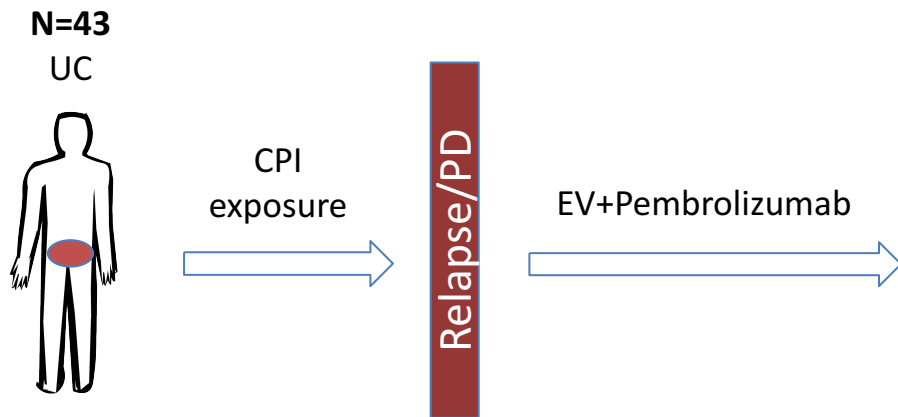
Recurrence after (**OFF**) CPI adjuvant treatment



Recurrence during (ON) CPI adjuvant treatment



UNITE STUDY (ASCO 2025)

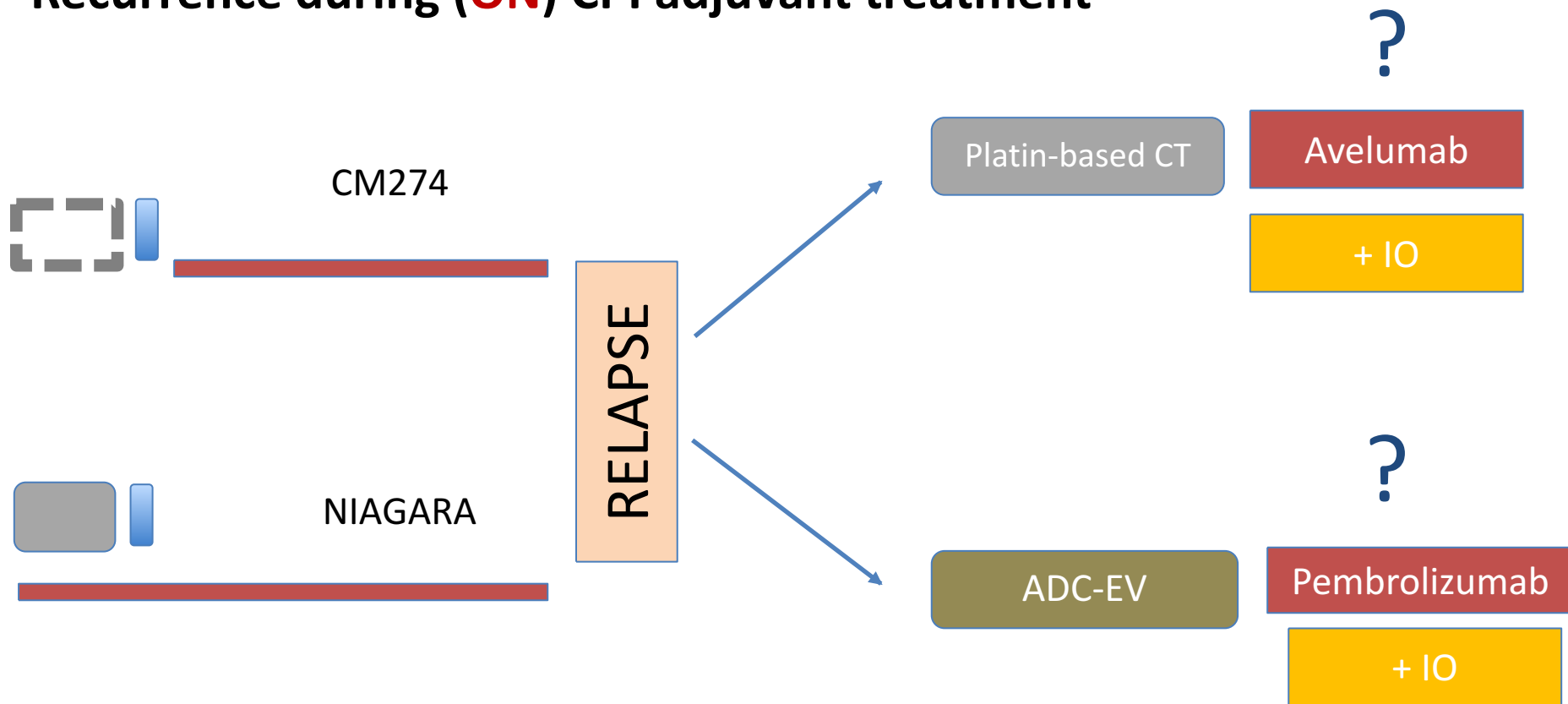


Treatment and Survival Outcomes (n=43)	
Median Follow Up	14 months
Median Overall Survival	15.4 mos (95% CI: 8.7 – NR)
Median Progression-Free Survival	6.9 mos (95% CI: 3.91 – 12.2)
Observed Response Rate	48% (95% CI: 31 - 66) [16/33]
Disease Control Rate (CR/PR/SD)	79% (95% CI: 65 - 93) [26/33]

Expected CPI-naïve mUC response and survival to EV+Pembrolizumab:

mOS: **36.5** mo (95% CI 32.2-NE)
mPFS: **12.5** mo (95% CI 10.4-16.6)
ORR: **67.7%** (95% CI 63.6-71.6)
DCR: **86.5%**

Recurrence during (ON) CPI adjuvant treatment

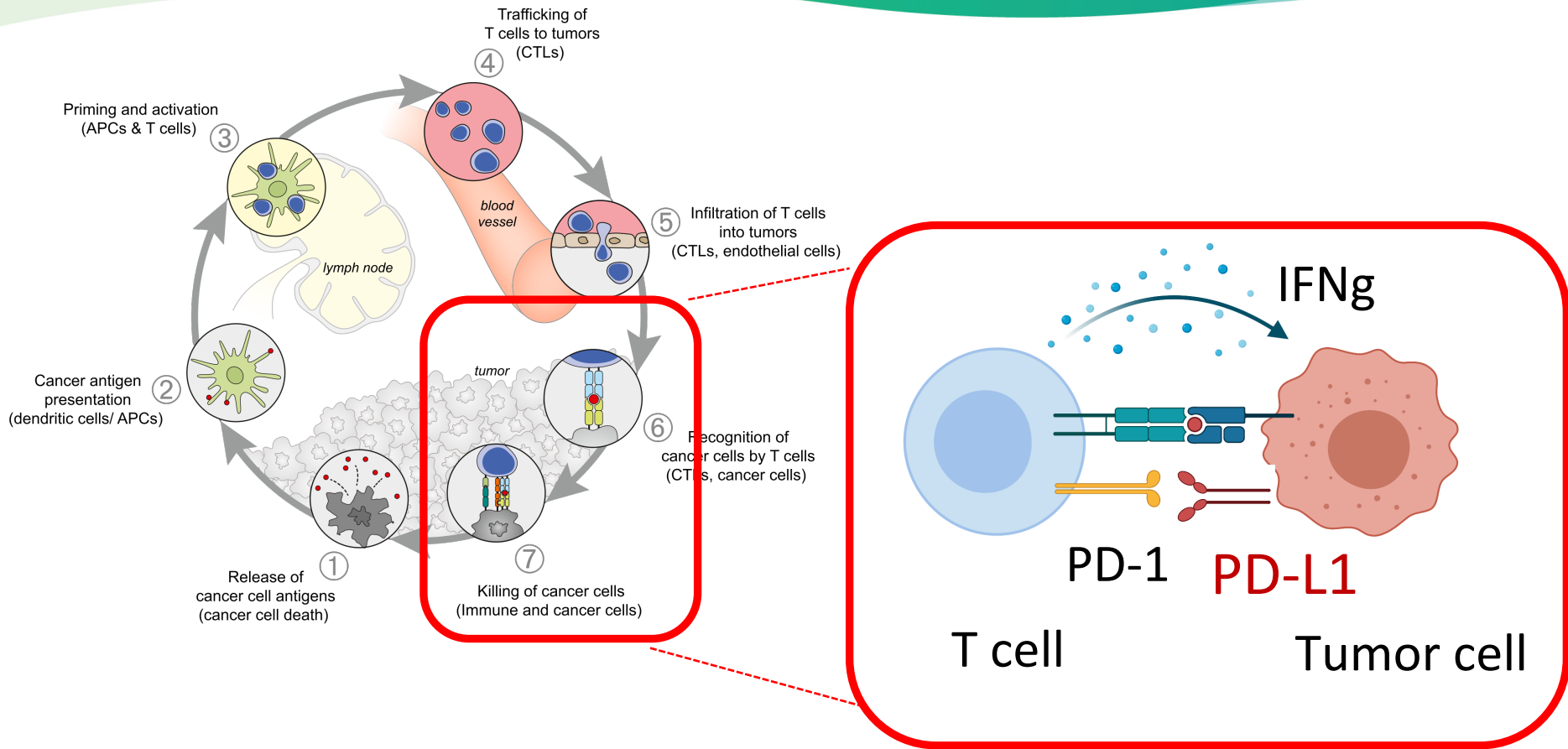


Aspects to consider

Time to relapse

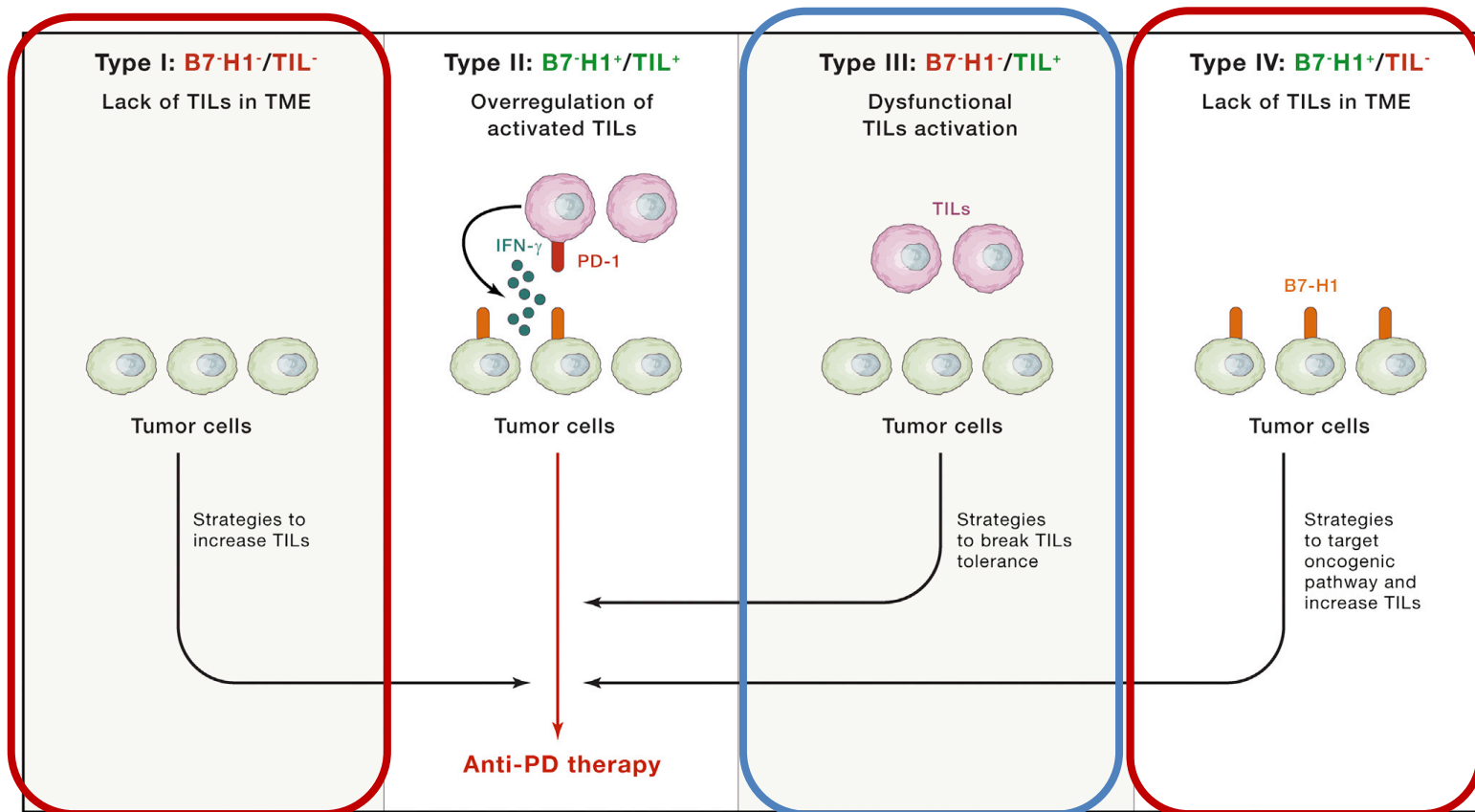
Adjuvant vs perioperative immunotherapy

Immune TME at the time of recurrence



Frame-work to analyze immune TME

B7-H1=PD-L1

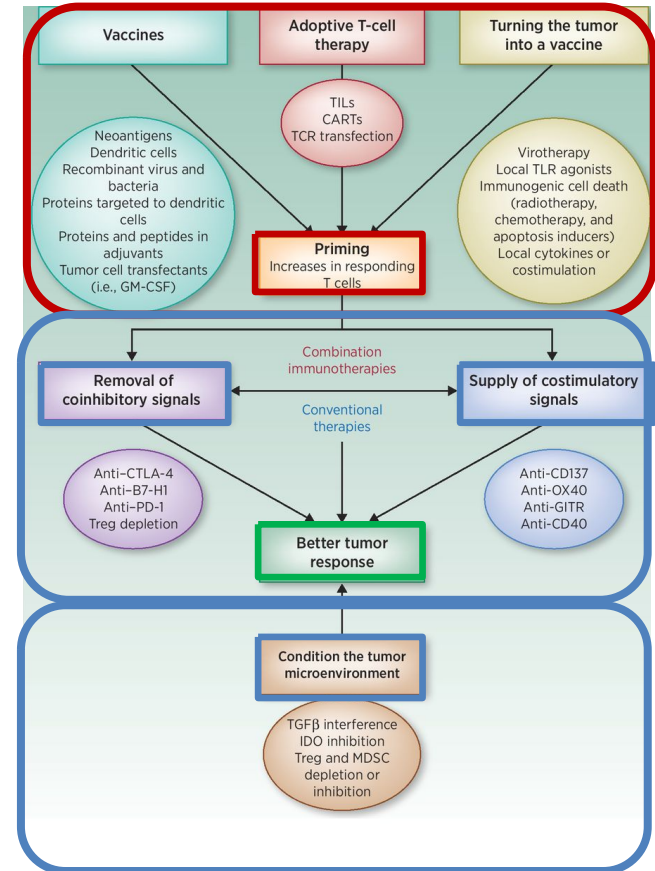


Many complementary strategies to CPI to enhance antitumor immune response

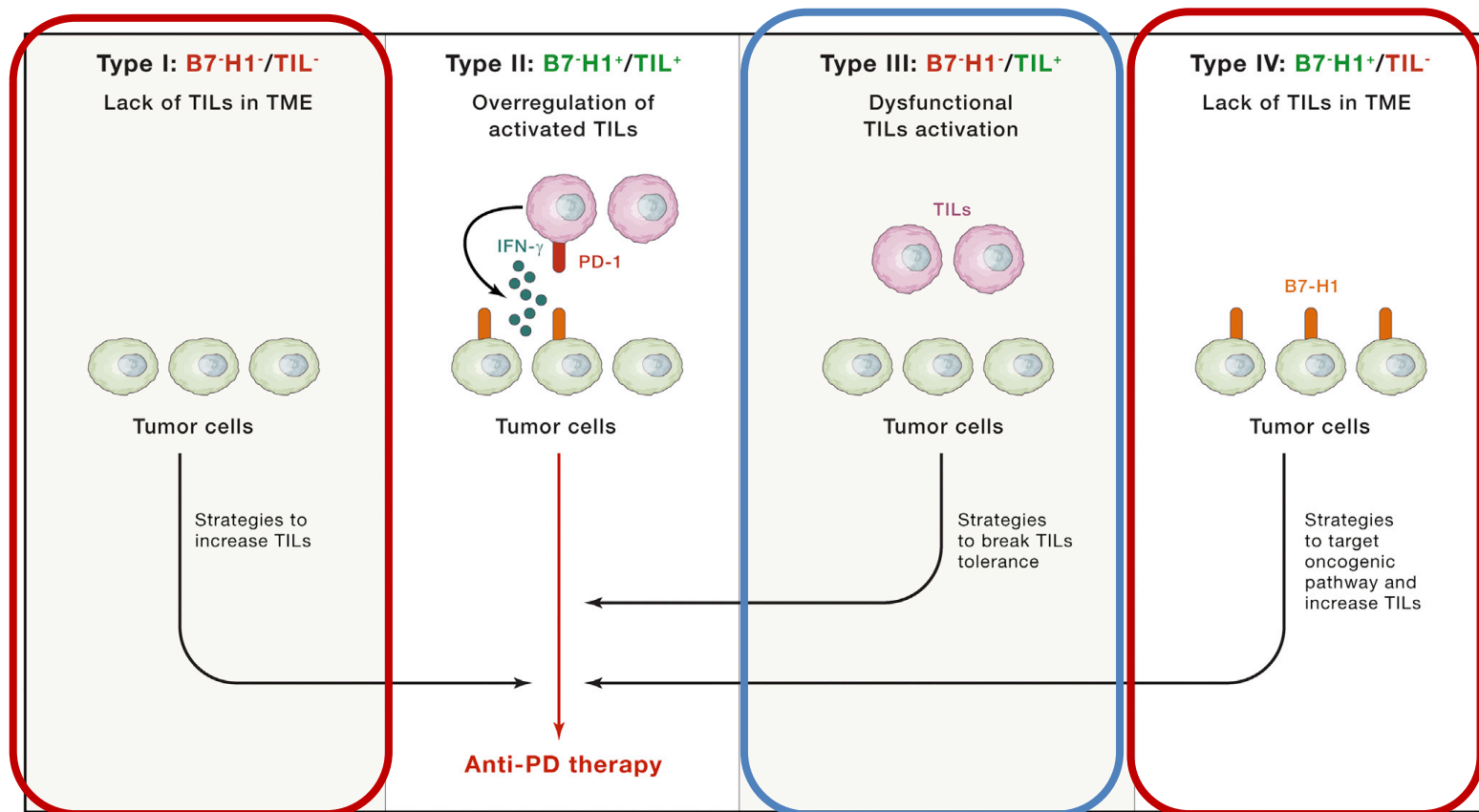
1. Expand tumour-specific T cells

2. T-cell co-stimulatory strategies

3. Targeting immunosuppressive TME



Frame-work to analyze immune TME



Adjuvant CPI exposure → relapse

OFF treatment
(6 months?)

ON treatment
(CPI resistant)

Platin-
based CT

+/-

CPI

ADC-EV

+

CPI

Platin-
based CT

+/-

CPI+IO

ADC-EV

+

CPI+IO

IO: Combinations driven by biomarker selection



Thanks