



Where **Science** Becomes **Hope**

USING PATHOLOGIC RESPONSE TO DETERMINE DE-ESCALATION OF SURGERY AND NEED FOR ADJUVANT THERAPY

PRO

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EMORY
WINSHIP
CANCER
INSTITUTE

National Cancer Institute-Designated
Comprehensive Cancer Center

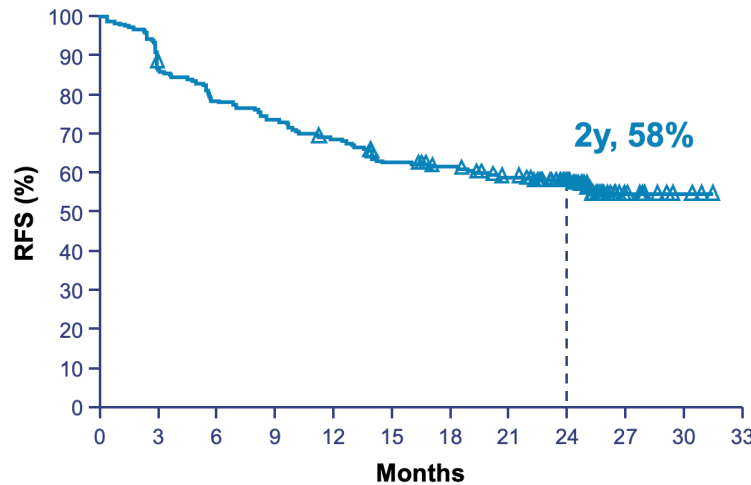
NCI

Designated
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Cancer Center

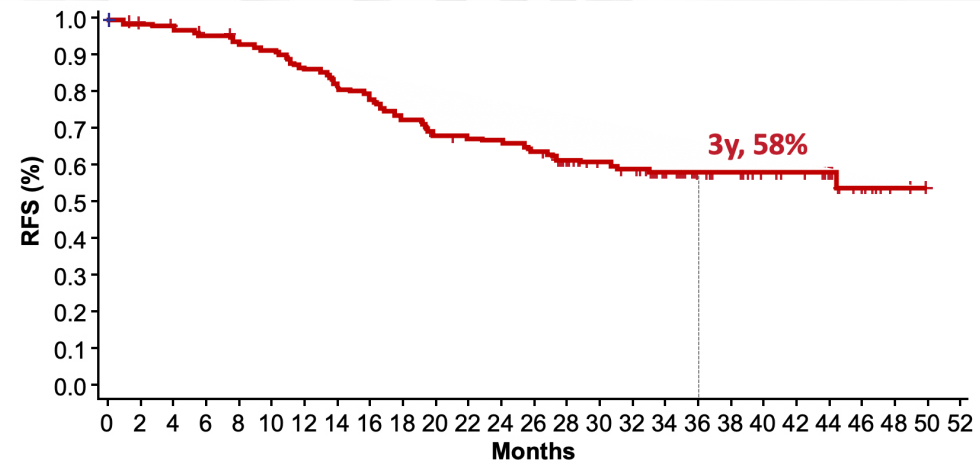
DISCLOSURES

- Advisory board: BMS, Merck, Philogen
- Research funding: Amgen, BMS, Delcath, Merck, Regeneron, Stryker, Vaccinex

RATIONALE FOR NEOADJUVANT THERAPY



Checkmate 238

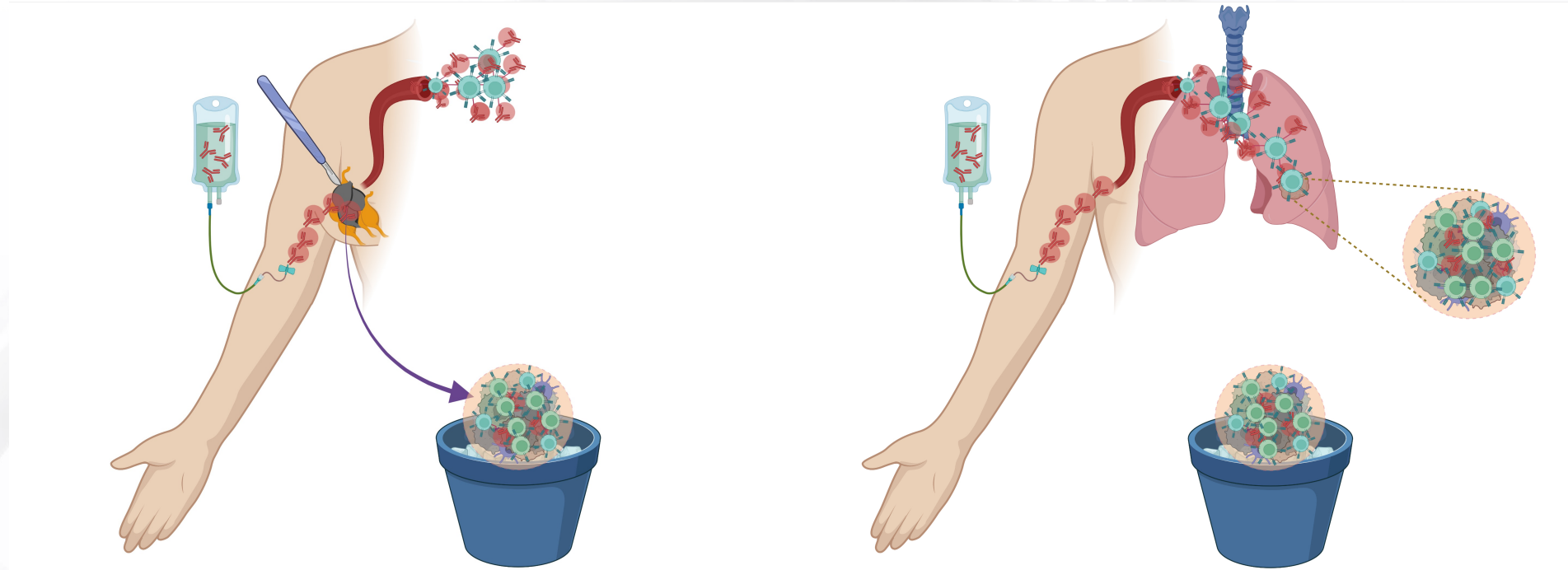


Combi-AD

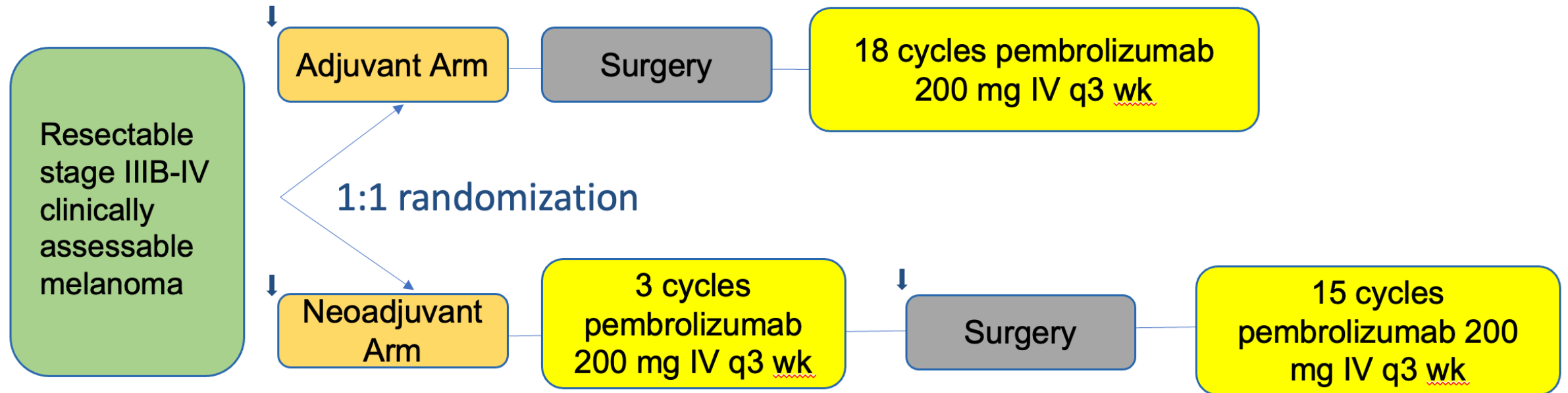
Outcomes for stage III disease remain relatively poor even with adjuvant therapies

RATIONALE FOR NEOADJUVANT THERAPY

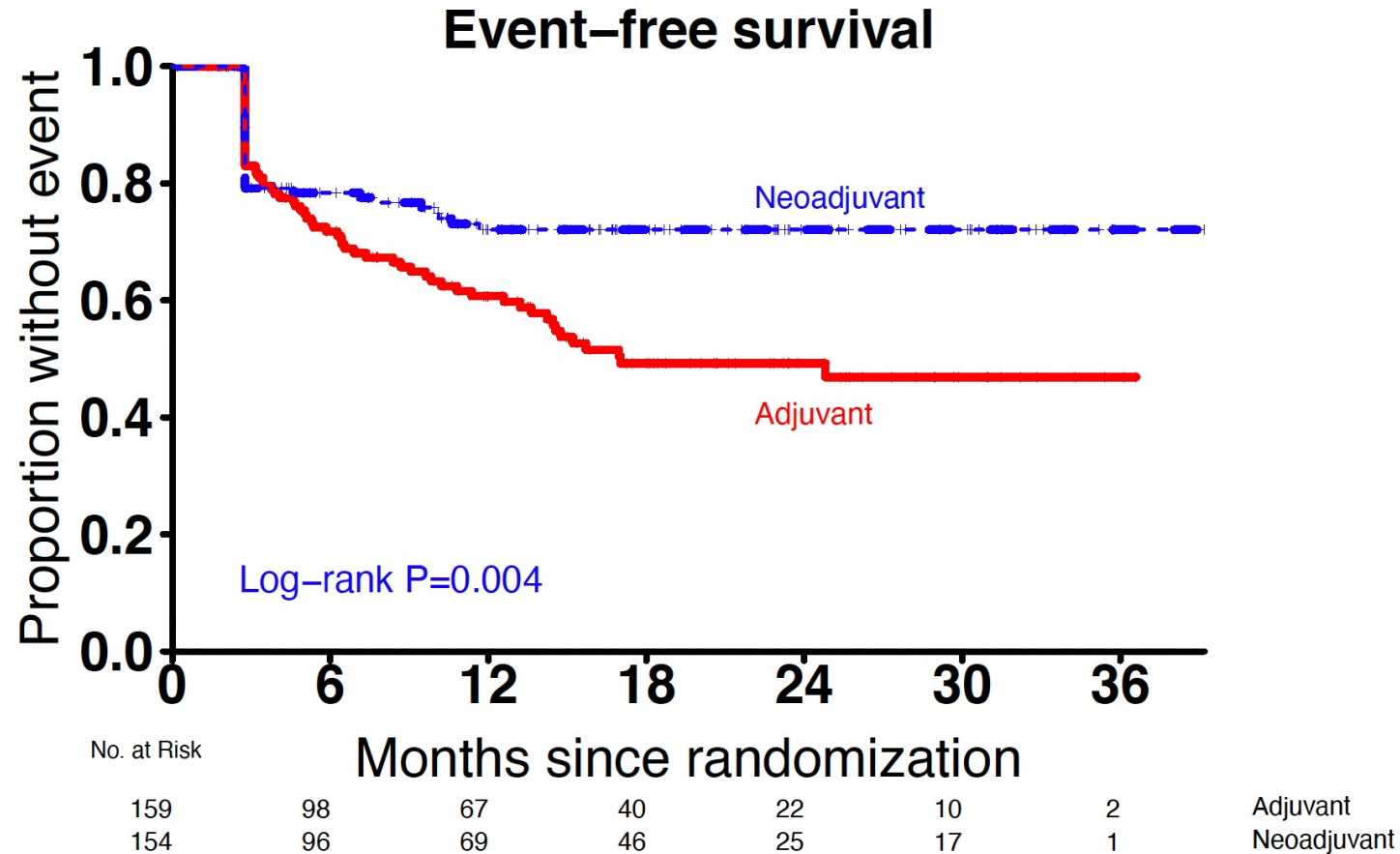
PD-1 blockade before surgery induces an immune response from a larger population of T cells that reside in the tumor and results in a systemic immune response at distant sites.



SWOG 1801

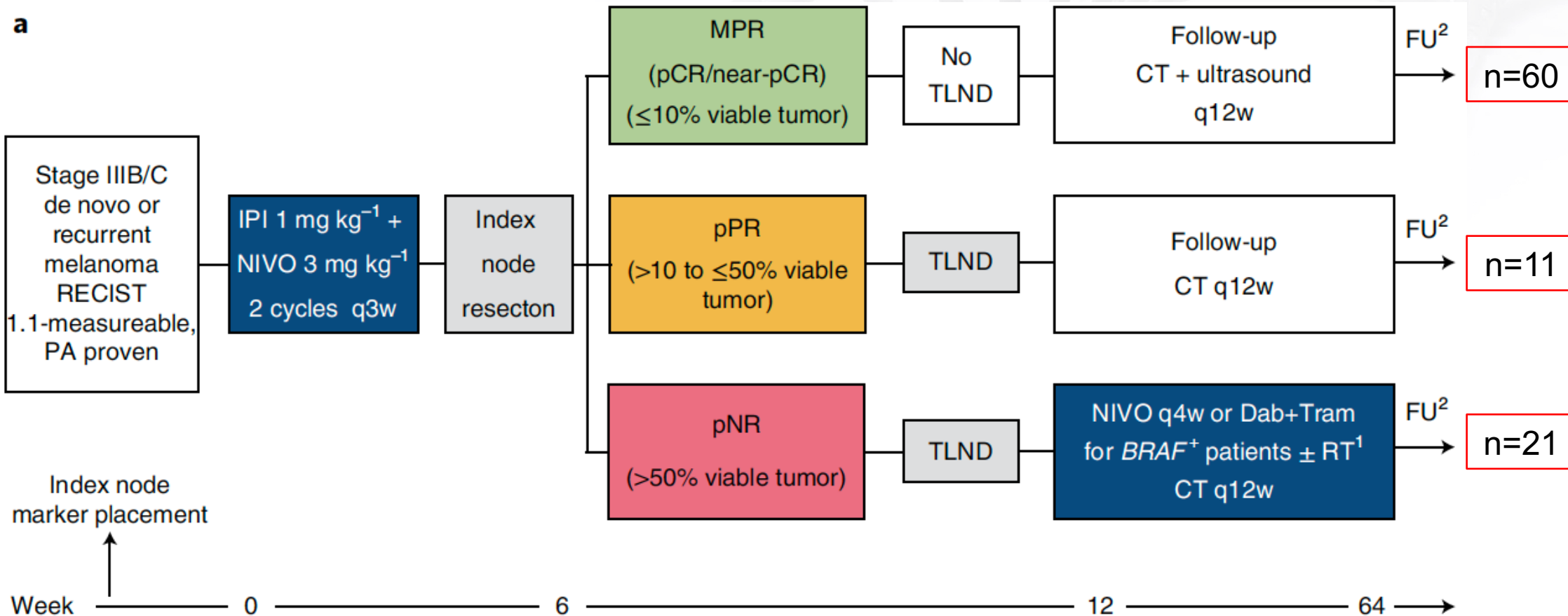


SWOG 1801 – IMPROVED EFS FOR PATIENTS RECEIVING NEOADJUVANT AND ADJUVANT THERAPY COMPARED TO ONLY ADJUVANT THERAPY

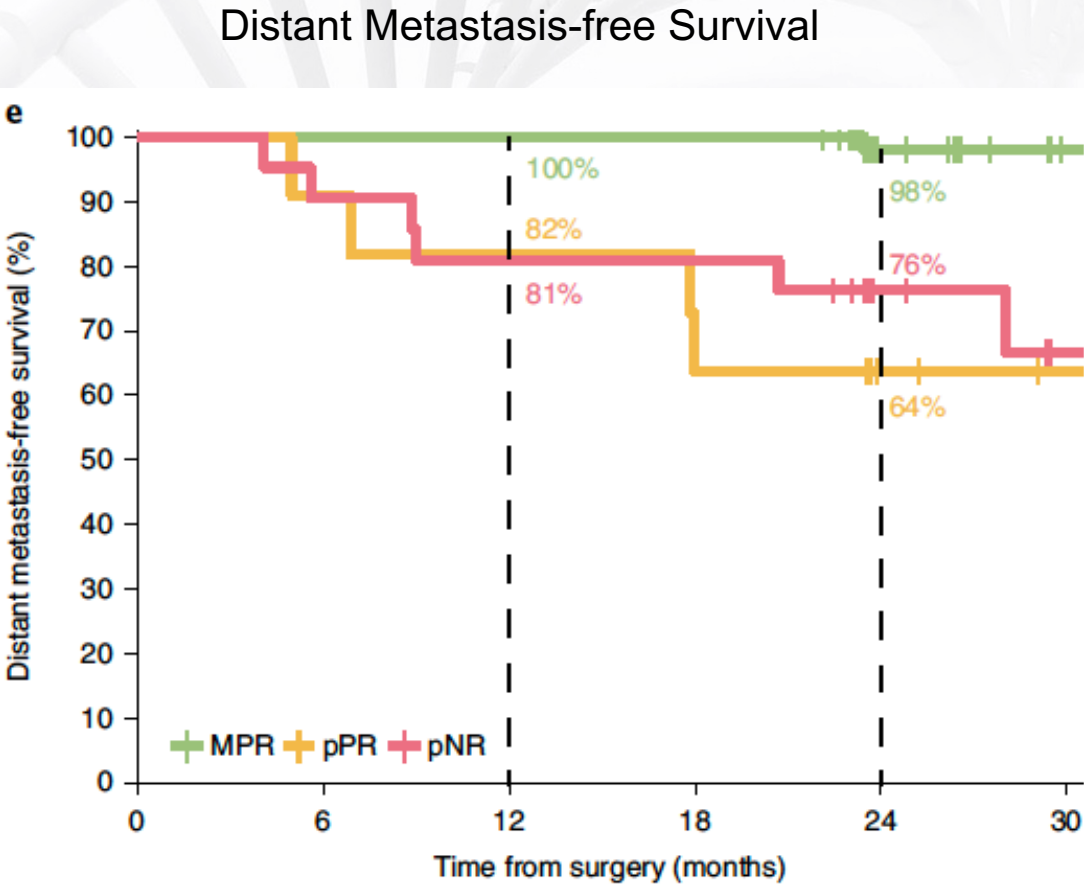
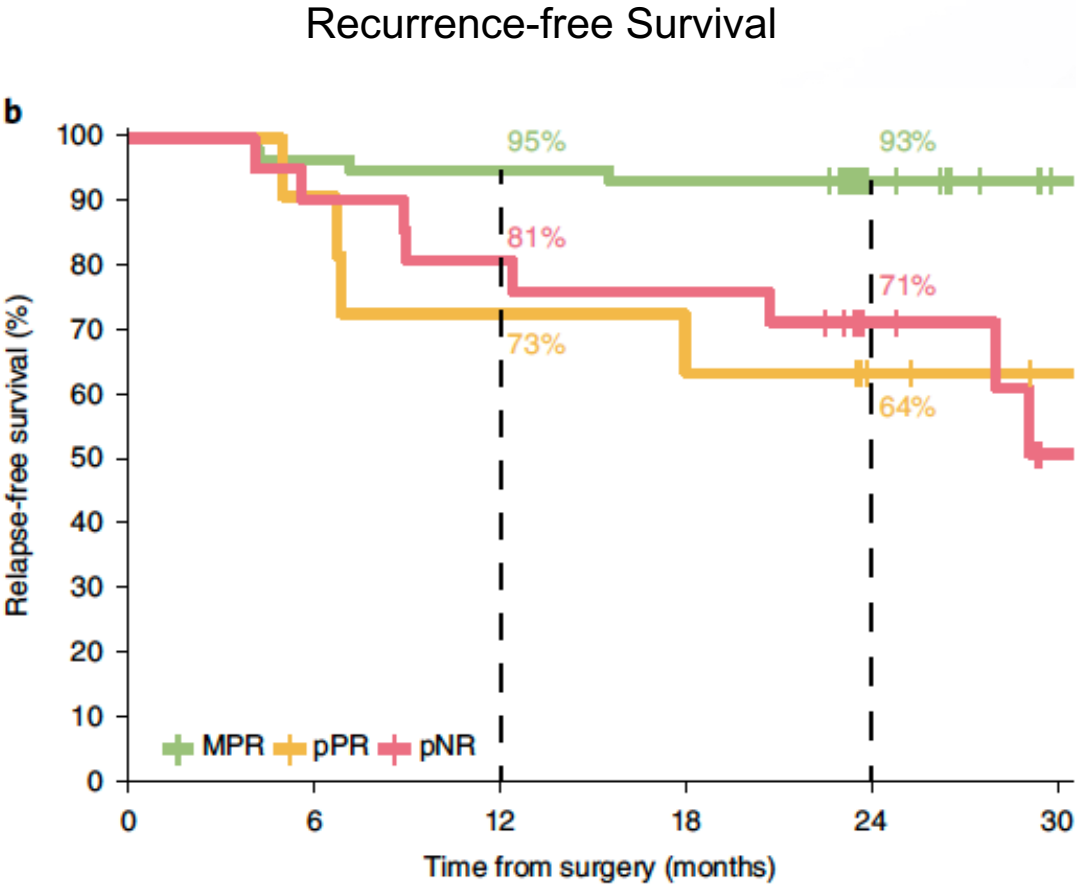


Patel, et al. *NEJM*. 2023;388:813-20.

SURGICAL AND ADJUVANT DE-ESCALATION – A PHASE II RESPONSE-DRIVEN STUDY OF SURGERY AND ADJUVANT THERAPY (PRADO)

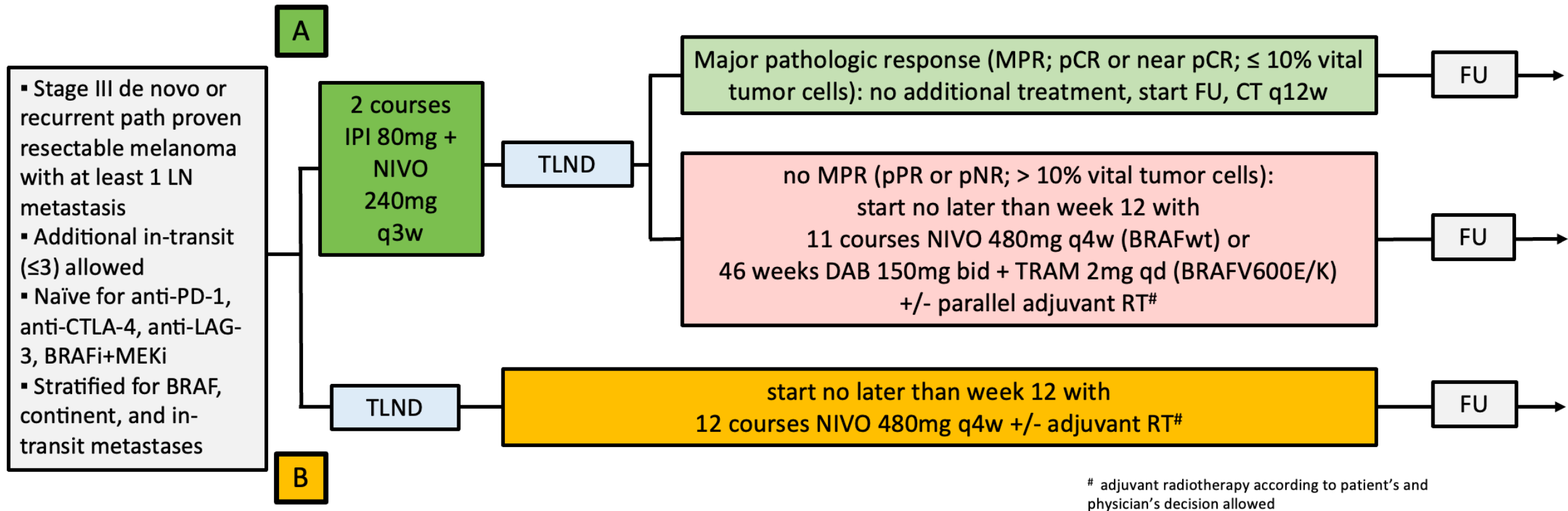


PRADO – PATIENTS WITH MAJOR PATHOLOGIC RESPONSE ARE AT LOW RISK OF DEVELOPING RECURRENCE OR DISTANT METASTASIS



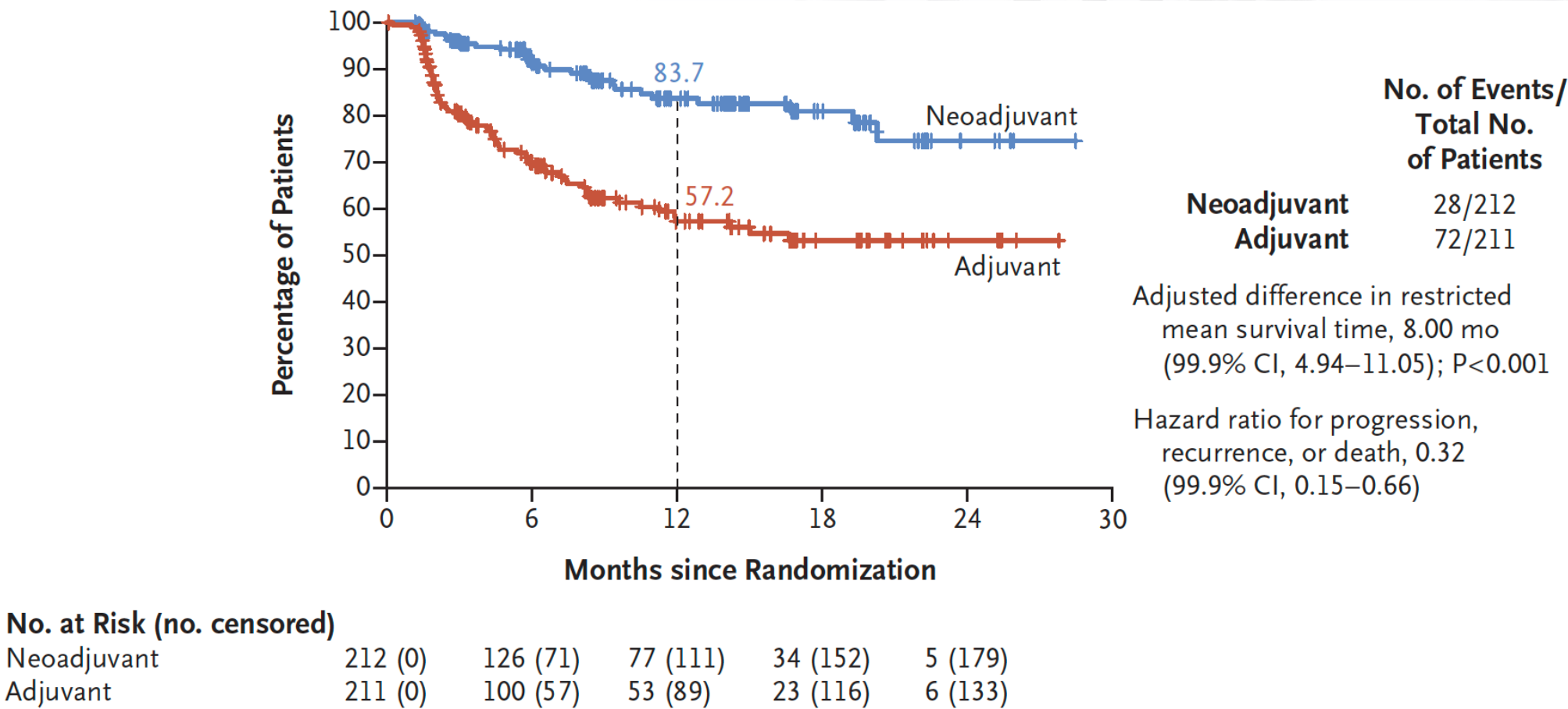
Reijers, et al. *Nature Medicine*. 2022;28:1178-88.

SURGICAL AND ADJUVANT DE-ESCALATION – A PHASE III STUDY OF NEOADJUVANT VERSUS ADJUVANT THERAPY (NADINA)



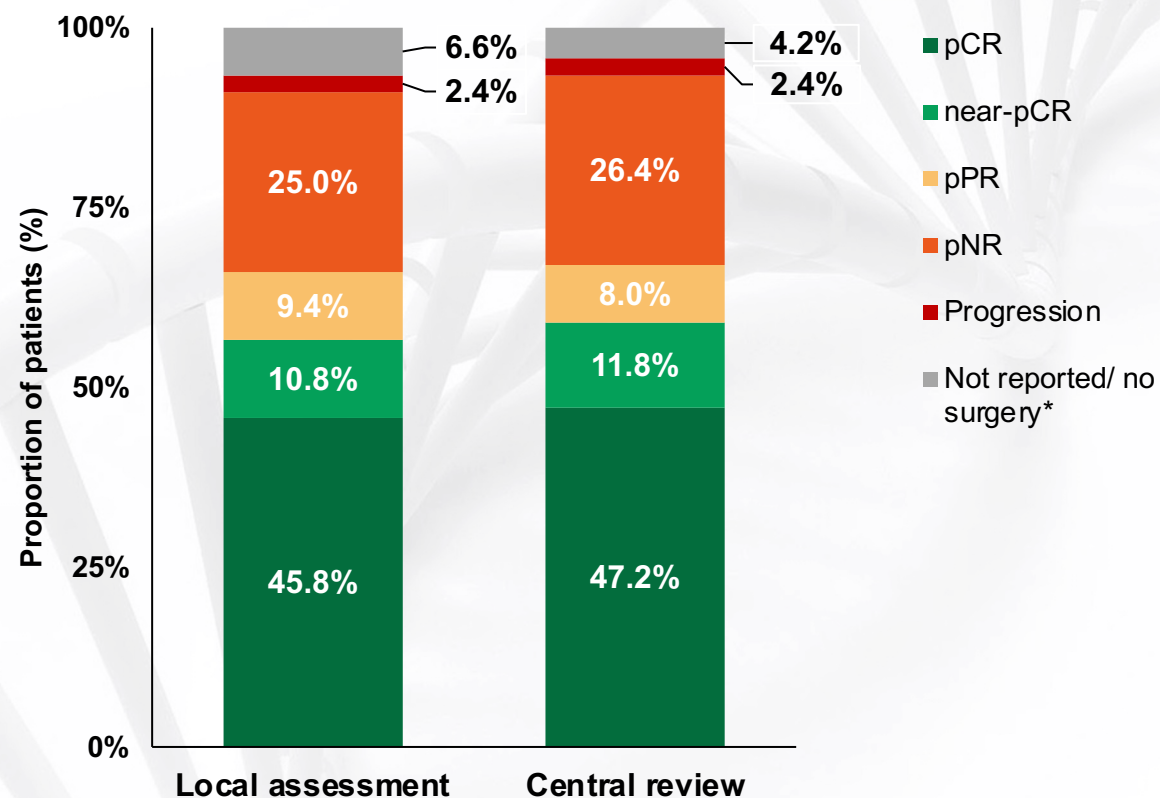
Primary endpoint: Event-free survival (time from randomization until an event, being defined as progression, recurrence, or death due to melanoma/treatment)

NADINA – PATIENTS RECEIVING NEOADJUVANT THERAPY HAD IMPROVED EFS COMPARED TO PATIENTS RECEIVING ONLY ADJUVANT THERAPY

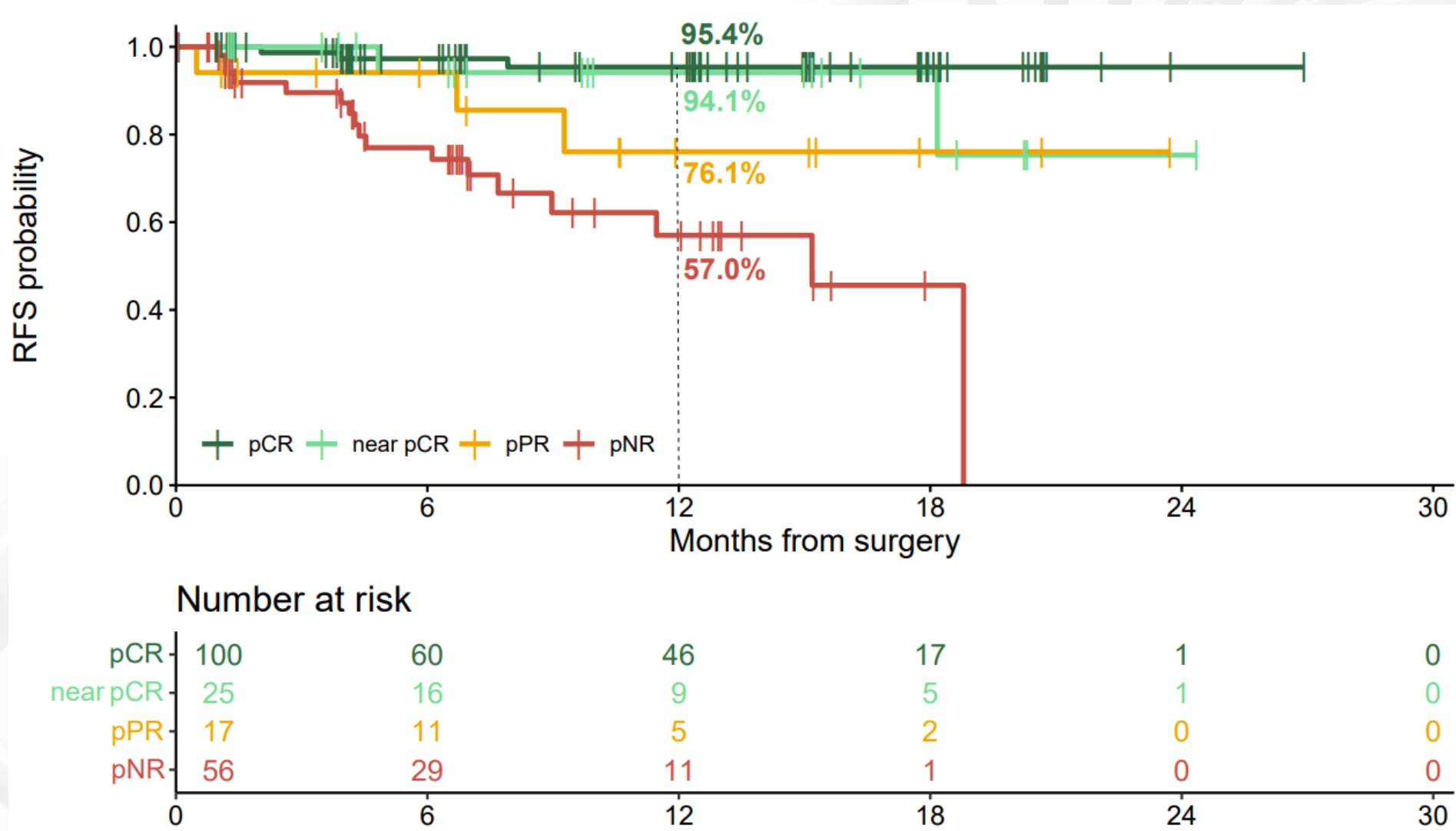


Blank, et al. *NEJM*. 2024;epub ahead of print.

NADINA – HIGH CONCORDANCE BETWEEN LOCAL AND CENTRAL PATHOLOGIC ASSESSMENTS



NADINA – LOW RATES OF RECURRENCE IN PATIENTS WITH COMPLETE OR NEAR COMPLETE PATHOLOGIC RESPONSE



NADINA – COMMENTARY BY ASCO EXPERT

“NADINA confirms and shows for the first time in a phase III study, that giving immunotherapy before surgery results in superior outcomes to giving immunotherapy only after surgery ... and that giving two immunotherapy drugs before surgery results in excellent responses. NADINA confirms that immunotherapy should be given to all patients with advanced melanoma before surgery when possible and establishes dual treatment with nivolumab and ipilimumab as the standard of care in the appropriate patient.”

- Michael Lowe, MD, MA, FASC, FSSO

CONCLUSIONS

- Event-free survival significantly improved for patients receiving neoadjuvant therapy compared to adjuvant therapy
 - SWOG – pembrolizumab
 - NADINA – flip dose nivolumab/ipilimumab
- Patients obtaining a complete or near complete pathologic response may be able to forego therapeutic lymphadenectomy and/or adjuvant systemic therapy
- Randomized clinical trials assessing these de-escalation strategies are absolutely necessary



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