NRG ONCOLOGY

Advancing Research. Improving Lives.™

HN014: Building on Translational Opportunities in CSCC

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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Disclosures

Scientific Advisory Board

- PDS Biotechnology

Research Funding

- Regeneron, Ascendis

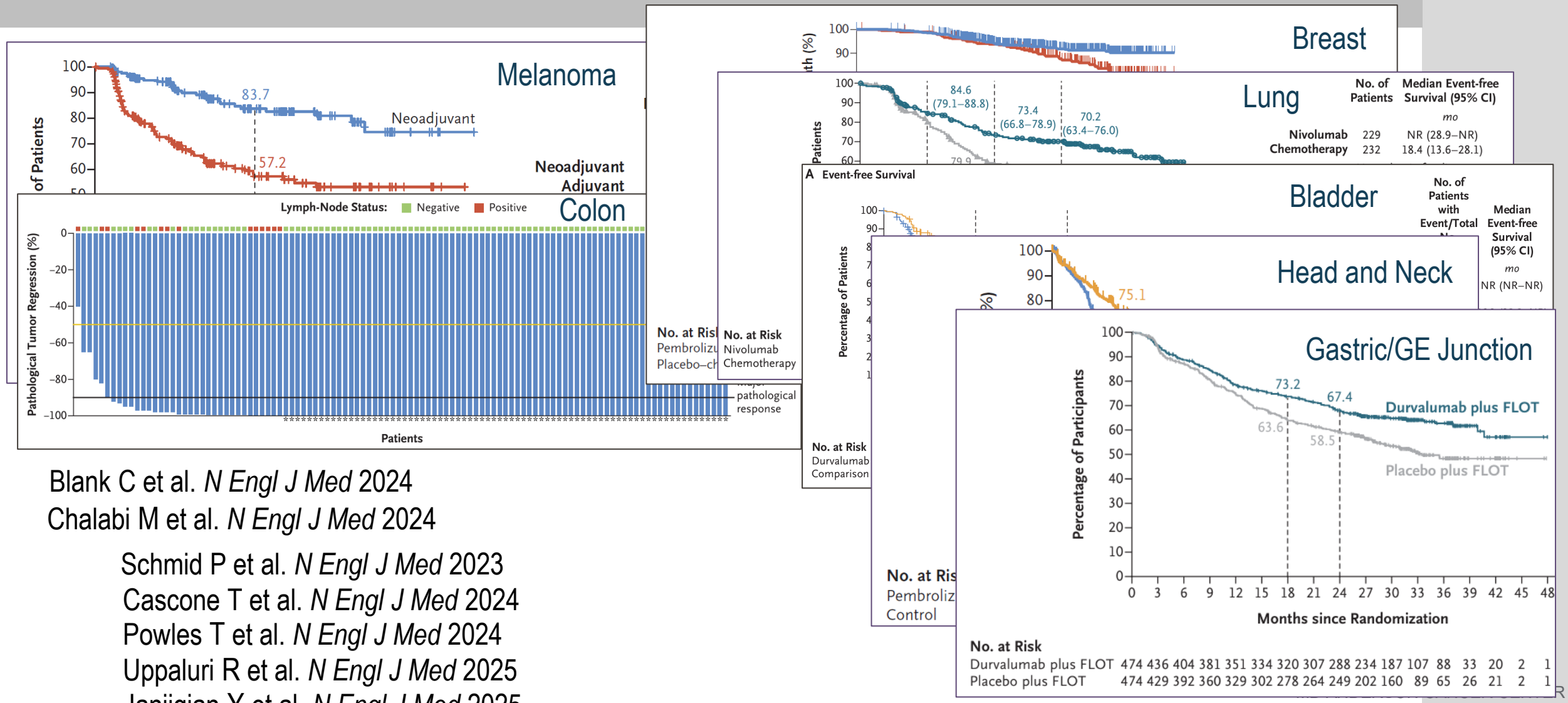
Consultant

- Regeneron, Merck, Sanofi-Genzyme, GeoVax

Speaker/Author

- OncLive, AiCME, Up-to-Date

Neoadjuvant/Perioperative Immunotherapy



Blank C et al. *N Engl J Med* 2024

Chalabi M et al. *N Engl J Med* 2024

Schmid P et al. *N Engl J Med* 2023

Cascone T et al. *N Engl J Med* 2024

Powles T et al. *N Engl J Med* 2024

Uppaluri R et al. *N Engl J Med* 2025

Janjigian Y et al. *N Engl J Med* 2025

Neoadjuvant Immunotherapy_CSCC

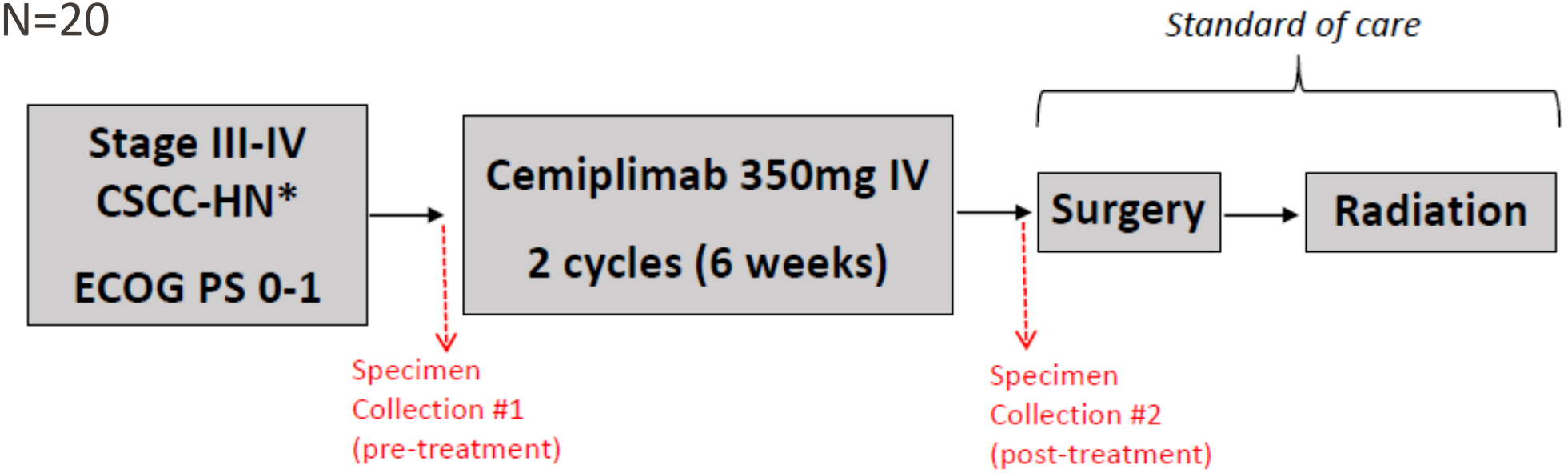
Pilot Study

Single institution

Open-label, non-randomized

Window-of-opportunity

N=20



ClincalTrials.gov: NCT03565783

Neoadjuvant Immunotherapy_CSCC

Pilot Study

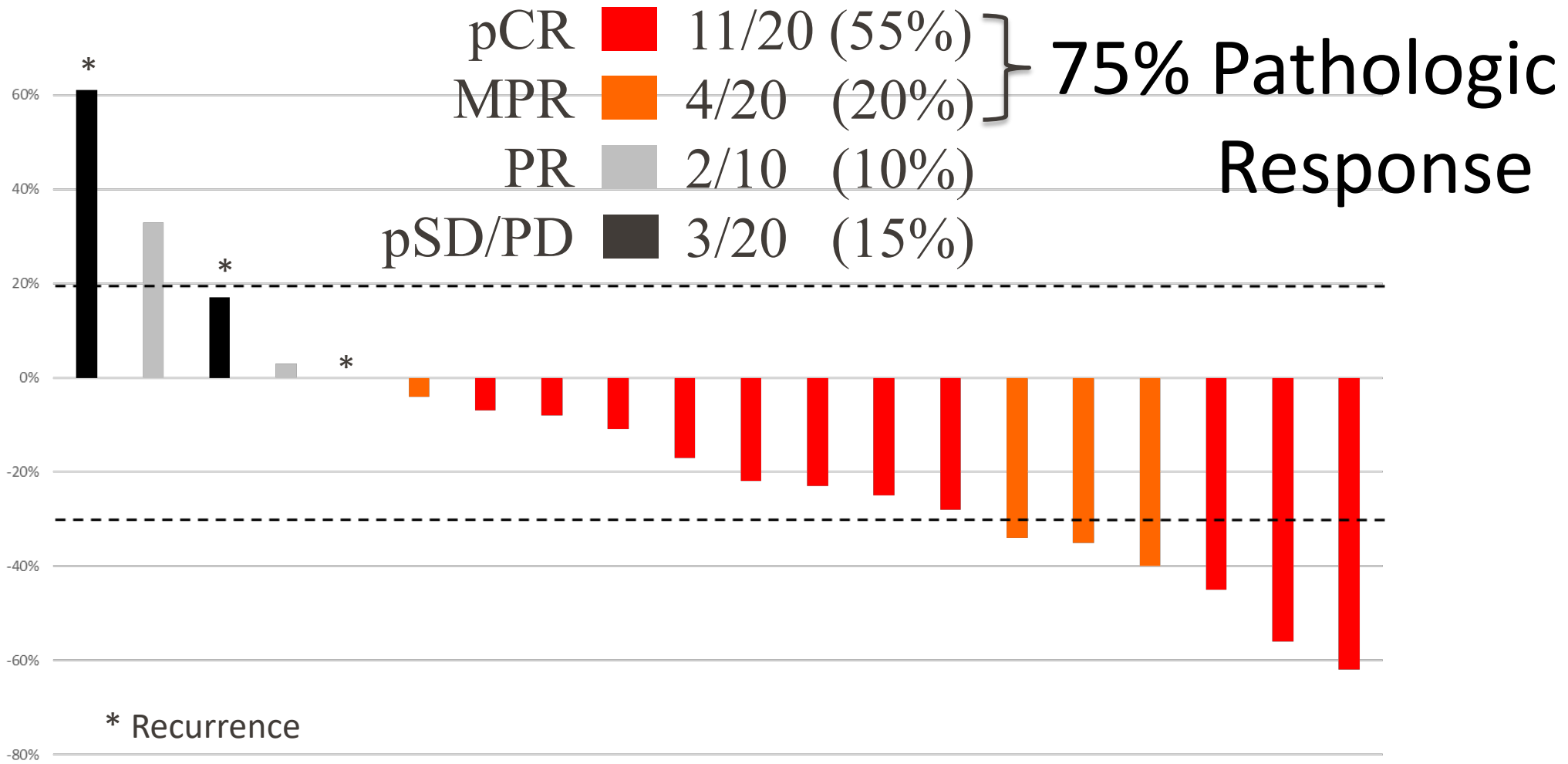
PRE

POST

ClincalTrials.gov: NCT03565783

Neoadjuvant Immunotherapy_CSCC

Pilot Study



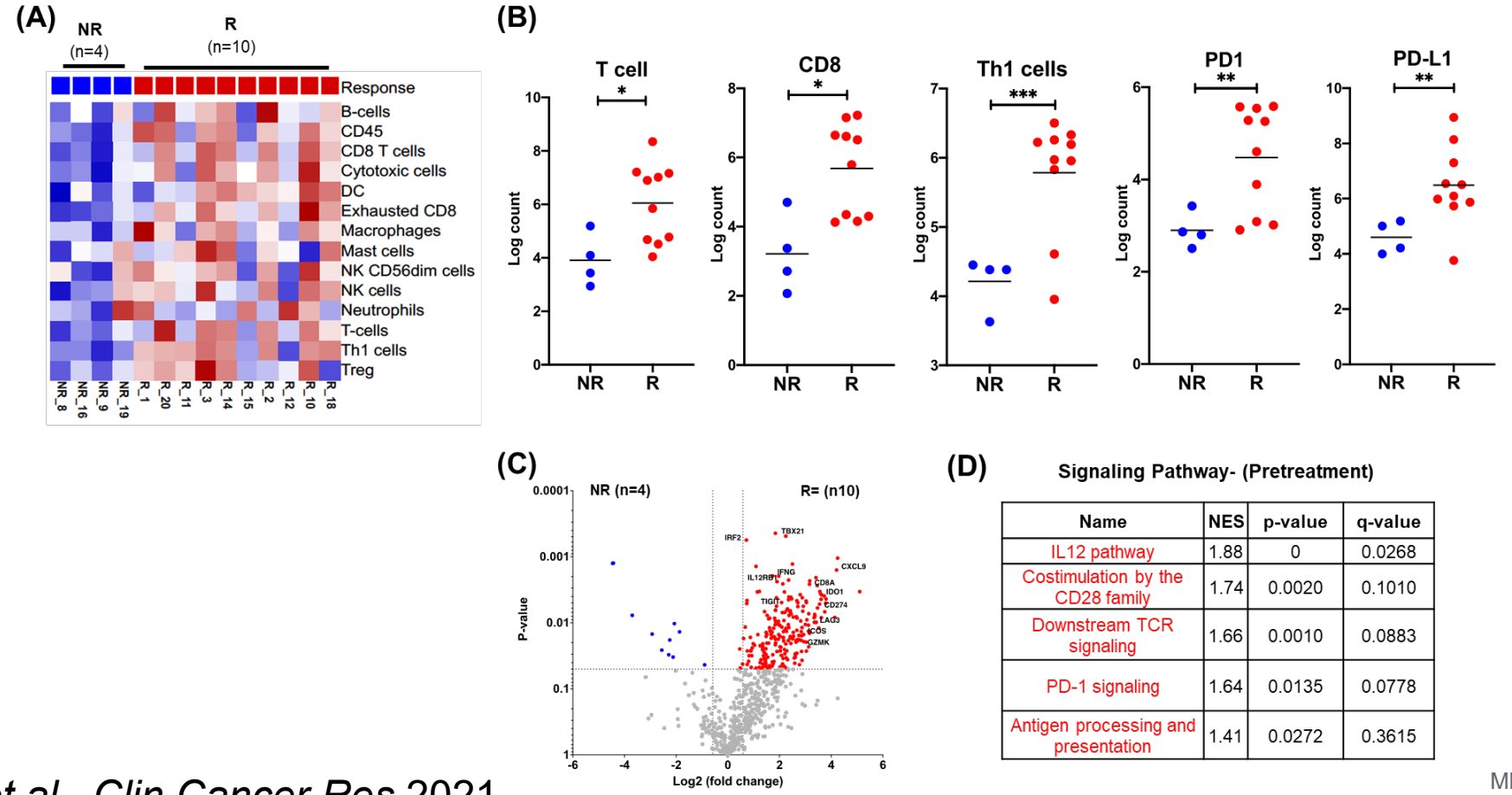
Gross N *et al*. EMSO 2019

Ferrarotto R *et al*. *Clin Cancer Res* 2021

Neoadjuvant Immunotherapy_CSCC

Pretreatment Gene Expression by NanoString

Favorable Immune Microenvironment Associated with Pathologic Responses



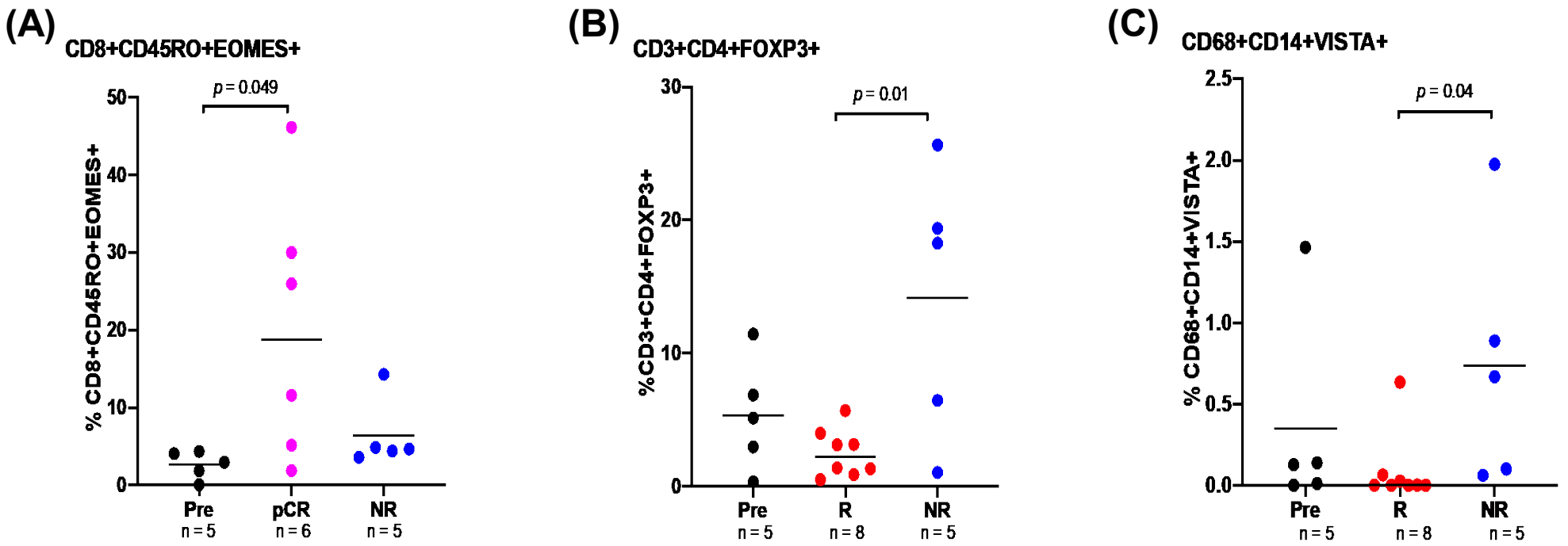
Name	NES	p-value	q-value
IL12 pathway	1.88	0	0.0268
Costimulation by the CD28 family	1.74	0.0020	0.1010
Downstream TCR signaling	1.66	0.0010	0.0883
PD-1 signaling	1.64	0.0135	0.0778
Antigen processing and presentation	1.41	0.0272	0.3615

Ferrarotto R *et al*. *Clin Cancer Res* 2021

Neoadjuvant Immunotherapy_CSCC

Pre and Post-Treatment CyTOF Analyses

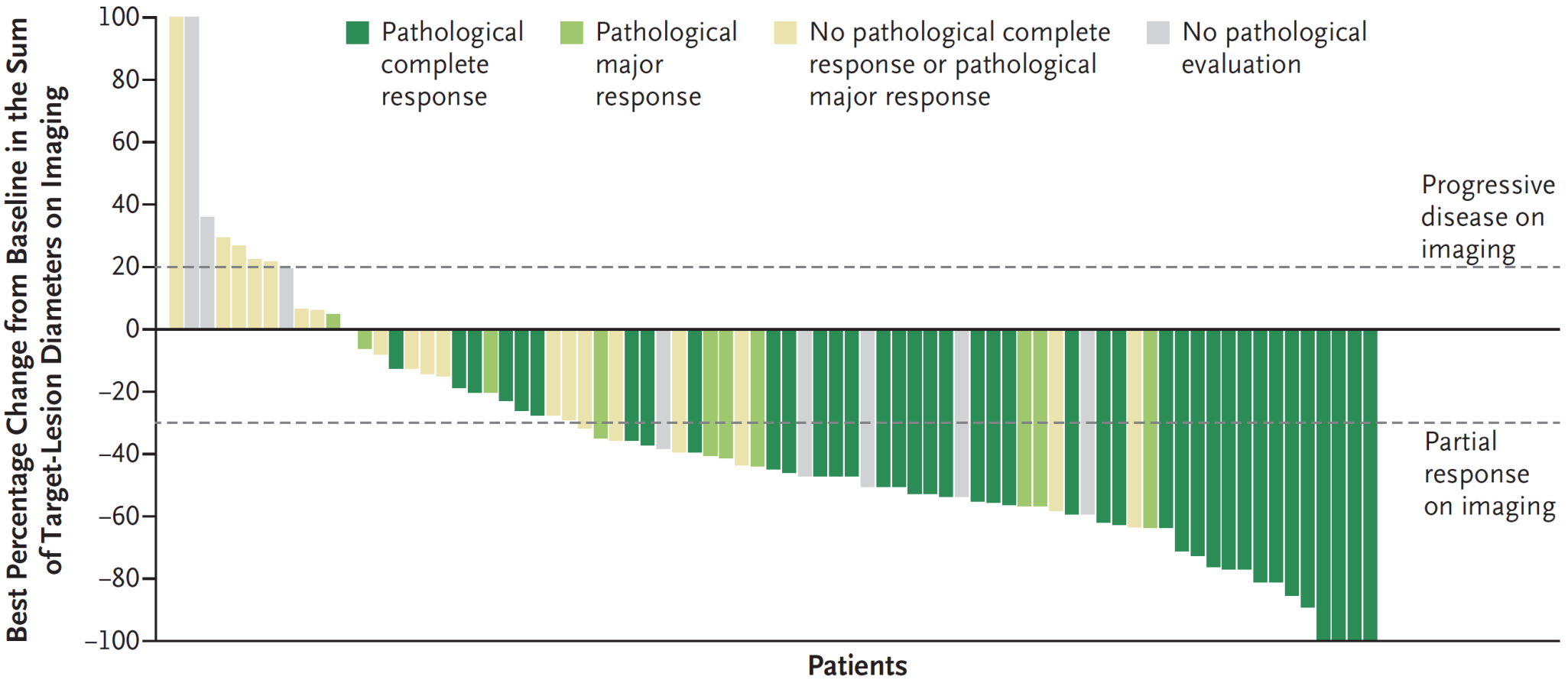
Memory CD8+ T-cell Subset Associated with Pathologic Responses



Ferrarotto R *et al*. *Clin Cancer Res* 2021

Phase 2 Neoadjuvant Immunotherapy_CSCC

Results

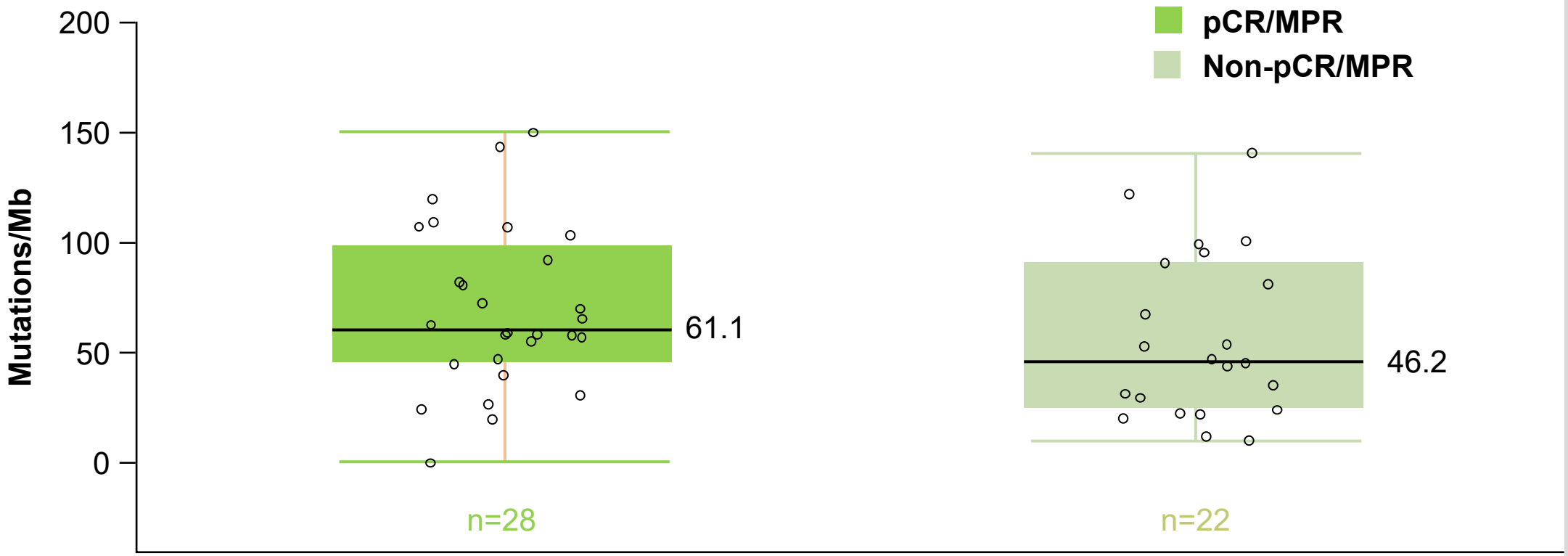


Gross N *et al*. *N Eng J Med* 2022

Phase 2 Neoadjuvant Immunotherapy_CSCC

Exploratory Analyses

Tumor mutational burden and pathologic response



Gross N *et al*. ESMO 2022

Phase 2 Neoadjuvant Immunotherapy_CSCC

Exploratory Analyses

PD-L1 status and pathologic response

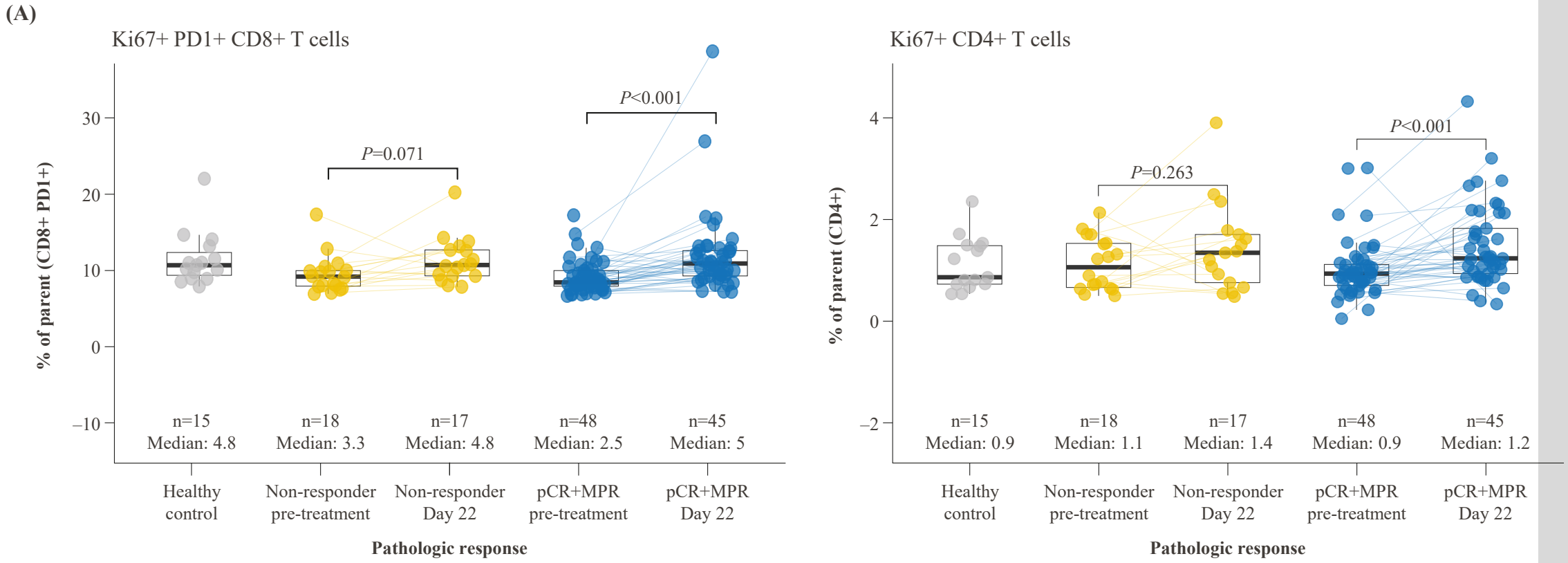
	Neoadjuvant Cemiplimab (N=79)	
	PD-L1 <1% (n=15)	PD-L1 ≥1% (n=41)
pCR (0% viable tumor		
Patients, no.	3	22
% (95% CI)	20 (4.3–48.1)	53.7 (37.4–69.3)
MPR (>0% and ≤10% viable tumor)		
Patients, no.	2	6
% (95% CI)	13.3 (1.7–40.5)	14.6 (5.6–29.2)
Non-pCR/MPR, no. (%)	8 (53.3)	10 (24.4)
Not evaluable, no. (%)*	2 (13.3)	3 (7.3)
Combined pathologic response (pCR + MPR)		
Patients, no.	5	28
% (95% CI)	33.3 (11.8–61.6)	68.3 (51.9–81.9)

Gross N *et al*. ESMO 2022

Phase 2 Neoadjuvant Immunotherapy_CSCC

Exploratory Analyses

Peripheral (A) CD8+ and (B) CD4+ T-cell activation/proliferation pre- and post-treatment by response status

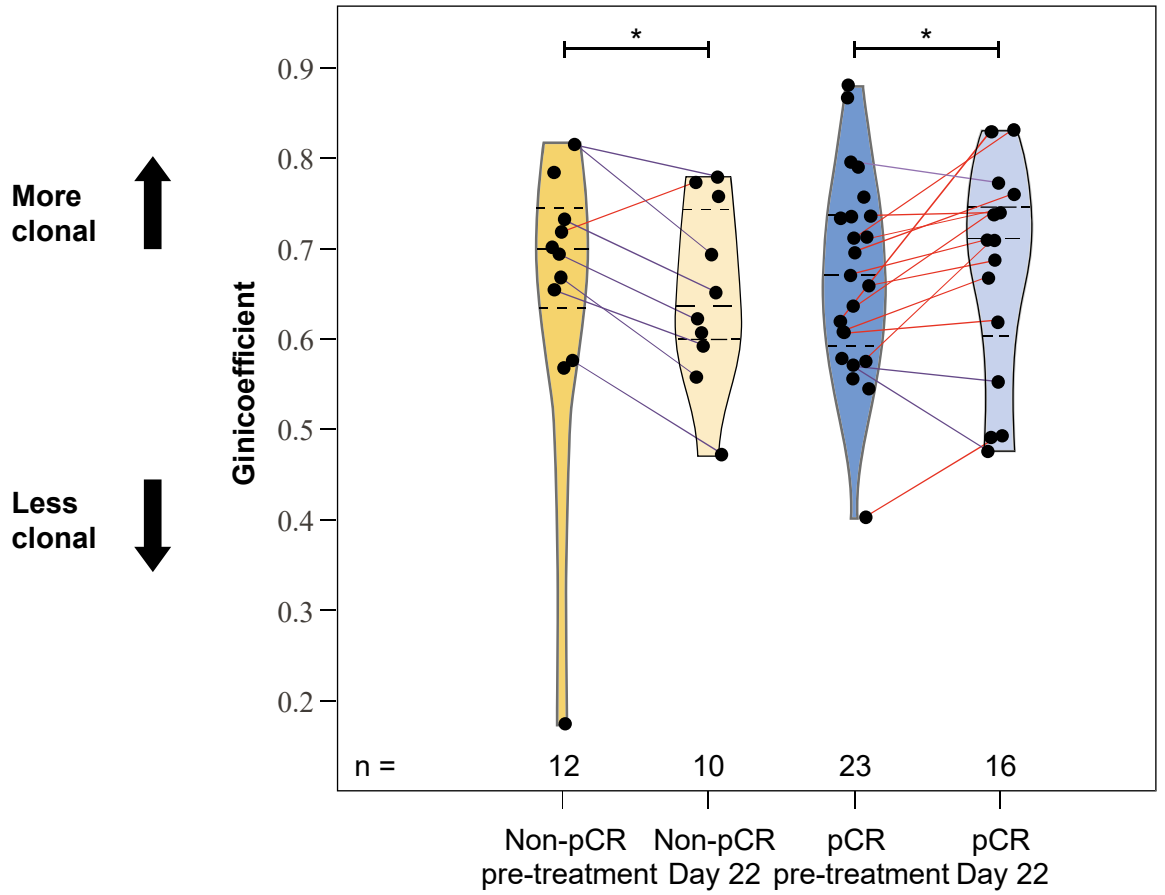


Rischin D *et al*. ESMO 2024

Phase 2 Neoadjuvant Immunotherapy_CSCC

Exploratory Analyses

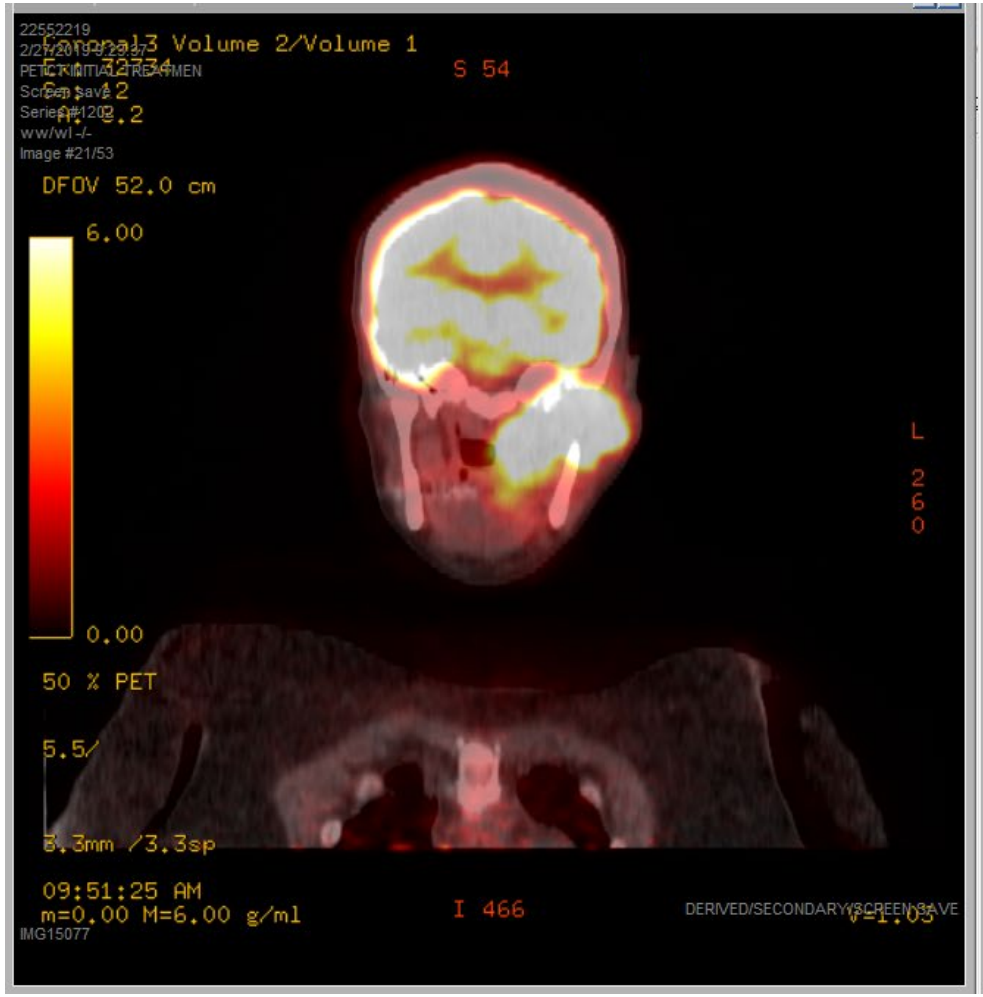
Clonality (Gini-coefficient) pre- and post-treatment by response status

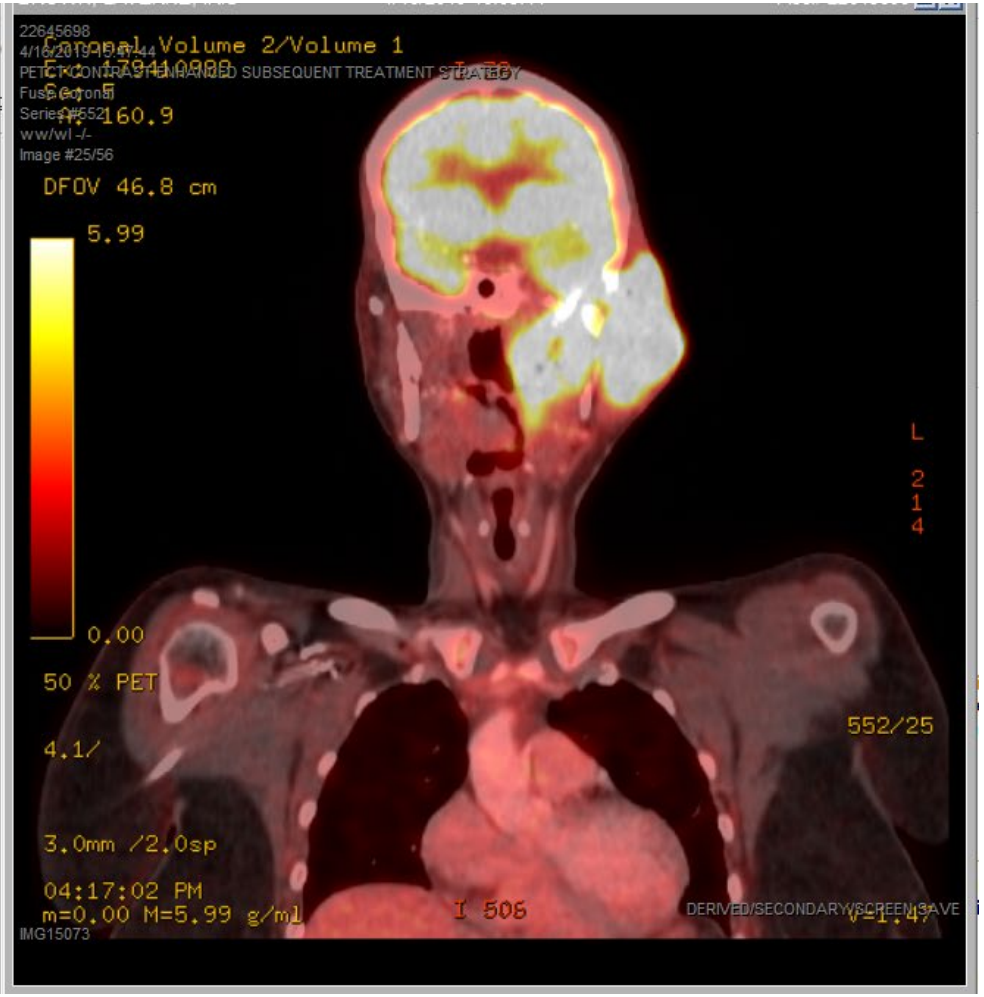


Rischin D *et al*. ESMO 2024

Neoadjuvant Immunotherapy_CSCC

Non-Responder

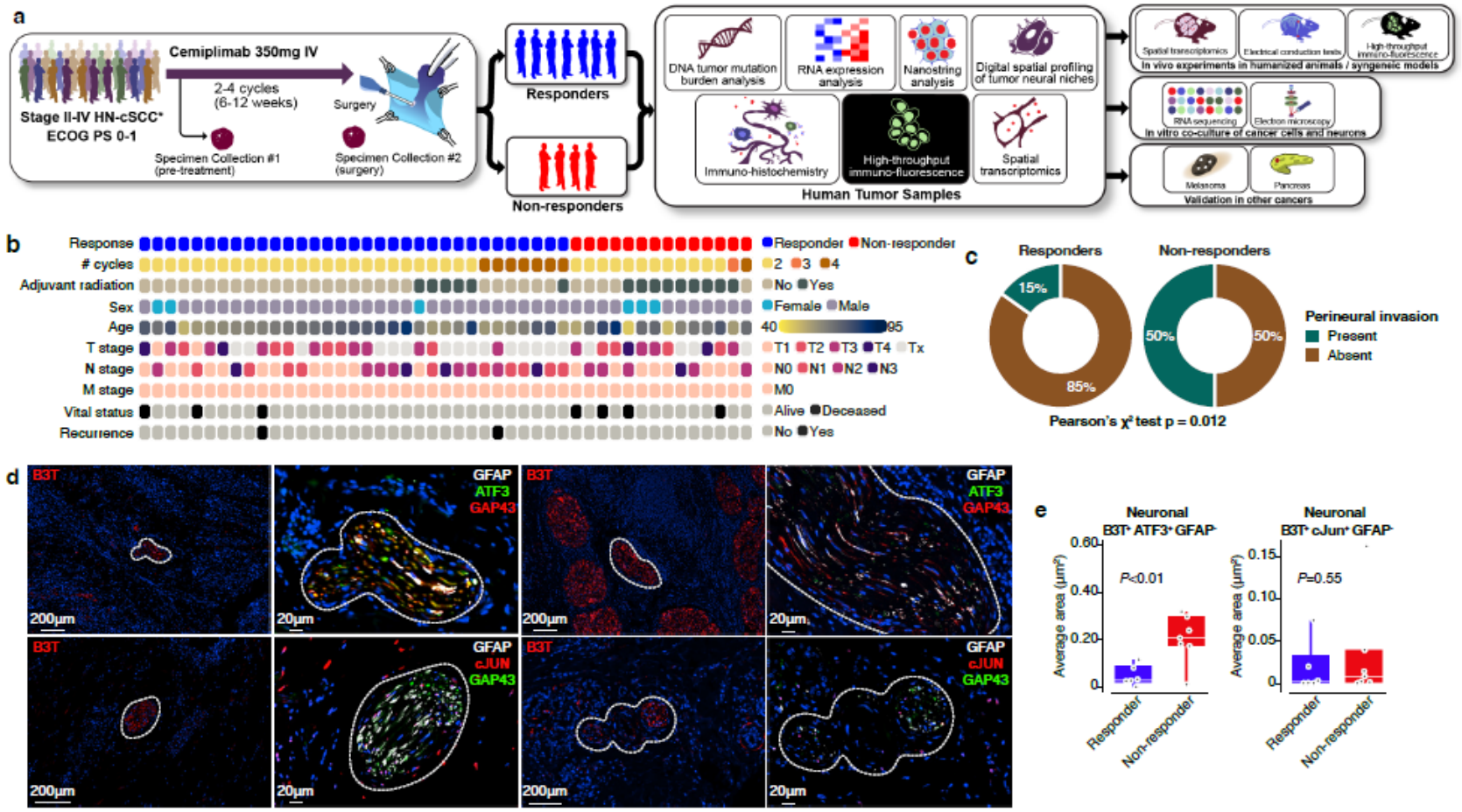




Translational Opportunity

Moran Amit, MD, PhD

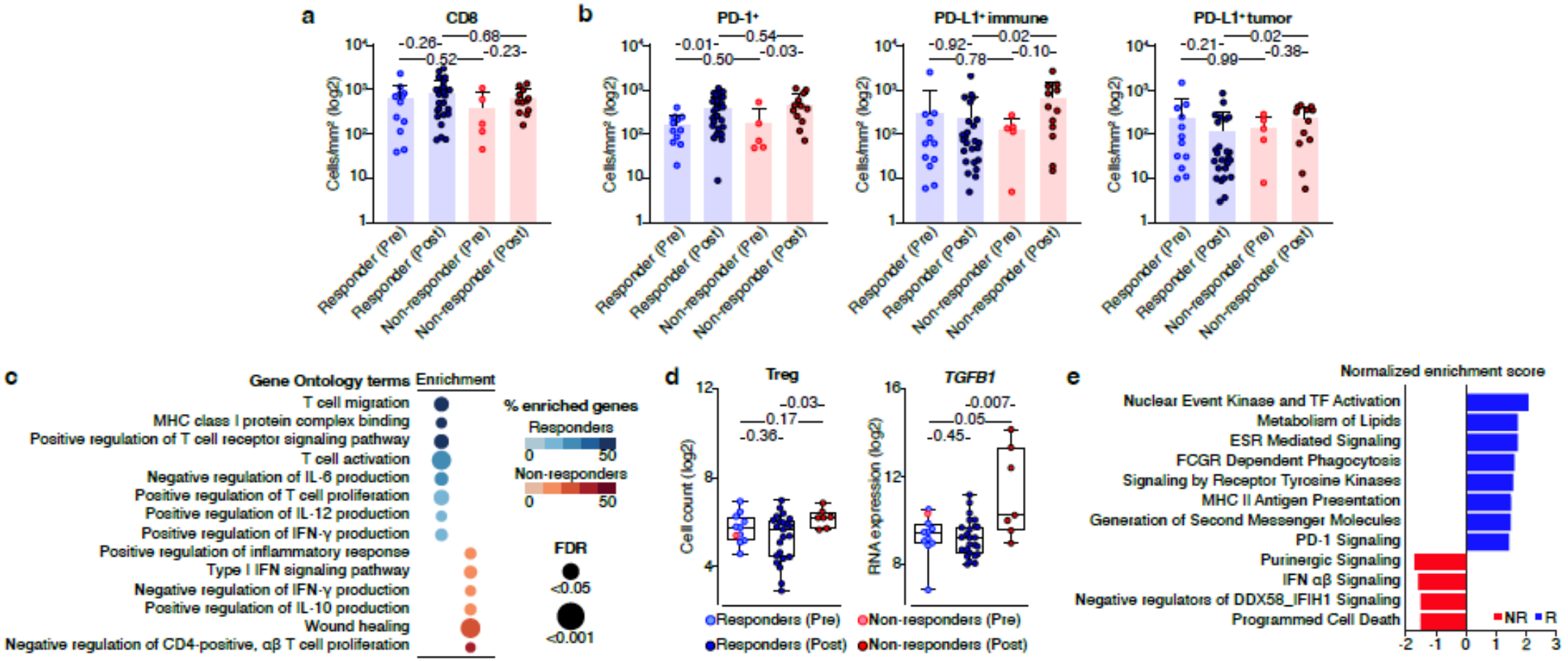
Cancer-induced nerve injury promotes resistance to anti-PD-1 therapy



Baruch E *et al*. *Nature* 2025 (in press)

Neoadjuvant Immunotherapy_CSCC

Biomarkers



Baruch E *et al*. *Nature* 2025 (in press)

NRG-HN014

Randomized Phase III Trial of Neoadjuvant Immunotherapy with Response-adapted Surgery versus Standard-of-Care (SOC) Surgery for Resectable Stage III/IV Cutaneous Squamous Cell Carcinoma (CSCC)

Neil D. Gross, MD, FACS

Trisha M. Wise-Draper, MD, PhD (co-chair)

Christopher A. Barker, MD (co-chair)

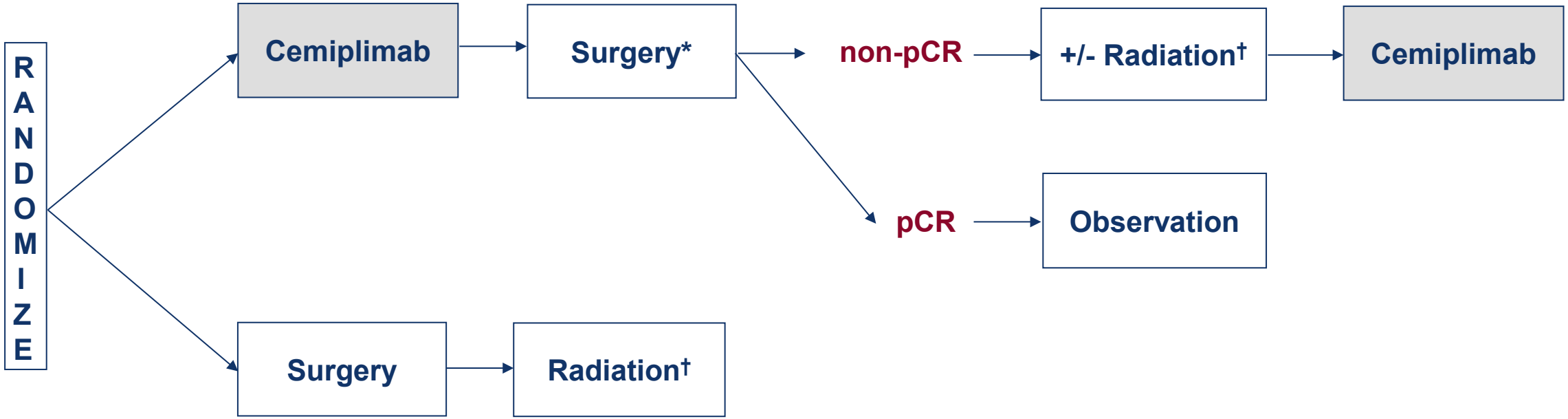
Bruce Ashford, MD (co-chair)

Danny Rischin, MD (co-chair)

NRG-HN014

Randomized Phase 3 Trial

N=420



Primary Endpoint:
Event-free Survival (EFS)

ClincalTrials.gov: NCT06568172

* Response-adapted oncologic surgery
† As indicated per protocol
pCR (pathologic complete response)

NRG-HN014 Biospecimen Collection

Biospecimen Type	Collection Time Point (Biospecimen Code)	Sites Ship Biospecimens to
Biospecimen Submission Required After Patient Registration and Bank ID Assignment		
H&E slide and FFPE block[1] from primary tumor tissue (can be from Lymph Node) Note: FNA or cytospin is not an acceptable specimen type	Pre-treatment biopsy (H&E: FP01; Block FP02) • Both Arms 1 and 2	Ambient to NRG Oncology Biospecimen Bank San Francisco, CA 94115*
H&E slide and FFPE Block[1] from Surgery: Surgical tumor tissue or biopsy of tumor tissue from resection or neck dissection specimen	During Treatment biopsy on day of surgery (H&E: FP03; Block FP04) • Both Arms 1 and 2	
Plasma (Blood collected in one 10 mL purple top EDTA tube, and processed for plasma and frozen at -80°C)	Pre-treatment: • Arm 1: prior to or on day of surgery (PB01) • Arm 2: prior to first neoadjuvant cycle (PB02)	Frozen on dry ice by priority overnight Monday to Wednesday to NRG Oncology Biospecimen Bank San Francisco, CA 94115*
	During treatment: • Arm 2: prior to second neoadjuvant cycle (PB03) and prior to or on day of surgery (PB04)	
Whole blood (Collect blood in one 5 mL purple top EDTA for DNA, mixed and aliquotted)	Pre-treatment: • Arm 1: prior to or on day of surgery (WB01) • Arm 2: prior to first neoadjuvant cycle (WB02)	
	During treatment: • Arm 2: prior to second neoadjuvant cycle (WB03)	

CSCC is ideal for translational research

Pathology remains the best biomarker of response to neoadjuvant immunotherapy

HN014 will bank specimens for future correlative studies

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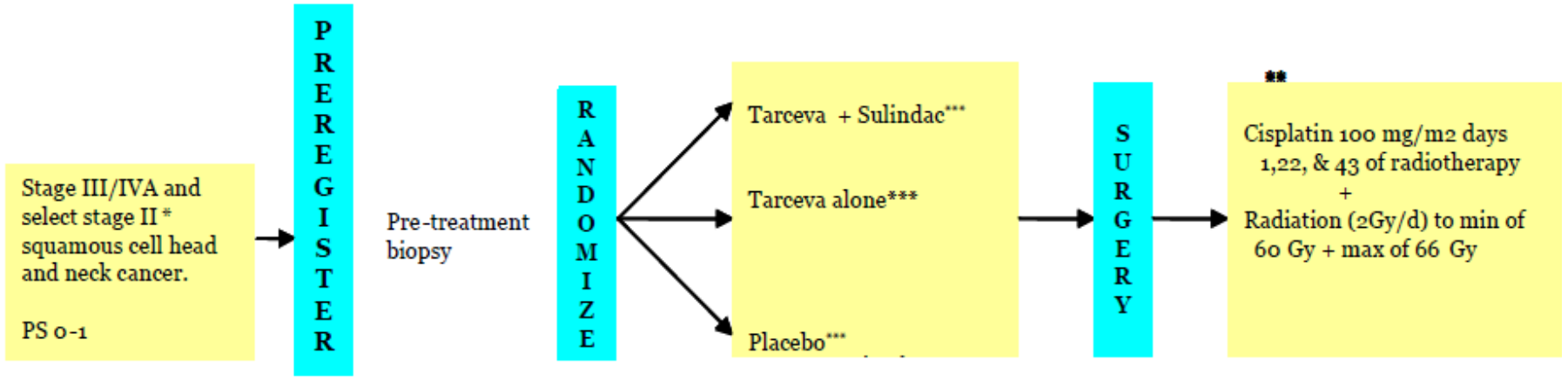
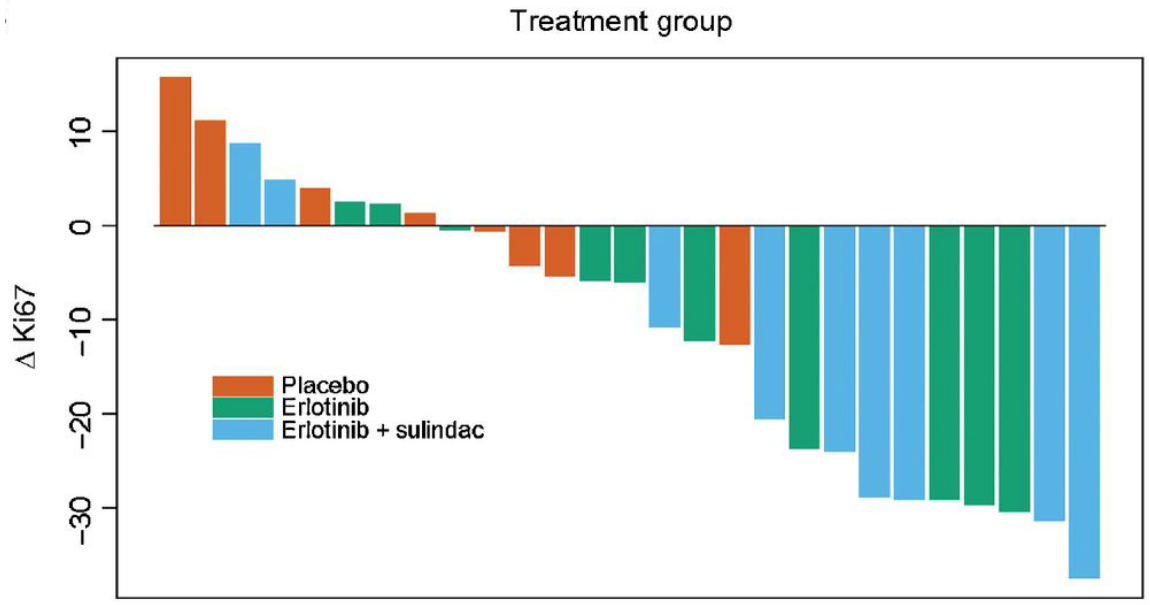
Head and Neck Squamous Cell Carcinoma (HNSCC)

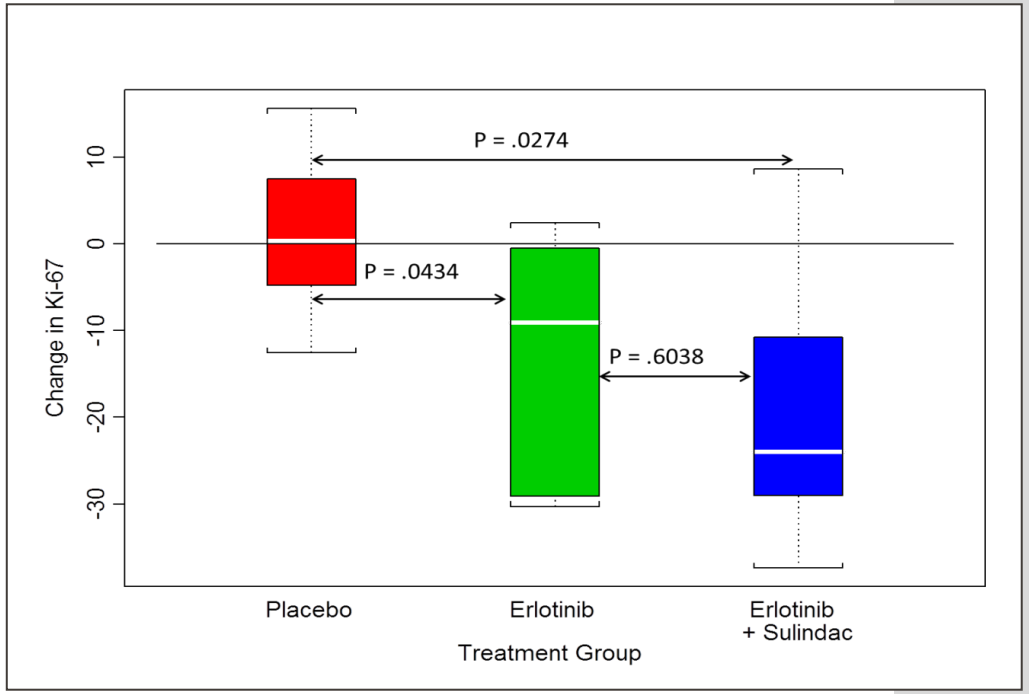
Multi institution
Phase 0 Study
N=49



Jennifer Grandis

Head and Neck Squamous Cell Carcinoma (HNSCC)





Gross ND *et al*. *Clin Cancer Res* 2014