


Neoadjuvant Immunotherapy for Early-Stage HR+, HER2- Breast Cancer

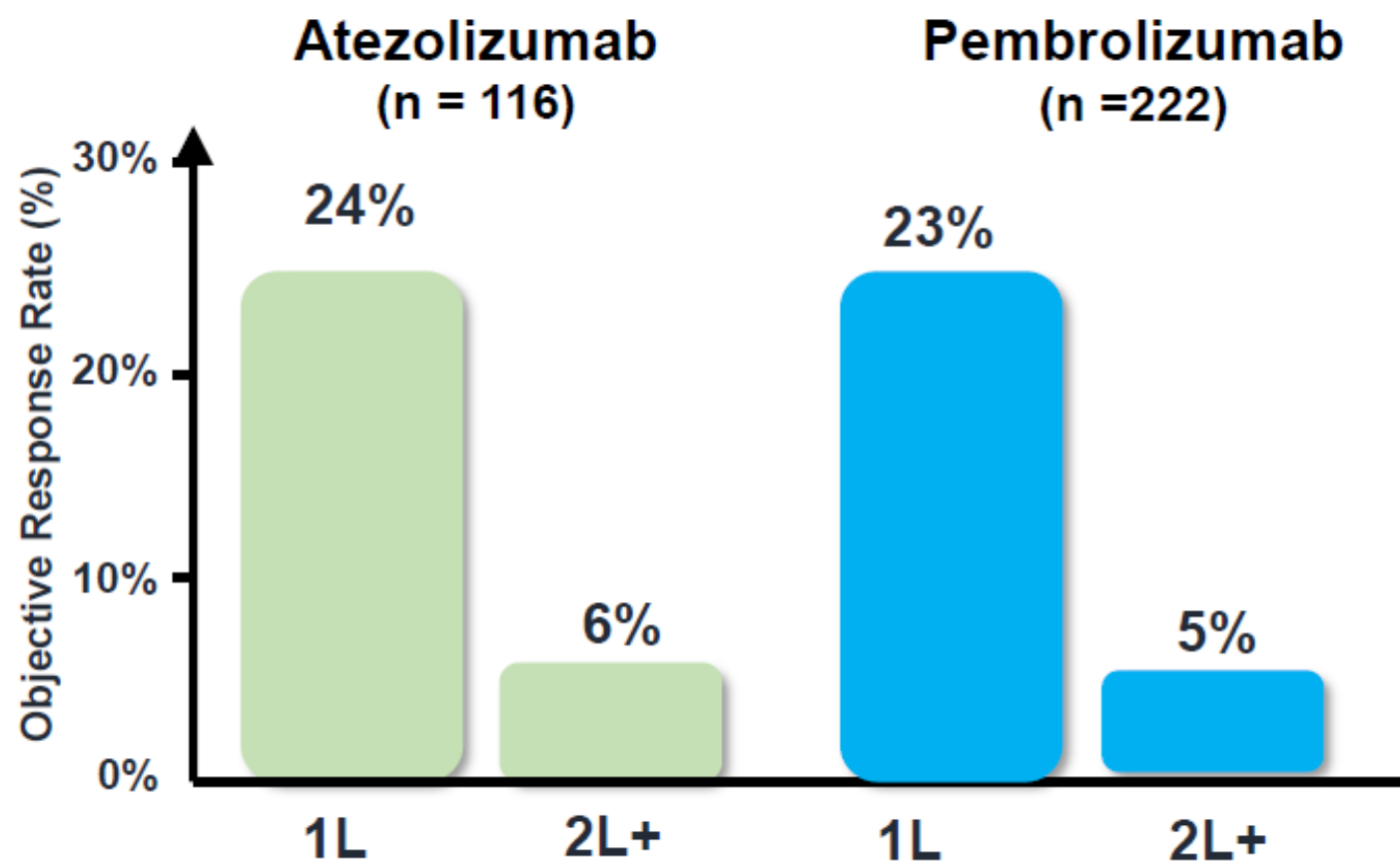
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Disclosures

I have the following relevant financial relationships to disclose:

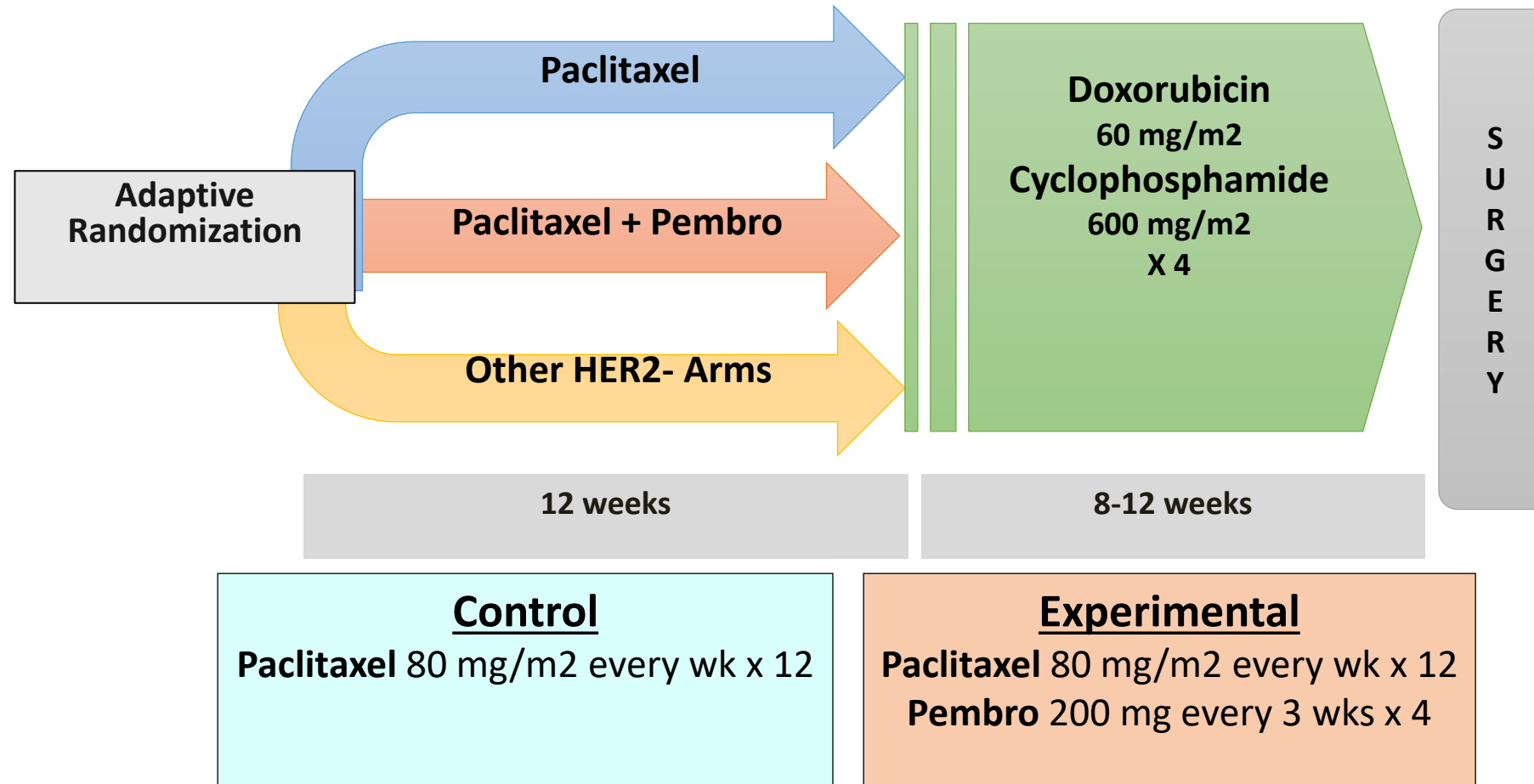
Consultant for: Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Genentech/Roche, Immunomedics, Merck, OBI Pharma, Pfizer, Puma, Spectrum Pharmaceuticals, Syndax Pharmaceuticals, Peregrine, Calithera, Daiichi-Sankyo, Seattle Genetics, AstraZeneca and TapImmune.

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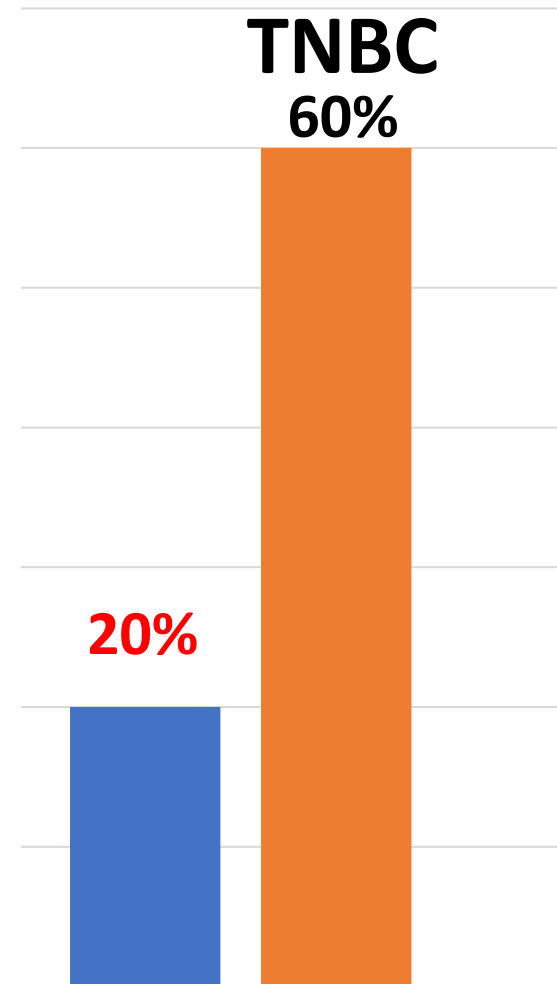


Metastatic Population	Agent	Evaluable (N)	ORR
TNBC	Avelumab	58	5%
HER2+	Avelumab	26	0%
HR+ HER2-	Pembrolizumab	25	12%
	Avelumab	72	3%

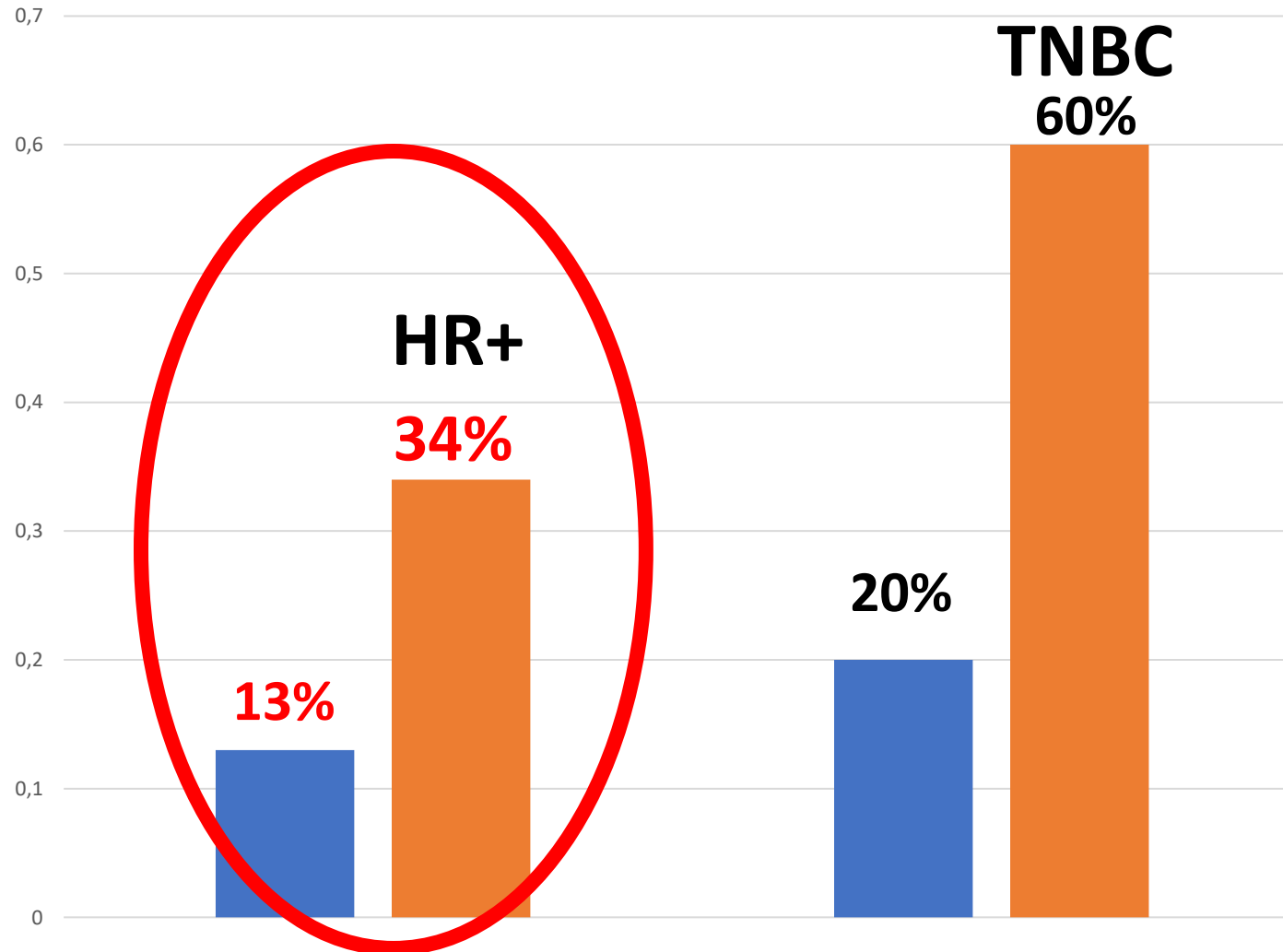
I-SPY2: Estimated pCR Rates in TNBC



Estimated Pathologic Complete Response Rates



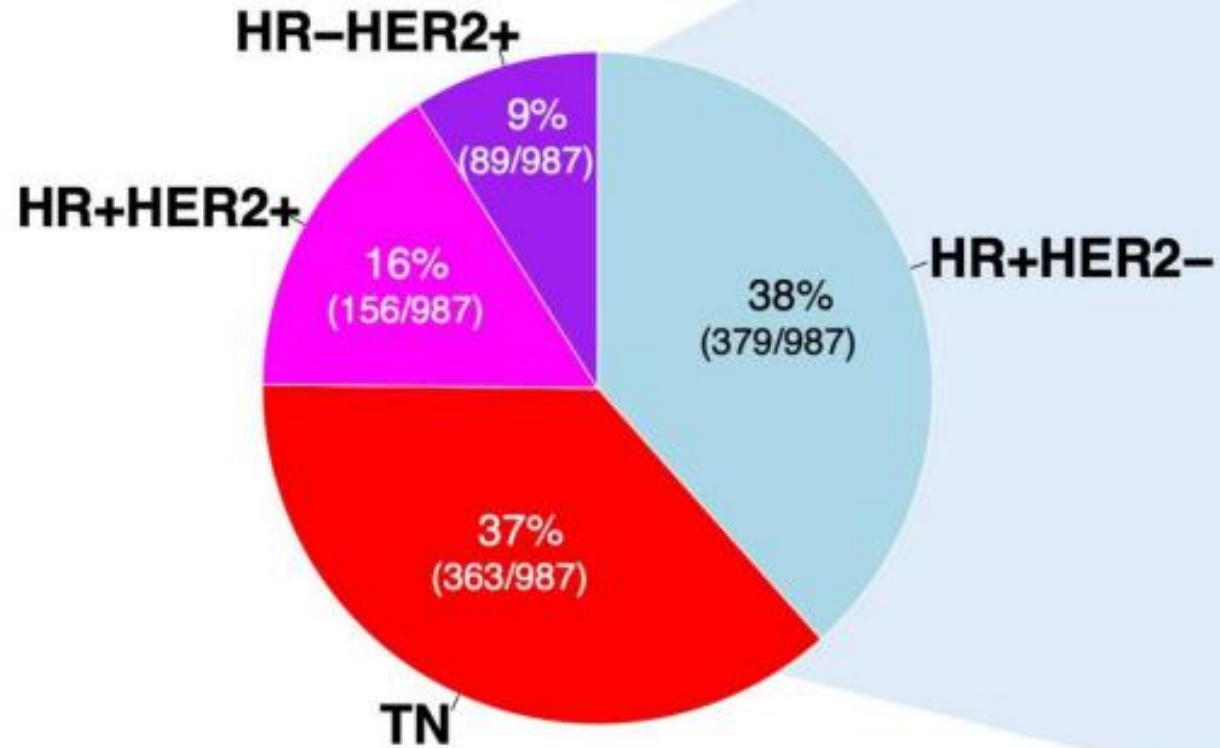
Estimated Pathologic Complete Response Rates



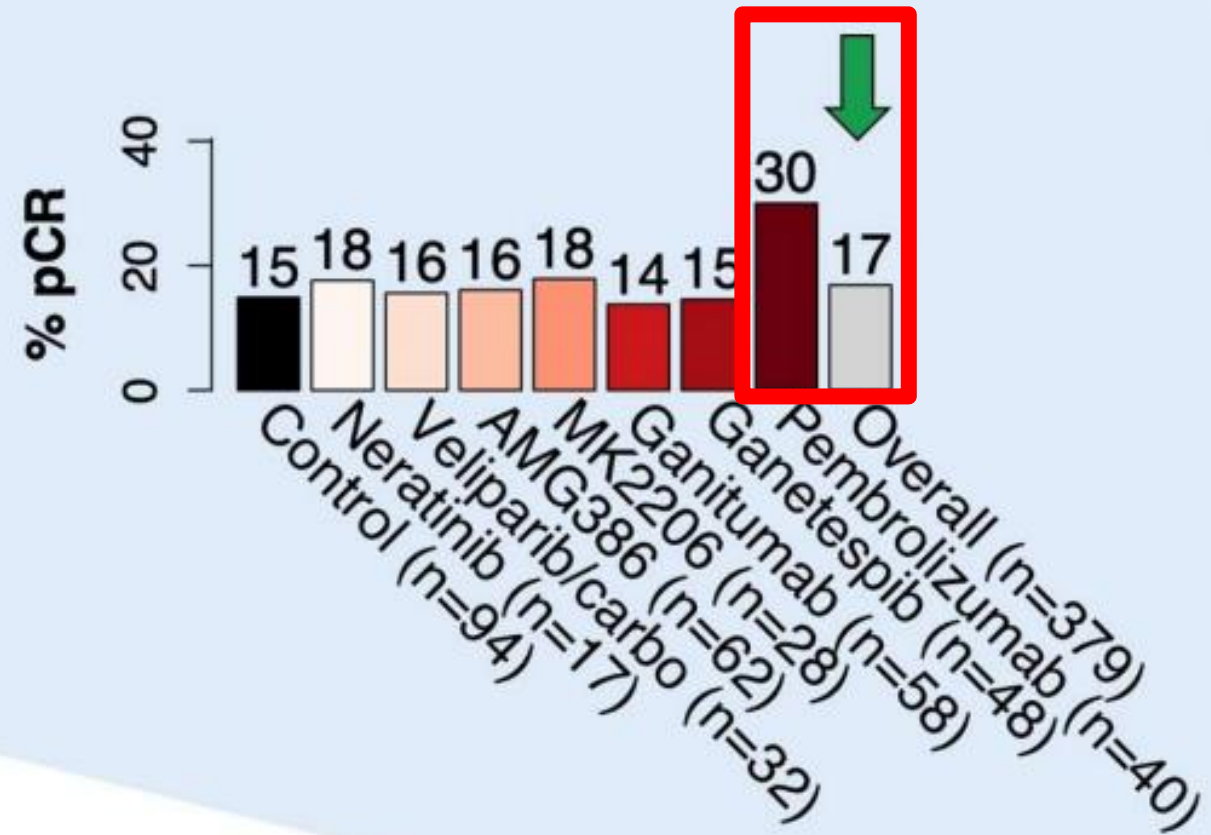
**Pembro graduates in all signatures
Including ER+**

Observed pCR rate by treatment arm in the HR+/HER2- cohort

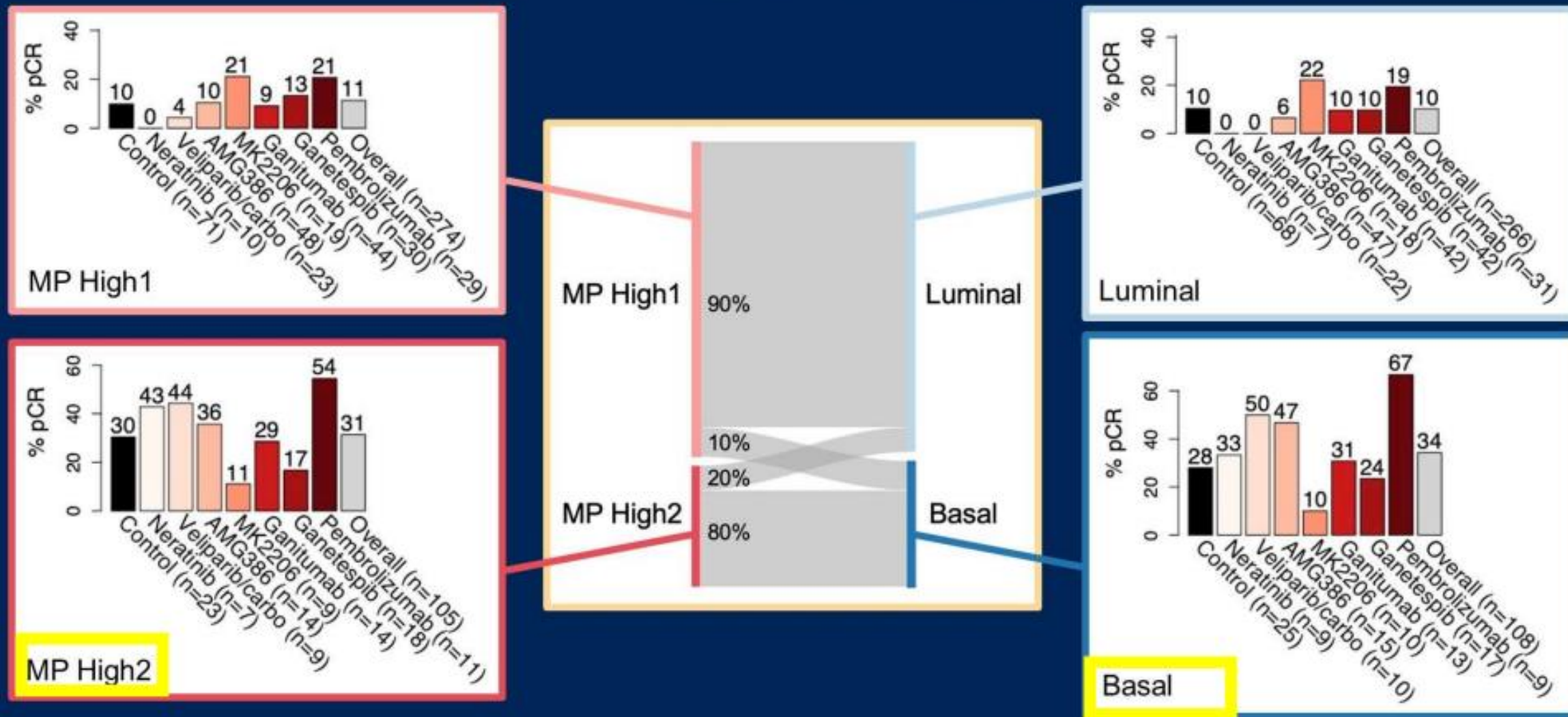
I-SPY2 participants by subtype (n=987)



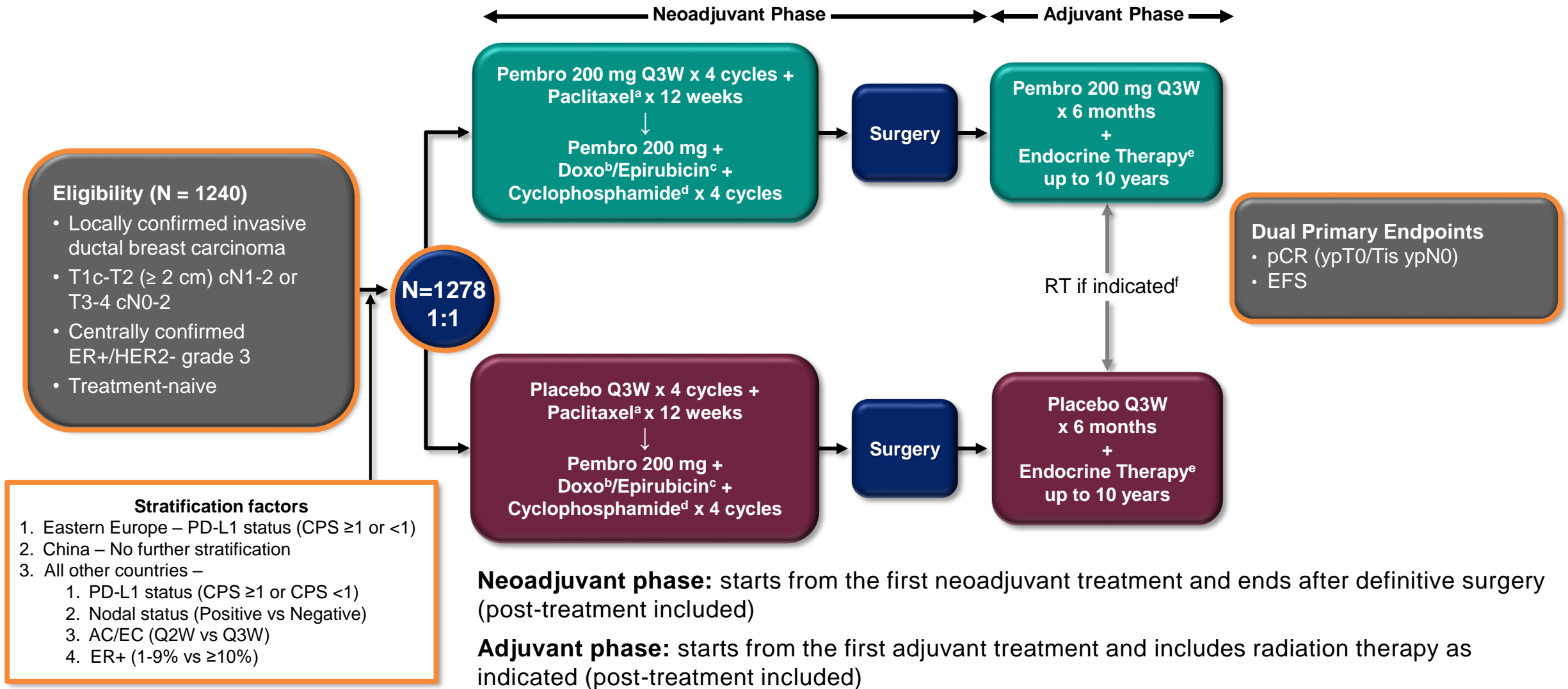
HR+/HER2- participants (n=379)



Observed pCR rate by MP High1 vs. High2 and BP-basal vs. luminal in the HR+/HER2- cohort



KEYNOTE-756 Study Design (NCT03725059)



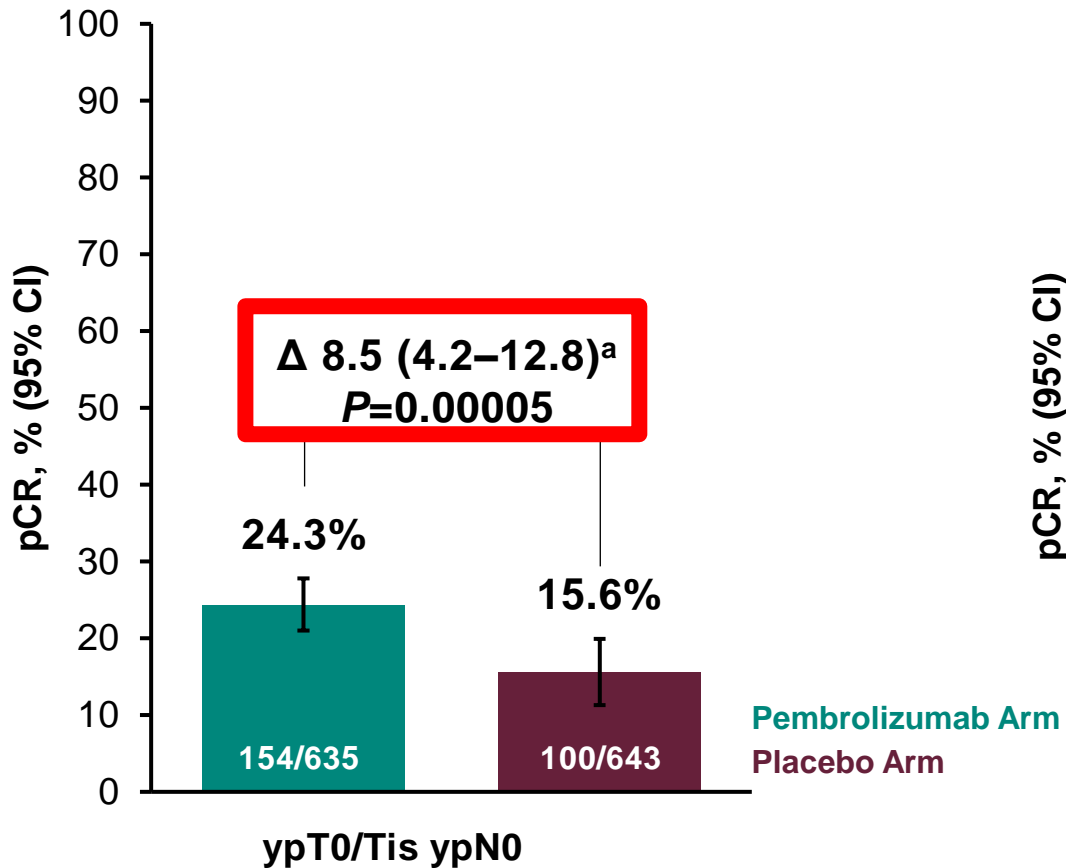
Baseline Characteristics, ITT Population

Characteristic, n (%)	All Participants ^a , N = 1278	
	Pembrolizumab Arm N = 635	Placebo Arm N = 643
Age, median (range), yrs	49 (24-82)	49 (19-78)
ECOG PS 1	65 (10.2)	55 (8.6)
PD-L1 ^b CPS ≥1	482 (75.9)	489 (76.0)
Anthracycline schedule		
Q3W	415 (65.4)	425 (66.1)
Q2W	183 (28.8)	187 (29.1)
Not started	37 (5.8)	31 (4.8)
Tumor size		
T1/T2	402 (63.3)	413 (64.2)
T3/T4	233 (36.7)	230 (35.8)
Nodal involvement		
Positive	570 (89.8)	582 (90.5)
Negative	65 (10.2)	61 (9.5)
ER positivity ≥10%	601 (94.6)	600 (93.3)

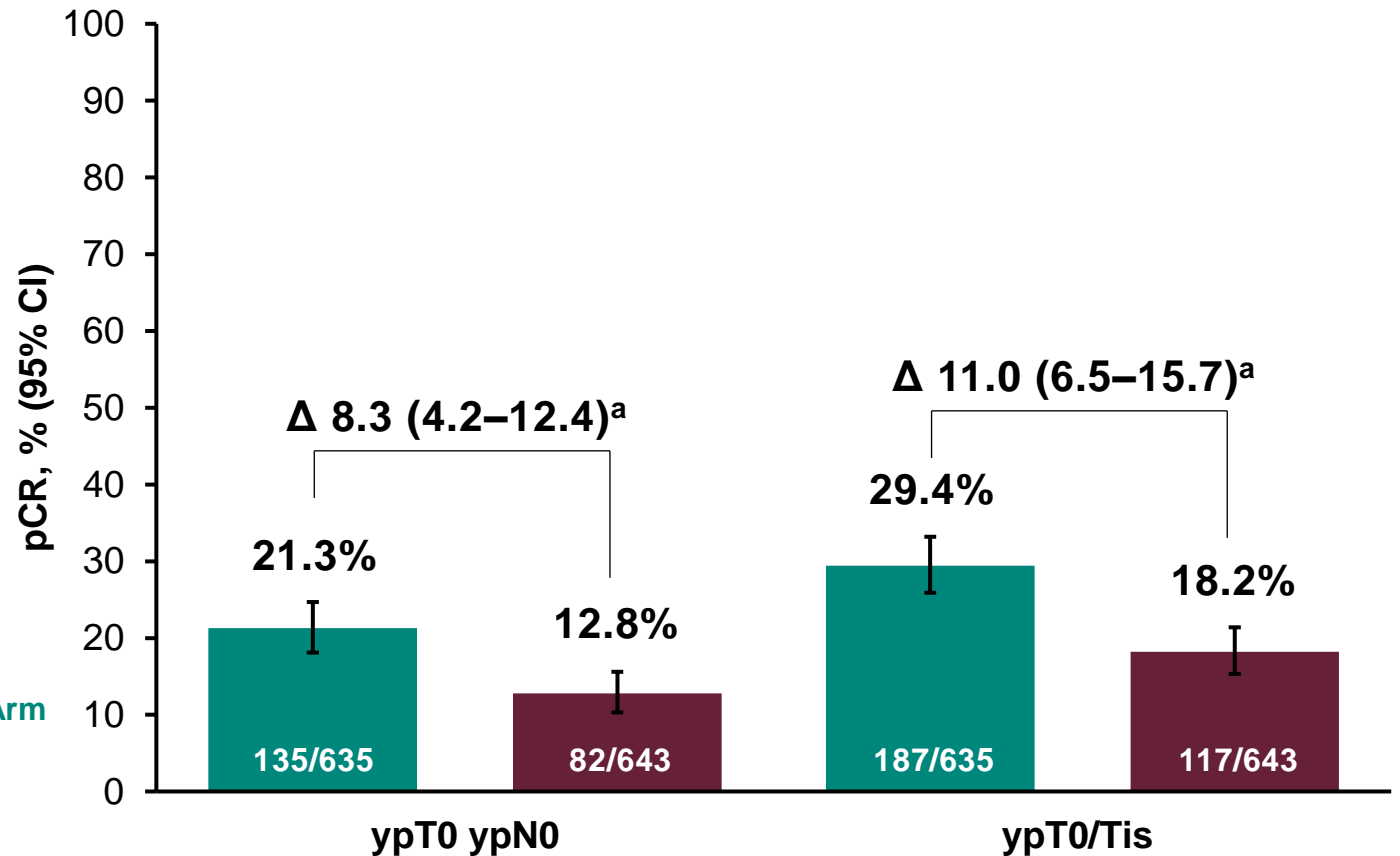
AII GRADE 3

Pathological Complete Response at IA1

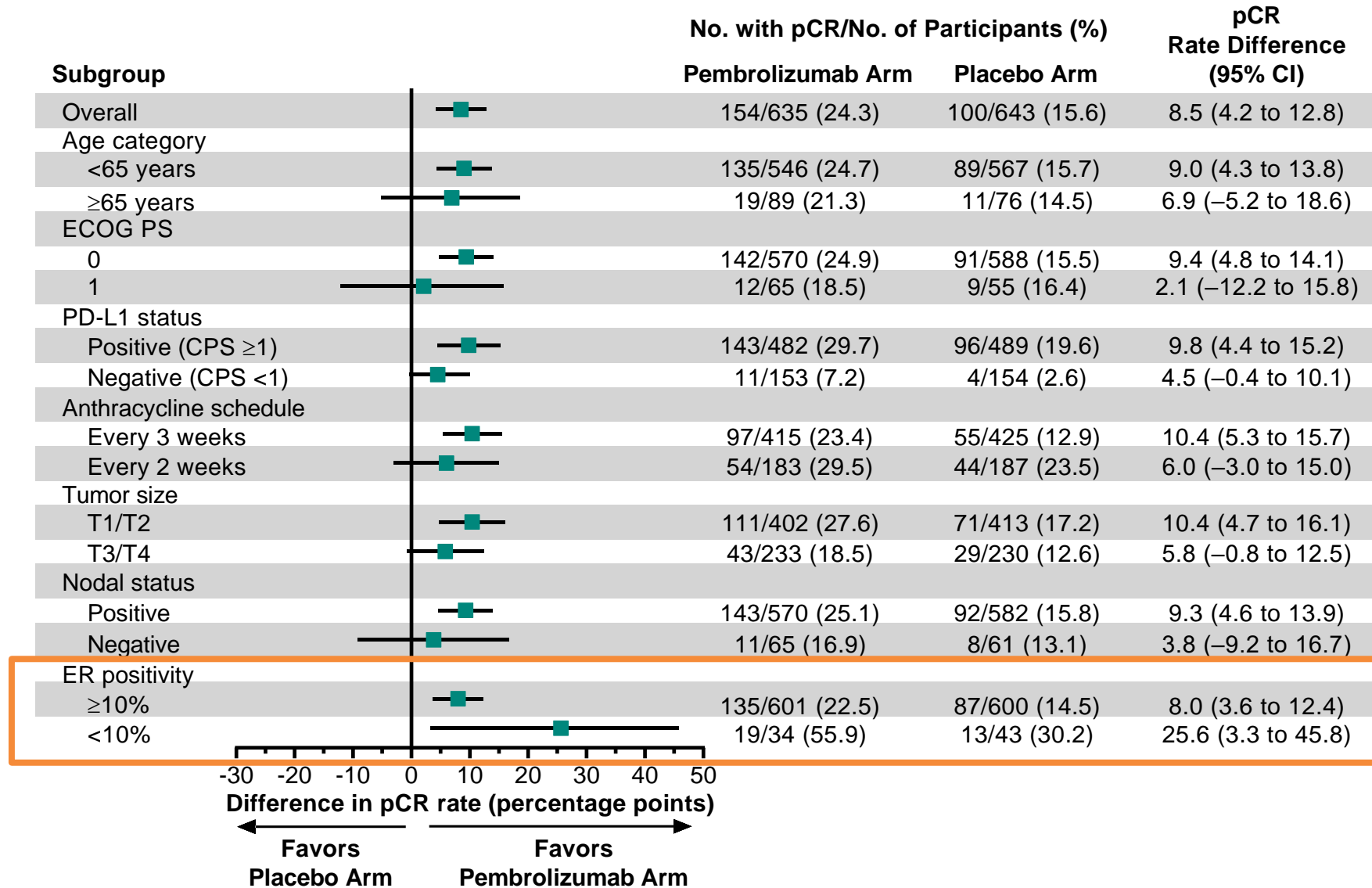
Primary Endpoint



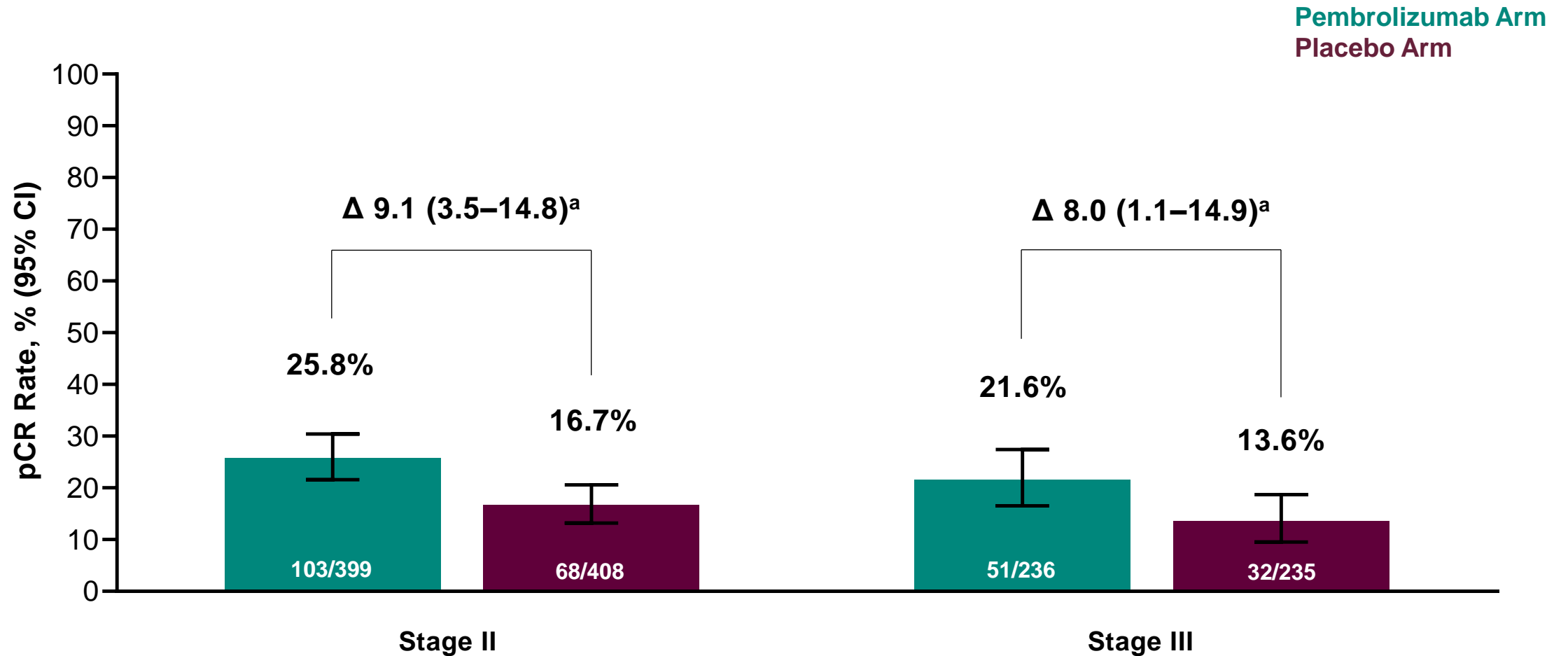
Secondary Endpoints: Other pCR Definitions



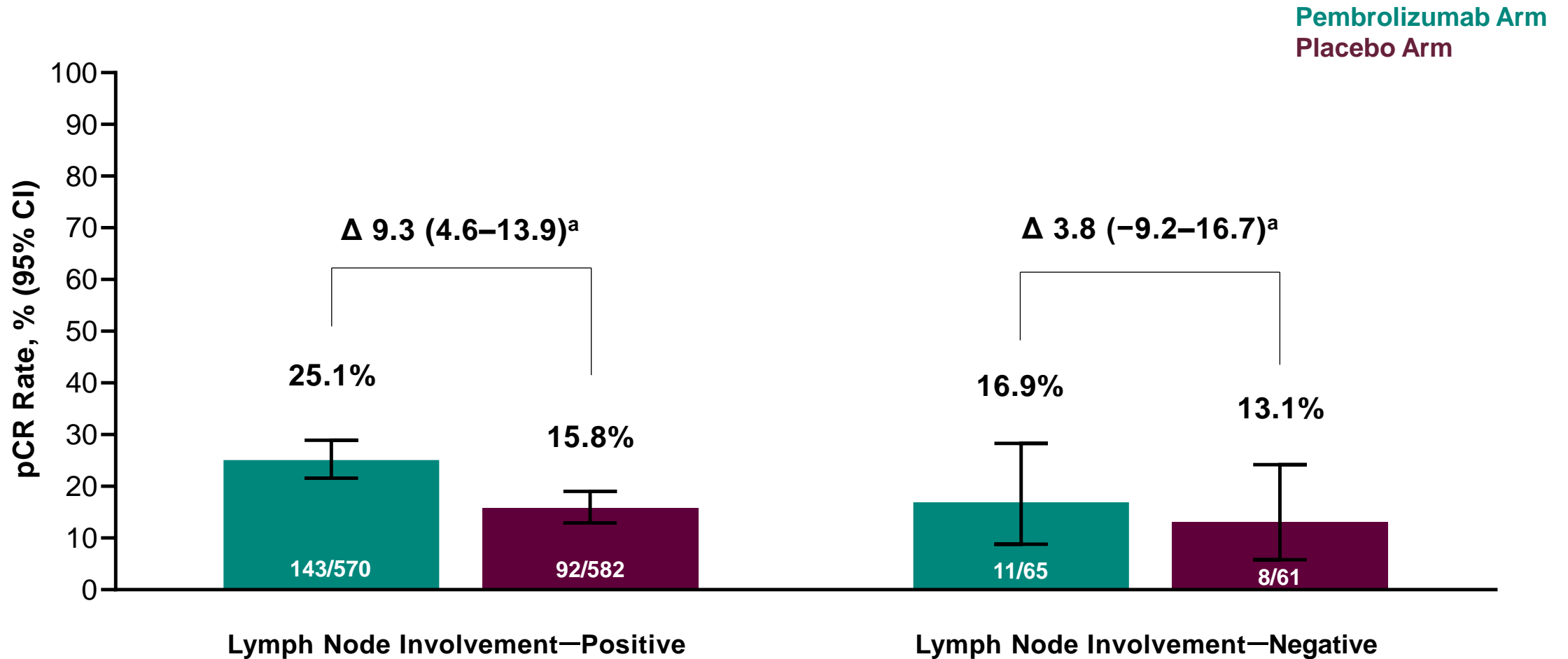
Pathological Complete Response (ypT0/Tis ypN0) in Subgroups



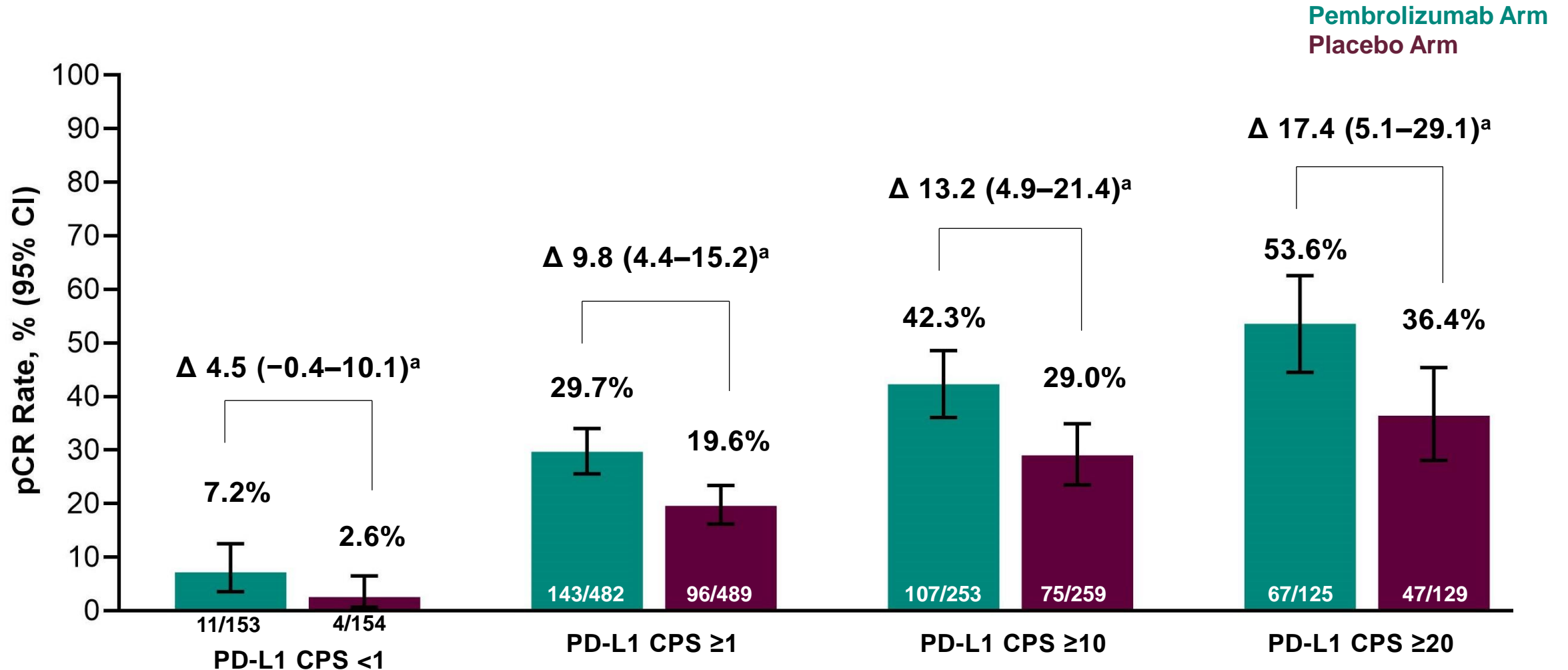
Pathological Complete Response at IA1 by Disease Stage



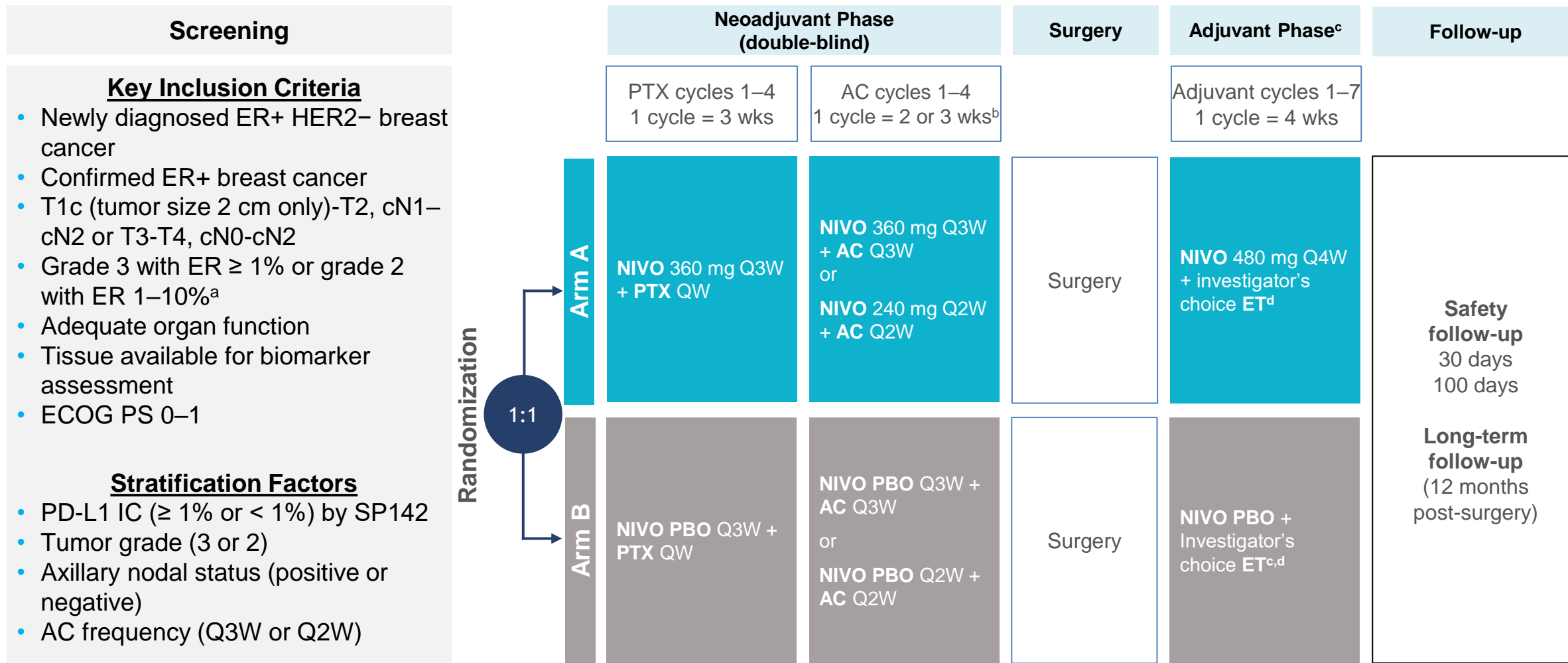
Pathological Complete Response at IA1 by Lymph Node Involvement



Pathological Complete Response at IA1 by PD-L1 Expression Level



CA209-7FL Study Design

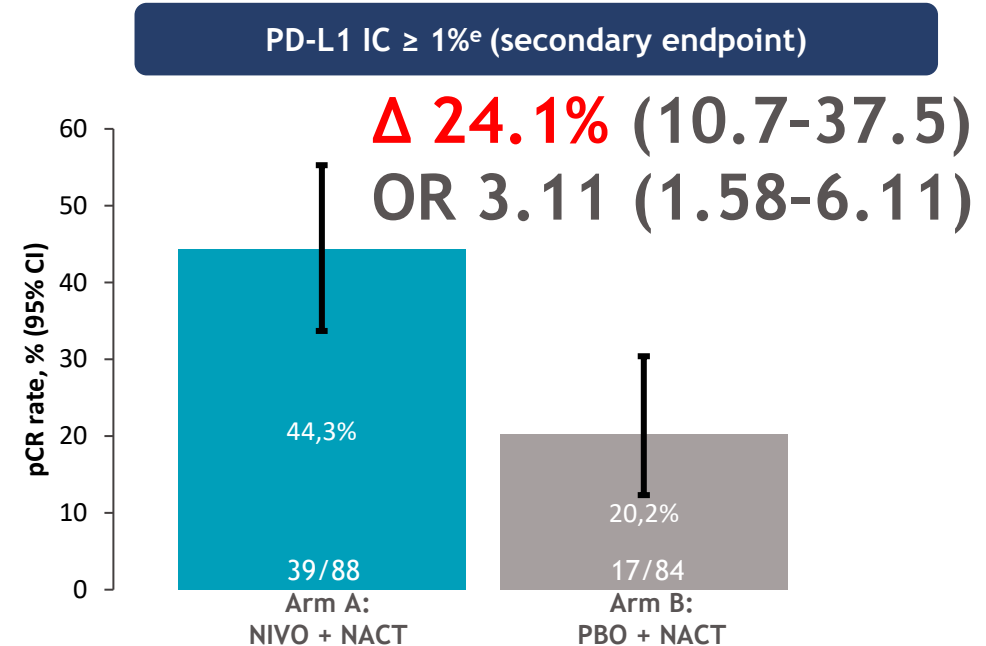
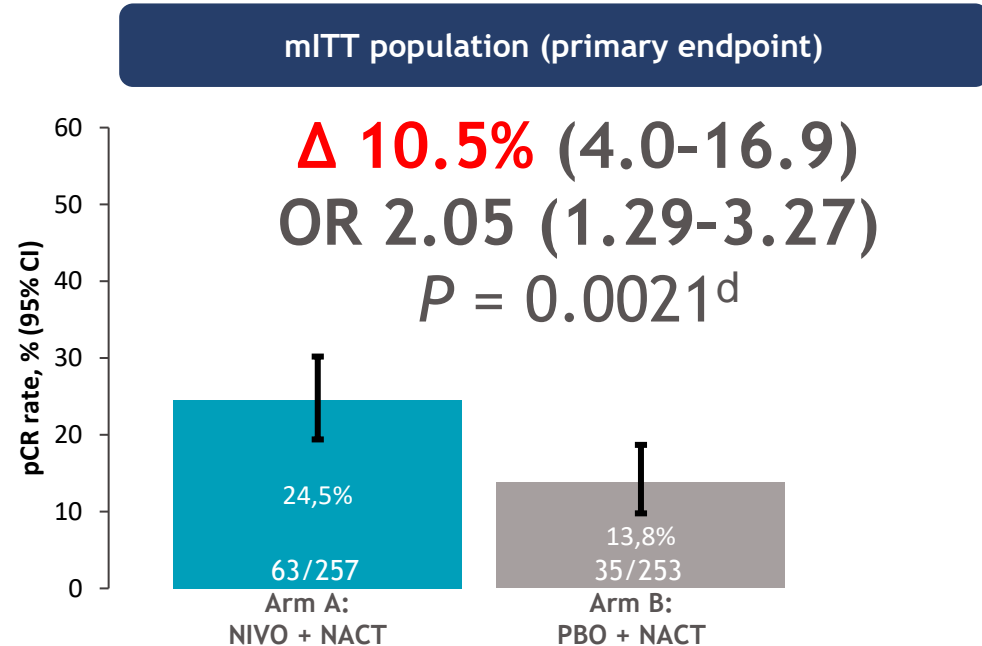


Patient Baseline Characteristics In mITT Population (N = 510) And in Patients With Quantifiable PD-L1 28-8 CPS (N = 349)

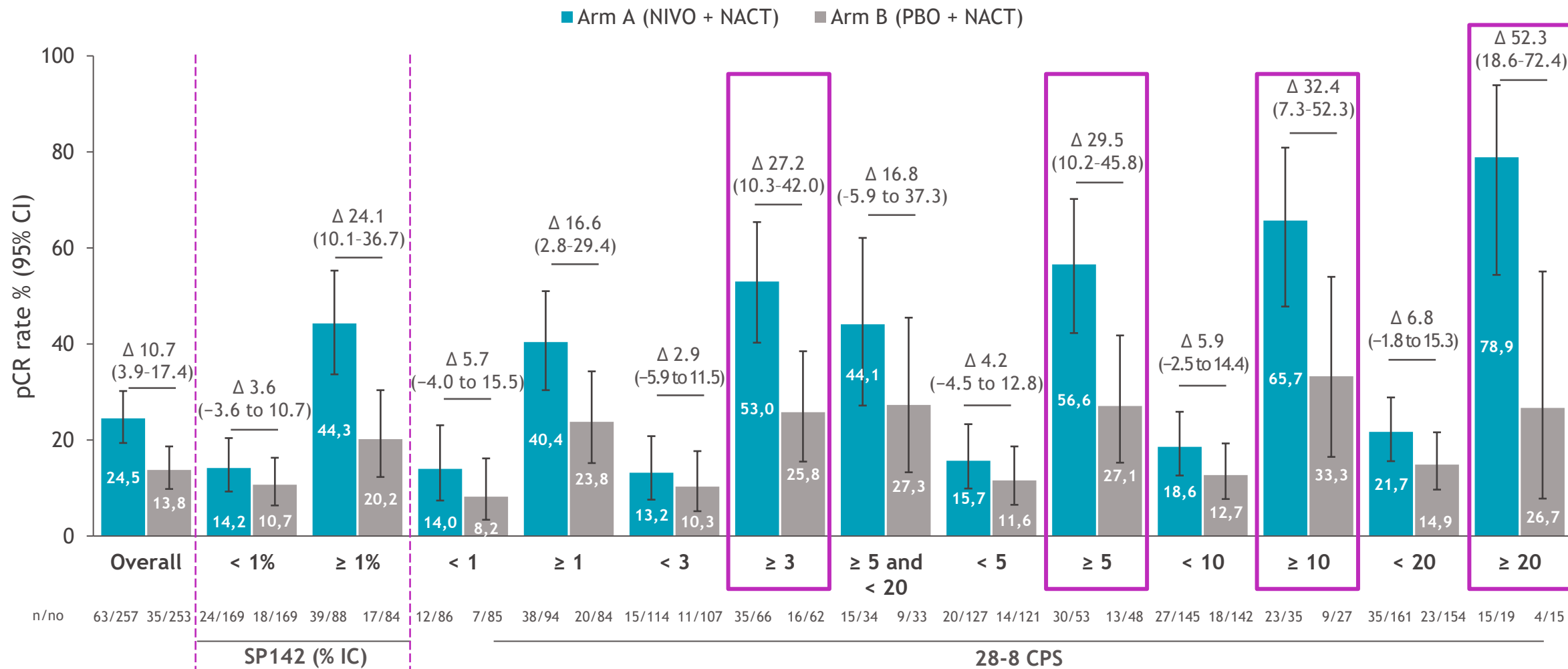
	Arm A: NIVO + NACT		Arm B: PBO + NACT	
	mITT population (n = 257)	Patients with quantifiable PD-L1 28-8 CPS (n = 180)	mITT population (n = 253)	Patients with quantifiable PD-L1 28-8 CPS (n = 169)
Median age, years (range)	50 (24–78)	51 (25–78)	51 (23–79)	51 (23–79)
ECOG PS, n (%)				
0	221 (86)	161 (90)	222 (88)	149 (88)
1	36 (14)	19 (11)	31 (12)	20 (12)
Tumor grade, ^a n (%)				
Grade 2	6 (2)	4 (2)	1 (< 1)	1 (1)
Grade 3	251 (98)	176 (98)	252 (> 99)	168 (99)
Stage ^b (TNM classification ¹), n (%)				
Stage II	135 (53)	87 (48)	138 (55)	92 (54)
Stage III	118 (46)	90 (50)	105 (42)	68 (40)
Not assigned/reported	4 (2)	3 (2)	7 (3)	6 (4)
Ki67, n (%)				
< 20%	72 (28)	72 (40)	72 (28)	71 (42)
≥ 20%	107 (42)	107 (59)	97 (38)	93 (55)
Not reported	78 (30)	1 (1)	84 (33)	5 (3)
Axillary nodal status, n (%)				
Positive	205 (80)	147 (82)	201 (79)	137 (81)
Negative	52 (20)	33 (18)	52 (21)	32 (19)
AC dose-frequency chemotherapy regimen ^c , n (%)				
Q2W	132 (51)	89 (49)	134 (53)	86 (51)
Q3W	125 (49)	91 (51)	119 (47)	83 (49)

CM-7FL: Efficacy

- CheckMate 7FL (NCT04109066) is a prospective, randomized, multicenter, double-blind, placebo-controlled trial investigating NIVO in combination with NACT and adjuvant ET in patients with high-risk, ER+ HER2- primary BC
- The primary endpoint (pCR) was met, resulting in a statistically significant improvement with added NIVO to NACT; RCB 0-1 rate was also meaningfully improved¹
- Benefit of NIVO was enriched in the PD-L1+ population (SP142 >1%)

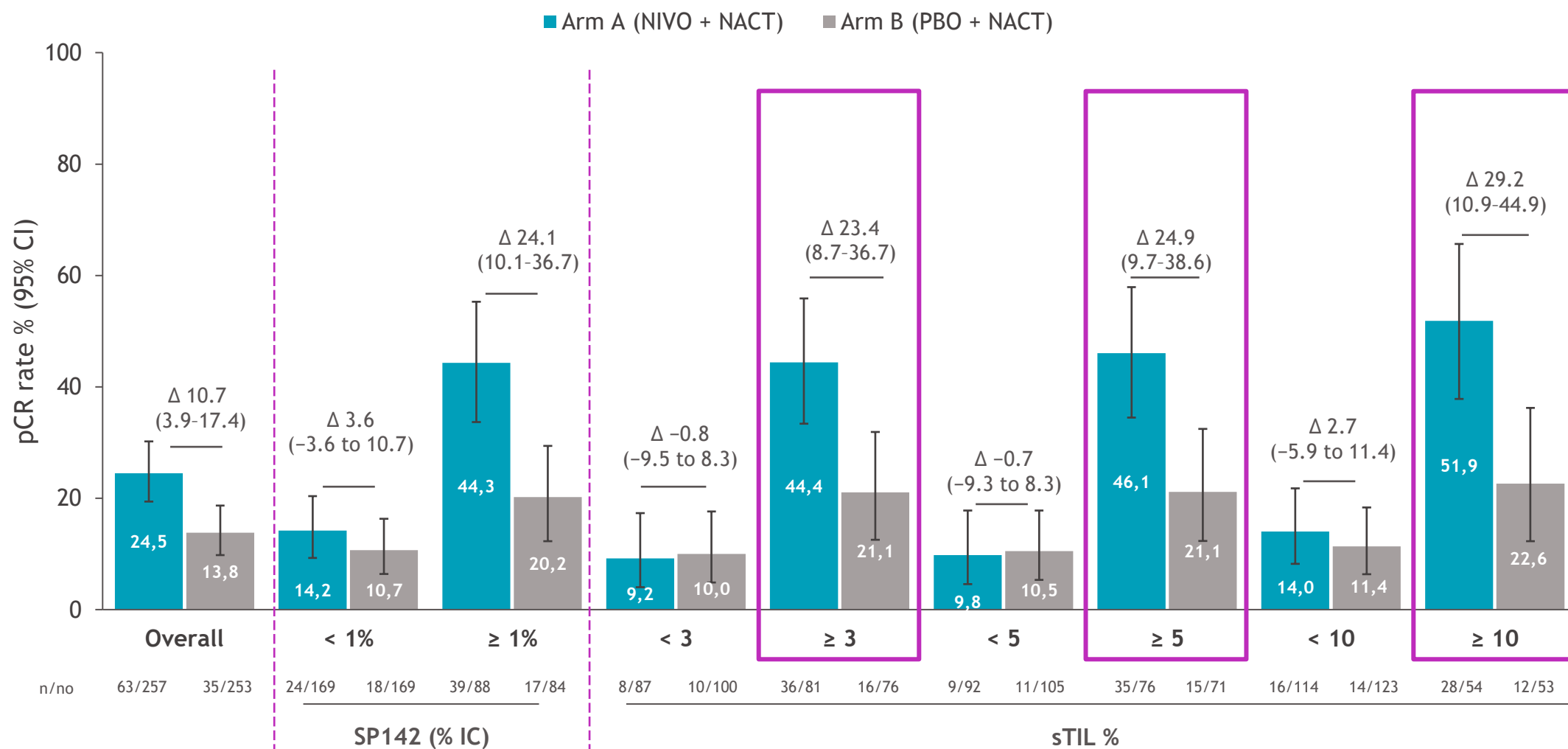


pCR by PD-L1 status determined by SP142 (IC%) and 28-8 CPS (cutoffs 1-20)



- PD-L1 CPS ≥ 3 was determined as the optimal cut-off for the prediction of NIVO benefit based on the ROC and lift plot analyses
- The benefit of NIVO was increased in patients with PD-L1+ tumors defined by both SP142 IC (≥ 1%) and 28-8 CPS (≥ 1); the benefit was greater with the increased CPS score

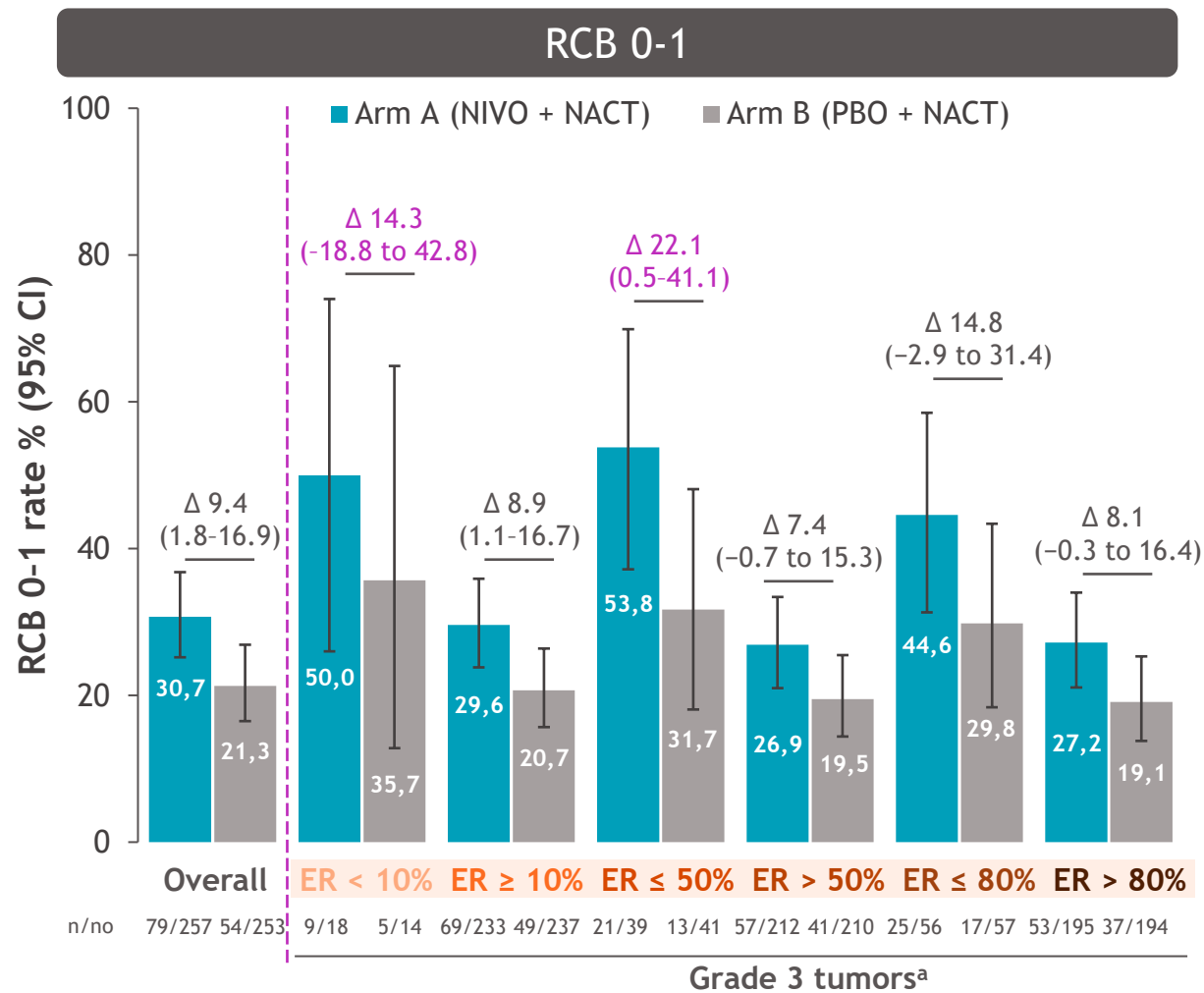
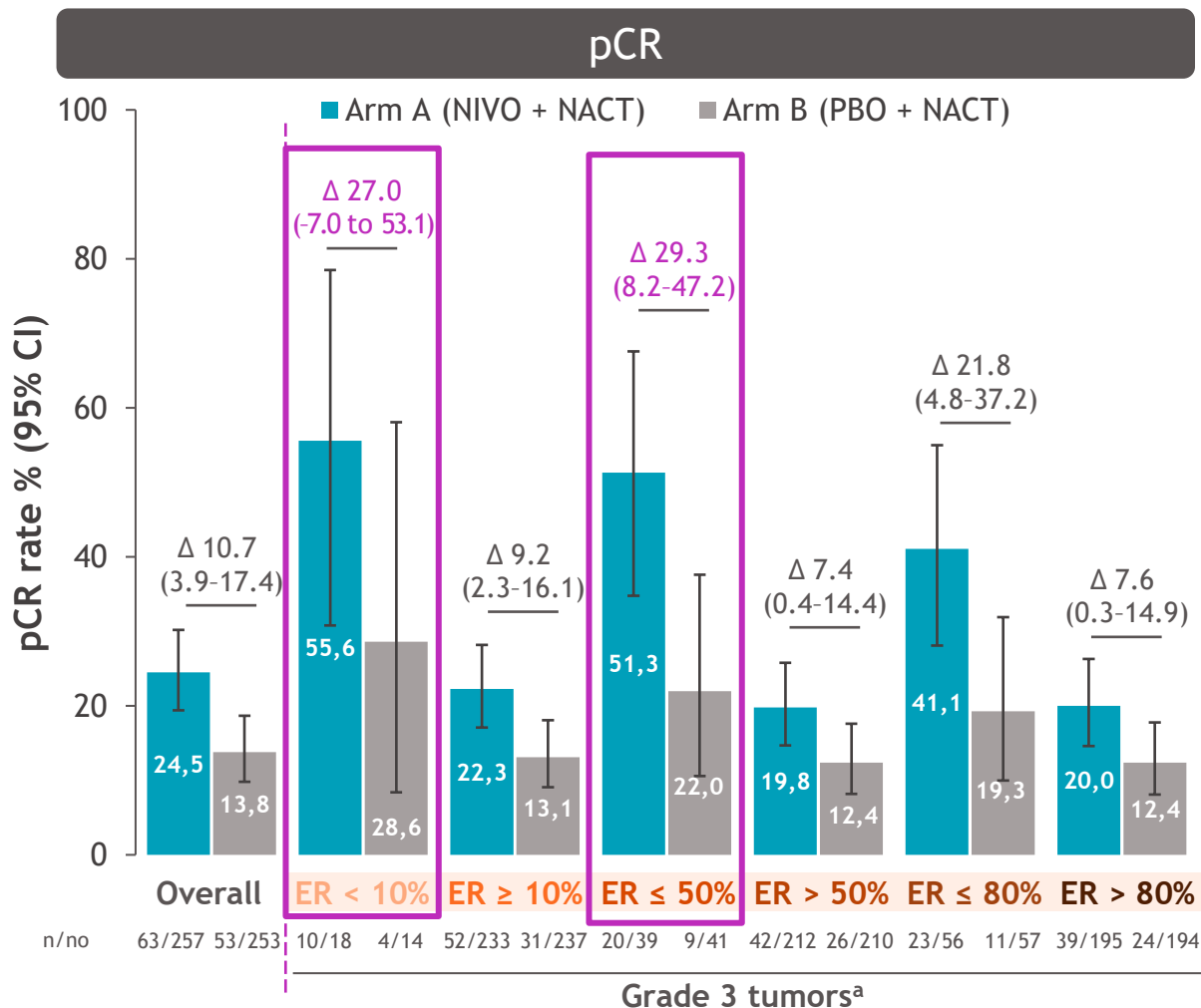
pCR by PD-L1 status determined by SP142 (IC%) and sTIL (cutoffs 3%, 5%, 10%)^a



- The benefit of NIVO was increased in patients with sTIL > 1% or greater; the data for RCB 0/1 were consistent

^aExploratory biomarker/analysis. N = 344; Median sTIL % (min-max): 1 (1-98); mean sTIL % (SD): 14.49 (24.35). IC, immune cell; NACT, neoadjuvant chemotherapy; NIVO, nivolumab; no, subpopulation total; PBO, placebo; pCR, pathological complete response; RCB, residual cancer burden; SD, standard deviation; SP142, Ventana PD-L1 SP142 assay; sTIL, stromal tumor-infiltrating lymphocyte.

pCR and RCB 0-1 by tumor ER expression

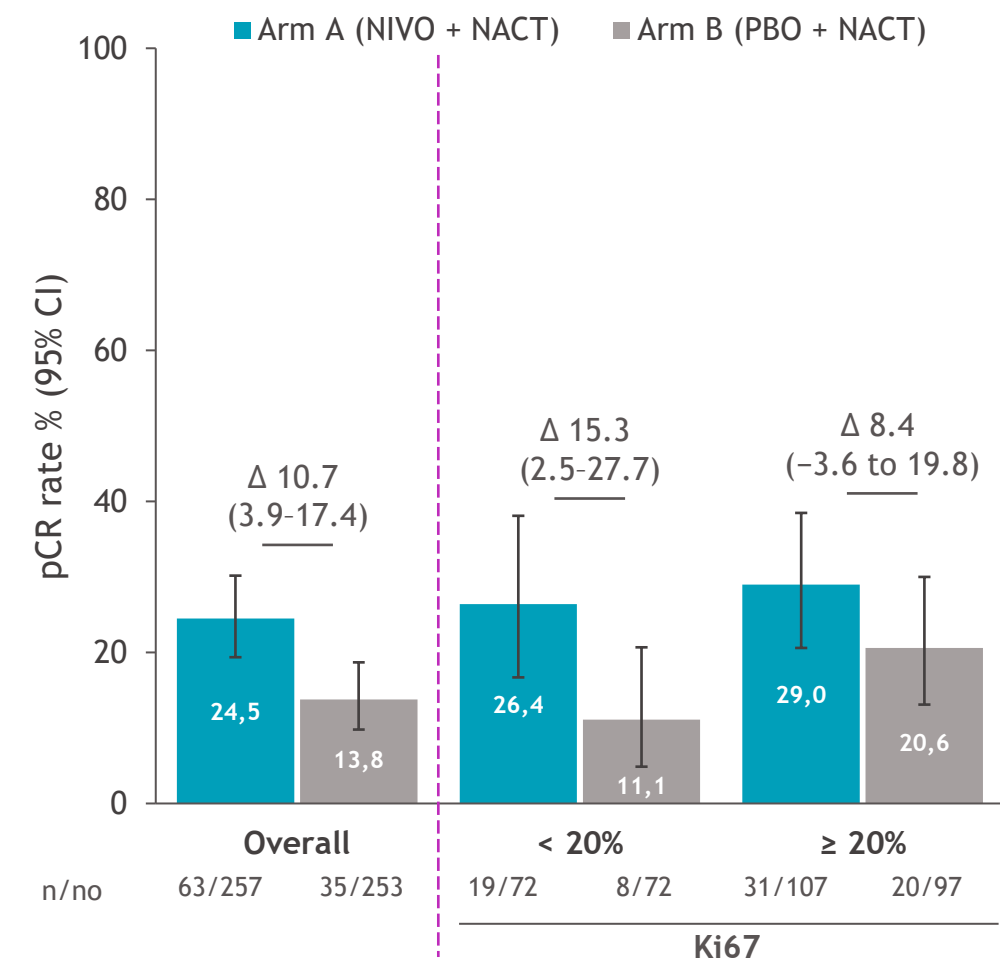


- ER > 50%, ER > 80% and PR ≥ 10% were exploratory cutoffs
- NIVO benefit on pCR and RCB 0-1 rates was the highest in patients with tumors with low ER (≤ 50%)

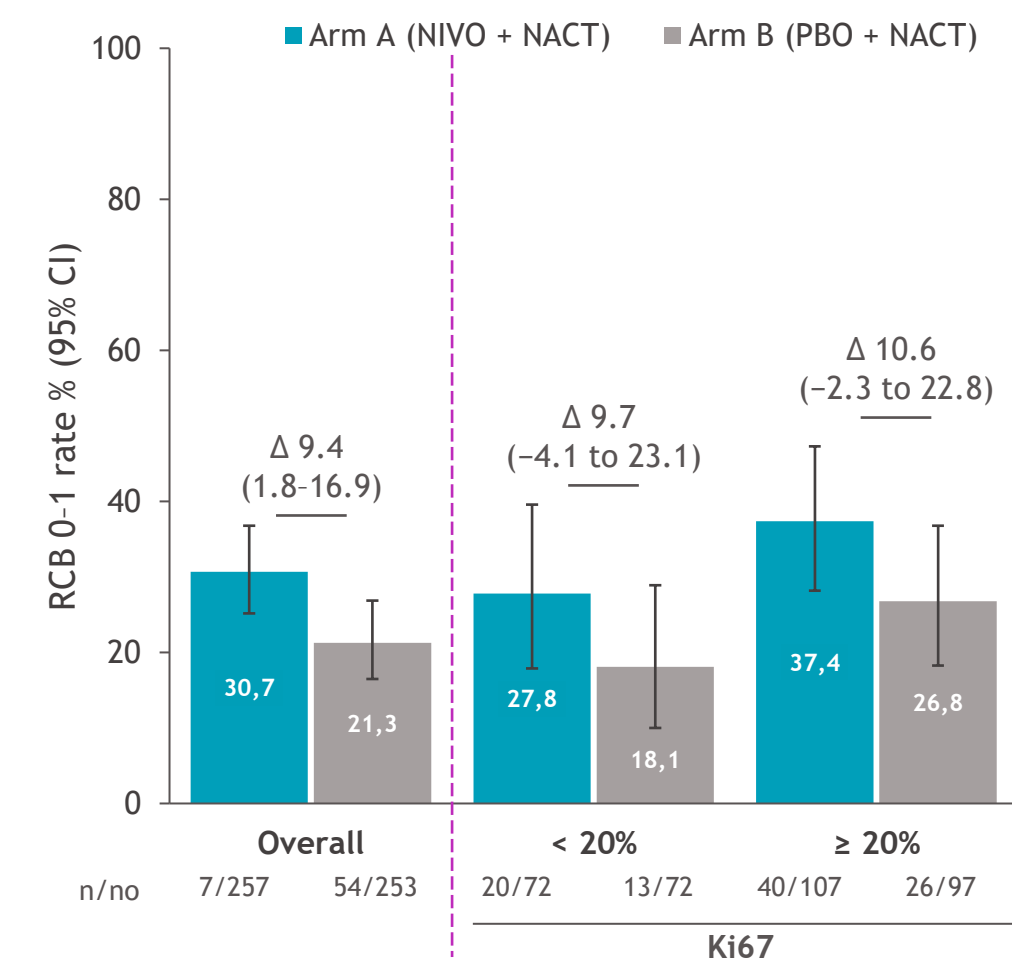
^aTumor grade as per the eCRF. eCRF, electronic case report form; ER, estrogen receptor; NACT, neoadjuvant chemotherapy; NIVO, nivolumab; no, subpopulation total; PBO, placebo; pCR, pathological complete response; RCB, residual cancer burden.

pCR and RCB 0-1 rates by Ki67 index^a

pCR



RCB 0-1



• No association between NIVO benefit and Ki67 index was observed

^aExploratory biomarker/analysis. NACT, neoadjuvant chemotherapy; NIVO, nivolumab; no, subpopulation total; PBO, placebo; pCR, pathological complete response; RCB, residual cancer burden.

TB04 Study Design: Ph3 Dato-DXd + Durva in Neoadjuvant/Adjuvant TNBC

Neoadjuvant

Surgery

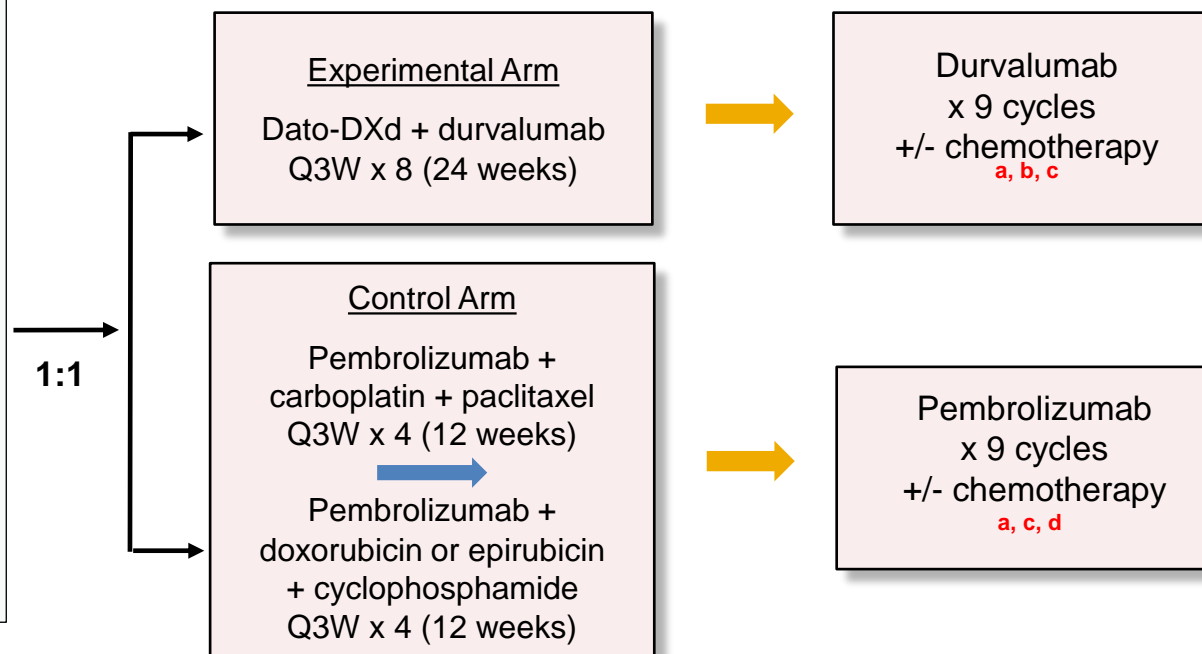
Adjuvant

Key Eligibility Criteria

- Histologically confirmed Stage II or III unilateral or bilateral primary invasive breast cancer.
- TNBC (ER and PR < 1%) or hormone receptor-low breast cancer (ER and/or PR 1% to < 10%, neither hormone receptor may be ≥ 10%), and HER2-negative.
- No evidence of distant disease.
- No prior surgery, radiation, or systemic anticancer therapy.
- ECOG PS 0 or 1.
- Adequate hematologic and organ function.

Stratification factors:

- Lymph node status (positive versus negative)
- Tumour stage (cT1 to cT2 versus cT3 to cT4)
- Hormone receptor status (hormone receptor-negative [ER and PR < 1%] versus hormone receptor-low (ER and/or PR 1% to < 10%, neither hormone receptor may be ≥ 10%])
- Geographic region (US/Canada/Europe/Australia versus Rest of World).



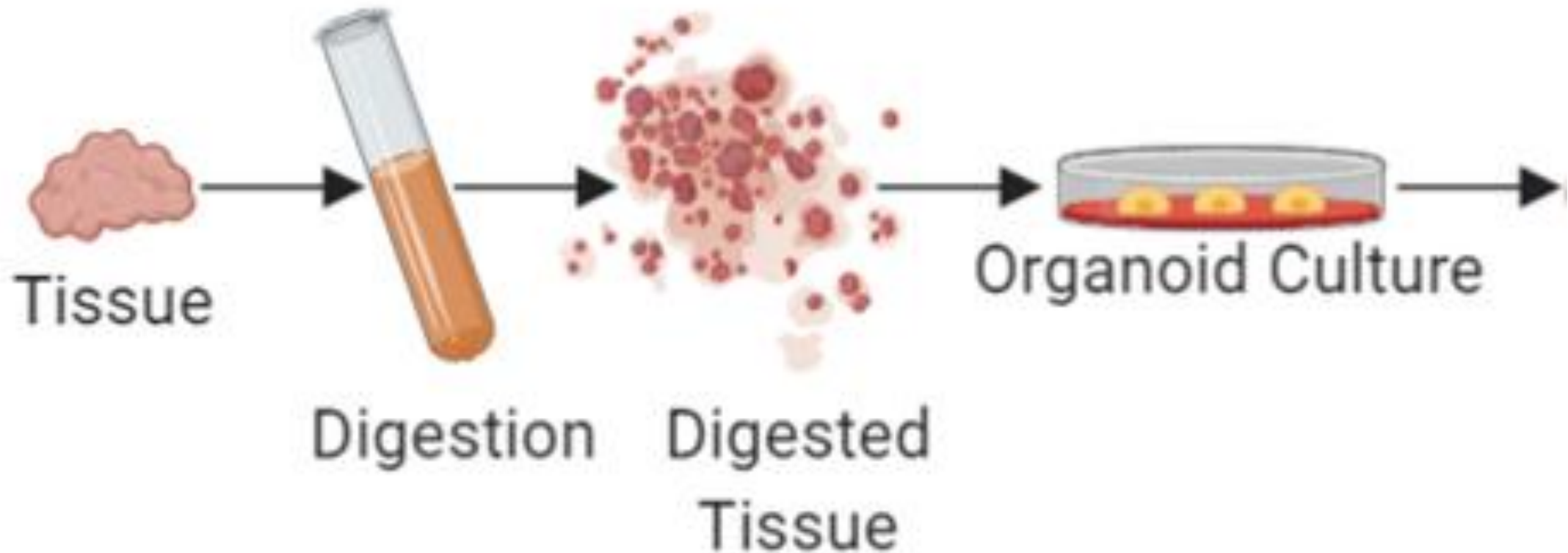
Dual primary endpoints:
pCR and EFS

Secondary endpoints:
OS, DDFS, safety and tolerability, PROs, PK, immunogenicity

Exploratory endpoints include but are not limited to:
TROP2, PD-L1

- a. Endocrine therapy is permitted for participants with hormone receptor-low tumours. No adjuvant CDK4/6 inhibitor (eg, abemaciclib, ribociclib).
- b. Adjuvant chemotherapy may be given in combination with durvalumab for participants with residual disease. Chemotherapy options at discretion of investigator, either: doxorubicin/epirubicin + cyclophosphamide, followed by paclitaxel + carboplatin; doxorubicin/epirubicin + cyclophosphamide followed by paclitaxel; carboplatin + paclitaxel; capecitabine.
- c. Olaparib may be administered to participants who are gBRCA-positive with residual disease.
- d. Adjuvant capecitabine may be given in combination with pembrolizumab for participants with residual disease, at the discretion of investigator.

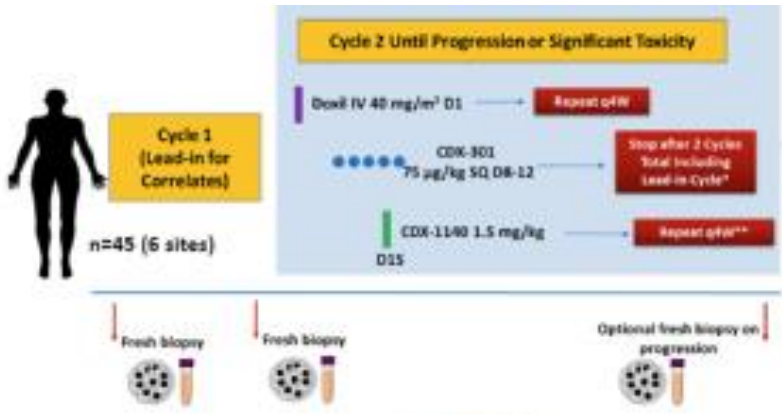
Laboratory to Clinic to Laboratory



A novel platform to discover new immune strategies



Breast Cancer Program: Focus on the Tumor Immune Microenvironment



- B-cell
- Dendritic cell
- CD4 T-cell
- CD8 T-cell
- Monocyte/Macrophage
- Mast cell
- NK-cell



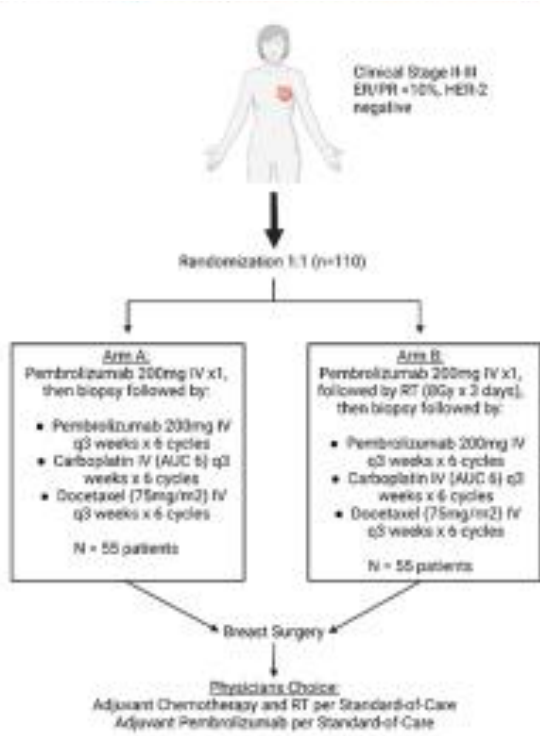
Alluri (ET)



McArthur (ET)



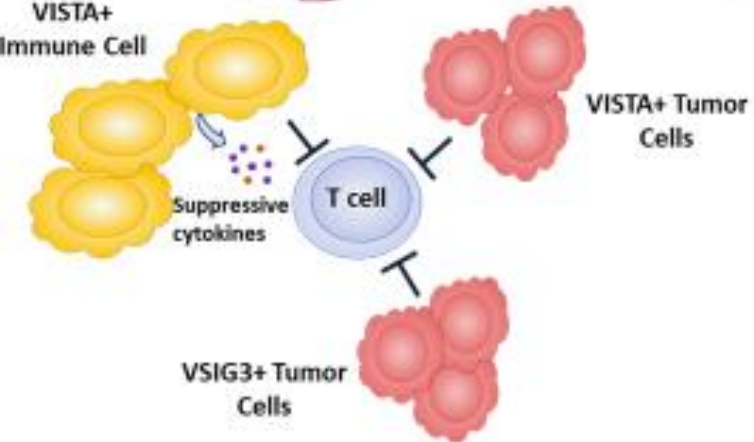
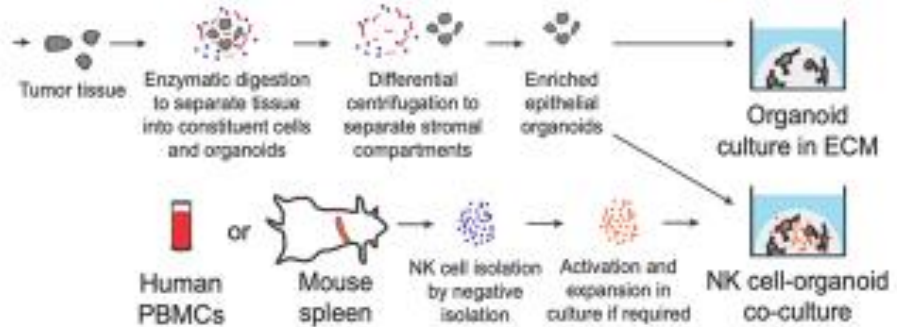
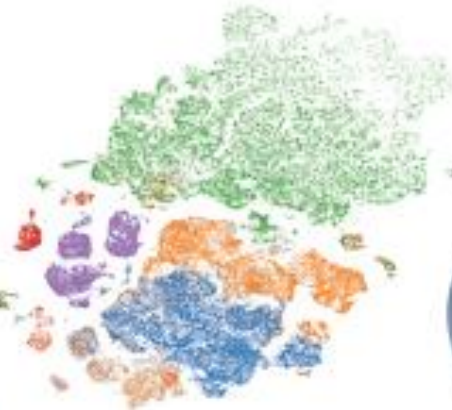
Gruber (CC)



Reddy (ET)



Chan (CNC)



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Breakthrough of the Year

**Cancer Cured with
Immunotherapy
Combinations**