



Where Science Becomes Hope®

IMMUNO-ONCOLOGY IN PERIOP THERAPY FOR EARLY E/GEJ/G CANCER: TO ADD

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EMORY
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INSTITUTE

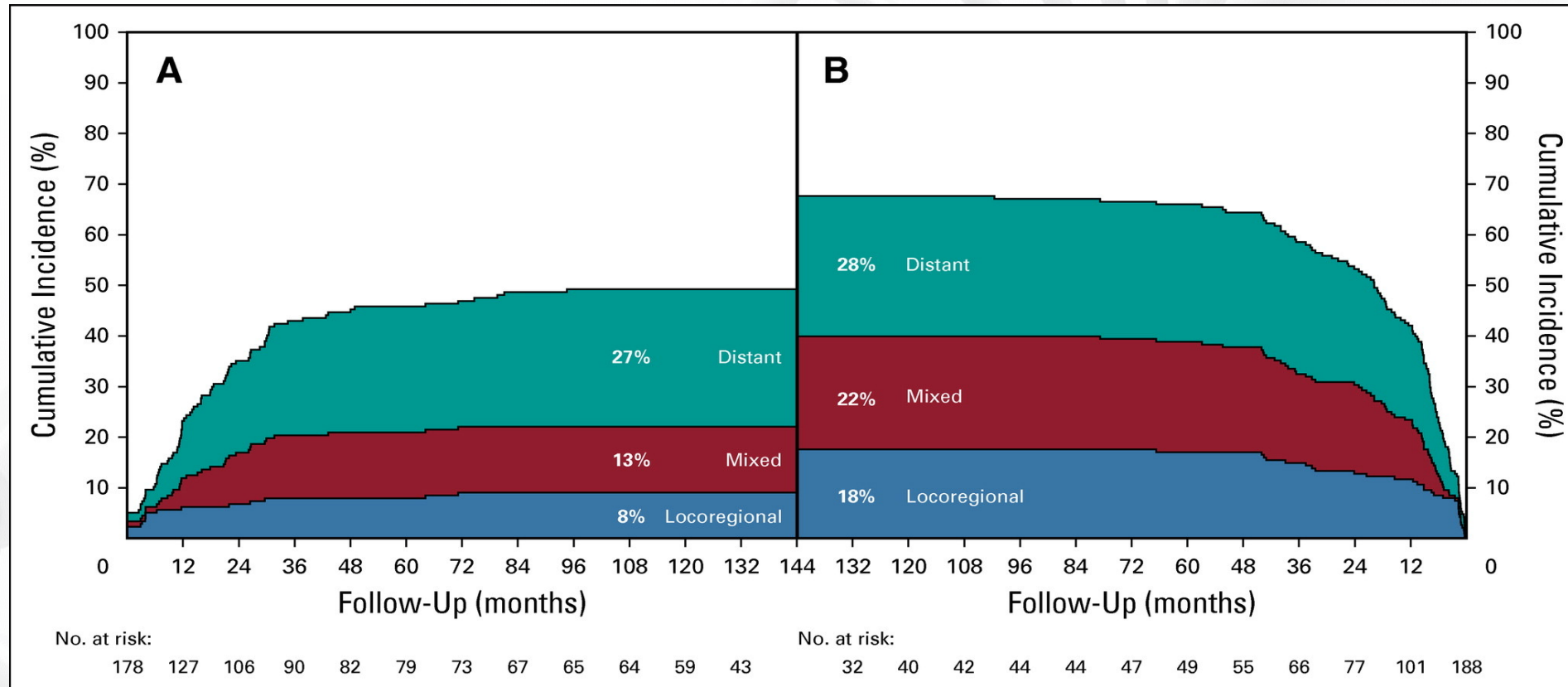
National Cancer Institute-Designated
Comprehensive Cancer Center

NCI

Designated
Comprehensive
Cancer Center

STATEMENT OF NEED

- Esophageal and Gastric cancer have high mortality (27,010 deaths, 49,260 new cases in 2024)



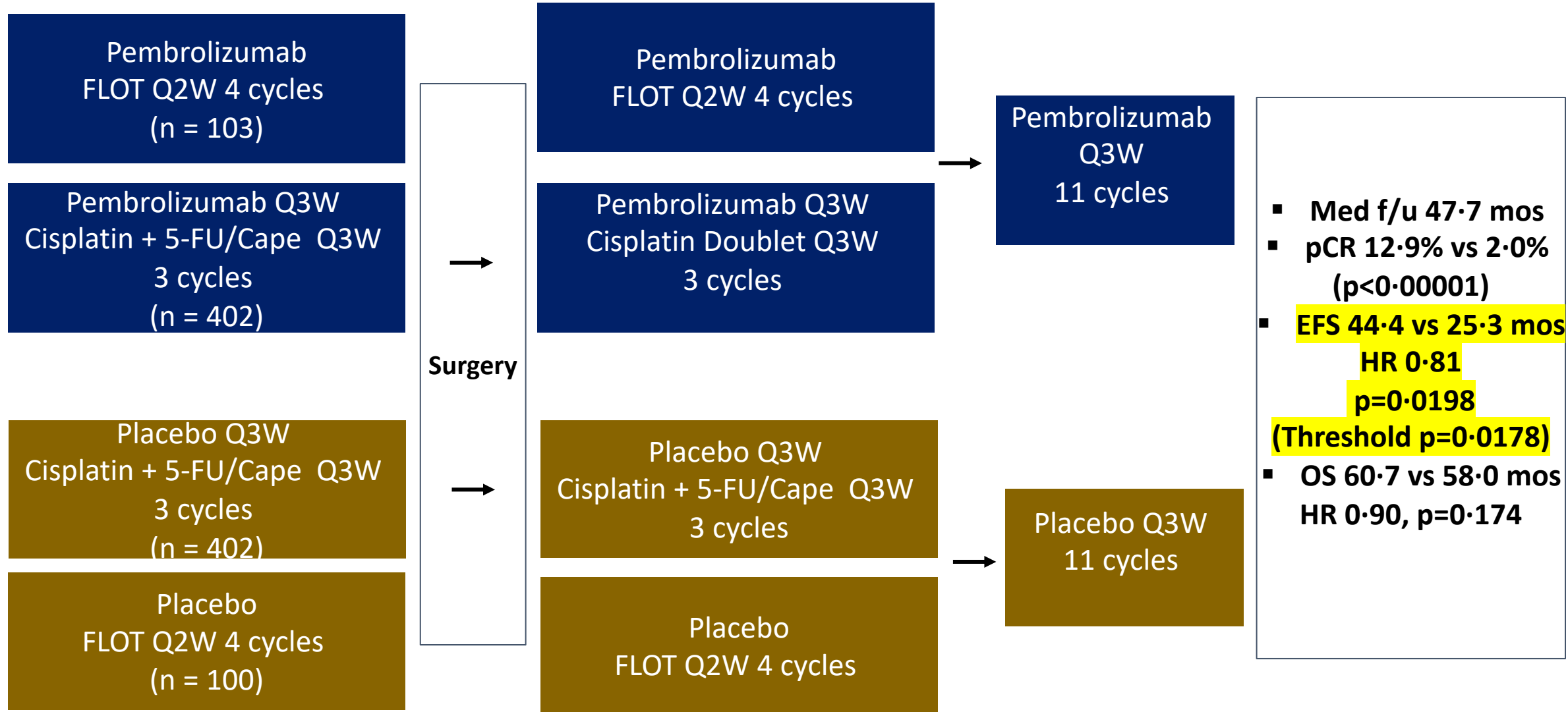
Siegel RL et al. Cancer Statistics 2024, Eyck BM et al, JCO 2021

RATIONALE FOR PERIOP IO

- Biological rationale for improved efficacy in the neoadjuvant setting
 - Intact primary tumor as a rich source of neoantigens to generate broader T cell response
 - Intact regional lymph nodes assist with robust antitumor immunity, especially uninvolved LNs
- Window of opportunity to assess individual tumor biology
- Less resistance to IO with reduced disease burden compared to metastatic disease
- Benefit from chemolO in metastatic GEJ Ca
- Increased immune cell infiltration due to IO component and not chemo (Verschoor YL et al. Nature Med 2024)

Luoma AM, et al. Cell. 2022, Nagasaki J, et al. Cell Rep. 2022, Rahim MK, et al. Cell. 2023, Janjigian Y et al. Lancet 2021, Rha SY et al. Lancet Oncol 2023

KEYNOTE-585

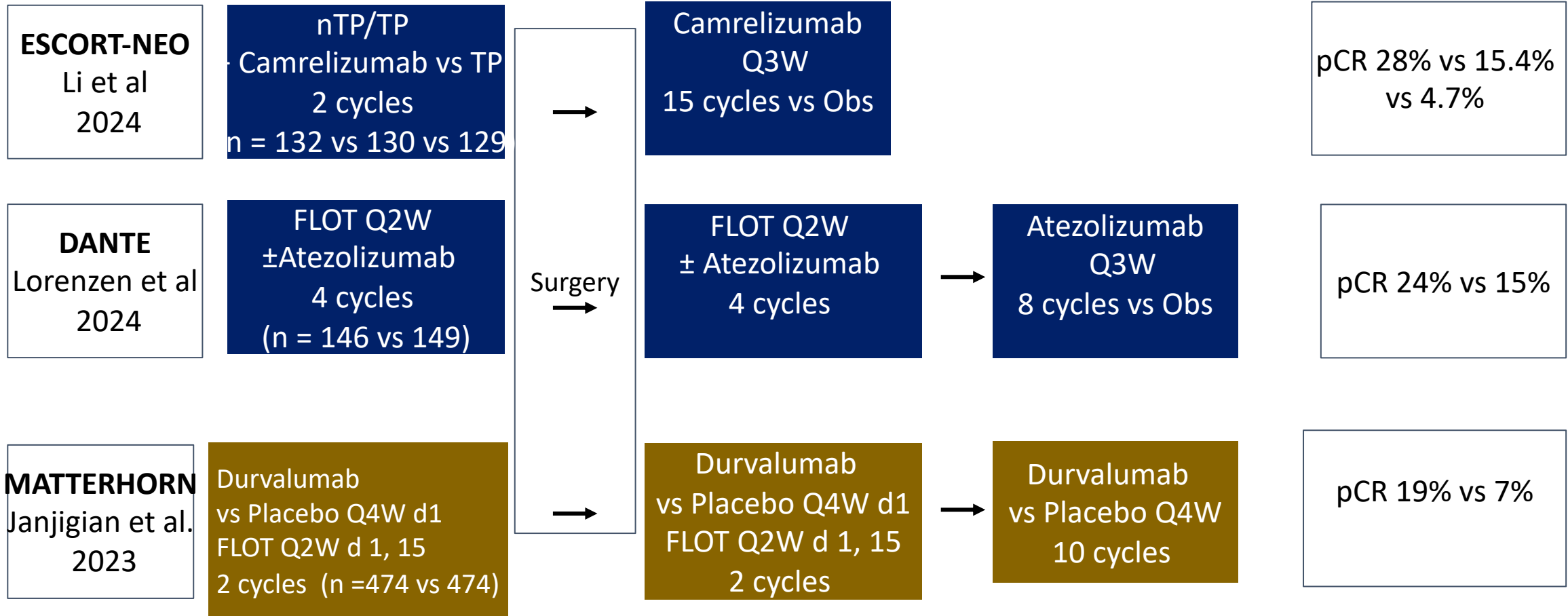


ESOPEC VS KEYNOTE-585

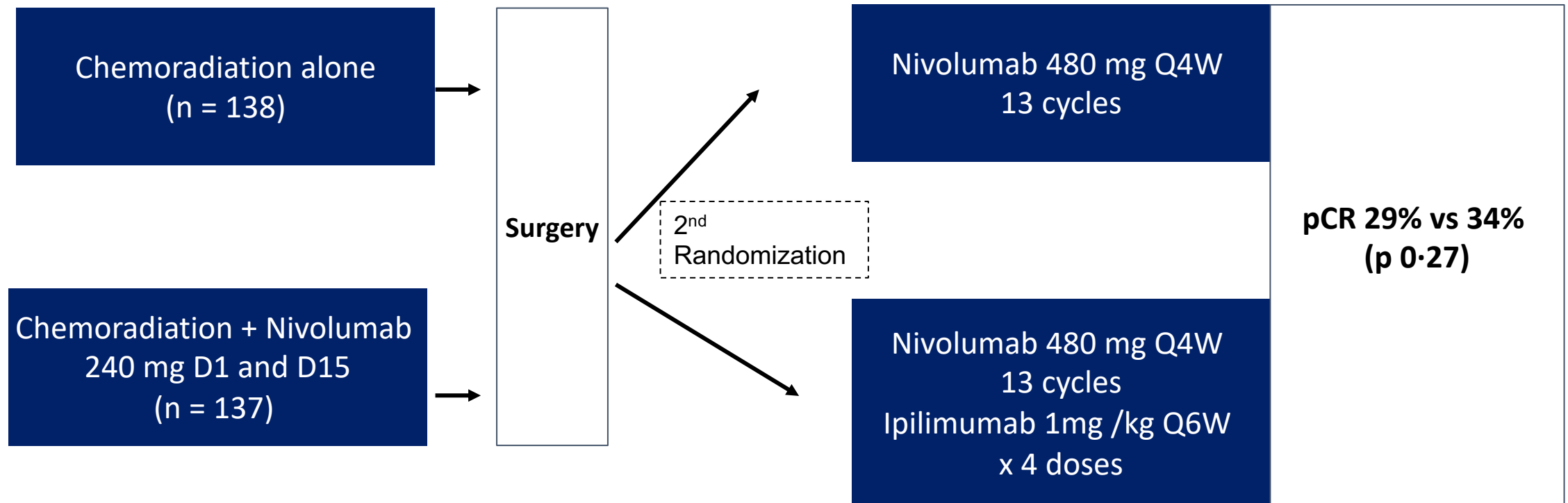
ESOPEC (Hoepfner et al. 2024)	KEYNOTE-585 (Shitara et al. 2024)
Periop Triplet chemo vs Neoadj Chemorad	Periop Chemo + IO vs Periop Chemo
Esophageal AdenoCa	GEJ and Gastric AdenoCa
Triplet chemo only in the chemo arm	Most patients received doublet chemo Primary endpoint analysis was in doublet chemo population
Median OS in FLOT arm = 66 mos	Median OS in doublet + IO arm = 60 mos

CANNOT CROSS-COMPARE
THESE TWO STUDIES

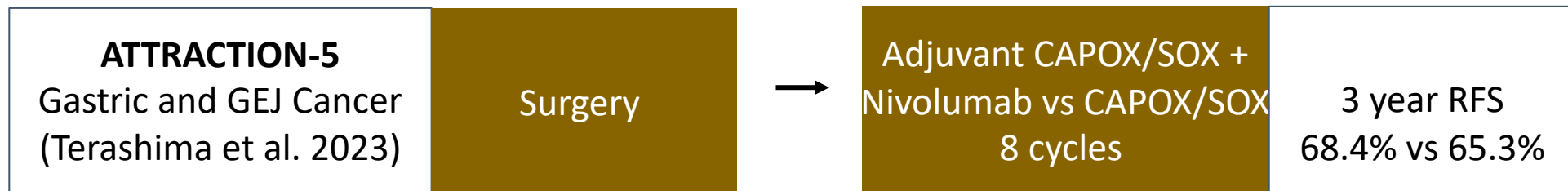
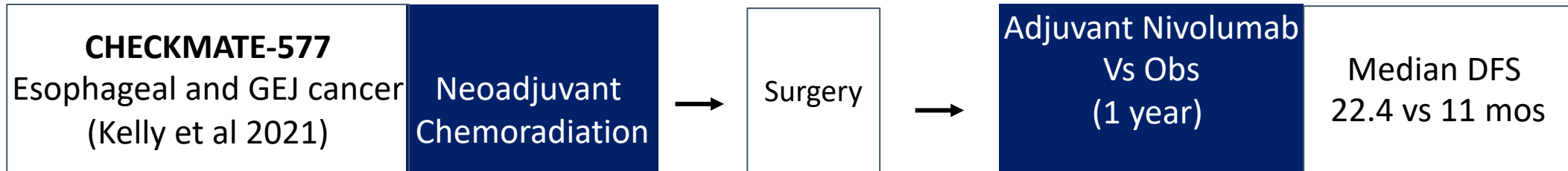
MORE PERIOP CHEMOIMMUNOTHERAPY RCTS



PERIOP CRT AND IMMUNOTHERAPY: EA2174

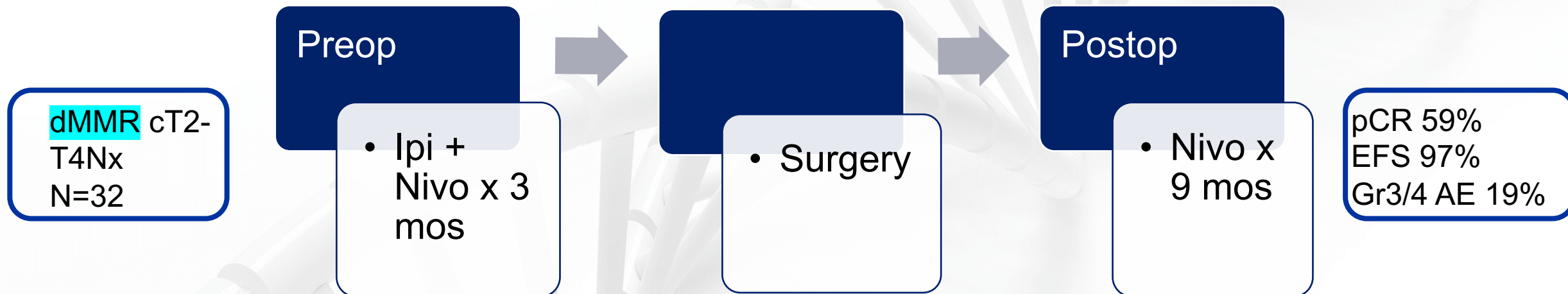


ADJUVANT IMMUNOTHERAPY



PERIOPERATIVE IO- **dMMR** GEJ CANCERS

NEONIPIGA



INFINITY

- Neoadjuvant Treme/Durva in dMMR/MSI-H GEJ/Gastric Ca followed by surgery (cohort 1) or non operative management (cohort 2)
- Cohort 1 N=18, evaluable n =15
 - pCR 60%, MPR 80%
 - Gr 3 AEs 17%

(Andre, Tougeron et al. JCO 2022, Pietrantonio F. et al, JCO 2023)

SAFETY AND CONCLUSIONS

Study	Chemo + IO	Chemo
KEYNOTE 585	78% Deaths 4 (1%)	74% Deaths 2 (<1%)
DANTE	Gr 3/4 AEs similar Deaths 4 (3%)	Gr 3/4 AEs similar Deaths 3 (2%)
MATTERHORN	Gr3/4AEs 69% Deaths 5%	Gr3/4AEs 68% Deaths 4%
ESCORT NEO	Gr3 AEs 34%, 29%	Gr3 AEs 29%
EA2174	Gr 3 AEs numerically increased cytopenias	Gr 3 AEs numerically fewer cytopenias

- Data support Periop IO in dMMR GEJ cancer
- The jury is still out on survival benefit from Triplet chemo+ IO combination in GEJ and gastric Ca, but DMFS benefit is anticipated.
- Treatment sequencing and biomarker improvements will be crucial