2022 ASCO ANNUAL MEETING

Integrating Immunotherapy in the Treatment Landscape of Patients With Triple-Negative Breast Cancer

Immunotherapy for Patients with Early Stage TNBC: Is the Presence of Immune/Tumor Cells Required

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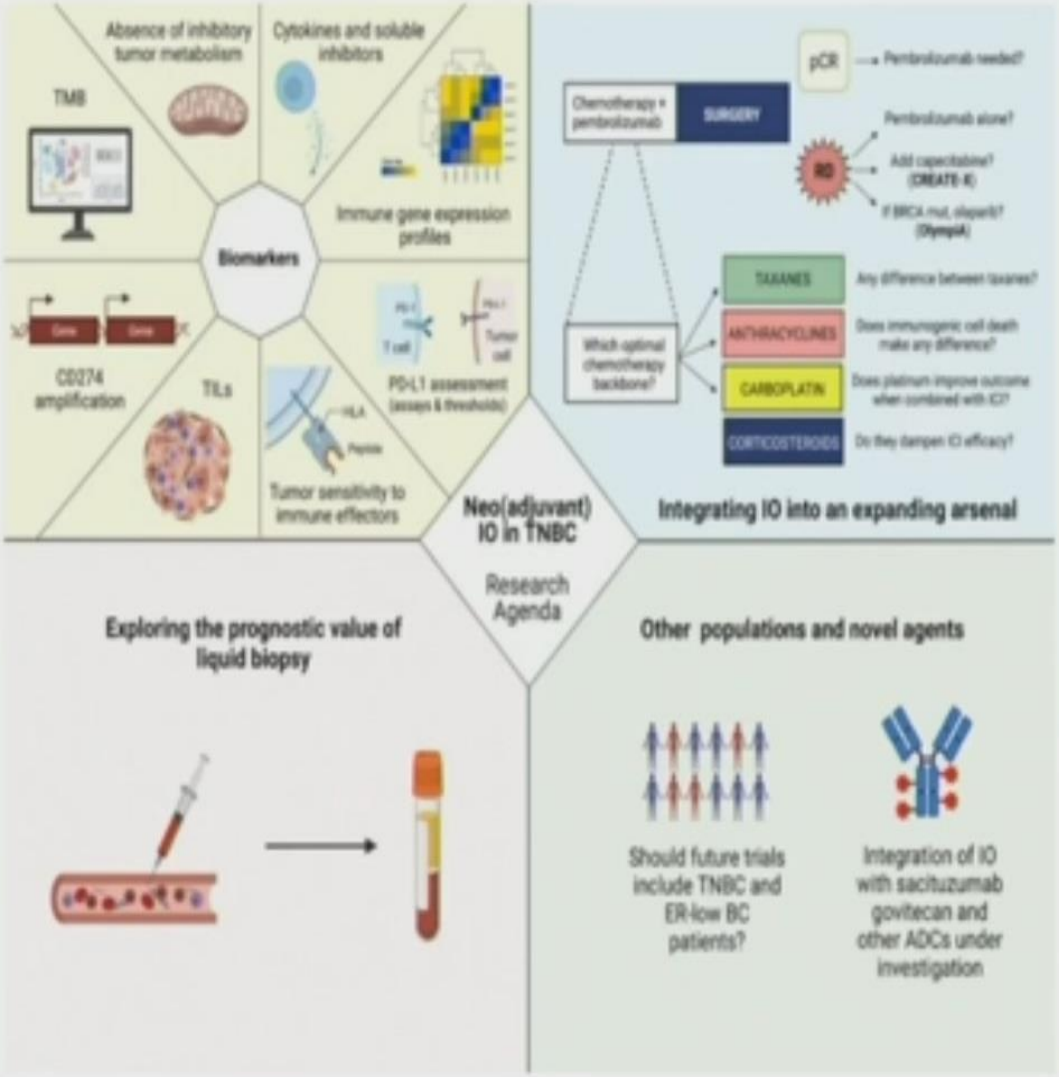
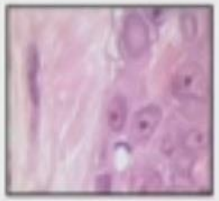
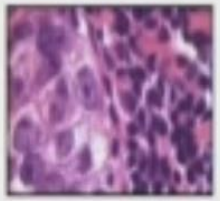
Where do we stand and what do we need to know

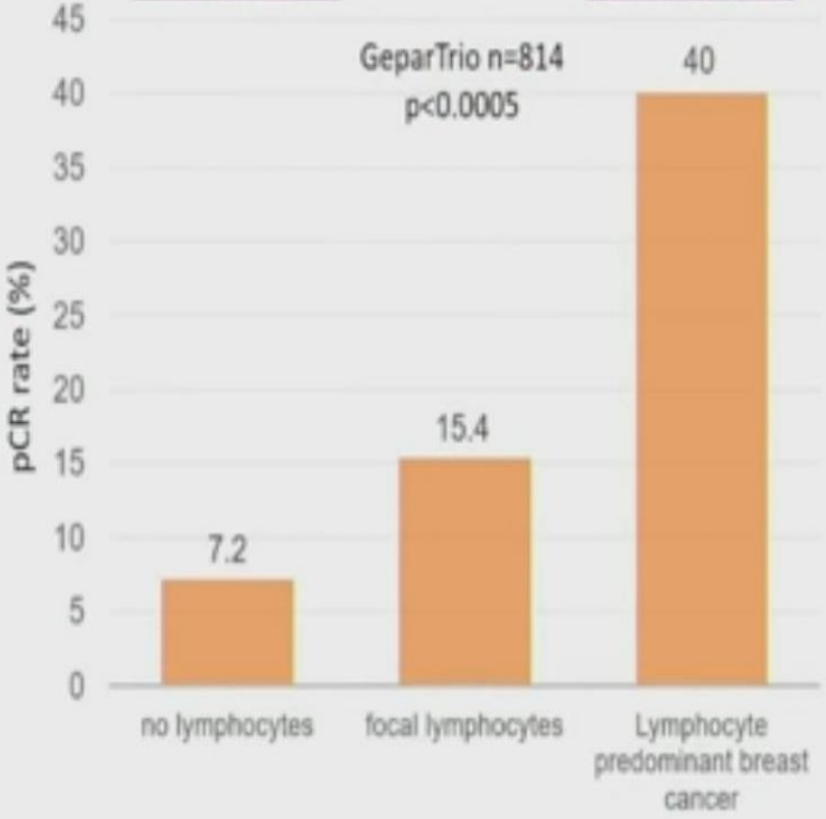


Tarantino P, et al. NPJ Breast Cancer 2022; doi: 10.1038/s41523-022-00386-1

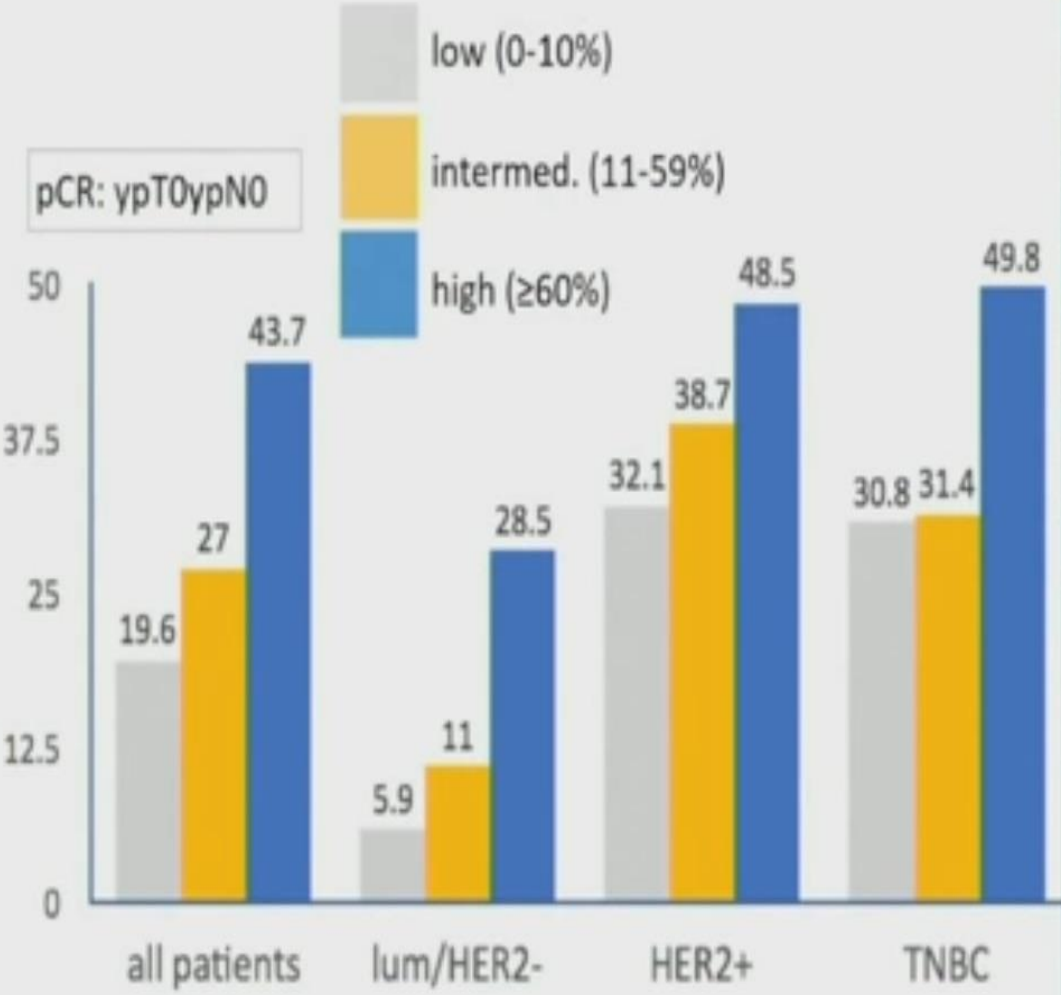
TILs are linked to response to neoadjuvant chemotherapy in all subtypes





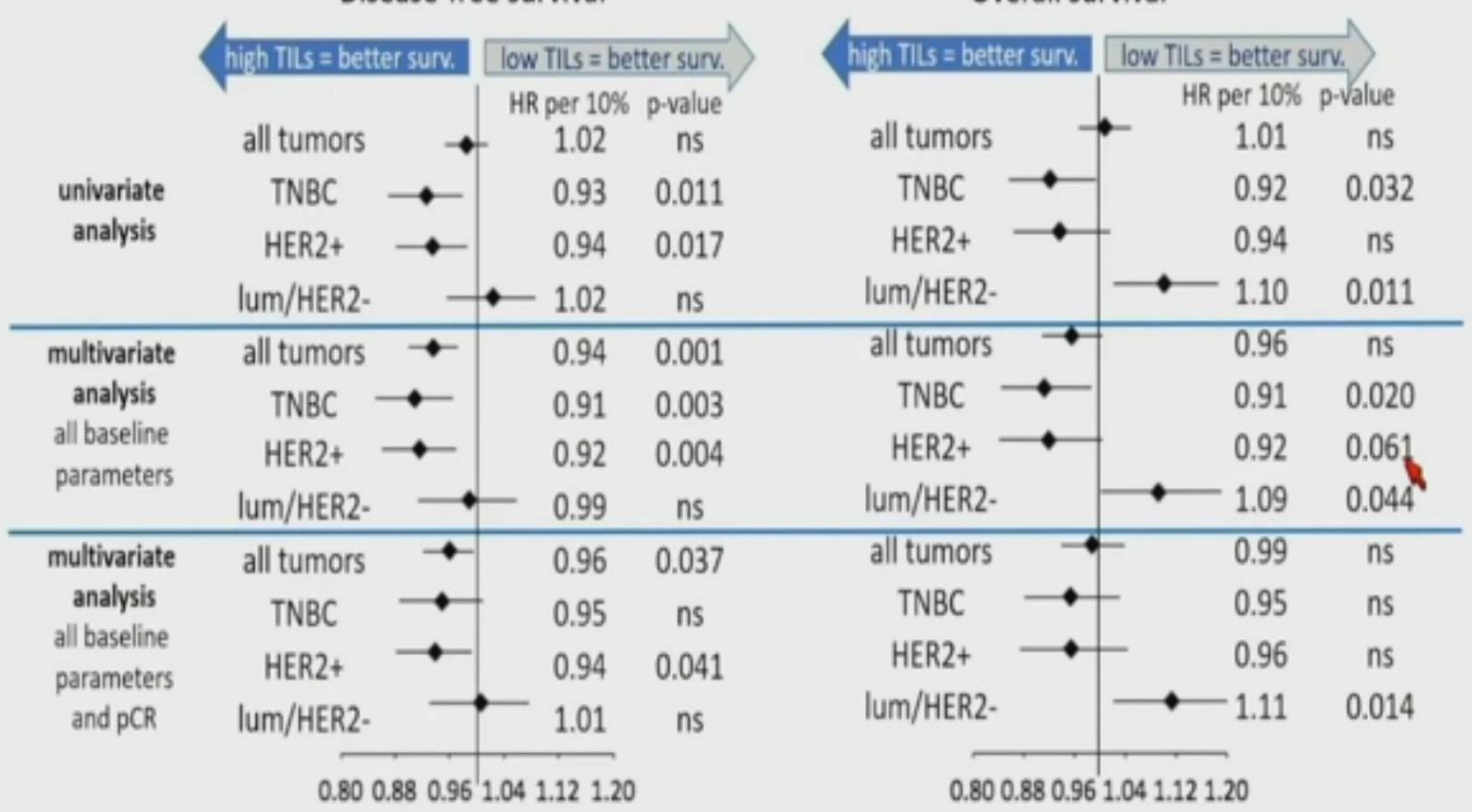


Denkert et al. J Clin Oncol 2010



Denkert et al. Loibl S. Lancet Oncol 2018

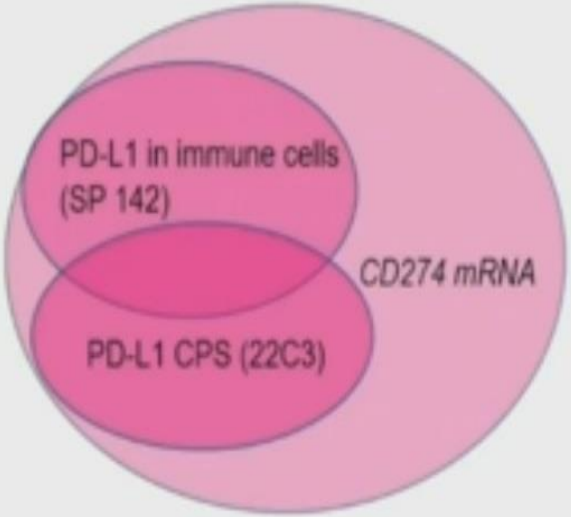
high TILs in pretreament samples→ improved survival in HER2+ and TNBC



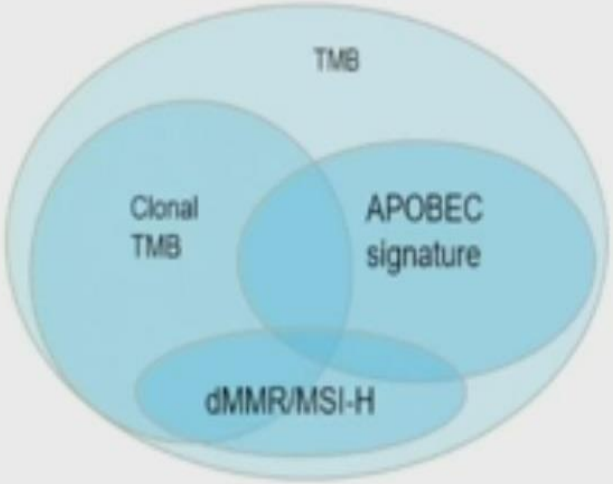
Denkert C et al. Loibl S. Lancet Oncol 2018

Markers Associated with Response to CPI

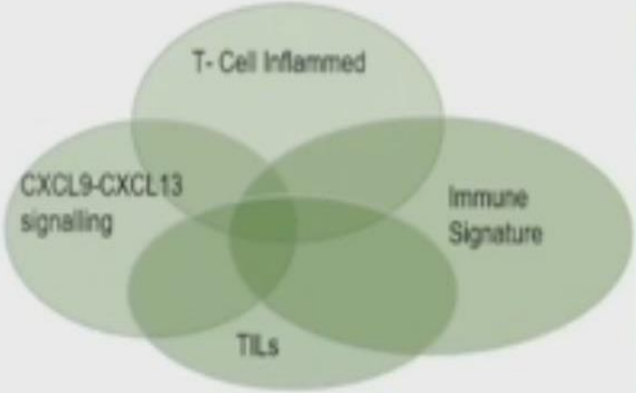
Immune Checkpoints



Tumor Mutations



Immune Cell Infiltration

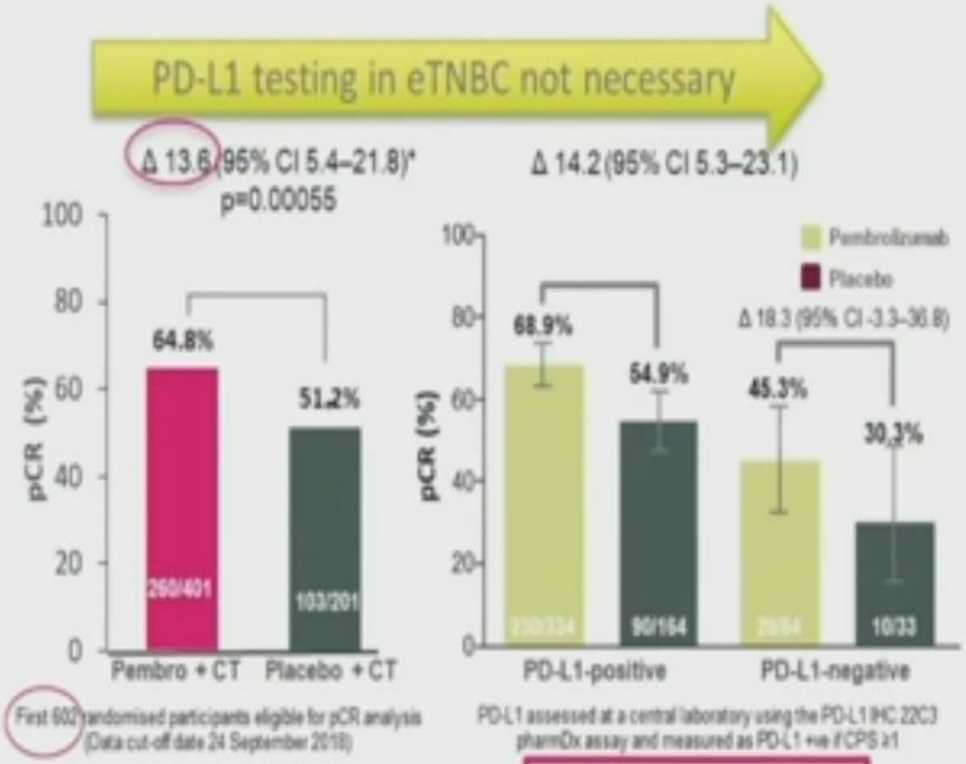


Adapted according to Bianchini G et al. Nature Reviews 2021

KN 522 pCR results

KEYNOTE-522[1] (IA1)
Pembrolizumab + CT vs placebo + CT in early TNBC

PD-L1 testing in eTNBC not necessary

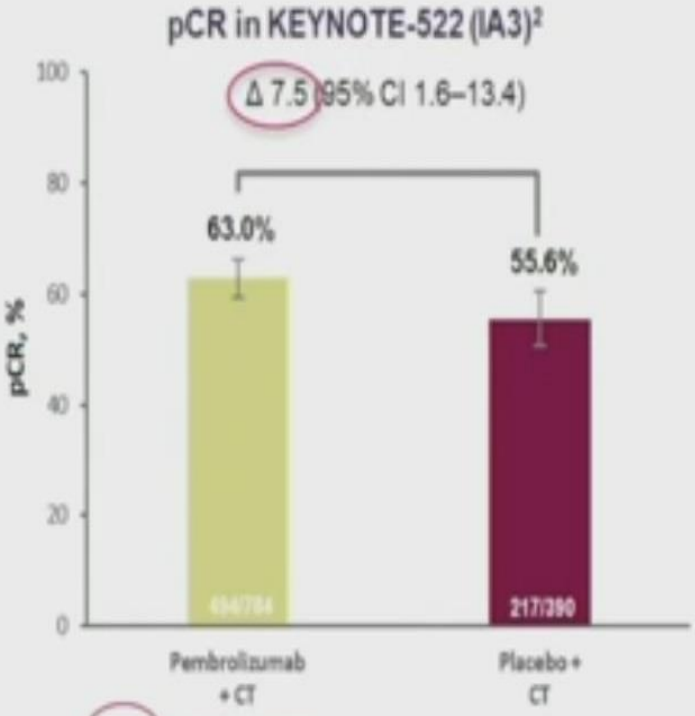


First 602 randomised participants eligible for pCR analysis (Data cut-off date 24 September 2018)

PD-L1 assessed at a central laboratory using the PD-L1 IHC 22C3 pharmDx assay and measured as PD-L1 +ve if CPS ≥1

83% PD-L1 +

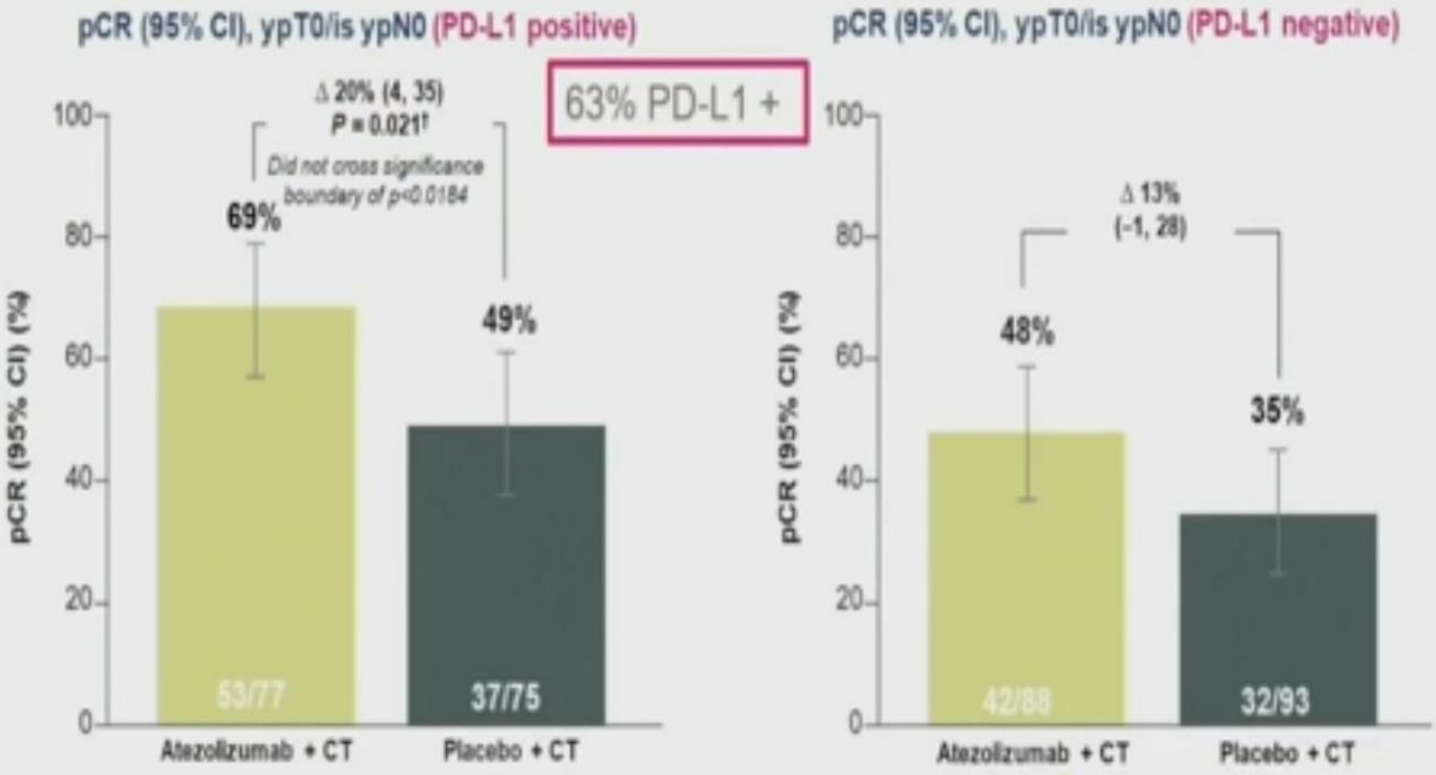
KEYNOTE-522 (IA3)*[2]
Pembrolizumab + CT vs placebo + CT in early TNBC



All 1174 participants in ITT (Data cut-off date 23 March 2020)

Results on pCR by PD-L1 status in Impassion031

IMpassion031
Atezolizumab + CT vs placebo + CT in early TNBC

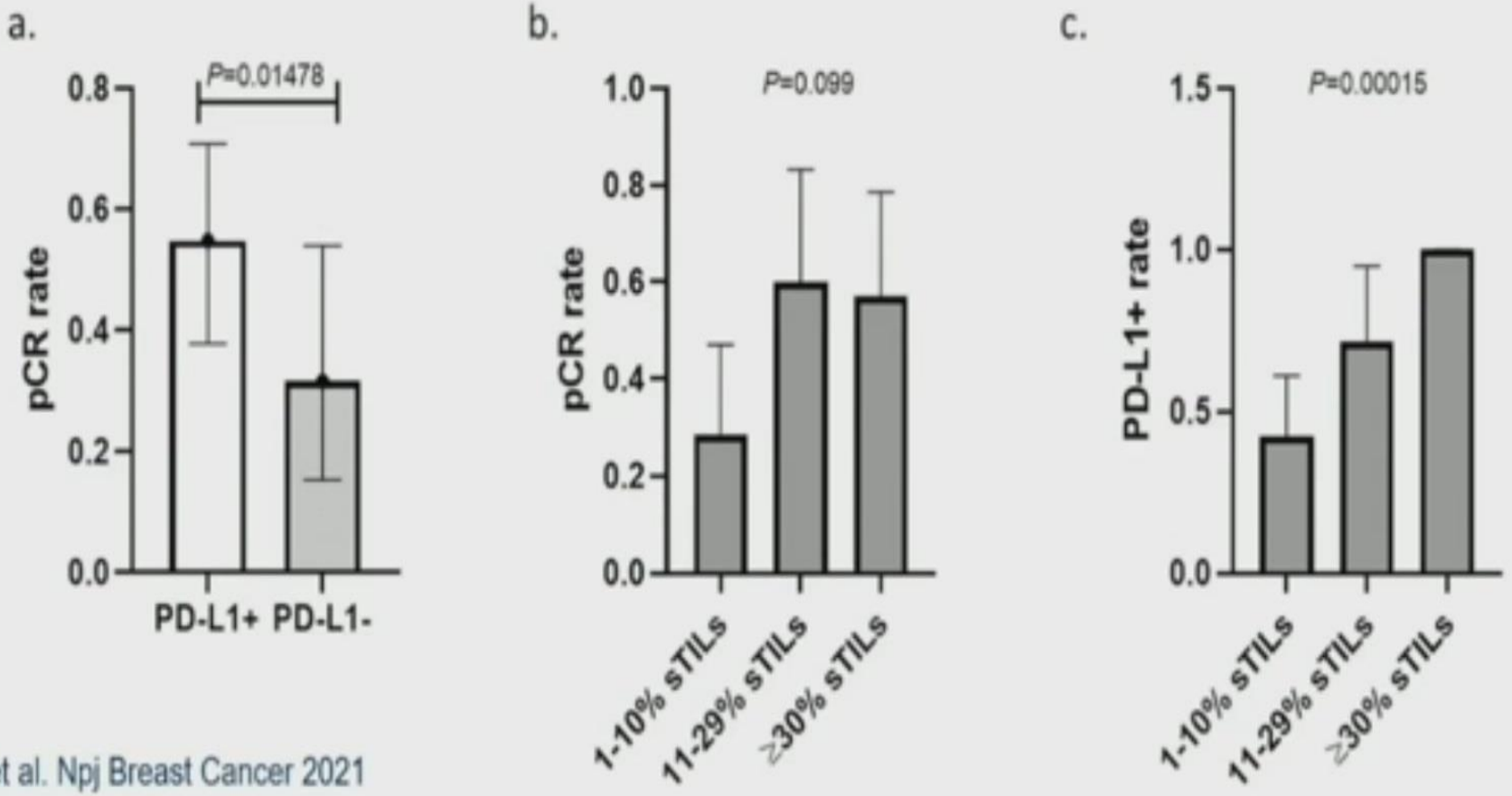


Mittendorf et al. Lancet 2020

PD-L1 testing in early TNBC not necessary

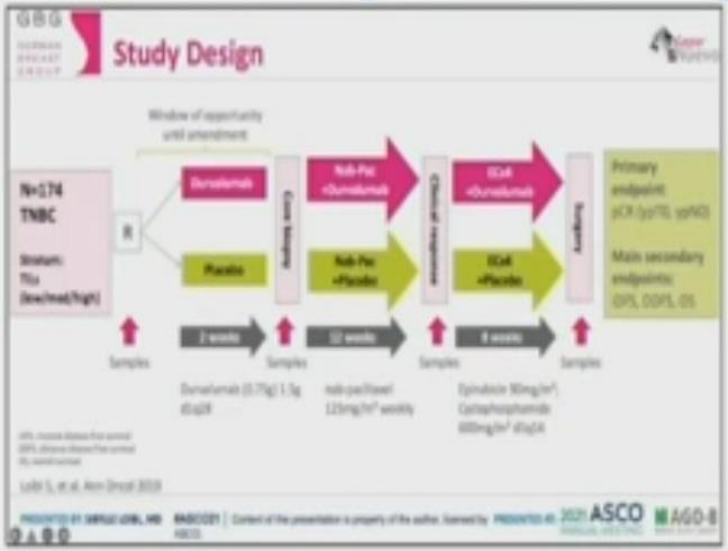
pCR in PD-L1 + and high TILs

Durvalumab 10mg/kg every 2 weeks plus nab-paclitaxel (100 mg/m²) and ddAC resulted in a pCR rate of **44%** (95% CI: 30–57%)



Foldi J et al. Npj Breast Cancer 2021

Evaluation of pCR according to sTILs, iTILs change, PD-L1



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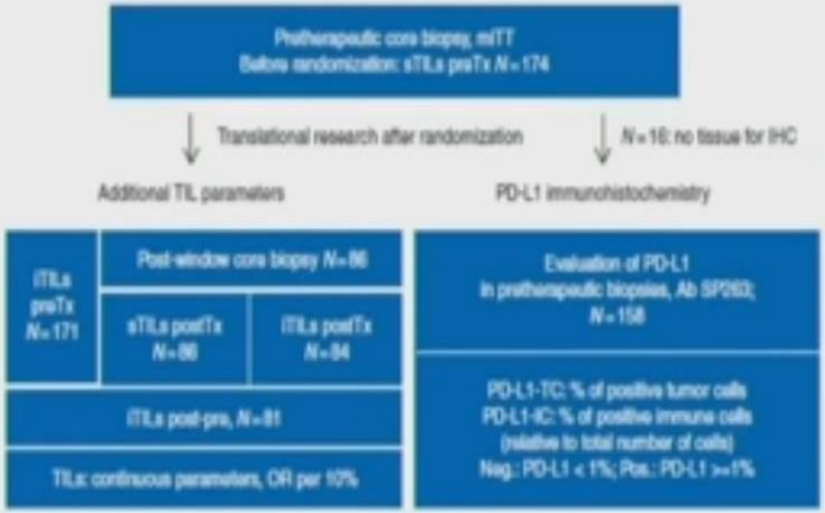

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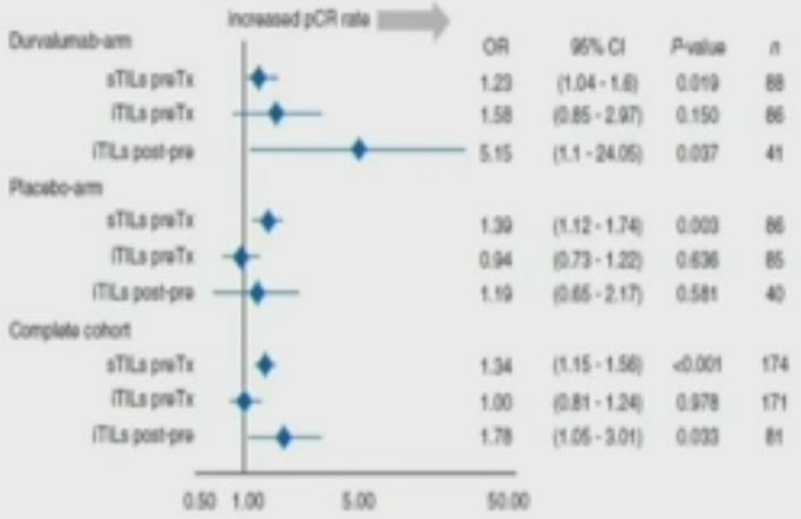

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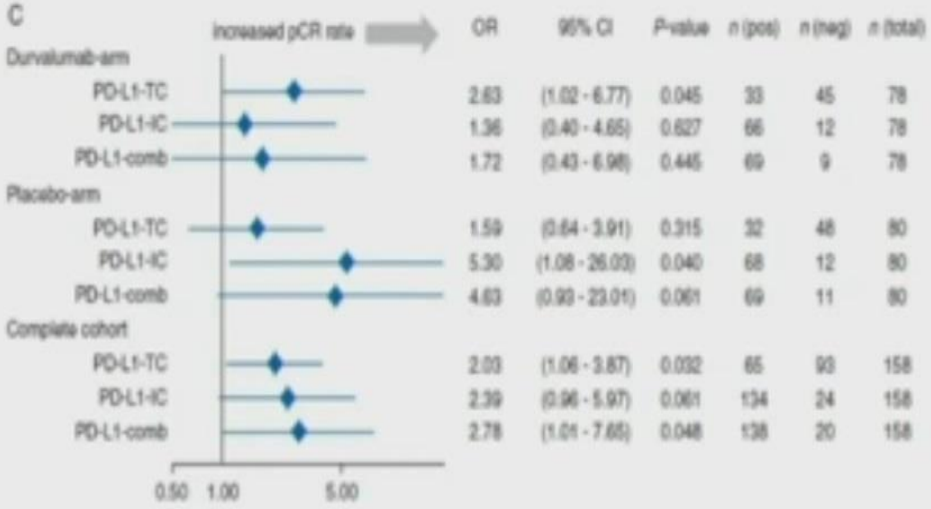
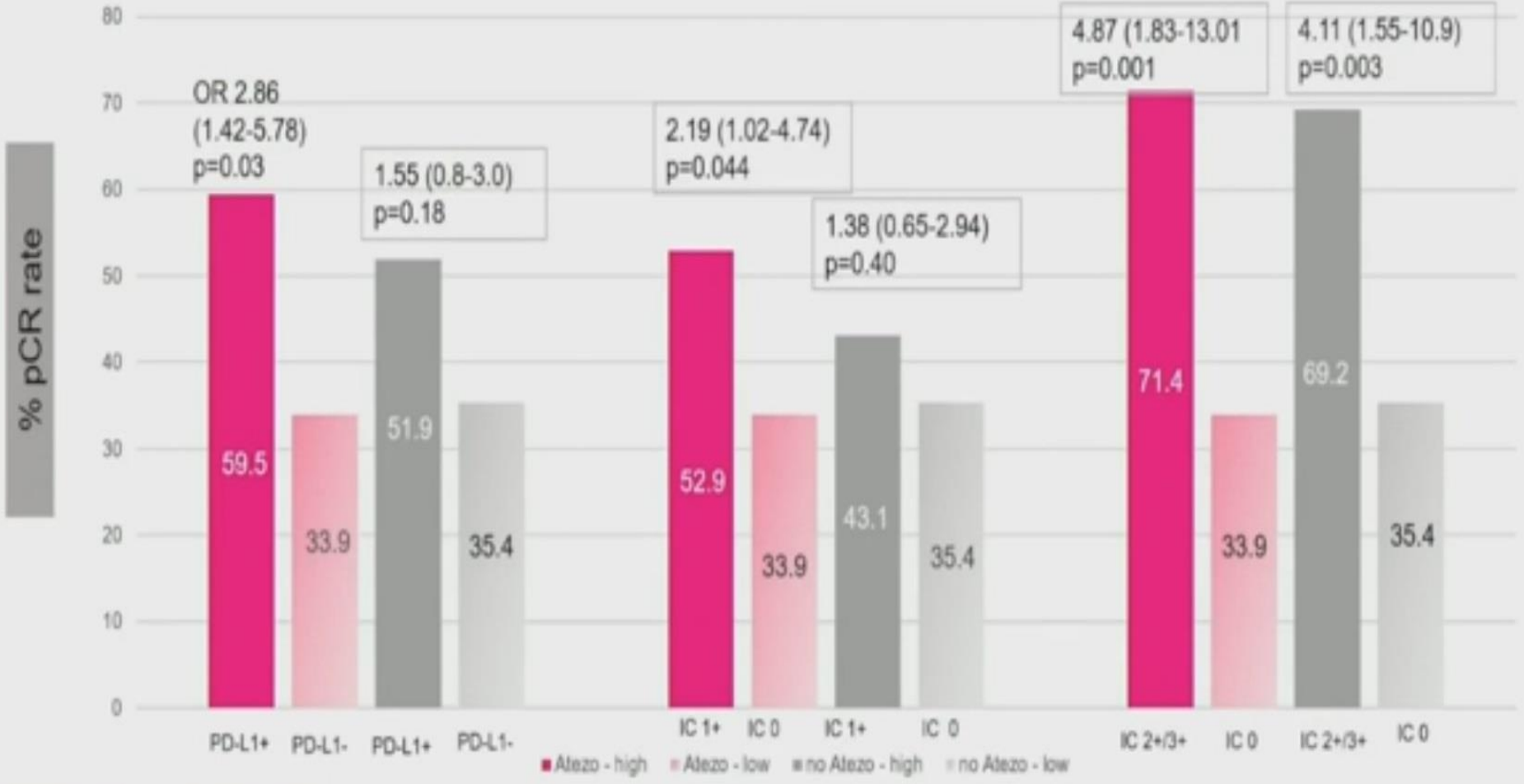


Loibl S et al. Annals Oncol 2019

NeoTrip PD-L1, IC score and pCR



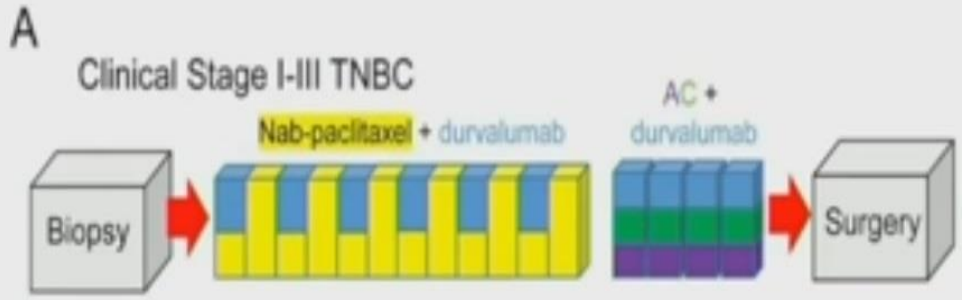
Gianni L et al. Annals Oncol 2022

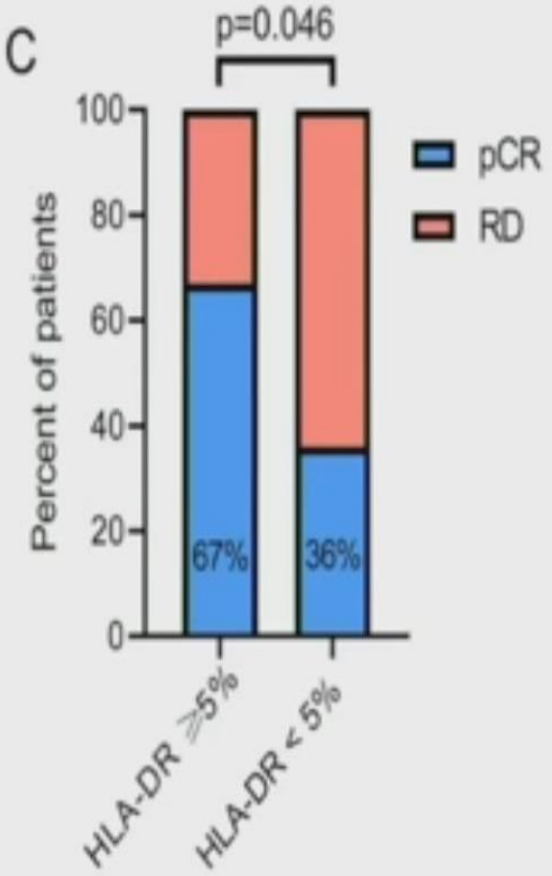
NeoTrip – Multivariate Analysis for pCR

Variable	Effect	Odds ratio (95% CI)	*P* value
Treatment	Atezo versus no atezo	1.11 (0.88-1.40)	0.39
PD-L1 expression	Positive versus negative	2.08 (1.64-2.65)	<0.0001
Disease stage	Early high risk versus locally advanced	0.84 (0.66-1.06)	0.14

Gianni L et al. Annals Oncol 2022

Tumor-specific MHC-II/HLA-DR expression is associated with pathologic complete response to NAC and anti-PD-L1 inhibition



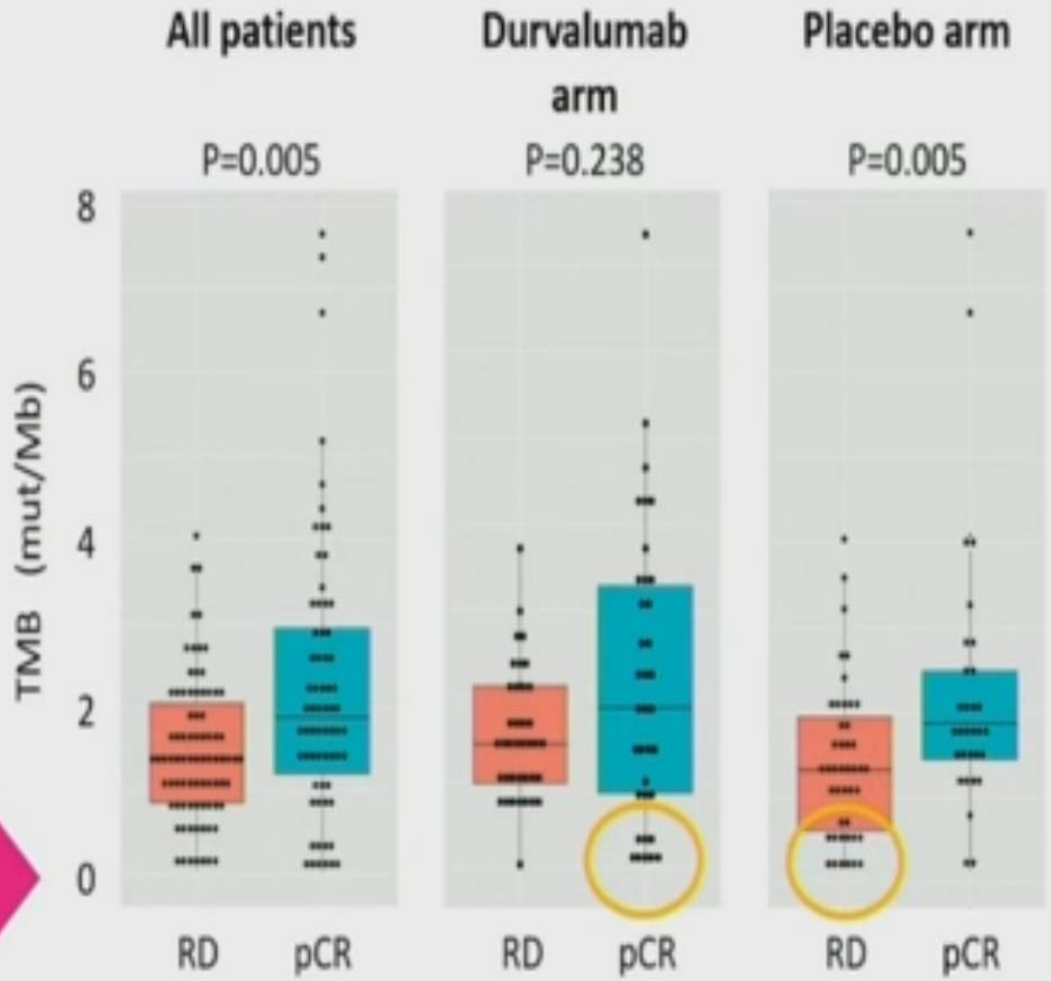


Gonzalez-Ericsson PI, et al. Clin Cancer Res 2022; https://doi.org/10.1158%2F1078-0432.CCR-21-0607

Association of pCR and TMB

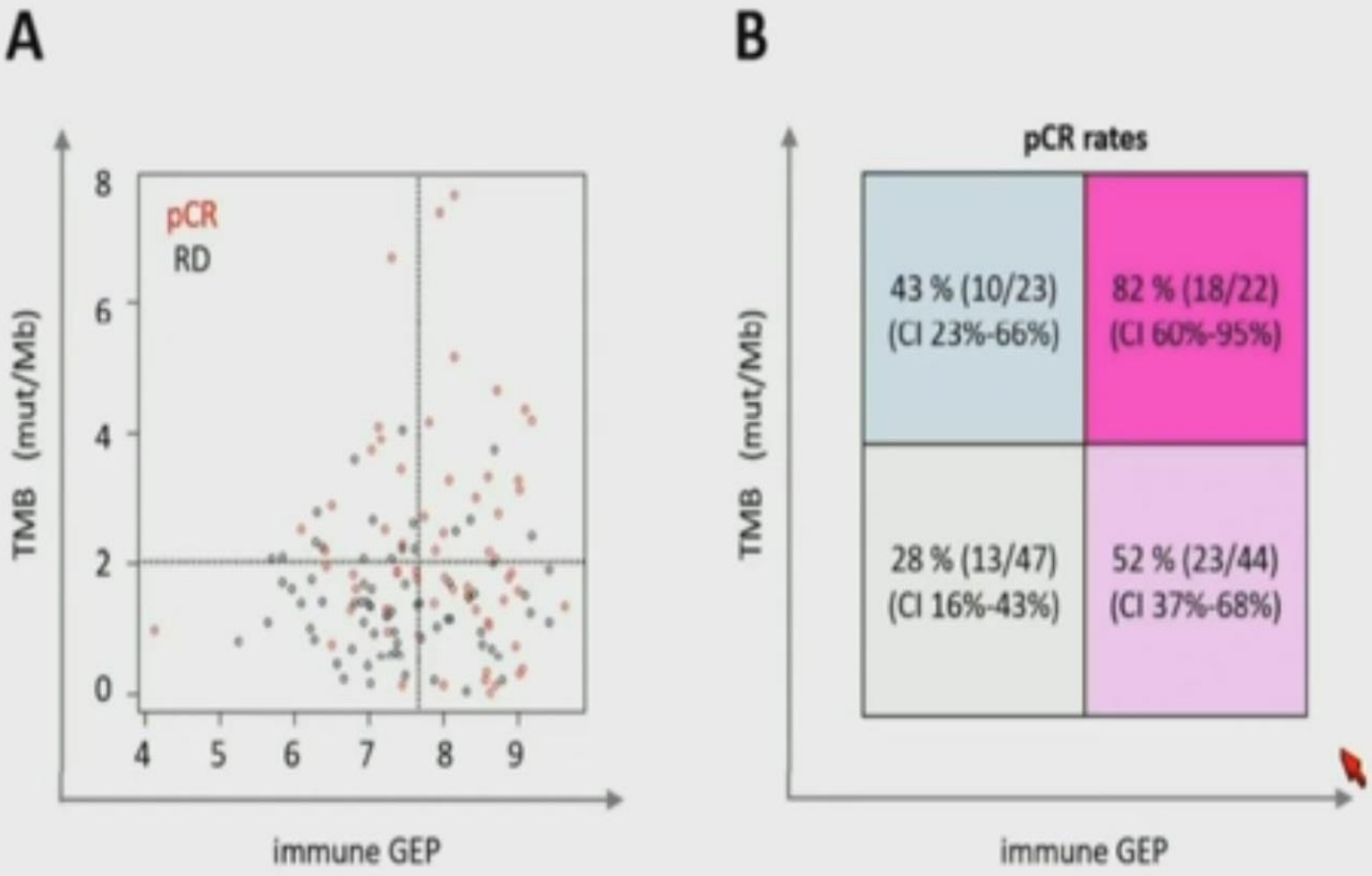
Gepar Nuevo

Cases with lowest TMB values experienced a pCR with durvalumab in contrast to placebo arm



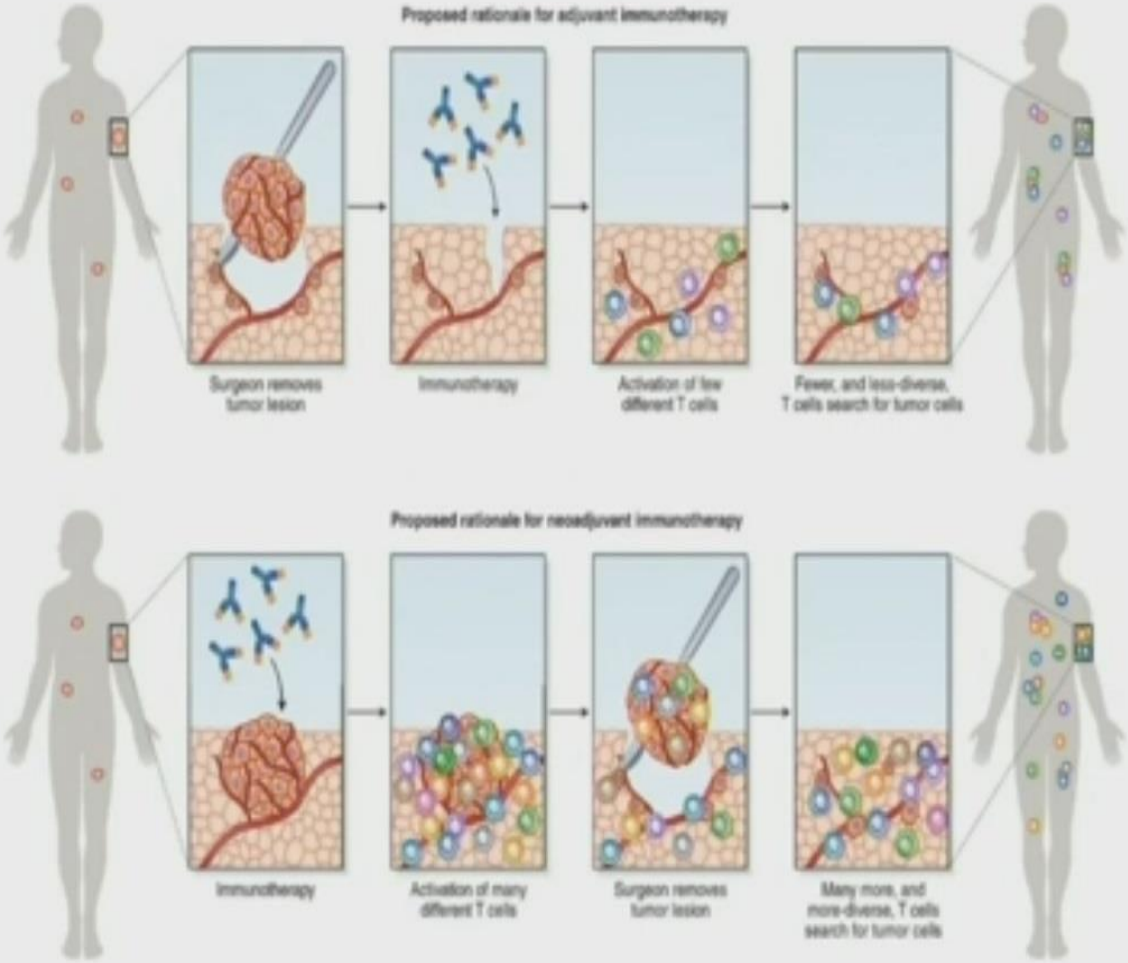
Karn et al. 2020 Ann Onc PMID 32461104

TMB and Immune gene expression predict pCR



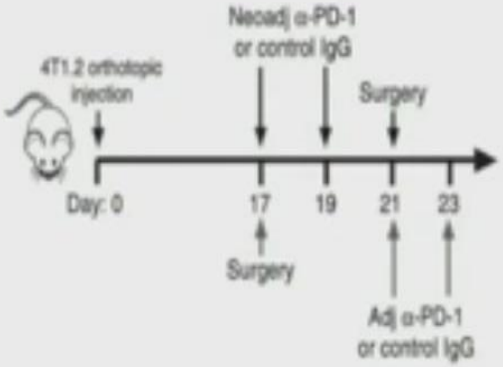
Karn T et al. Annals Oncol 2020

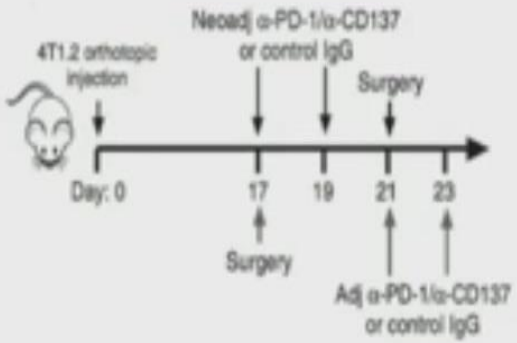
Adjuvant vs Neoadjuvant CPI Therapy

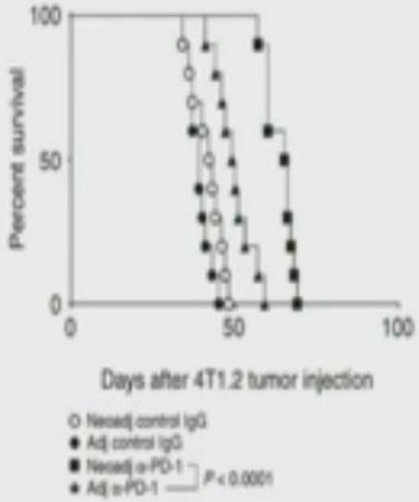


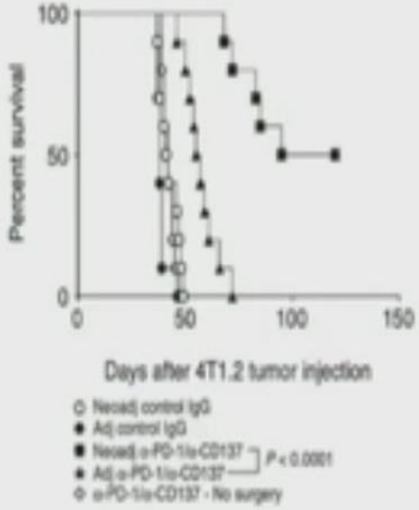
Versluis JM et al. Nature Med 2020

Mice receiving neoadjuvant IO live longer









Liu et al. Cancer Discovery 2016

Survival Data with CPI as neoadjuvant therapy

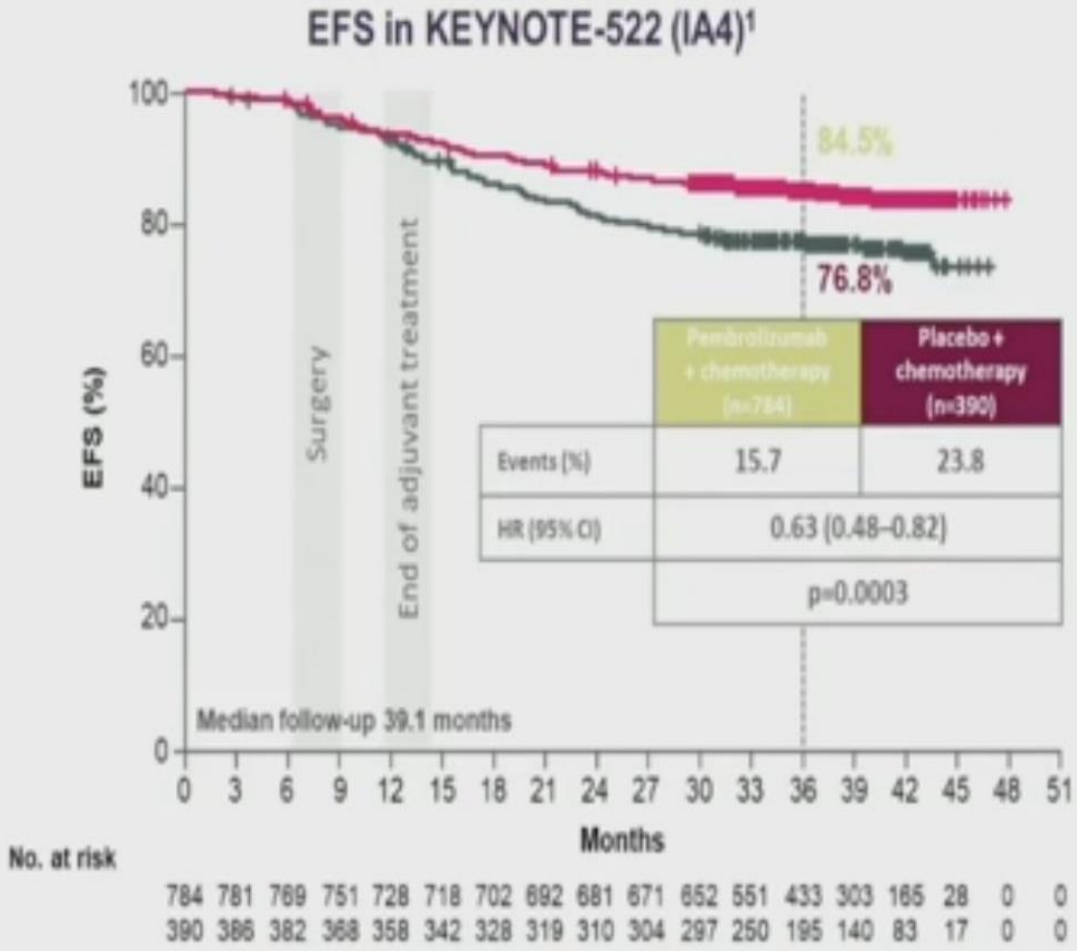
PRESENTED BY: Sibylle Loibl, MD PhD

EFS KN 522

KEYNOTE-522[1] (IA4)
Pembrolizumab + CT vs placebo + CT in early TNBC

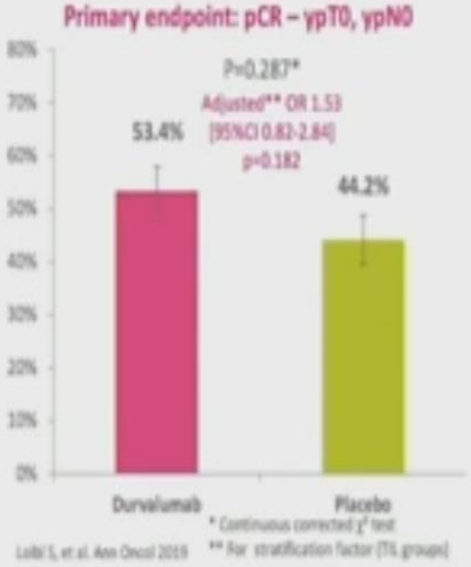
PD-L1 $_{negative}$ (HR 0.48, 95% CI 0.28–0.85)

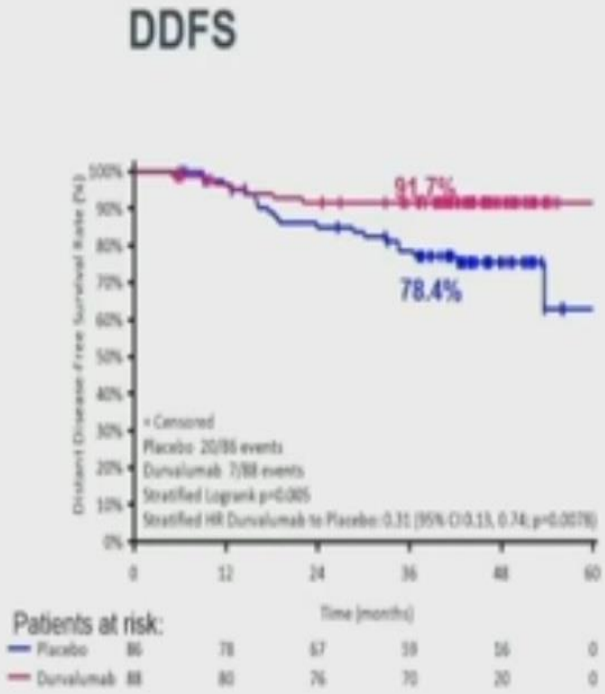
PD-L1 $_{positive}$ (HR 0.67, 95% CI 0.49–0.92)

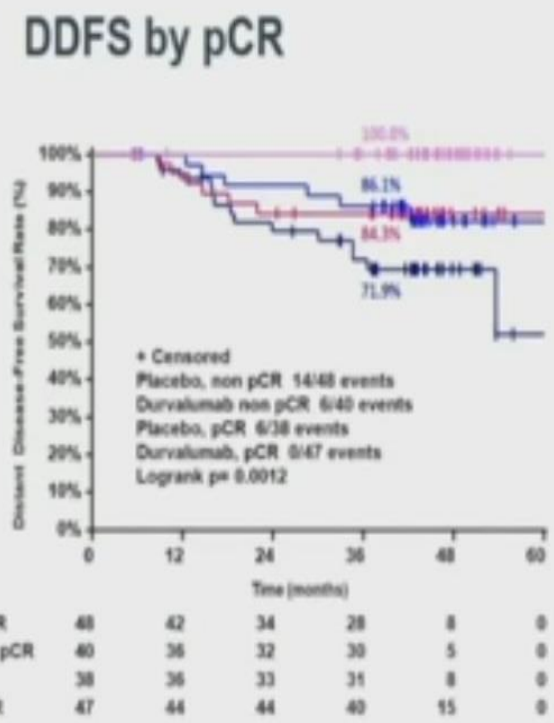


Schmid P et al. New Engl J Med 2022

GeparNUEVO clinical results



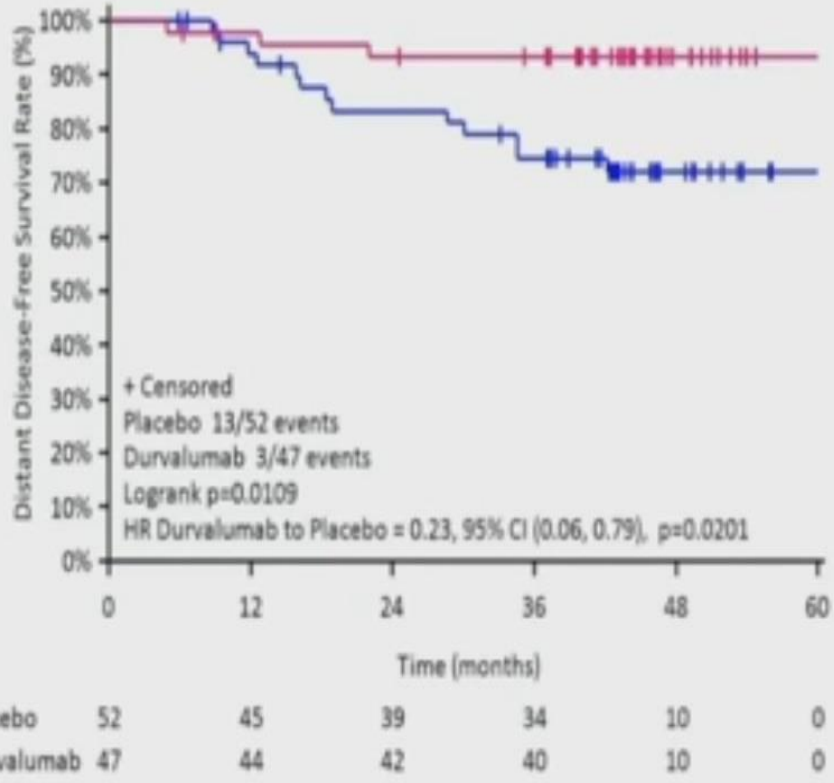




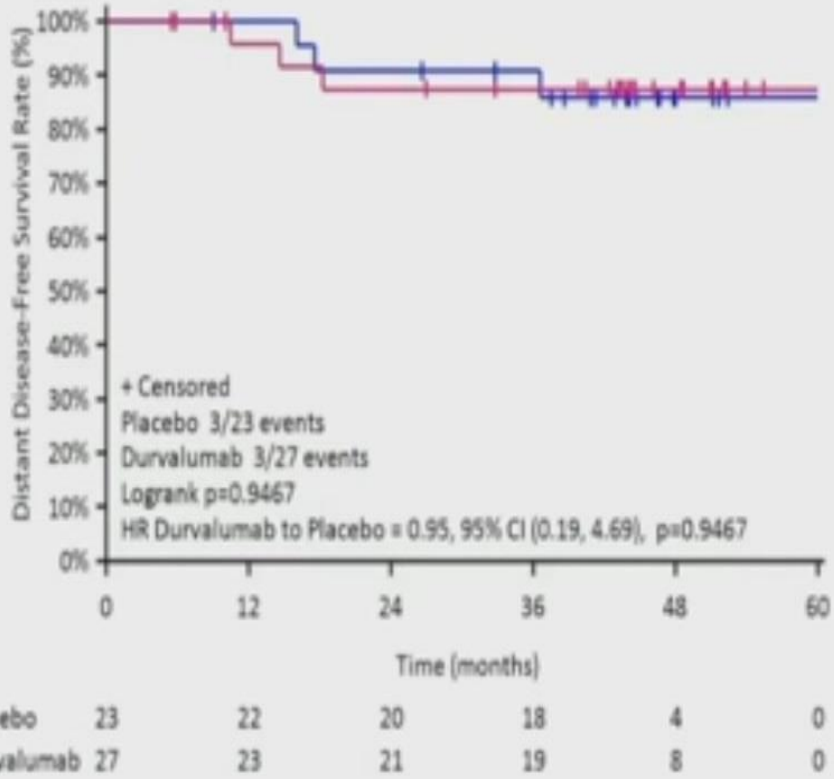
Loibl S et al. Annals Oncol 2019 and ASCO 2021

DDFS according to treatment in TMB subgroups

Low TMB (Tertile 1 & 2)

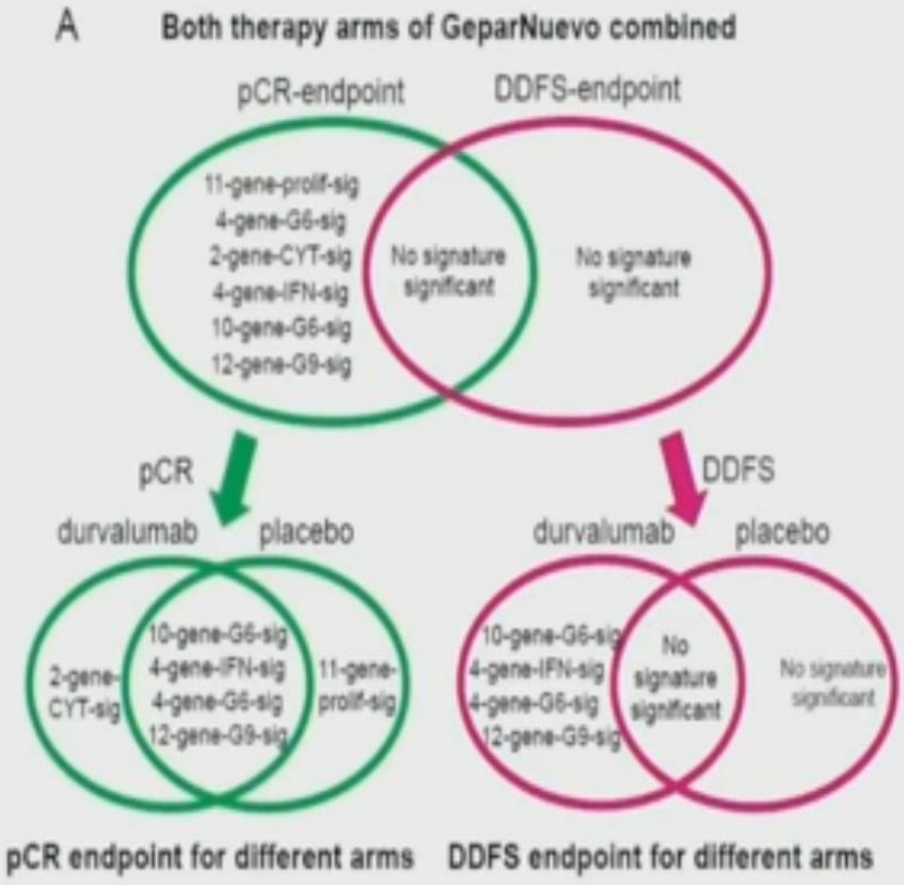


High TMB (Tertile 3)

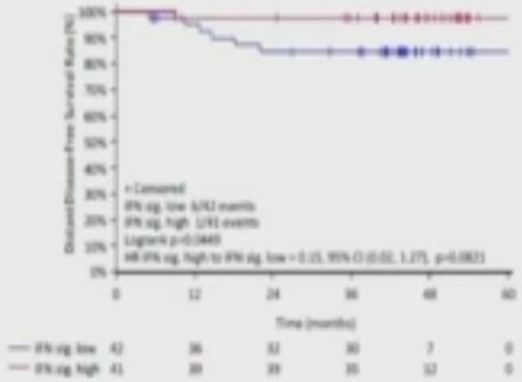


Karn T et al. ASCO 2022 #581

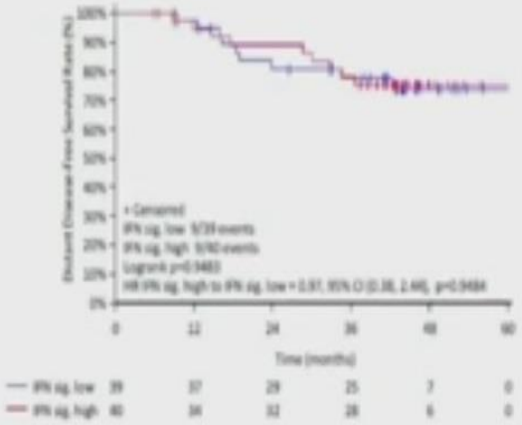
Immune genes predict response to Durvalumab



B: IFN-signature in durvalumab arm



C: IFN-signature in placebo arm



Denkert C et al. ASCO 2022 #583

Conclusion

- Role of Immune Cells/Tumor Cells as Response Predictor for CPI in Early TNBC unclear at this point in time.
- Patients with sTILS at baseline and in residual tumor have a very good prognosis
- Immune Cells, Immune Genes, PD-L1 Expression and TILs **predict** pCR rate after NACT+/-CPI
- Immune Cells, PD-L1 Expression and TILs **do not predict** treatment effect of CPI added to NACT
- Immune signatures might be able **to predict** response to Durvalumab
- pCR **does not correlate** well with long-term outcome in TNBC after NACT+ CPI in contrast to chemotherapy alone
- Neoadjuvant CPI therapy might be superior to adjuvant CPI therapy – no evidence from clinical trials yet
- More biomarker data needed for long term outcome after CPI

Open Questions and Potential Trials

Do we need CPI after neoadjuvant therapy?

- TNBC
- NACT +CPI
- pCR
- No pCR with high TILs in RD

R

- Continue CPI after surgery as per SOC
- No further treatment

Is neoadjuvant CPI therapy better than adjuvant?

- TNBC

R

- Adjuvant CPI
- Neoadjuvant CPI