

Immunotherapy: Wait, Why Wait?

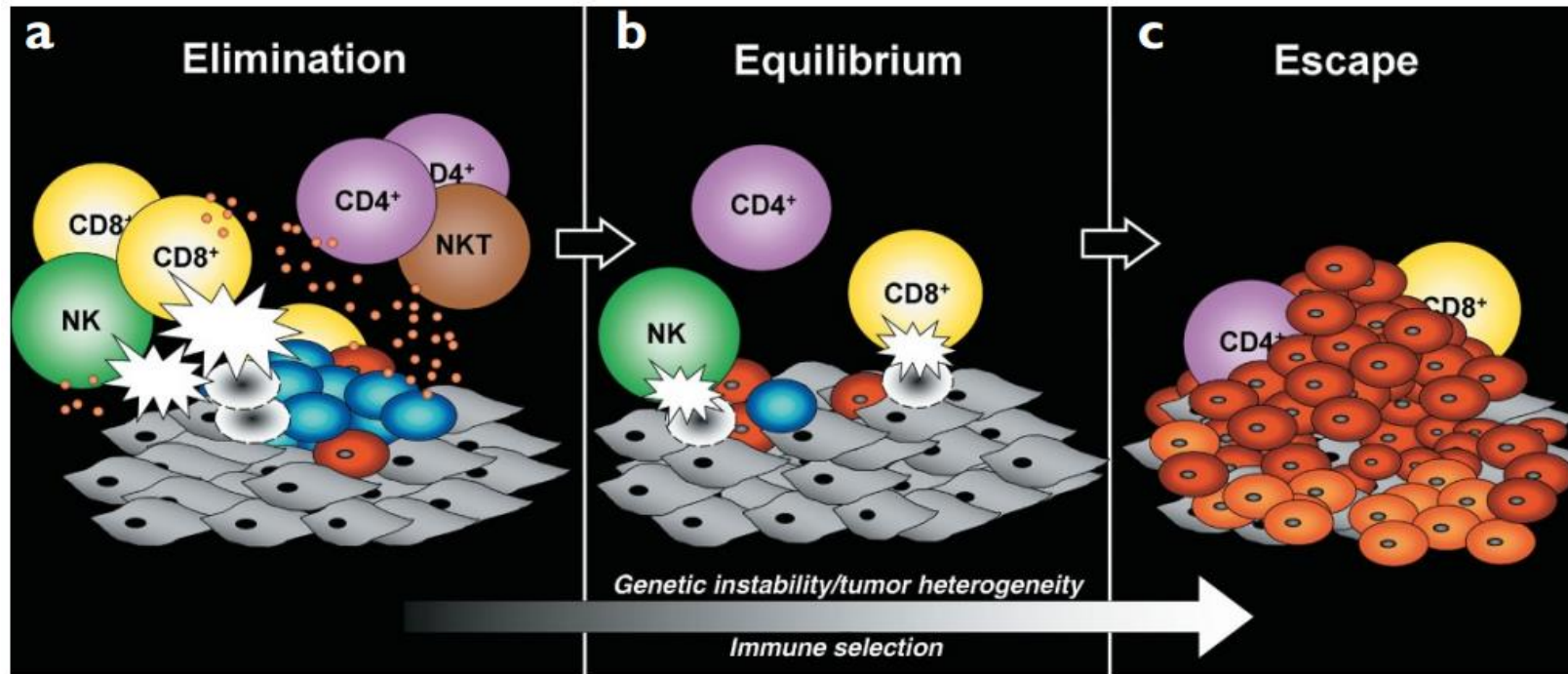
V.K. Gadi, MD PhD

Deputy Director, U of Illinois Cancer Center

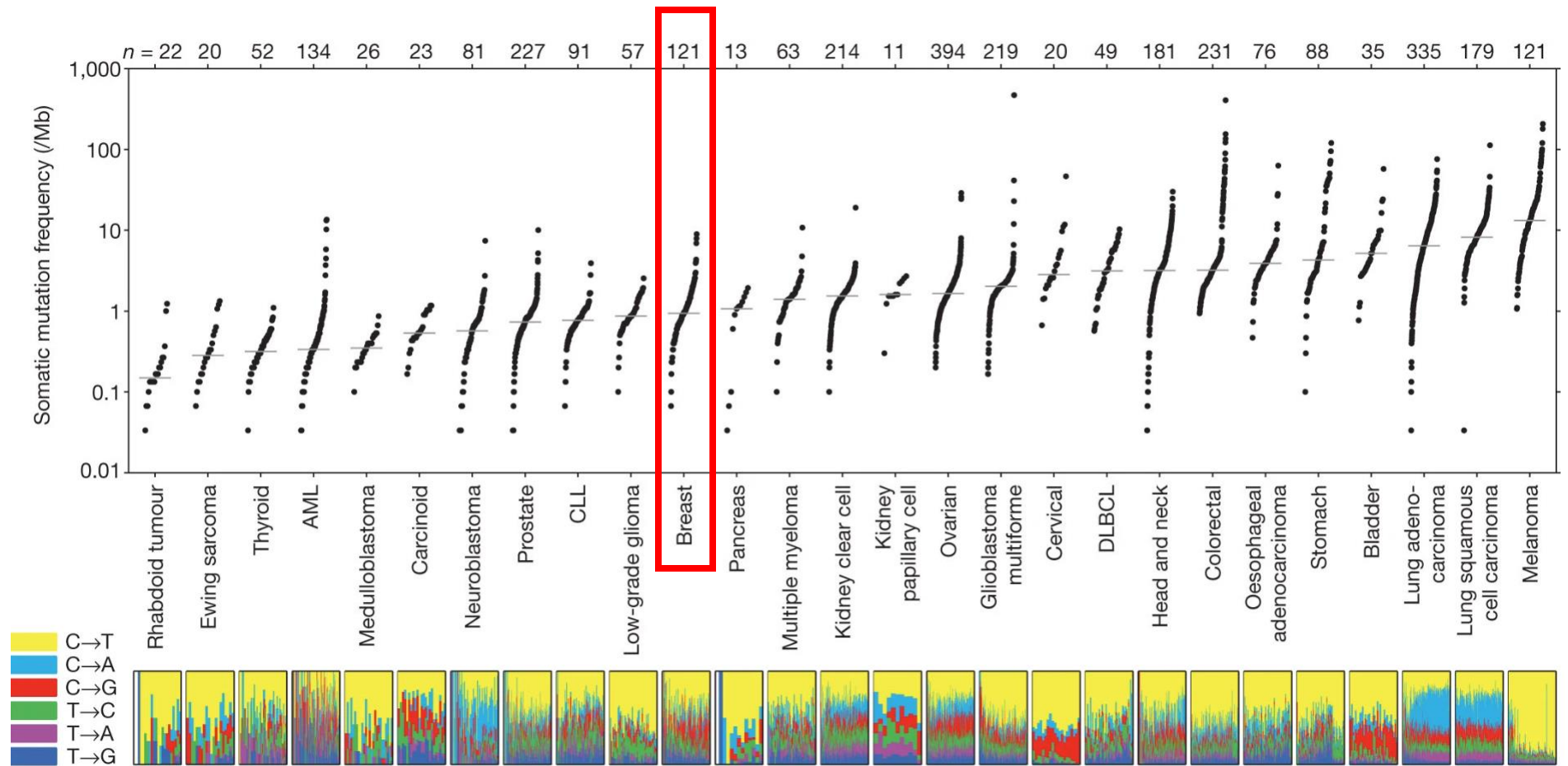
October 20, 2024



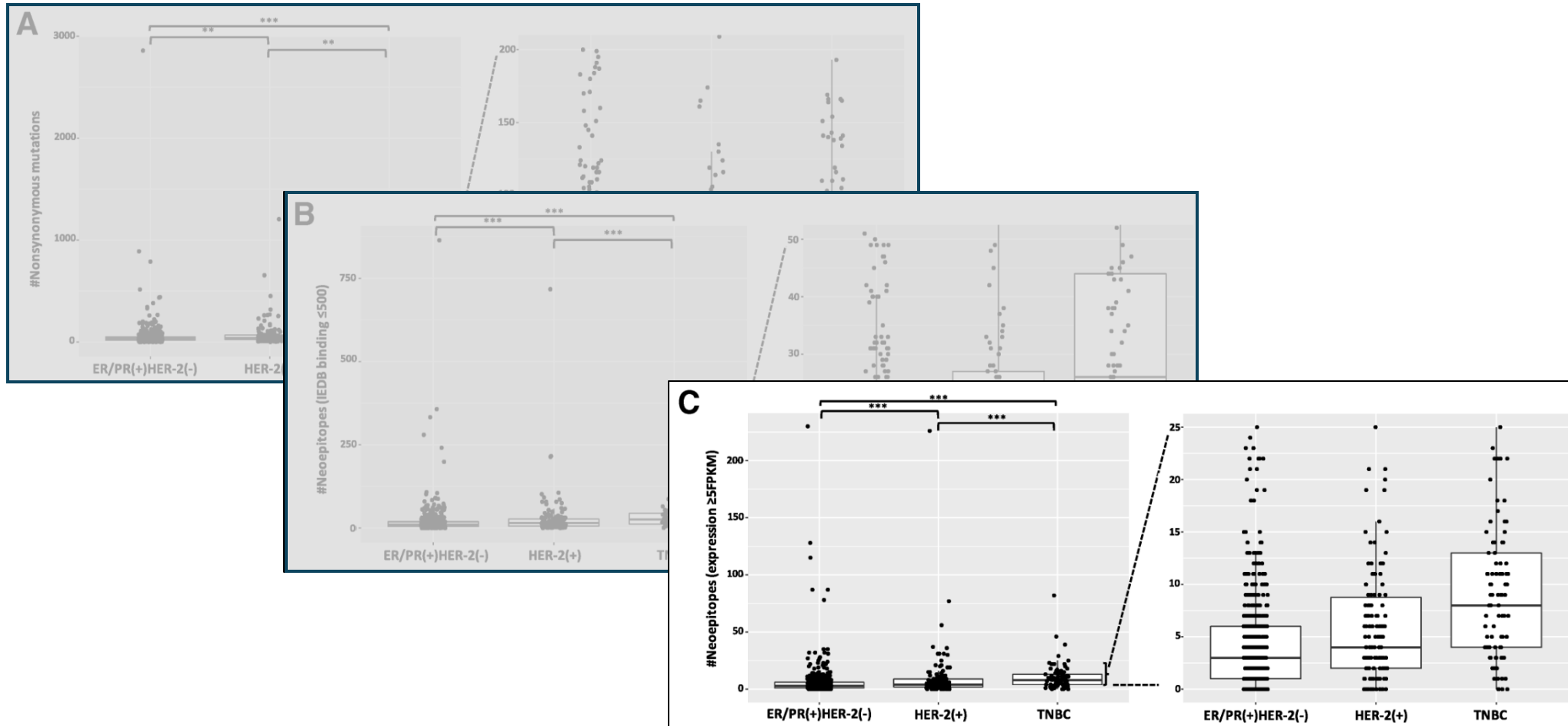
Immunoediting: The immune system as a selection pressure



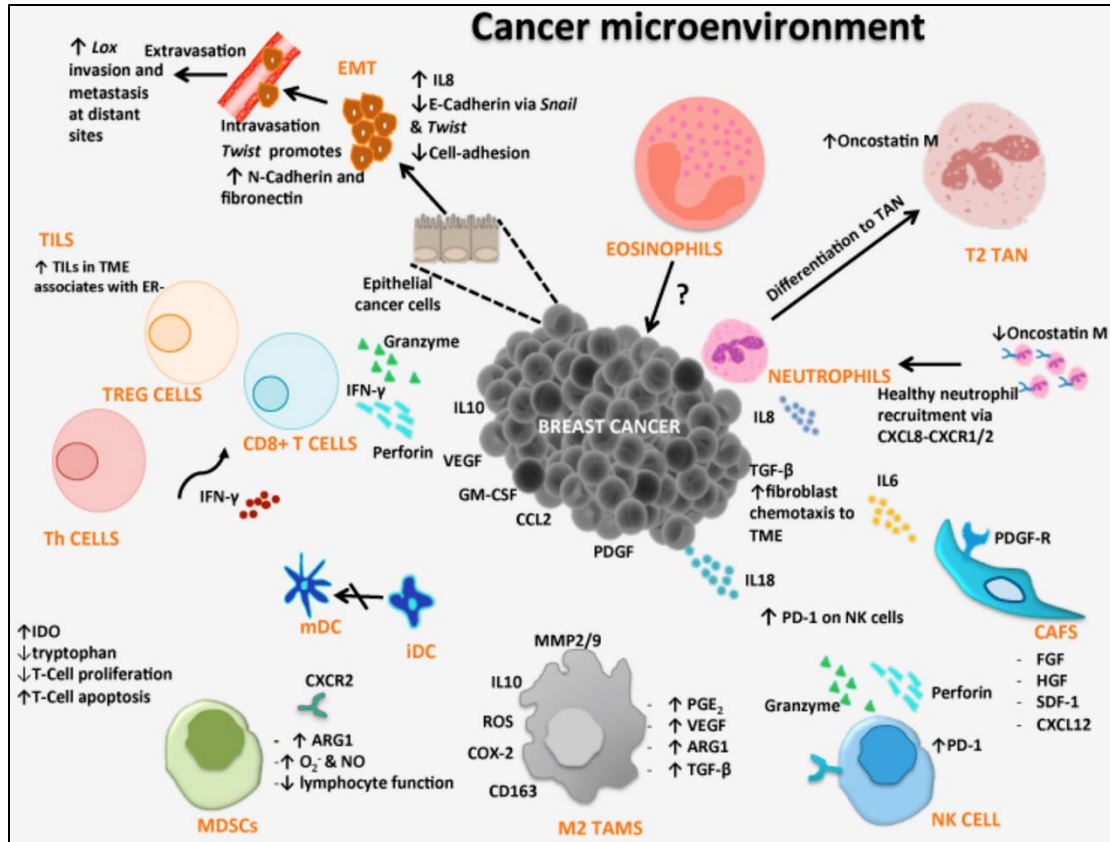
TMB: Breast isn't the worst



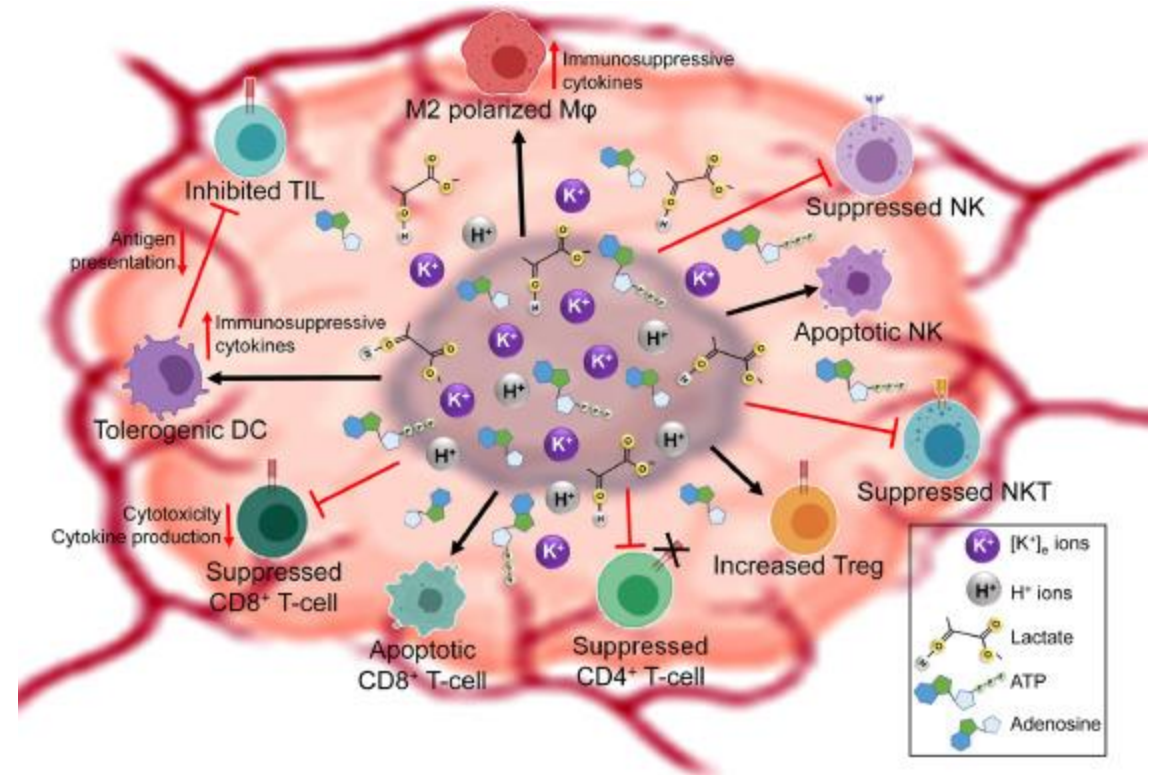
Funny looking DNA -> Funny looking proteins



The Obligatory TME slide



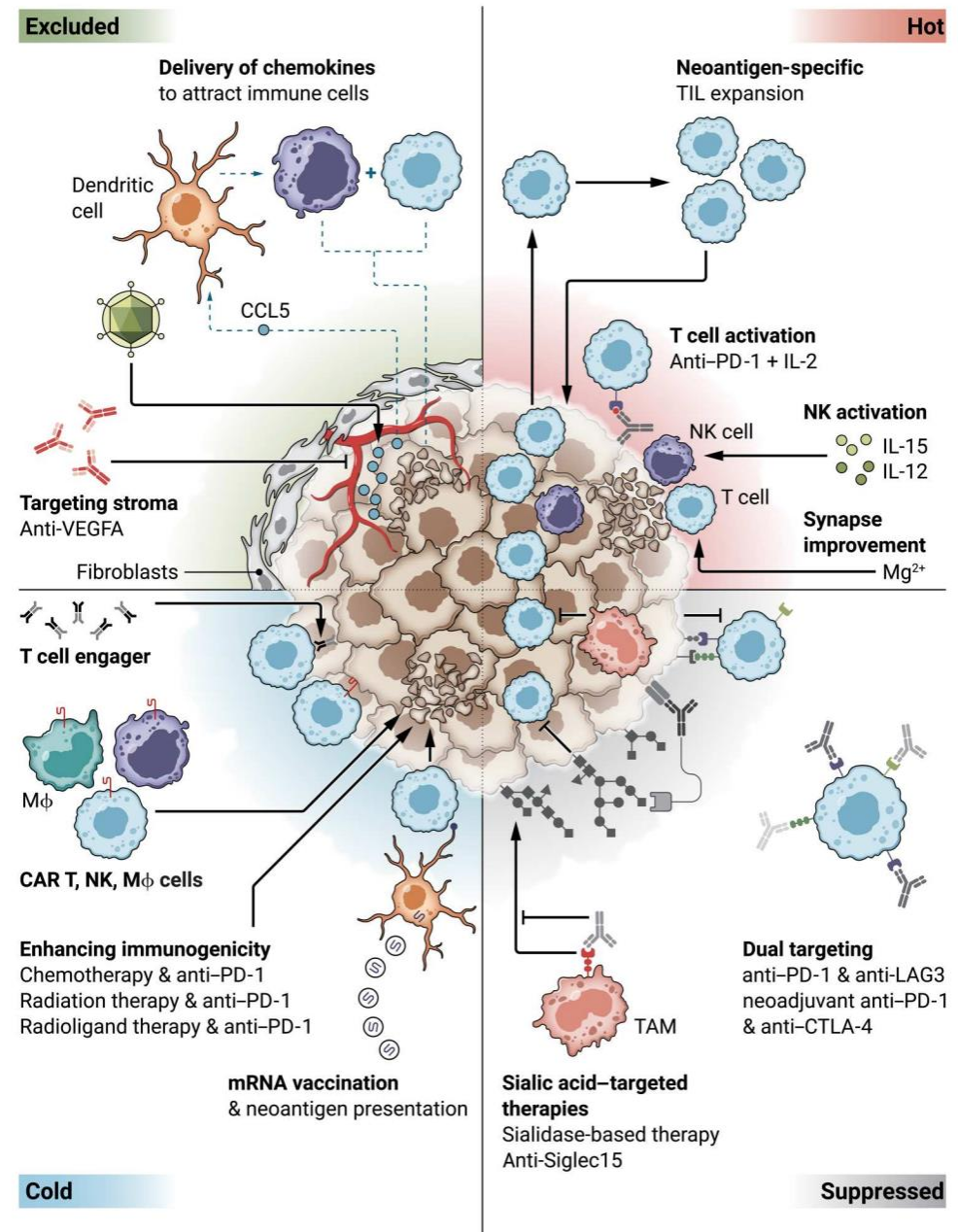
Barriga, Cancers, 2019



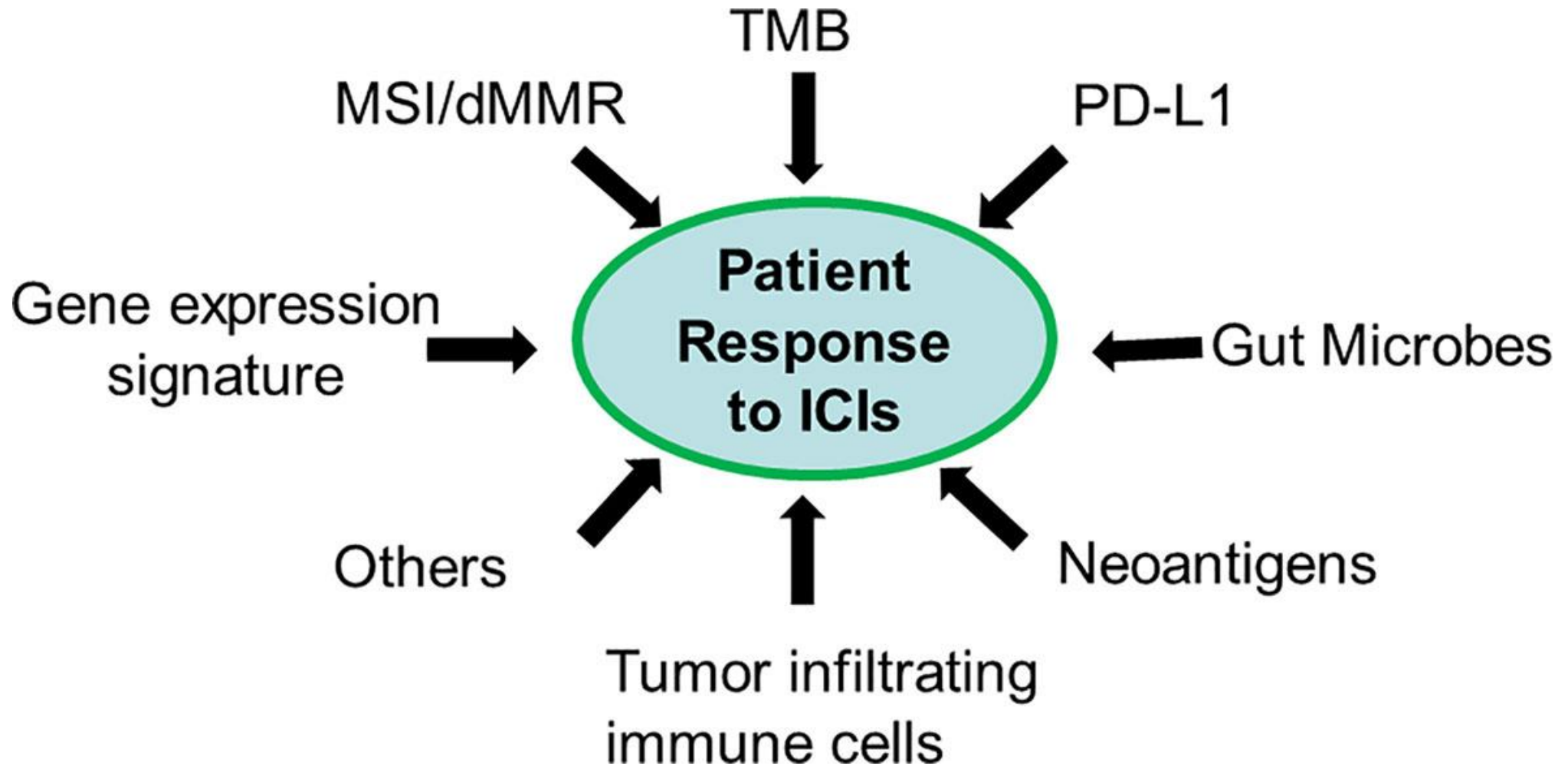
Verma, EBioMedicine, 2022

TME terms

- Hot – primed and ready
- Cold – turn the temp up
- Excluded – open the door
- Suppressed – multiple checkpoints at play



Biomarkers

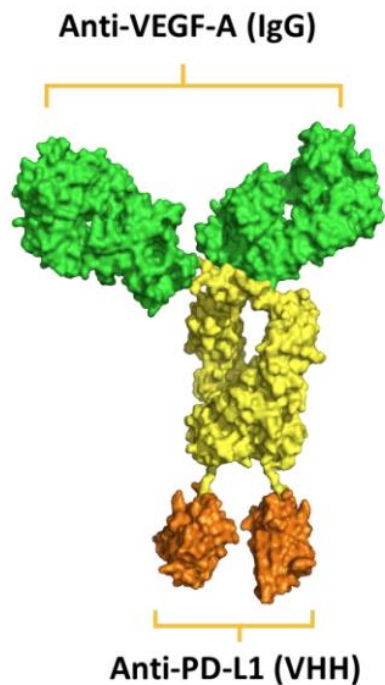


Immune Tools

- Checkpoint inhibitors
- Vaccines
 - Adjuvants
 - mRNA
- Oncolytic viruses
- Cell therapies
 - APC
 - Tcell
 - NKcell
 - Stem cell transplant

A Couple of Updates

A Phase Ib/II Study to Assess the Safety and Efficacy of PM8002/BNT327 in Combination with Nab-Paclitaxel for First Line Treatment of Locally Advanced or Metastatic Triple-Negative Breast Cancer



- Open-label Single-arm, Phase Ib/II Study of PM8002/BNT327 + nab-paclitaxel for 1L TNBC (NCT05918133)

Key Eligibility Criteria

- Patients with locally advanced or metastatic TNBC who have not received prior systemic therapy for unresectable locally advanced or metastatic advanced TNBC
- Age \geq 18 years
- ECOG score 0-1
- Adequate organ function

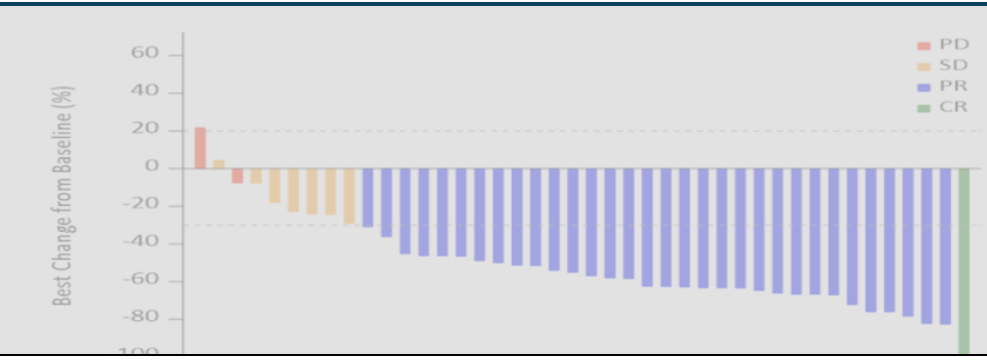
PM8002/BNT327 20mg/kg Q2W on Day 1, 15 of 28-day cycle
+
nab-paclitaxel 100mg/m² on Day 1, 8, 15 of 28-day cycle

until disease progression/
unacceptable toxicity

- ✓ **Primary endpoints:** ORR (RECIST V1.1), safety (CTCAE 5.0)
- ✓ **Secondary endpoints:** PFS, DCR, OS

Patient Characteristics (n=42)	
Median age, years (Q1, Q3)	53.5 (41.0, 60.0)
Number of metastatic sites, n (%)	
0-2	17 (40.5)
\geq 3	25 (59.5)
Liver metastasis, n (%)	
Yes	16 (38.1)
No	26 (61.9)
Brain metastasis, n (%)	
Yes	2 (4.8)
No	40 (95.2)
Neo/adjuvant Paclitaxel treatment, n (%)	
Yes	28 (66.7)
No	14 (33.3)

Variable	ITT	PD-L1 CPS<1	PD-L1 1≤CPS<10	PD-L1 CPS≥10	NOT DETECTED
Population (n)	42	13	16	9	4
CR	1 (2.4)	0 (0.0)	1 (6.3)	0 (0.0)	0 (0.0)
PR	32 (76.2)	10 (76.9)	10 (62.5)	9 (100.0)	3 (75.0)
SD	7 (16.7)	3 (23.1)	4 (25.0)	0 (0.0)	0 (0.0)
PD	2 (4.8)	0 (0.0)	1 (6.3)	0 (0.0)	1 (25.0)



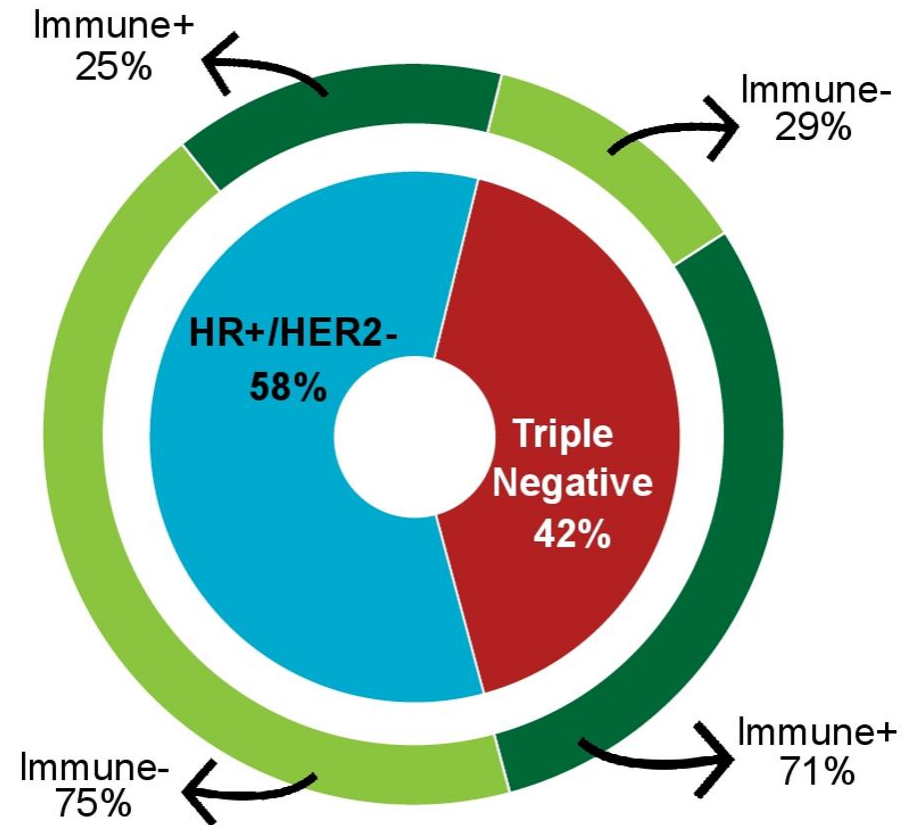
ORR % (95% CI)
cORR % (95% CI)
DCR % (95% CI)
mPFS (Mo), (95% CI)

Variable	BLIS	IM	LAR	MES	Unclassified	Unknown
Population (n)	12	4	13	2	3	8
CR	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)
PR	8 (66.7)	4 (100.0)	10 (76.9)	1 (50.0)	2 (66.7)	7 (87.5)
SD	4 (33.3)	0 (0.0)	2 (15.4)	0 (0.0)	1 (33.3)	0 (0.0)
PD	0 (0.0)	0 (0.0)	1 (7.7)	0 (0.0)	0 (0.0)	1 (12.5)
ORR, % (95% CI)	66.7 (34.9, 90.1)	100.0 (39.8, 100.0)	76.9 (46.2, 95.0)	100.0 (15.8, 100.0)	66.7 (9.4, 99.2)	87.5 (47.3, 99.7)
cORR, % (95% CI)	58.3 (27.7, 84.8)	100.0 (39.8, 100.0)	69.2 (38.6, 90.9)	100.0 (15.8, 100.0)	66.7 (9.4, 99.2)	87.5 (47.3, 99.7)
DCR % (95% CI)	100.0 (73.5, 100.0)	100.0 (39.8, 100.0)	92.3 (64.0, 99.8)	100.0 (15.8, 100.0)	100.0 (29.2, 100.0)	87.5 (47.3, 99.7)



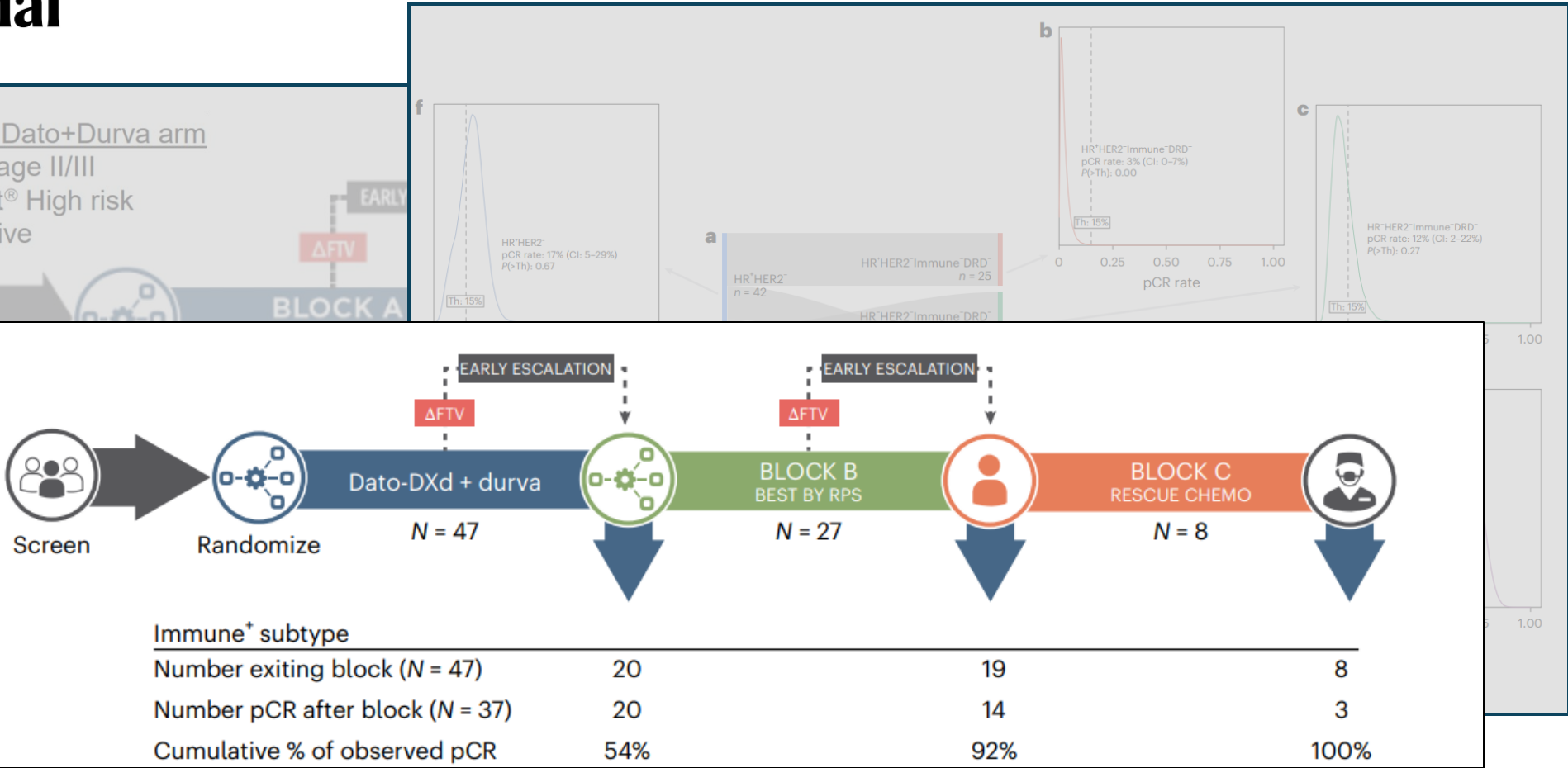
irAE	15 (35.7)
Grade ≥3 irAE	4 (9.5)

ImPrint Signature: I-SPY2.2



Datopotamab–deruxtecan plus durvalumab in early-stage breast cancer: the sequential multiple assignment randomized I-SPY2.2 phase 2 trial

Eligibility for Dato+Durva arm
 Anatomic Stage II/III
 MammaPrint® High risk
 HER2 negative



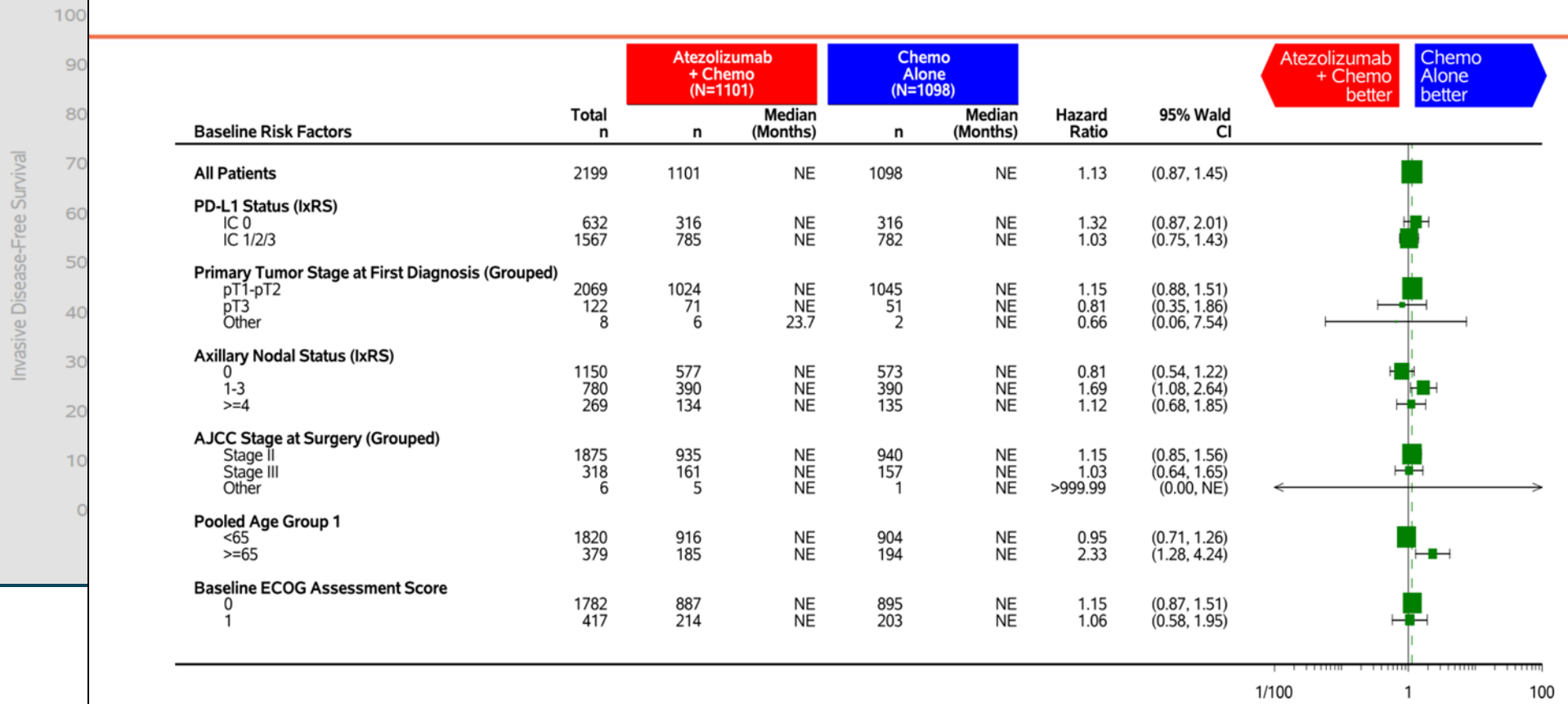
Alexandra/IMpassion030 phase 3 open-label study design

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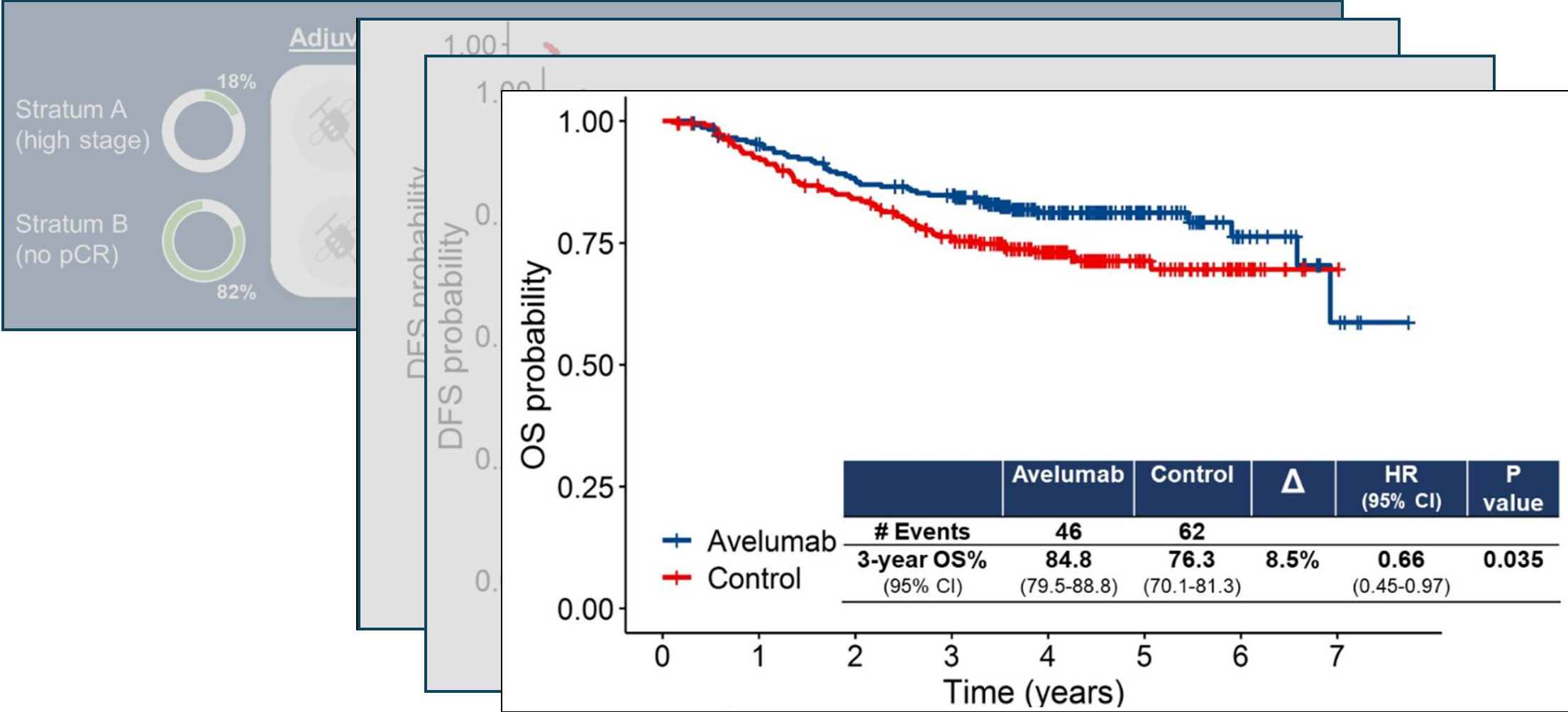
Primary efficacy endpoint: iDFS^a (ITT population)

iDFS subgroup analysis (ITT Population)



Stratification factors:
 Axillary node status (0 vs. 1-3 vs. >=4)
 Surgery (breast-conserving vs. mastectomy)
 Tumor PD-L1 status (IC0 vs. IC1-3 vs. IC4-9)

A-BRAVE trial: A phase III randomized trial with avelumab in early triple-negative breast cancer with residual disease after neoadjuvant chemotherapy or at high risk after primary surgery and adjuvant chemotherapy.



Summary

IO is a work in progress

- Neoadj IO but not adj IO in TNBC
- Better Signatures
- More Tools
 - Additional checkpoints
 - More developments in other tumor types

