

UNIVERSITY OF ILLINOIS CANCER CENTER

Immunotherapy: Wait, Why Wait?

V.K. Gadi, MD PhD

Deputy Director, U of Illinois Cancer Center

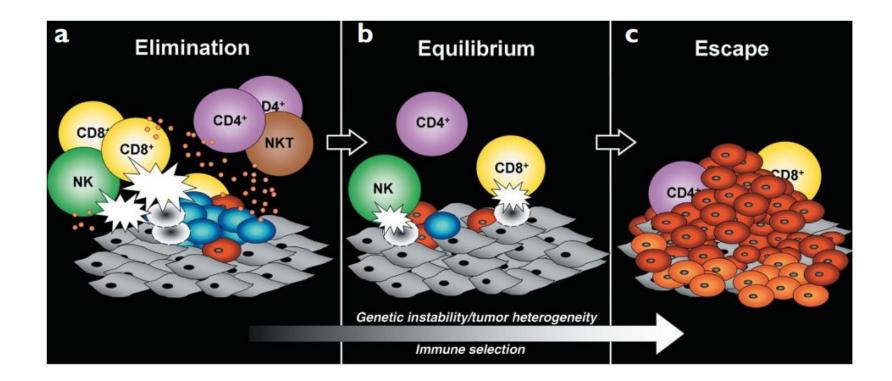
October 20, 2024

6th Annual BREAST CANCER SYMPOSIUM YESTERDAY, TODAY AND TOMORROW

OCTOBER 18- 20, 2024 HUDSON HALL HUDSON, NY

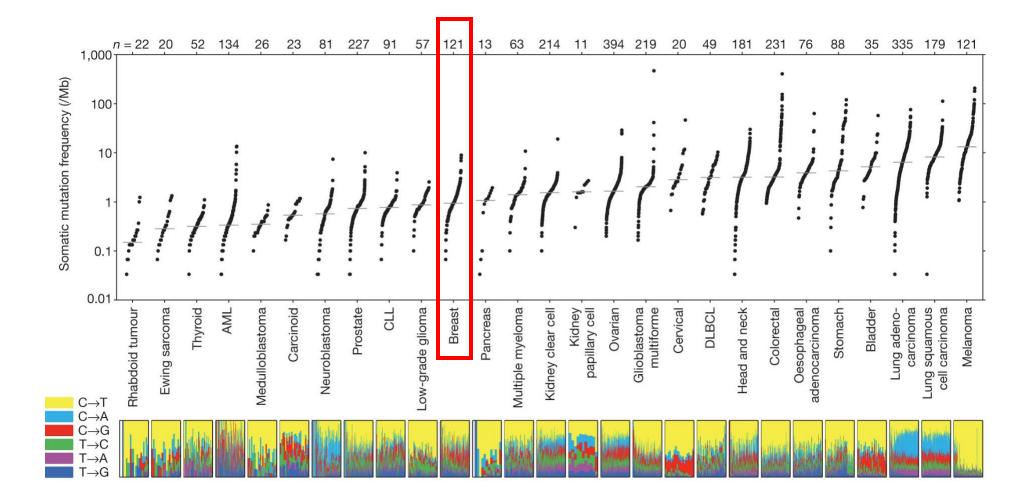
PROGRAM DIRECTOR Maria Theodoulou, MD Breast Cancer Medicine New York Oncology Hematology Albany, NY

Immunoediting: The immune system as a selection pressure



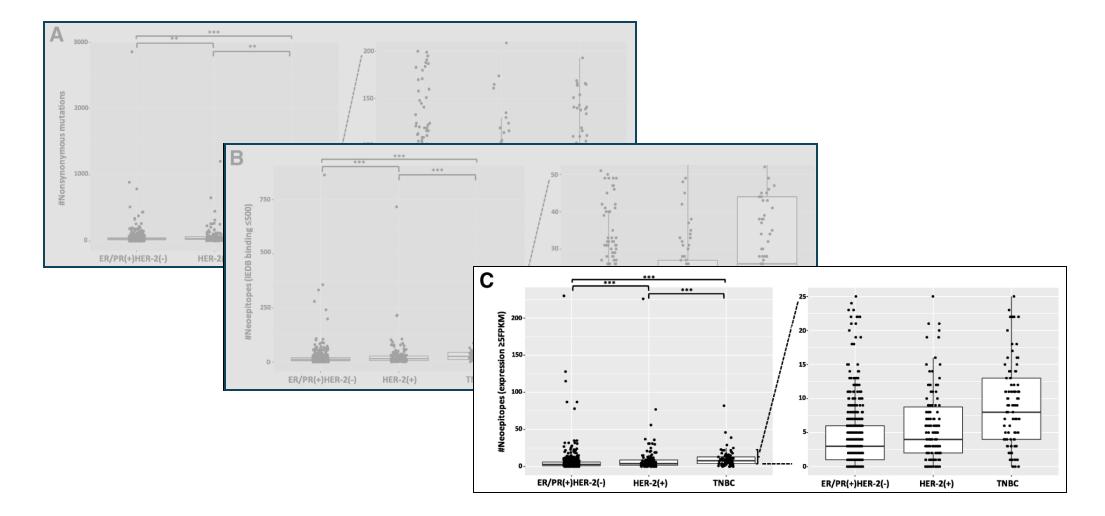
Dunn, et al, Nat Immunol, 2002

TMB: Breast isn't the worst



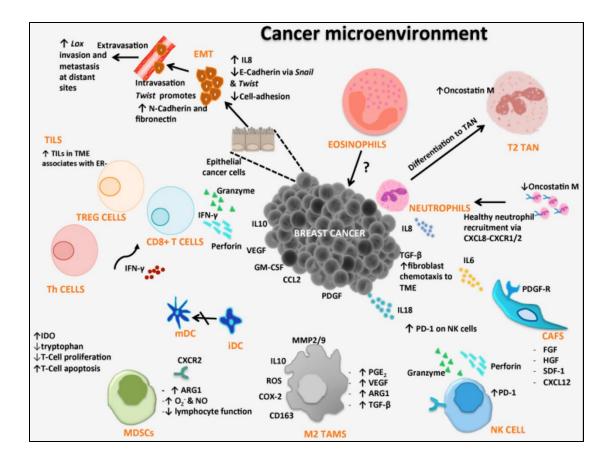
Lawrence, Nature, 2013

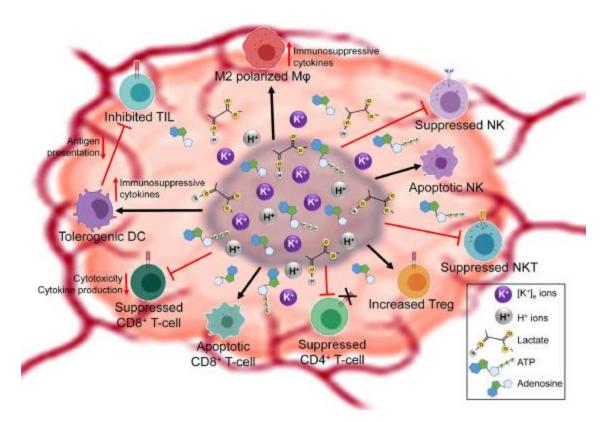
Funny looking DNA -> Funny looking proteins



Narang, BMC Cancer, 2019

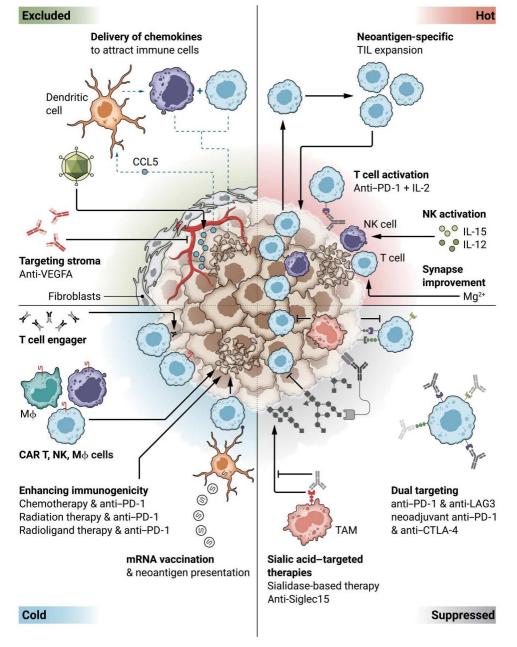
The Obligatory TME slide



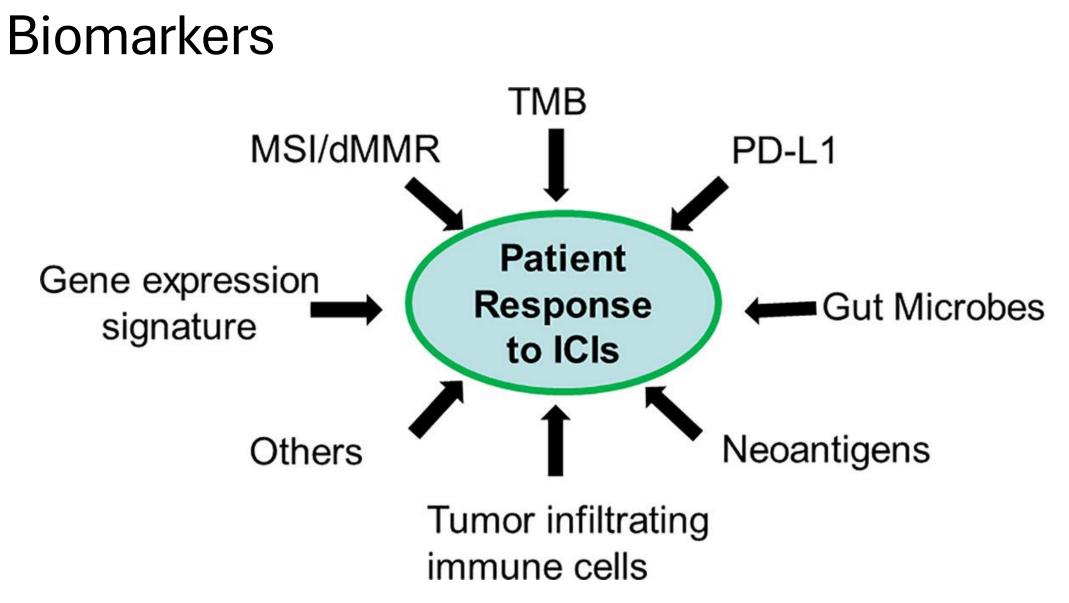


TME terms

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



Kirchammer, Sci Transl Med, 2022



Wang, Front. Oncol., 2021

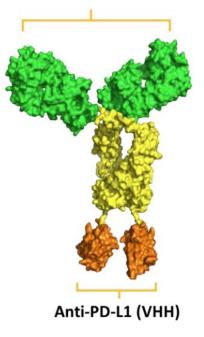
Immune Tools

- 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

Anti-VEGF-A (IgG)



 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 ≥ 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

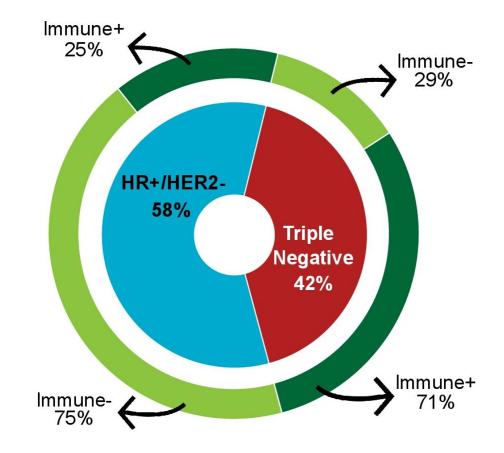
Patient Characteristics (n=42)							
Median age, years (Q1, Q3)	53.5 (41.0, 60.0)						
Number of metastatic sites, n (%	6)						
0-2	17 (40.5)						
≥ 3	25 (59.5)						
Liver metastasis, n (%)							
Yes	16 (38.1)						
No	26 (61.9)						
Brain metastasis, n (%)							
Yes	2 (4.8)						
No	40 (95.2)						
Neo/adjuvant Paclitaxel treatme	ent, n (%)						
Yes	28 (66.7)						
No	14 (33.3)						

Variable	ITT	PD-L1 CPS<1	PD-L1 1≤CPS<1	PD-L 0 CPS≥		OT (%)	20			PD SD PR CR
Population (n)	42	13	16	9		4 au	-20 _	- 11		
CR PR SD	1 (2.4) 32 (76.2) 7 (16.7)	0 (0.0) 10 (76.9) 3 (23.1)	1 (6.3) 10 (62.5) 4 (25.0)	0 (0 9 (10 0 (0	0.0) 3 ((0.0) (75.0) (0.0)	-40 -60 -80			
	2 (4.8) Variable	0 (0.0) BLIS	1 (6.3) IM	0 (0 LAR	0) 1 MES	Unclassified	Unknown		60 –	BLIS IM LAR MES
cORR % (95% CI)	Population (n)	12	4	13	2	3	8	(%) e	40 _	UK 🔳 Unclassified
DCR % (95% Cl)	CR PR	0 (0.0) 8 (66.7)	0 (0.0) 4 (100.0)	0 (0.0) 10 (76.9)	1 (50.0) 1 (50.0)	0 (0.0) 2 (66.7)	0 (0.0) 7 (87.5)	Baseline	20 0	
mPFS VIo), (95%C	SD PD	4 (33.3) 0 (0.0)	0 (0.0) 0 (0.0)	2 (15.4) 1 (7.7)	0 (0.0) 0 (0.0)	1 (33.3) 0 (0.0)	0 (0.0) 1 (12.5)	ge from	-20 _	
	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)	Best Change from Baseline (%)	-40 _ -60 _	and the second se
	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)	Bes	-80 _	
	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)	,	-100 _	

 irAE
 15 (35.7)

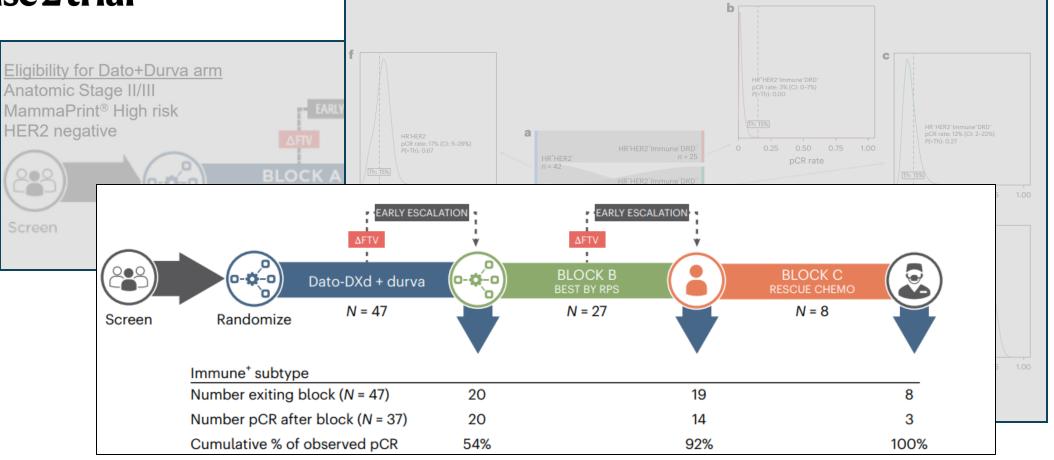
 Grade ≥3 irAE
 4 (9.5)

ImPrint Signature: I-SPY2.2



Esserman, ASCO 2022

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



Shatsky, Nature Med 2024

Alexandra/IMpassion030 phase 3 open-label study design

Ea

Stratification

Surgery

Tumor PD-(IC0 vs. IC1

Axillary no (0 vs. 1-3 v 100

80

60

50

40

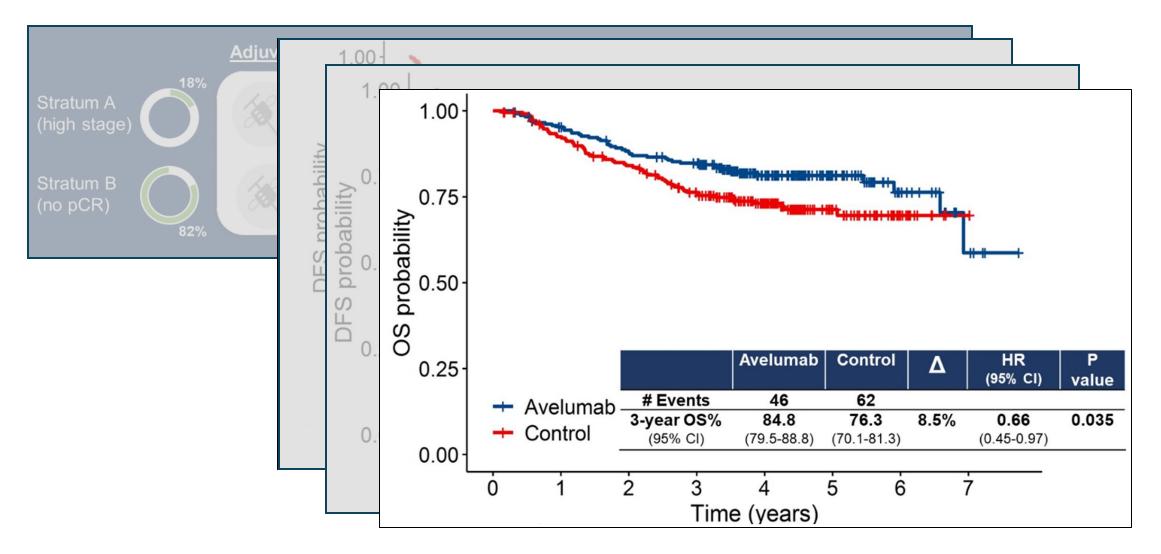
ee Surviva

asive

Primary efficacy endpoint: iDES^a (ITT population) iDFS subgroup analysis (ITT Population)

		Atezolizumab + Chemo (N=1101)		Chemo Alone (N=1098)				Atezolizumab + Chemo better better
Baseline Risk Factors	Total n	n	Median (Months)	n	Median (Months)	Hazard Ratio	95% Wald Cl	
All Patients	2199	1101	NE	1098	NE	1.13	(0.87, 1.45)	, I
PD-L1 Status (IxRS) IC 0 IC 1/2/3	632 1567	316 785	NE NE	316 782	NE NE	1.32 1.03	(0.87, 2.01) (0.75, 1.43)	
Primary Tumor Stage at First Diagnosis (Grouped) pT1-pT2 pT3 Other	2069 122 8	1024 71 6	NE NE 23.7	1045 51 2	NE NE	1.15 0.81 0.66	(0.88, 1.51) (0.35, 1.86) (0.06, 7.54)	
Axillary Nodal Status (IxRS) 0 1-3 >=4	1150 780 269	577 390 134	NE NE	573 390 135	NE NE	0.81 1.69 1.12	(0.54, 1.22) (1.08, 2.64) (0.68, 1.85)	₽ <mark>₩</mark> ₩ ₩₩₩ ₩₩₩
AJCC Stage at Surgery (Grouped) Stage II Stage III Other	1875 318 6	935 161 5	NE NE	940 157 1	NE NE	1.15 1.03 >9999.99	(0.85, 1.56) (0.64, 1.65) (0.00, NE)	<
Pooled Age Group 1 <65 >=65	1820 379	916 185	NE NE	904 194	NE NE	0.95 2.33	(0.71, 1.26) (1.28, 4.24)	
Baseline ECOG Assessment Score 0 1	1782 417	887 214	NE NE	895 203	NE NE	1.15 1.06	(0.87, 1.51) (0.58, 1.95)	
								1/100 1

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.



Conte PF, ASCO 2024

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

