

Clarifying the position of immunotherapies in metastatic UCa

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Disclosures

- **Travel, research funding:**
Roche, Genentech, MSD, Pfizer, BMS
- **Honoraria:**
Merck, Roche, Pfizer, Ellipses, Ipsen
- **Participating investigator** on studies with Roche/GNE, Pfizer, MSD, Exelixis, BMS, Astellas, AstraZeneca

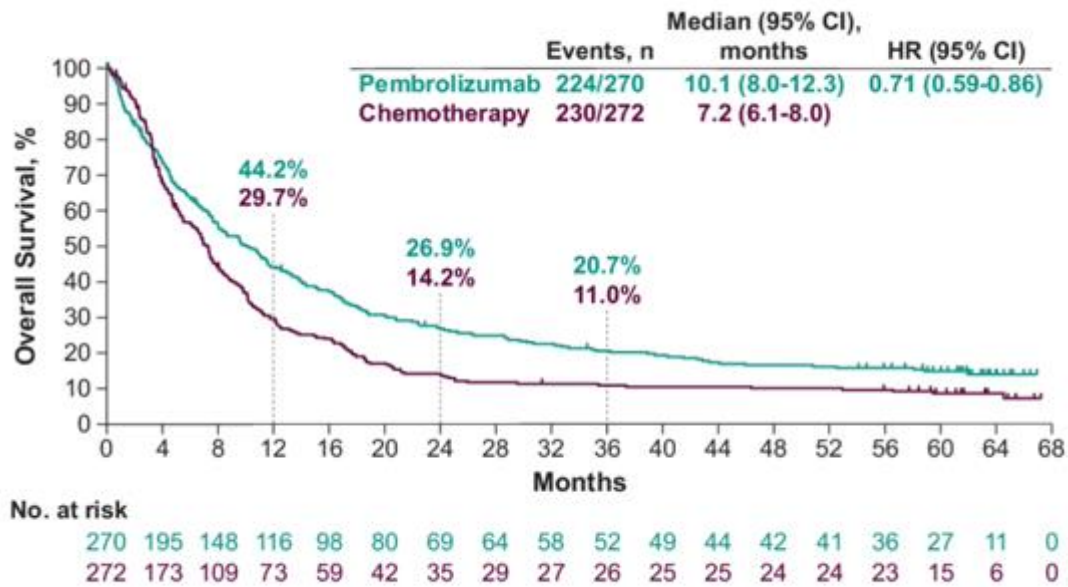
WHEN?

WHICH?

BIOMARKERS?

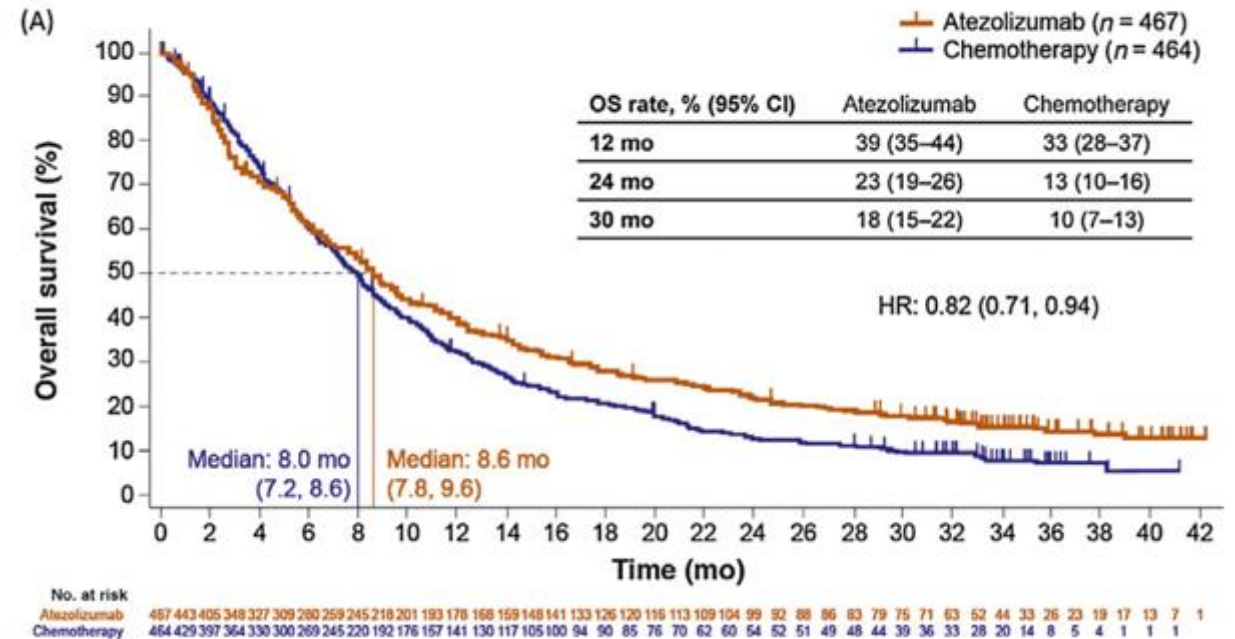
WHEN? – 2L

KN-045 – 5y update



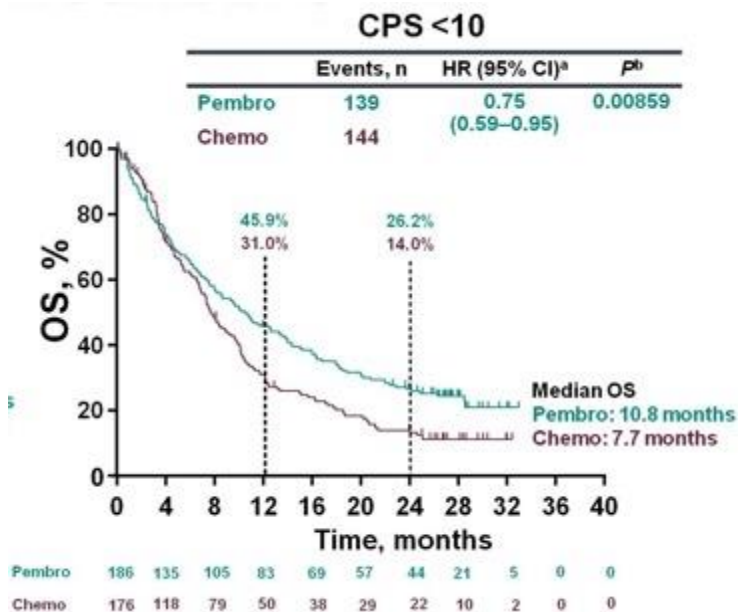
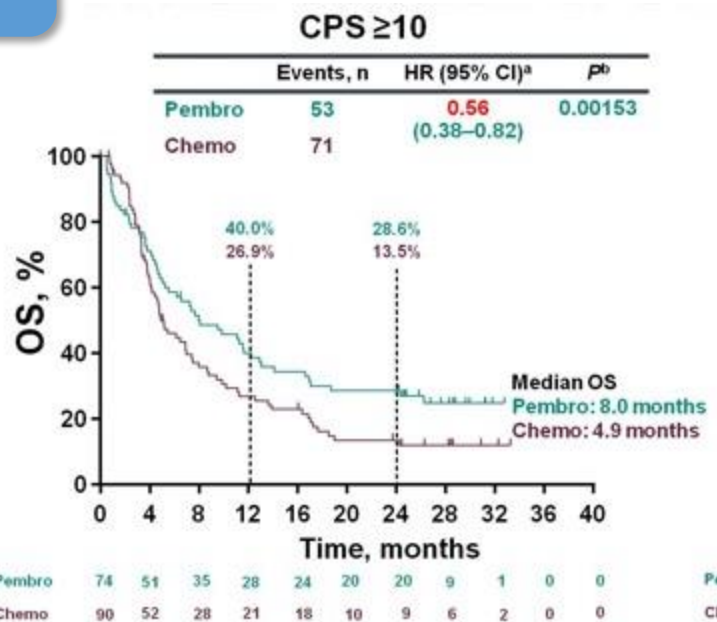
HR, hazard ratio.

Imvigor 211 – 30m update

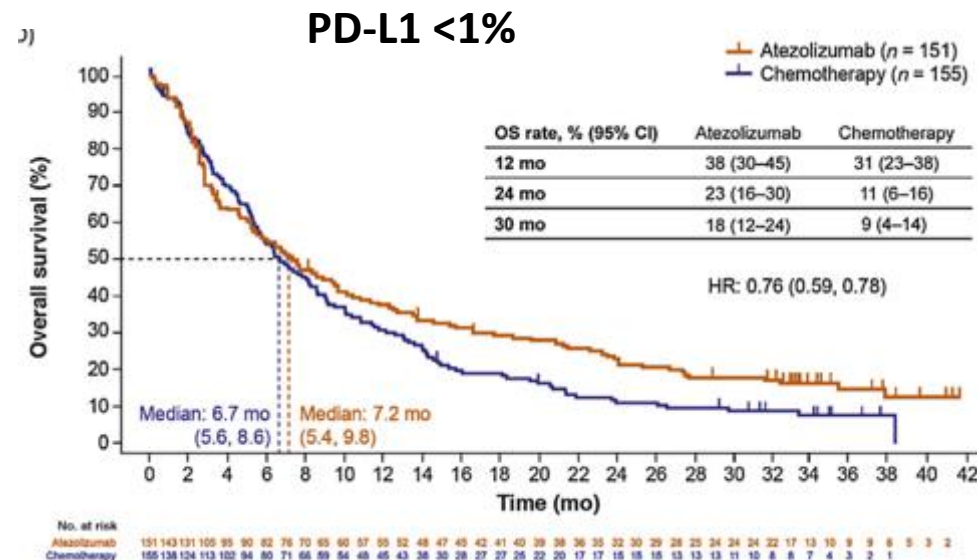
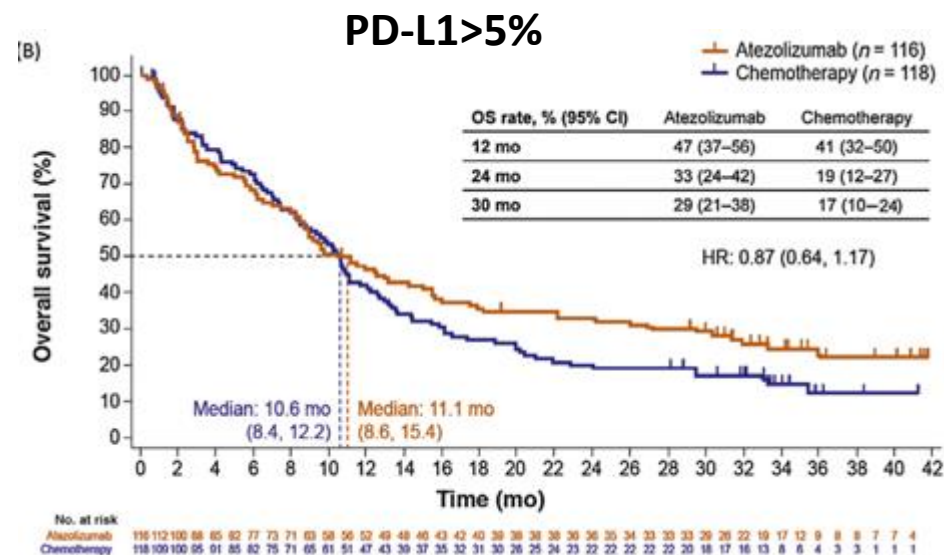


WHEN? – 2L

KN-045 – 5y update

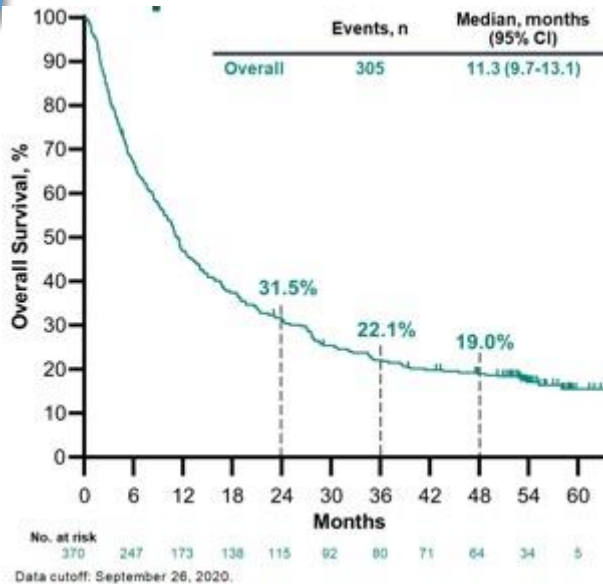


Imvigor 211 – 30m update

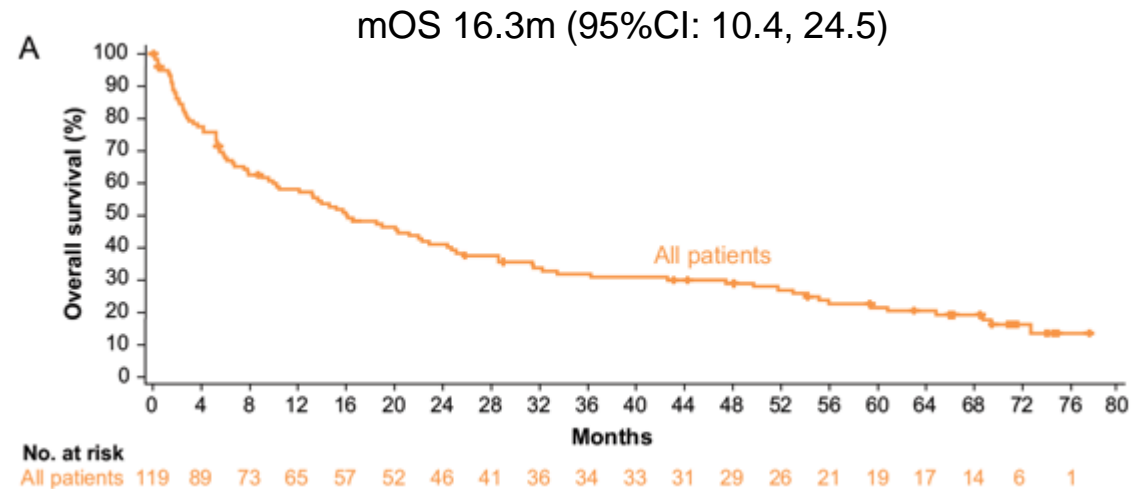


WHEN? – 1L

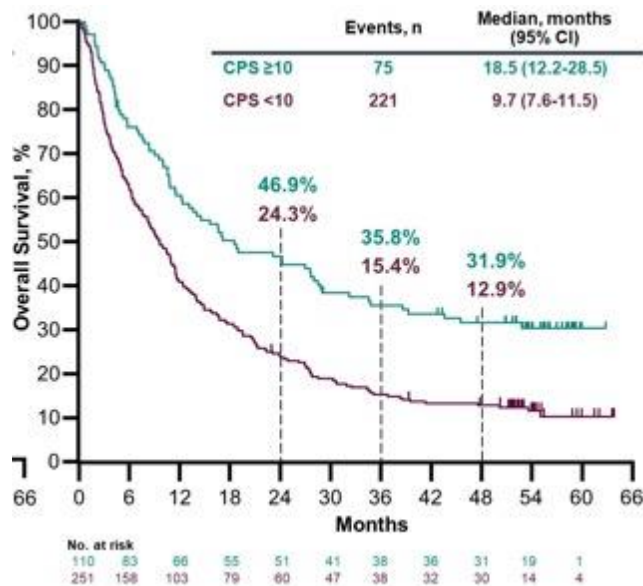
KEYNOTE – 052 – 5y update



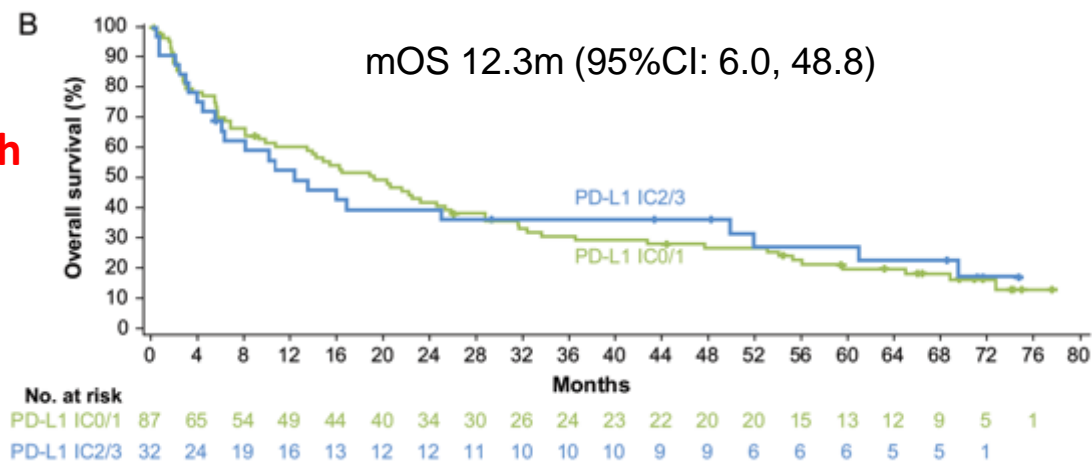
IMvigor 210 – 6y update



PD-L1 high
N=110

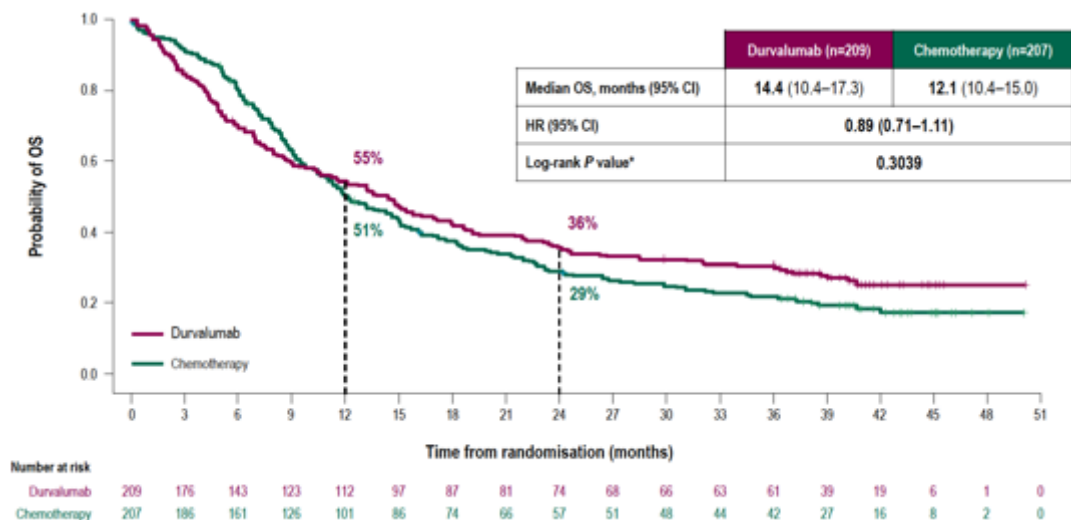


PD-L1 high
N=32

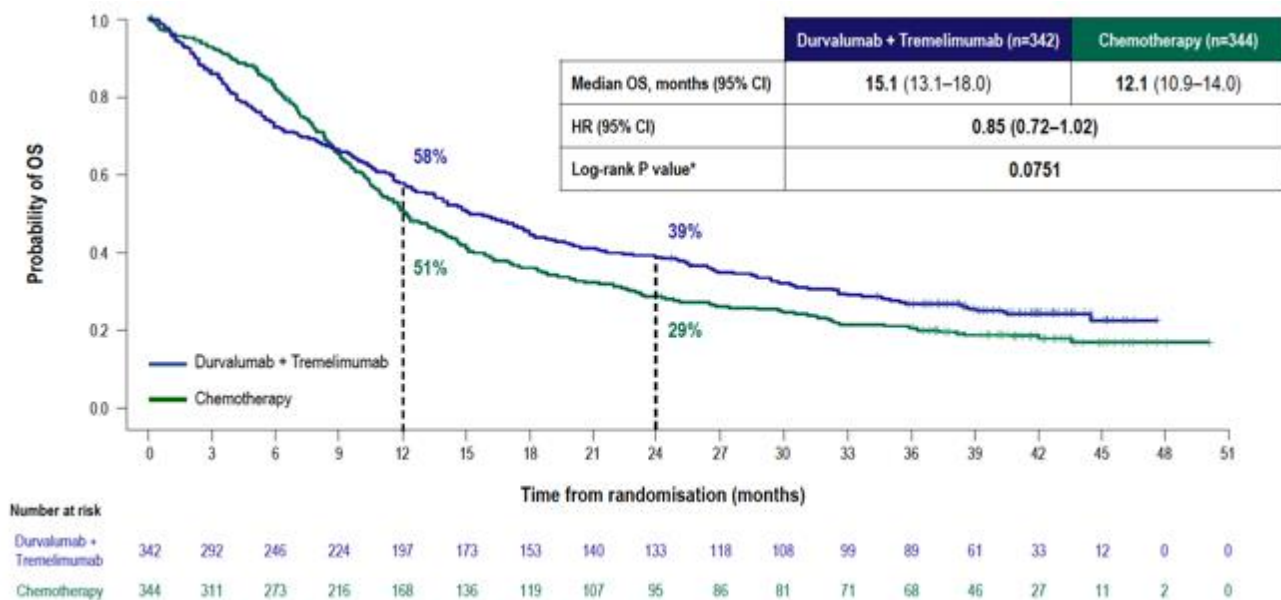


WHEN? – 1L

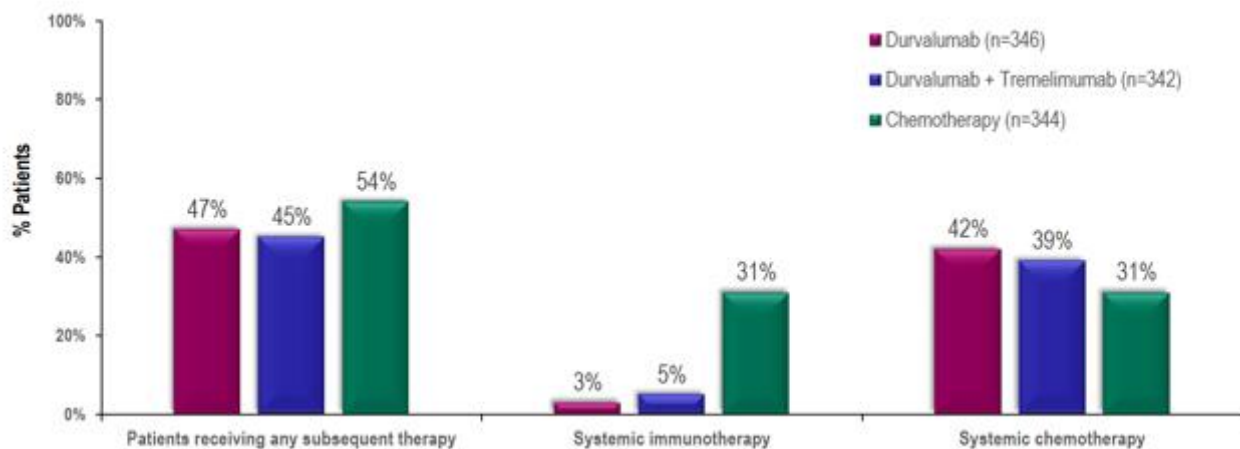
DANUBE in PD-L1 high



DANUBE - ITT



SUBSEQUENT ANTI-CANCERTHERAPIES



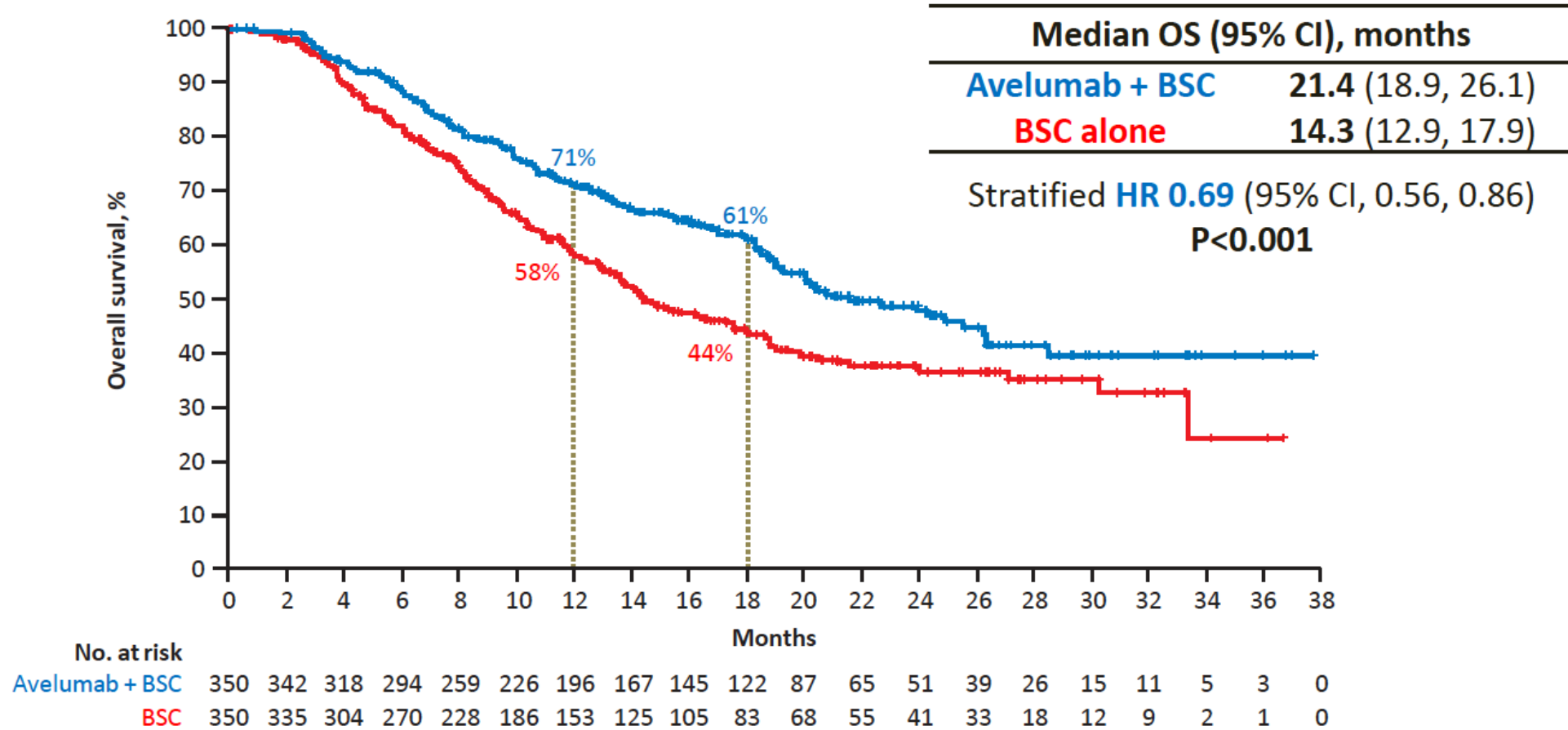
Overall, only **49%** had subsequent therapies.

WHEN?



WHEN? – Maintenance

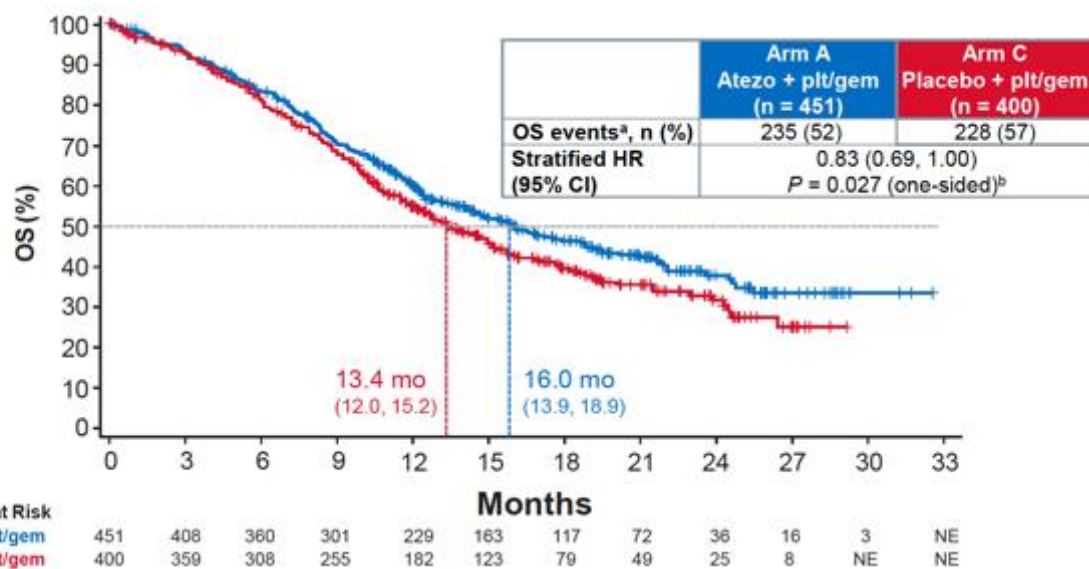
JAVELIN Bladder 100



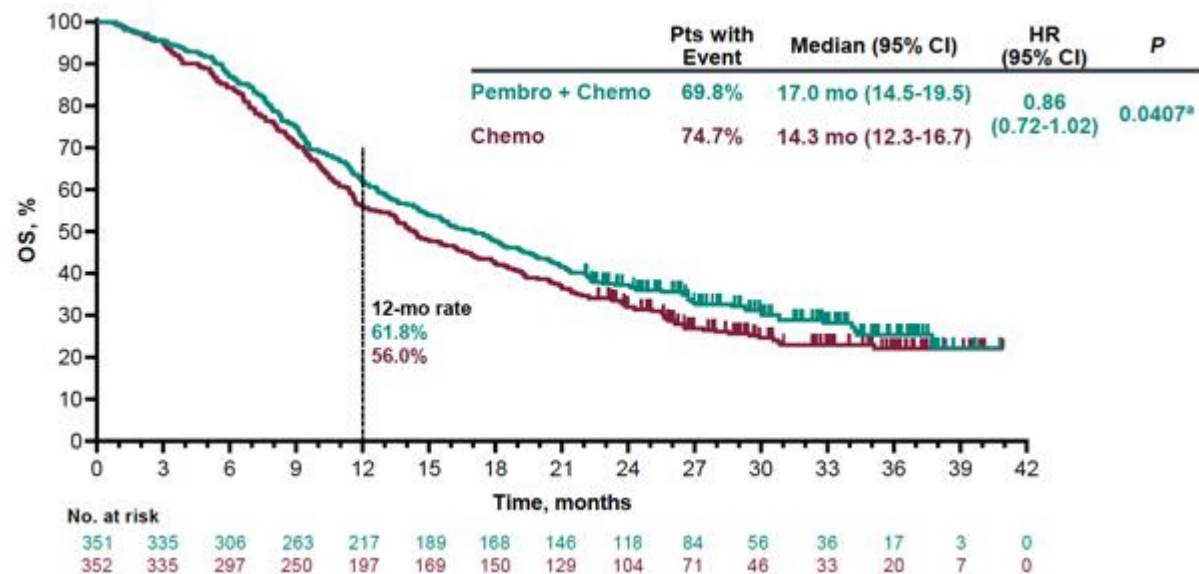
OS was measured post randomization (after chemotherapy); the OS analysis crossed the prespecified efficacy boundary based on the alpha-spending function (P<0.0053)

WHICH? – COMBINATION WITH CHEMOTHERAPY

IMvigor 130

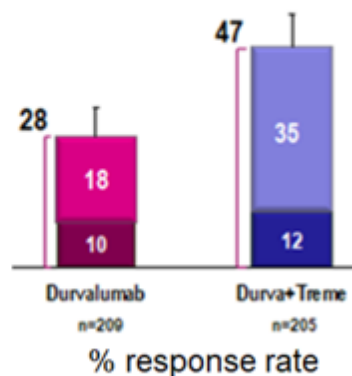
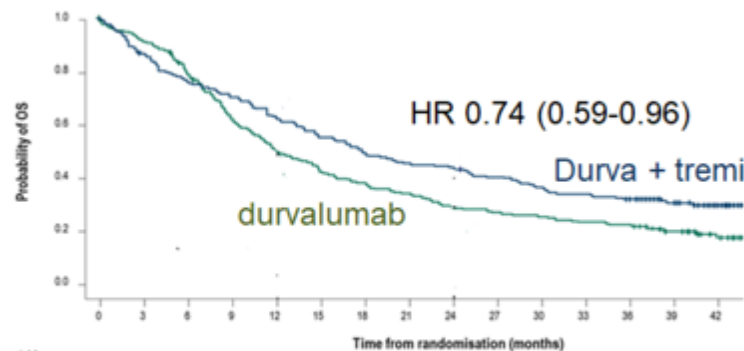


KEYNOTE-361

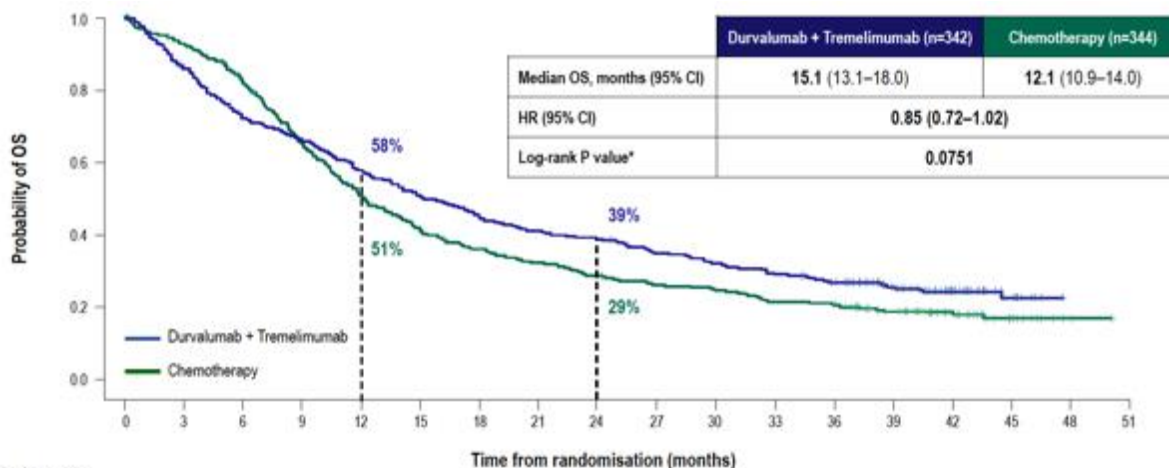


WHICH? – COMBINATION with CTLA-4

Durvalumab and tremilimumab in PD-L1+ve



Ipilimumab and nivolumab in PD-L1+ve vs chemo is being prospectively tested.



Number at risk

	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51
Durvalumab + Tremelimumab	342	292	246	224	197	173	153	140	133	118	108	99	89	61	33	12	0	0
Chemotherapy	344	311	273	216	168	136	119	107	96	86	81	71	68	46	27	11	2	0



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Bristol Myers Squibb Provides Update on CheckMate -901 Trial Evaluating Opdivo (nivolumab) Plus Yervoy (ipilimumab) as First-Line Treatment for Patients with Unresectable or Metastatic Urothelial Carcinoma

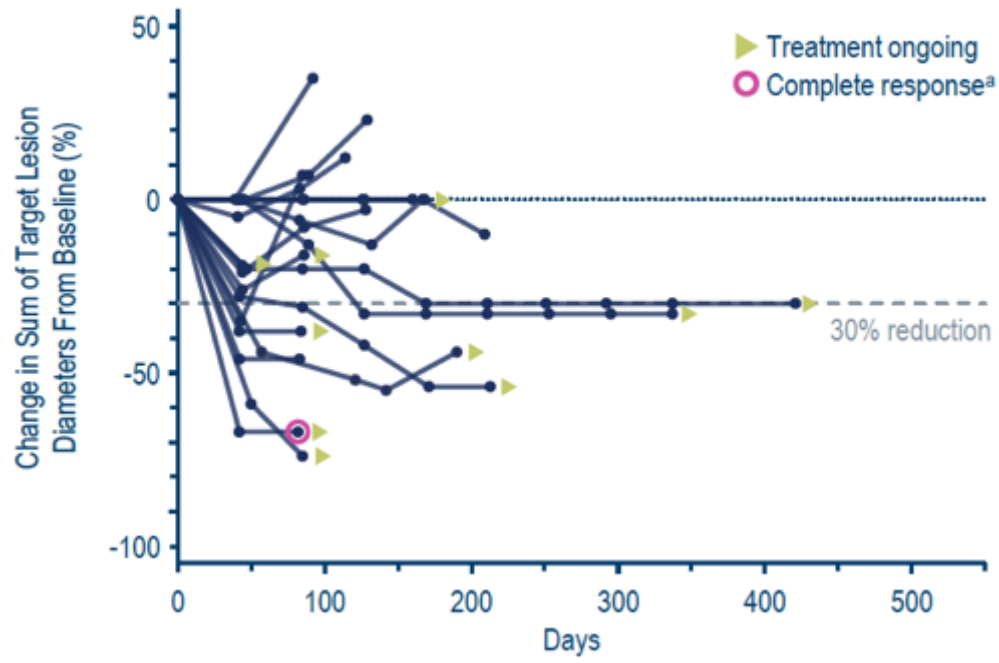
05/16/2022

CATEGORY: [Corporate/Financial News](#)

PRINCETON, N.J.--(BUSINESS WIRE)-- [Bristol Myers Squibb](#) (NYSE: BMY) today announced the Phase 3 CheckMate -901 trial, comparing *Opdivo* (nivolumab) plus *Yervoy* (ipilimumab) to standard-of-care chemotherapy as a first-line treatment for patients with untreated unresectable or metastatic

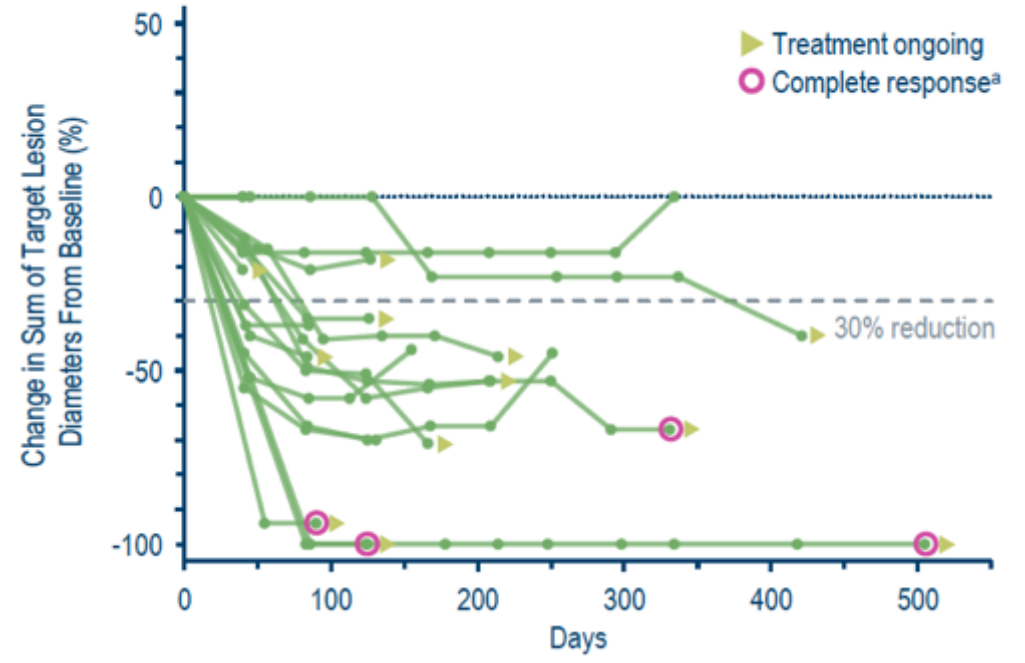
WHICH? – COMBINATION with FGFRi

Erdafitinib



NORSE

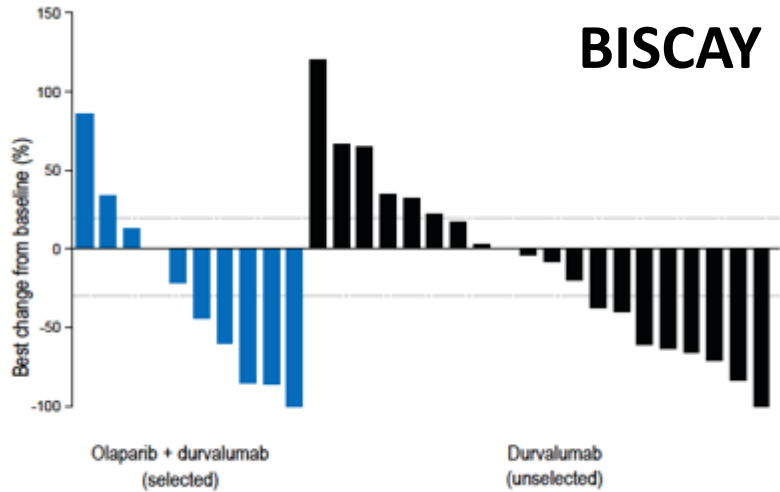
Erdafitinib + Cetrelimab



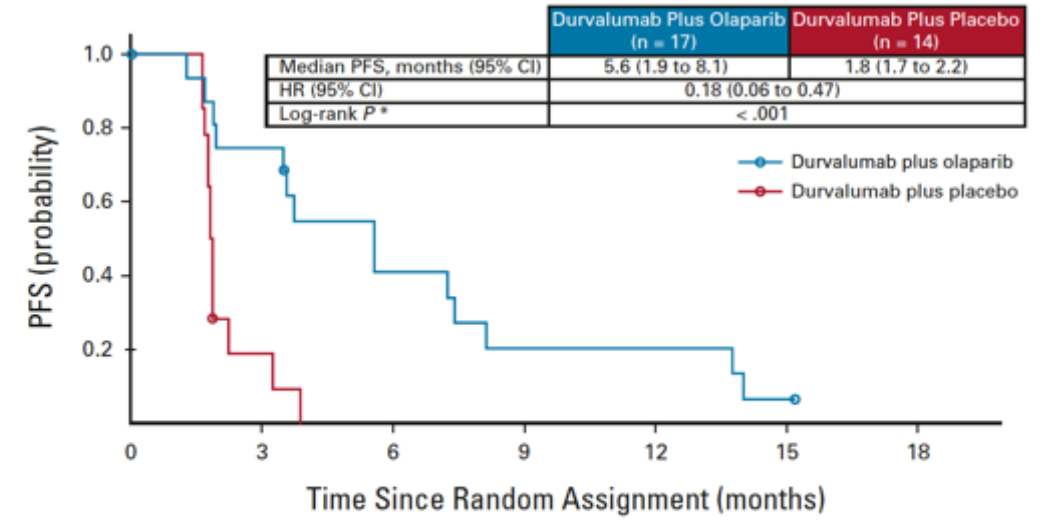
ORR 33% vs 68%

WHICH? – COMBINATION with PARPi

BISCAY

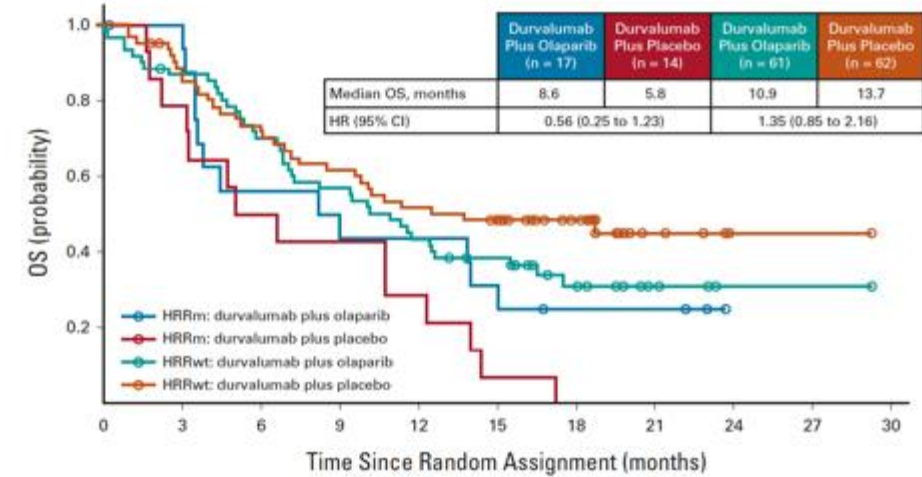
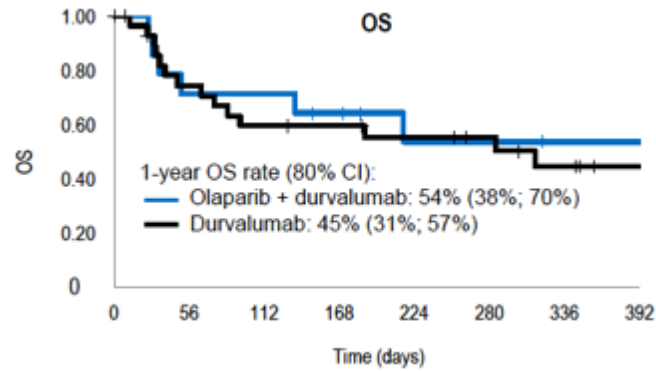
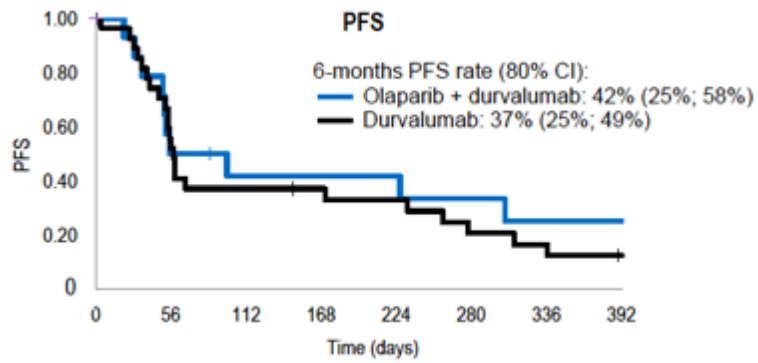


BAYOU



No. at risk:

	0	3	6	9	12	15	18
Durvalumab plus olaparib 17	17	12	6	3	3	1	0
Durvalumab plus placebo 14	14	2	0	0	0	0	0

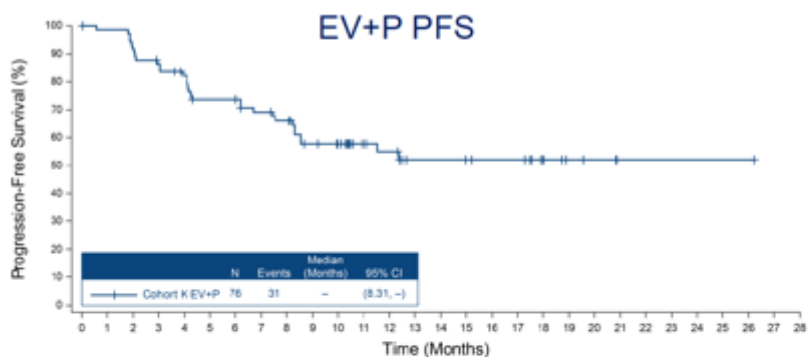
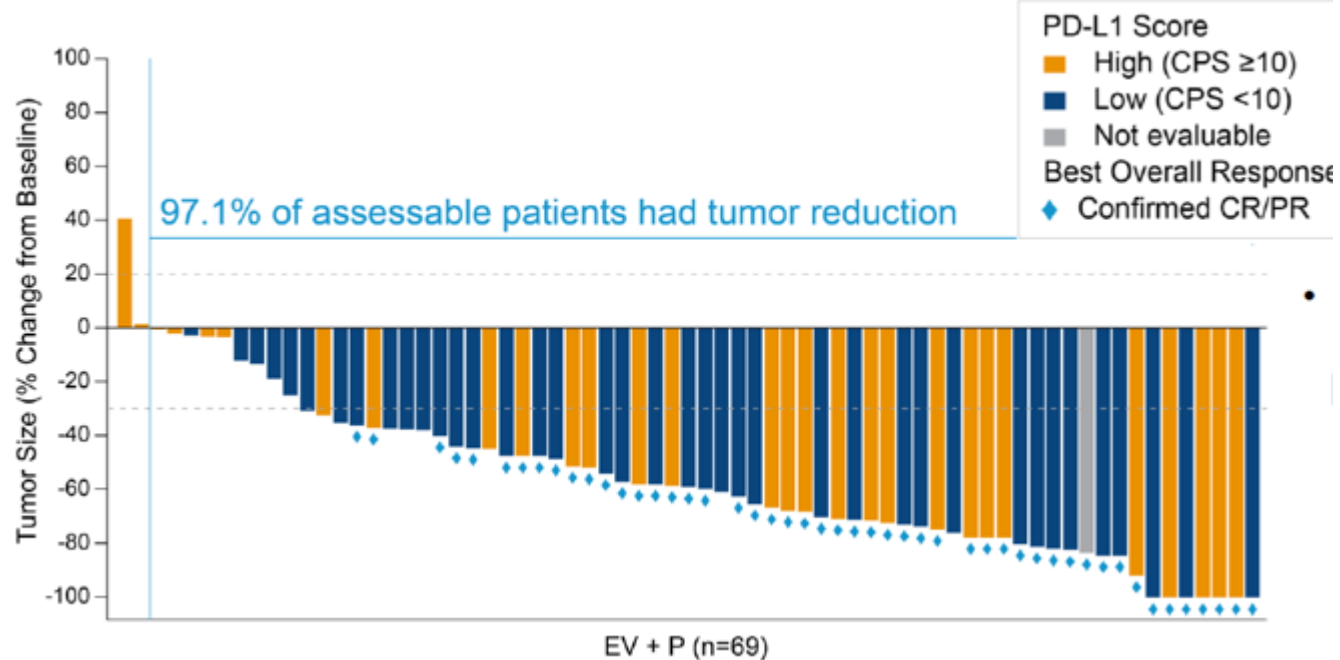


No. at risk:

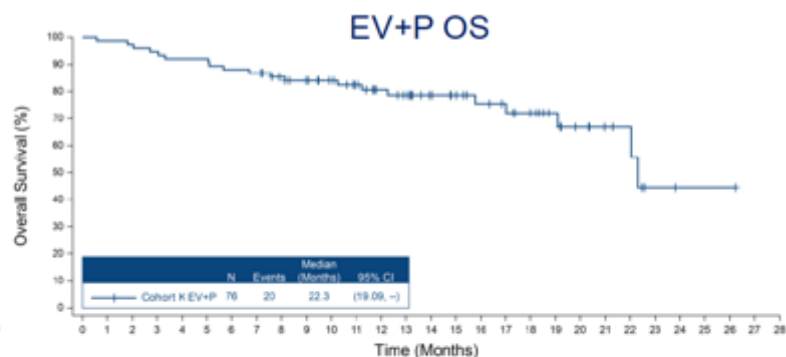
	0	3	6	9	12	15	18	21	24	27	30
HRRm: durvalumab plus olaparib 17	17	15	9	8	7	5	3	3	0	0	0
HRRm: durvalumab plus placebo 14	14	11	7	6	4	1	0	0	0	0	0
HRRwt: durvalumab plus olaparib 61	61	52	42	34	26	21	11	5	1	1	0
HRRwt: durvalumab plus placebo 62	62	52	44	37	31	28	18	5	1	1	0

WHICH? – COMBINATION with ADC

EV-103 (EV + Pembrolizumab)



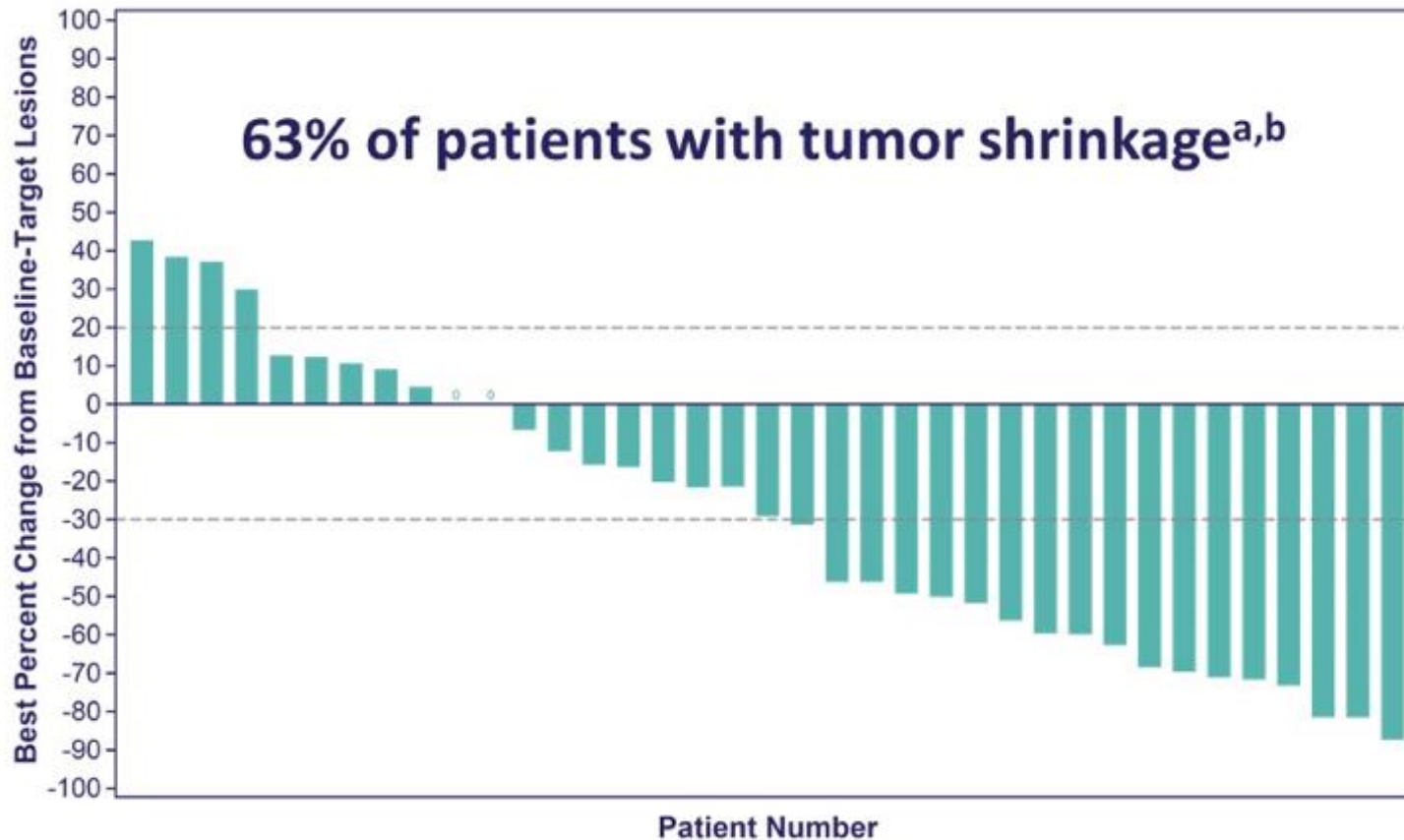
	EV+P (N=76)	EV Mono (N=73)
PFS events, n	31	38
mPFS (95% CI), mos	- (8.31, -)	8.0 (6.05, 10.35)
PFS at 12 mos, %	55.1%	35.8%



	EV+P (N=76)	EV Mono (N=73)
OS Events, n	20	26
mOS (95% CI), mos	22.3 (19.09, -)	21.7 (15.21, -)
OS at 12 mos, %	80.7%	70.7%
Median follow-up time, mos	14.8	15.0

WHICH? – COMBINATION with ADC

TROPHY-U-01 Cohort 3 SG + Pembrolizumab

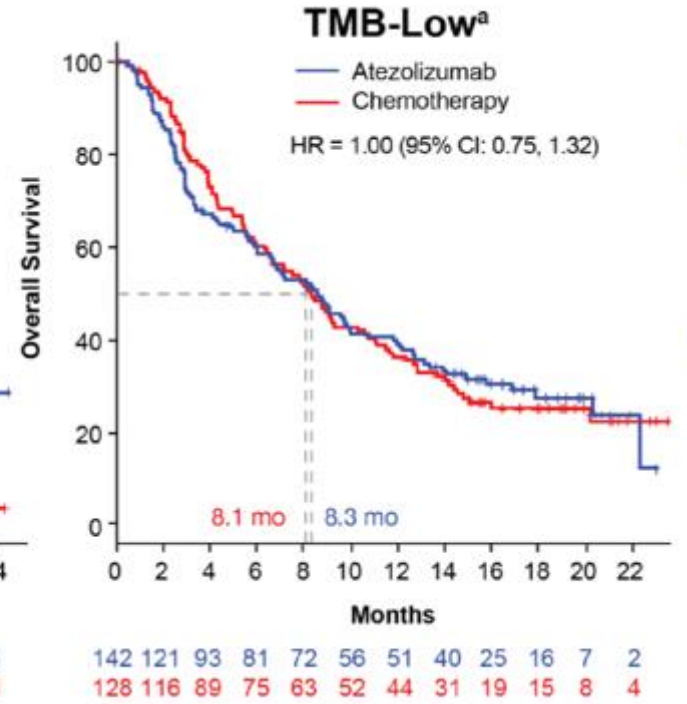
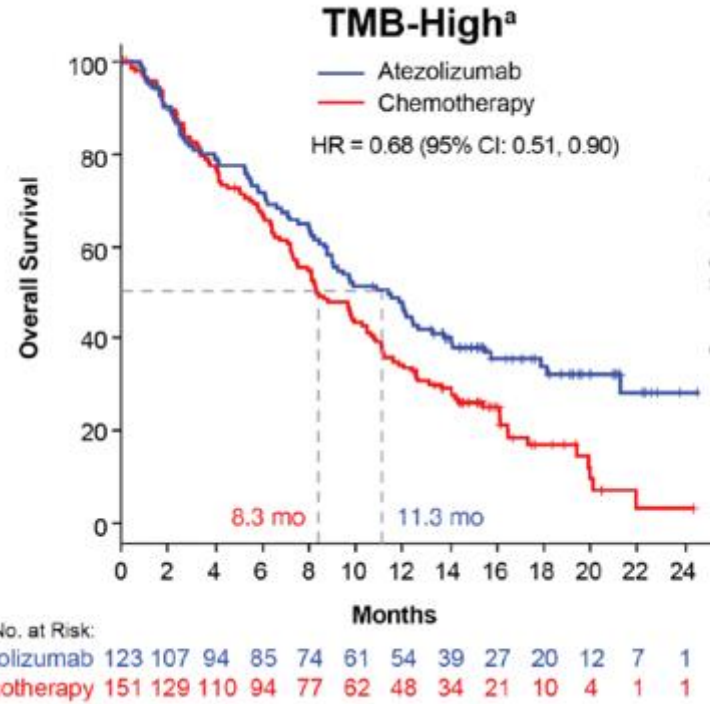
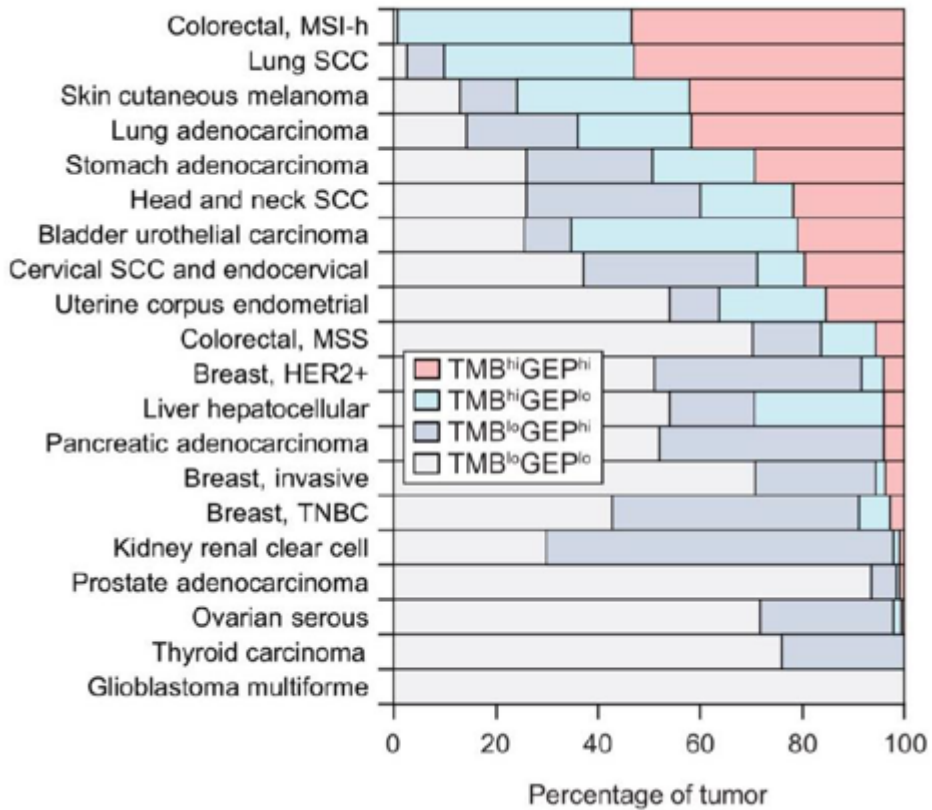


	Cohort 3 ^a (N=41)
Objective response rate (CR + PR), n (%) [95%CI]	14 (34) [20.1-50.6]

mPFS: 5.5m (95%CI: 1.7 - NR)

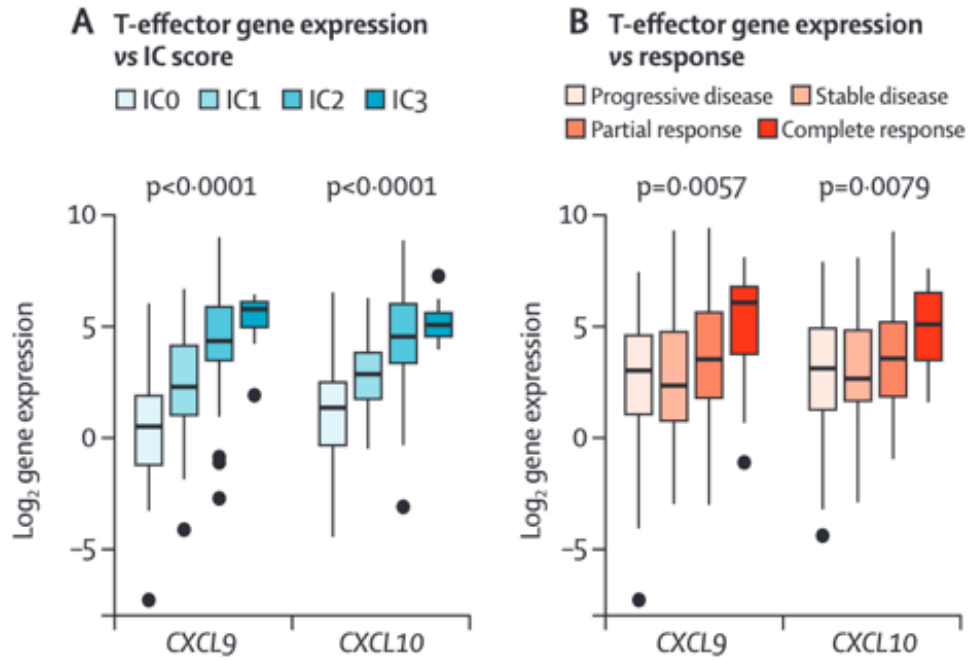
mOS: NR

BIOMARKERS? - TMB

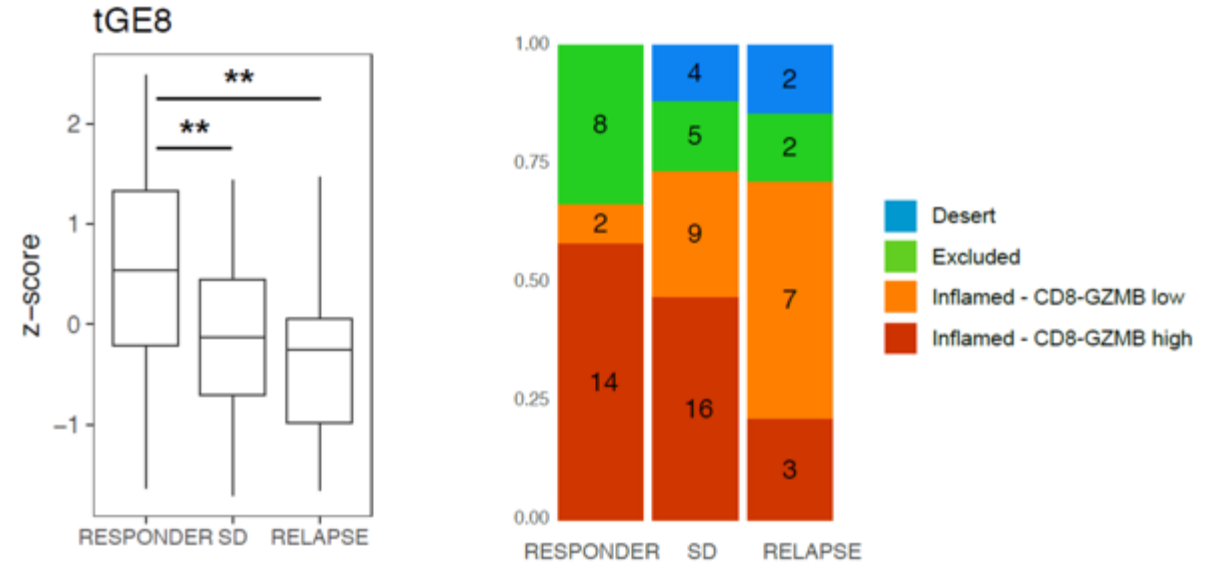


BIOMARKERS? – T effector signature

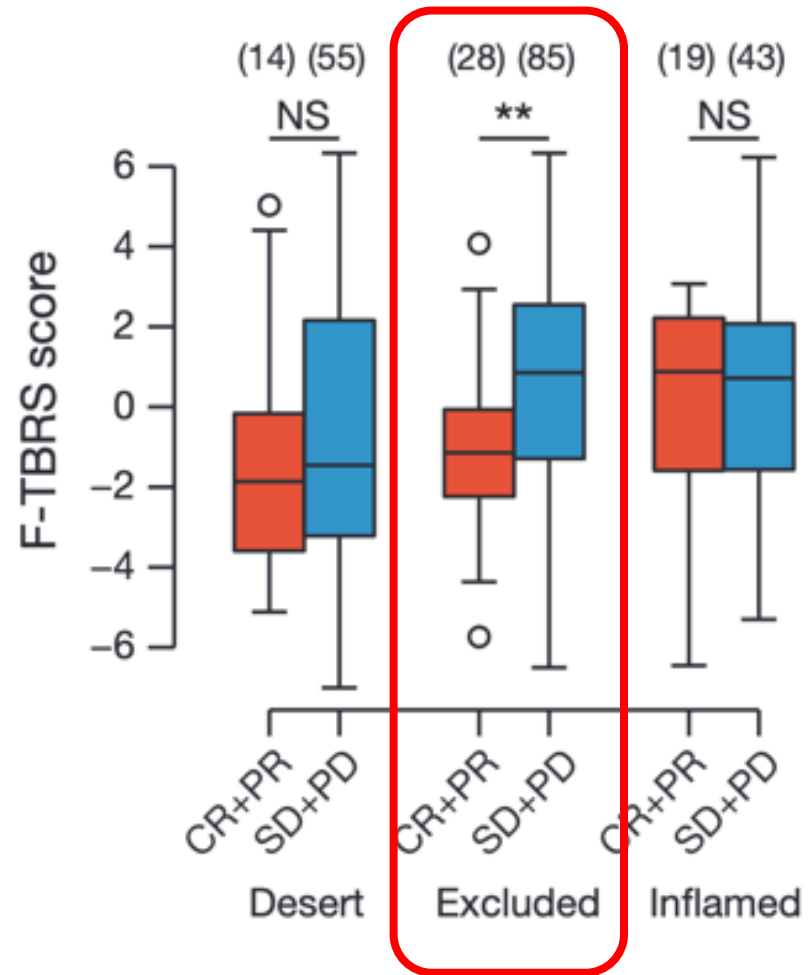
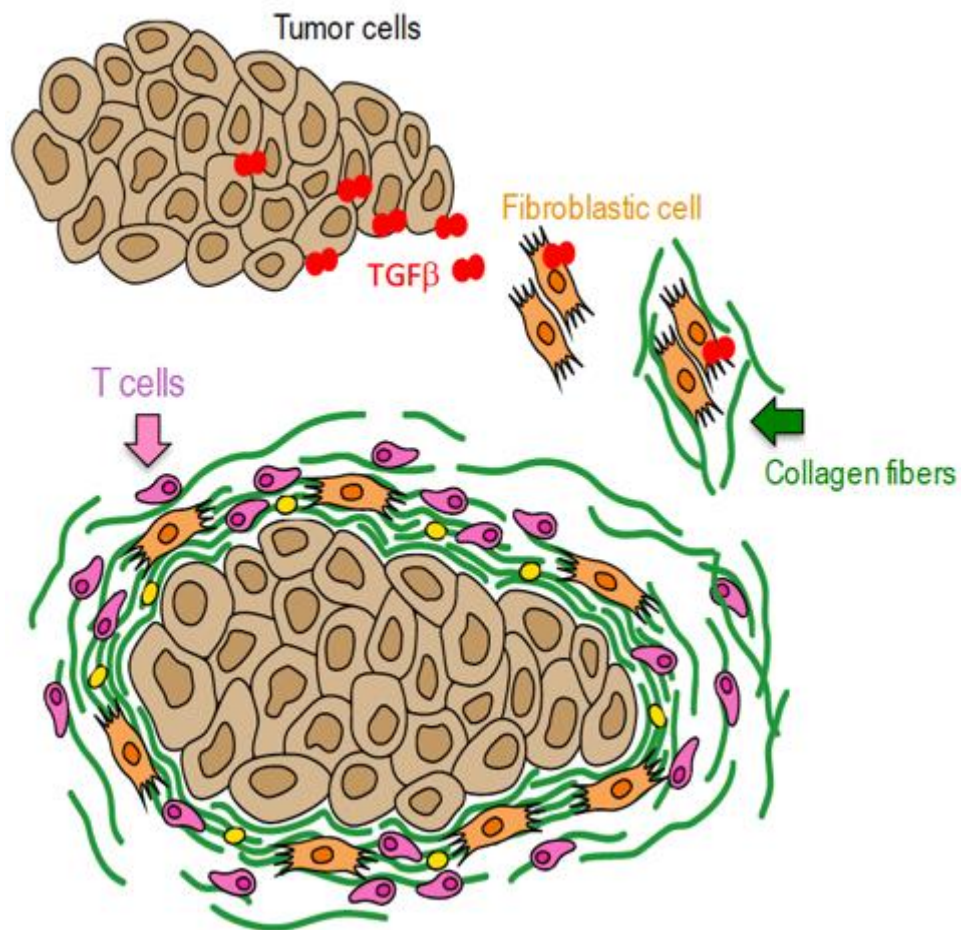
IMvigor 211



ABACUS



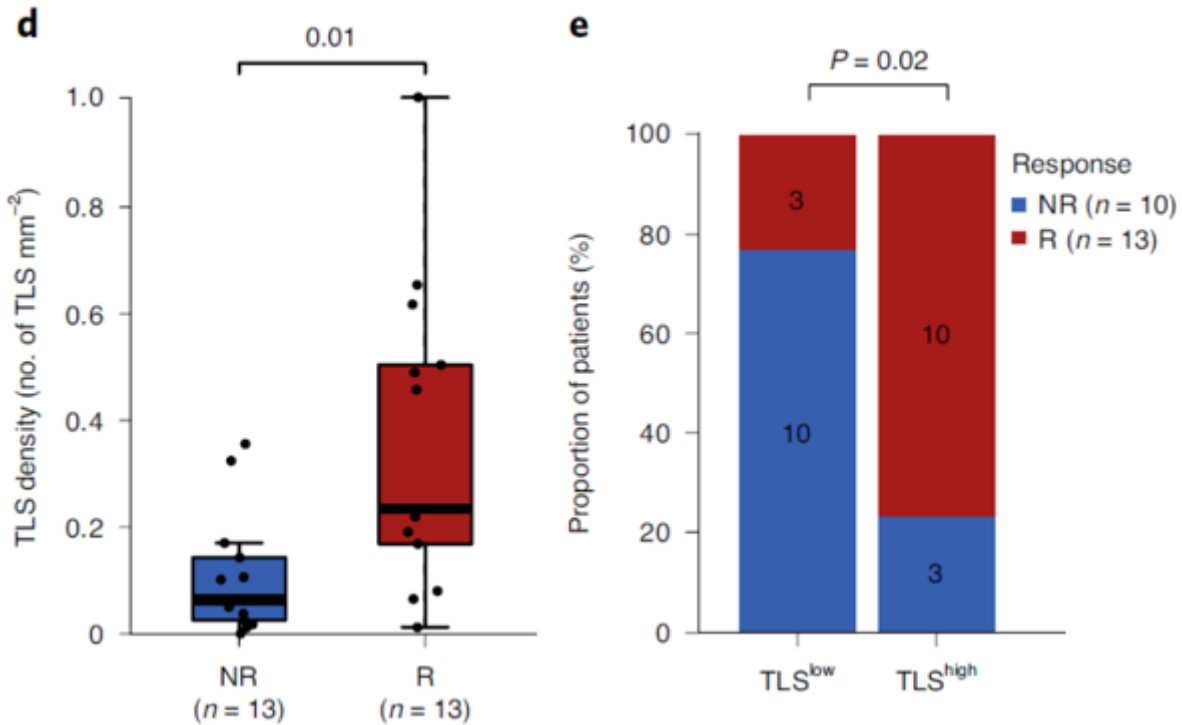
BIOMARKERS? - TGFB



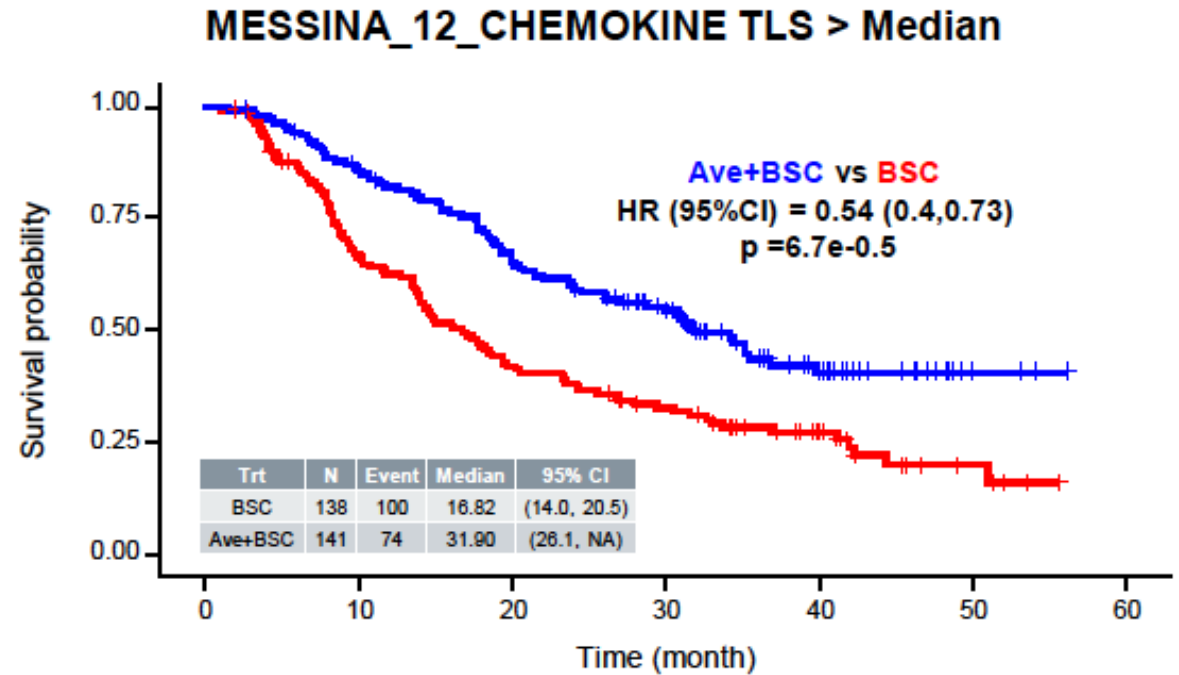
BIOMARKERS? – Tertiary Lymphoid Structures

- Ectopic lymphoid tissues arising in inflamed tissue and cancer.
- Characterized by variably organized lymphoid regions with B cell zones and adjacent T cells.

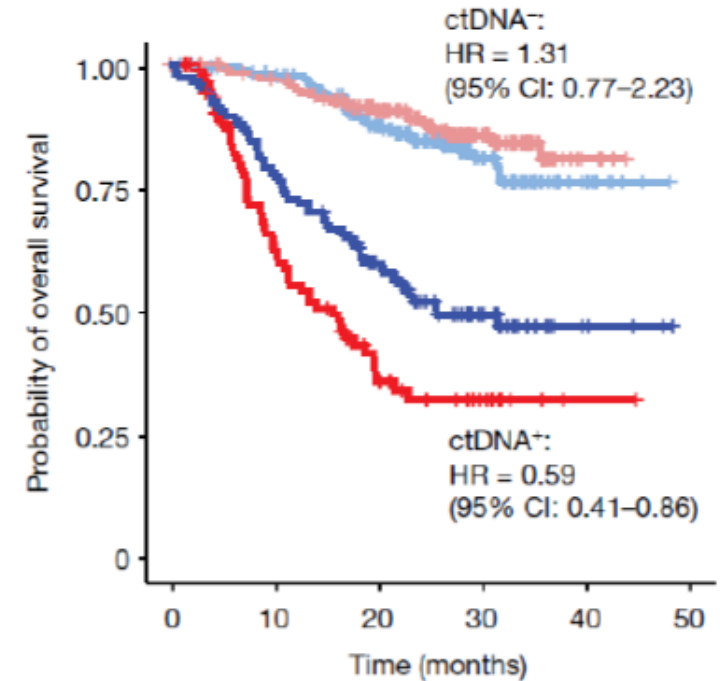
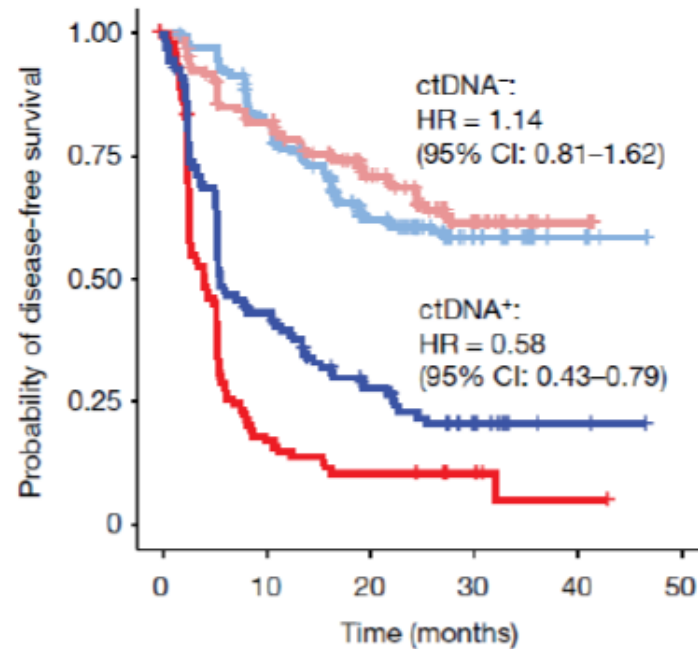
Neoadjuvant durva/treme



Javelin Bladder 100



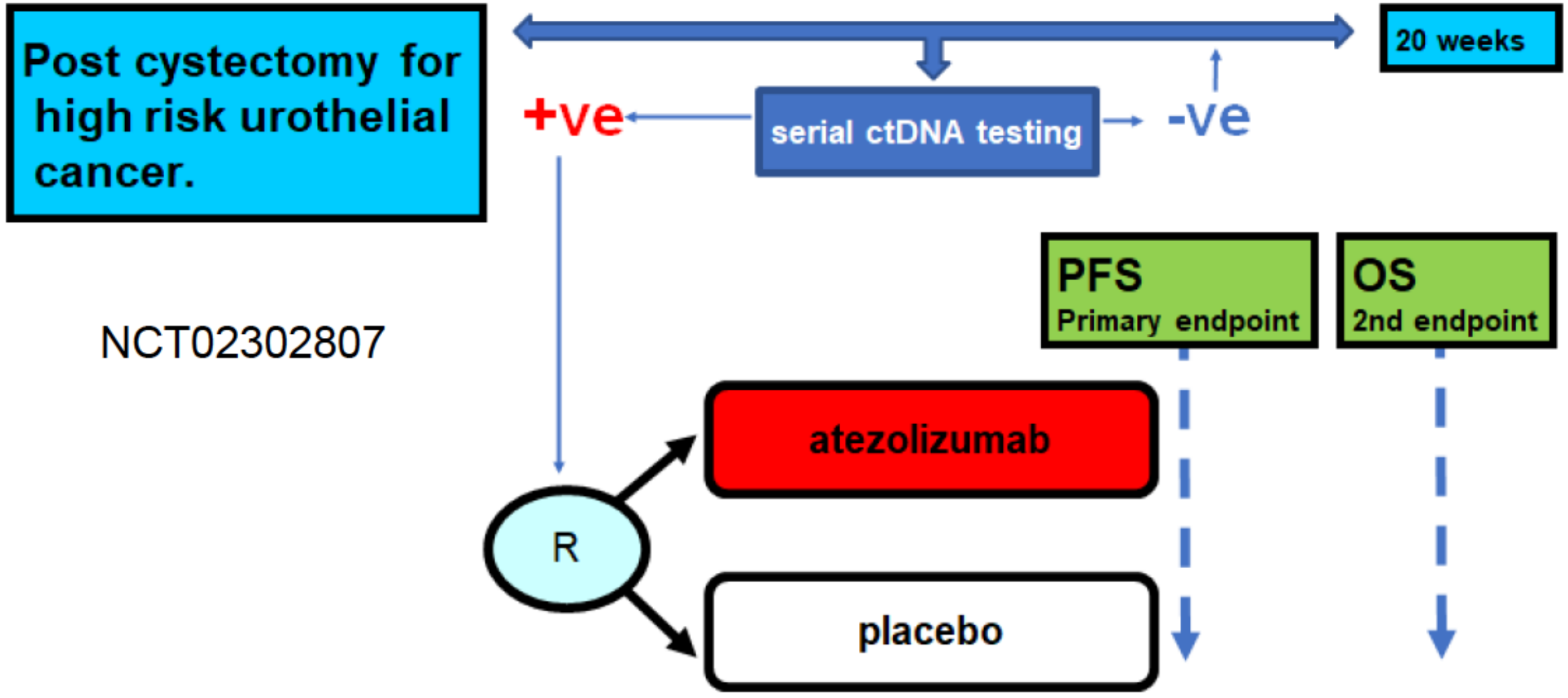
ctDNA guiding adjuvant immunotherapy in urothelial carcinoma



No. at risk		Time (months)					
		0	10	20	30	40	50
— Atezolizumab	ctDNA ⁻	184	144	85	44	5	0
		183	140	90	46	6	0
— Atezolizumab	ctDNA ⁺	116	48	25	13	2	0
		98	17	10	5	1	0

184	174	129	57	10	0
183	170	130	65	7	0
116	88	55	25	4	0
98	54	24	11	1	0

Adjuvant Atezolizumab vs Placebo in High-Risk Muscle-Invasive Bladder Cancer Who Are ctDNA Positive Following Cystectomy (IMvigor011)



SUMMARY

WHEN?

- First line is too early – not able to get in control of the disease.
- Second line is too late.
- Currently the best position of immunotherapy in mUC is the maintenance setting with avelumab.

WHICH?

- ICIs/ ADC combinations look the most promising.

BIOMARKERS?

- 1st generation of biomarkers for single agent ICIs (PD-L1 and TMB) have not changed therapy in mUC.
- 2nd generation of biomarkers remain exploratory (Teff RNA signature) and yet utilized routinely.
- Tissue based and circulating biomarkers in combination may be the best option.