Immunotherapy Advances in NSCLC

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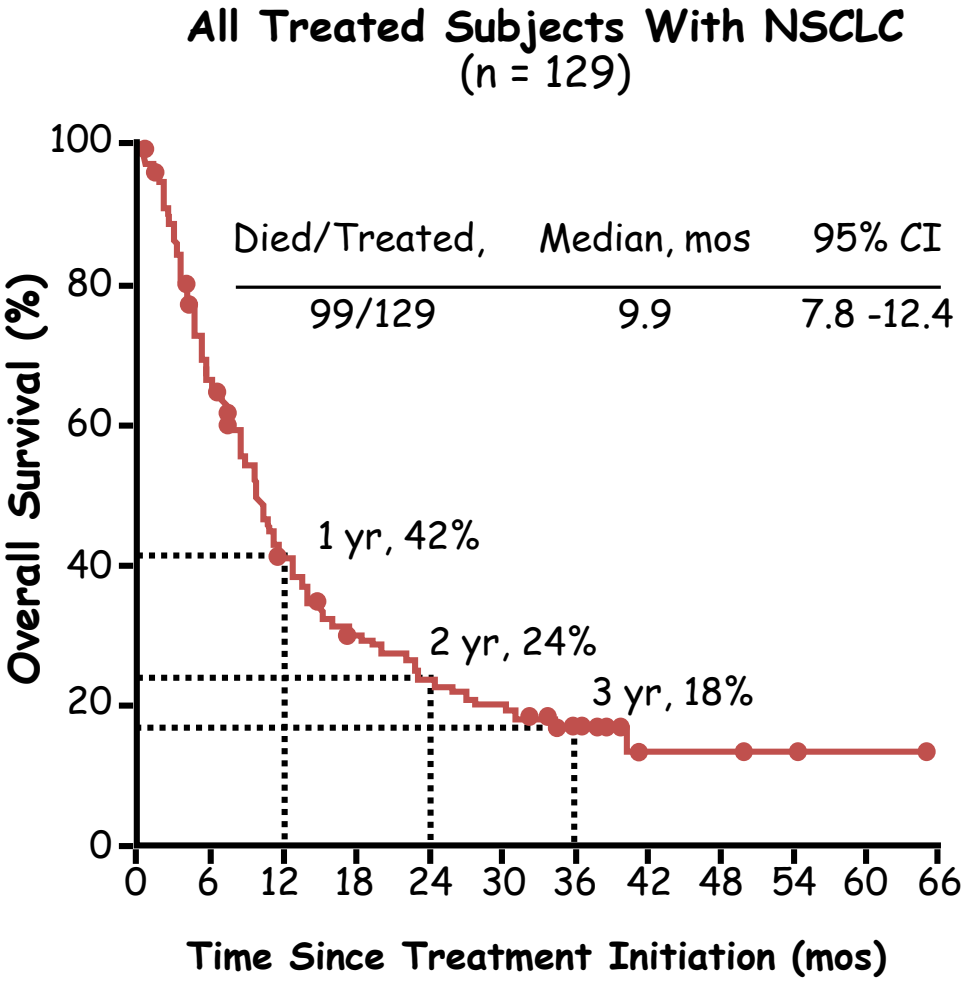
Disclosures

- Consulting fees: AstraZeneca, Merck & Co., Inc., Novartis Pharmaceuticals, Roche
- Ownership interest: Gritstone Oncology
- I **will** be discussing non-FDA approved treatments.

A Phase 1 Study of Nivolumab (MDX1106-03)



Gettinger SN, et al. J Clin Oncol. 2015

Nivolumab 017 and 057

	Docetaxel	Nivolumab			
017	All	All	PD-L1 < 1%	PD-L1 > 1%	PD-L1>10%
ORR	9%	20%	17%	18%	19%
mPFS (mo.)	2.8	3.5			
mOS (mo.)	6.0	9.2	8.7	9.3	11
057					
ORR	12%	19%	9%	31%	37%
mPFS (mo.)	4.2	2.3			
mOS (mo.)	9.4	12.2	10.4	17.2	19.4

Brahmer et al NEJM 2015
Borghaei et al NEJM 2015

Nivolumab 017 and 057 2 year OS

	Docetaxel	Nivolumab				
017	All	All	PD-L1 < 1%	PD-L1 > 1%	PD-L1 > 5%	PD-L1>10%
2 year OS	8%	23%				
057						
2 year OS	16%	29%	25%	37%	44%	45%

Borghaei et al ASCO 2016

KEYNOTE-001

	All patients	PS≥50%	PS 1%-49%	PS <1%
Prevalence	N=824	23	37	39
All patients	N=495	n=73	n=103	n=28
ORR	19%	45%	17%	11%
mPFS (mo.)	3.7	6.3	3	2
mOS (mo.)	12	NR	8.5	8.5

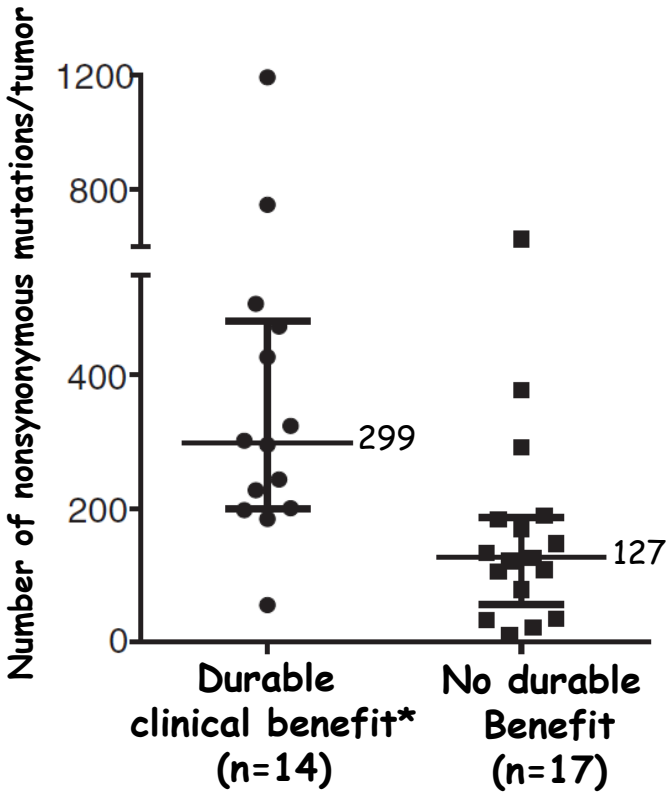
Garon et al NEJM 2015

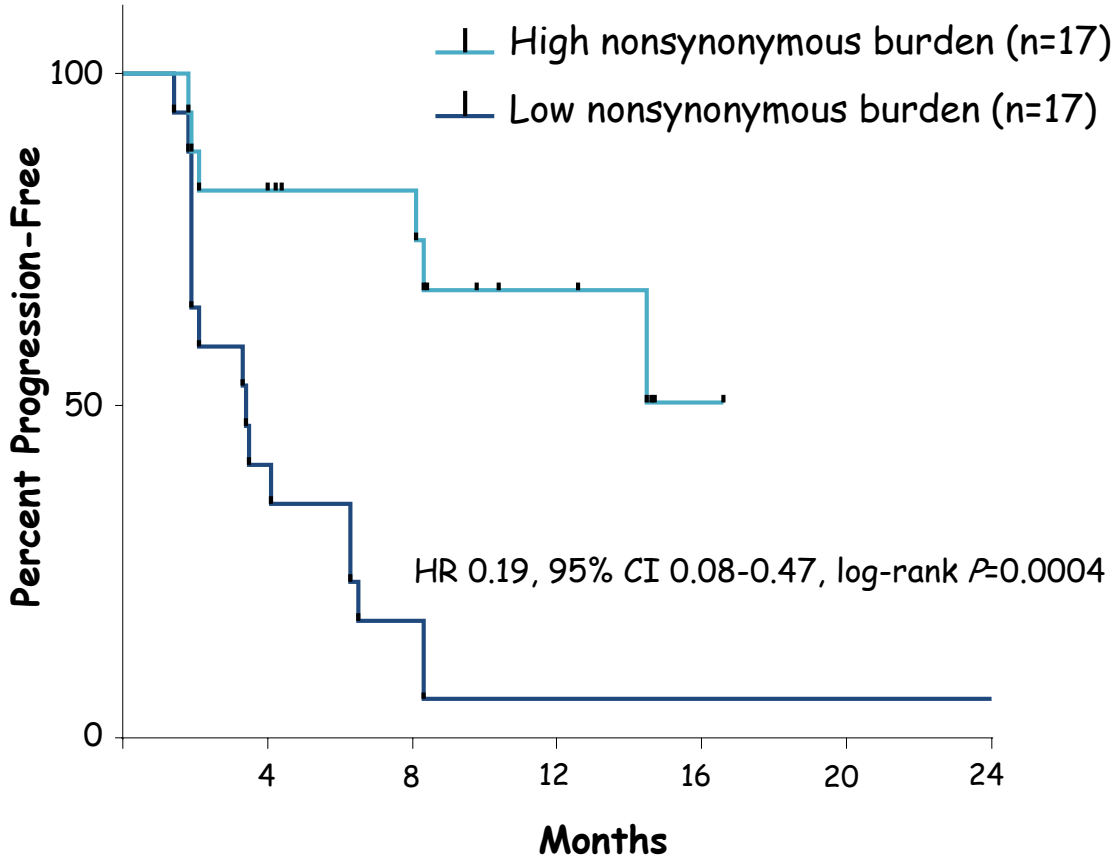
KEYNOTE-001 Overall Survival

	PS≥50%	PS 1%-49%	PS <1%
Squamous	14	14	14.7
Non-squamous	15.4	10.5	8.6
+ Smoking history	15.7	13.2	8.6
- Smoking history	8.2	7.3	9.1
EGFR WT	15.7	13.2	9.1
EGFR mutated	6.5	6.5	5.7

Hui et al ASCO 2016

Mutation Burden Determines Sensitivity to PD-1 Blockade in NSCLC

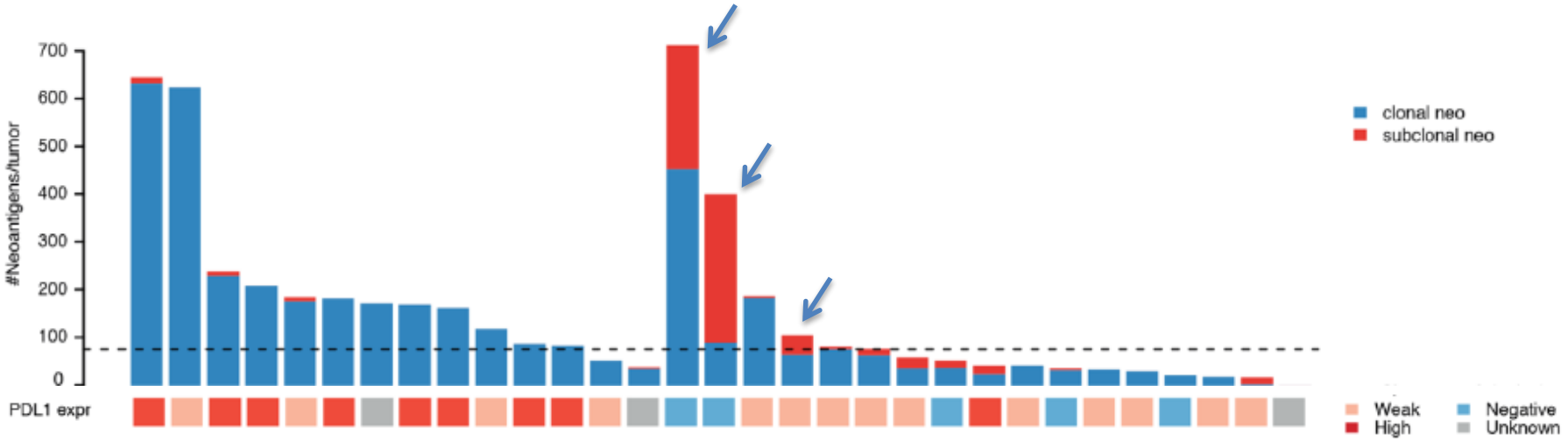


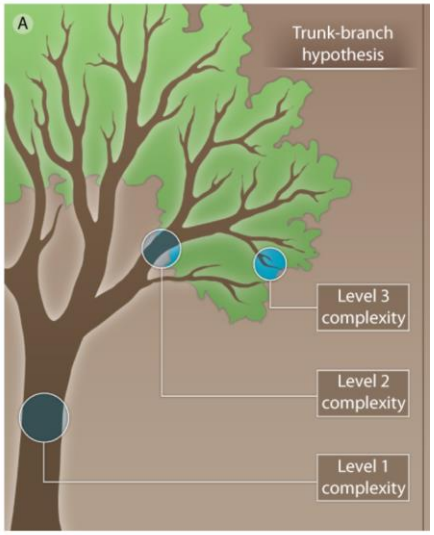


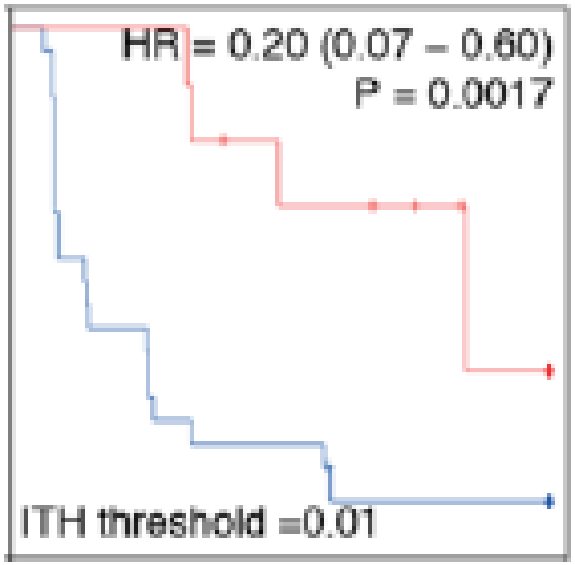
*Partial or stable response lasting >6 months.

Rizvi N, et al. *Science.* 2015;348(6230):124-128.

Neoantigen clonality and PD-1 benefit

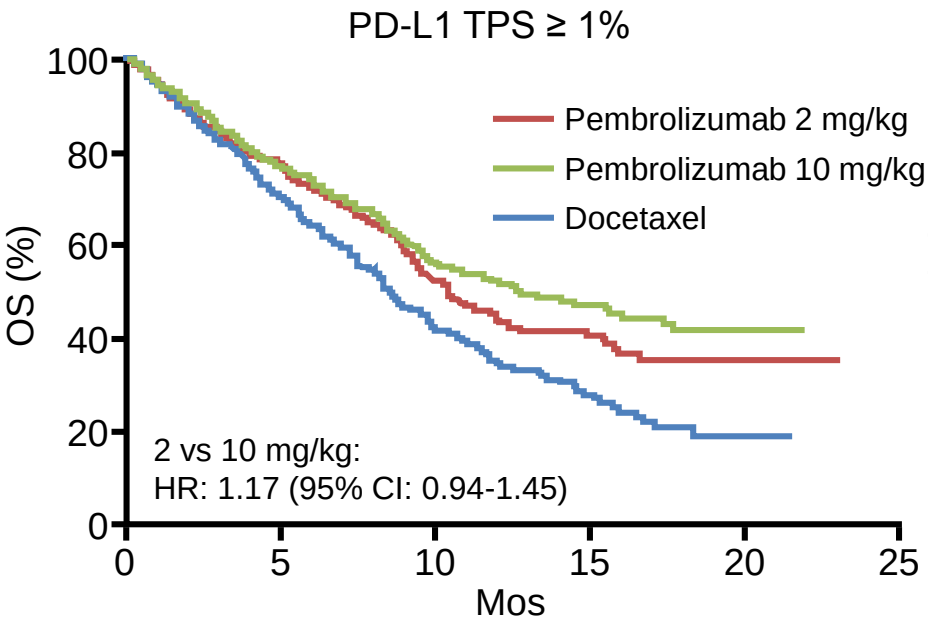




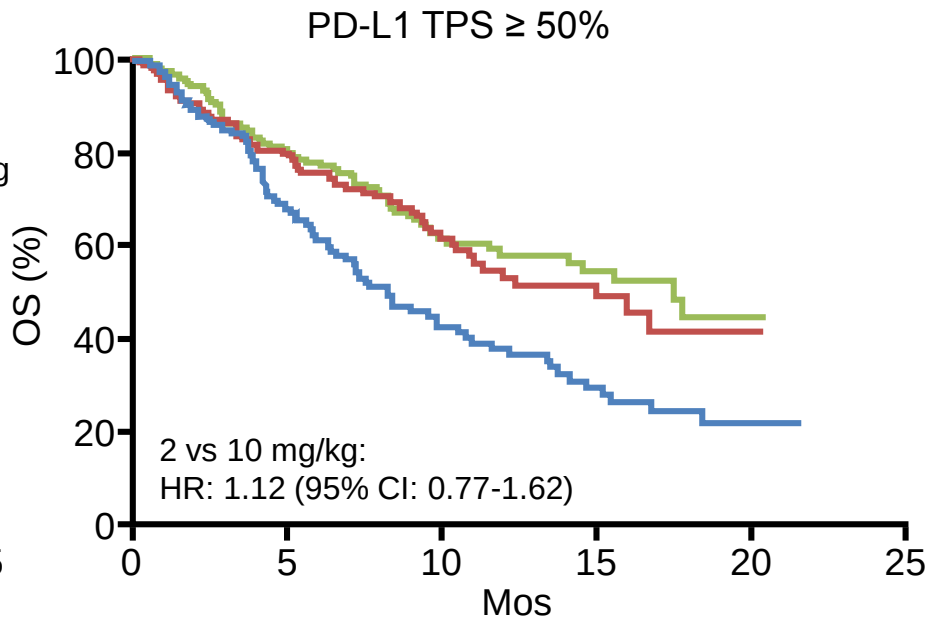


Swanton et al, Science 2016

KEYNOTE-010: OS With Pembrolizumab in NSCLC by PD-L1 Expression



Treatment Arm	Median OS, Mos (95% CI)	1-Yr OS, %	HR vs docetaxel (95% CI; P Value)
Pembro 2 mg/kg	10.4 (9.4-11.9)	43.2	0.71 (0.58-0.88; .0008)
Pembro 10 mg/kg	12.7 (10.0-17.3)	52.3	0.61 (0.49-0.75; < .0001)
Docetaxel	8.5 (7.5-9.8)	34.6	–



Treatment Arm	Median OS, Mos (95% CI)	HR vs Docetaxel (95% CI; P Value)
Pembro 2 mg/kg	14.9 (10.4-NR)	0.54 (0.38-0.77; .0002
Pembro 10 mg/kg	17.3 (11.8-NR)	0.50 (0.36-0.70; < .0001
Docetaxel	8.2 (6.4-10.7)	–

Herbst RS, et al. Lancet. 2016;387:1540-1550.

Key outcomes (total population)

	KEYNOTE 010		057		017	
RR	Pembro 2mg/kg Pembro 10mg/kg Docetaxel	18% 18.5% 9.3%	Nivo Doc	19% 9%	Nivo Doc	20% 9%
PFS (Total)	Pembro 2mg/kg Pembro 10mg/kg Docetaxel	3.9m 4.0m 4.0m	Nivo Doc	4.2m 2.3m	Nivo Doc	3.5m 2.8m
OS (Total)	Pembro 2mg/kg Pembro 10mg/kg Docetaxel	10.4m 12.7m 8.5m	Nivo Doc	12.2m 9.2m	Nivo Doc	9.2m 6.0m

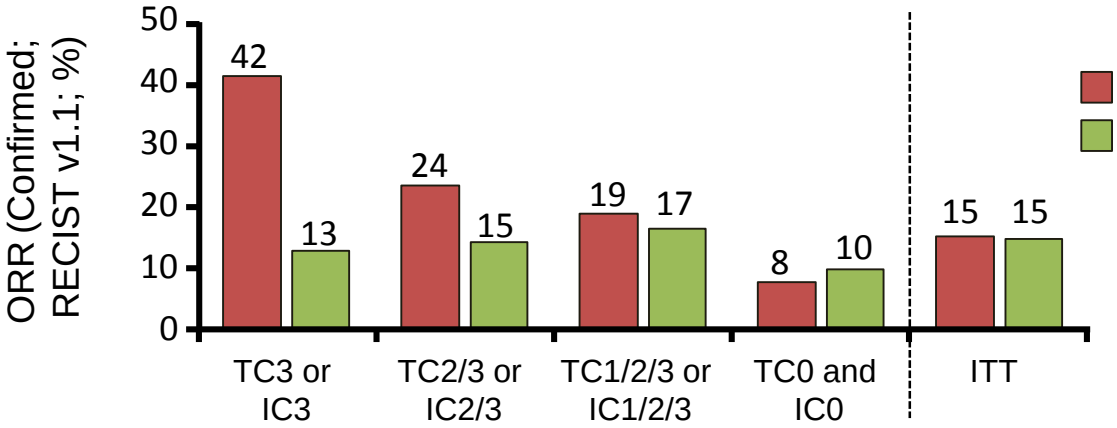
Courtesy of Tony Mok

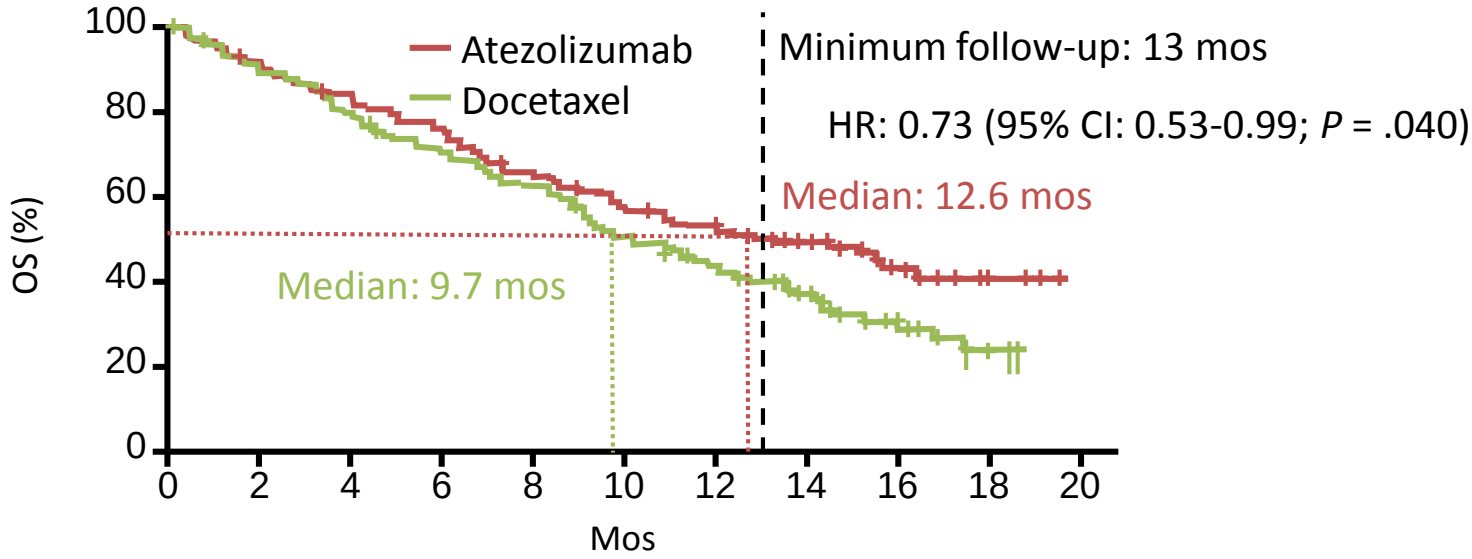
Key distinctive features

	KEYNOTE 010	Checkmate 057	Checkmate 017
Line of chemotherapy	One line or more	One line	One line
PD-L1 expression	≥ 1%	No selection	No selection
Histology	Non-squamous and squamous cell	Non-squamous cell	Squamous cell
Biomarker (PDL1 expression)	Prospective (44% archival, 56% new biopsy)	Retrospective	Retrospective
Drug dose	2mg/kg q3w 10mg/kg q3w	3mg/kg q2w	3mg/kg q2w
Primary Endpoints	PFS/OS Total population PFS/OS >50% stratum	OS Total population	OS Total population

Courtesy of Tony Mok

POPLAR: ORR and OS





Smith D, et al. ASCO 2016. Abstract 9028.
Fehrenbacher L, et al. Lancet. 2016;387:1837-1846.

First line NSCLC

Pembrolizumab				
	All patients	PS≥50%	PS 1%-49%	PS <1%
n		24	46	10
mOS (mo.)	22	NR	19.5	14.7
ORR	19%	45%	17%	11%

Hui et al ASCO 2016

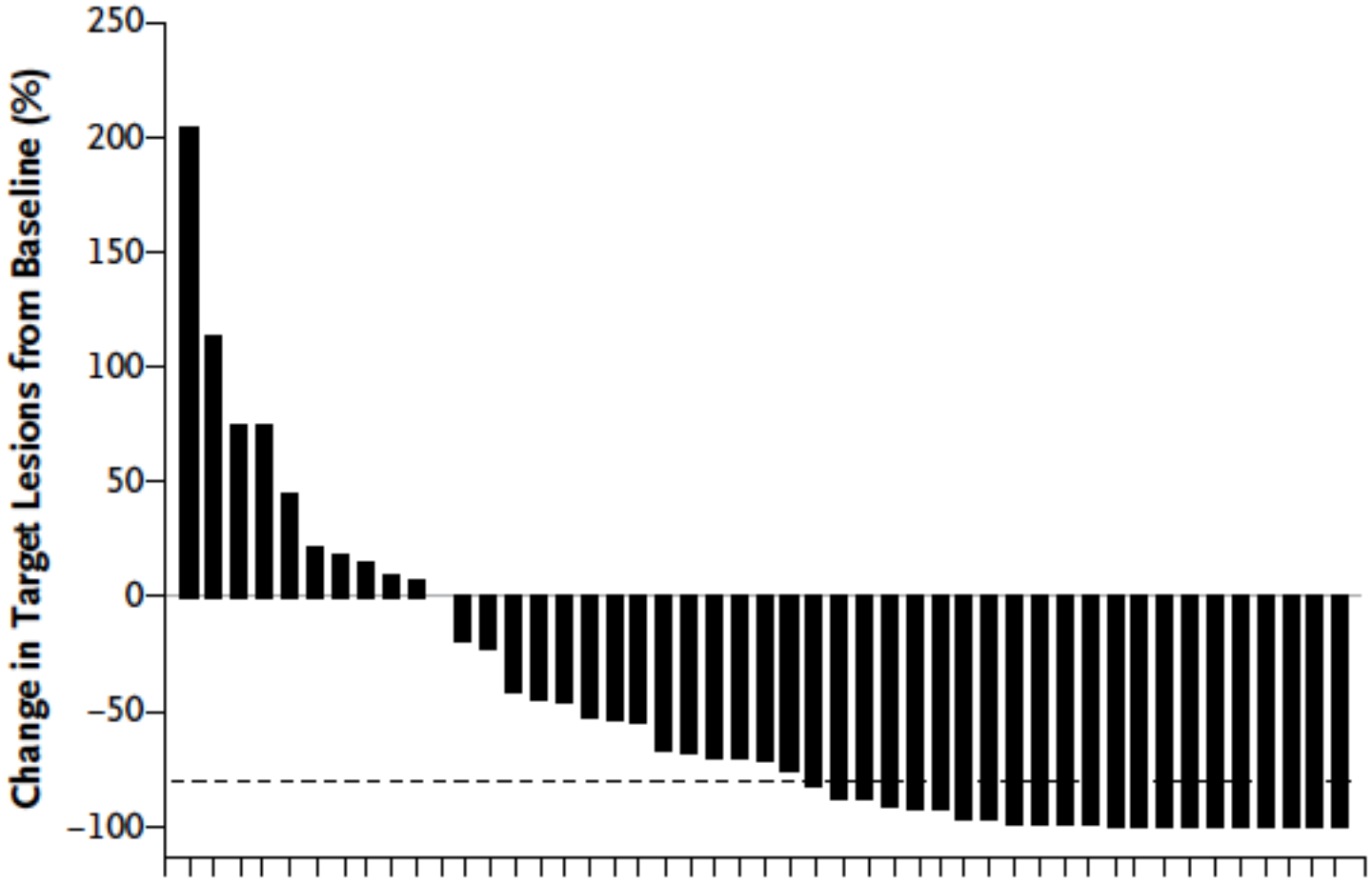
Nivolumab						
	All patients	≥50%	≥25%	≥10%	≥5%	≥1%
n	52	12	18	20	26	32
mOS (mo.)	19.4					
ORR (%)	23%	50	44	40	31	28

Gettinger et al JCO 2016

Phase III first line trials: PD-L1 +

Trial	VS. SOC	Cutoff	Endpoint	
CheckMate 026	nivolumab		PFS	Negative trial
KEYNOTE-024	pembrolizumab	50%	PFS	Positive trial
KEYNOTE-042	pembrolizumab	1%	OS	
Impower110 (non-squamous)	atezolizumab		PFS	
Impower111 (squamous)	atezolizumab		PFS	

Nivolumab + Ipilimumab in Melanoma



Wolchok et al NEJM 2013

Combination I-O in NSCLC

Previously treated NSCLC
Durvalumab 10–20 mg/kg q 2 – 4 weeks Tremelimumab 1 mg/kg q 4 weeks
ORR 28% (n=39)

Antonia et al. Lancet Oncology 2015

Chemotherapy naïve NSCLC
Nivolumab 3 mg/kg q 2 weeks Ipilimumab q 6-12 weeks
ORR 39-47% (n=86)

Hellmann et al, ASCO 2016

Phase 3 first-line combination trials in advanced NSCLC (all PD-L1 unselected)

Treatment	N*	Arms			Primary endpoint
Checkmate 227[1]	1980	Nivolumab, ipilimumab	Nivolumab	Plt-doublet chemotherapy	OS
MYSTIC[2]	675	Durvalumab, tremelimumab	Durvalumab	SOC Plt-based chemotherapy	PFS
NEPTUNE[3]	800	Durvalumab, tremelimumab	SOC Plt-based chemotherapy	-	OS
IMpower 130[4]	550	Atezolizumab, nab-paclitaxel/carboplatin	nab-paclitaxel/carboplatin	-	PFS
IMpower 150[5]	1200	Atezolizumab, paclitaxel/carboplatin, bevacizumab	Atezolizumab, paclitaxel/carboplatin	Paclitaxel/ carboplatin, bevacizumab	PFS
IMpower 131[6]	1200	Atezolizumab, nab-paclitaxel/carboplatin	Atezolizumab, paclitaxel/carboplatin	Nab-paclitaxel/carboplatin	PFS

*Estimated enrolment

Plt, platinum; SOC, standard of care

1. NCT02477826; 2. NCT02453282; 3. NCT02542293; 4. NCT02367781; 5. NCT02366143; 6. NCT02367794