Lung Cancer: Frontline Cancer, Predictive Markers, and Novel Combinations

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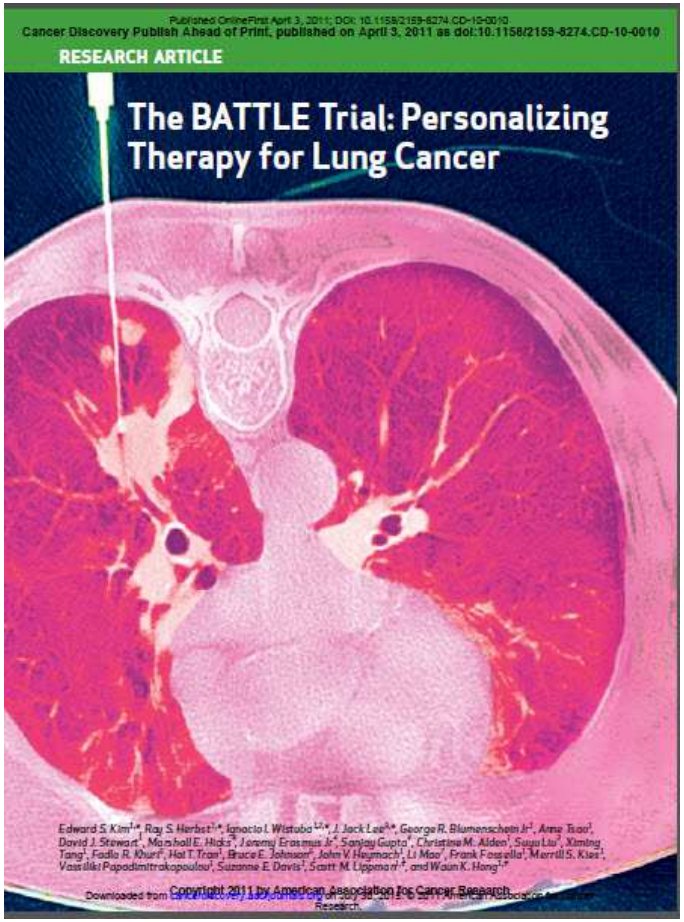
Disclosures

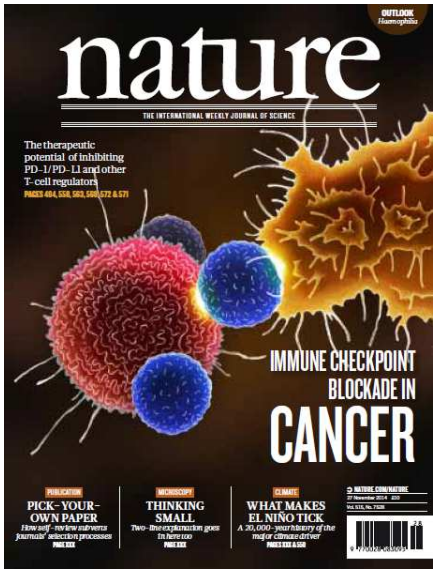
Consulting: Astra Zeneca, BMS, Lilly, Merck, Novartis, Pfizer, Roche

Scientific Advisory Board

Kolltan, Diatech, Biothera

The 10 Year Journey From Targeted Therapy (Battle) to Immunotherapy for Lung Cancer





Biomarkers don't just involve the tumor anymore!

Plan for this Presentation

- Historical progress of new drug development for Advanced NSCLC
- Novel Clinical Trial Designs for Biomarker Development (BATTLE 1, 2 and Master Protocols)
- Immunotherapy for NSCLC: New Standards of Care in the Refractory and Front Line Settings
- Bringing it all together: Doing BATTLE Using Immunotherapy in NSCLC: The "I" BATTLE Trial, and the Development of Rational Combinations

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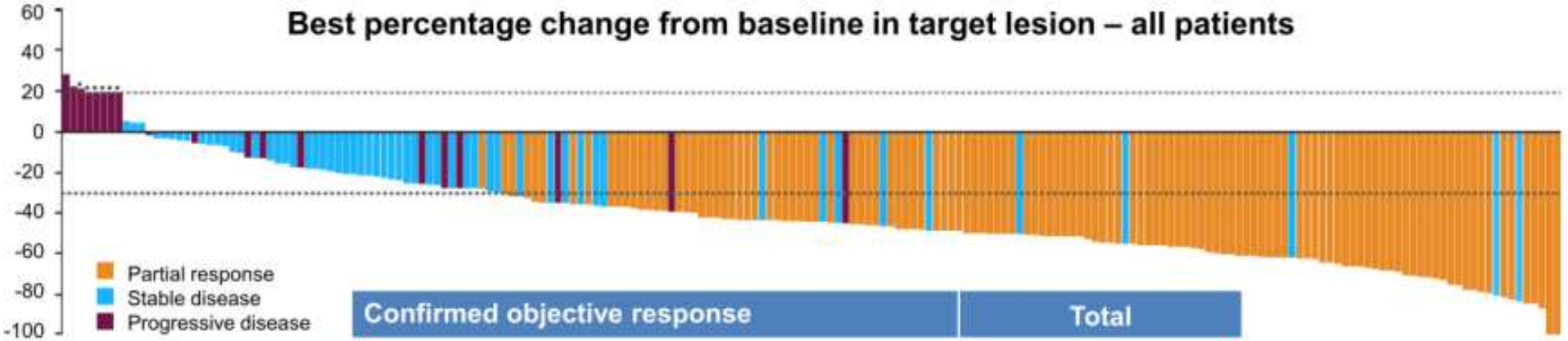
Lung Cancer:
The Leading Cause of Cancer Death in Most Countries

- US Lung Cancer: [1]
  - 221,200 new cases (13% of all cancer cases)
  - 158,040 deaths (27% of all cancer deaths)
- Worldwide Lung Cancer: [2]
  - 1.8 Million new cases
  - 1.6 Million deaths
- 87% of lung cancer is NSCLC (13% small cell) [3]
- 42.1 Million adults in the US currently smoke cigarettes [4]

[1] Cancer Facts and Figures, American Cancer Society 2015
[2] Lung Cancer Fact Sheet, International Agency for Research on Cancer, World Health Organization 2012
[3] Lung Cancer (Non-small cell), American Cancer Society 2014
[4] Current Cigarette Smoking Among Adults- United States 2005-2013. Centers for Disease Control and Prevention 2014

Osertimib response in pre-treated EGFR+ NSCLC patients with T790M mutation



Confirmed objective response	Total
ORR†	61% (95% CI 54, 68)
Complete response,‡ n (%)	0
Partial response,§ n (%)	122 (61%)
Stable disease ≥6 weeks,§ n (%)	58 (29%)
Progressive disease, n (%)	19 (10%)
DCR	91% (95% CI 85, 94)

Is anyone cured?

Yang JC, et al. Presented at WCLC 2015. Abstract 943.

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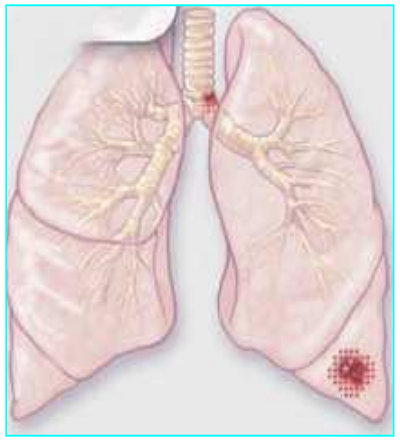
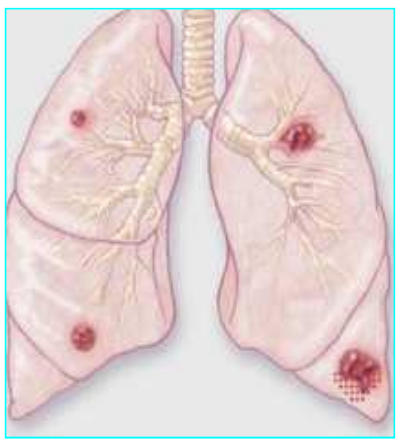
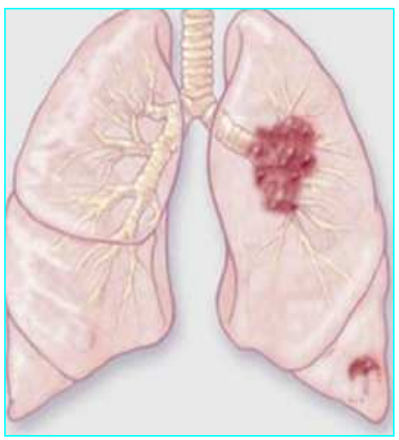
Natural History of Lung Cancer

Stages I-III Surgically Resected	Advanced – Stage IV Untreated	Advanced - Stage IV Refractory to Chemotherapy





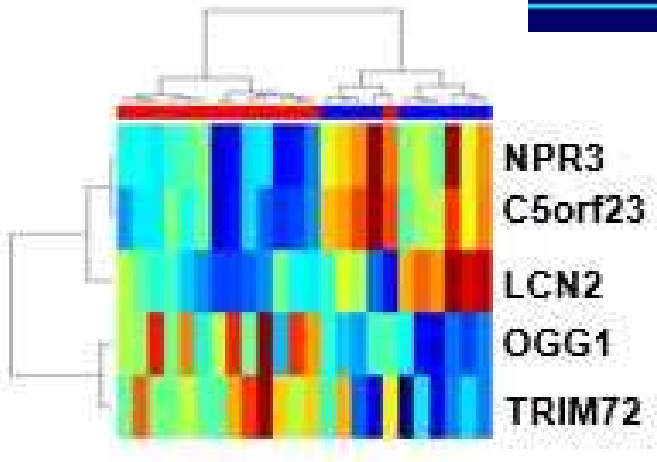


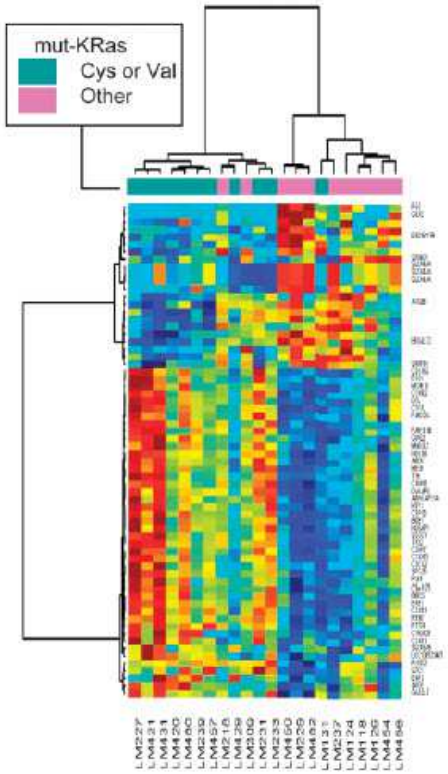
Tissues Available	Frequent	Infrequent	Rare

Adapted from Herbst, Heymach and Lippman; N Engl J Med 359:1367, 2008

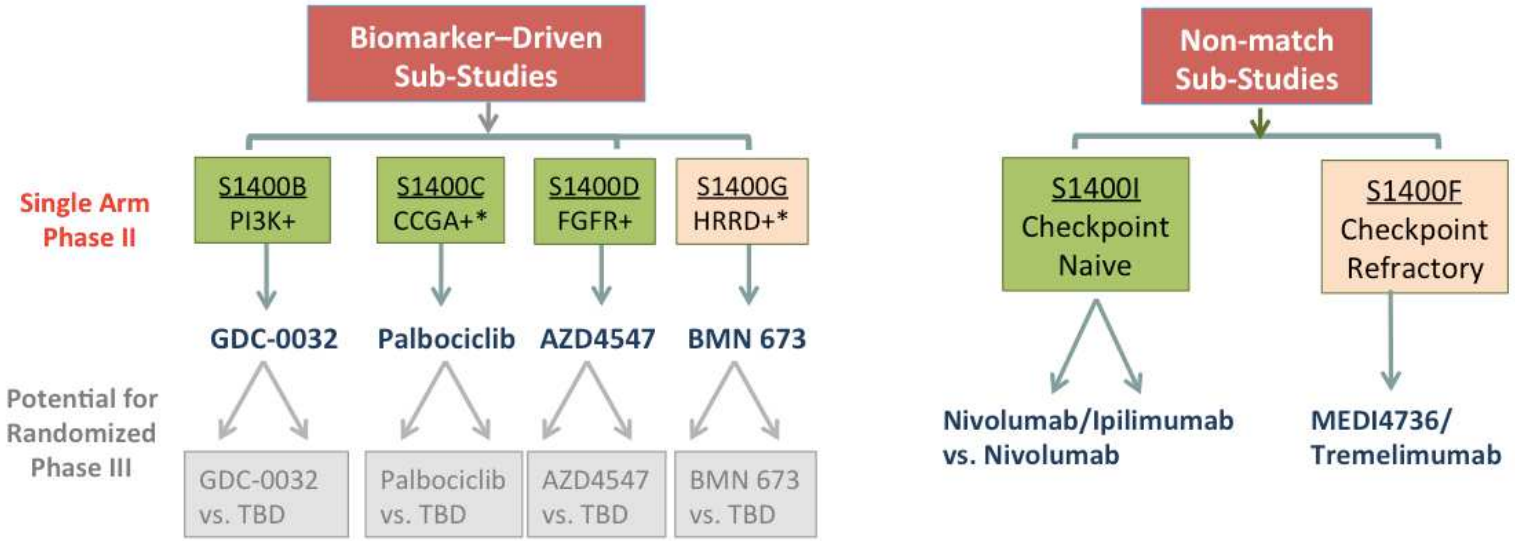
BATTLE-1 Identification of Predictive Markers and Gene Signatures

Drug Treatment	Biomarker	P–value	DC
Erlotinib	*EGFR* mutation	0.04	Improved
Vandetanib	High VEGFR-2 expression	0.05	Improved
Erlotinib + Bexarotene	High Cyclin D1 expression	0.001	Improved
	EGFR FISH Amp	0.006	Improved
Sorafenib	*EGFR* mutation	0.012	Worse
	EGFR high polysomy	0.048	Worse





Up-coming Protocol Schema



Two new sub-studies – S1400G and S1400F – added within 6-12 months

*CCGA = Cell Cycle Gene Alternation, HRRD = Homologous Recombinant Repair Deficiency

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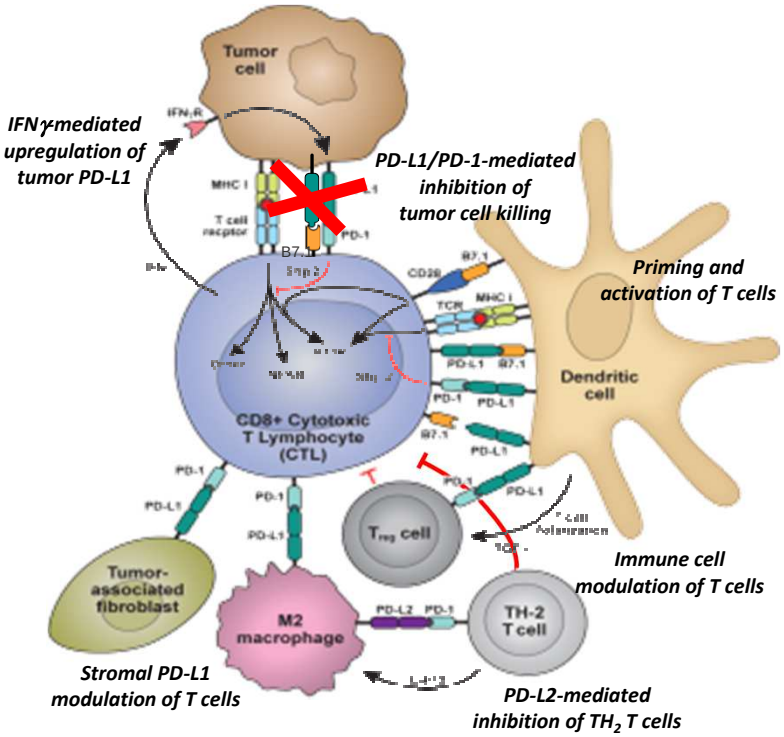
Mechanism of immune checkpoint inhibitors

Key attributes of the immune system

- Specificity
- Memory
- Adaptive

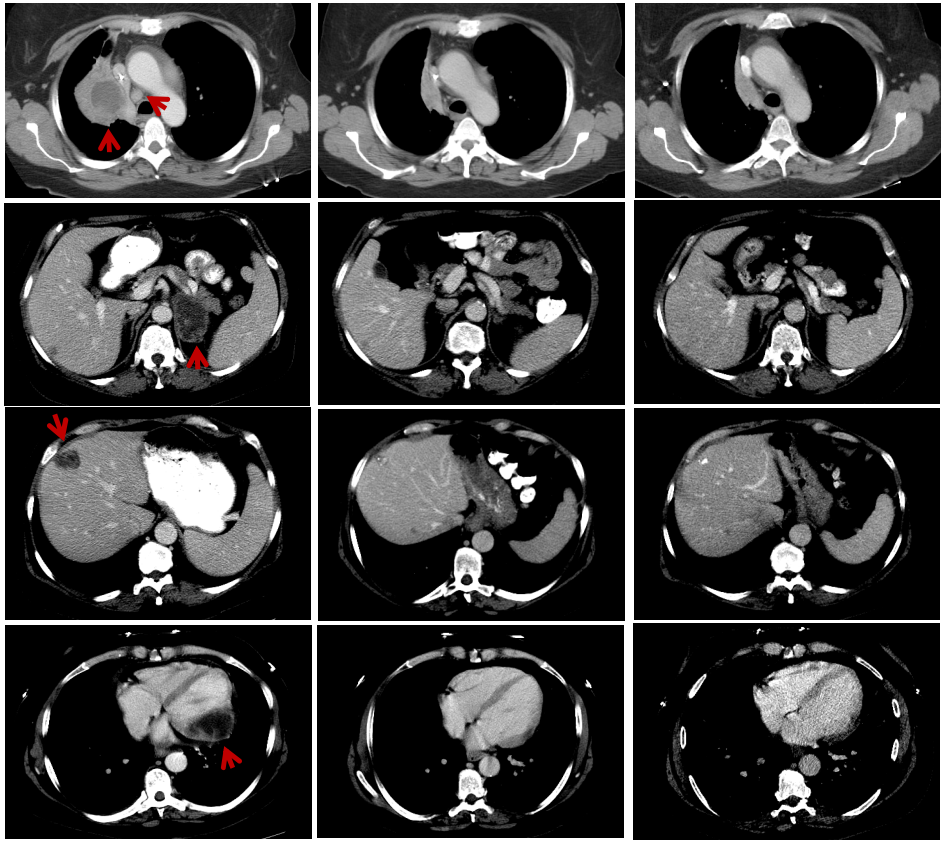


- Cancer cells develop many mutations that can make them appear foreign to the immune system
- T cells can recognize, attack, and kill these "foreign" cancer cells
- Cancer cells can evade immune attack by expressing PD-L1
- Adaptive tumour expression of PD-L1 turns the immune system OFF
- Clinically, we want to block PD-1 or PD-L1 to **reactivate** the immune system
- PD-L1 plays an important role in dampening the anti-tumour immune response

IFN, interferon.

Herbst RS, et al. J Clin Oncol. 2013;31 Suppl;abstract 3000.

Early Patient on Nivolumab June 2010

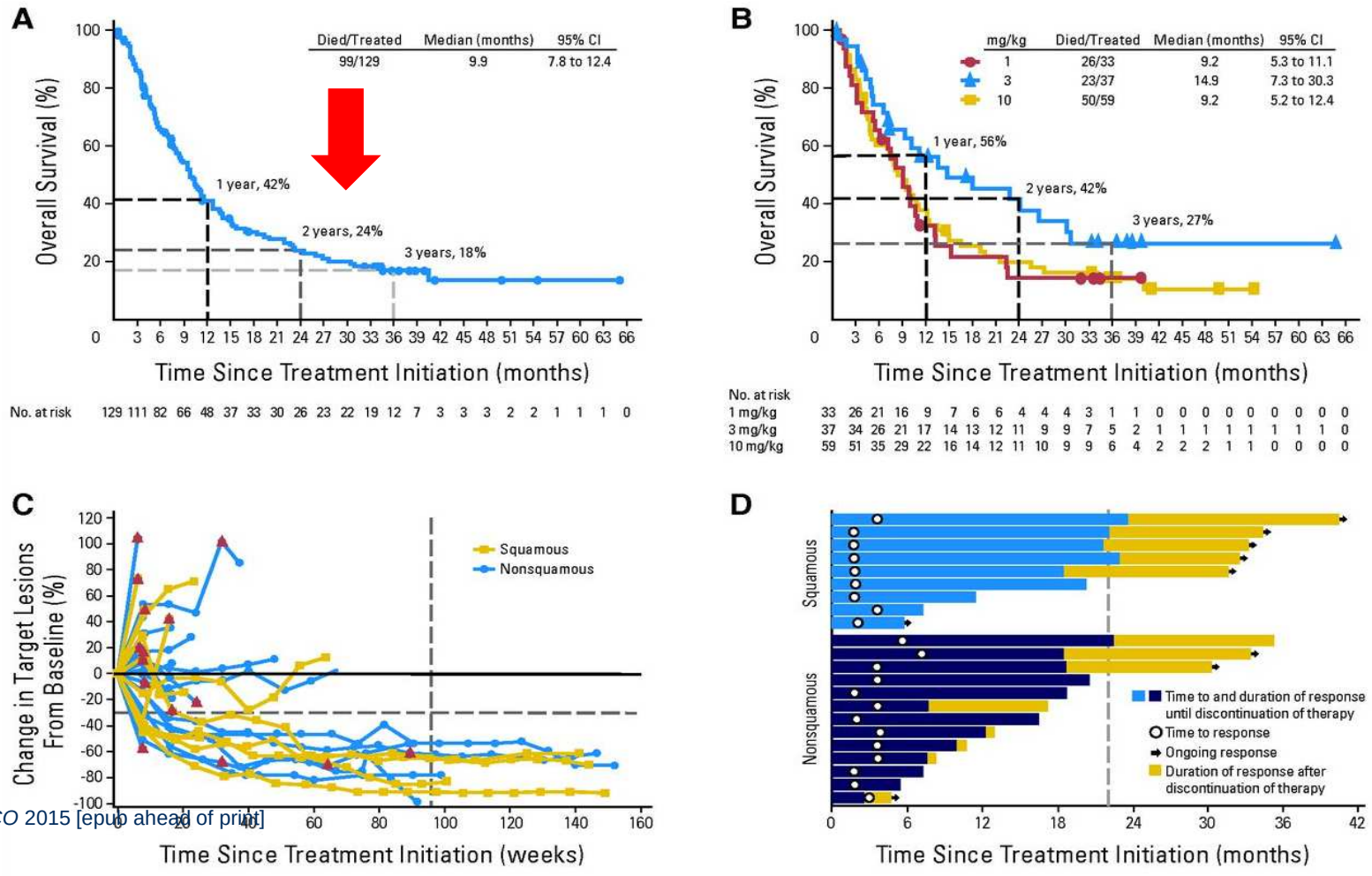


Pre- Nivolumab | 2 Years on Nivolumab | Last month, > 4 Years off Nivolumab

- 63 y/o ex-smoker (15 pack years, quitting in 1983)
- Stage IV Squamous NSCLC dx in Jan. 2009; metastatic to hilum/ mediastinum, liver, adrenal, bone and later, myocardium
- 3 prior chemotherapy regimens
- Nivolumab initiated June 2010

Cure?

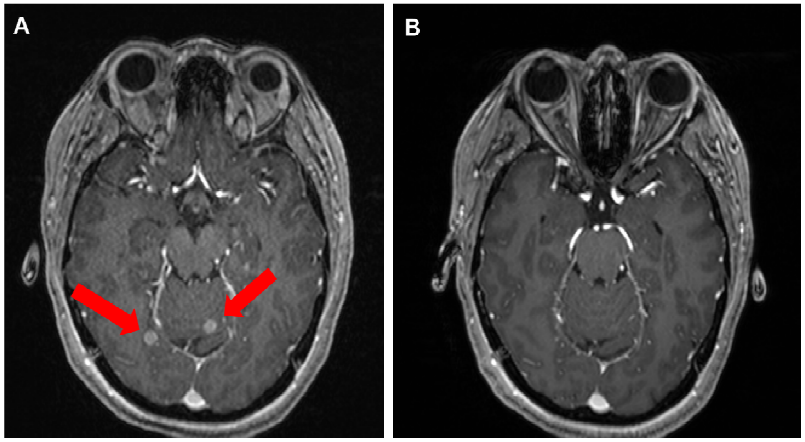
A large Phase 1 experience provided the preliminary data for this randomized study



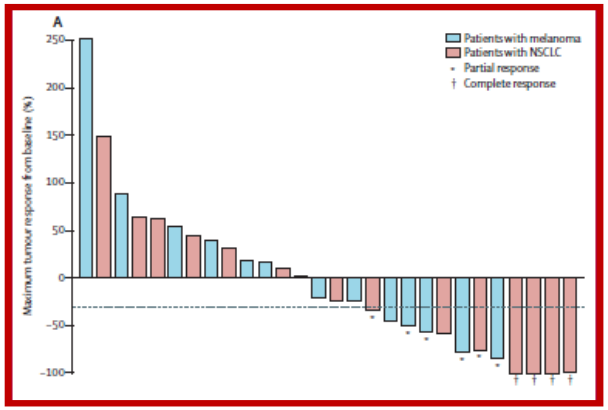
Gettinger SN et al. *JCO* 2015 [epub ahead of print]

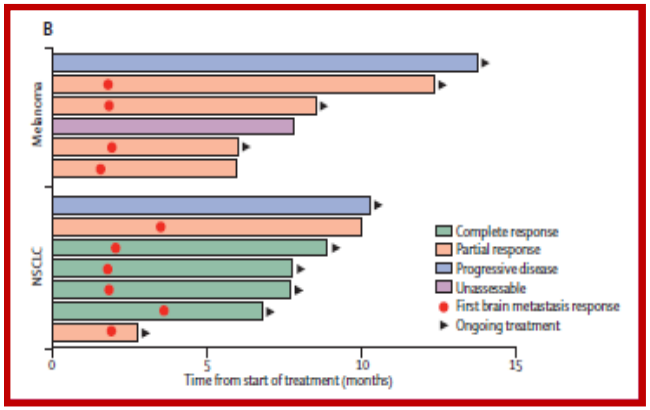
Immunotherapy for NSCLC Brain Metastasis

Immunotherapy and Brain Metastases



- 51-year-old woman with adenocarcinoma
- Previously treated with SRS to several brain metastases and 1 line of chemotherapy
- Pembrolizumab resulted in systemic and CNS responses that are ongoing at 7+ months of treatment

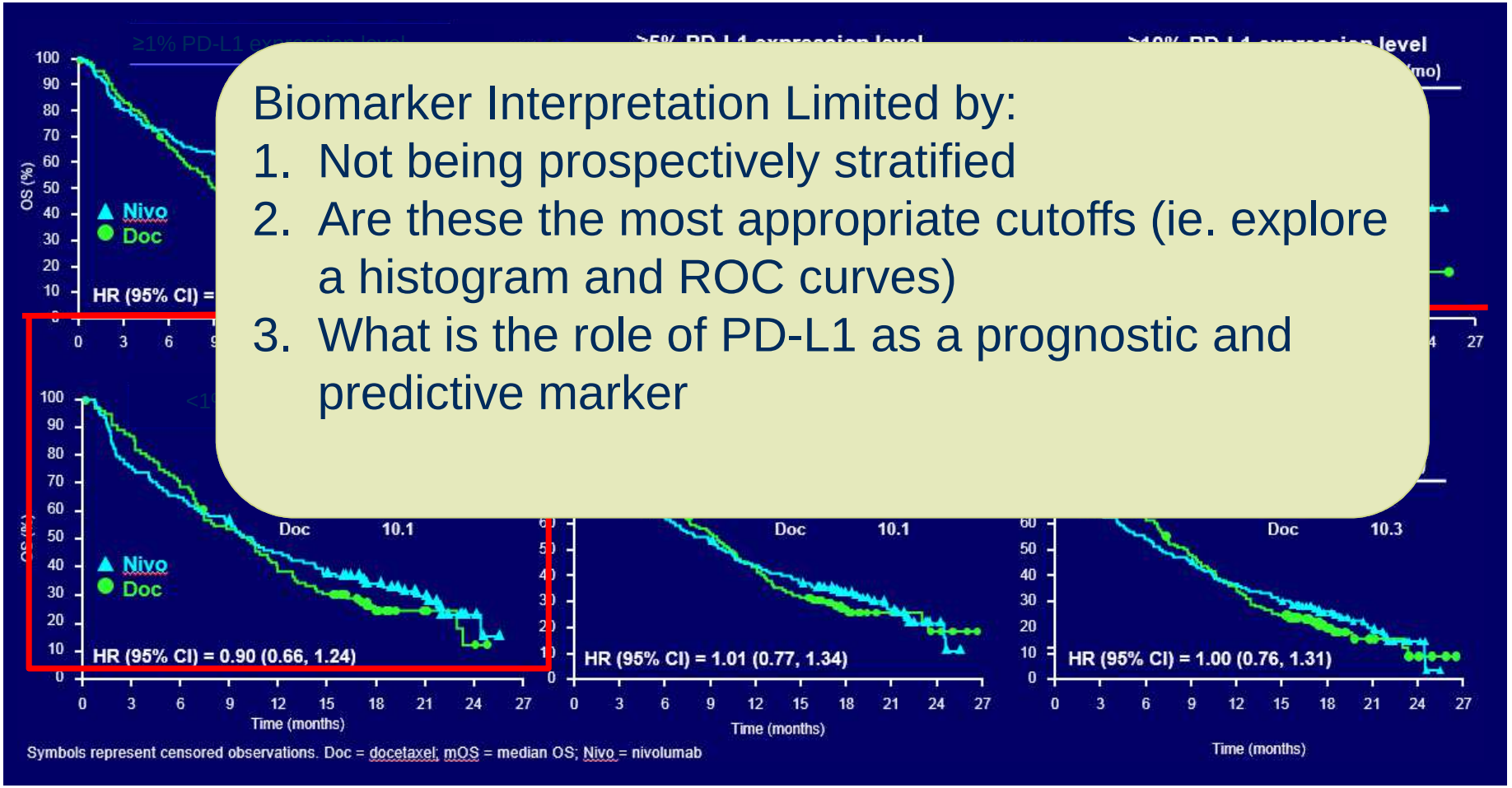




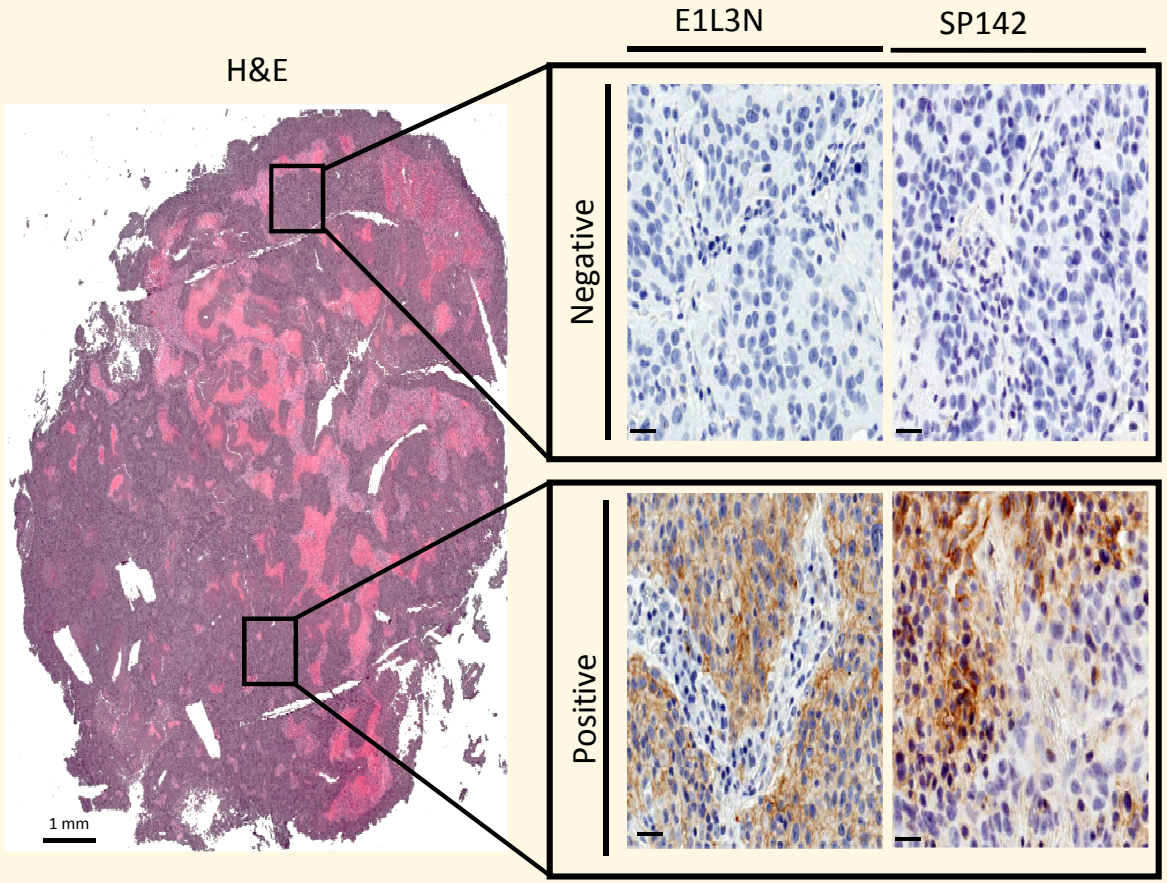
Goldberg SB, et al. *Lancet Oncol*. 2016;17:976-983.

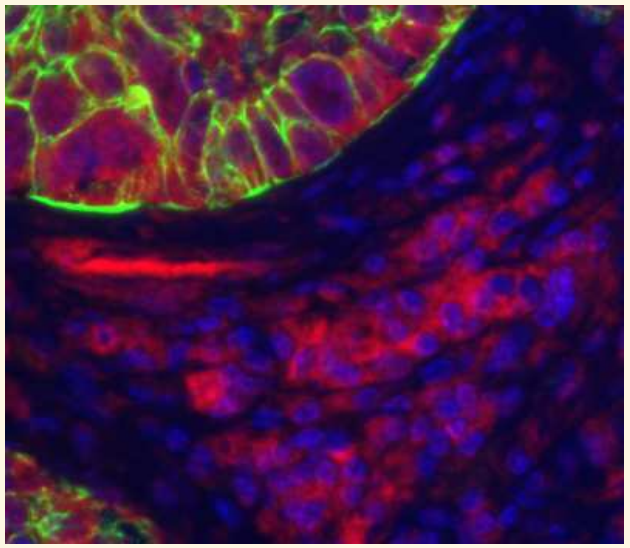
IS PDL1 a Biomarker?

ASCO 2015: Overall Survival by PD-L1 Expression (Checkmate 57- Non Squamous)



Expression of PD-L1 is heterogeneous and varies with antibody used





Immunofluorescence shows stroma and epithelial staining are often concordant and adjacent

Green = Cytokeratin

Blue = Nuclei

Red = PD-L1 (SP142)

McLaughlin, K Schalper, R. Herbst and D Rimm (Yale Pathology)

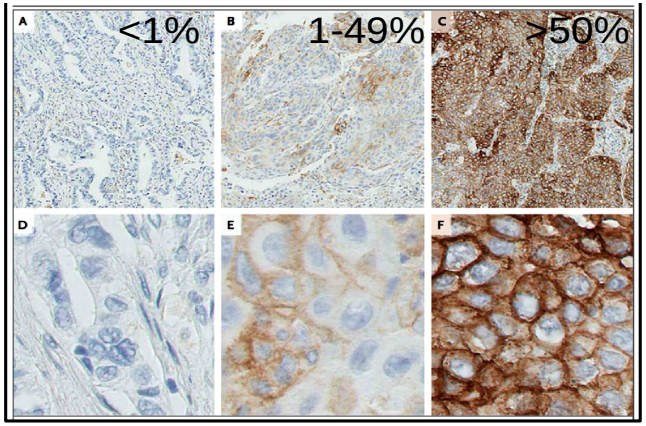
Issues with the PDL1 Biomarker

- Heterogeneity – multiple tumors and multiple passes within a tumor
- Interval between biopsy and treatment
- Primary versus metastatic disease
- Antibody and staining conditions

- Defining a positive result (cut-offs):
  - Cell type expressing PD-L1 (immune cell versus tumor or both)
  - Location of expression – cell surface versus intracellular versus stromal
  - Intensity, percent of cells ‘positive’
  - Distribution - patchy versus diffuse, intratumoral versus peripheral

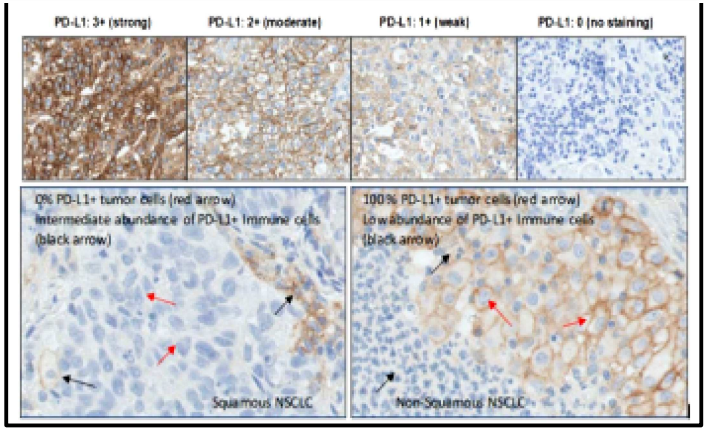
FDA approved PD-L1 assays

Clone 22C3 (pembrolizumab, **companion**)



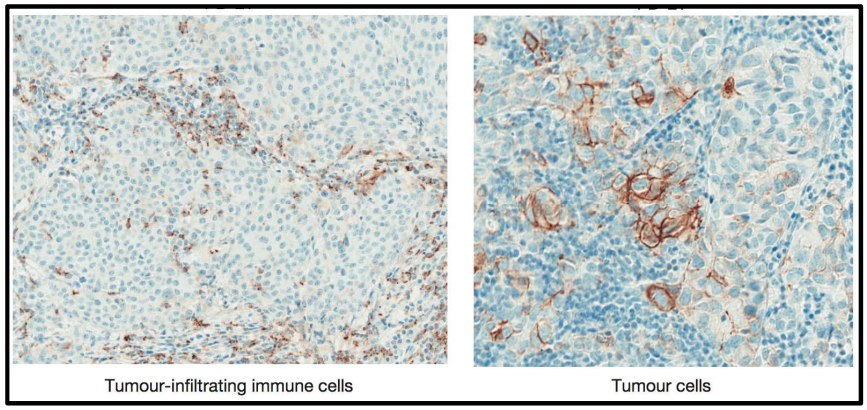
Garon et al., 2015, NEJM

Clone 28-8 (nivolumab, **complementary**)



Philips et al., 2015, AIMM

Clone SP142 (atezolizumab, **complementary**)



Powles et al., 2014, Nature

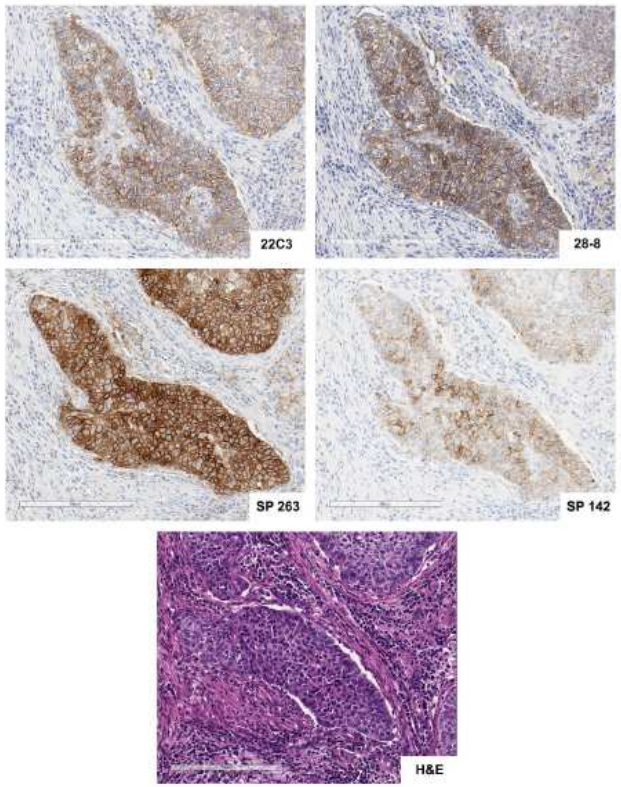
The Blueprint Project: Comparing PD-L1 IHC Diagnostics For Immune Checkpoint Inhibitors

Dr. Fred R. Hirsch MD, Pl

Blueprint Team:

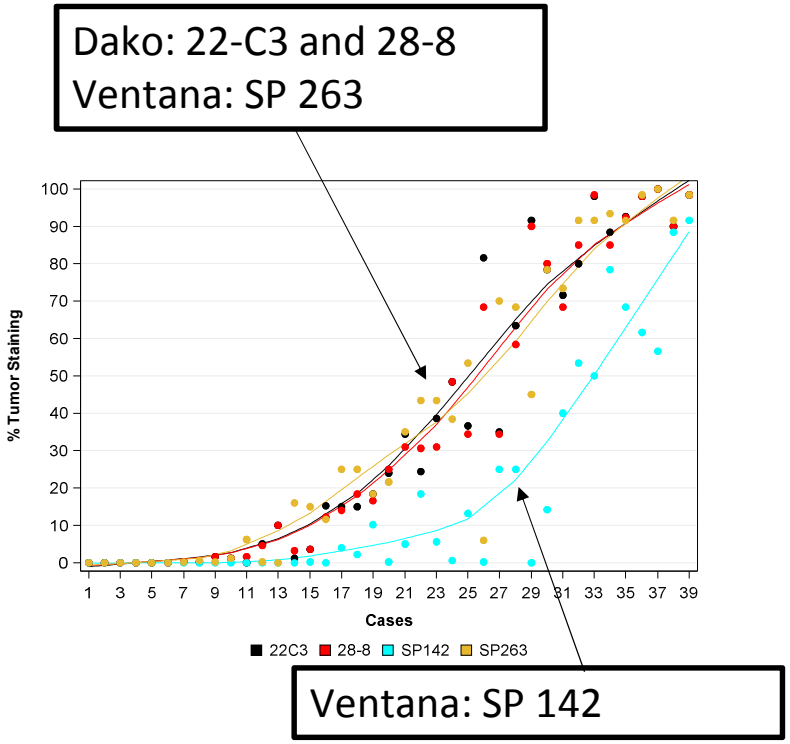
AACR
AstraZeneca
Bristol-Myers Squibb
Dako/Agilent
Genentech/Roche
IASLC **: COORDINATOR**
Merck
Ventana/Roche Tissue Diagnostic

FIGURE 2F



Analytical Evaluation Results: Mean Tumor Proportion Score (TPS) per case based on three readers

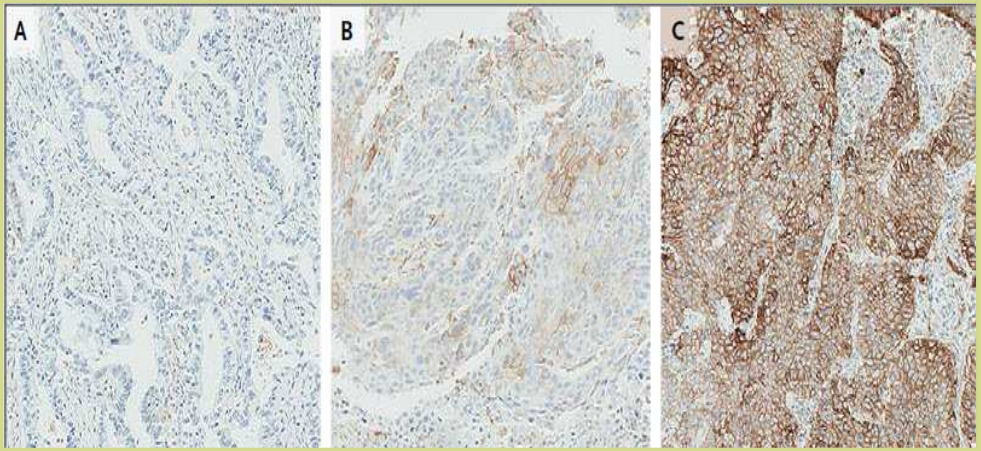
- Analytical comparison of % tumor cell staining (Tumor Proportion Score), by case, for each assay
- **Data points represent the mean score from three pathologists for each assay on each case**
- Superimposed lines / points indicate identical TPS values
- No clinical diagnostic cut-off applied
- **Conclusion:** 3 of 4 assays are analytically similar for tumor cell staining.

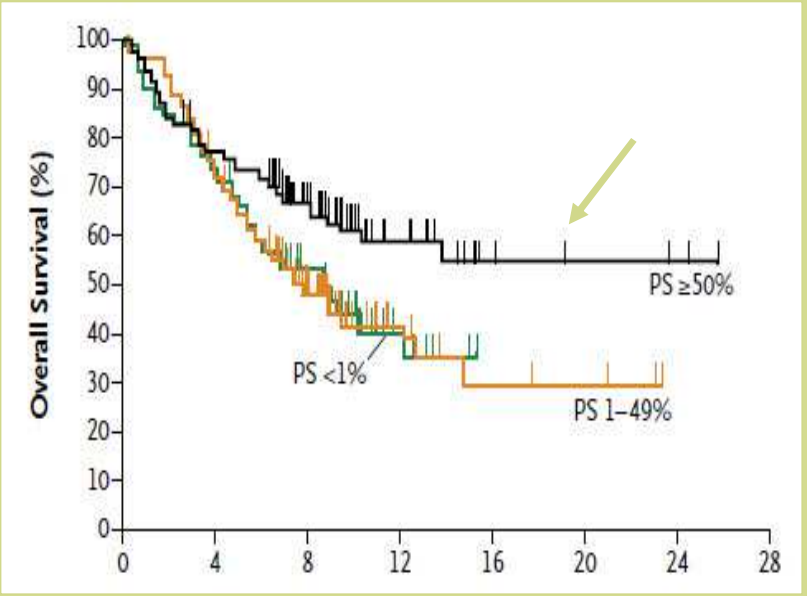


Hirsch FR et al: AACR 2016

Pembrolizumab Biomarker Development

Pembrolizumab[1] DAKO-22c3 Ab





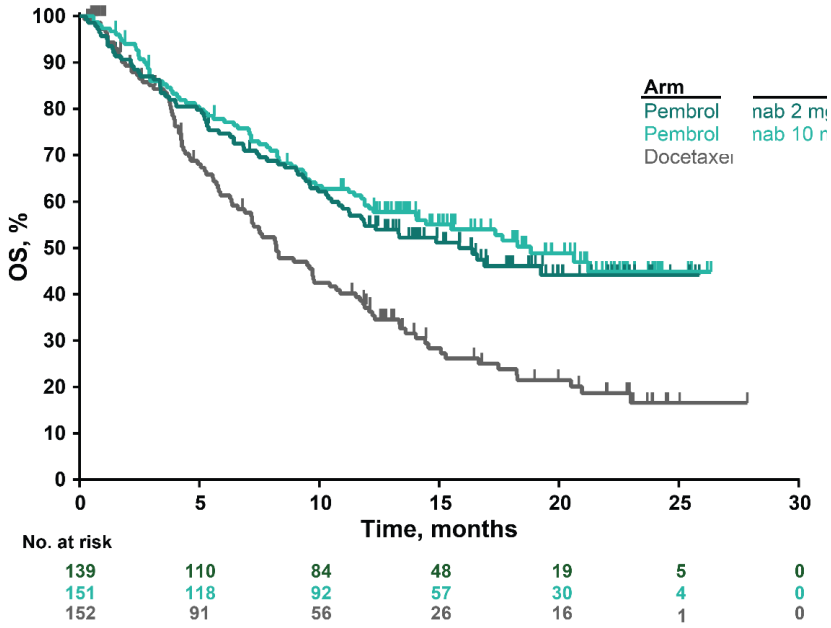
0 1-49% low > 50% high

[1] Garon EB et al. *N Engl J Med* 2015 372:2018-2028

Overall Survival: Updated Analysis

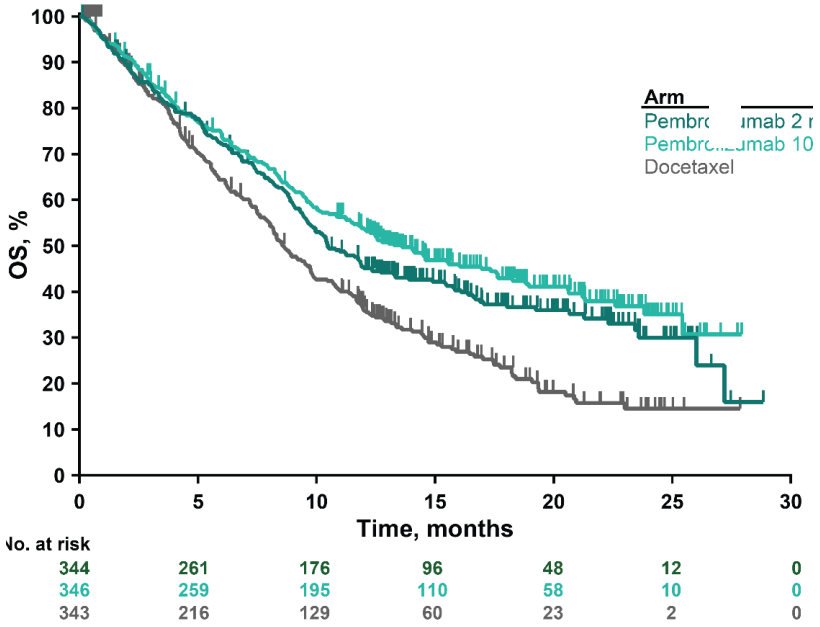
TPS ≥50%

Arm	Median, mo	18-mo Rate, %	HR (95% CI)	P[a]
Pembrolizumab 2 mg/kg	15.8	46	0.54 (0.39-0.73)	0.00004
Pembrolizumab 10 mg/kg	18.8	52	0.48 (0.35-0.66)	<0.00001
Docetaxel	8.2	24	—	—



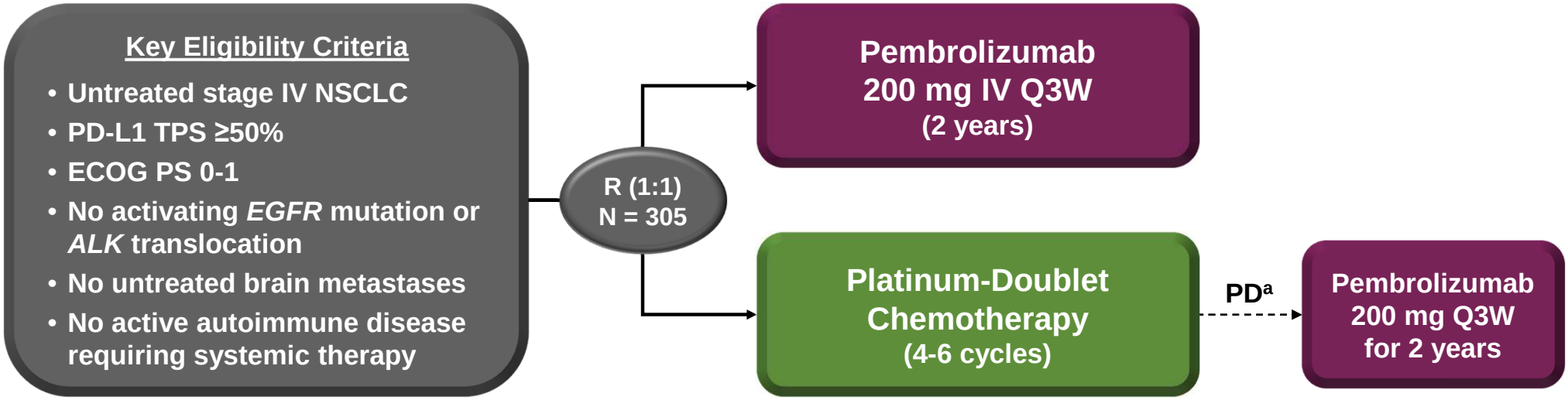
TPS ≥1%

Arm	Median, mo	18-mo Rate, %	HR (95% CI)	P[a]
Pembrolizumab 2 mg/kg	10.5	37	0.72 (0.60-0.87)	0.0003
Pembrolizumab 10 mg/kg	13.6	43	0.60 (0.50-0.73)	<0.00001
Docetaxel	8.6	24	—	—



Herbst et al, Lancet 2015, updated ESMO 2016

KEYNOTE-024 Study Design (NCT02142738)



Key End Points

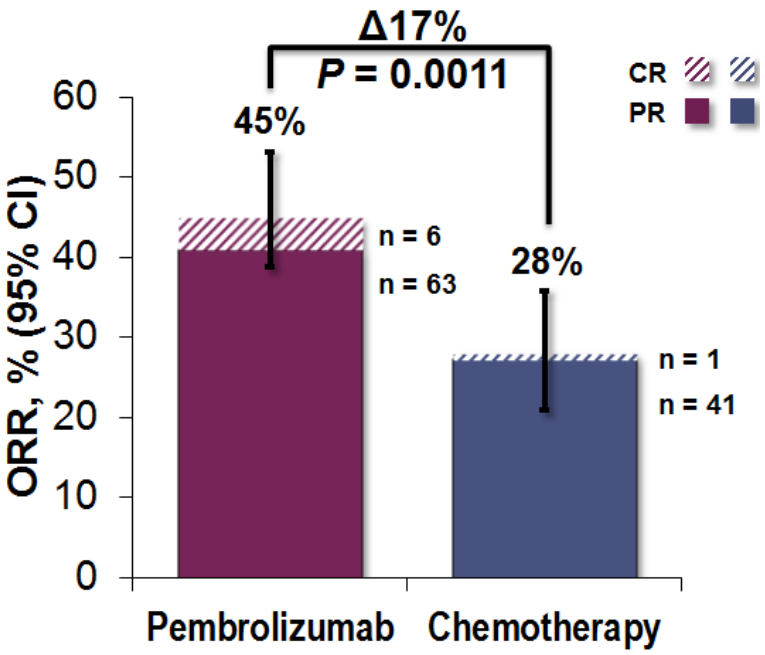
Primary: PFS (RECIST v1.1 per blinded, independent central review)

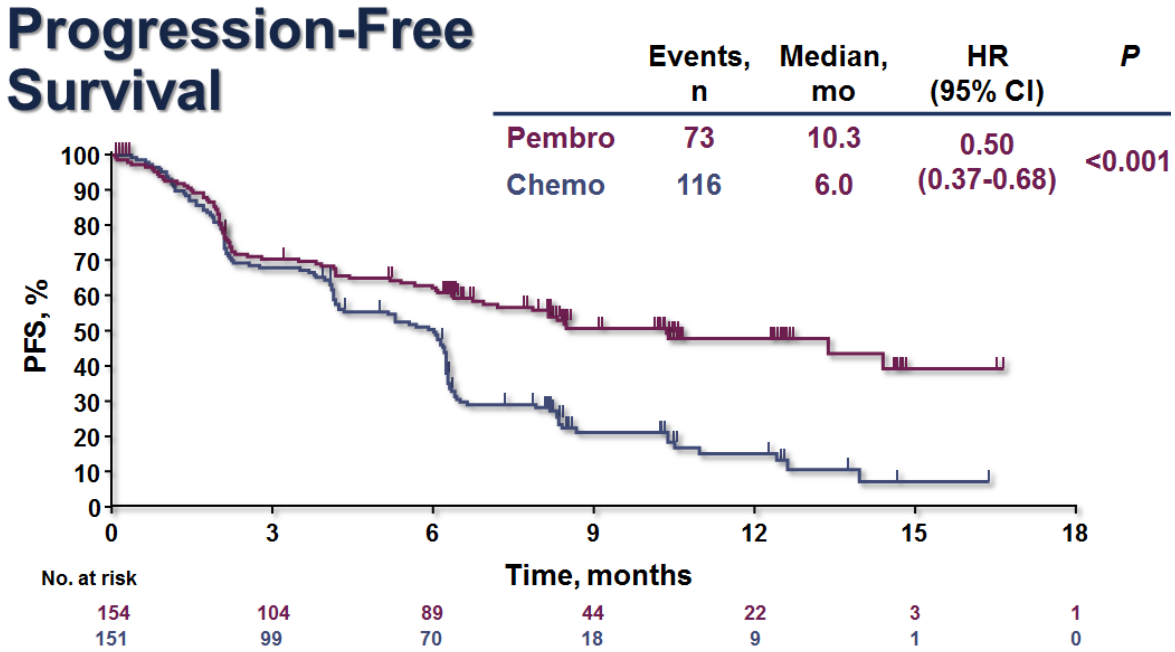
Secondary: OS, ORR, safety

Exploratory: DOR

[a]To be eligible for crossover, progressive disease (PD) had to be confirmed by blinded, independent central radiology review and all safety criteria had to be met.

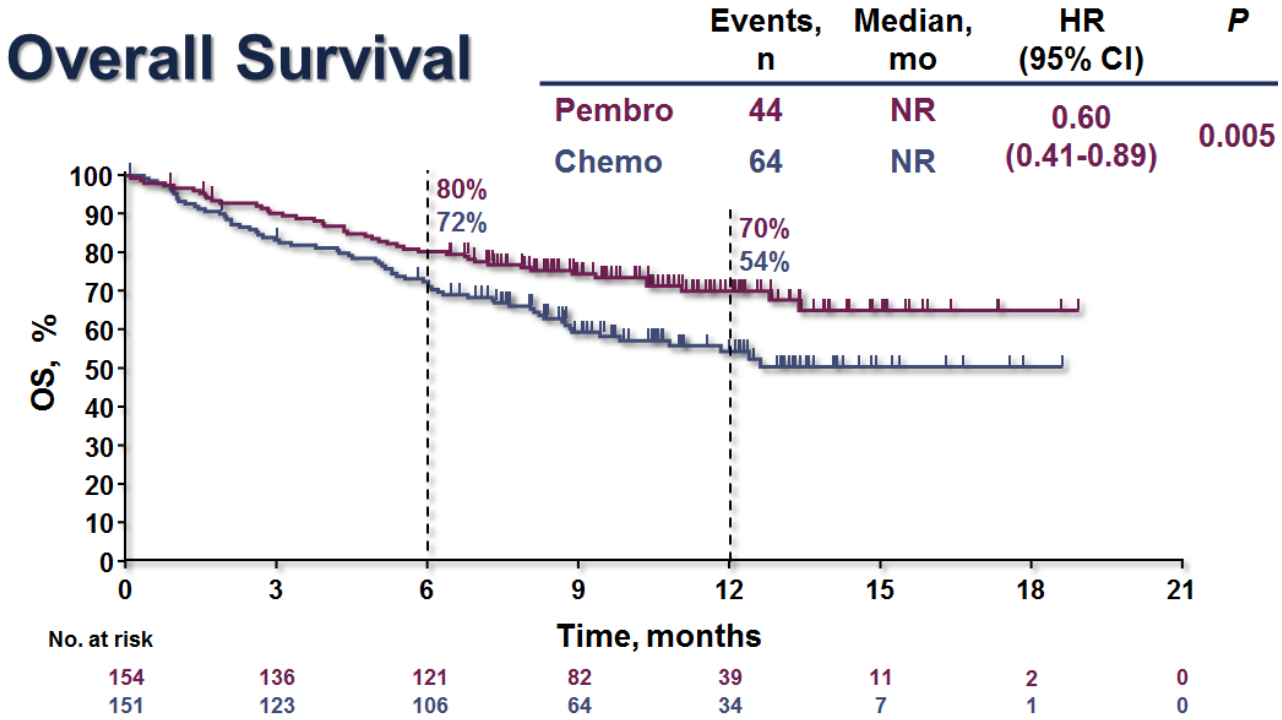
Efficacy data





Reck et al, NEJM 2016

Survival data



- Clear survival benefit
  - Estimated rate of OS @ 12 months: 70% (Pembro) vs 54% (CT)
  - HR for death: **0.60**
  - cross-over **in 50% of the patients**

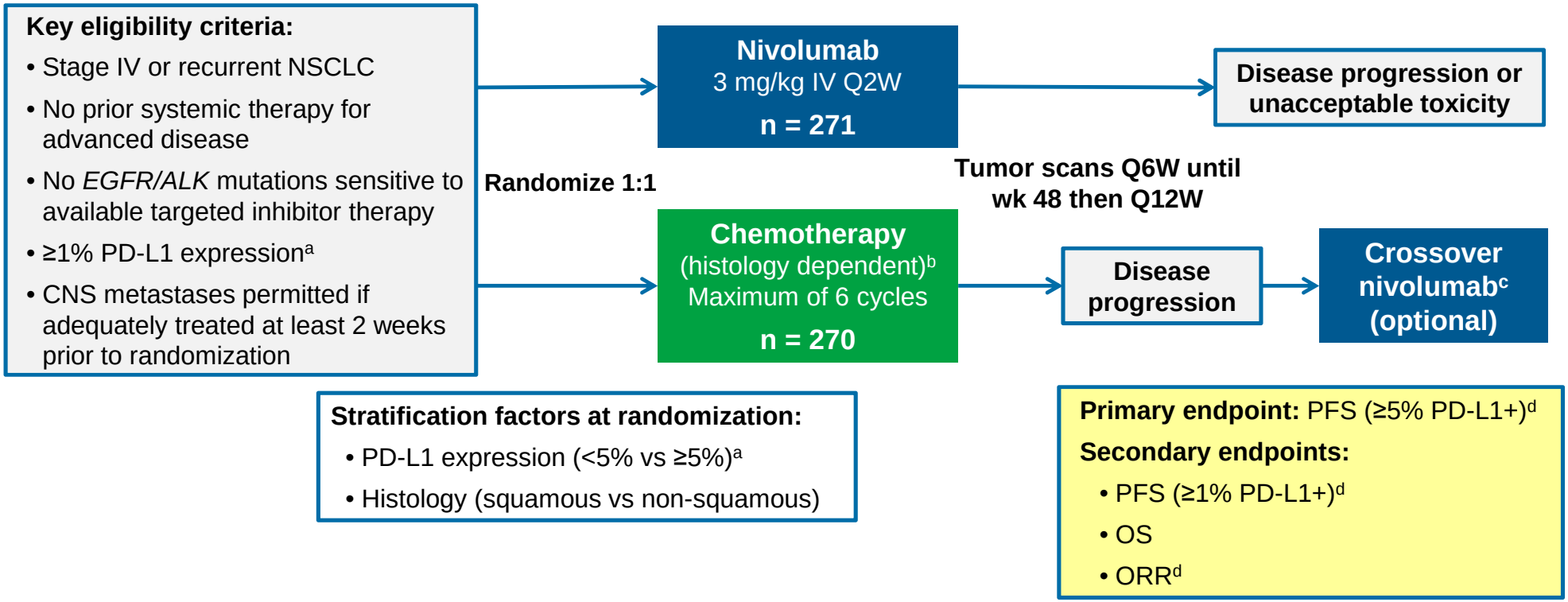
Biomarker Testing for PDL1 is Now Clearly Indicated in NSCLC

FDA APPROVAL

Immunotherapy for Front Line NSCLC

October 25, 2016!

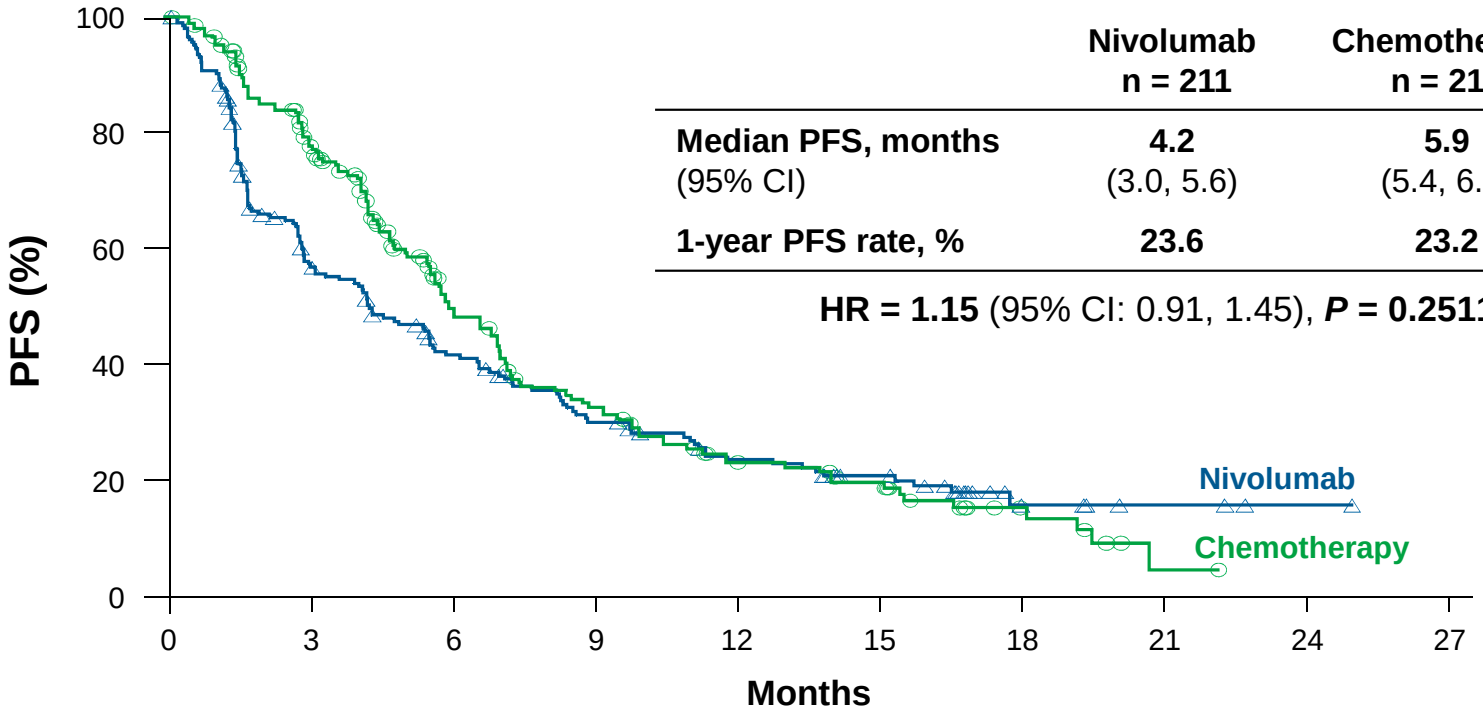
Phase 3 CheckMate 026 Study Design: Nivolumab vs Chemotherapy in First-line NSCLC



[a]Dako 28-8 validated; archival tumor samples obtained ≤6 months before enrollment were permitted; PD-L1 testing was centralized
[b]Squamous: gemcitabine 1250 mg/m^2 + cisplatin 75 mg/m^2; gemcitabine 1000 mg/m^2 + carboplatin AUC 5; paclitaxel 200 mg/m^2 + carboplatin AUC 6; Non-squamous: pemetrexed 500 mg/m^2 + cisplatin 75 mg/m^2; pemetrexed 500 mg/m^2 + carboplatin AUC 6; option for pemetrexed maintenance therapy
[c]Permitted if crossover eligibility criteria met, including progression confirmed by independent radiology review
[d]Tumor response assessment for PFS and ORR per RECIST v1.1 as determined by independent central review

Primary Endpoint (PFS per IRRC in ≥5% PD-L1+)

CheckMate 026: Nivolumab vs Chemotherapy in First-line NSCLC



	Nivolumab n = 211	Chemotherapy n = 212
Median PFS, months (95% CI)	**4.2** (3.0, 5.6)	**5.9** (5.4, 6.9)
1-year PFS rate, %	**23.6**	**23.2**

HR = 1.15 (95% CI: 0.91, 1.45), ***P* = 0.2511**

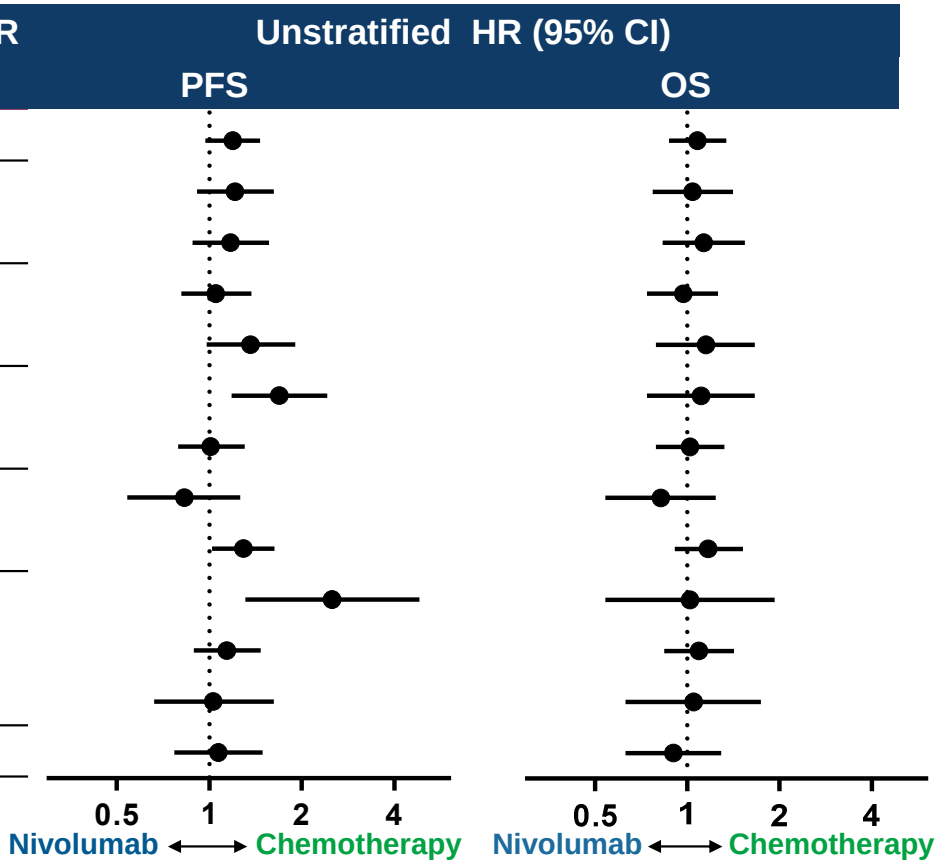
No. of patients at risk:										
Nivolumab	211	104	71	49	35	24	6	3	1	0
Chemotherapy	212	144	74	47	28	21	8	1	0	0

All randomized patients (≥1% PD-L1+): HR = 1.17 (95% CI: 0.95, 1.43)

PFS and OS Subgroup Analyses (All Randomized Patients)

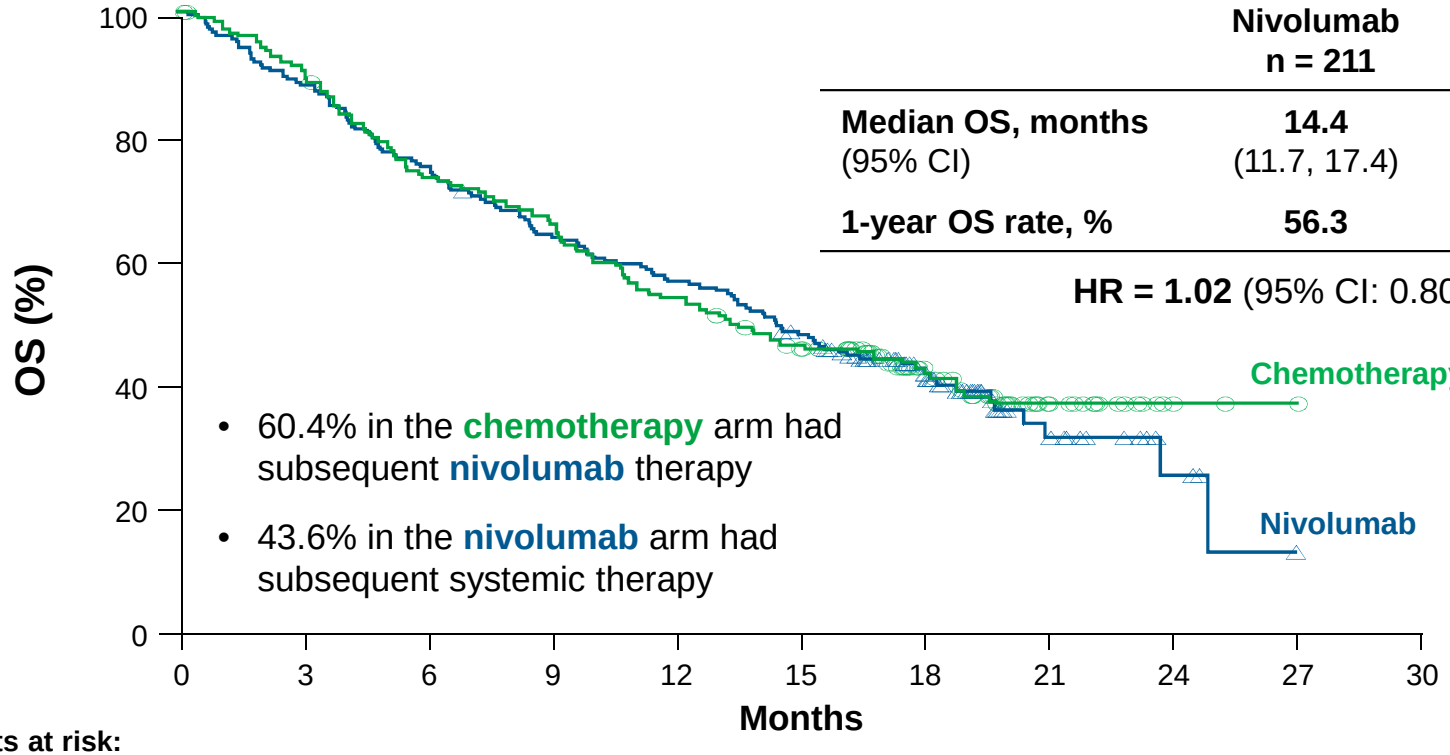
CheckMate 026: Nivolumab vs Chemotherapy in First-line NSCLC

Subgroup	Patients, n		Unstratified HR	
	Nivolumab	Chemotherapy	PFS	OS
Overall	271	270	1.19	1.08
≥65 years	123	137	1.21	1.04
<65 years	148	133	1.17	1.13
Male	184	148	1.05	0.97
Female	87	122	1.36	1.15
ECOG PS = 0	85	93	1.69	1.11
ECOG PS ≥1	185	177	1.01	1.02
Squamous	65	64	0.83	0.82
Non-squamous	206	206	1.29	1.17
Never smoker	30	29	2.51	1.02
Former smoker	186	182	1.14	1.09
Current smoker	52	55	1.03	1.05
≥50% PD-L1+	88	126	1.07	0.90



OS (≥5% PD-L1+)

CheckMate 026: Nivolumab vs Chemotherapy in First-line NSCLC



	Nivolumab n = 211	Chemotherapy n = 212
Median OS, months (95% CI)	**14.4** (11.7, 17.4)	**13.2** (10.7, 17.1)
1-year OS rate, %	**56.3**	**53.6**

HR = 1.02 (95% CI: 0.80, 1.30)

No. of patients at risk:											
Nivolumab	211	186	156	133	118	98	49	14	4	0	0
Chemotherapy	212	186	153	137	112	91	50	15	3	1	0

All randomized patients (≥1% PD-L1+): HR = 1.07 (95% CI: 0.86, 1.33)

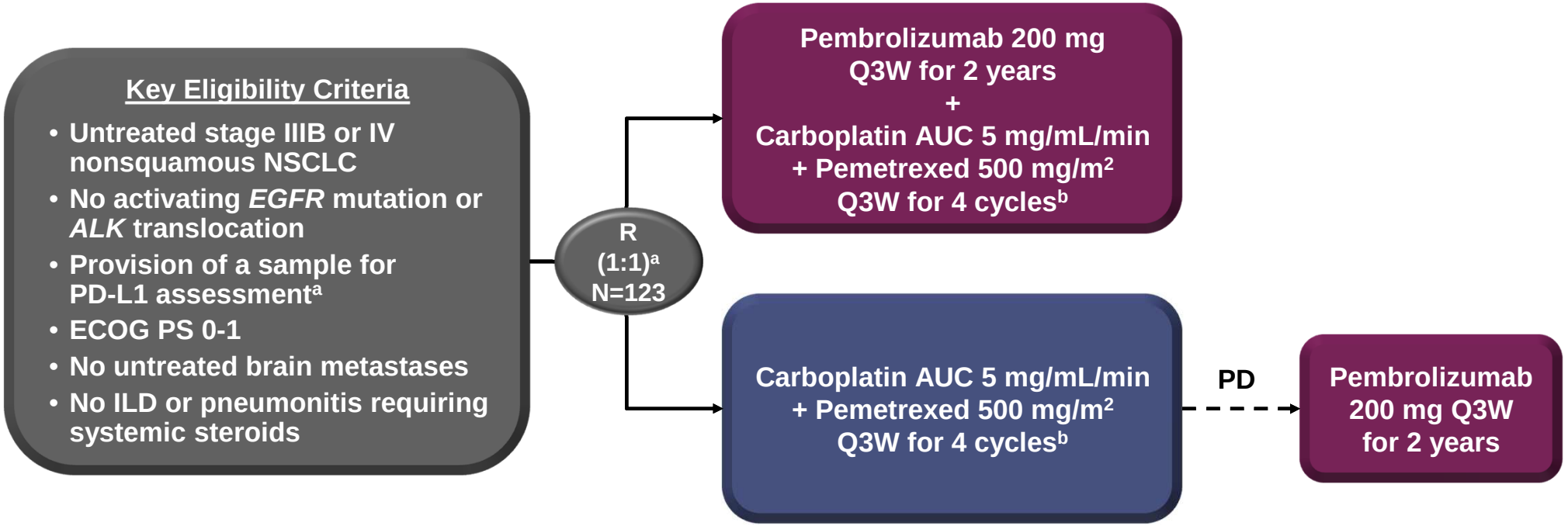
CM 026 vs. KN 024

	KN 024	CM 026
Tumor biopsy	After metastatic diagnosis	Within 6 months
PD-L1 cut off	50% (22C3 clone)	5% (28-8 clone)
Prevalence	30%	50%
Imaging interval	Q 9 weeks	Q 6 weeks for first 48 weeks
Primary endpoint	PFS (RECIST)	PFS (IRRC)
Never smokers (PD-1)	3%	11%
Squamous histology	19%	24%
Time from diagnosis to treatment	?	2 months
Prior radiation	? [1]	37.6 %

[1] Prior radiation therapy of > 30 Gy disallowed within 6 months of first dose of trial treatment

Socinski et al, ESMO 2016
Reck et al, ESMO 2016, NEJM 2016

KEYNOTE-021 Cohort G



End Points

Primary: ORR (RECIST v1.1 per blinded, independent central review)

Key secondary: PFS

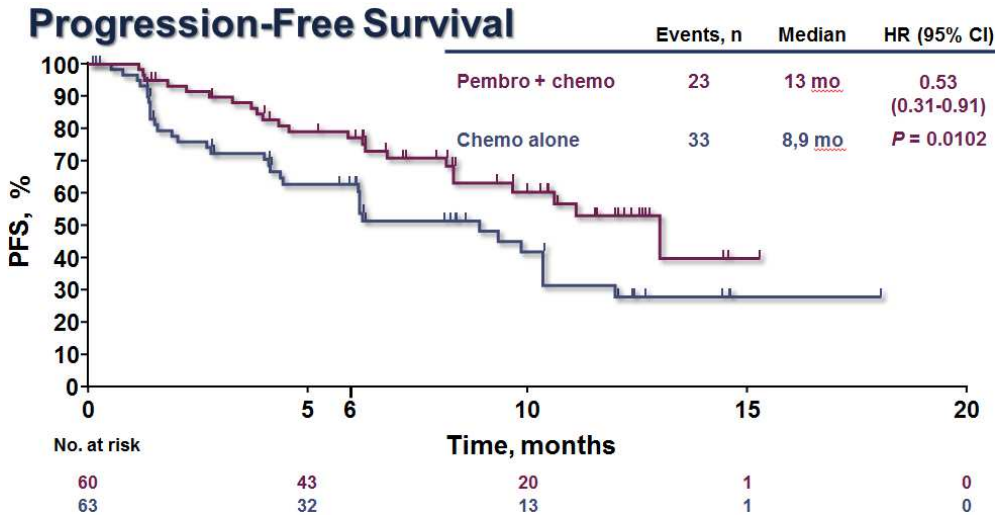
Other secondary: OS, safety, relationship between antitumor activity and PD-L1 TPS

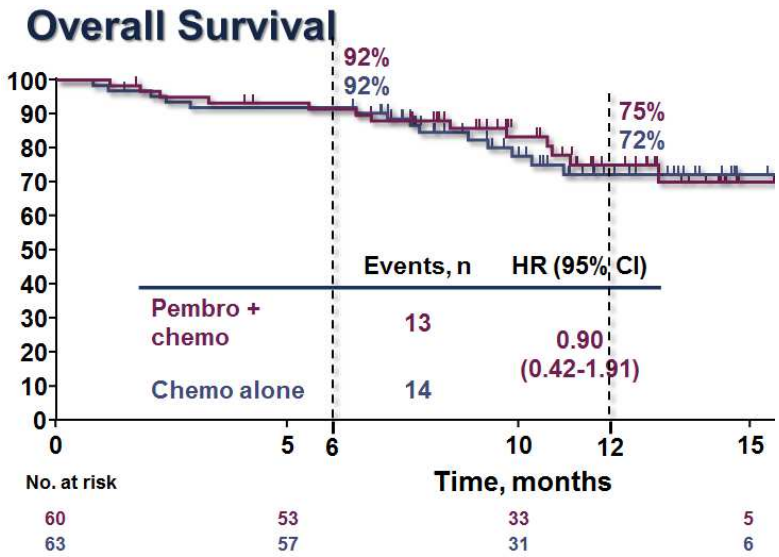
PD=progressive disease.

[a]Randomization was stratified by PD-L1 TPS <1% vs ≥1%.

[b]Indefinite maintenance therapy with pemetrexed 500 mg/m² Q3W permitted.

Survival data



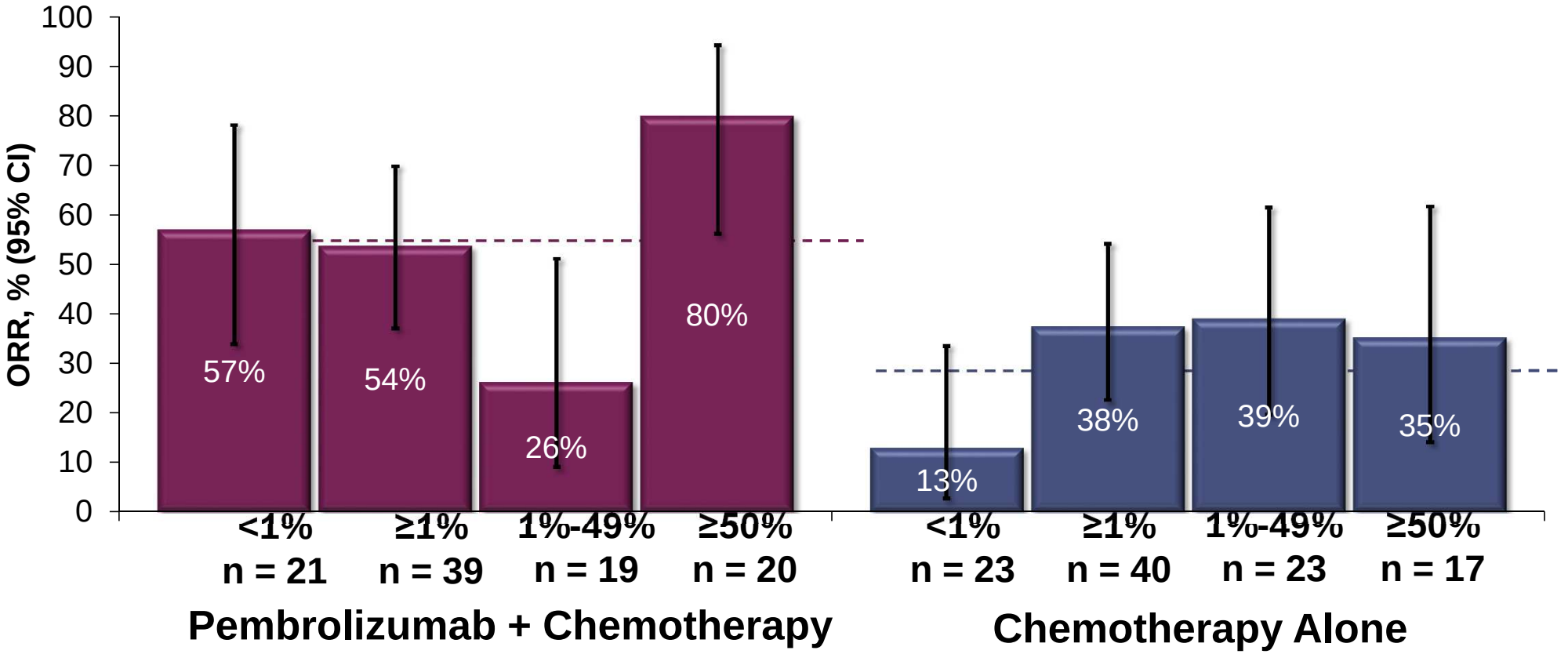


- Clear PFS benefit and no OS advantage
  - **Median PFS improved by 4.1 months**
  - PFS HR is 0.53
  - No difference for OS
  - Estimated rate of OS @ 12 months: 75% (Combo) vs 72% (CT)
  - In CT arm cross-over is 51% to PD(L)1 therapies (pembro & others)

Langer et al, 2016

Objective Response Rate by PD-L1 Status

(RECIST v1.1 by Blinded, Independent Central Review)



Horizontal dotted lines represent the ORR in the total population.

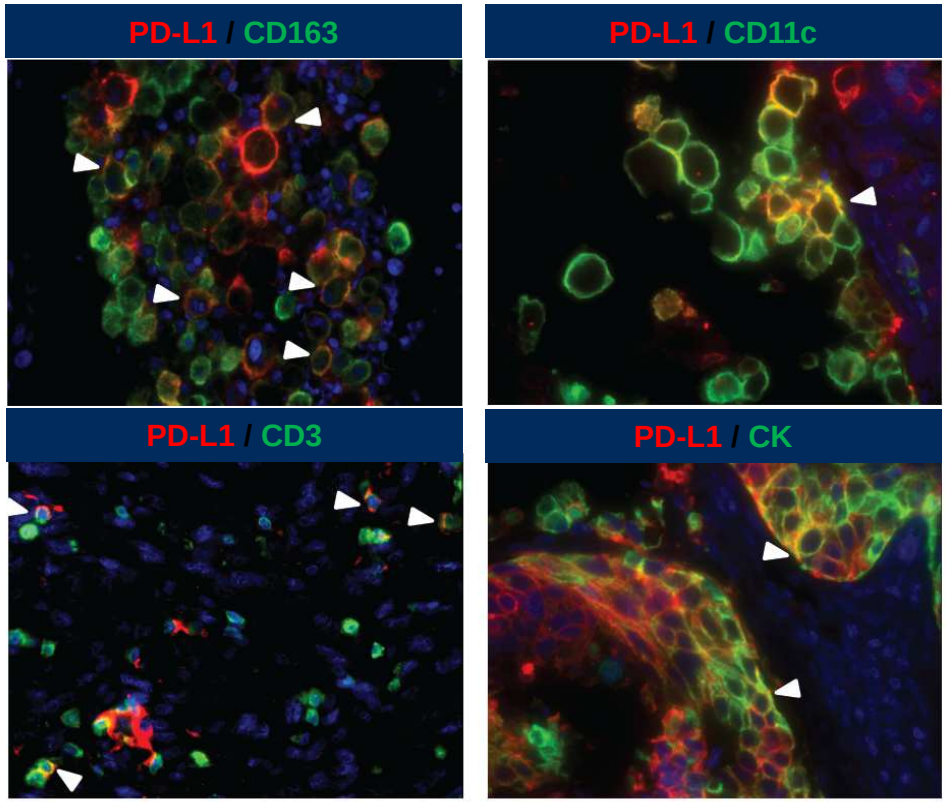
Data cut-off: August 8, 2016.

COPENHAGEN 2016 ESMO congress

Plan for this Presentation

- Historical progress of new drug development for Advanced NSCLC
- Novel Clinical Trial Designs for Biomarker Development (BATTLE 1, 2 and Master Protocols)
- Immunotherapy for NSCLC: New Standards of Care in the Refractory and Front Line Settings
- Bringing it all together: Doing BATTLE Using Immunotherapy in NSCLC: The "I" BATTLE Trial, and the Development of Rational Combinations

PD-L1 Expression in ICs and TCs by Immunofluorescence



PD-L1 localized with macrophages, dendritic cells and T cells, but not B cells

IC, tumor-infiltrating immune cell; TC, tumor cell.
Markers of ICs: CD3, T cells; CD11b, dendritic cells; CD163, macrophages.
Marker of TCs: CK, cytokeratin.
Red: PD-L1 staining; Green: IC and TC markers; Blue: DAPI staining.

Herbst et al. Nature 2014 515: 563-567;

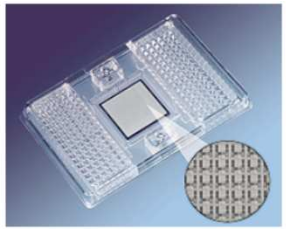
Understanding Anti-Cancer Immunity: Focus on Biomarkers

The Phase Ia trial is providing key information on the safety, tolerability and activity of MPDL3280A

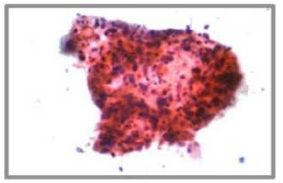
However, understanding the impact on immune biology is critical to determine who is expected to benefit from MPDL3280A

This information will help to guide future development of MPDL3280A, as well as other cancer immunotherapies, as monotherapy or combination therapy

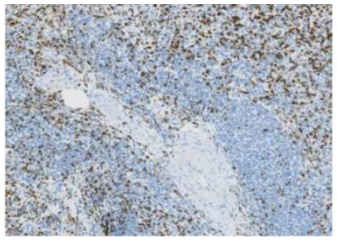
Gene Expression - iChip



High throughput and comprehensive evaluation of tumor and immune genes

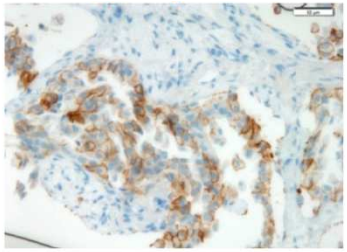


CD8 IHC



Spatial assessment of CD8 in response to treatment

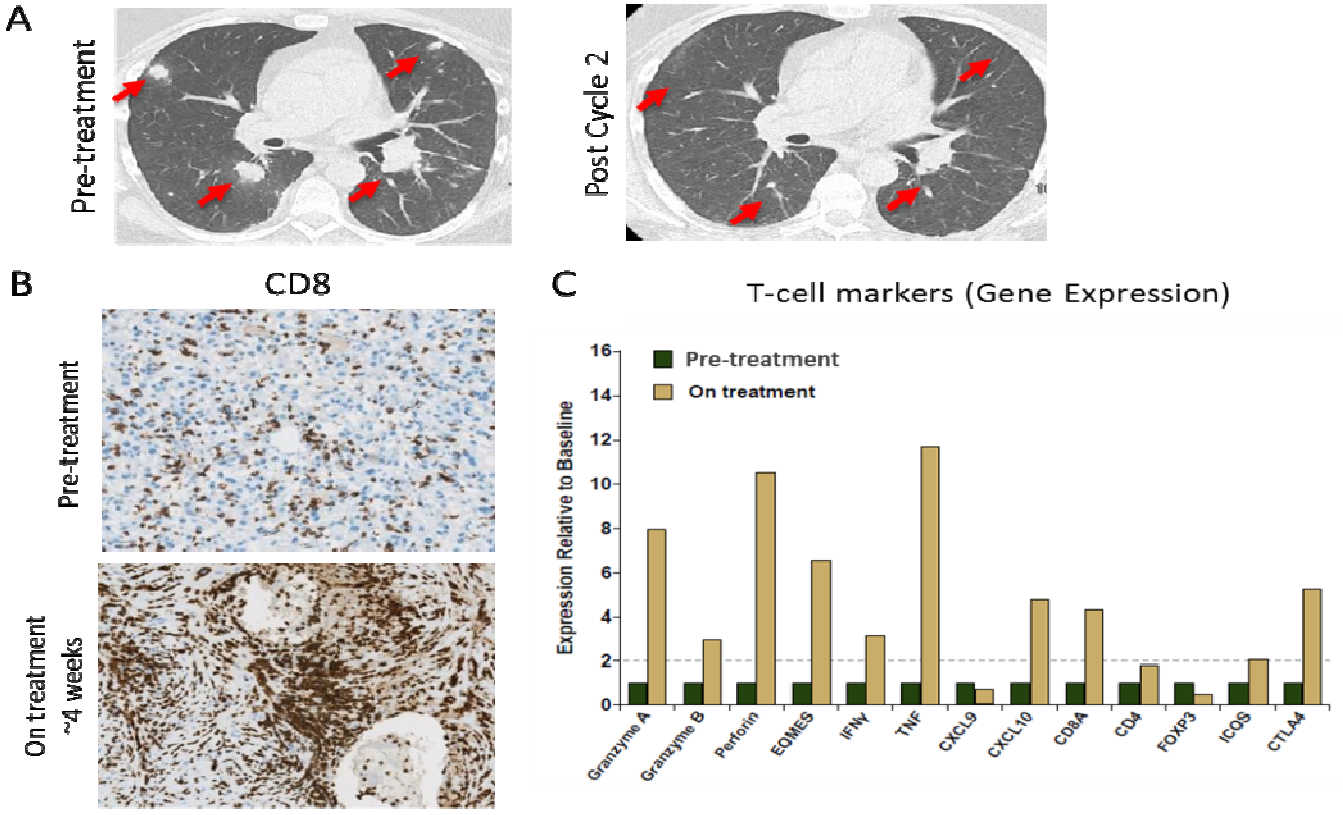
Target expression



Dx grade assays for assessment of target expression

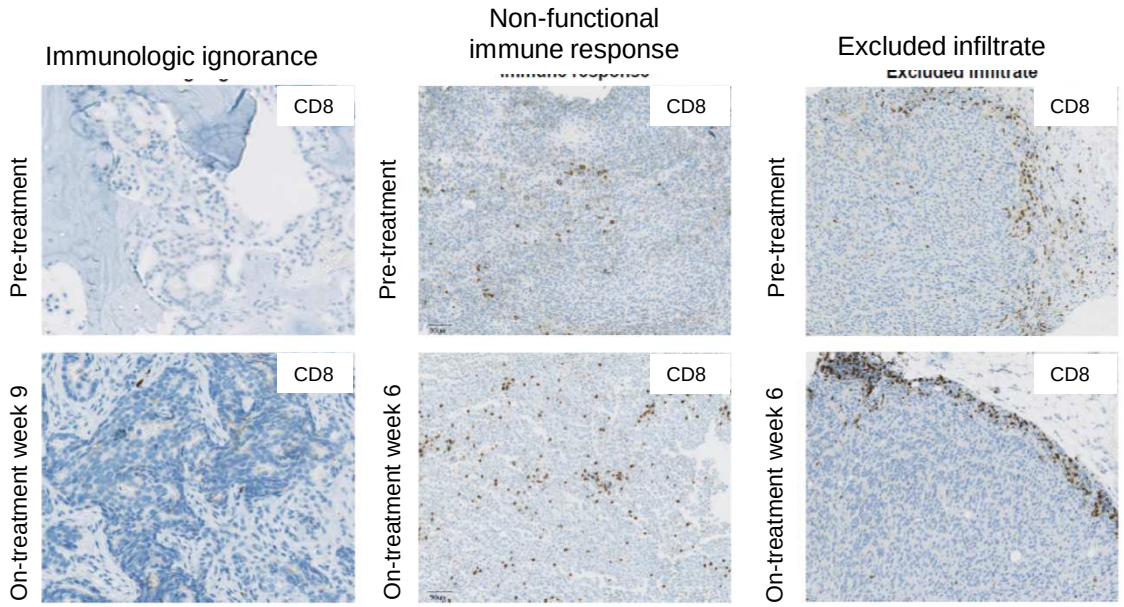
Biomarker Analyses for PD-L1 Treatment

Mechanistic studies using pre and post biopsies



Herbst RS et al. *Nature* 2014;515: 563-567;

Biomarker Analyses
Defining the Profile of Non-responders

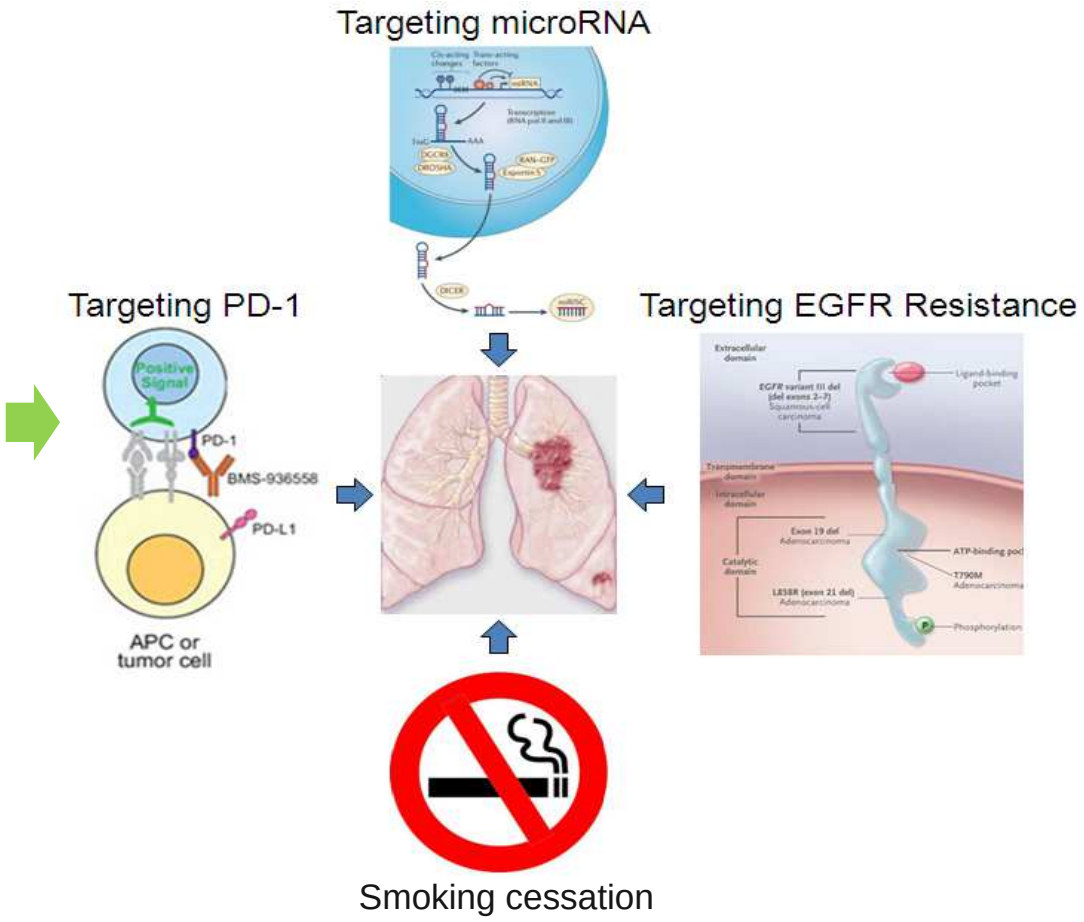


- Three distinct patterns of nonresponse were observed
- Most patients who progressed failed to show up-regulation of PD-L1 or evidence of activated T cells
- These results provide evidence for the “inflamed tumor” hypothesis

Herbst RS et al. *Nature* 2014;515: 563-567;

Yale SPORE in Lung Cancer (YSILC)

L. Chen
S. Gettinger
D. Rimm
K. Politi
K. Schalper



8/1/15

Four Categories of Tumors Based on Presence of PD-L1 and TILS (450 samples analyzed)

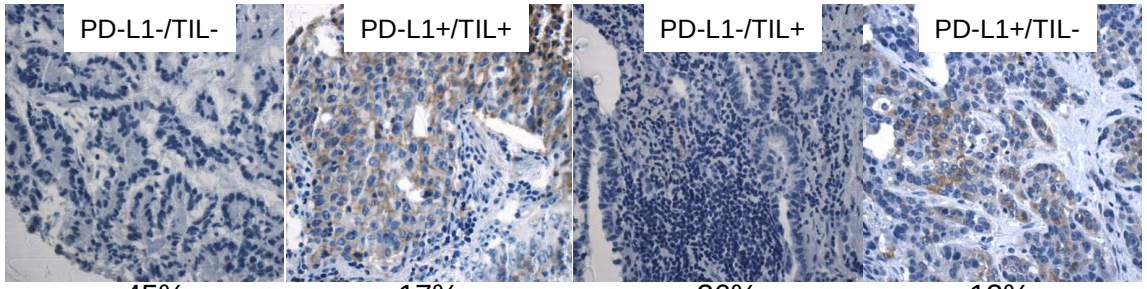
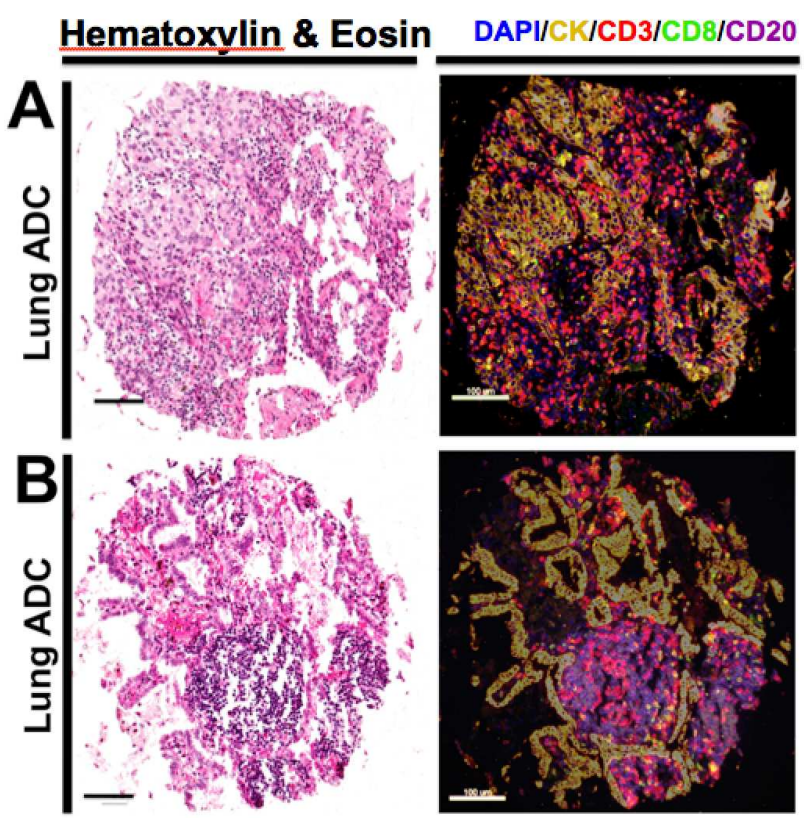


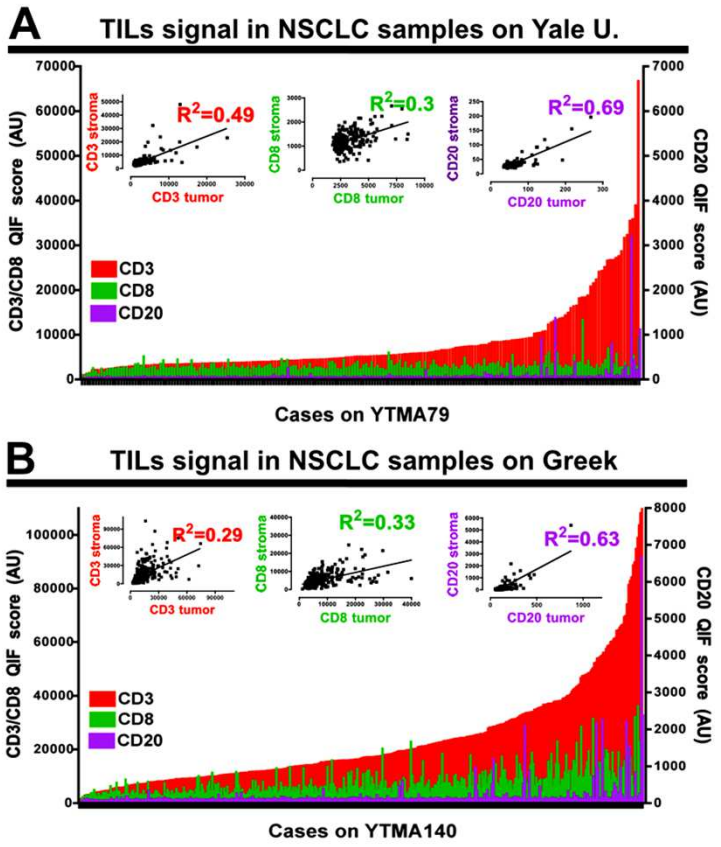
Table 3. Proposed mechanisms associated with NSCLC resistance to anti-PD-1/B7-H1 therapy

Subgroup		Type	Tumor Distribution	Possible Resistance Mechanism(s)	Analysis
B7-H1	TIL				
-	-	I	45%	Poor priming of general T cell responses	Peripheral CD4+ and CD8+ T cell responses to autologous tumor cells
				Lack of inflammatory cell recruitment	Chemokine expression in biopsy or FFPE samples
+	+	II	17%	Incomplete PD-1/B7-H1 pathway blockade and activation of alternate immune suppressive pathways	CD80 expression on TILs, expression of alternate suppressive pathways in TME
-	+	III	26%	Alternate immune suppressive pathways	Expression of select molecules in pathways with roles in evasion of NSCLC immunity
+	-	IV	12%	Intrinsic induction of B7-H1 by oncogenes	Expression of molecules triggering aberrant signaling events

Velcheti et al (Rimm)

TIL subtype quantification in FFPE defines the “Inflamed” phenotype in NSCLC

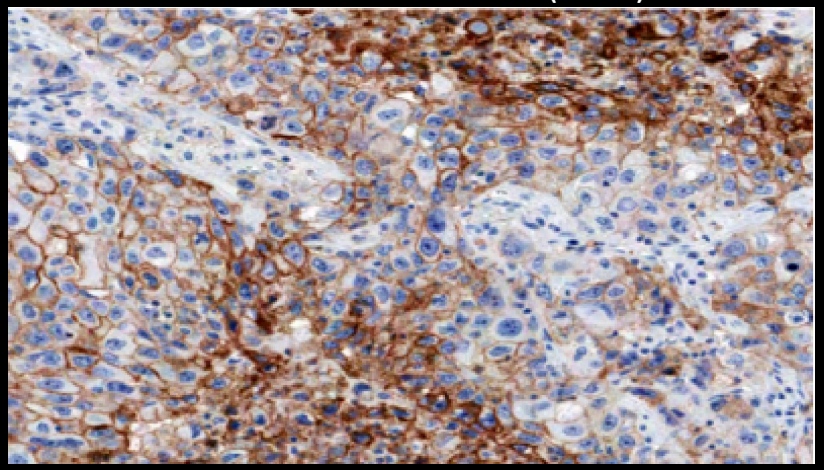




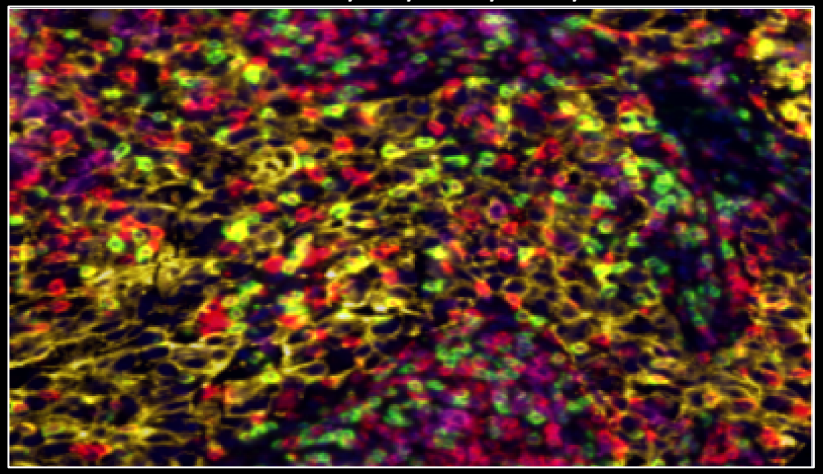
Schalper et al., 2015, JNCI, 107(3)

SU2C Immunoprofiling assay/panels

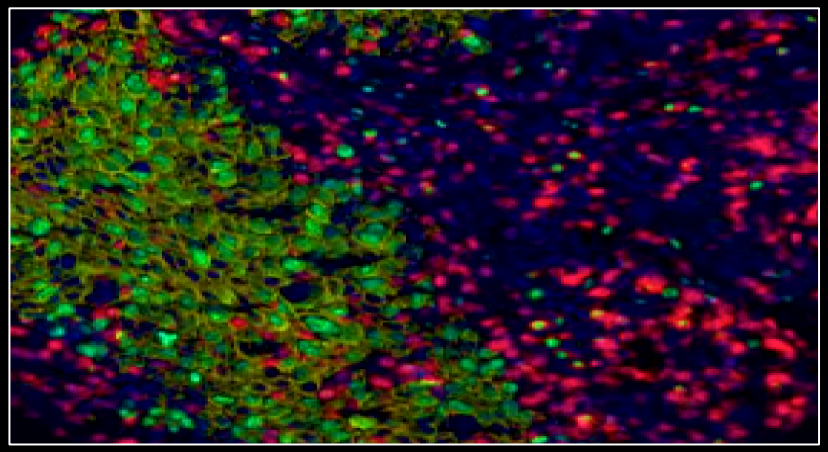
Marker #1 : PD-L1 IHC (22c3)



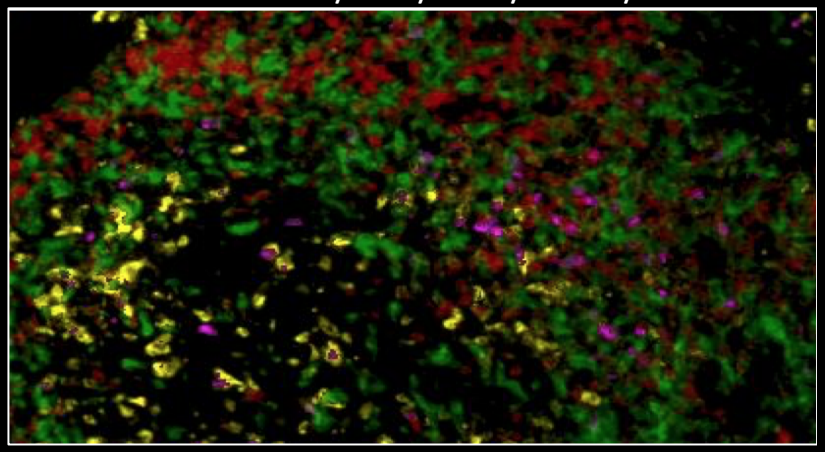
Panel #2: DAPI/CK/CD4/CD8/CD20

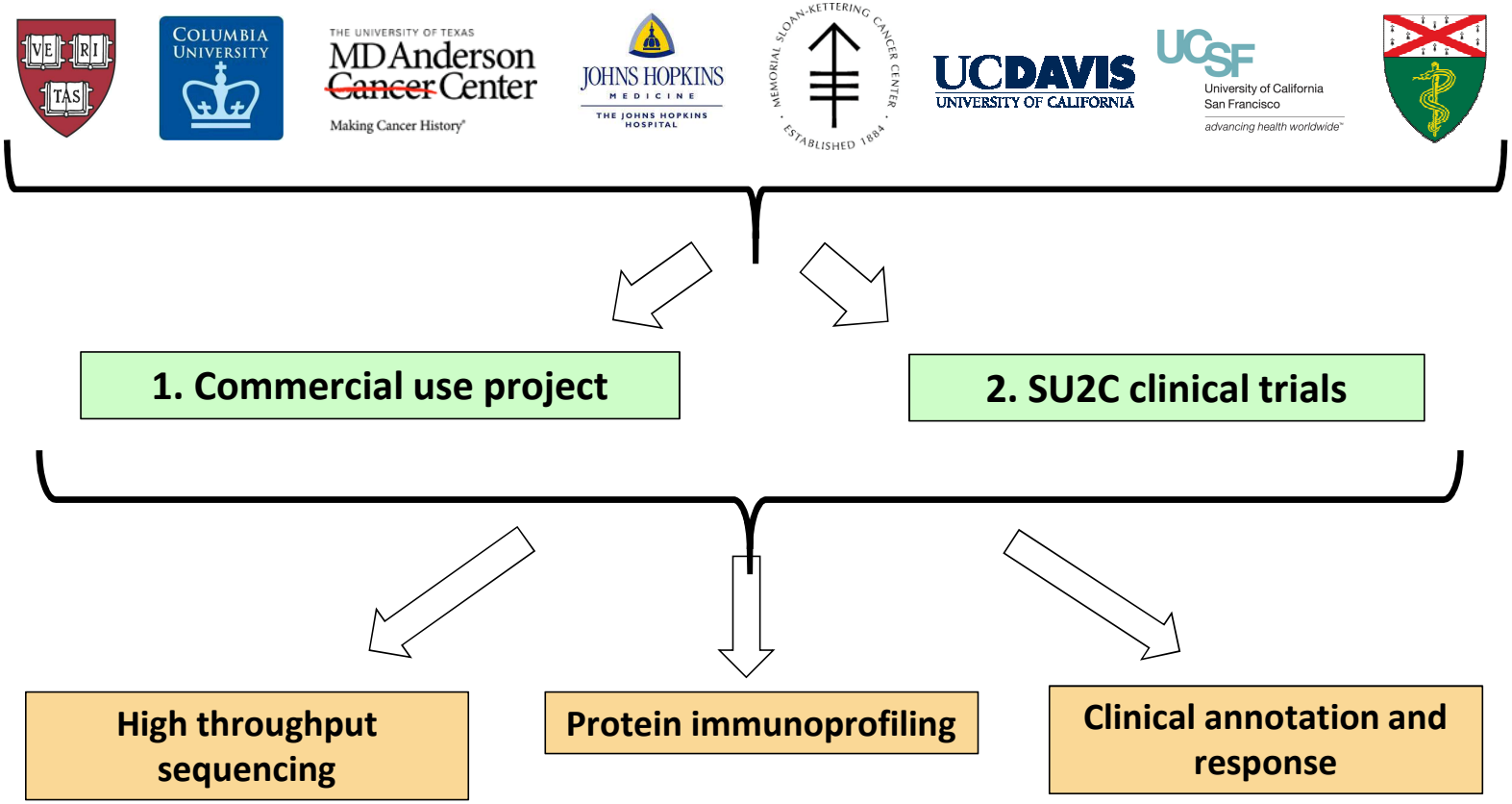


Panel #3: DAPI/CK/CD3/Ki-67/GZMB



Panel #4: DAPI/CD3/PD-1/TIM-3/LAG-3




1. Commercial use project
2. SU2C clinical trials
High throughput sequencing
Protein immunoprofiling
Clinical annotation and response

Experimental outline Yale NSCLCs:

45 NSCLC cases

-24 resections, 21 biopsies
-7 non-smokers, 38 smokers
-20 EGFR/KRAS mutations
-13 without germline pair

Review & Selection

-Tumor and non-tumor
-Amount of tumors
-Sections
-Prioritization

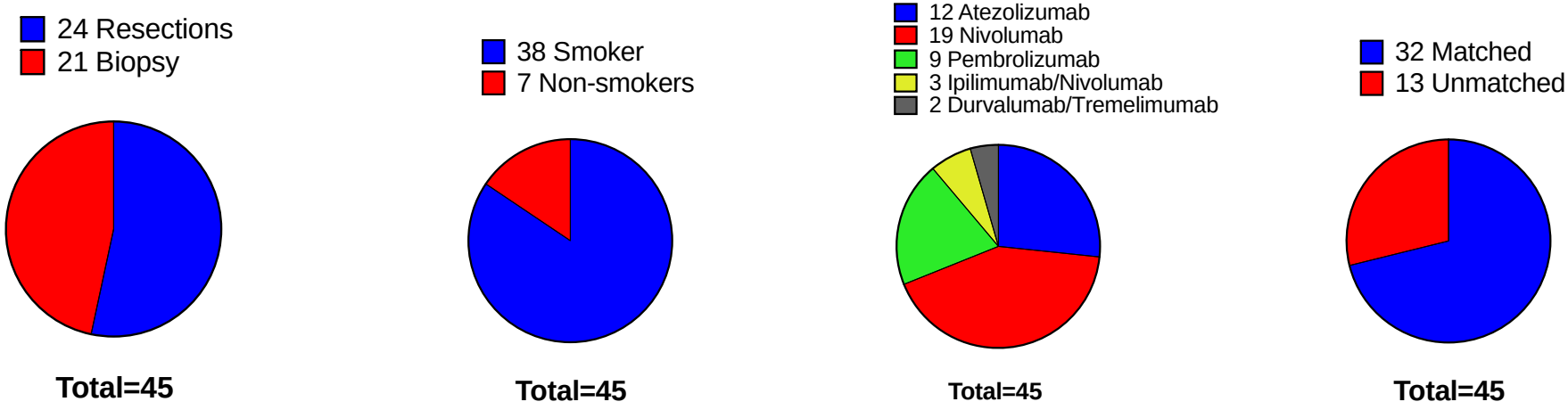
Whole exome sequencing

-Mutation load
-Class I and II neoantigens
-Mutations key genes

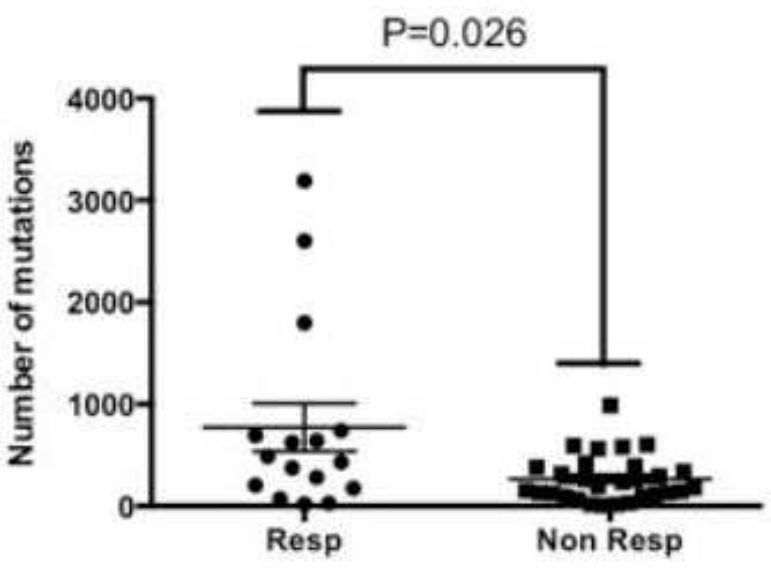
TIL profiling & function

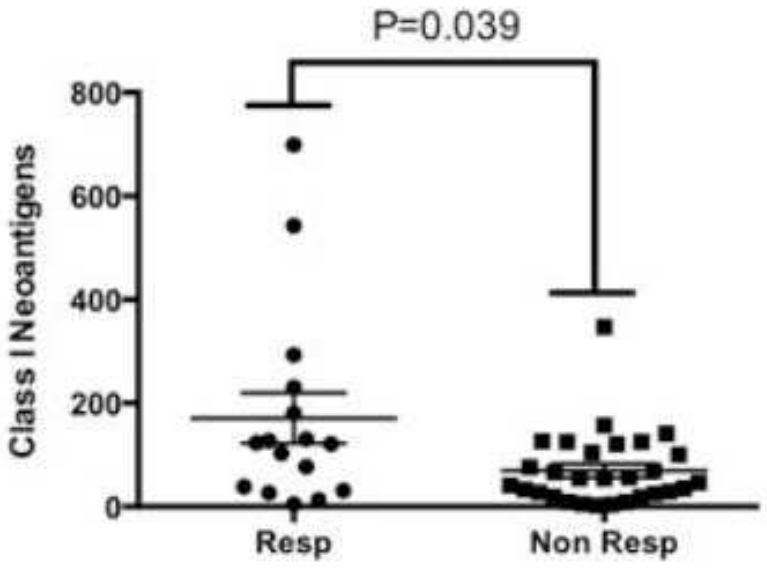
-QIF for TILs
-TIL activation
-TIL proliferation

Integrative analysis



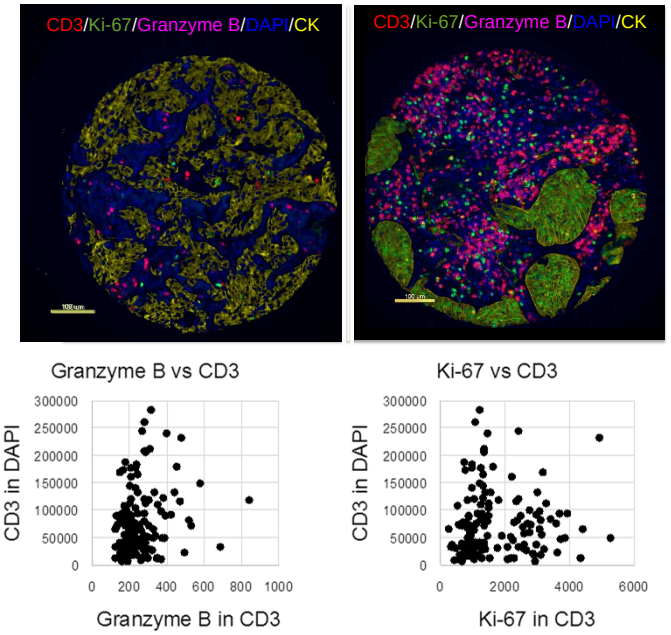
Mutation load and class I neoantigens

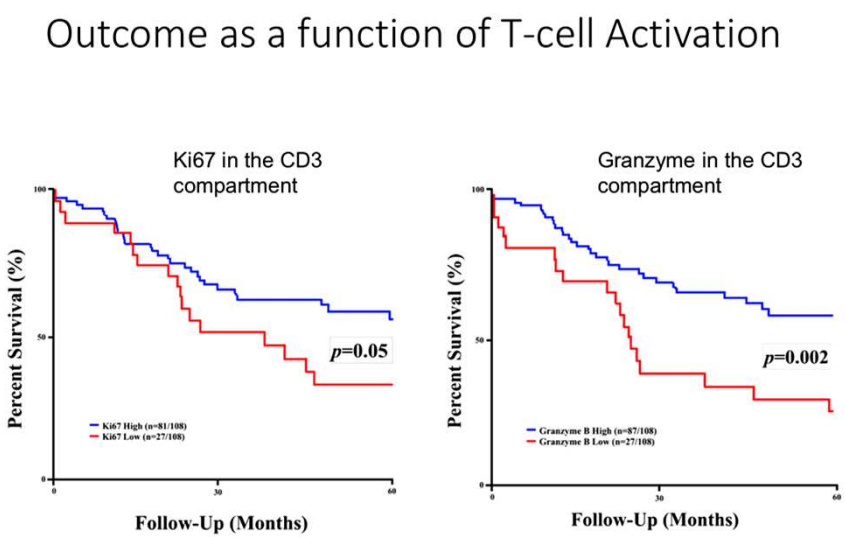




Schalper et al, unpublished

The TIL activation panel in historical cohort without PD-1 axis therapy (n=204)



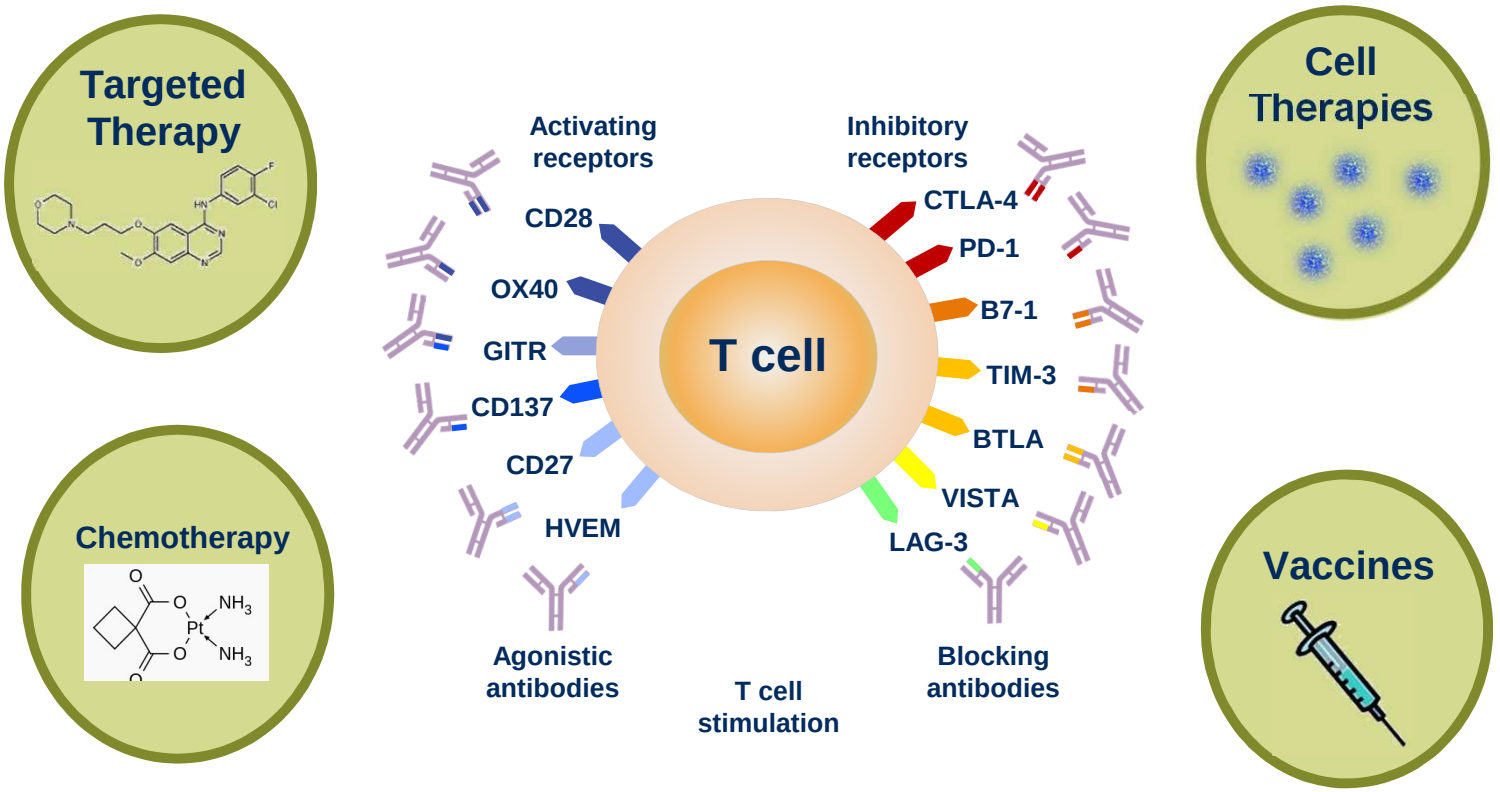


- In situ T-cell activation/proliferation is not correlated with T-cell content and is associated with better prognosis in NSCLC

Schalper et al, unpublished

The crossroads of immunotherapy and targeted therapy (and chemotherapy/Radiotherapy…)

T-Cell Immune Checkpoints as Targets for Immunotherapy

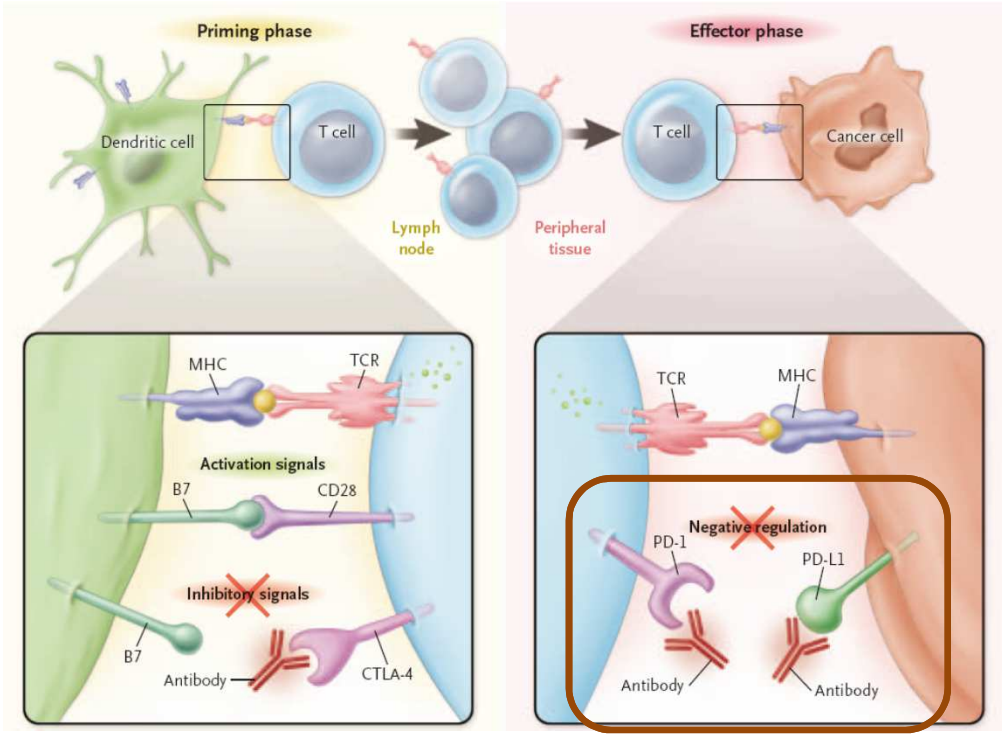


Adapted from Mellman I et al. *Nature*. 2011;480:481–489.

Anti-PD/PDL1 as Backbone to Combination Tx?

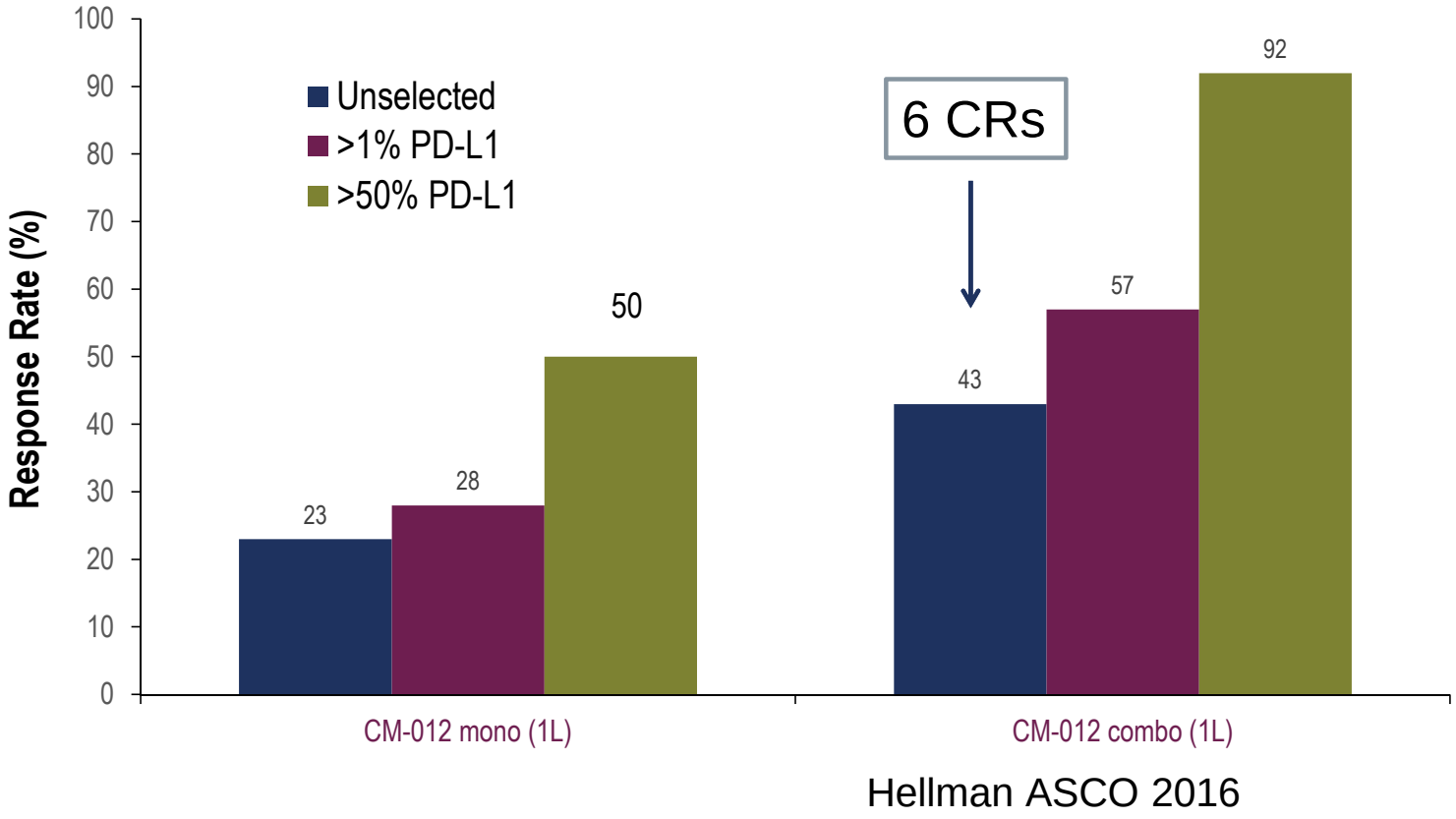
Nivolumab	Pembrolizumab	Atezolizumab	Durvalumab
- Chemotherapy - Radiation/ Ablation - EGFR/ ALK TKI - Anti-VEGF/ VEGFR inhibitor - Vasc Disrupt Agent - Hypomethylating Agent - HDAC inhibitor - SPK Inhibitor - C-Met inhibitor - Glutaminase inhibitor - Dasatinib - Vaccine - Gene therapy - IL15 agonist - PEG IL10 - $TGF_{\beta}R1$ inhibitor - Anti-CD27 - Ant-CXCR4 - Anti-CSF-1R - IDO-1 inhibitor - Anti-CTLA4 - Anti-LAG - Anti-TIM-3 - Anti-KIR	- Chemotherapy - Radiation - EGFR/ ALK TKI - Anti-VEGF/VEGFR inhibitor - Hyomethylating Agent - HDAC inhibitor - CDK Inhibitor - BTK inhibitor - PI3K Inhibitor - KIT/CSF1R/FLT3 Inh - FGFR inhibitor - JAK1 Inhibitor - CRM1 Inhibitor - FAK Inhibitor - Anti-EGFR - Anti-CEACAM1 - PEG hyaluronidase - Vaccine - Oncolytic - PEG IL10 - Anti-CSF-1 - IDO1 Inhibitor - Anti-CTLA4 - Anti-B7-H3	- Chemotherapy - Radiation - EGFR/ ALK TKI - Anti-VEGF/Ang-2 - MEK Inhibitor - Vaccine - Adoptive Cell Therapy - Anti-CEA/CD3 - Anti-CEA/ IL-2 - Anti-OX40 - Anti-CD40 - Anti-CD27 - Anti-CSF-1 - Adenosine A2A Inhibitor - IDO-1 Inhibitor - Anti-CTLA4 - Anti-TIGIT	- Chemotherapy - Radiation - EGFR/ALK TKI - VEGFR Inhibitor - BTK Inhibitor - MEK Inhibitor - HAD Inhibitor - PARP Inhibitor - WEE1 Inhibitor - ATR Inhibitor - Anti-OX40 - CXCR4 Inhibitor - CSF - Anti-CD73 - Anti-CCR4 - Anti-CSF1R - Anti-NKG2A - Adenosine A2a Inhibitor - IDO1 Inhibitor - Anti-CTLA4 - Anti-PD1
		Avelumab: ALK inhibitor (crizotinib and lorlatinib), Anti-41BB, Anti-OX40	

Dual Checkpoint Blockade



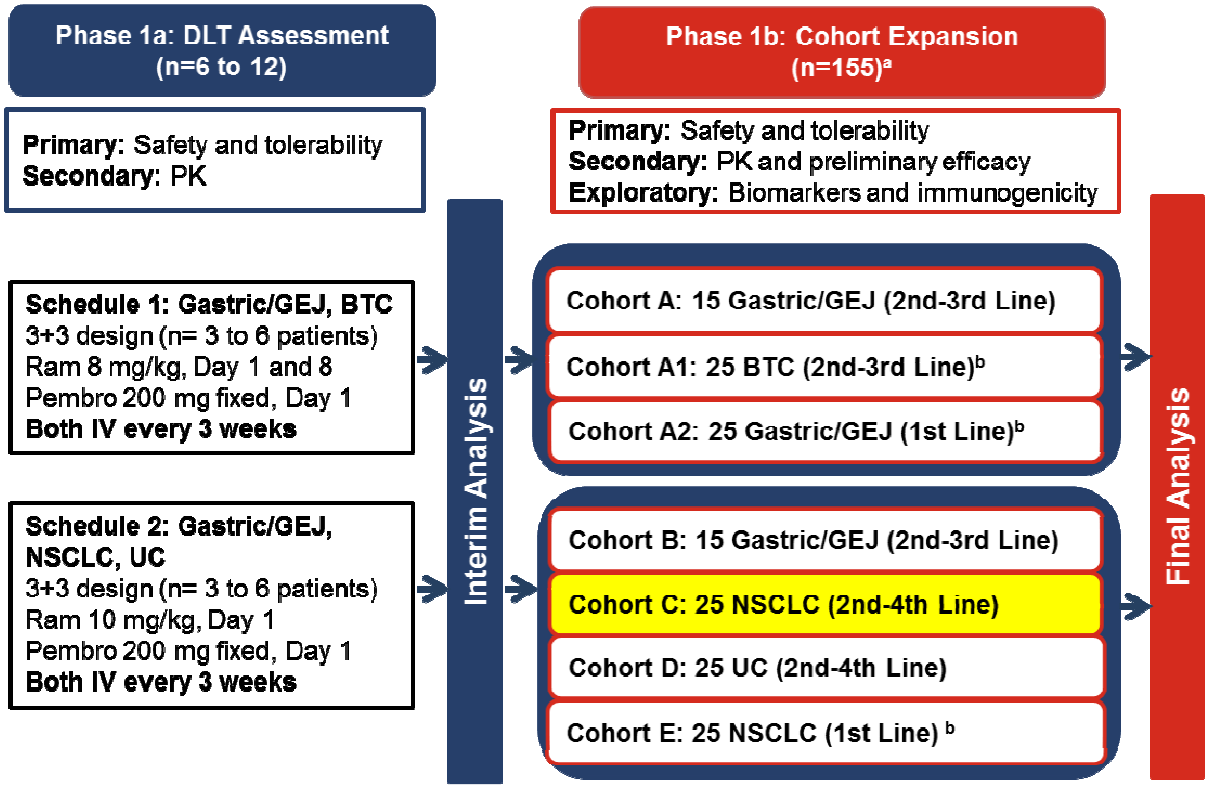
Ribas A et al NEJM 2012

Combination I-O (IPI/NIVO) potential in first line?



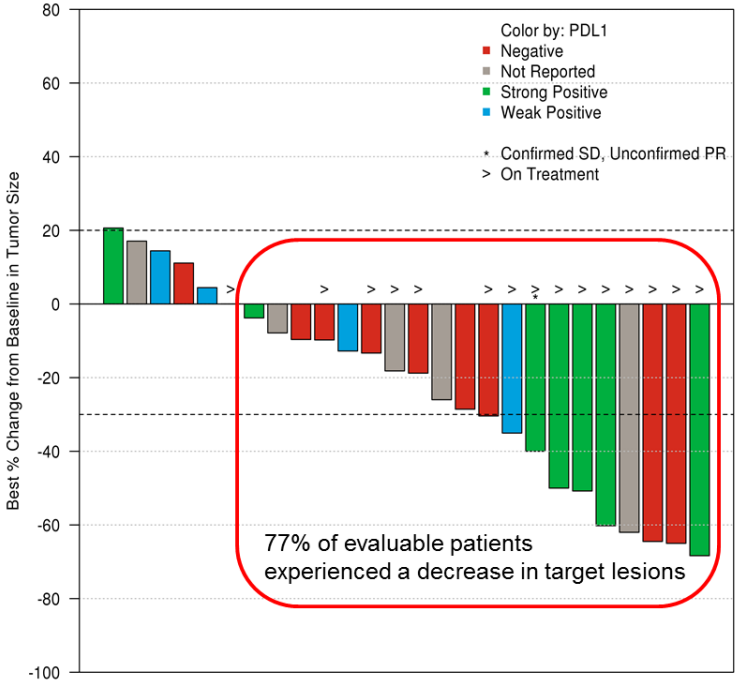
Hellman ASCO 2016

STUDY JVDF (NCT02443324) PHASE 1A/B STUDY DESIGN

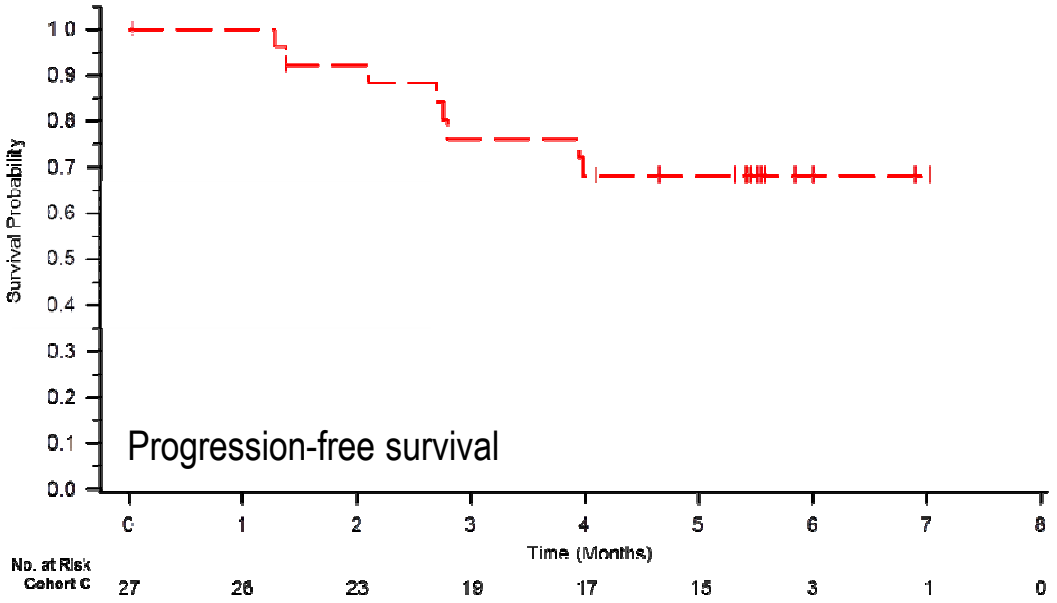


[a]Patients may continue treatment for up to 35 cycles, until confirmed progressive disease or discontinuation for any other reason. [b]Protocol was recently amended to add cohorts A1, A2 and E; cohorts are currently enrolling. DLT dose-limiting toxicity; PK pharmacokinetics; Ram ramucirumab; Pembro pembrolizumab

COHORT C: INTERIM CLINICAL ACTIVITY RAMUCIRUMAB + PEMBROLIZUMAB



ITT Population	Cohort C NSCLC (n=27)
Objective response rate, n (%)	8 (30%)
Disease control rate, n (%)	23 (85%)



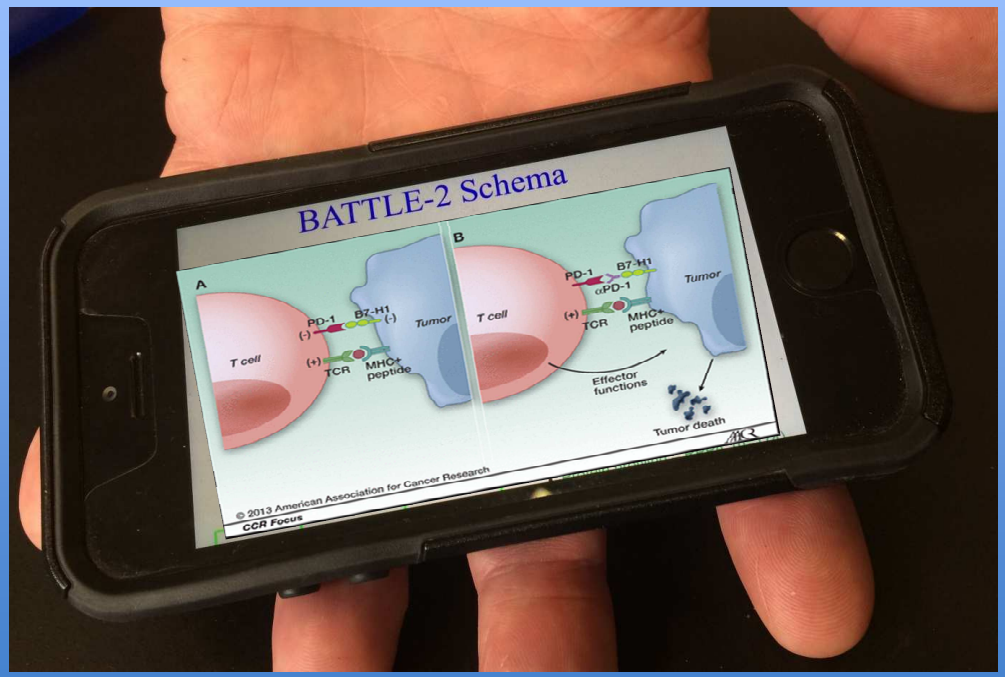
PD-L1 Status	Patients	Events	Median PFS, Mo (95% CI)
All Patients	27	8	NR (3.98, --)
Negative	10	2	NR
Weak positive	4	2	3.98 (2.76, --)
Strong positive	7	2	NR
Not reported	6	2	NR

COPENHAGEN 2016 ESMO congress

Herbst et al, 2016 ESMO

BATTLE-2 Schema

iBATTLE –Coming Soon!



EML4-ALK
Fusion or
EGFR Mut ex

Statistical

Erlotinib

Primary e

p-AKT
LKB1

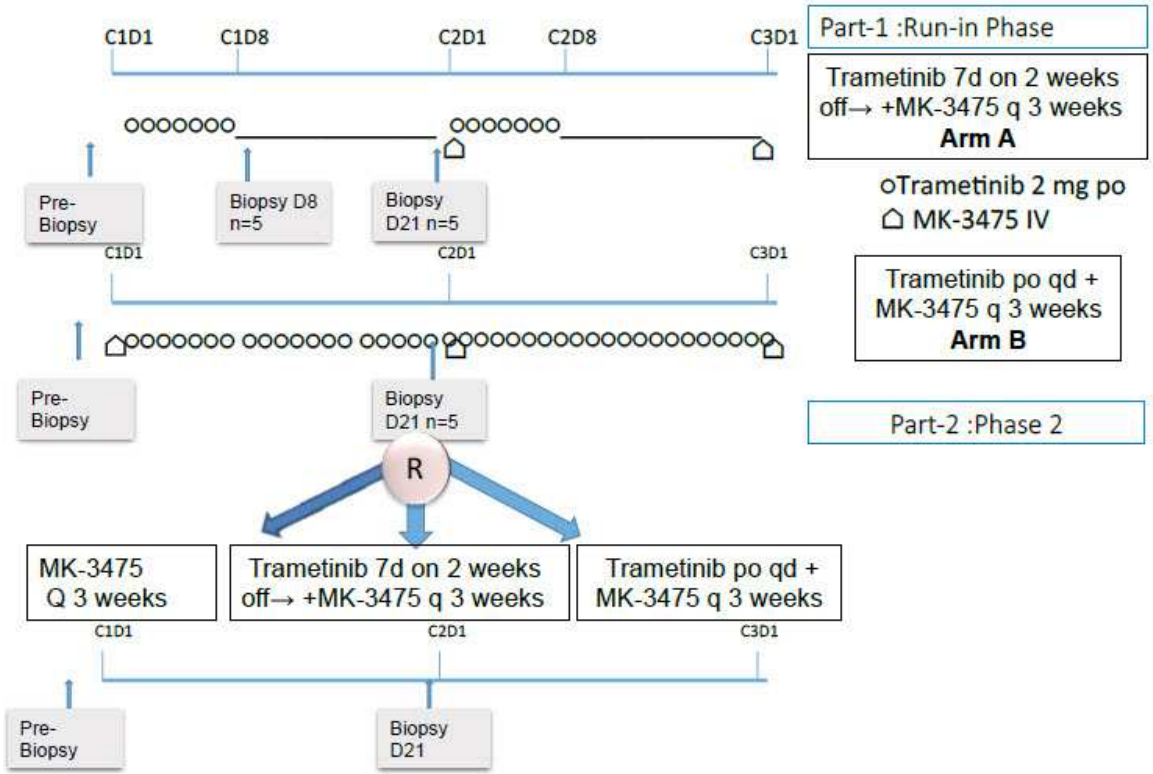
nom):
RAS,
MET,

n

rafenib
very”

(n=174)
e

The "I" BATTLE TRIAL



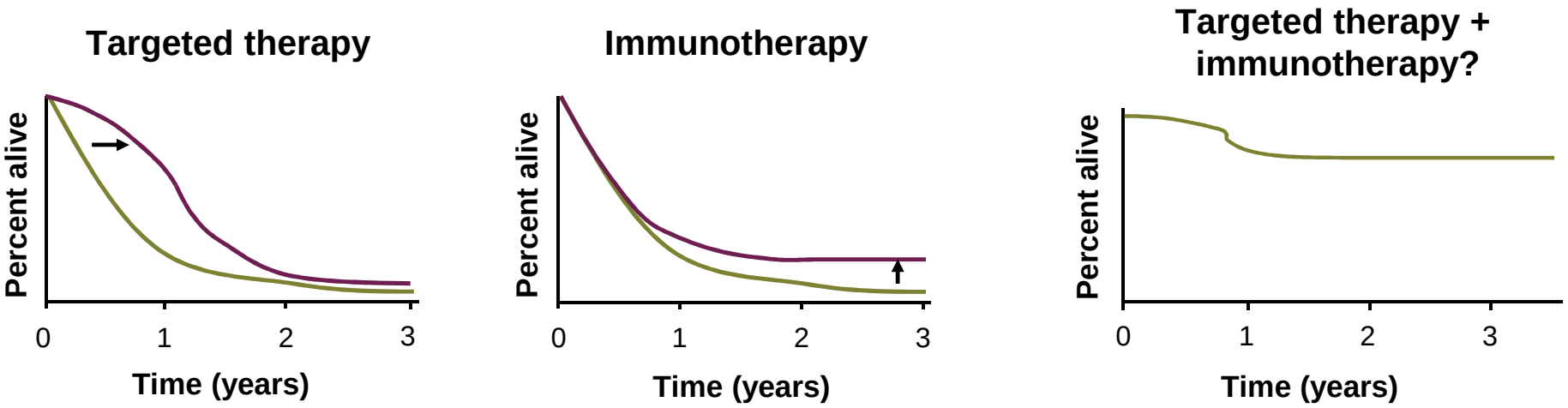
Papadimitrakopoulou and Herbst

Support from Merck/Novartis, NCI RO1

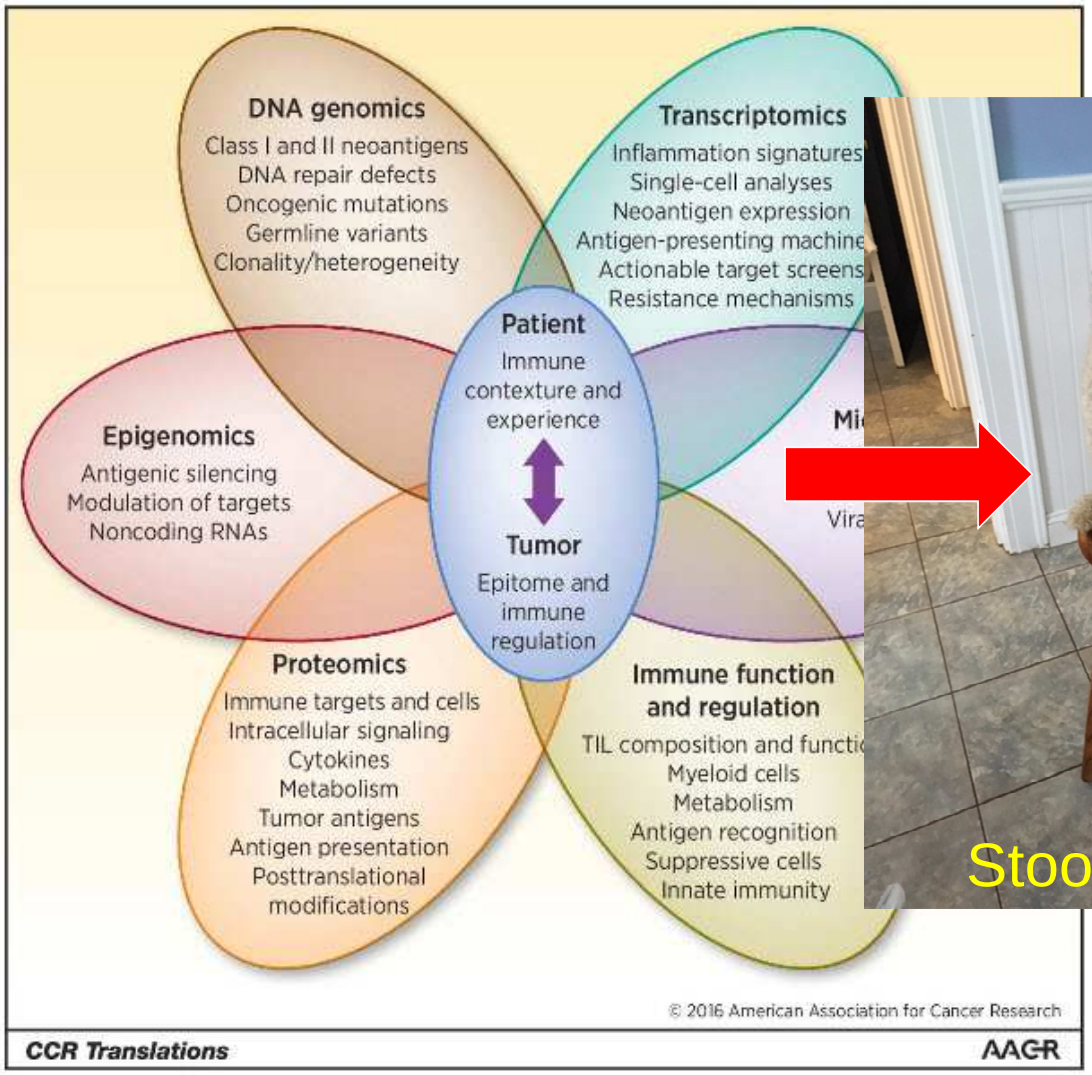
PD-1 Axis Inhibition for NSCLC: Questions

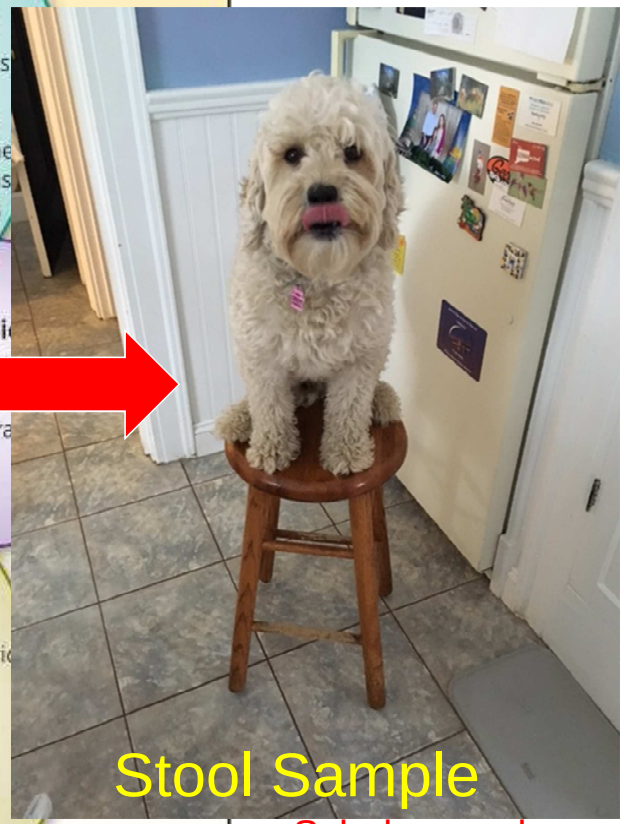
- Schedule (q 2, 3, 4 weeks)? How long?
- Treat patients with pre- existing autoimmune conditions?
- Treat beyond initial progression- pseudo-progression?
- Treatment of oligo-progression- add local therapy?
- Nivolumab vs Pembrolizumab- vs Atezolizumab vs Durvakumab vs ….
- Anti-PD-1 vs anti-PD-L1?
- Approach to PD-L1 negative disease?
- Role in EGFR/ ALK/ ROS1 and non-smoking related NSCLC
- Benefit in Stage I-III disease? Stage IV as maintenance?
- Should we combine with other therapies? Which patients?

Rationale for combining targeted therapy and immunotherapy



Ribas A, et al. Clin Cancer Res. 2012;18:336-41. Sharma P, Allison JP. Cell. 2015;161:205-14.





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THANK YOU

Disease Aligned Research Team Retreat and Symposium

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