MADRID 2014 ESMO congress

Immunotherapy Current Status

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Disclosure slide

Honoraria for lectures:

- Hoffmann-La Roche, Lilly, BMS, AstraZeneca, Pfizer, Boehringer-Ingelheim

Advisory Board (compensated):

- Hoffmann-La Roche, Lilly, BMS, AstraZeneca, Pfizer, Novartis, Clovis, BMS, Boehringer-Ingelheim, Daiichi-Sankyo

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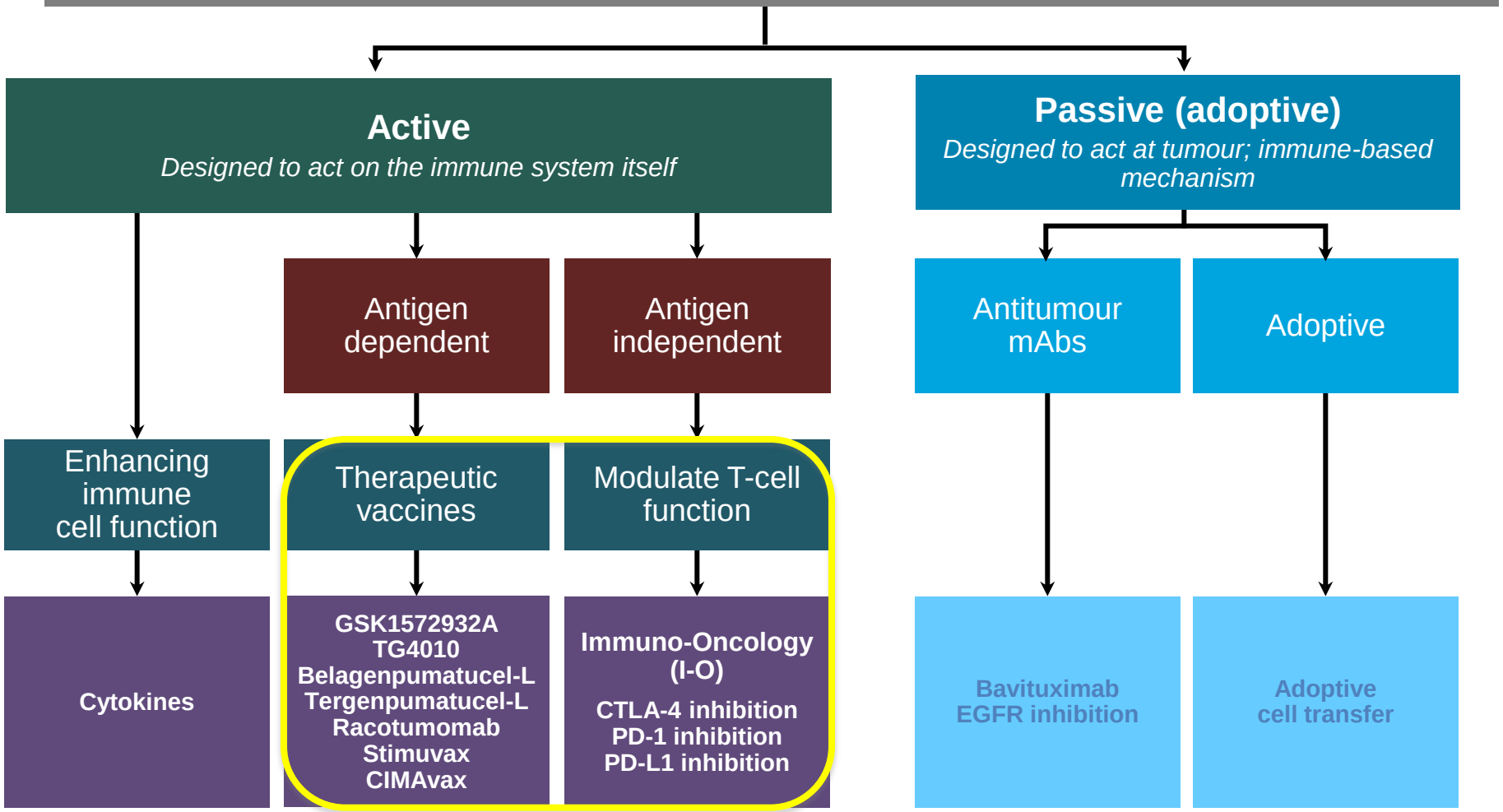
NSCLC: An immune driven tumor?

Tumour type	Prognostic[a] tumour infiltrating lymphocytes[b]	Immune-related spontaneous tumour regression[c]
NSCLC	**Yes[1]**	**Yes[13] (rare)**
CRC	**Yes[2]**	**Yes[14]**
Breast	**Yes[3,4]**	**No**
Melanoma	**Yes[5,6]**	**Yes[15]**
Renal	**Yes[7,8]**	**Yes[16,17]**
Prostate	**Yes[9]**	**No**
Ovarian	**Yes[10]**	**No**
Head and neck	**Yes[11]**	**No**
Cervical	**Yes[12]**	**Evidence for cervical intraepithelial neoplasia 2/3[18,19]**

[a]Covers correlation with improved overall or progression-free survival, disease stage, or therapy outcome
[b]The type of lymphocyte dictates where there is a correlation with improved or worsened outcome
[c]Based on PubMed search conducted in October 2013 using the terms 'spontaneous regression' and the tumour type

1. Hiraoka K, et al. *Br J Cancer*. 2006;94:275–280; 2. Galon J, et al. *Science*. 2006;29:1960–1964; 3. Mahmoud SM, et al. *J Clin Oncol*. 2011;29:1949–1955; 4. Loi S, et al. *J Clin Oncol*. 2013;31:860–867; 5. Piras F, et al. *Cancer*. 2005;104:1246–1254; 6. Azimi F, et al. *J Clin Oncol*. 2012;30:2678–2683; 7. Siddiqui SA, et al. *Clin Cancer Res*. 2007;13:2075–2081; 8. Donskov F, et al. *Br J Cancer*. 2002;87:194–201; 9. Flammiger A, et al. *APMIS*. 2012;120:901–908; 10. Zhang L, et al. *N Engl J Med*. 2003;348:203–213; 11. Badoual C, et al. *Clin Cancer Res*. 2006;12:465–472; 12. Piersma SJ, et al. *Cancer Res*. 2007;67:354–361; 13. Nakamura Y, et al. *Lung Cancer*. 2009;65:119–122; 14. Bir AS, et al. *Anticancer Res*. 2009;29:465–468; 15. Kalialis LV, et al. *Melanoma Res*. 2009;19:275–282; 16. Kawai K, et al. *Int J Urol*. 2004;11:1130–1132; 17. Kumar T, et al. *Respir Med*. 2010;104:1543–1550; 18. Øvestad IT, et al. *Mod Pathol*. 2010;23:1231–1240; 19. Castle PE, et al. *Obstet Gynecol*. 2009;113:18–25.

Immunotherapy in lung cancer

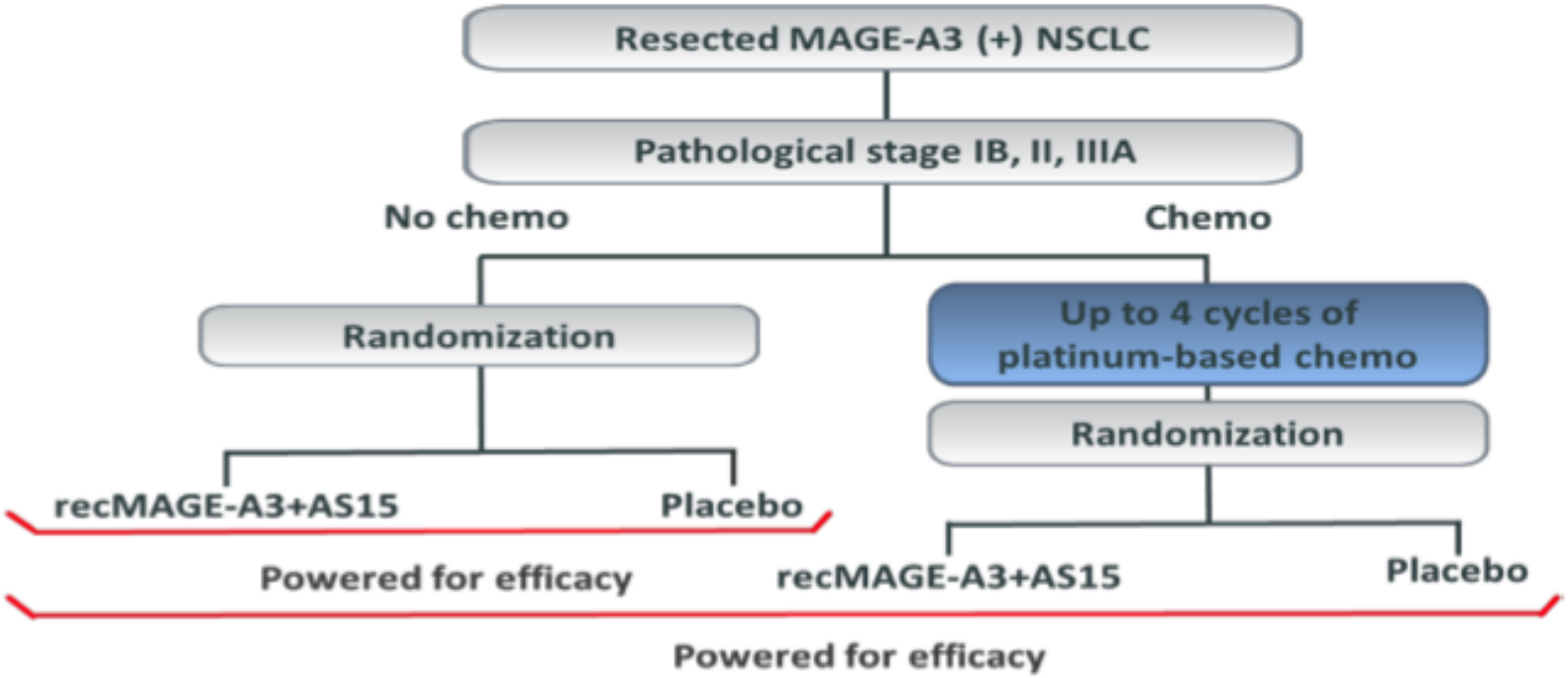


CTLA-4 = cytotoxic T-lymphocyte antigen-4; PD-1 = programmed death-1; PD-L1 = programmed death ligand-1.
www.clinicaltrials.gov accessed November 6, 2013; NCCN Guidelines®. NSCLC. V2.2013; Peters S, et al. *Ann Oncol*. 2012;23:vii56–vii64.

Vaccination strategies?

- Mage-A3 Vaccine
- (combination MAGE-A3 recombinant protein + immunological adjuvant system)

MAGRIT: Phase III Study - MAGE-A3 as Adjuvant Non-Small Cell LunG CanceR ImmunoTherapy



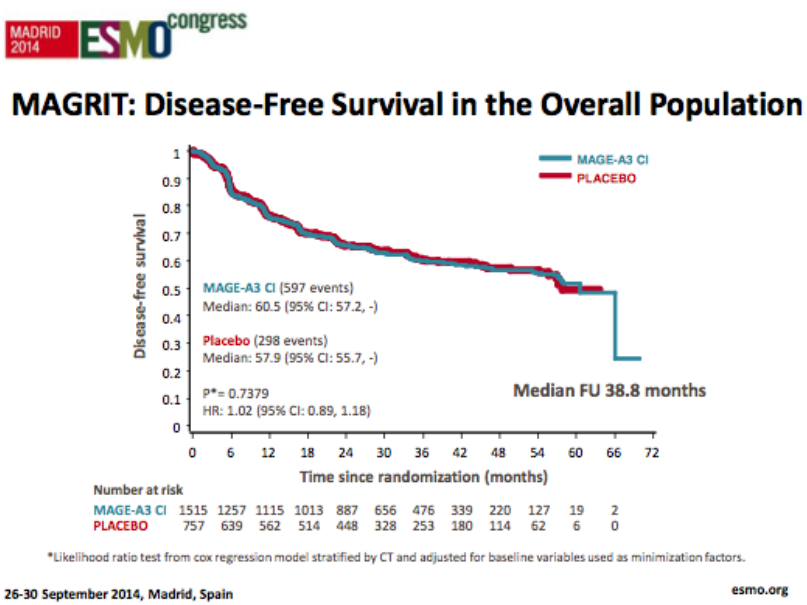
13 administrations over 27 months - 2,312 patients randomized (screened >13,000 patients)

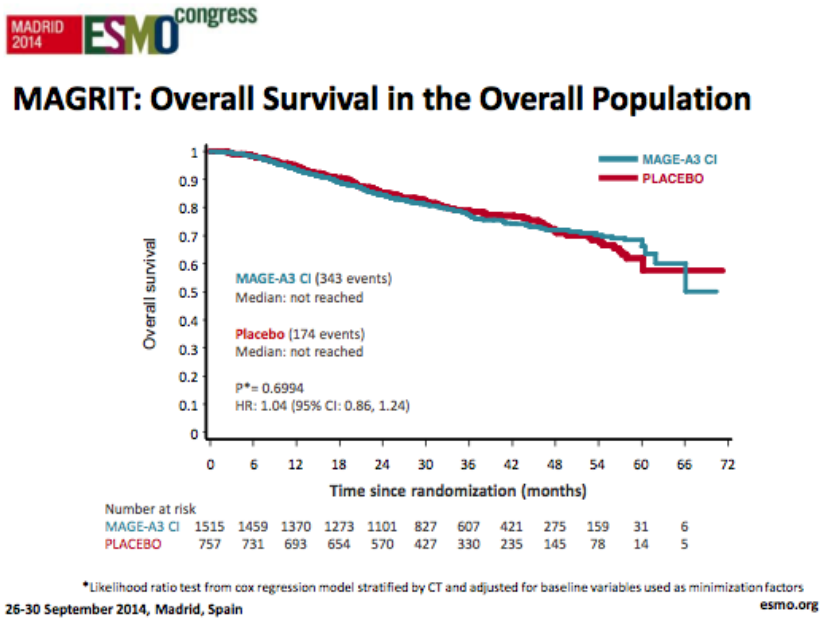
Stratification factor: chemotherapy (CT)/no-CT

Minimization factors: nb of CT cycles (1-2 *vs* 3-4), stage of disease (IB *vs* II *vs* IIIA), type of lymph-node sampling (radical *vs* sampling), PS (0,1 *vs* 2), smoking status (never *vs* past *vs* current)

Vansteenkiste J et al, ESMO 2014

MAGRIT – Key results





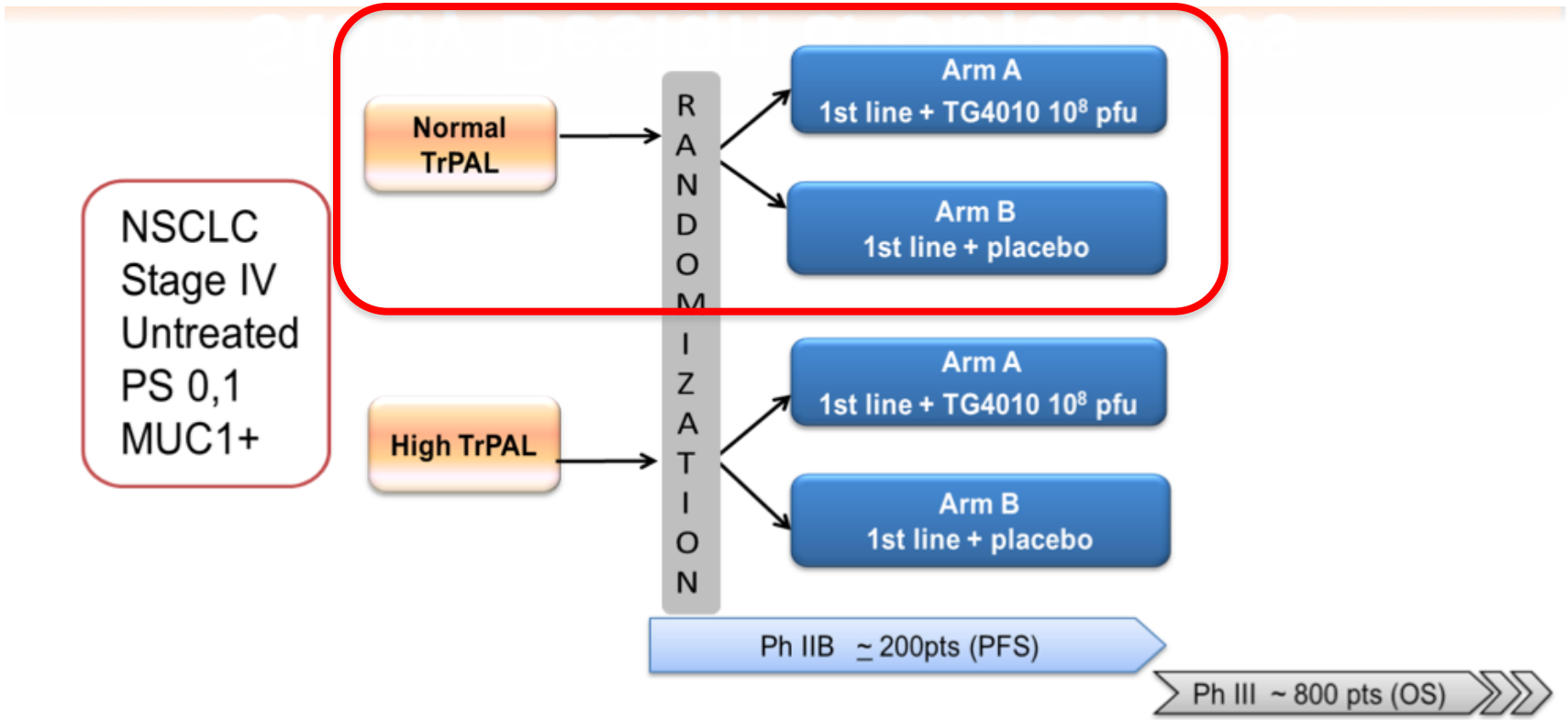
Due to the absence of treatment effect no assessment of Gene signature feasible.

Vansteenkiste J et al, ESMO 2014

Vaccination strategies?

- Mage-A3 Vaccine
- MUC-1 Vaccine

TG4010
Design: TIME Trial



Quoix E et al, ESMO 2014: abstr. 5152

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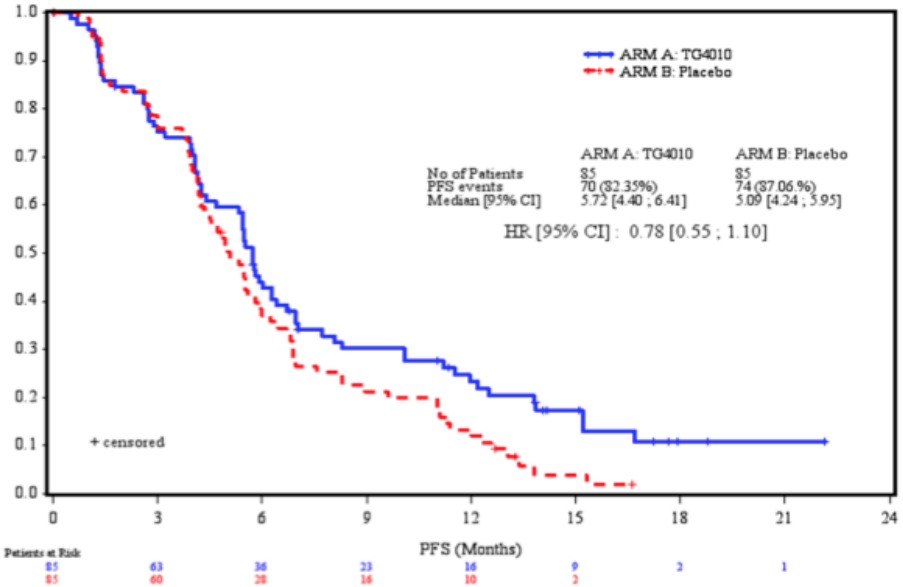
TG4010
First results

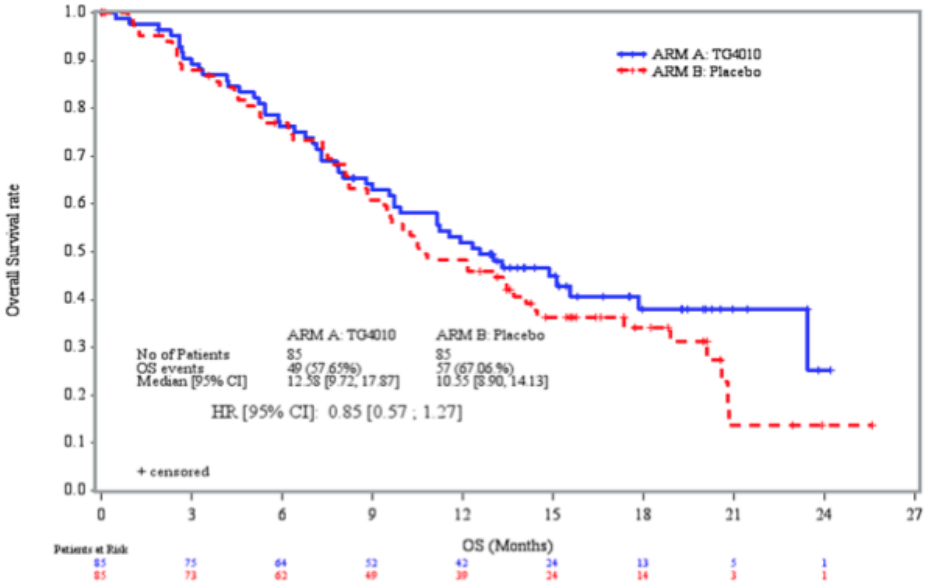
PFS & OS in Normal TrPAL patients (N=170)-Frequentist analyses

HR from stratified Cox model



HR from stratified Cox model

HR from stratified Cox model



HR from stratified Cox model

Quoix E et al, ESMO 2014: abstr. 5152

START: A phase III study of L-BLP25 cancer immunotherapy for unresectable stage III non-small cell lung

Randomised, double-blind, placebo-controlled, Phase III study

Objective: To evaluate the MUC1 antigen-specific cancer immunotherapy, L-BLP25, in patients with stage III NSCLC who had not progressed after primary chemoradiotherapy

Key patient inclusion criteria

- Unresectable stage III NSCLC
- ECOG 0-1
- No progression after chemoradiotherapy (≥2 cycles of platinum based and ≥50 Gy)

(n=1,239)

R 2:1

L-BLP25 806 µg lipopeptide SC weekly then x8 q6w (n=829) → PD

Placebo SC weekly then x8 q6w (n=410) → PD

Stratification

- Stage IIIA vs. IIIB at first diagnosis; CR/PR vs. SD to initial chemo/RT; concurrent vs. sequential chemo/RT; geographical region

Primary endpoint

- OS

Secondary endpoints

- TTSP, TTP
- Safety

Butts et al. Lancet Oncology 2014; 15: 59-68

Key efficacy data: OS

- **Key results**
  - 1,239 patients were included in the primary analysis population (median age 61 years; 39% stage IIIA and 61% IIIB; 65% concurrent and 35% sequential chemoradiotherapy)

	L-BLP25 + BSC	Placebo +BSC	HR (95% CI)	p value
OS, months				
All patients	25.6	22.3	0.88 (0.75–1.03)	0.123
Concurrent chemo/RT	30.8	20.6	0.78 (0.64–0.95)	0.016
TTP, months				
All patients	10.0	8.4	0.87 (0.75–1.00)	0.053

  - Median OS: 25.6 months with L-BLP25 vs. 22.3 months with placebo (adjusted HR 0.88, 95% CI 0.75–1.03, p=0.123)
  - In the prespecified sub group analysis, concurrent chemoradiotherapy (n=808) followed by L-BLP25 resulted in a 10.2-month difference in median OS (HR 0.78, 95% CI 0.64–0.95)
- **Key conclusions**
  - L-BLP25 maintenance therapy in stage III NSCLC was well tolerated, but did not significantly prolong OS except in the subgroup of patients treated with a concurrent chemoradiotherapy strategy

BSC, best standard of care

Butts et al. Lancet Oncology 2014; 15: 59-68

Vaccination strategies?

- Mage-A3 Vaccine
- MUC-1 Vaccine
- Other Vaccines (Belagenpumatucel, EGF-Vaccine...)

Strategies of Immunotherapy

Antigen-Dependent Therapies

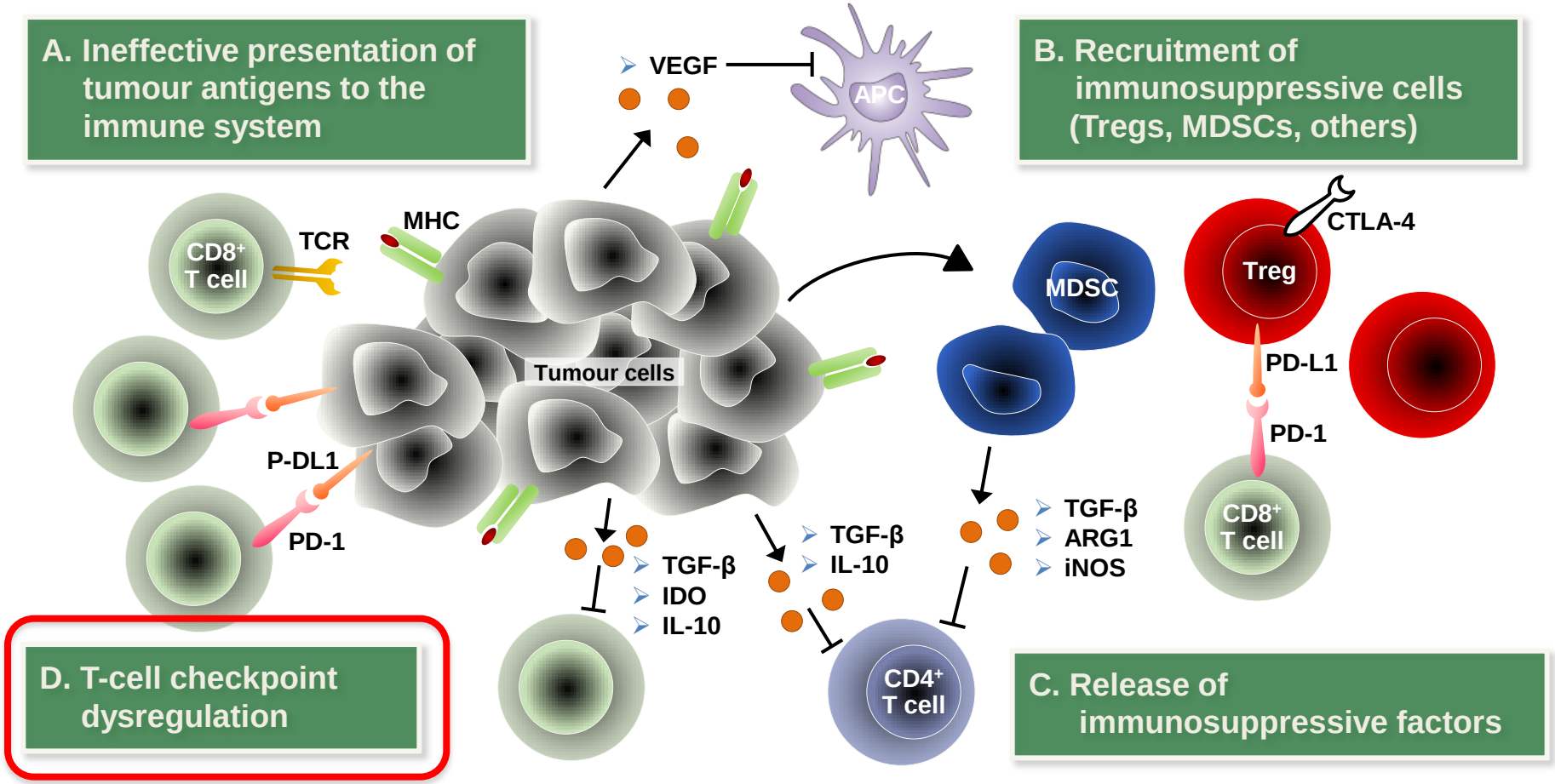
- Vaccines

Antigen-Independent Therapies

- Checkpoint-Inhibitors

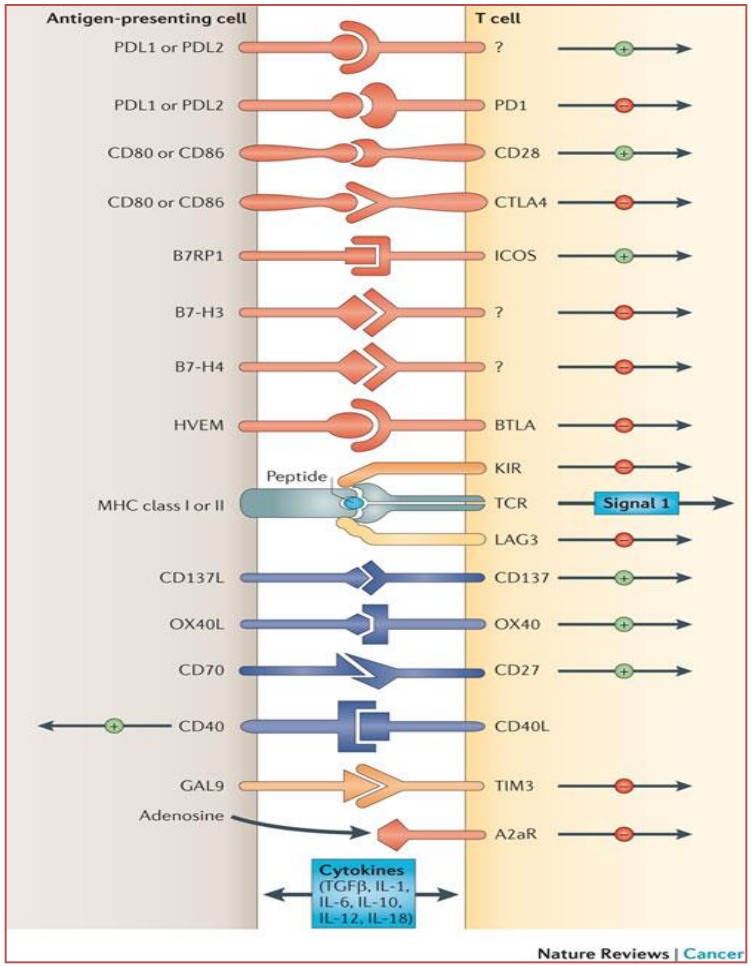
Tumours use various mechanisms to escape the immune system

- Immune escape mechanisms are complex and frequently overlapping



Vesely MD, et al. *Ann Rev Immunol* 2011;29:235–271

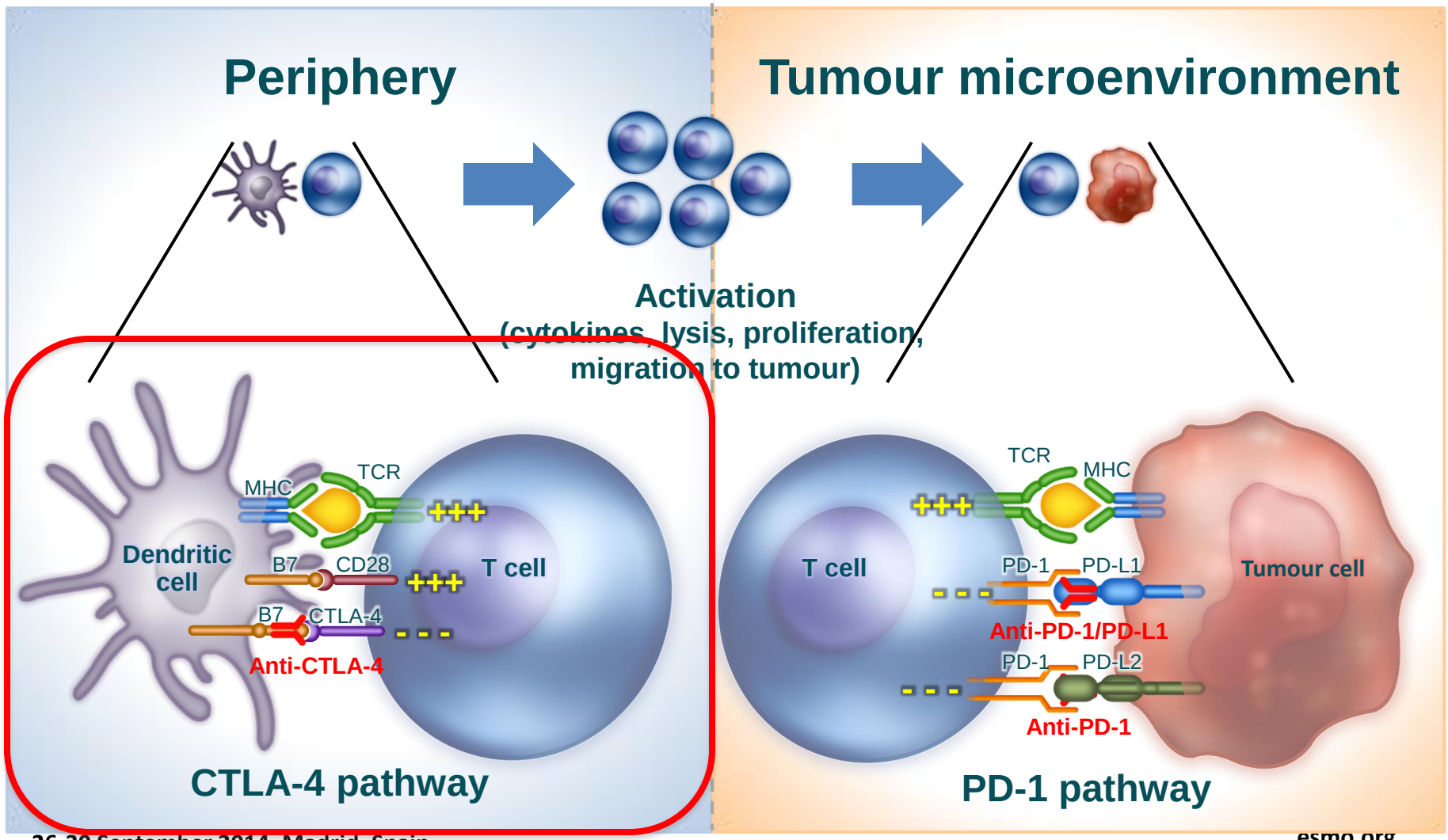
Regulation of the T cell immune response



- T cell responses are regulated through a complex balance of inhibitory ('checkpoint') and activating signals
- Tumours can dysregulate checkpoint and activating pathways, and consequently the immune response
- Targeting checkpoint and activating pathways is an evolving approach to cancer therapy, designed to promote an immune response

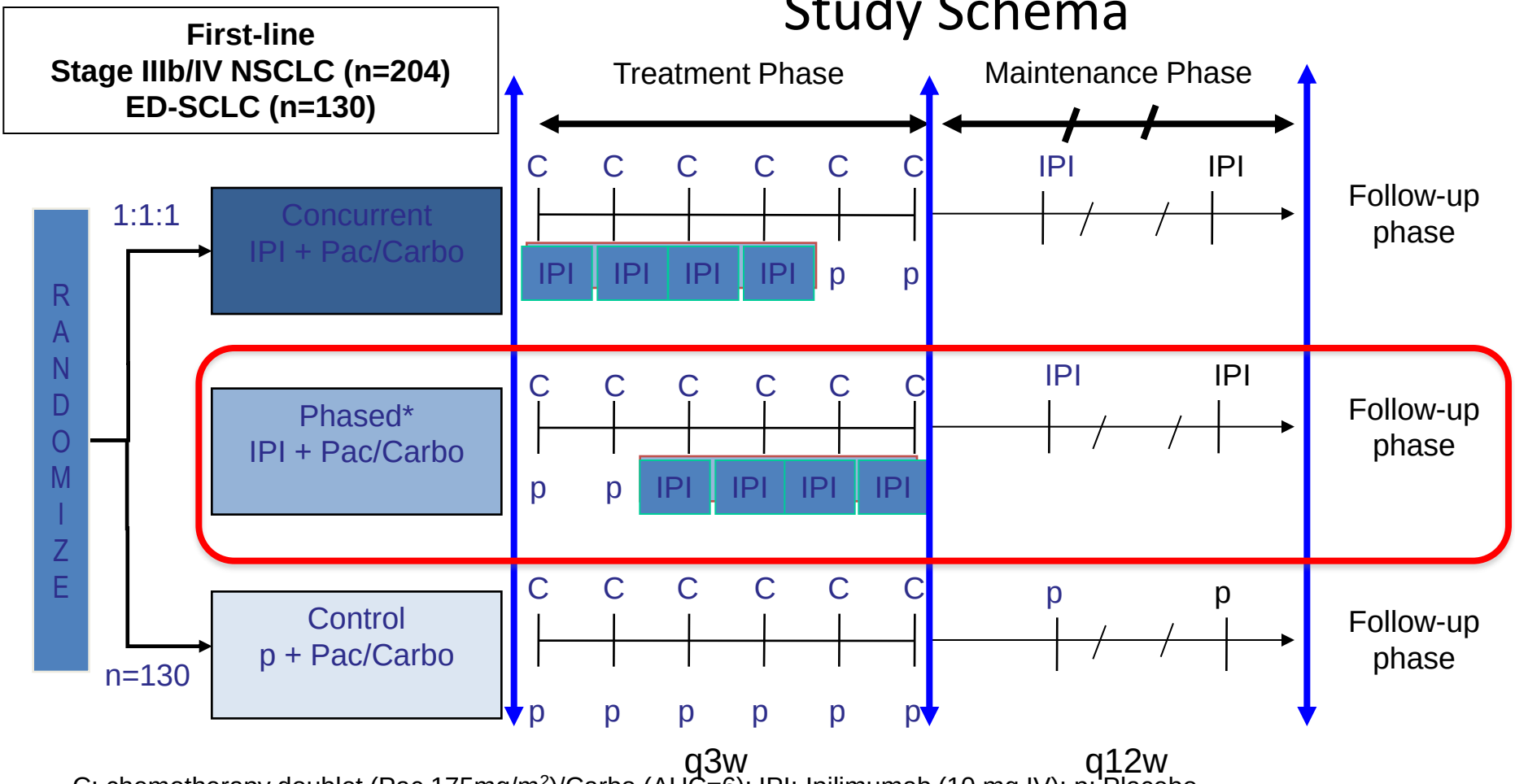
Pardoll DM. *Nat Rev Cancer* 2012;12:252–26

Targeting CTLA-4 and PD-1 pathways



Wolchock J, et al. *J Clin Oncol* 2013;31(Issue 15_suppl); abstr 9012^

Phase 2 CA184-041: Study Schema



C: chemotherapy doublet (Pac 175mg/m^2)/Carbo (AUC=6); IPI: Ipilimumab (10 mg IV); p: Placebo
*Phased : 2 doses of paclitaxel /carboplatin given prior to start of ipilimumab
Note: Steroids were given as premedication for chemotherapy

Lynch T, et al. J Clin Oncol. 2012;30(17):2046-54

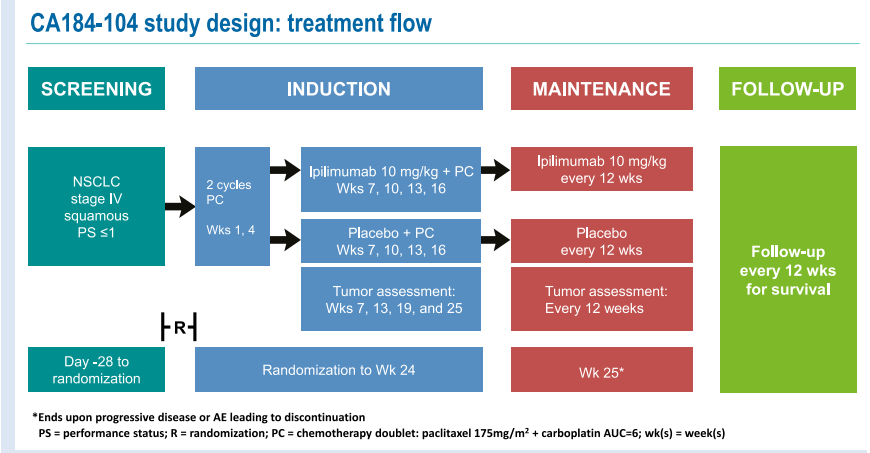
Summary Efficacy Results CA184041

End-point	NSCLC		SCLC	
	Concurrent	**Phased**	**Concurrent**	**Phased**
irPFS HR versus control (95%CI)	0.806 (0.553, 1.174)	**0.724 *** **(0.495, 1.059)**	0.751 (0.475, 1.188)	**0.640 *** **(0.403, 1.016)**
mWHO PFS HR versus control (95%CI)	0.882 (0.612, 1.271) ,	**0.691 *** **(0.478, 0.999)**	0.933 (0.588, 1.481)	0.927 (0.591, 1.453)
OS HR versus control (95%CI)	0.988 (0.669, 1.460)	0.866 (0.587, 1.278)	0.947 (0.585, 1.536)	0.753 (0.461, 1.232)
irBORR % change versus control	+3.2	+14	-4.5	+18.1
mWHO BORR % change versus control	+7.8	+18.8	-16.3	+8.2

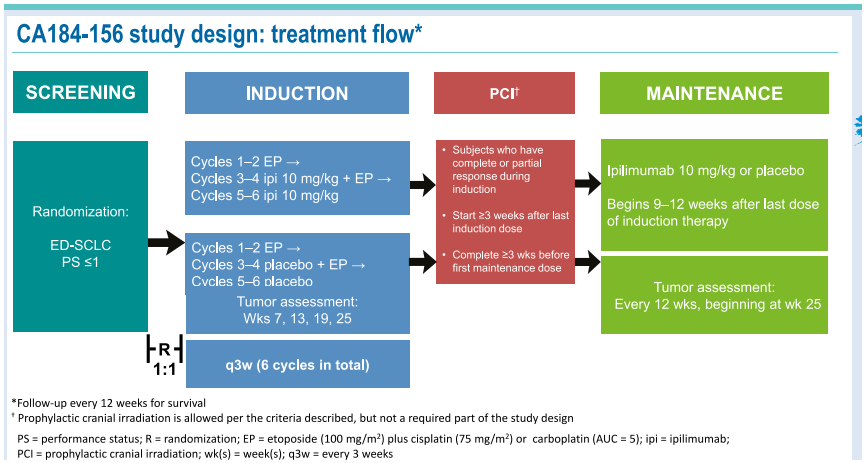
*statistically significant

Lynch T, et al. J Clin Oncol. 2012;30(17):2046-54; Reck M et al. Ann Oncol 2012, published online August 2

Ipilimumab: Phase III trials



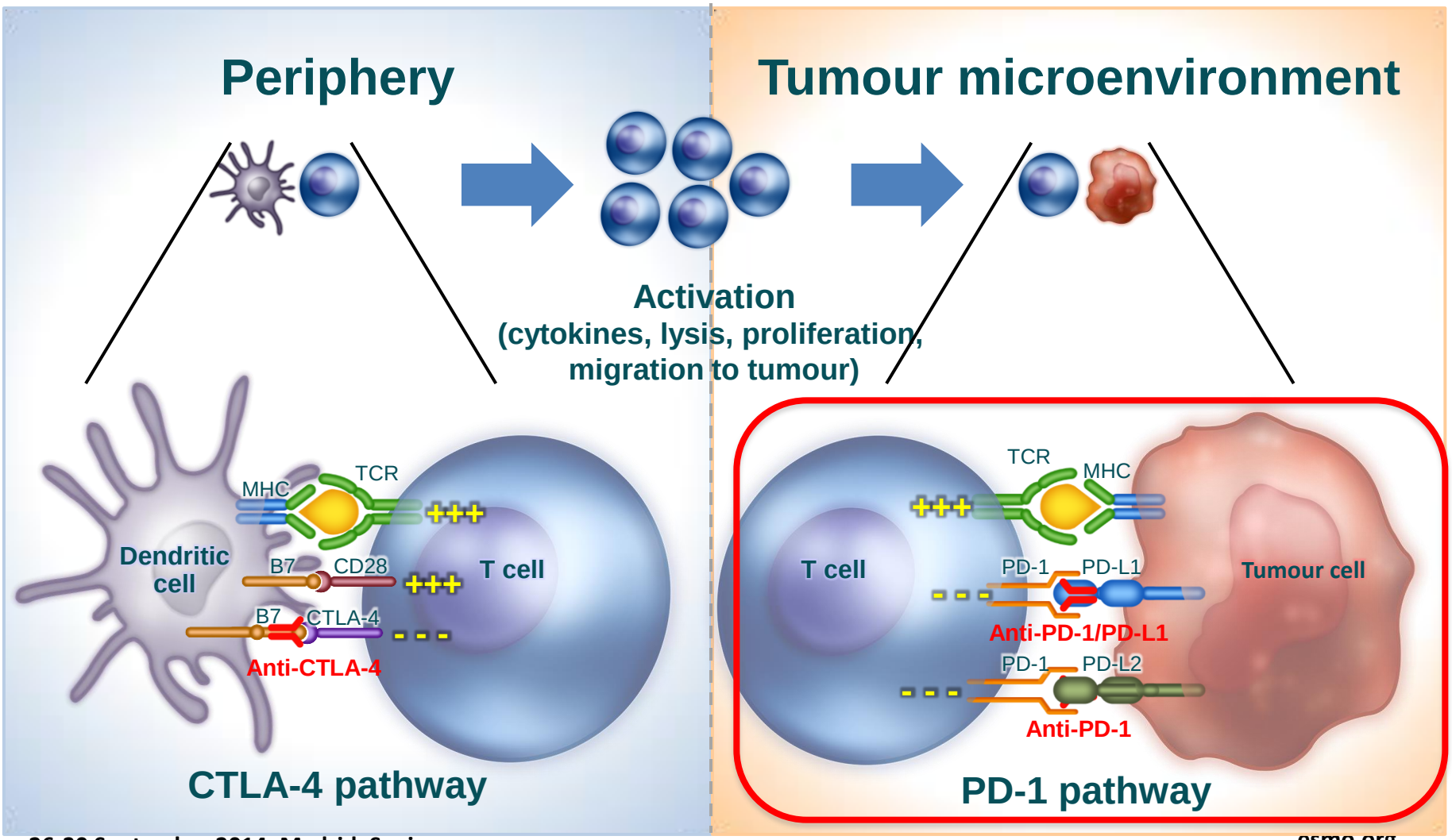
Squamous Cell
NSCLC, stage IV
Primary EP: OS



SCLC
Stage IV
Primary EP: OS

Spigel D et al ASCO 2012, Reck M et al ASCO 2013

Targeting CTLA-4 and PD-1 pathways



Wolchock J, et al. *J Clin Oncol* 2013;31(Issue 15_suppl); abstr 9012^

Efficacy according so far in pretreated patients...

	Anti PD1		Anti PD-L 1	
	MK-3475 ORR n/N (%)	Nivolumab ORR n/N (%)	MEDI4736 ORR n/N (%)	MPDL3280A ORR n/N (%)
All patients	(21%)	22/129 (17.1%)	9/58 (16%)	12/53 (23%)
PD-L1 Status (evaluable pts.)				
Positive	37/159 (23%)	5/31 (16%)	5/20 (25%)	8/26 (31%)
Negative	3/35 (9%)	4/32 (13%)	1/29 (3%)	4/20 (20%)

Horn L, J Thorac Oncol 2013; 8 (Suppl 2), #MO18.01; Brahmer JR, J Thorac Oncol 2013; 8 (Suppl2), #MO1803; Antonia SJ, J Thorac Oncol 2013 (Suppl 2), #P2 11-034; Garon E, ASCO 2014; #8020; Brahmer J, ASCO 2014, #8021

Randomized confirmation pending…

CA209-017
NCT01642004
(Phase III; N = 264)

Patients with stage IIIb/IV squamous cell NSCLC

→ **Docetaxel**
→ **Nivolumab**

Primary objective
- OS

Secondary objectives
- ORR
- PFS
- ORR, OS and PFS by PD-L1 status
- QoL

CA209-057
NCT01673867
(Phase III; N = 582)

Patients with stage IIIb/IV non-squamous cell NSCLC

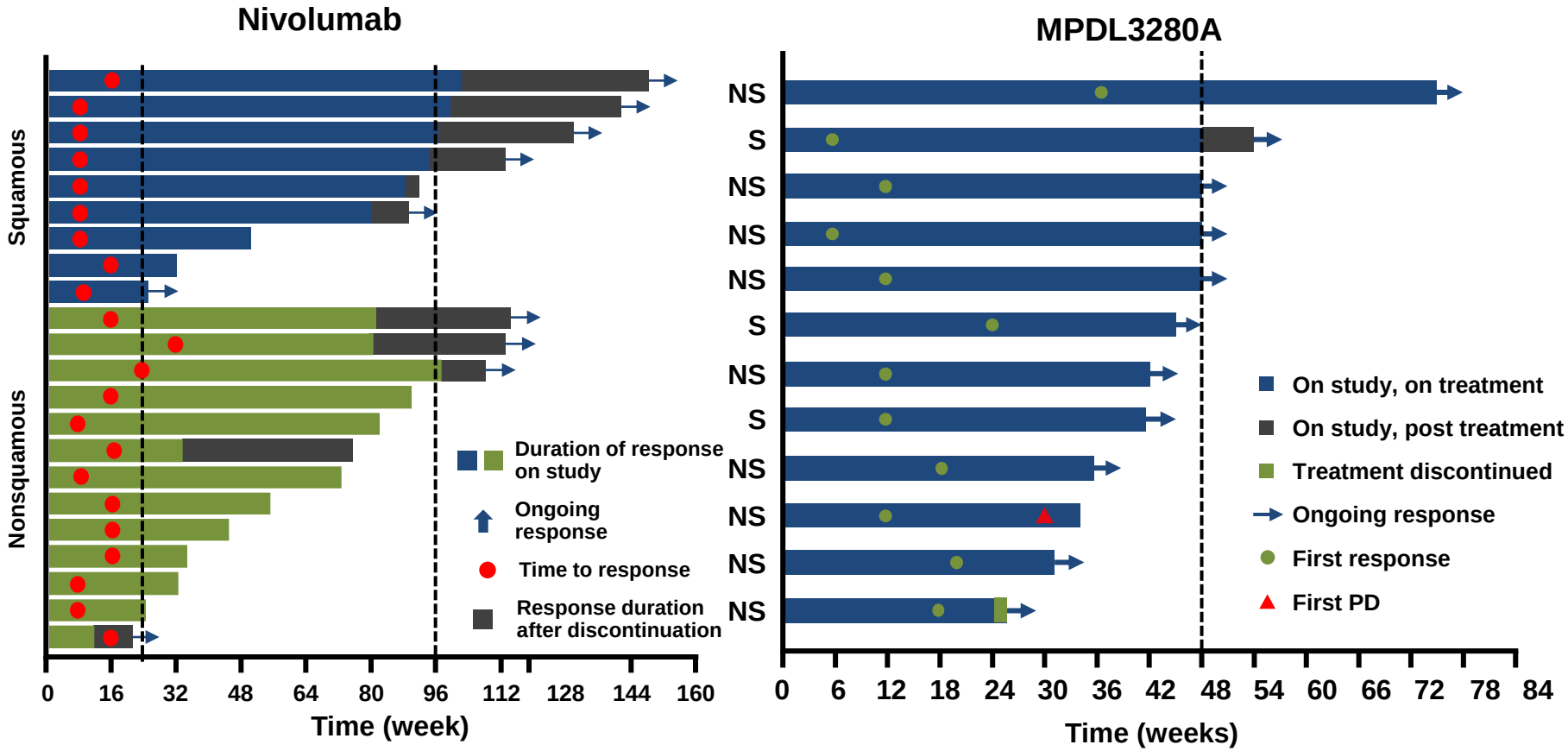
→ **Docetaxel**
→ **Nivolumab**

Primary objective
- OS

Secondary objectives
- ORR
- PFS
- PD-L1 status
- Disease-related symptom improvement rate (measured using Lung Cancer Symptom Scale)

http://www.clinicaltrials.gov

Impact of Histology
Efficacy of Anti PD1/PD-L1 Antibodies

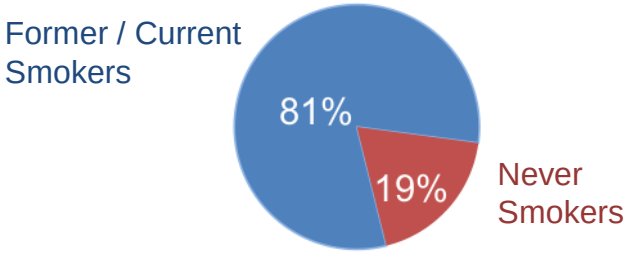


Adapted from Brahmer JR, et al. Mini-Oral presentation at WCLC 2013. *J Thorac Oncol.* 2013;8(Suppl 2):abstract: MO18.03
Horn L, et al. Mini-Oral presentation at WCLC 2013. *J Thorac Oncol.* 2013;8(Suppl 2):abstract: MO18.01.

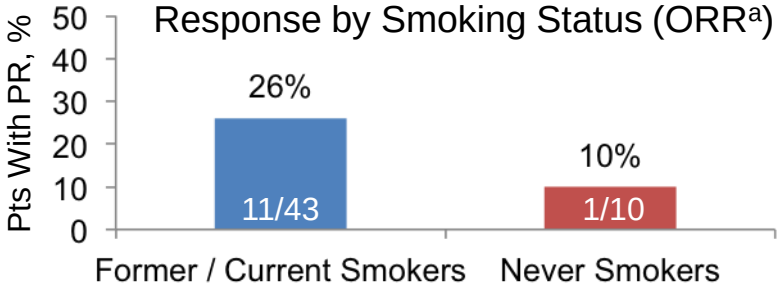
Impact of Molecular Marker?

MPDL3280A

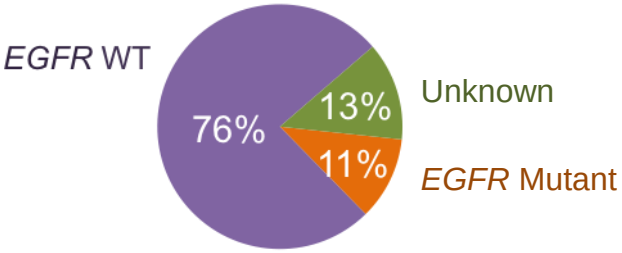
Smoking Status (NSCLC; n = 53)



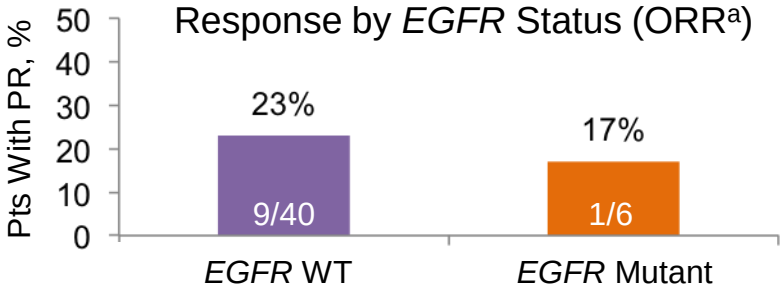
Response by Smoking Status (ORR[a])



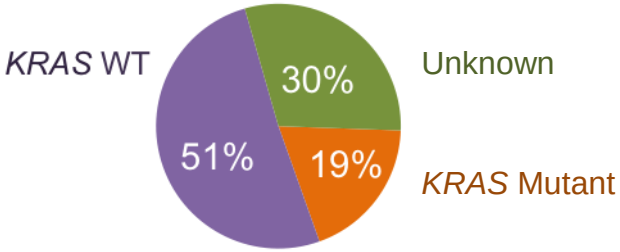
EGFR Status (NSCLC; n = 53)



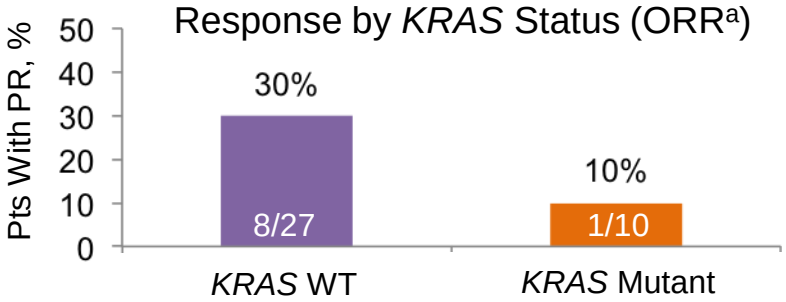
Response by *EGFR* Status (ORR[a])



KRAS Status (NSCLC; n = 53)

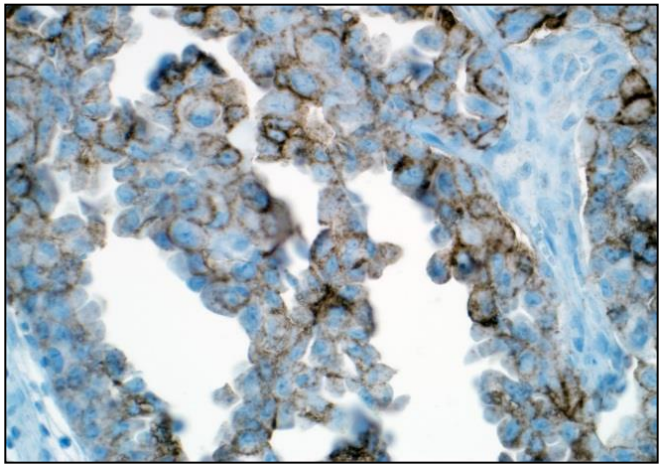


Response by *KRAS* Status (ORR[a])

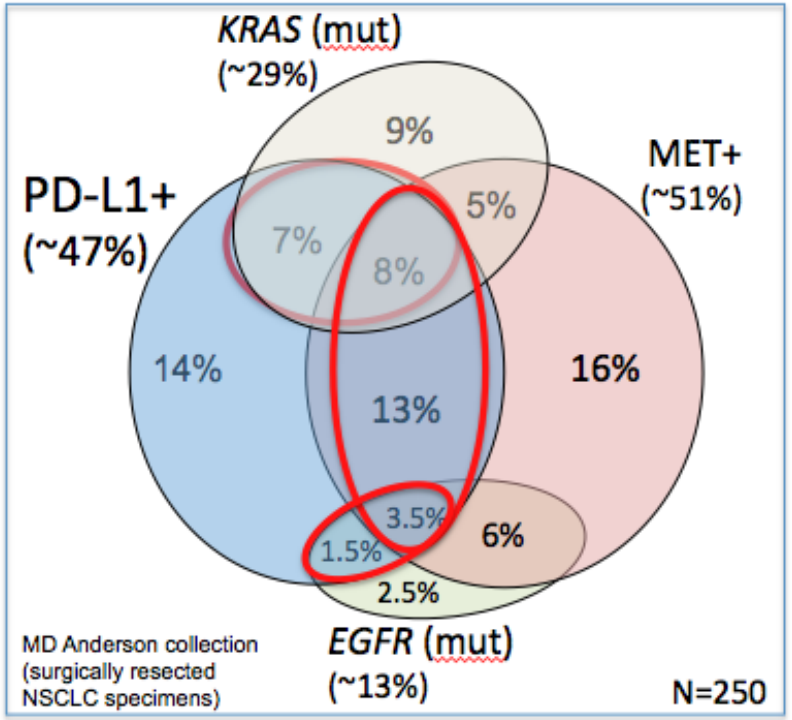


Horn L, WCLC 2013, MO18.01

Any predictive marker?



PD-L1 positive



Adenocarcinoma

Horn L, WCLC 2013, Kowanetz WCLC 2013

Problems with assessment of PD-L1 expression

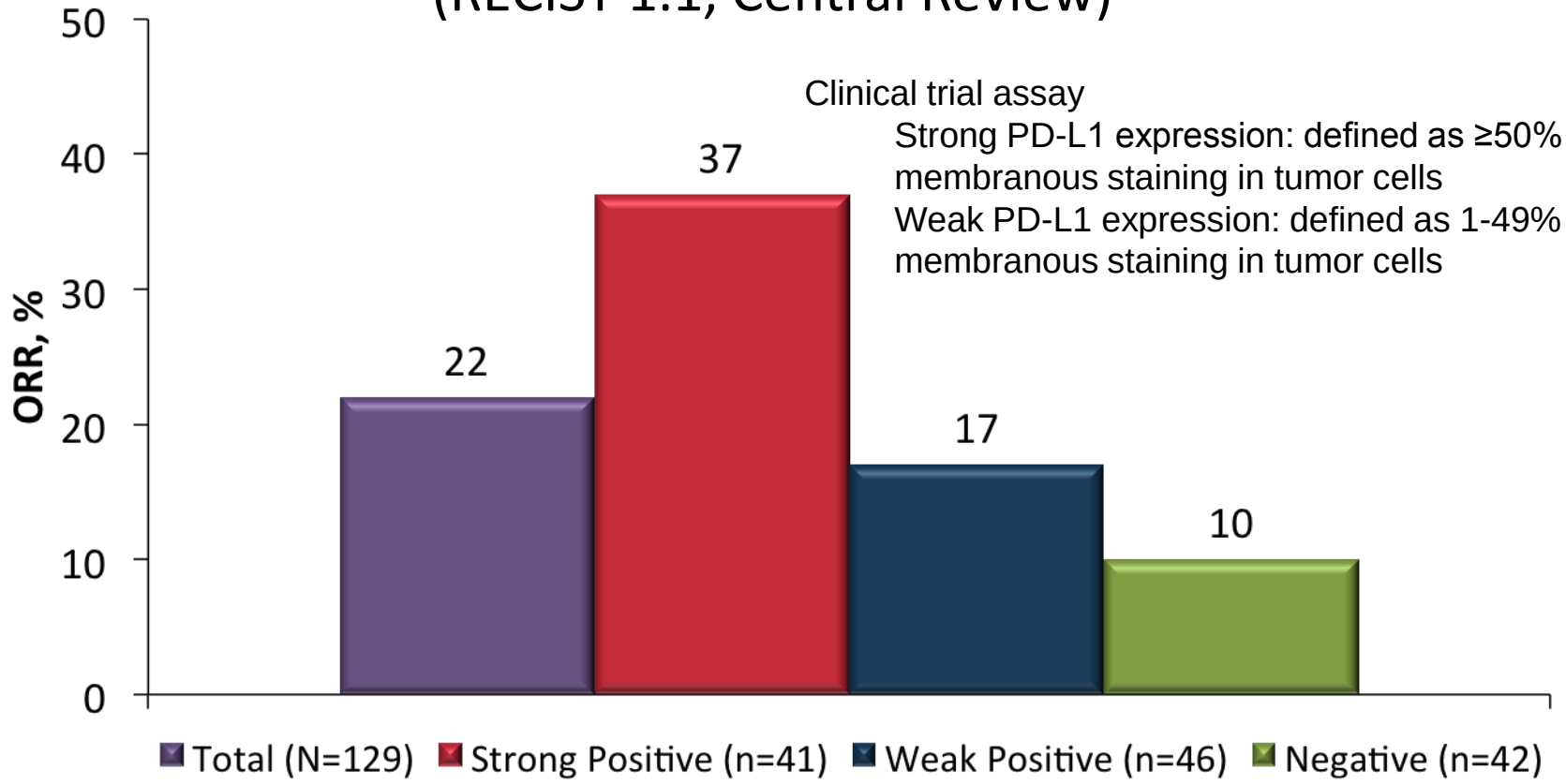
	Anti PD1		Anti PD-L 1	
	MK-3475 ORR n/N (%)	Nivolumab ORR n/N (%)	MEDI4736 ORR n/N (%)	MPDL3280A ORR n/N (%)
All patients	(21%)	22/129 (17.1%)	9/58 (16%)	12/53 (23%)
PD-L1 Status (evaluable pts.)				
Positive	37/159 (23%)	5/31 (16%)	5/20 (25%)	8/26 (31%)
Negative	3/35 (9%)	4/32 (13%)	1/29 (3%)	4/20 (20%)

Key questions about PD-L1 assessment

- Variability in tissue collection timing, cell sampling, mAb used for staining, IHC criteria

Horn L, J Thorac Oncol 2013; 8 (Suppl 2), #MO18.01; Brahmer JR, J Thorac Oncol 2013; 8 (Suppl2), #MO1803; Antonia SJ, J Thorac Oncol 2013 (Suppl 2), #P2 11-034; Garon E, ASCO 2014; #8020; Brahmer J, ASCO 2014, #8021

Pembrolizumab
Response Rate by Level of PD-L1 Expression
(RECIST 1.1, Central Review)



[a]Evaluable patients were those patients in the training set with evaluable tumor PD-L1 expression who had measurable disease at baseline per imaging assessment criteria. Analysis cut-off date: March 3, 2014.

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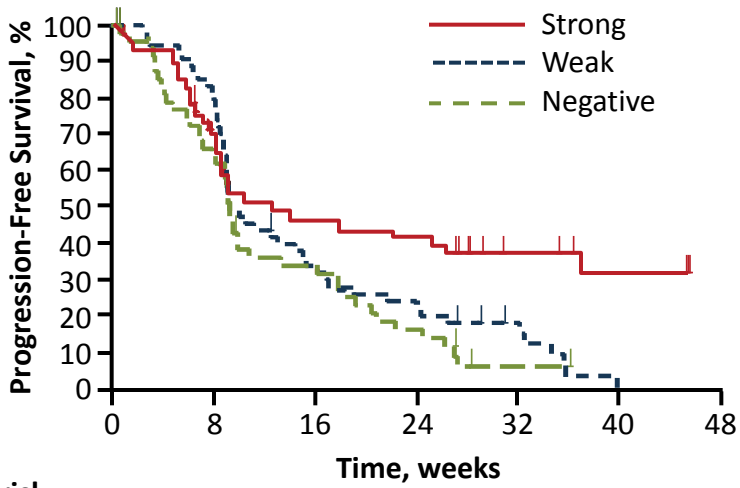
Pembrolizumab
Kaplan-Meier Estimates of Survival

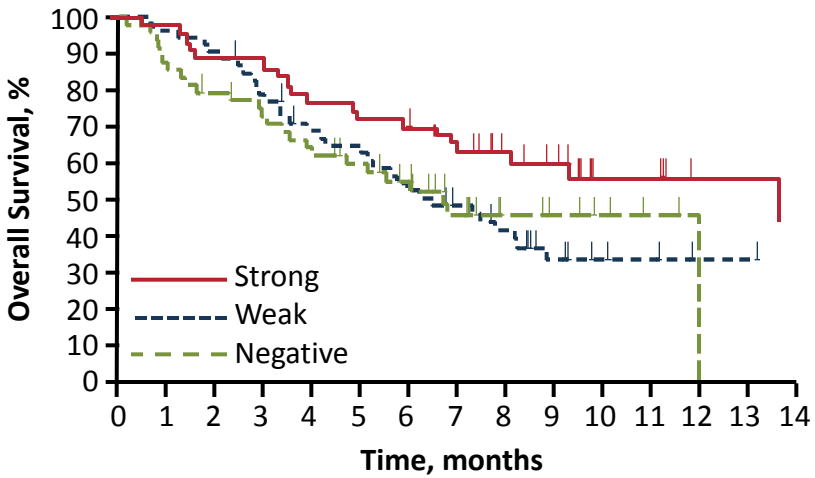
PFS (RECIST v1.1, Central Review)



n at risk

Strong	44	28	18	17	9	6	3
Weak	53	43	17	12	6	0	0
Negative	49	30	15	7	1	0	0

OS



Strong	44	43	38	38	34	32	30	27	21	18	9	8	5	5	4
Weak	53	51	48	40	34	31	26	22	18	11	8	7	5	5	4
Negative	49	42	38	34	29	26	21	14	8	6	4	2	0	0	0

- PFS was longer in patients with PD-L1 strong-positive versus PD-L1 weak-positive/ negative tumors (HR, 0.52; 95% CI, 0.33-0.80)
- OS was longer in patients with PD-L1 strong-positive versus PD-L1 weak-positive/ negative tumors (HR, 0.59; 95% CI, 0.35-0.99)

[a]Evaluable patients were those patients in the training set with evaluable tumor PD-L1 expression.
Strong PD-L1 positivity defined as staining in ≥50% of tumor cells, and weak PD-L1 positivity as staining in 1-49% of tumor cells. Negative staining is no PD-L1 staining in tumor cells.
Data cut-off: March 3, 2014.

Garon E, ESMO 2014: LBA 43

Next steps...

First-Line Efficacy?

	MK-3475 Pembrolizumab		BMS-936558 Nivolumab
Patients	45		20
Squamous	22% / 10		45% / 9
Non-Squamous	76% / 34		55% / 11
Unknown	2% / 1		-
RR (RECIST 1.1)	26%	47% (IrRC)	30% / 10% CR
DCR	64%	78% (IrRC)	65%
Med PFS (95% CI)	27 w (13.6-45)		36 w (5.9-80.7+)
1 year OS (95% CI)			75% (50, 89)

Rizvi N et al, J Clin Oncol 2014; 32 (suppl 5, abstr. 8007), Gettinger S et al, J Clin Oncol 2014; 32 (suppl 5, abstr. 8024)

Sometimes things become difficult: Exploratory analysis BMS 936558 (Nivolumab)

	Baseline PD-L1 Expression[a]	
	PD-L1+	PD-L1-
Samples sufficient for PD-L1 analysis, n	10	7
ORR,[b] n (%)	5 (50)	0
Median DOR, weeks (range)	NR (24.0, 71.4+)	–
Stable disease, n (%) [duration ≥24 weeks, n]	3 (30) [1]	4 (57) [4]
PFS rate at 24 weeks, % (95% CI)	70 (33, 89)	**57** (17, 84)
Median PFS, weeks (range)	45.6 (8.0, 80.7+)	**36.1** (6.1, 54.0)
1-year OS rate, % (95% CI)	80 (41, 95)	**71** (26, 92)
Median OS, weeks (range)	NR (42.7, 82.4+)	NR (13.3, 89.1+)

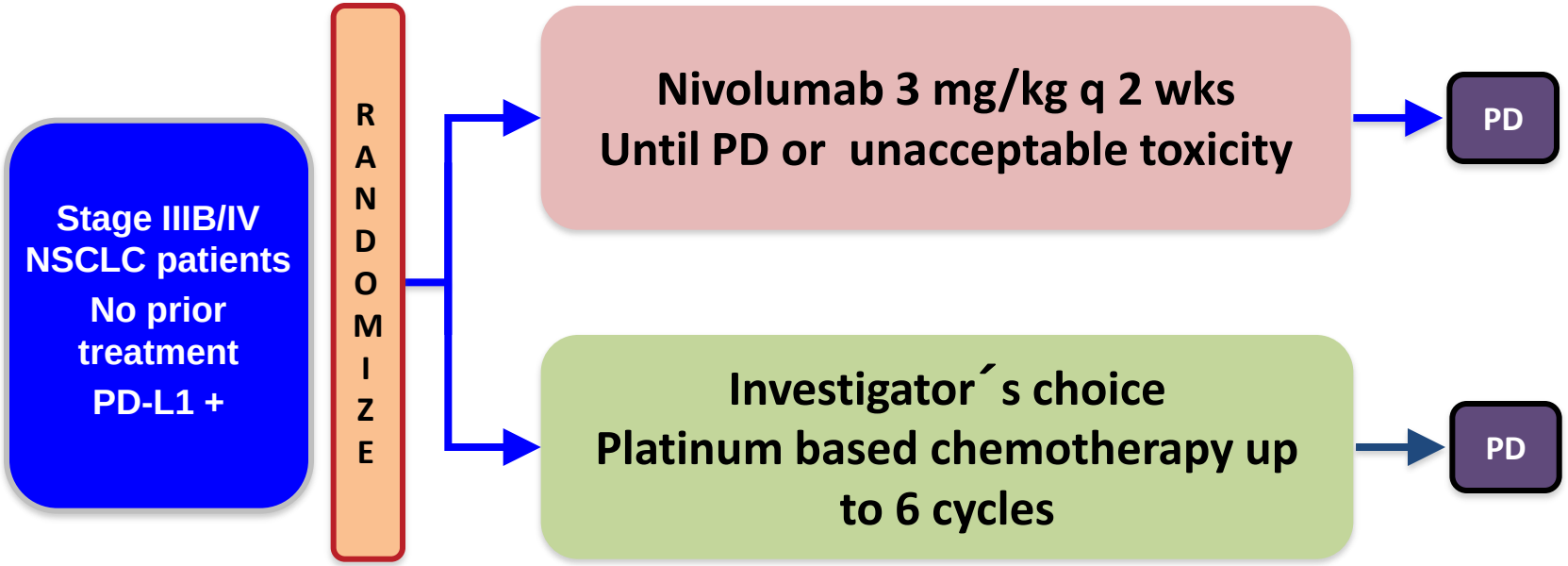
Gettinger et al. J Clin Oncol 2014; 32 (suppl 5; abstr 8024)

First-Line PD1 / PD-L1 Inhibition?

- How strong is the oncogenic addiction, which is characterized by PD-L1 expression?
- How strong is the impact of PD1 / PD-L1 checkpoint inhibition?
- How reliable is the test for PD-L1 expression?
- Will PD1 / PD-L1 inhibition be superior to platinum-based chemotherapy....

One Example

Nivolumab vs chemotherapy in first-line treatment of NSCLC (CA 209-026)



Optional Maintenance, optional crossover to nivolumab

ClinicalTrial.gov NCT01154140; Carbone D, ASCO 2014; TPS 8128

Other areas...?

PD-1 Inhibition + EGFR-TKI in EGFR mutant patients?

- 21 Patients (20 patients refractory after previous EGFR TKI)
- 7 Patients T790M mutation
- RR 19%
- PFS-Rate 24w: 51%, med PFS: 29.4 w
- 1-year OS: 73%
- Option for patients without T790M mutation?

Rizvi NA, J Clin Oncol 2014; 32 (suppl 5, Poster 36), Gettinger S, ESMO 2014: abstr 1054PD

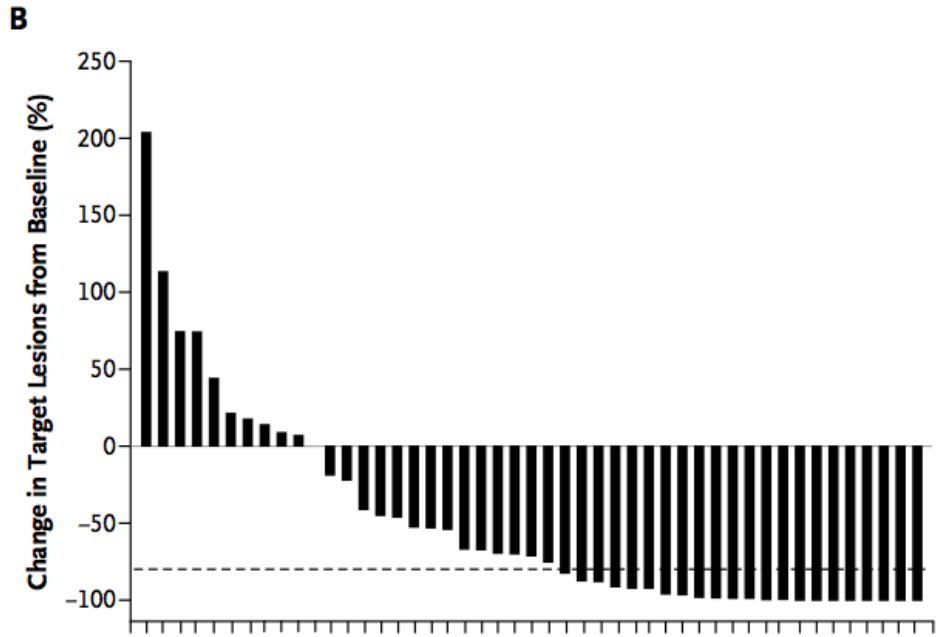
Other areas...?
PD-1 Inhibition + Chemotherapy

- Combinations:
  - Gem/Cis; Pem/Cis; Pac/Carbo + Nivo 10 mg/kg (42 pts)
  - Pac/Carbo + Nivo 5 mg/kg (14 pts)
- Response rate: 33% - 47%
- PFS rate at 6 months: 38% - 71%
- Median PFS: 5.25 – 7.75 m
- 1-year OS rate: 50% - 87%

Gettinger S, ESMO 2014: abstr 1054PD

Other areas – Combination of checkpoint inhibitors

Background



- Improved efficacy for combination of ipilimumab and nivolumab patients with advanced melanoma
- Response rate: 40%
- Cinical activity: 65%
- Optimal dose:
  - Concurrent treatment
  - Ipilimumab: 3 mg/kg (4 doses)
  - Nivolumab: 1 mg/kg (8 doses)
  - Subsequent treatment cykles
- Grade 3,4 AEs: 53%

Wolchok JD, NEJM 2013; 369: 122-33

Tumor response	Nivolumab 1 mg/kg + ipilimumab 3 mg/kg		Nivolumab 3 mg/kg + ipilimumab 1 mg/kg	
	Squamous n = 9	Non-squamous n = 15	Squamous n = 9	Non-squamous n = 16
ORR, n (%) [95% CI]	1 (11) [0.3, 48]	2 (13) [2, 41]	3 (33) [8, 70]	2 (13) [2, 38]
PFS				
PFS rate at 24 weeks % (95% CI)	25 (4,56)	51 (21, 74)	44 (14,72)	20 (5,43)
Median PFS, weeks (range)	8.9 (0.1+, 44.7)	32.9 (0.1+, 54.1+)	20.6 (9.7, 33.3+)	9.9 (4.1+, 58.1+)
	16.1(0.1+, 54.1+)		14.4 (4.1+, 58.1+)	

Safety

- Treatment-related AEs (all grades) reported in 43 patients (88%), most commonly fatigue (45%)
- **Pneumonitis** (all grades) was reported in 6 patients (12%)
- **Grade 3/4 in 3 patients (6%)**; all cases were reversible with corticosteroids and drug discontinuation
- **Grade 3/4 treatment-related AEs were reported in 24 patients (49%), most commonly diarrhea (10%)**
- **18 patients (37%) discontinued due to AEs related to any study medication**
- 17 patients died (**3 due to drug-related toxicities: respiratory failure following grade 3 colitis; pulmonary hemorrhage; and toxic epidermal necrolysis**)

Antonia et al. J Clin Oncol 2014; 32 (suppl 5; abstr 8023)

Open spaces...
(partly covered by clinical trials)

- Early stage (Adjuvant treatment)
- Local advanced stage (Maintenance after chemoradiotherapy)
- Maintenance Setting
- Combination with antangiogenic drugs
- Combination with targeted therapies
- SCLC
- Mesothelioma

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Ongoing trials...

Table 1. Select active immunotherapies in clinical development for non-small cell lung cancer.

Drug	Target	Phase	Setting	Planned accrual†	Ref.
T-cell checkpoint blockade (monotherapy)					
Ipilimumab	CTLA-4	II	Recurrent/stage IV non-squamous	–	[118]
Nivolumab	PD-1	II	Advanced or metastatic squamous cell NSCLC who have received at least two prior systemic regimens	100	[62]
		III	Previously treated advanced or metastatic squamous NSCLC	264	[63]
		III	Non-squamous cell NSCLC after failure of prior platinum-based chemotherapy	574	[64]
		III	Stage IV or recurrent PD-L1-positive as a first-line treatment	495	[65]
		III	Advanced or metastatic NSCLC who have progressed	780	[119]
Pembrolizumab (MK-3475)	PD-1	I	Progressive locally advanced or metastatic carcinoma, melanoma or NSCLC	1137	[120]
		I	Advanced NSCLC	24	[121]
		II	Metastatic melanoma and NSCLC with untreated brain metastases	64	[122]
		II/III	Previously-treated NSCLC	920	[68]
		III	Metastatic NSCLC	300	[123]
MPDL3280A (RG7446)	PD-L1	II	PD-L1-positive locally advanced or metastatic NSCLC	128	[70]
		II	PD-L1-positive locally advanced or metastatic NSCLC	300	[124]
		II	Locally advanced or metastatic NSCLC who have failed platinum therapy	300	[71]
		III	Locally advanced or metastatic NSCLC who have failed platinum therapy	850	[72]
MEDI4736	PD-L1	II	Stage III unresectable NSCLC who have received at least 2 prior systemic treatment regimens	210	[125]
		III	Stage III unresectable NSCLC who have not progressed following definitive, platinum-based, concurrent chemoradiation therapy	880	[126]
Dual T-cell checkpoint blockade					
Ipilimumab + nivolumab	CTLA-4 + PD-1	I	Stage IIIB/IV NSCLC	412	[85]
Tremelimumab + MEDI4736	CTLA-4 + PD-L1	I	Advanced NSCLC	208	[127]
Pembrolizumab + ipilimumab	PD-1 + CTLA-4	I	Locally advanced or metastatic NSCLC	320	[86]
T-cell checkpoint blockade combined with chemotherapy					
Ipilimumab + paclitaxel/carboplatin	CTLA-4	I	Japanese patients, stage IIIB or recurrent/stage IV	15	[128]

Table 1. Select active immunotherapies in clinical development for non-small cell lung cancer (cont.).

Drug	Target	Phase	Setting	Planned accrual†	Ref.
T-cell checkpoint blockade combined with chemotherapy					
Ipilimumab + paclitaxel/carboplatin/cisplatin	CTLA-4	I	Neoadjuvant, stage IB, IIA/IIB or III NSCLC	30	[129]
Nivolumab + chemotherapy‡	PD-1	I	Stage IIIB/IV NSCLC	412	[85]
Pembrolizumab + pemetrexed or paclitaxel/carboplatin	PD-1	I	Advanced NSCLC	30	[130]
			Unresectable or metastatic NSCLC	320	[86]
Ipilimumab + paclitaxel/carboplatin	CTLA-4	III	Squamous NSCLC	920	[9]
T-cell checkpoint blockade combined with targeted therapy					
Nivolumab + bevacizumab	PD-1 + VEGF	I	Stage IIIB/IV NSCLC	412	[85]
Ipilimumab + erlotinib	CTLA-4 + EGFR	I	EGFR or ALK mutated stage IV NSCLC	46	[131]
Nivolumab + erlotinib	CTLA-4 + EGFR	I	Stage IIIB/IV NSCLC	412	[85]
MPDL3280A (RG7446) + erlotinib	PD-L1 + EGFR	I	NSCLC	32	[132]
MEDI4736 + gefitinib	PD-1 + EGFR	I	EGFR mutant NSCLC	47	[133]
MEDI4736 + AZD9291§	PD-1 + EGFR	I	EGFR mutant NSCLC	300	[134]
Tremelimumab + gefitinib	CTLA-4 + EGFR	I	EGFR mutant NSCLC	24	[135]
Ipilimumab + crizotinib	CTLA-4 + ALK	I	EGFR or ALK mutated stage IV NSCLC	46	[131]
Pembrolizumab + INCB024360	PD-1 + IDO1	I/II	Selected solid tumors (Phase I), stage IIIb, IV or recurrent NSCLC (Phase II)	120	[136]
Pembrolizumab + erlotinib	PD-1 + EGFR	I/II	Locally advanced or metastatic NSCLC	320	[86]
Pembrolizumab + gefitinib	PD-1 + EGFR	I/II	Locally advanced or metastatic NSCLC	320	[86]
Pembrolizumab + bevacizumab	PD-1 + VEGF	I/II	Locally advanced or metastatic NSCLC	320	[86]
Switch from targeted therapy to T-cell checkpoint blockade					
Gefitinib, AZD9291, selumetinib + docetaxel or tremelimumab to MEDI4736	PD-1	II	Stage IIIB–IV NSCLC	72	[137]

26-30 September 2014, Madrid, Spain

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Heigener DF, Reck M, Expert Rev Anticancer Ther 2014

Summary

- Fascinating new approach
- Place of vaccination strategies has to be validated
- Response best surrogate marker for efficacy?
  - Difficult assessment (RECIST?, irResponse Criteria?)
  - PFS or TTP better marker? (MOA)
- Strong request for harmonized development of companion diagnostics
  - For economical reasons
  - For scientific reasons
  - For medical reasons (the maximum benefit for the patient still is the center of therapeutical efforts!)
- Randomized evaluation undebatable