Multidisciplinary management of thoracic malignancies

Thursday, 04/14/2016, 04:45 PM - 06:15 PM
Room A
Discussant abstracts 98O and 208O_PR

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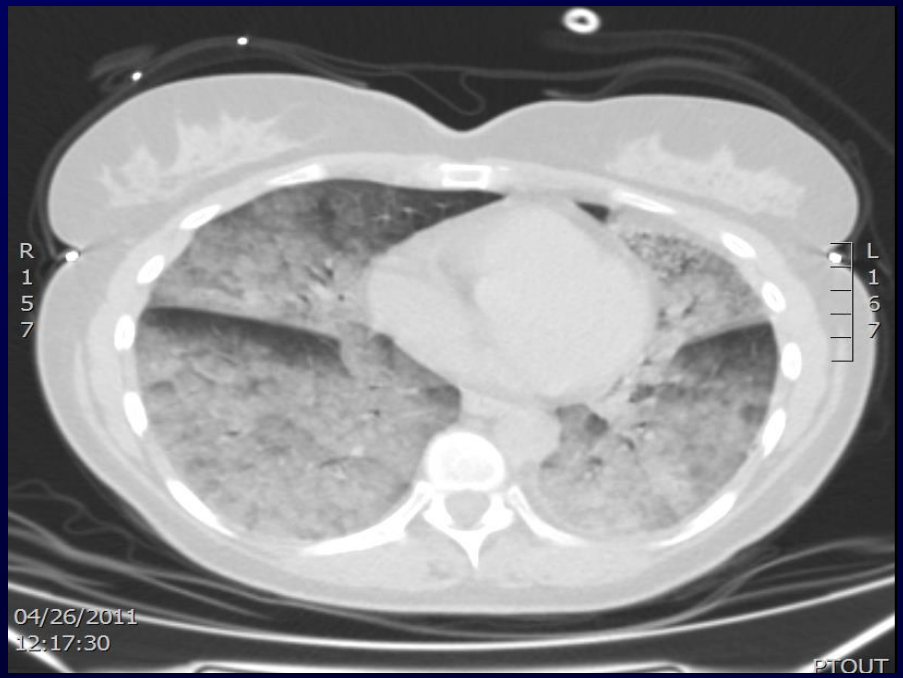
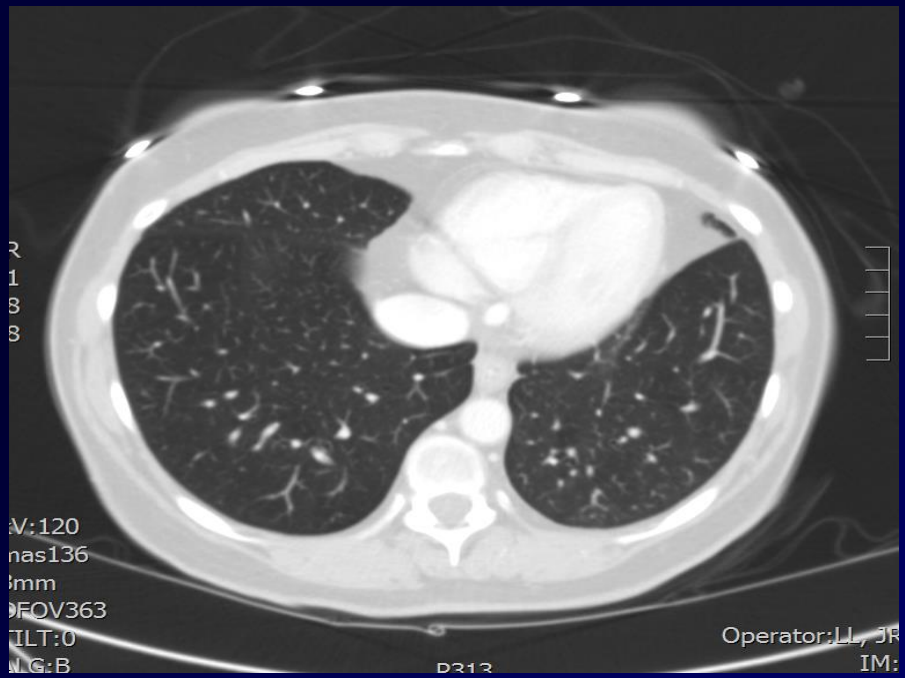
Disclosures

- Consulting/honoraria from:
  - Genentech/Roche
  - Pfizer
  - Novartis
  - BioDesix
  - Merck
  - EMD Serono
  - GSK
  - Boehringer Ingelheim
  - Amgen

Response to crizotinib (Xalkori) in ALK+ patient



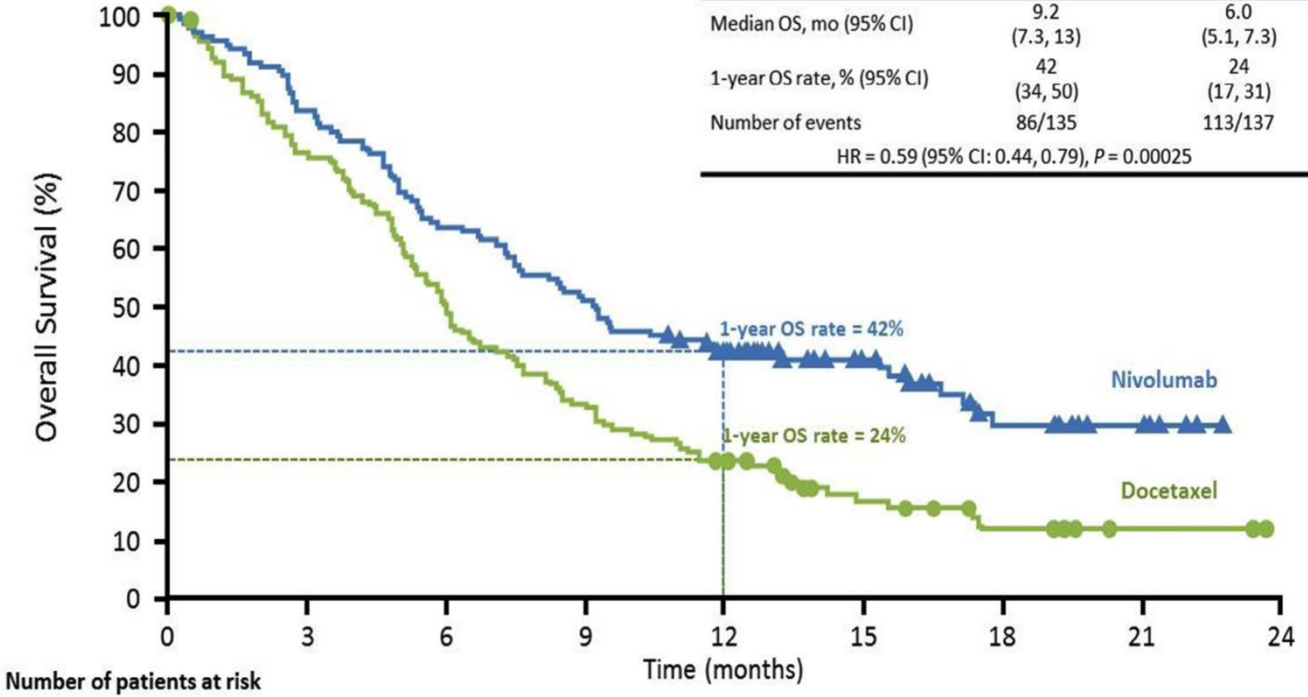
4/26/2011



9/27/2011

Nivolumab in second line squamous - OS

	Nivolumab n = 135	Docetaxel n = 137
Median OS, mo (95% CI)	9.2 (7.3, 13)	6.0 (5.1, 7.3)
1-year OS rate, % (95% CI)	42 (34, 50)	24 (17, 31)
Number of events	86/135	113/137
HR = 0.59 (95% CI: 0.44, 0.79), *P* = 0.00025		



Number of patients at risk									
Nivolumab	135	113	86	69	52	31	15	7	0
Docetaxel	137	103	68	45	30	14	7	2	0

Brahmer, NEJM 2015

EUROPEAN LUNG CANCER CONFERENCE 2016

CHARACTERIZATION OF TUMOR INFILTRATING LYMPHOCYTES IN RESECTABLE EARLY-STAGE NON-SMALL CELL LUNG CANCER

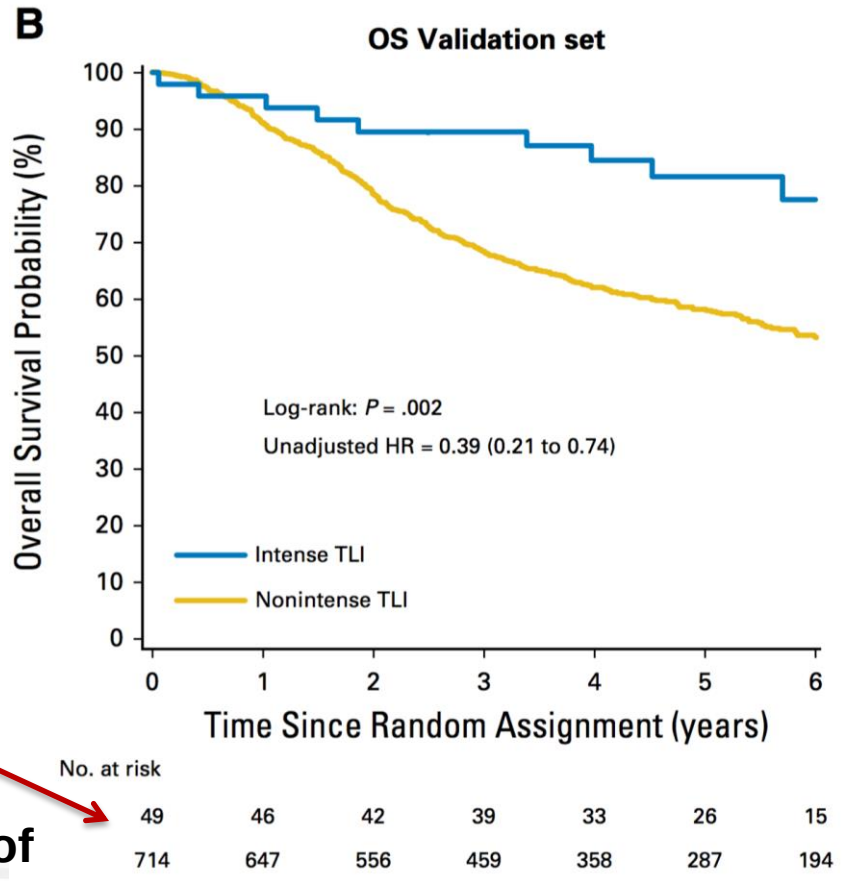
Sean Hall
Division of Thoracic Surgery,
University Hospital of Bern

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
HOPITAL UNIVERSITAIRE DE BERNE
BERN UNIVERSITY HOSPITAL

The immunology of early vs. late stage tumors

- Resection of lung cancer results in only about 50% cures
- Immunotherapy has the potential to increase the number of cures
- The host response observable in tumors presenting as early stage and those presenting as late stage may be different and even perhaps cause and effect
  - A 4 cm stage I tumor may have an ongoing immune response that has kept it from metastasizing
  - A 5 mm tumor that presents with bone, liver and brain metastases may not have the same responses
- Most of the data to date are on overtly metastatic patients
- Understanding responses in early stage tumors is important for optimizing immunotherapy of early stage disease

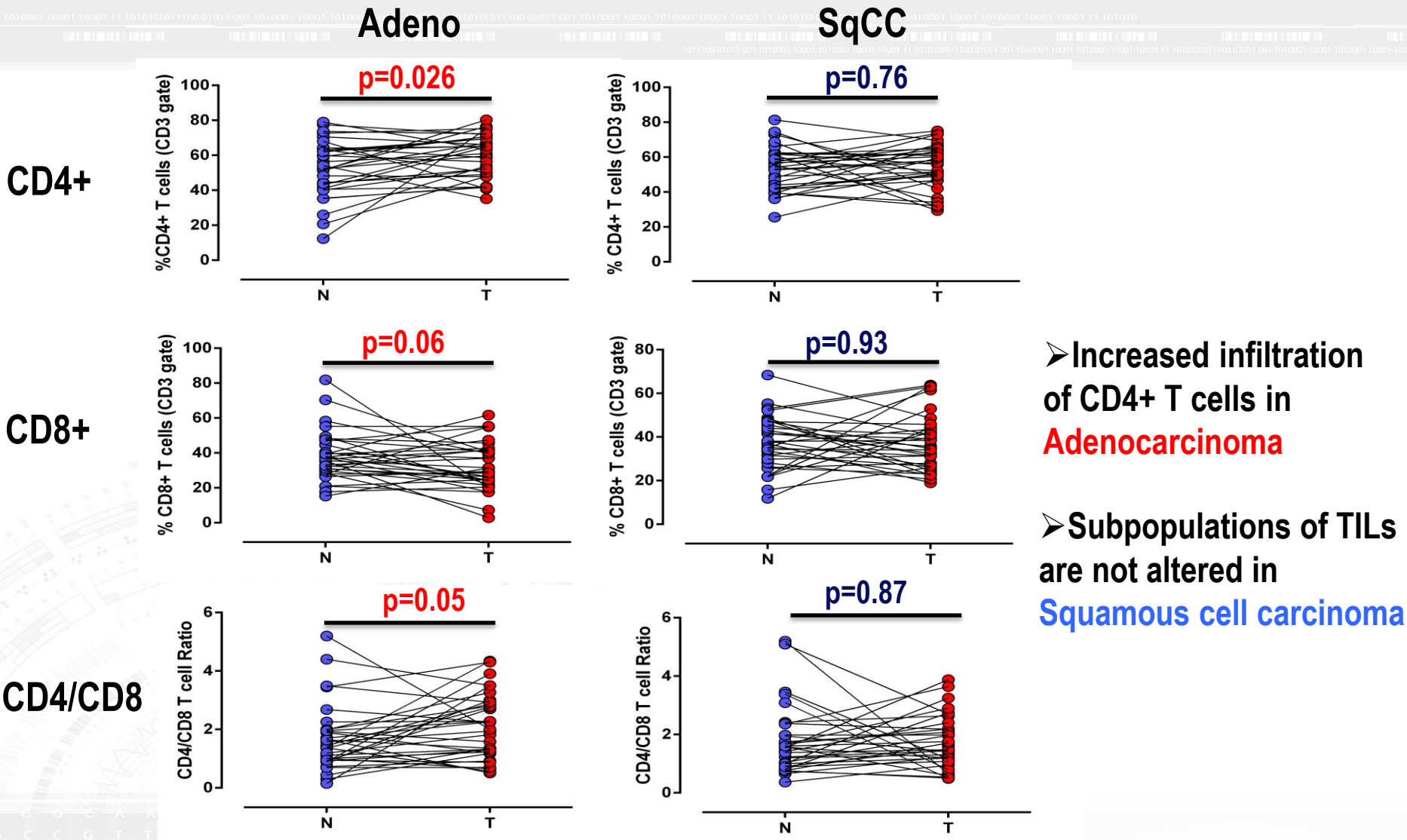
Lymphocyte infiltration correlates with good outcome



But only a small subset has intense lymphocytic infiltration

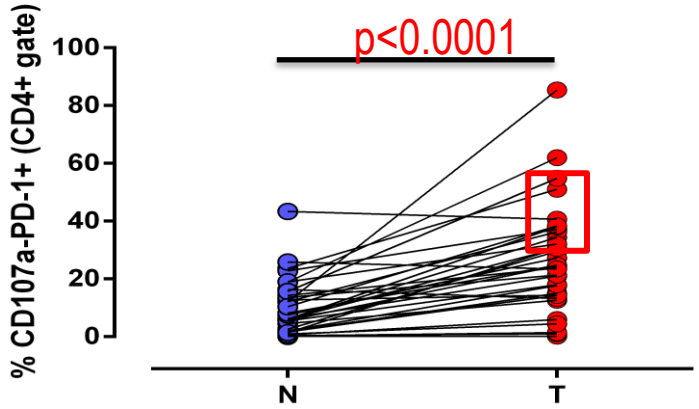
What are the characteristics of these cells??

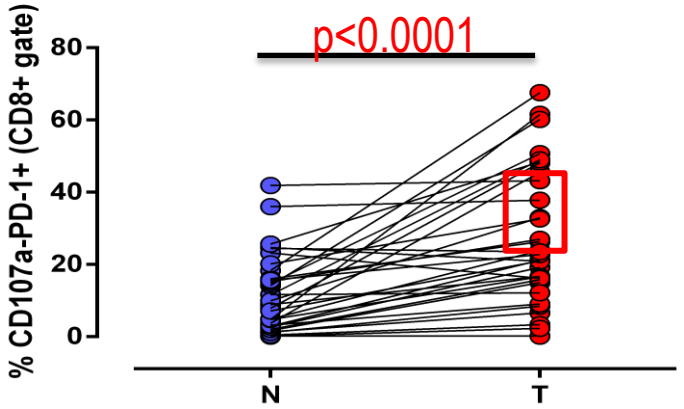
Brambilla, JCO 2016

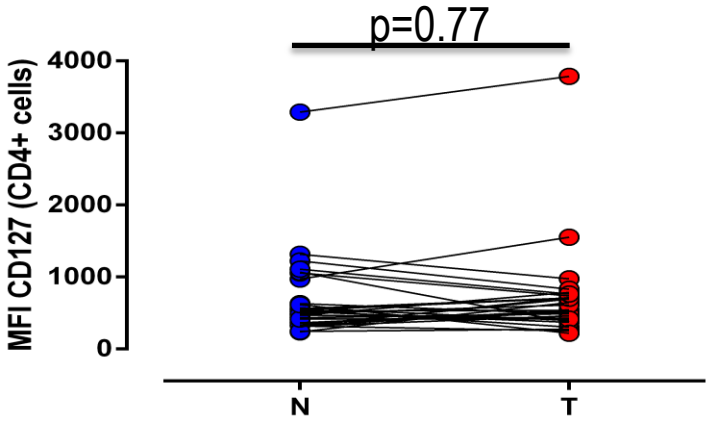


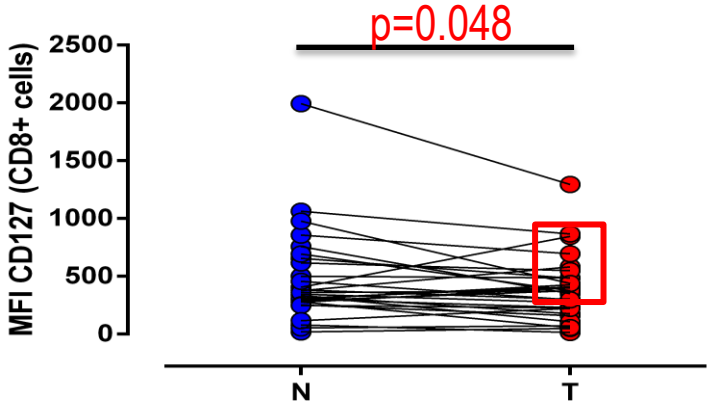
- Increased infiltration of CD4+ T cells in Adenocarcinoma
- Subpopulations of TILs are not altered in Squamous cell carcinoma

TIL subpopulations: Evidence of exhaustion in Adenocarcinoma







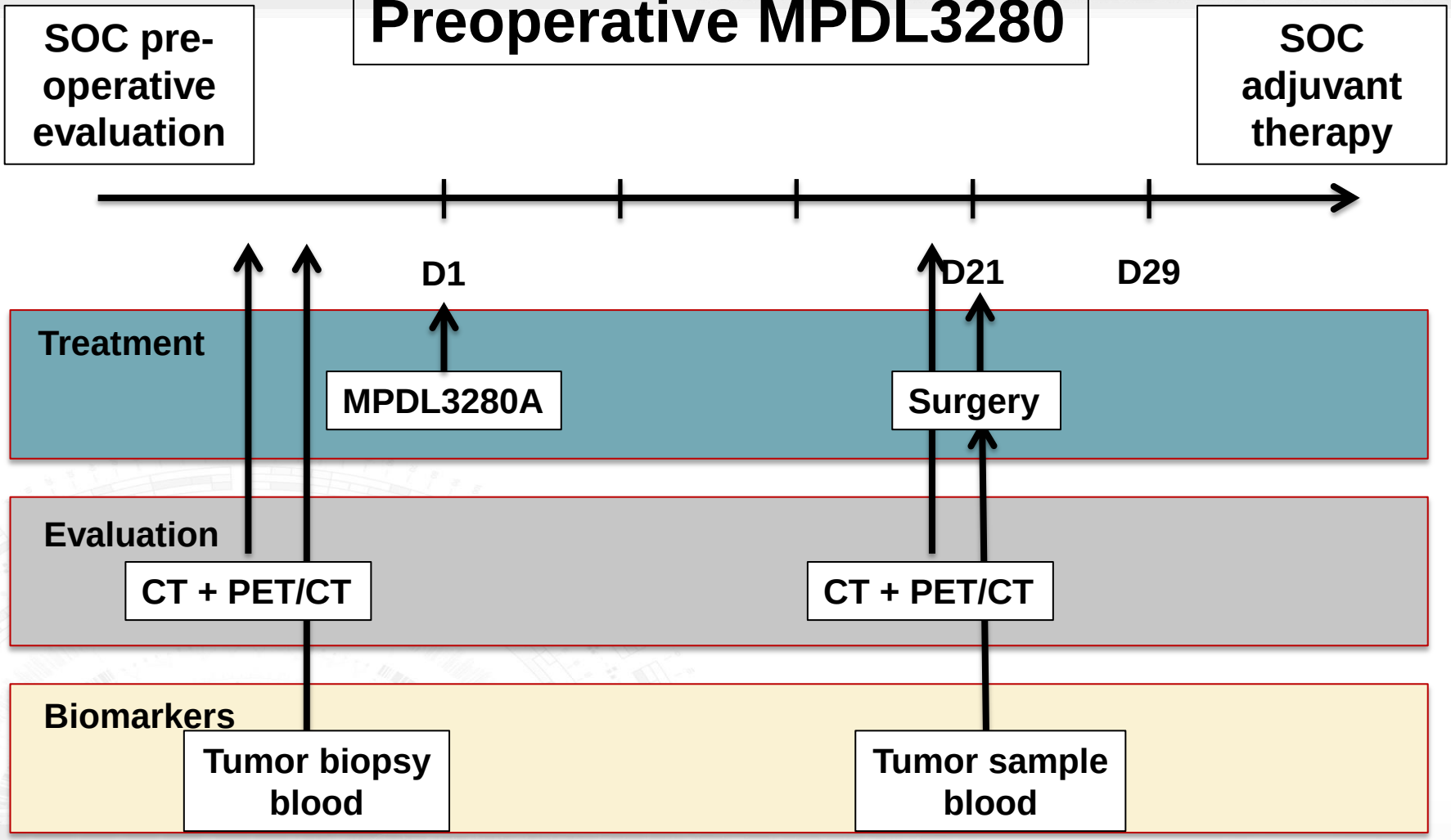


Adenocarcinoma, N=33, paired t-test, two sided

TILS in early stage NSCLC

- T-cell subsets seem different in adenocarcinoma and squamous
- Exhaustion markers present in both
- Implications for adjuvant/neoadjuvant PD-1 pathway intervention is unclear
- Implications for intervention with other immune modulators, informed by these analyses, is an exciting potential of these studies.

Preoperative MPDL3280



If no progression is seen at D20 CT, an additional 2 cycles are given before surgery

CRS-207 with Chemotherapy in Malignant Pleural Mesothelioma (MPM): Results from a Phase 1b Trial

Thierry Jahan[1], Raffit Hassan[2], Evan Alley[3], Hedy Kindler[4], Scott Antonia[5], Chan Whiting[6], Lisa M. Coussens[7], Aimee Luck Murphy[6], Anish Thomas[2], Dirk G. Brockstedt[6]

[1]Department of Medicine, Division of Hematology Oncology, University of California, San Francisco, San Francisco, CA; [2]Thoracic and GI Oncology Branch, National Cancer Institute, Bethesda, MD; [3]Division of Hematology/Oncology, University of Pennsylvania, Philadelphia, PA; [4]Gastrointestinal Oncology and Mesothelioma Programs, Section of Hematology/Oncology, University of Chicago, Chicago, IL; [5]Thoracic Oncology Department, Moffitt Cancer Center, Tampa, FL; [6]Aduro Biotech, Inc., Berkeley, CA; [7]Oregon Health & Science University, Portland, OR

CRS-207

- Live-attenuated *Listeria monocytogenes*– expressing mesothelin
- Induces innate and adaptive immunity
- Tested prime/boost vaccination with GVAX and CRS-207 in pancreatic adenocarcinoma (Le et al, JCO 2015).
  - Randomized 2:1 to two doses of Cy/GVAX followed by four doses of CRS-207 (arm A) or six doses of Cy/GVAX (arm B) every 3 weeks.
  - OS was 6.1 months in arm A versus 3.9 months in arm B (hazard ratio [HR], 0.59; *P* .02).

Key points on cancer vaccines

- Prevention vs. therapy
  - Treatment is more challenging
- Active vs. passive immunity
- Cellular vs. humoral immunity
  - T-cells vs. antibodies
- Antigens
  - TSA, TAA, whole cell vaccines
- Antigen is necessary but not sufficient
  - Adjuvants (chemical or cellular), viral/bacterial vectors
- Tumors suppress immunity
  - Overcoming immunosuppression (e.g. PD1)

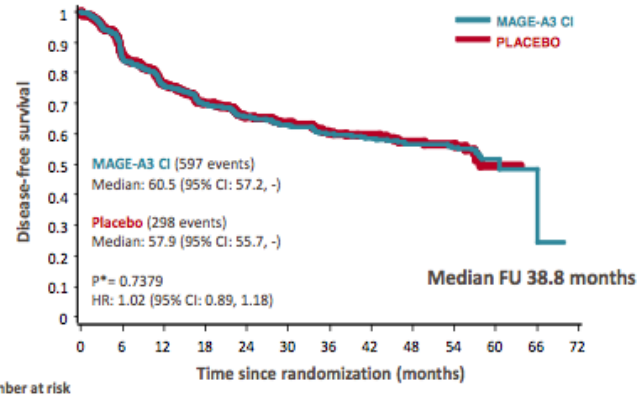
Lung cancer vaccination
> phase 3 trials (ca. 8000 R patients)

Stage	Phase 3	Status
Completely resected IB-IIIA	MAGE-A3 ASCI MAGRIT target 2270	Recruited (reported ESMO 14)
Stage IIIA-B treated by radiochemotherapy	Tecemotide (L-BLP25) START target 1300	Recruited (reported ASCO 13)
III (not amenable to radicatl teratment) and IV Strategies with chemotherapy	Belagenpumatucel-L STOP target 700	Recruited (reported ECCO/ESMO 13)
	rEGF target 1000	Ongoing
	TG4010 TIME target 1000	Ongoing
	Racotumomab (1E10) target 1082	Ongoing

MAGRIT – Key results

MADRID 2014 ESMO congress

MAGRIT: Disease-Free Survival in the Overall Population



Number at risk

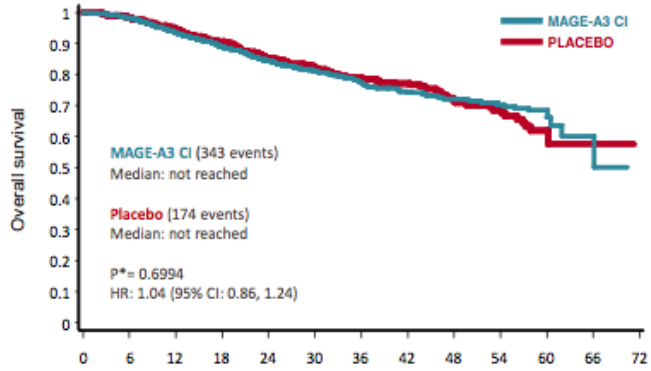
MAGE-A3 CI	1515	1257	1115	1013	887	656	476	339	220	127	19	2
PLACEBO	757	639	562	514	448	328	253	180	114	62	6	0

*Likelihood ratio test from cox regression model stratified by CT and adjusted for baseline variables used as minimization factors.

26-30 September 2014, Madrid, Spain esmo.org

MADRID 2014 ESMO congress

MAGRIT: Overall Survival in the Overall Population



Number at risk

MAGE-A3 CI	1515	1459	1370	1273	1101	827	607	421	275	159	31	6
PLACEBO	757	731	693	654	570	427	330	235	145	78	14	5

*Likelihood ratio test from cox regression model stratified by CT and adjusted for baseline variables used as minimization factors

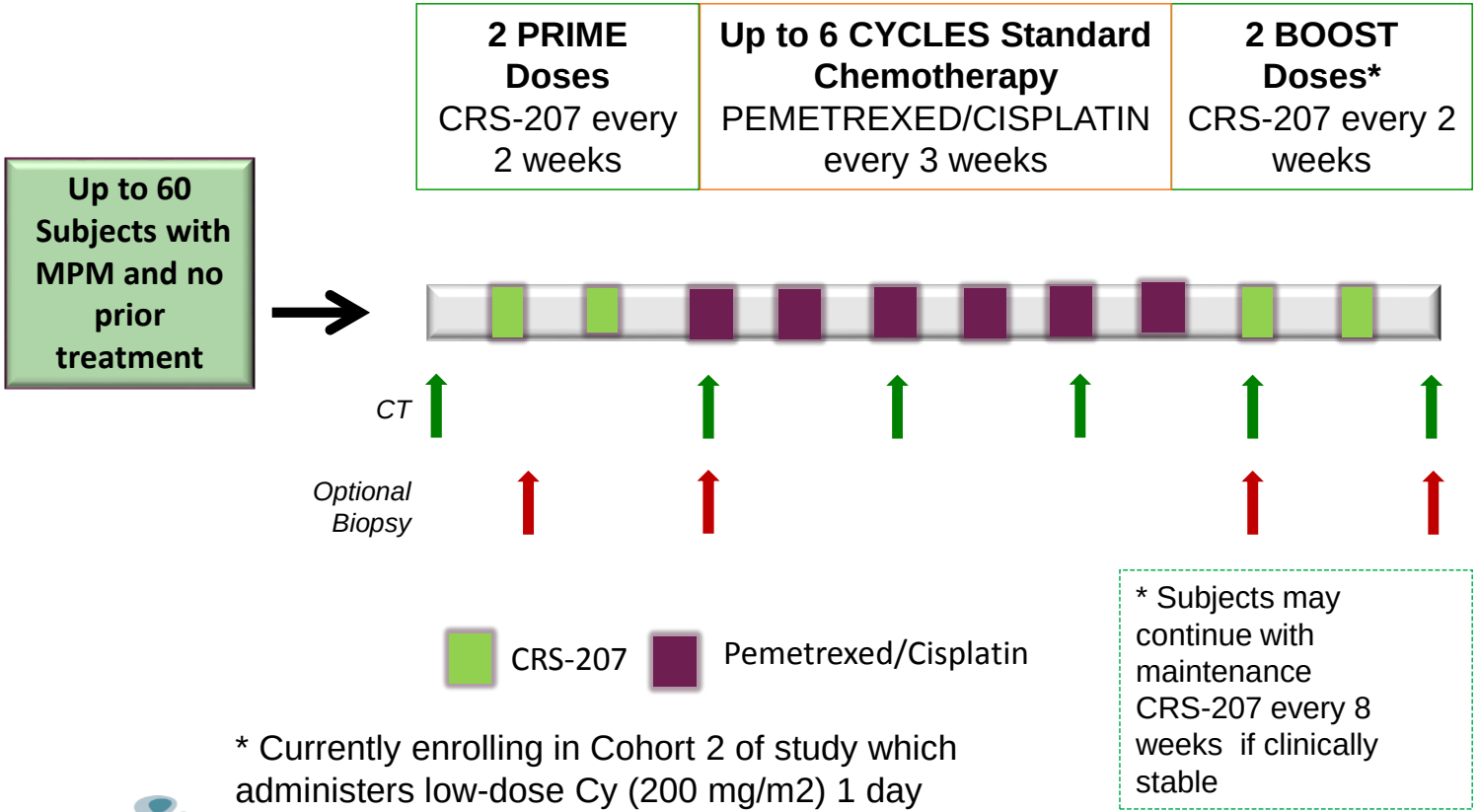
26-30 September 2014, Madrid, Spain esmo.org

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

Vansteenkiste J et al, ESMO 2014

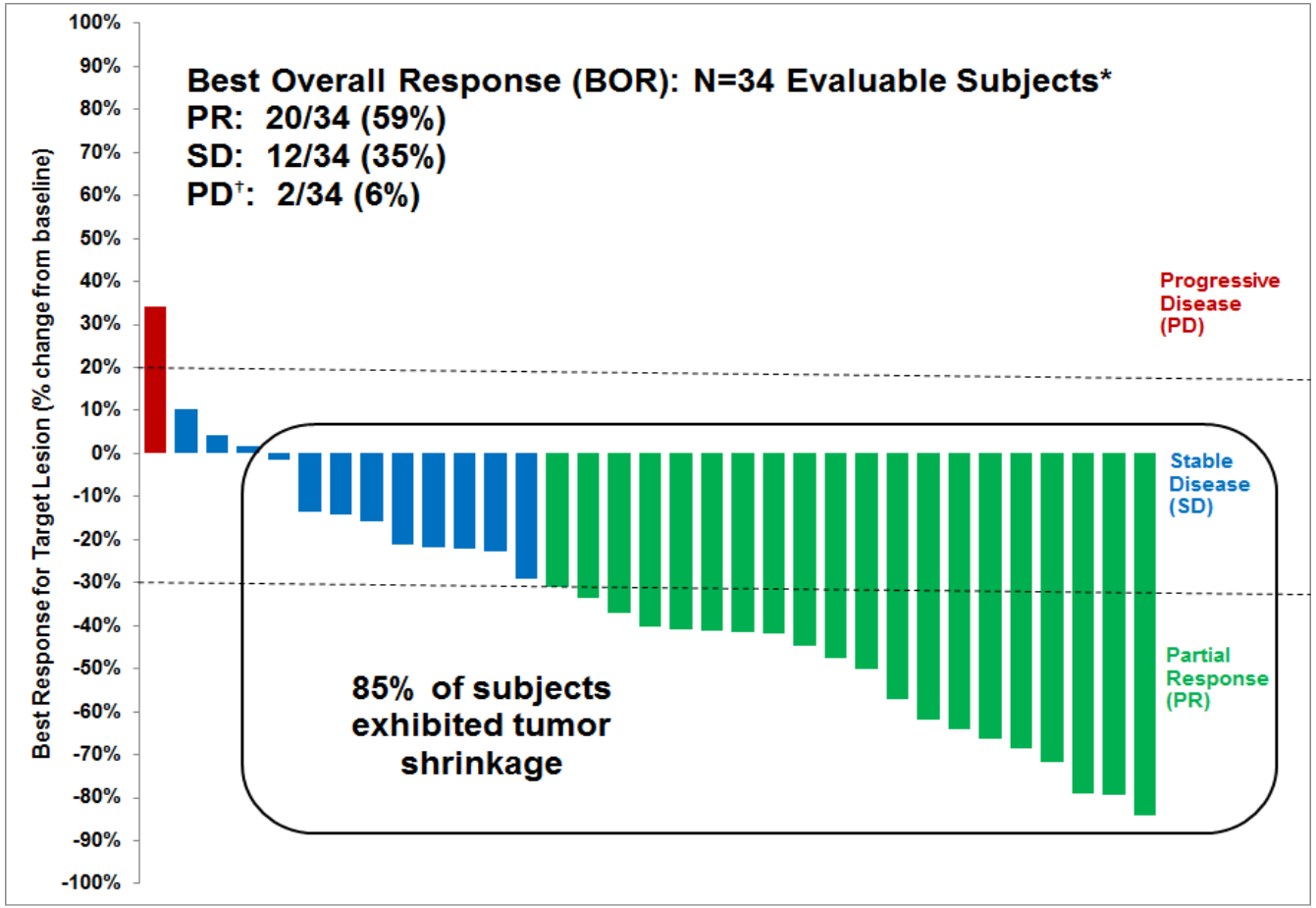
Study Design

Phase 1B study to evaluate the safety and induction of immune response of CRS-207 in combination with pemetrexed and cisplatin in front-line therapy of adults with MPM



* Currently enrolling in Cohort 2 of study which administers low-dose Cy (200 mg/m2) 1 day prior to CRS-207

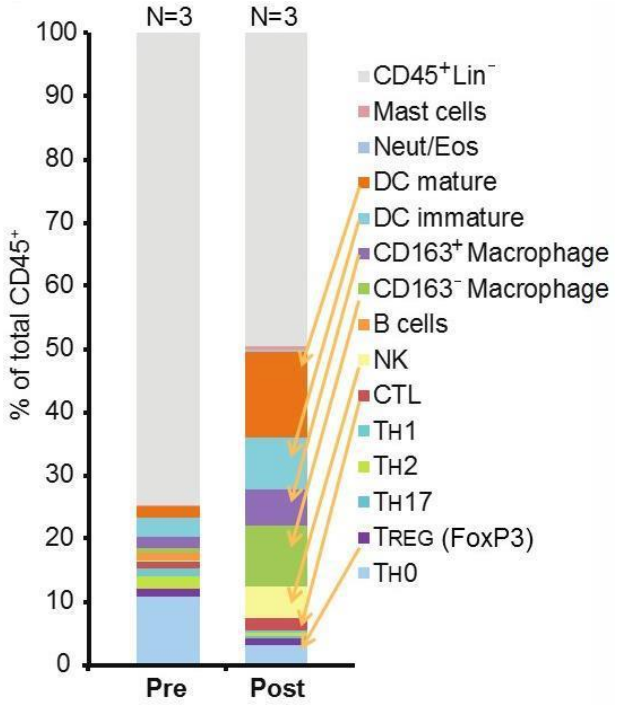
Best Overall Response

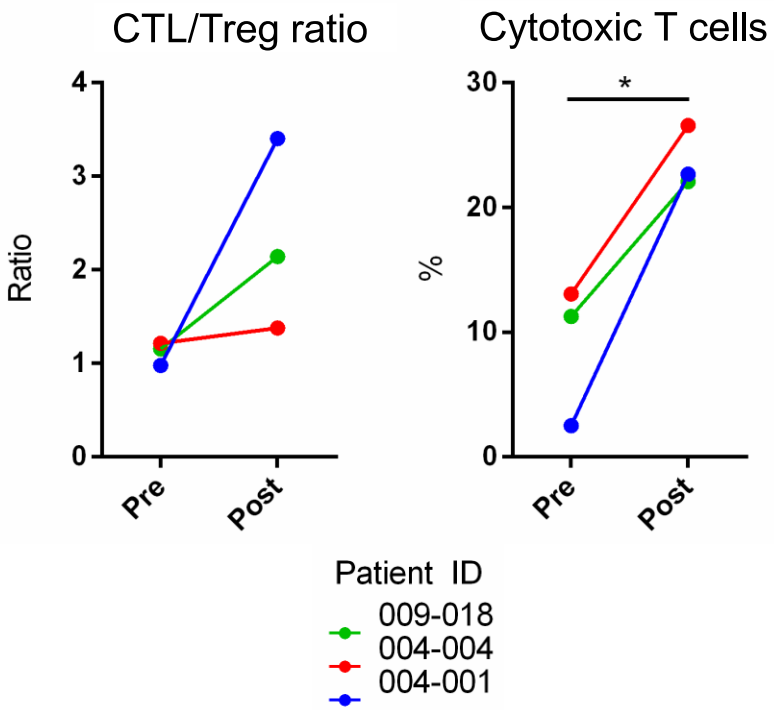


*34/38 subjects evaluable for response; 4 subjects did not have post-baseline tumor measurements

†1 subject had clinical progression and did not have post-baseline tumor measurements

CRS-207 Induced Immune Cell Recruitment and Activation in the Tumor Microenvironment





Conclusions:

- Response rate, waterfall plot, PFS, remarkable
- No data on mesothelin-specific CTL
- BUT – single arm trial, so caution is in order.
  - Untreated, good PS patients
  - Sarcomatoid-predominant histology excluded
- Randomized study planned

16TH WORLD CONFERENCE ON LUNG CANCER

IASLC

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

PHOTOGRAPH PROVIDED BY DENVER INTERNATIONAL AIRPORT

WWW.IASLC.ORG

Abstract Submission Open	January 2015
Registration Open	January 2015
Abstract Submission Deadline	April 24, 2015
Abstract Notifications	June 22, 2015
Early Registration Deadline	June 26, 2015
Late Breaking Abstract Submission Deadline	July 10, 2015
Regular Registration Deadline	July 24, 2015

SEPTEMBER 6–10, 2015

DENVER, COLORADO, USA

CURE FOR LUNG CANCER