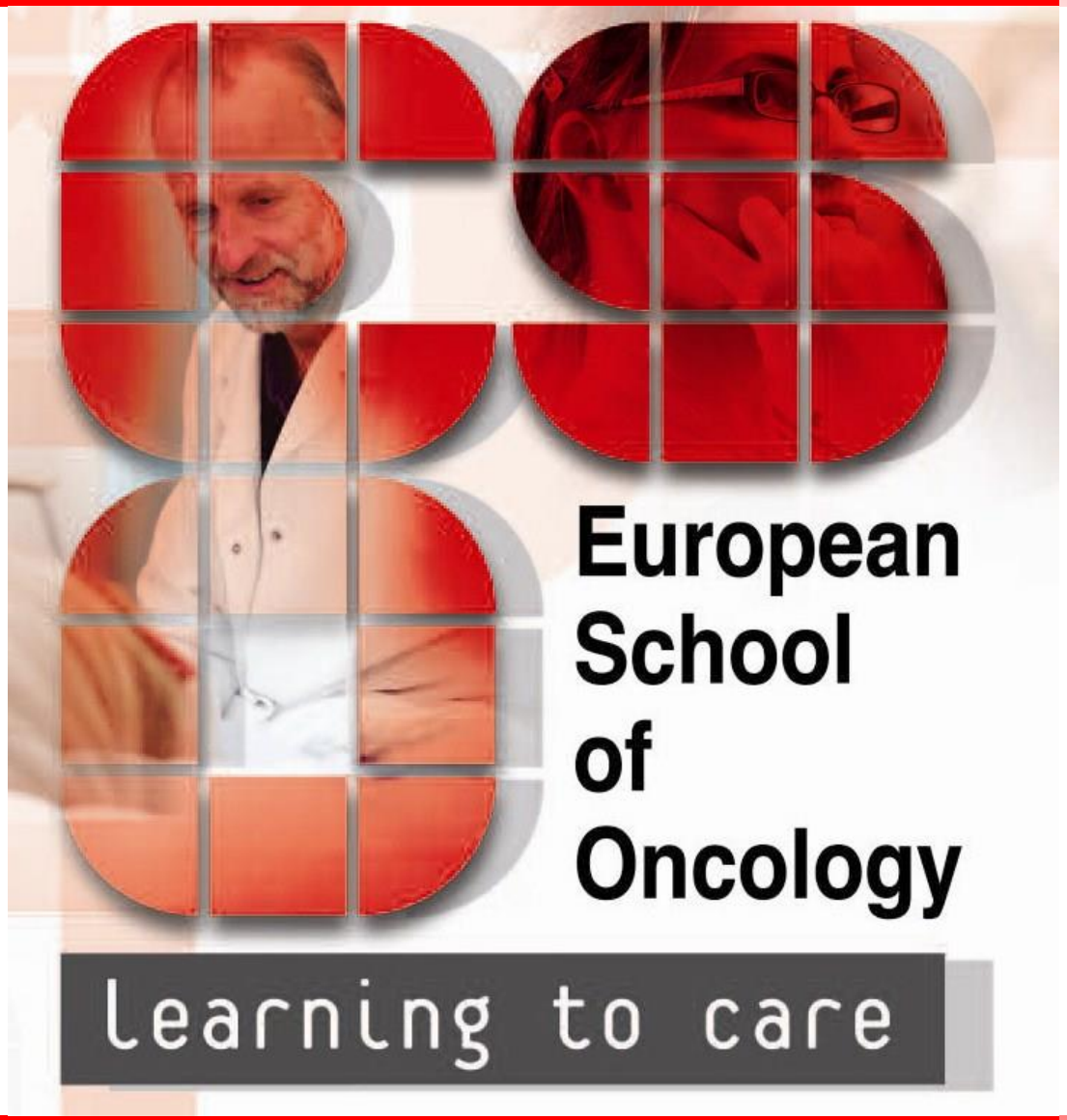
European
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ESO OBSERVATORY

2ND ESO LUNG CANCER OBSERVATORY:

Innovation and care in the next 12 months

16 April 2015
Geneva, Switzerland

Chairs: M.S Aapro, CH - J. Vansteenkiste, BE

The Observatory will be held during the
ELCC 2015 European Lung Cancer Conference

16:30 - 18:00
Palexpo, Room X

For information on other ESO events visit
www.eso.net

European School of Oncology
Learning to care

PANELLISTS

M.S. Aapro
Clinique de Genolier, CH

R. Dziadziuszko
University of Gdansk, PL

D. Grunenwald
Hospital Tenon, University of Paris, FR

F. Johansson
Swedish Lung Cancer Association "Stödet", Stockholm, SE

K. Kerr
Aberdeen Royal Infirmary, Foresterhill, Aberdeen, UK

S. Peters
Centre Hospitalier Universitaire Vaudois, Lausanne, CH

J. Vansteenkiste
University Hospital Gasthuisberg, Leuven, BE

elcc European Lung Cancer Conference

Chairs: M.S Aapro, CH - J. Vansteenkiste, BE

TOPICS

Screening and surgery advances
D. Grunenwald, FR

Radiotherapy in extensive disease SCLC
R. Dziadziuszko, PL

Anti-PD1 and anti-PDL1 strategies in NSCLC, its potential role in NSCLC treatment
S. Peters, CH

Predictive markers in NSCLC
K. Kerr, UK

Long-term lung cancer survivors, patient's needs
F. Johansson, SE

Attendance is granted to all participants registered to the ELCC 2015 European Lung Cancer Conference.

The conclusion of the Observatory will be made available on the ESO website www.eso.net

Detailed information available at: www.eso.net

2014-2015 Predictions

- Individualized therapy for NSCLC beyond EGFR and ALK, including immunotherapy approaches, will be a reality within the next year
- Strong anti-tobacco programmes are needed, particularly in Central and Eastern Europe
- Elderly patients with lung cancer should be included in further specific studies
- Surgery modulated by tumour biology should be a reality
- The studies to evaluate the immune modulating capacity of radiation therapy should have started
- Next generation sequencing should have provided the first clinically relevant results
- Immunological treatment of lung cancer should have its first success
- By end of 2015 all European patients should have access to all treatments recognized in Europe

2nd ESO Lung Cancer Observatory: Innovation and care in the next 12 months

Thursday 16th April 2015, 16.30 – 18.00

Panellists:

Dominique Grunenwald, FR
Rafal Dziadziuszko, PL
Solange Peters, CH
Keith Kerr, UK
Fredrik Johansson, SE

Chair: M.S. Aapro, CH – J. Vansteenkiste, BE

2nd ESO Lung Cancer Observatory: Innovation and care in the next 12 months

Dominique Grunenwald

Hospital Tenon, University of Paris

Paris, France

View of a Surgical Oncologist

Screening and surgery advances

screening and staging

- due to the low dose computed tomography (LDCT) low rate of specificity complementary biomarkers are required to properly define patients at risk and to reduce the number of further radiological examinations
- miRNA signature could reduce the false-positive rate of LDCT, thus improving the efficacy of lung cancer screening
- programs must integrate smoking cessation interventions to maximize the clinical efficacy and cost-effectiveness of screening
- preoperative invasive mediastinal procedures to discover unexpected pN2 disease in patients with clinical stage IA NSCLC is not justified, considering their good survival
- endosonography (EBUS/EUS) with fine needle aspiration is the first choice for tissue confirmation needed in CT-enlarged or PET-positive mediastinal lymph nodes

Screening and surgery advances

Early stage NSCLC

- whether or not sub lobar resection constitutes adequate treatment for small-sized lung cancer or for the radiographic "early" lung cancer such as a GGO-dominant lesion is still being prospectively investigated
- lobectomy should still be considered the standard operation of choice for solid lesions (type 4)
- VATS lobectomy may offer significantly more favourable long-term outcomes than SBRT in potentially operable patients with biopsy-proven clinical stage I NSCLC
- SBRT could be offered to all high-risk surgical patients, and for patients not willing to take the risk of lobectomy and therefore refusing surgery

Screening and surgery advances

Multimodal therapy

- in patients with clinical N2 disease who are potential candidates for a lobectomy, both definitive and induction concurrent chemotherapy/RT are appropriate treatments
- results from 47 trial comparisons and 11,107 patients demonstrate the clear benefit of adjuvant chemotherapy for completely resected stage II-III patients, irrespective of whether chemotherapy was given in addition to surgery or surgery plus radiotherapy (NSCLC Collaborative group meta-analysis)
- intravenous or oral administration of vinorelbine in combination with cisplatin after surgery for NSCLC appear equally effective in terms of overall and disease-free survival
- PORT in N2 completely resected patients is still being prospectively investigated (Lung-ART trial)

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Rafal Dziadziuszko

Medical University of Gdansk

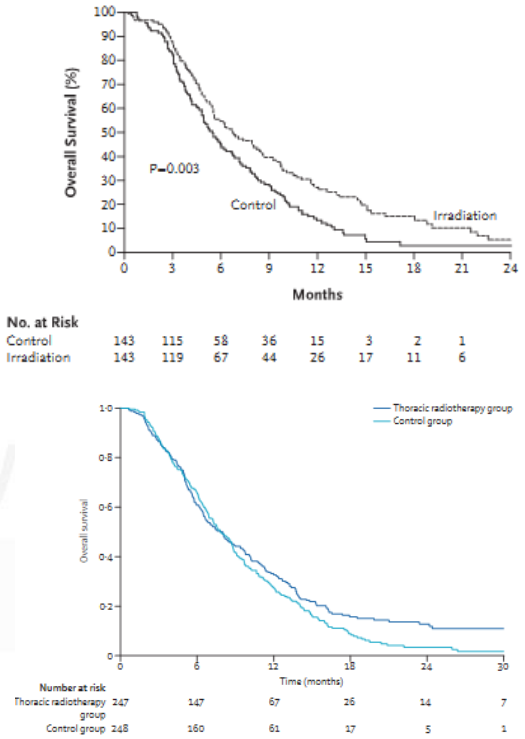
Gdansk, Poland

View of a Radiation Oncologist

Radiotherapy in extensive disease SCLC

Recent advances in extensive disease SCLC came from local therapies:

1. **Prophylactic cranial irradiation**
   (Slotman et al. NEJM 2007)



2. **Chest RT**
   (Slotman et al. Lancet 2015)

Radiotherapy in extensive disease SCLC

Controversies and future directions:

1. Relatively small benefits at the cost of additional procedures with their toxicities – better identification of patients who benefit?

2. More effective systemic therapies sorely needed, despite many failures in this field. Immunotherapies and cyclin kinase inhibitors?

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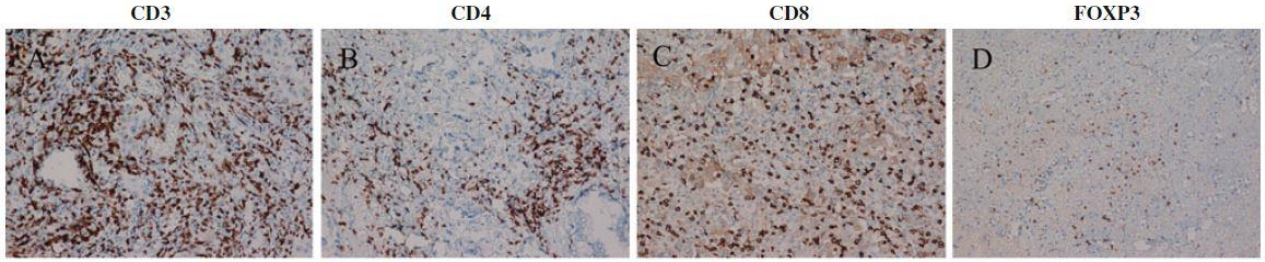
Solange Peters

Centre Hospitalier Universitaire Vaudois

Lausanne, Switzerland

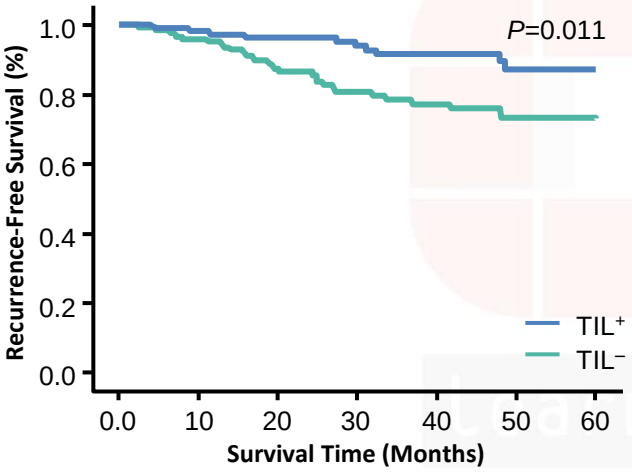
View of a Medical Oncologist

Anti-PD1 and PDL1 strategies in NSCLC: Rational

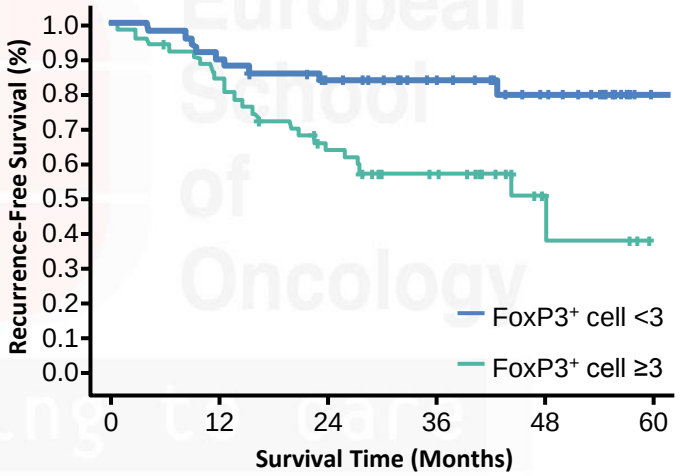


Liu H et al. *Cancer Immunol Immunother* 2012

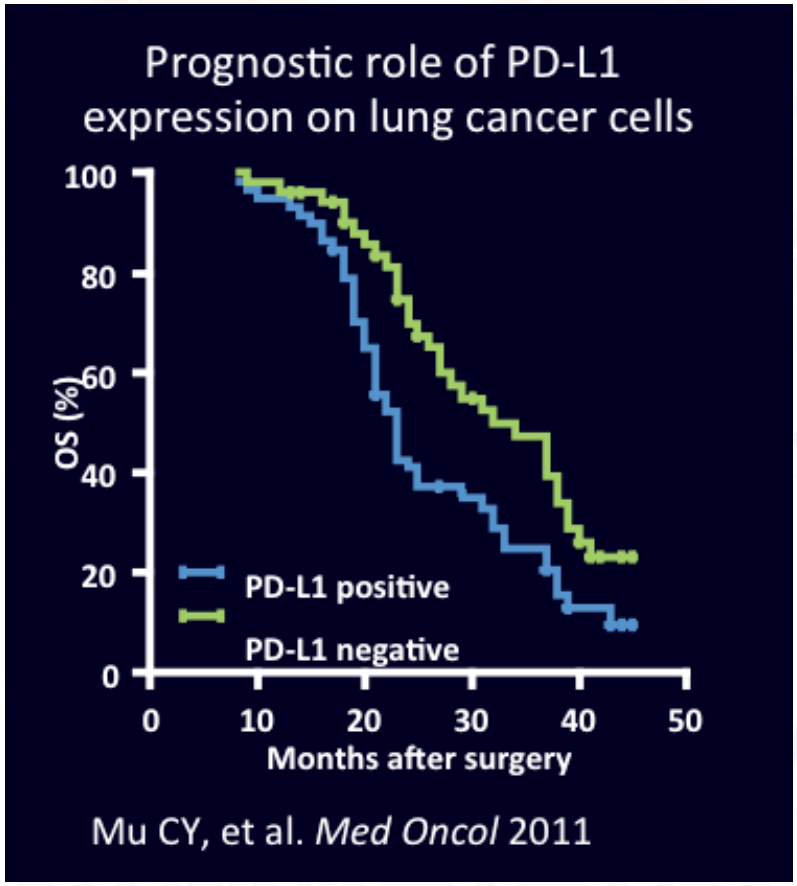
Presence of TILs associated with increased recurrence-free survival[1]



Higher NSCLC-Infiltrating Tregs associated with worse recurrence-free survival[2]



Anti-PD1 and PDL1 strategies in NSCLC: Rational

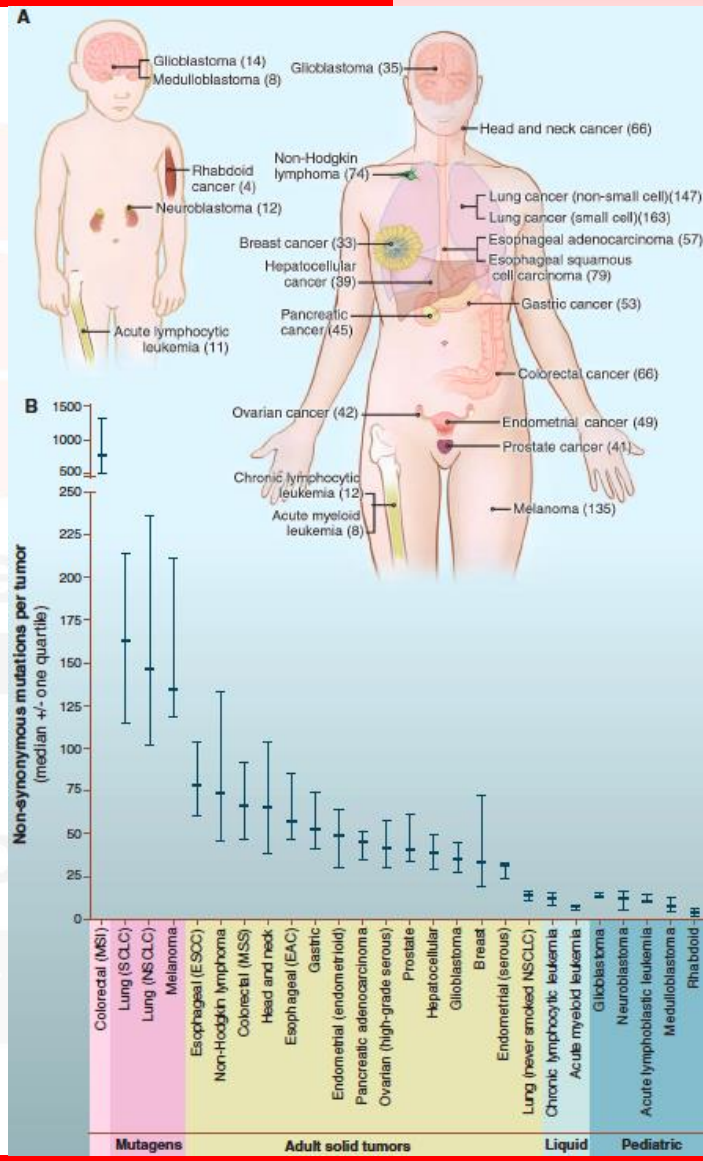


1. Shimizu K, et al., *J Thorac Oncol.* 2010
2. Horne ZD, et al., *J Surg Res.* 2011

Anti-PD1 and PDL1 strategies in NSCLC: Mutagens?

Melanomas and lung tumors display many more mutations than average, with~200 non-synonymous mutations per tumor.

These larger numbers reflect the involvement of potent mutagens. Accordingly, lung cancers from smokers have 10 times as many somatic mutations as those from non-smokers.



Vogelstein, Science 2013

Anti-PD1 and PDL1 strategies in NSCLC: Drugs in competition

PD-1	Nivolumab-BMS-936558	Fully human IgG4 mAb	Bristol-Myers Squibb	Phase III multiple tumors
	Pidilizumab CT-011	Humanized IgG1 mAb	CureTech	Phase II multiple tumors
	Pembrolizumab MK-3475	Humanized IgG4 mAb	Merck	Phase III
	AMP-224	Recombinant PD-L2-Fc fusion protein	GlaxoSmithKline	Phase I
PD-L1	BMS-936559	Fully human IgG4 mAb	Bristol-Myers Squibb	Phase I
	MedI-4736	Engineered human IgG1 mAb	MedImmune	Phase II (III)
	MPDL-3280A	Engineered human IgG1 mAb	Genentech	Phase III
	MSB0010718C	Engineered human IgG1 mAb	EMD Serono	Phase II

Anti-PD1 and PDL1 strategies in NSCLC: PFS/OS in phase 1

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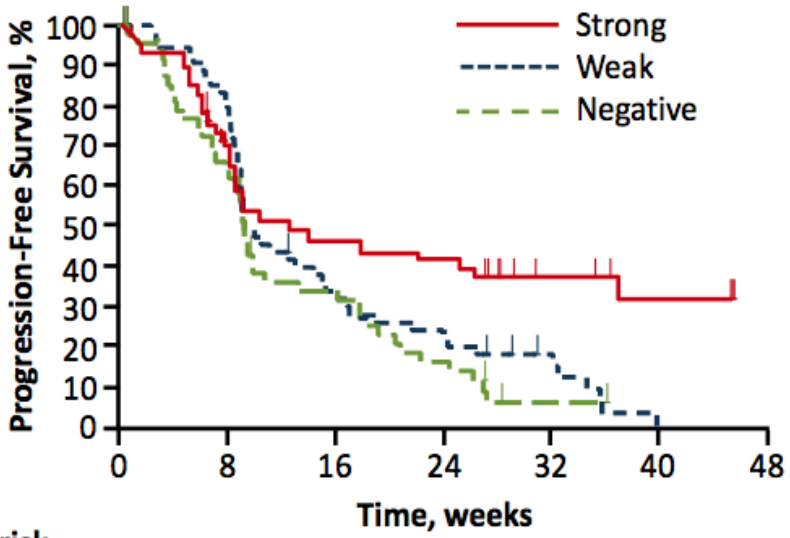
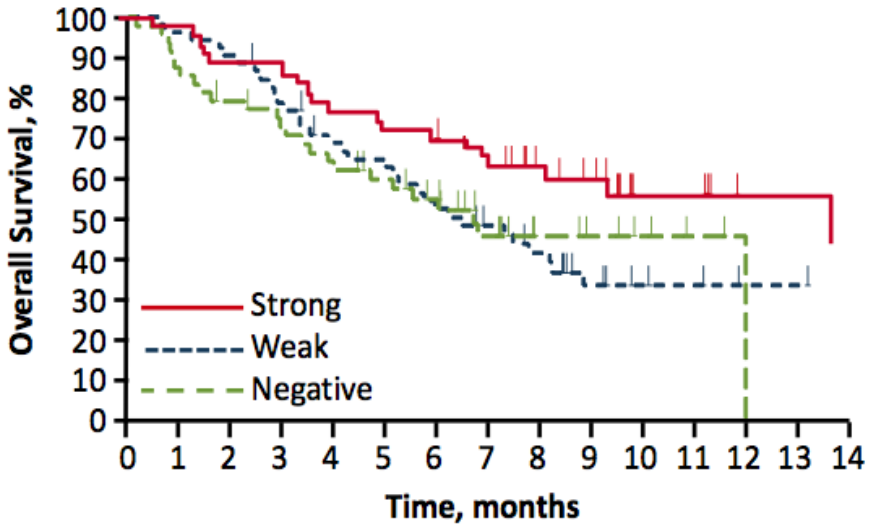
PFS (RECIST v1.1, Central Review)



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

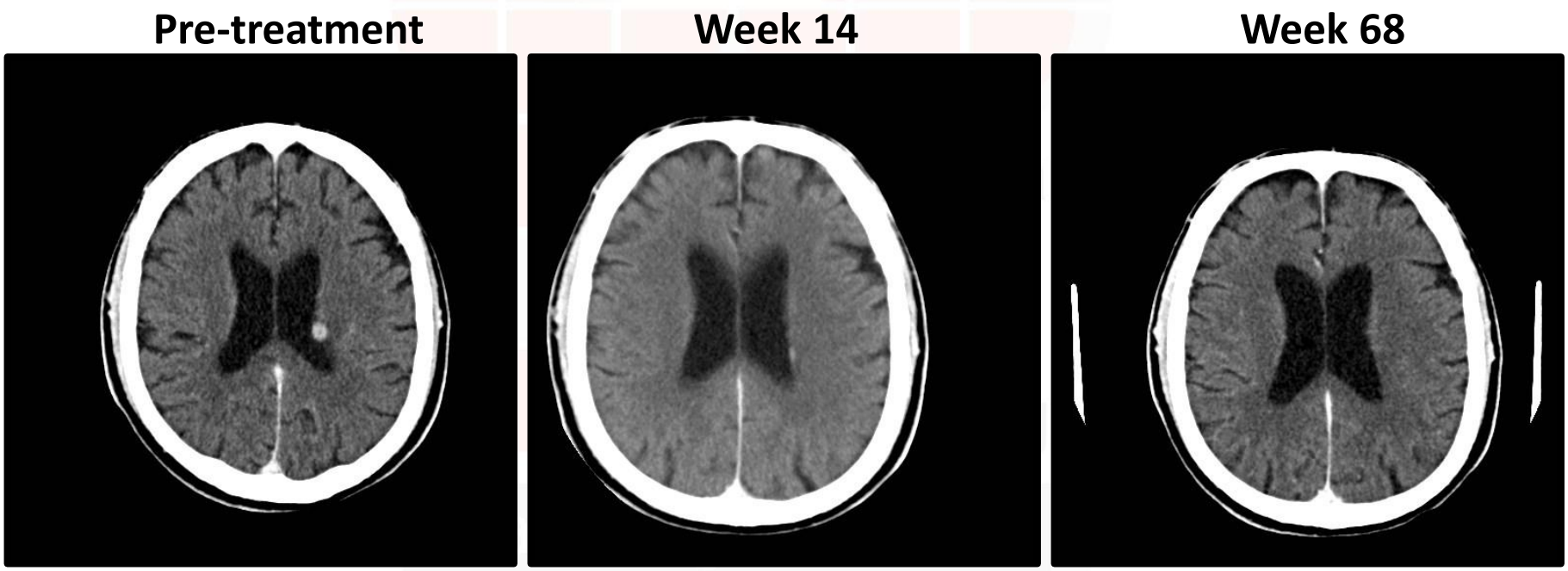
OS



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

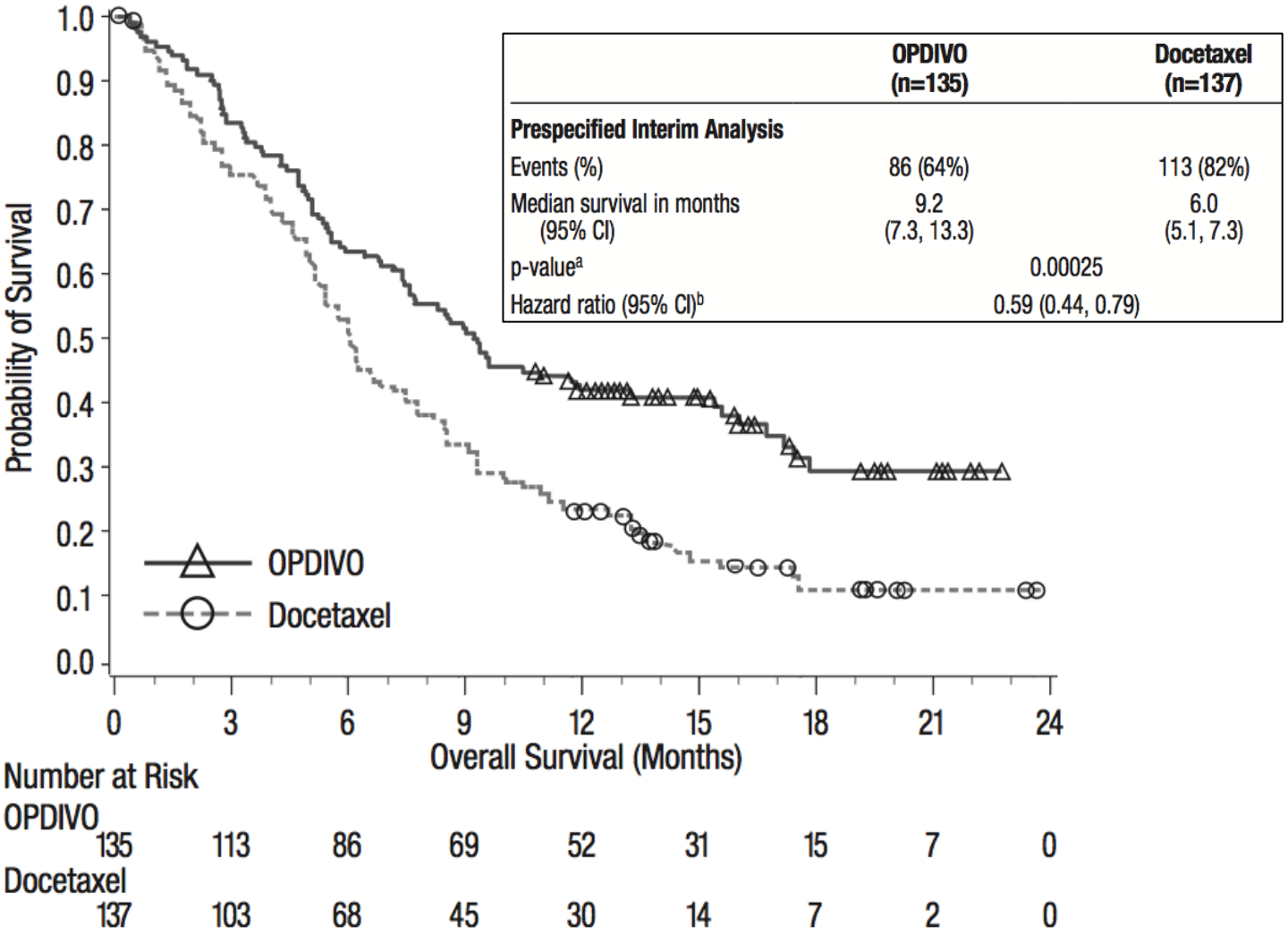
- PFS was longer in patients with PD-L1 strong-positive versus PD-L1 weak-positive/ negative tumors (HR, 0.52; 95% CI, 0.33-0.80)
- OS was longer in patients with PD-L1 strong-positive versus PD-L1 weak-positive/ negative tumors (HR, 0.59; 95% CI, 0.35-0.99)

Anti-PD1 and PDL1 strategies in NSCLC: Brain activity



No prior CNS-directed radiotherapy

Nivolumab phase III data, before ASCO. No biomarker selection!



	OPDIVO (n=135)		Docetaxel (n=137)
Prespecified Interim Analysis			
Events (%)	86 (64%)		113 (82%)
Median survival in months (95% CI)	9.2 (7.3, 13.3)		6.0 (5.1, 7.3)
p-value[a]		0.00025	
Hazard ratio (95% CI)[b]		0.59 (0.44, 0.79)	

1st ESO Lung Cancer Observatory: Innovation and care in the next 12 months

Keith Kerr

Aberdeen University Medical School

Aberdeen Royal Infirmary,

Foresterhill, Aberdeen,UK

View of a Pathologist

Predictive markers in NSCLC (beyond EGFR and ALK)

Emerging molecular biomarkers as targets

Adenocarcinoma

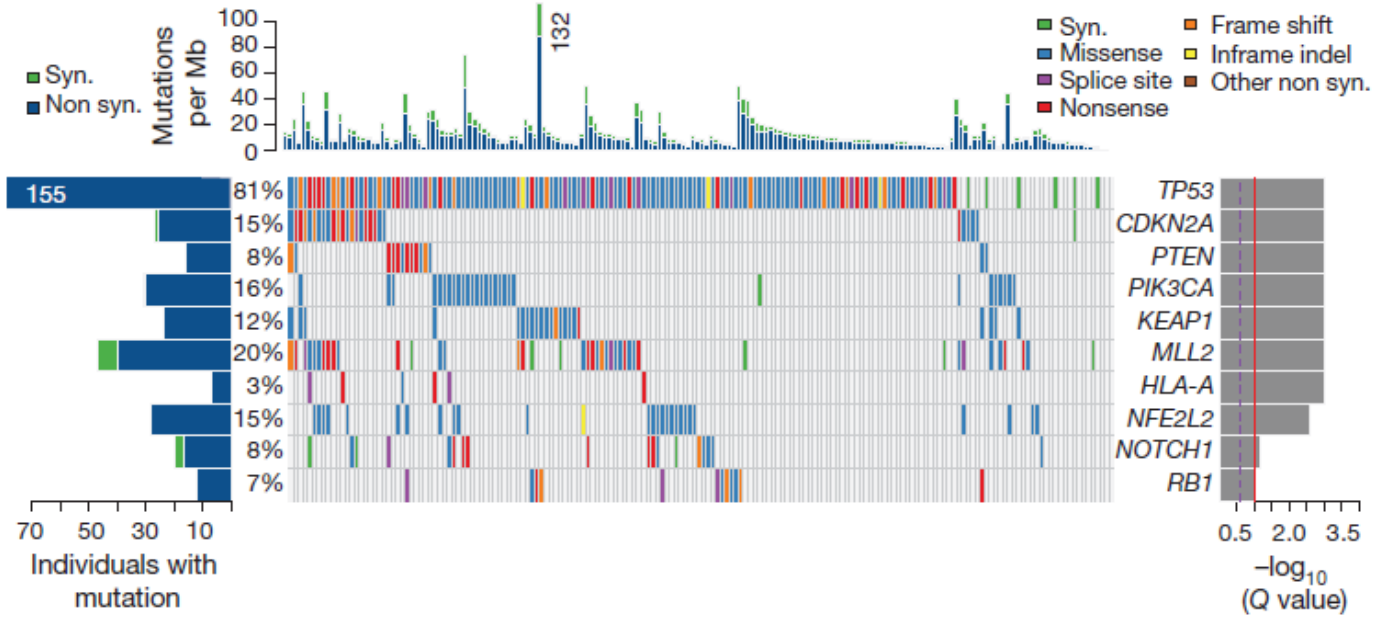
- ROS1 fusion
- KRAS mutation
- RET fusion
- HER2 mutation
- NTRK fusion

Squamous Cell Carcinoma

- FGFR1 amplification
- CDNK2

Next Generation Sequencing as a multiplex technology platform
Will MET make it?
PI3K, AKT, PTEN: are they good targets and biomarkers?
The liquid biopsy?

Mutated Genes in Squamous Cell Carcinoma



Hammerman et al (TGCA) Nature 2012; 489, 519-525

Some potential drug targets……

……but NOT addictive oncogenes

Immunomodulatory therapy

- Is a predictive biomarker needed?
- If so, is PD-L1 expression that biomarker?
- If so, how should it be measured?
  - Tumour cells or tumour-infiltrating immune cells?
  - How to define a ‘positive’ test?
  - Specific IHC biomarker for each drug?
- Prospects for ‘test equivalence’?
- Other biomarkers?
- Other co-factors?

2nd ESO Lung Cancer Observatory: Innovation and care in the next 12 months

Fredrik Johansson

The Swedish Lung Cancer Association www.stodet.se

Stockholm, Sweden

View of an Advocate Representative

Lung Cancer Europe

Long-term lung cancer survivors – patient's needs

Most important thing: Hope

After being diagnosed, it is important to continue to live - for Yourself, your Family, your Friends, and to proceed with your Life Goals/Bucketlist.

Find Hope, Inspiration and Support in your family, friends and from patient organizations such as Stödet.

Long-term lung cancer survivors – patient's needs

The IT-boom of Pharmaceutics

Cytotoxics are good, but Immunotherapy and Targeted Inhibitors are the future - and needs to be adopted faster - not delayed in local administration.

Increase of cost should consider decrease of patient hospital needs and increase of tax revenue - patients expect to be offered the latest, and the best.

2015-2016 Predictions