The European Thoracic Oncology Platform Lungscape project: A way to bridge NSCLC molecular characteristics and clinical data

S. Peters, U. Dafni, L. Bubendorf, P. Meldgaard, K.J. O'Byrne, A. Wrona, W. Weder, M. Canela, S. Malatesta, J.F. Vansteenkiste, A-M.C. Dingemans, M.C. Nicolson, S. Savic, P. Baas, R. Peck, S. Lu, E.F. Smit, E. Jantus-Lewintre, R. Rosell and R. Stahel, on behalf of ETOP

Disclosures

S. Peters / ETOP declare no conflict of interest

Aims

- Lungscape addresses the challenges of studying the molecular epidemiology of lung cancer
  - By coordinating and harmonizing the procedures of lung cancer specialists working in translational research across Europe
  - By performing analysis of larger series of cases.
- This will:
  - Expedite knowledge of the prevalence and context of current and emerging molecular biomarkers
  - Facilitate more rapid application of biomarker usage in the clinic
  - Provide a platform for biomarker-driven trials of novel therapeutics.

Overall Objectives

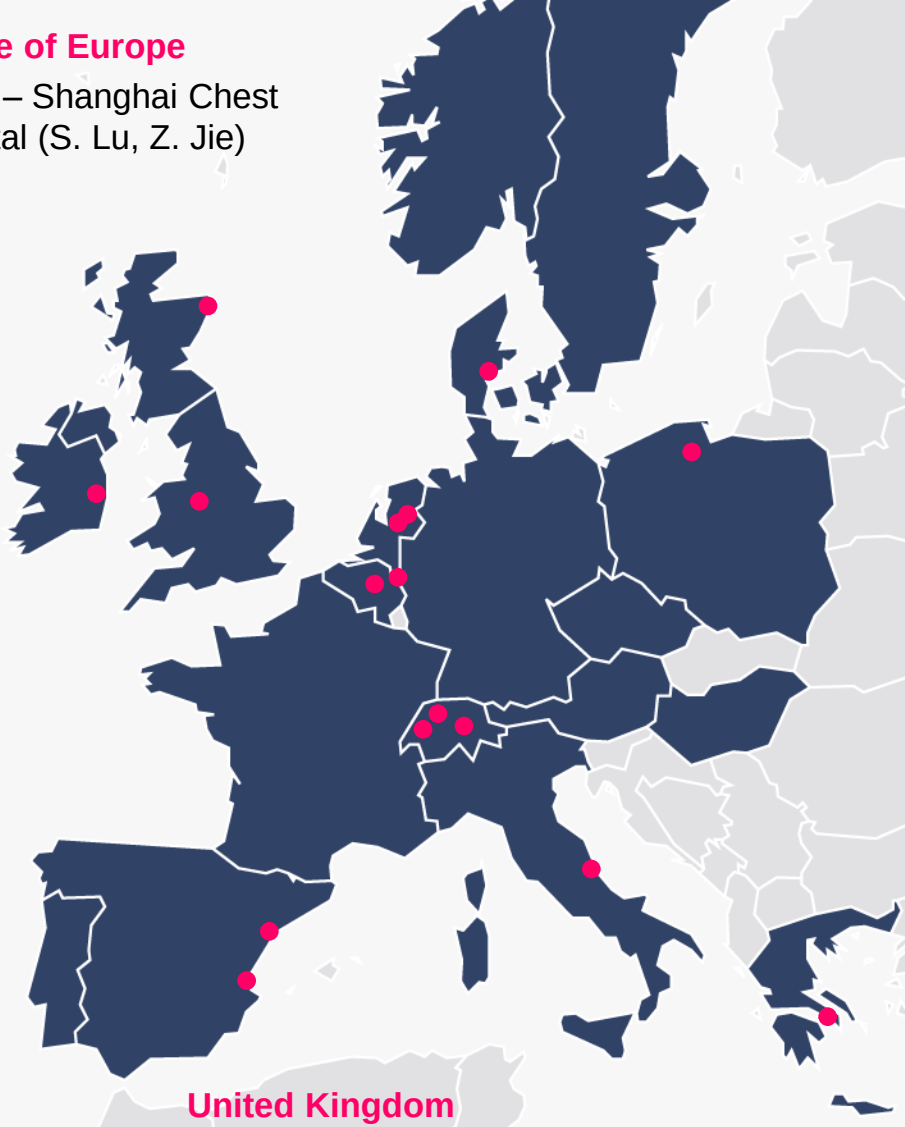
- Establish a decentralized NSCLC biobank (iBiobank)
- Generate new biological hypotheses
- Establish a clinical trial platform (ETOPdata)
- Develop practical diagnosis algorithms

Methodology: Case inclusion criteria

- Histological diagnosis of NSCLC
- Radically resected non-pretreated stage IA-IIIB NSCLC
- Diagnosis after January 2003 (10% before 2003)
- Adequate quantity and quality of formalin-fixed paraffin embedded tissue
- Documented ethical approval for tissue sample and associated clinical data
- 3 years of follow-up
- Mandatory clinical data available

Methodology: Sites selection

- Survey to ETOP members
  - 20 institutions replied
- Additional requirements for site selection:
  - Patient consent for biobanking according to local regulations
  - TMA building capability
  - External Quality Assessment acceptance (ALK lungscape abstract 193P)
  - (Matched fresh frozen tissue available)
- Number of selected sites:
  - 14 European sites and one Chinese site



Outside of Europe

- China – Shanghai Chest Hospital (S. Lu, Z. Jie)

Belgium

- Leuven:
  J. Vansteenkiste,
  E. Verbeken, C. Dooms

Denmark

- Aarhus:
  P. Meldgaard, H. Hager

Greece

- Frontier Science Hellas:
  U. Dafni

Ireland

- Dublin:
  K. O'Byrne, S. Finn,
  S. Gray

Italy

- Chieti:
  A. Marchetti, S. Malatesta

Poland

- Gdansk:
  R. Dziadziuszko,
  W. Biernat, A. Sejda,
  A. Wrona

United Kingdom

- Aberdeen:
  K.M. Kerr, N. Price,
  M. Nicolson
- Manchester:
  F. Blackhall, D. Nonaka,
  R. Peck

Spain

- Barcelona:
  E. Felip, J. Hernandez-Losa, M. T. Salcedo, M. Canela
- Badalona:
  R. Rosell, M. Taron
- Valencia:
  C. Camps, M. Martorell,
  E. Jantus-Lewintre

Switzerland

- ETOP Coordinating Center:
  A. Hiltbrunner, S. Peters,
  R. Kammler, R. King,
  R. Stahel
- Basel:
  L. Bubendorf, S. Savic
- Zurich:
  W. Weder, A. Soltermann

The Netherlands

- Amsterdam VU (E. Thunnissen, E. Smit
- Amsterdam NKI:
  P. Baas, J. de Jong
- Maastricht:
  A.-M. Dingemans,
  E-J.M. Speel

Lungscape project responsibilities

Project design and guidance:

- Lungscape steering committee

Project execution:

- ETOP office
- Frontier Science Foundation-Hellas

Lungscape financial support:

- Consortium approach
- Contributions for this specific project:

  Roche, Pfizer

Methodology: iBiobank mandatory parameters

Patient Demographics and Characteristics	DATE OF BIRTH GENDER ETHNICITY SMOKING HISTORY
NSCLC pathology	DATE OF SURGERY HISTOLOGY (ADENOCARCINOMA, SQUAMOUS, LARGE CELL, UNDIFFERENTIATED, MIXED) LOCALISATION OF PRIMARY TUMOUR PATHOLOGY (7th TNM + report attached)
Treatment Information	ADJUVANT CHEMOTHERAPY ADJUVANT RADIOTHERAPY
Patient status at last FU	DATE OF LAST FOLLOW UP PATIENT STATUS AT LAST FOLLOW UP DATE OF DEATH (IF APPLICABLE)
1st line treatment at recurrence	ADMINISTRATION OF ANTITUMOUR TREATMENT AT RECURRENCE
2nd line treatment at recurrence	ADMINISTRATION OF ANTITUMOUR TREATMENT AT RECURRENCE
Subsequent line of treatment	ADMINISTRATION OF ANTITUMOUR TREATMENT AT RECURRENCE

Data Acquisition Workflow: Focus on Upstream Quality Control

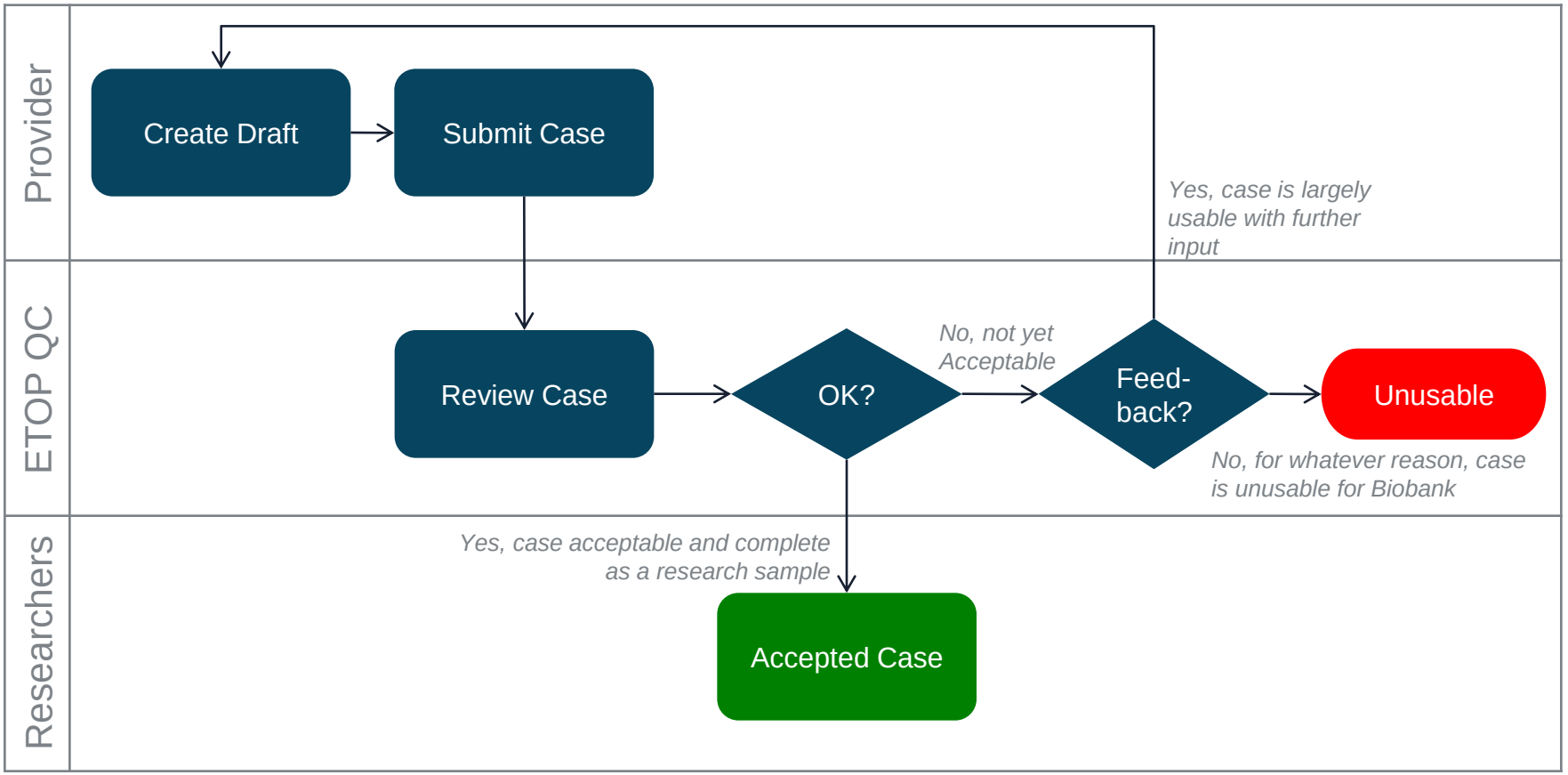


Table example

ETOPdata

Home | Cases | Analysis | Projects | Sites | Admin | Help | Dr. Solange Peters | ETOP Secretariat
Role: Administrator

BEL015 University Hospital Leuven - Case ID: 3701

Identification | Patient | Tissue Tracking | Surgery | **Pathology at Surgery** | Molecular Pathology | Adjuvant Chemotherapy | Adjuvant Radiotherapy | Patient at Last Follow-up

Printer-friendly Form

Histology

Date of Surgery:	03.10.2006
Histology:	Squamous cell
Histology Notes:	

Stage at Diagnosis: Tumour

Tumor Size, Largest Diameter (cm):	4	
Involves Main Bronchus:	No	
Invasion of neighboring other structures:	(•) No	( ) Yes
Associated with atelectasis or obstructive pneumonitis:	No	
Separate tumor nodule(s):	No	
Pathology, Subsequent TNM Staging (7th TNM classification): T:	T2a	

Stage at Diagnosis: Nodes

Lymph node involvement:	(•) No	( ) Yes
Number of lymph nodes examined:	12	
Pathology, Subsequent TNM Staging (7th TNM classification): N:	0	

Stage at Diagnosis: Metastasis

Set Status to: Feedback | Set Status to: Accepted | Set Status to: Ineligible

Methodology: Current report statistics (1)

Descriptive statistics for the Lungscape cohort:

- Demographic and clinical data - Histology
- Outcome: Primary: OS
  Secondary: RFS and TTR

Outcome Definitions:

- ***Overall Survival (OS):*** date of surgery to death from any cause
- ***Relapse Free Survival (RFS):*** date of surgery to first relapse or death from any cause
- ***Time to Relapse (TTR):*** time from date of surgery to first relapse.

  TTR is measuring direct clinical benefit, by censoring deaths without documented relapse. It is useful, when the majority of deaths are unrelated to lung cancer.

Methodology: Current report statistics (2)

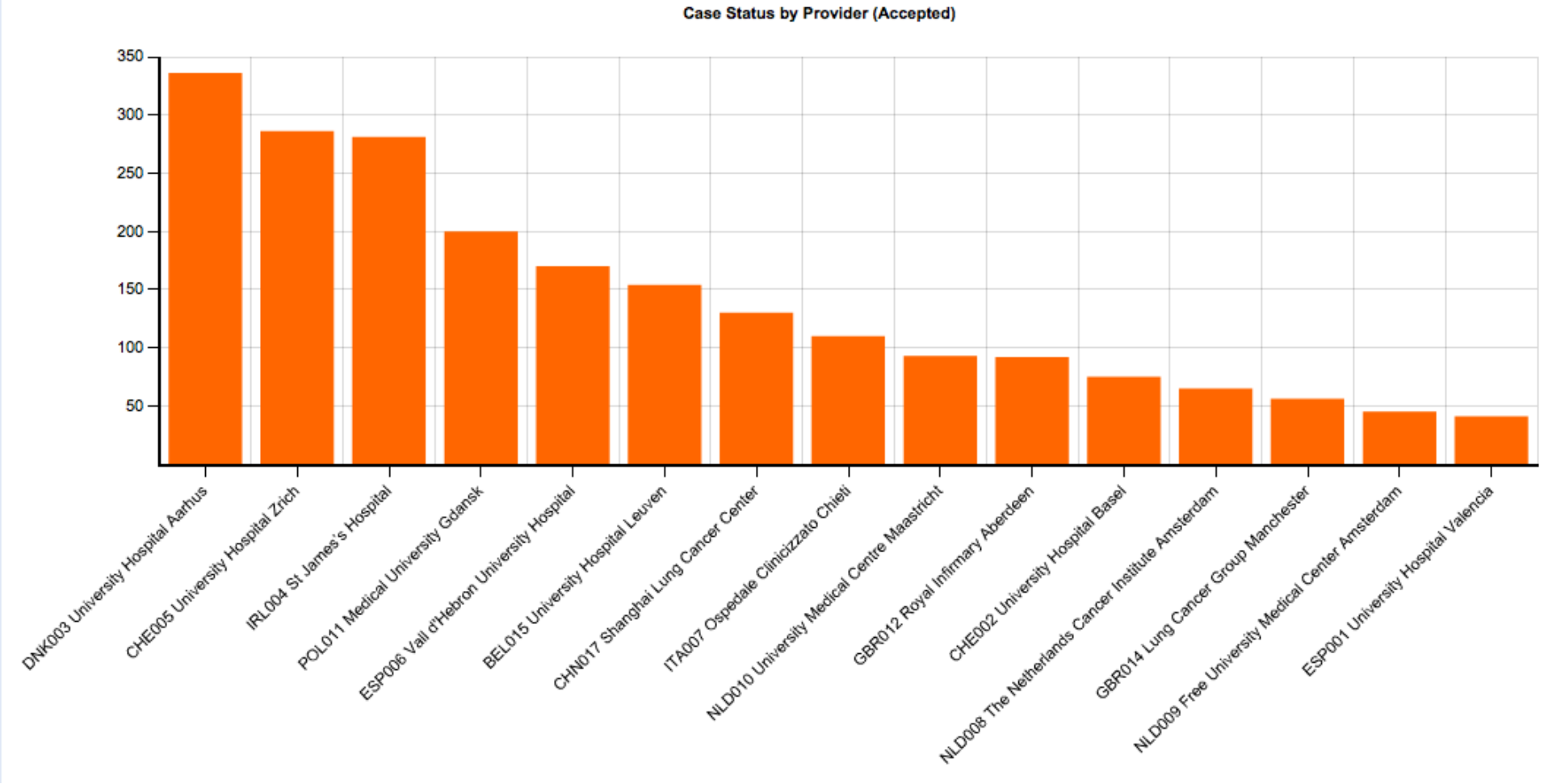
Outcome analysis according to characteristics of interest, including:

- Age
- Gender
- PS
- Stage
- Smoking history
- Histology

- Kaplan-Meier estimates
- Multivariate Cox Regression Analysis with backward selection ($p<0.10$)

Cases by provider (n=2130)

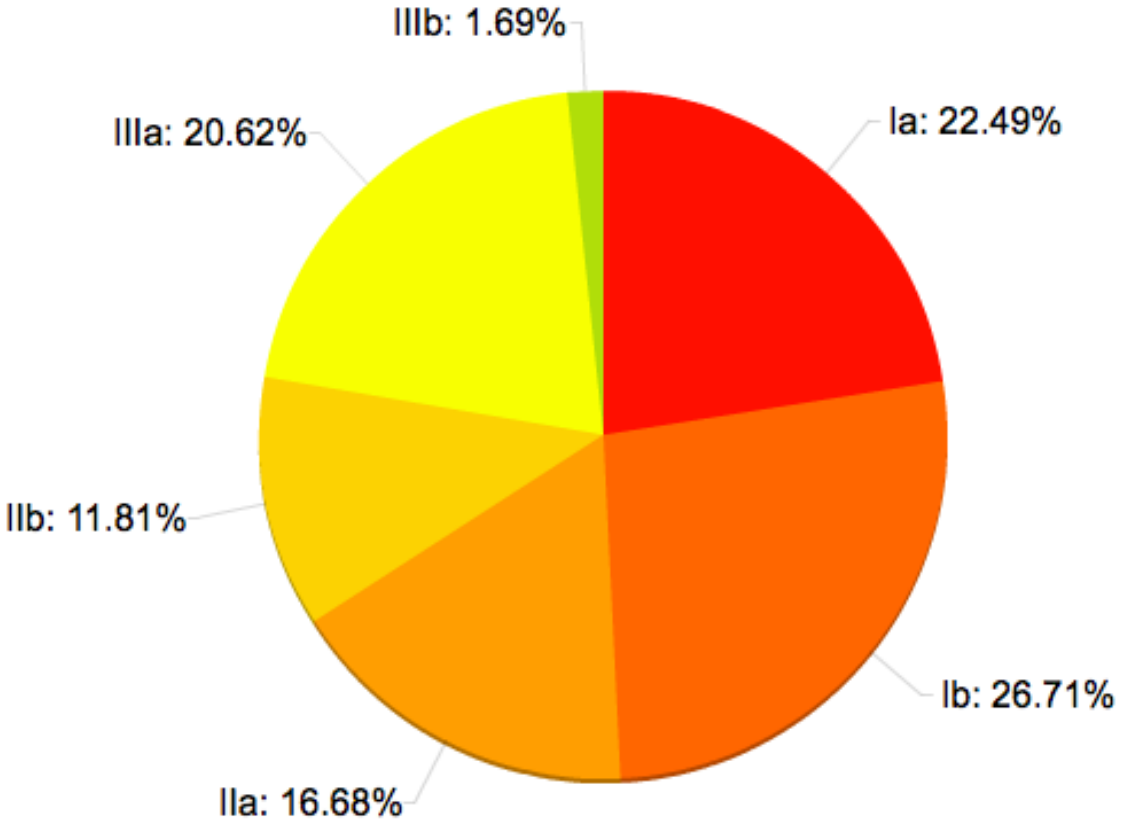
Median follow-up: 58 months



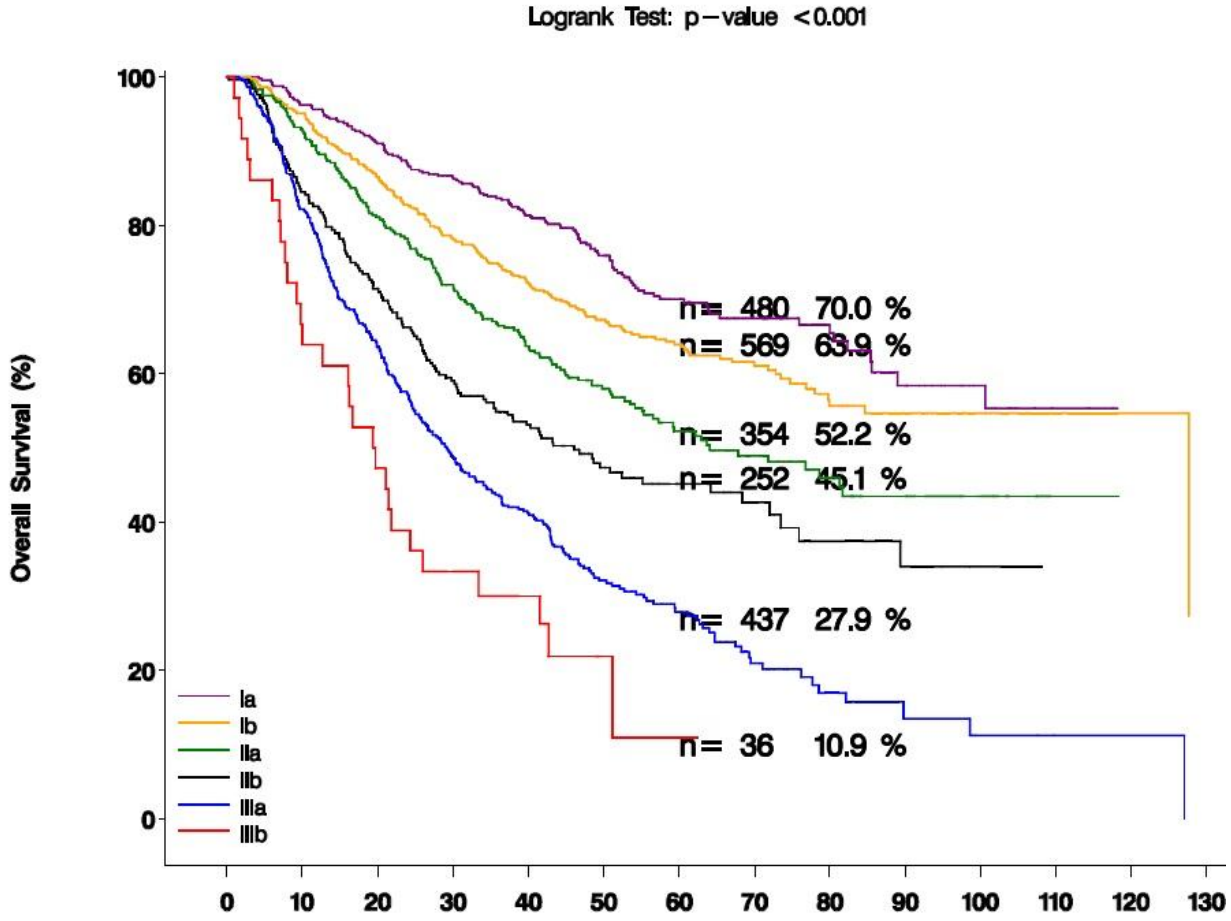
Patient characteristics (N=2130)

Gender (%)	*Male* *Female*	*63.8* *36.2*
Ethnicity (%)	*Caucasian* *East Asian* *Other*	*93.4* *6.2* *0.4*
Age at surgery – yrs	*Median (Min-Max)*	*65.5 (22.6-89.5)*
Smoking History *N=2058* *(%)*	*Current* *Former* *Never*	*33.2* *50.7* *16.1*
Performance status at diagnosis *N= 1134* *(%)*	*0* *1* *2* *3*	*62.2* *35.0* *2.2* *0.6*

Stage grouping



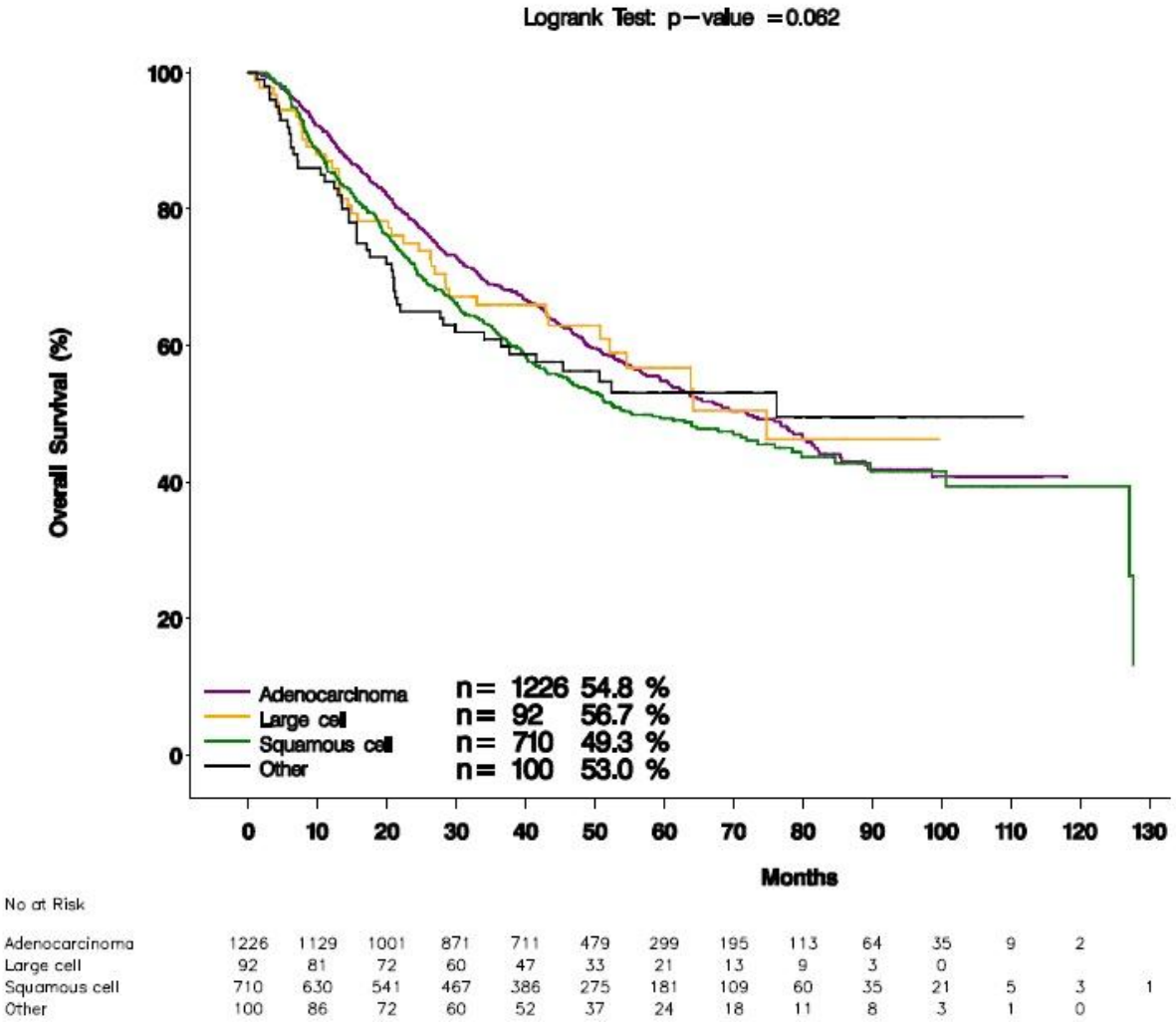
OS by Stage



No at Risk														
Ia	480	462	437	408	342	244	159	98	58	30	19	5	1	
Ib	569	540	490	437	364	262	178	121	67	41	21	6	2	1
IIa	354	329	287	251	206	148	89	62	38	23	12	2	0	
IIb	252	213	180	144	117	75	44	27	15	10	4	1		
IIIa	437	358	275	207	159	92	54	27	15	6	3	1	1	0
IIIb	36	24	17	11	8	3	1	0						

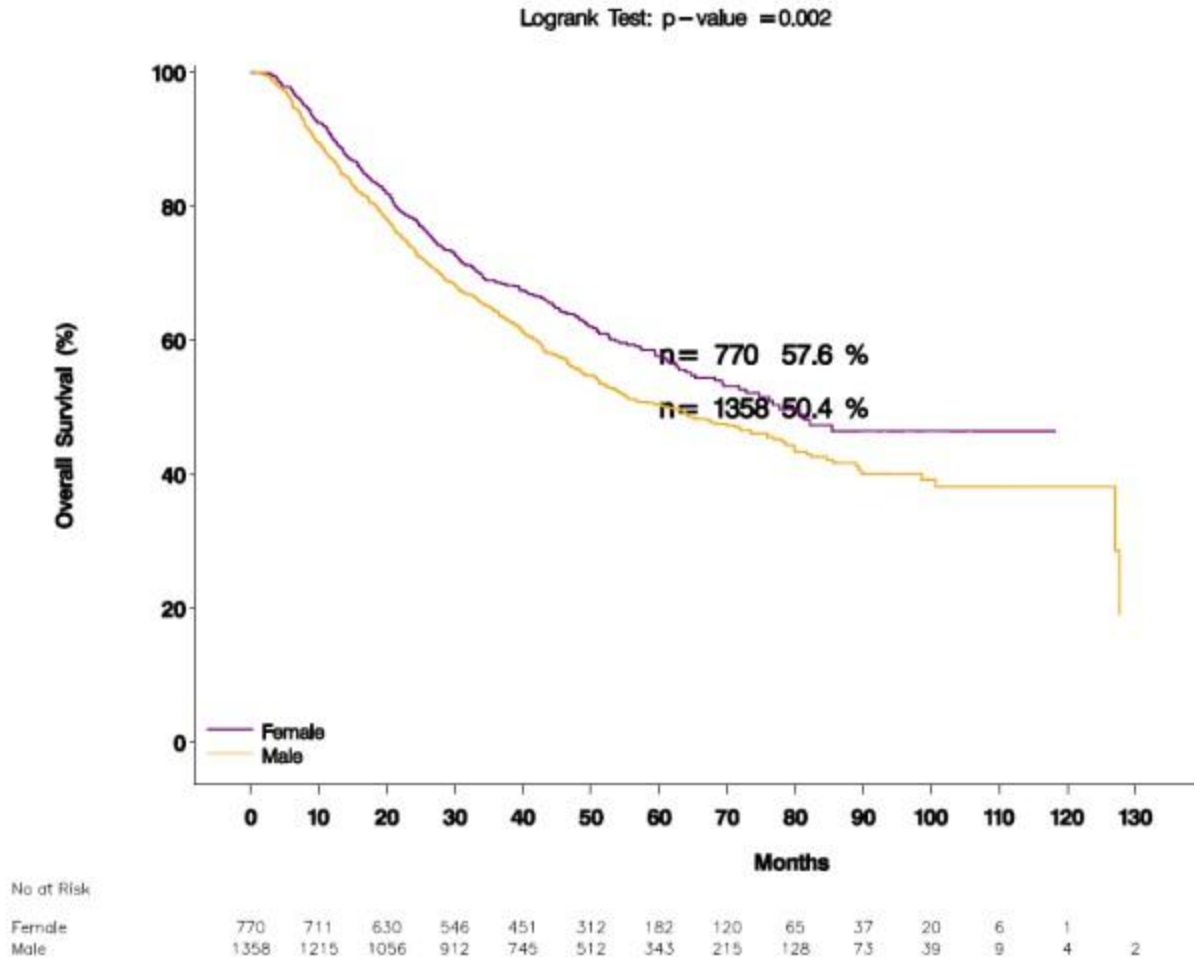
Note: Number of patients and 5-year OS by stage, depicted in the figure

OS by Histology



Note: Number of patients and 5-year OS by Histology, depicted in the figure

OS by Gender

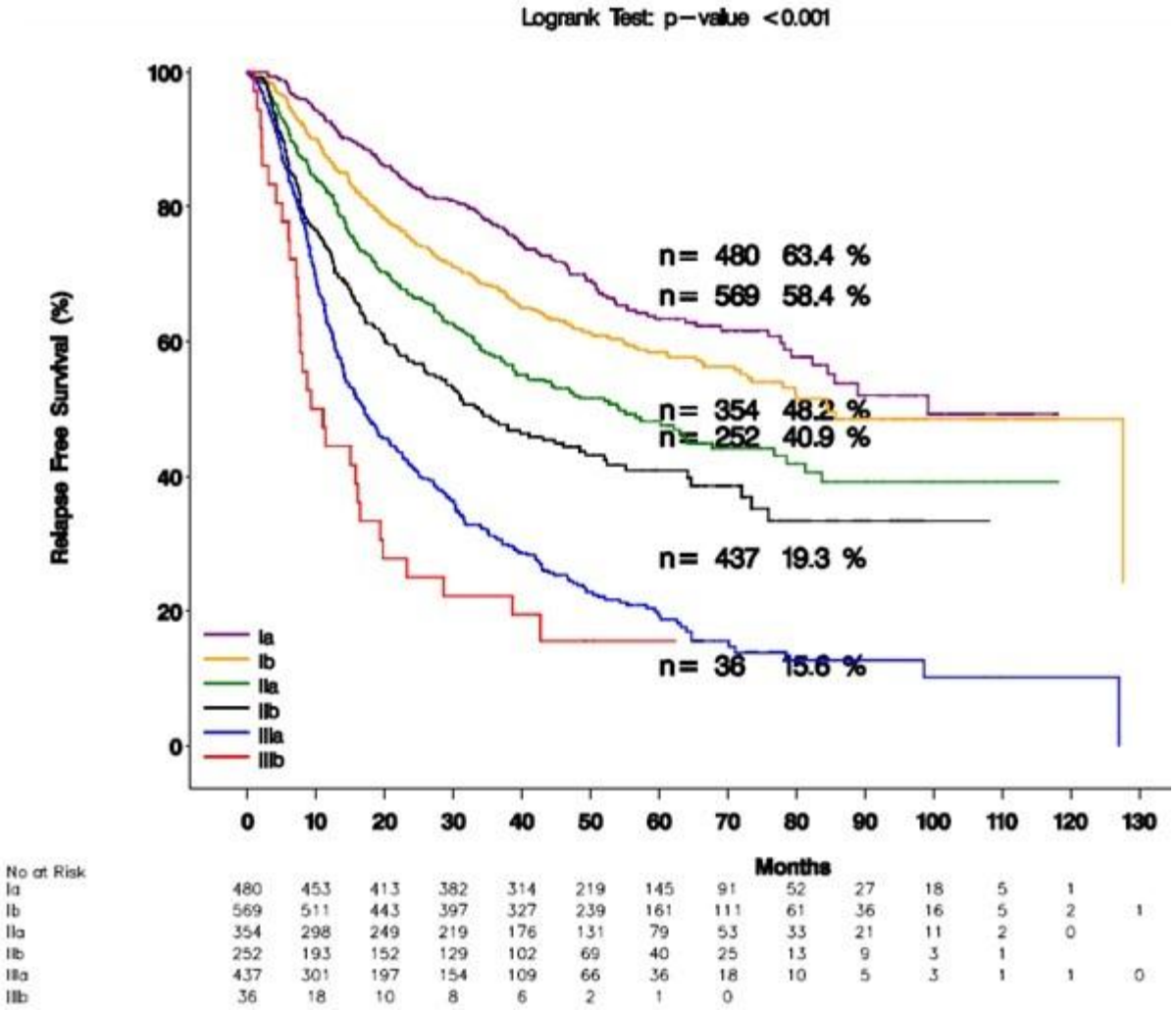


Note: Number of patients and 5-year OS by gender, depicted in the figure

Multivariate Cox model for OS (N=2128, deaths=991)

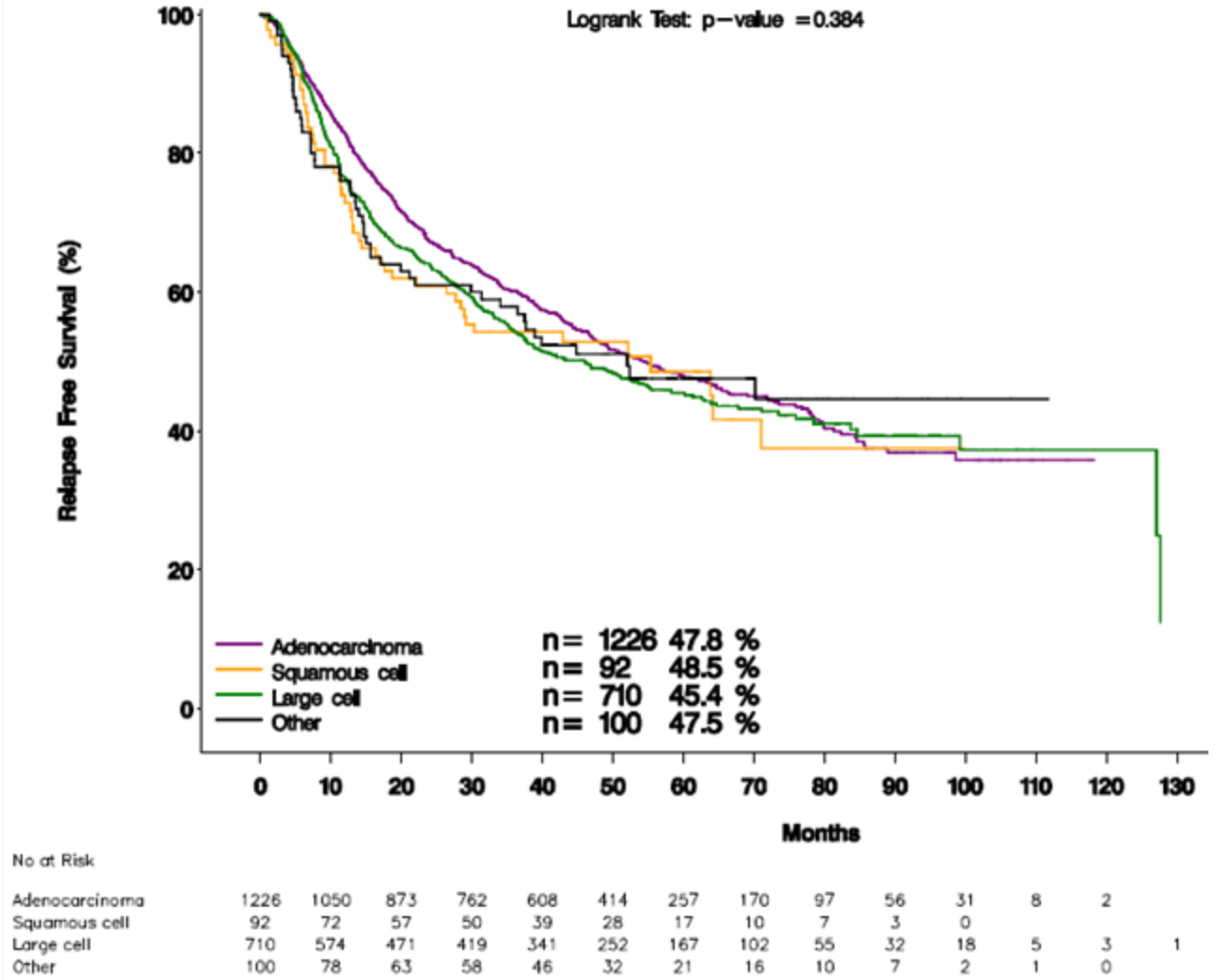
Variable	HR	95% CI	p-value
Age – cat			
"60-70" vs "<60"	*1.39*	*(1.19, 1.64)*	***<0.001***
">70" vs "<60"	*1.50*	*(1.27 1.77)*	***<0.001***
Gender			
Male vs Female	*1.13*	*(0.98, 1.30)*	***0.032***
Performance status at diagnosis			
1 vs 0	*1.31*	*(1.08, 1.59)*	***0.0071***
2&3 vs 0	*1.83*	*(1.16,2.90)*	***0.018***
Unknown vs 0	*1.25*	*(1.04,1.50)*	***0.012***
Missing vs 0	*1.66*	*(1.41,1.97)*	***<0.001***
Smoking history			
Current vs Never	*1.26*	*(1.02, 1.56)*	***0.032***
Former vs Never	*1.20*	*(0.98, 1.47)*	***0.079***
Unknown vs Never	*1.42*	*(0.98, 2.06)*	***0.063***
Stage			
Ib vs Ia	*1.38*	*(1.11,1.71)*	***0.0035***
IIa vs Ia	*1.90*	*(1.51,2.38)*	***<0.001***
IIb vs Ia	*2.56*	*(2.01,3.24)*	***<0.001***
IIIa vs Ia	*4.11*	*(3.36,5.03)*	***<0.001***
IIIb vs Ia	*6.44*	*(4.28,9.71)*	***<0.001***

RFS by Stage



Note: Number of patients and 5-year RFS by stage, depicted in the figure

RFS by histology

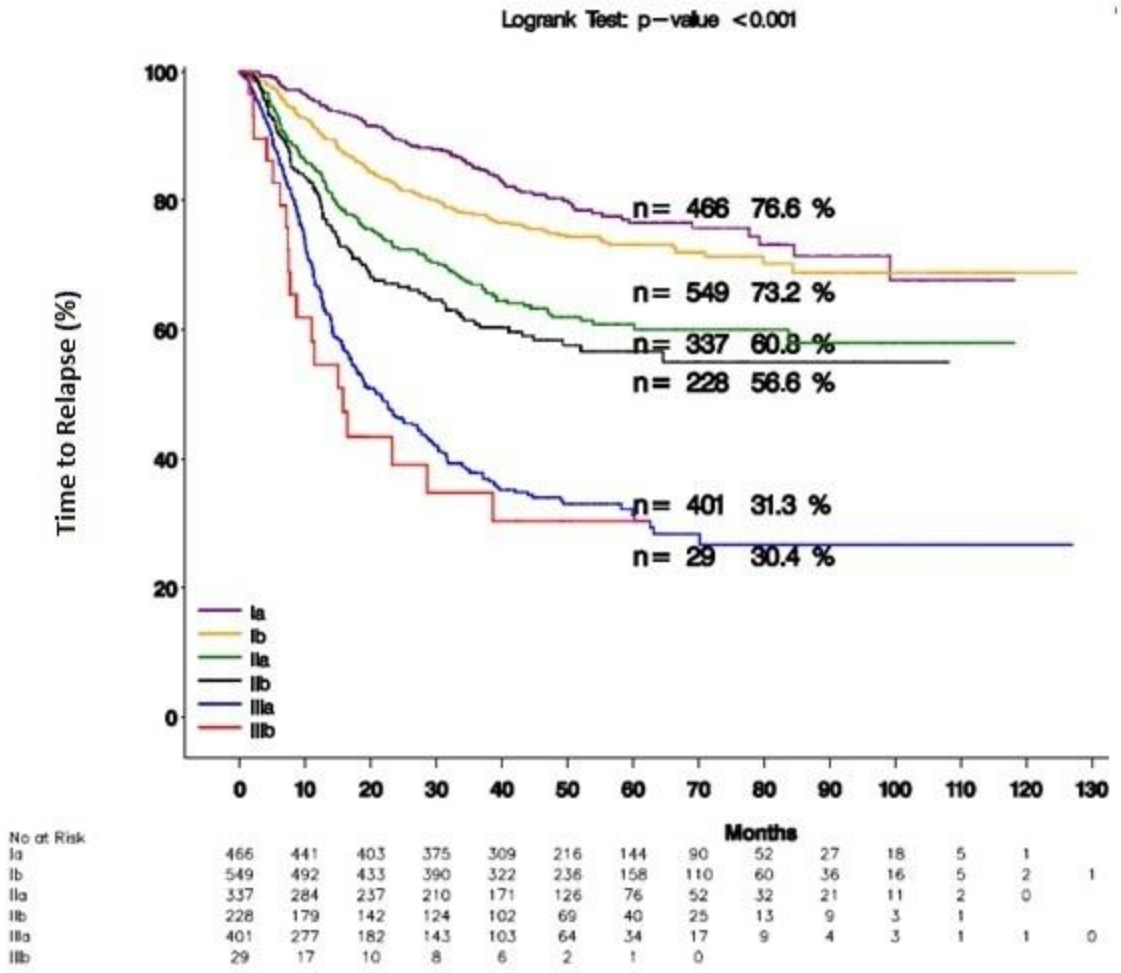


Note: Number of patients and 5-year RFS by histology, depicted in the figure

Multivariate Cox model for RFS (N=2128, RFS events=1119)

Variable	HR	95% CI	p-value
Age			
"60-70" vs "<60"	1.29	(1.11, 1.50)	**<0.001**
">70" vs "<60"	1.34	(1.15, 1.56)	**<0.001**
Gender			
Male vs Female	1.13	(0.99, 1.28)	**0.057**
Performance status at diagnosis			
1 vs 0	1.31	(1.10 1.57)	**0.0029**
2&3 vs 0	1.93	(1.25, 3.00)	**0.0031**
Unknown vs 0	1.32	(1.12, 1.56)	**0.0013**
Missing vs 0	1.55	(1.32, 1.81)	**<0.001**
Stage			
Ib vs Ia	1.31	(1.08, 1.60)	**0.007**
IIa vs Ia	1.80	(1.46, 2.22)	**<0.001**
IIb vs Ia	2.29	(1.83,2.86)	**<0.001**
IIIa vs Ia	3.99	(3.32,4.81)	**<0.001**
IIIb vs Ia	5.58	(3.77,8.26)	**<0.001**

TTR by Stage



Note: Excluding 118 patients with missing date of death or relapse diagnosis and 2 patients without reported "Status at last follow-up"

Conclusions (1) : Lungscape collection

- Through Lungscape, we have collected a large clinical dataset of resected NSCLC including not only raw survival data but also OS, RFS and TTR outcomes according to main clinical and pathological characteristics.

- All patients have tissue available for biomarker analysis and determination of their impact on outcome (ALK lungscape, ESMO abstract 1670)

- Application of the 7th TNM classification has been successful in distinguishing prognostic categories in our dataset and OS similar to published data

Conclusions (2) : Lungscape data report

- We report on the first multivariate survival analysis of OS identifying age, gender, PS and smoking status as independent prognostic characteristics in addition to TNM stage

- TTR outcome, by omitting deaths from other causes, allows to evaluate direct clinical benefit in lung cancer, especially for older age patient

- TTR will represent an optimal parameter to define the impact of biomarkers in NSCLC outcome definition

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