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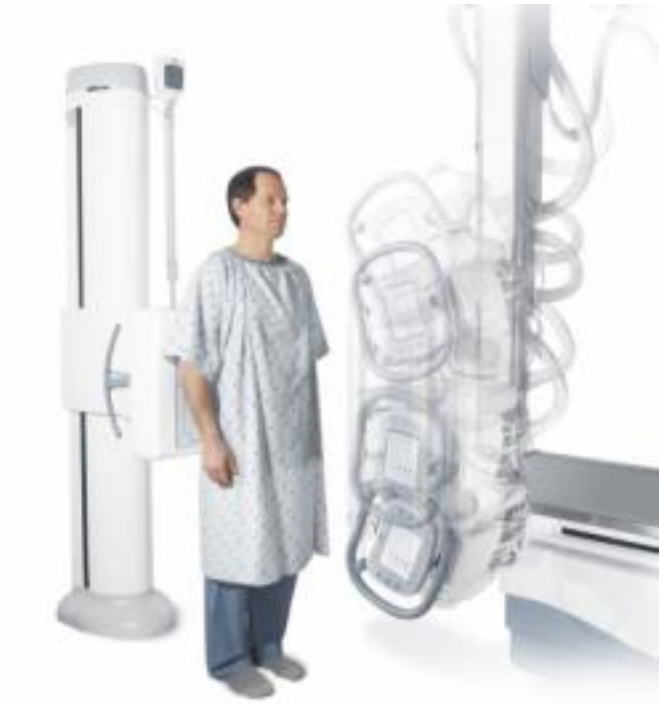
Poster Discussion 2

Oliver Gautschi

Cantonal Hospital Luzern and University of Bern, Switzerland

27PD: background

- Digital tomosynthesis DTS
- 3D-images from limited-angle 2D-scans
- Advantages: speed, cost, radiation dose, high coronal resolution



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Studio OSservazionale DIAGNOSI PRECOCE DEL TUMORE POLMONARE
PROGETTO SOS
il sorriso che salva la vita

Lung Cancer Detection with Chest Digital Tomosynthesis: Results from the SOS Observational Study

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26-29 March 2014, Geneva, Switzerland

Organisers

IASLC International Association for the Study of Lung Cancer

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

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Background

- Low-Dose Computed Tomography (LDCT) screening for Lung Cancer (LC) currently suggested
  - Grade of recommendation = 2B
  - Radiation exposure and costs still problems
- Chest Digital Tomosynthesis (DT) limited angle tomography
  - Allows reconstruction of multiple image planes
  - Provides high-resolution images in coronal planes
- Baseline results of SOS study
  - Single-arm observational study of DT in LC at-risk population
  - LC detection rate comparable to LDCT: 0.98%
  - Low effective radiation dose: 0.13 mSv
  - Costs:1/6 of LDCT

Lung Cancer Detection with Digital Chest Tomosynthesis

Baseline Results from the Observational Study SOS

Alberto Terzi, MD, Luca Bertolaccini, MD, PhD,* Andrea Viti, MD,* Liliana Comello, MD,† Donatella Ghirardo, MD,† Roberto Priotto, MD,† and Maurizio Grosso, MD,† for the SOS Study Group*

Introduction: Observational studies consistently support strategies for early cancer diagnosis and treatment. Owing to its high prevalence, mortality rate, and easily identifiable at-risk population groups, lung cancer seems ideal for early detection programs. We present the baseline results of the SOS study, a single-arm observational study of digital chest tomosynthesis for lung cancer detection in an at-risk population.

Methods: Accrual of study participants started in December 2010 and ended in December 2011. Participants considered eligible were smokers or former smokers aged 45 to 75 years, with a smoking history of at least 20 pack-years, without malignancy in the 5 years before the start of the study. A tomosynthesis examination was performed at baseline and another the year after.

Results: Of the 1919 candidates assessed, 1843 (96%) were enrolled into the study: the mean age was 61 years (range, 48–73 years); 1419 (77%) were current smokers. The most prevalent comorbidities were hypertension, chronic obstructive pulmonary disease, and cardiovascular diseases. A total of 1843 tomosynthesis studies were obtained. Pulmonary abnormalities were detected in 268 subjects (14.5%). First-line basal computed tomography (CT) was subsequently carried out in 132 subjects (7.2%), 68 (4.9%) of which were referred for follow-up CT. Positron-emission tomography/CT was performed on 27 individuals (1.46%), and lung cancer was detected in 18 (0.98%) of them.

Conclusion: The detection rate of noncalcified lung nodules for tomosynthesis was comparable with rates reported for CT. A small subgroup underwent low-dosage CT and entered a follow-up program. Overall, lung cancer was detected in approximately 1% of cases. Digital chest tomosynthesis holds promise as a first-line lung cancer screening tool.

Key Words: Lung cancer screening, Digital chest tomosynthesis.

Thorac Oncol. 2013;8: 685-692)

Lung cancer is the leading cause of cancer-related deaths in the United States and most of the western and developing countries. Most lung cancers are detected when patients become symptomatic and have late-stage disease. However, recently, computed tomography (CT) screening for lung cancer has been reported to reduce lung cancer mortality.[1] In this regard, the National Lung Screening Trial (NLST)[1] showed a 20% reduction in lung cancer-specific deaths in those patients who had screening performed with chest CT. However, CT is associated with the disadvantages of high radiation dosage and cost. Digital chest tomosynthesis (DT), a tomographic technique, may offer an alternative to CT screening. DT uses a conventional radiograph tube, a flat-panel detector, a computer-controlled tube mover, and special reconstruction algorithms to produce section images. Compared with conventional chest radiography, chest tomosynthesis improved sensitivity in the detection of CT-proven lung nodules. DT is able to detect most lung nodules larger than 5 mm, in particular 91% of nodules, whose sizes were between 4 mm and 6 mm, and 100% of nodules larger than 6 mm, detected in a CT scan.[2,3] In addition, the effective radiation dosage to patients from chest examination with DT is low (approximately 0.13 mSv compared with 0.1 mSv for a postero-anterior and lateral chest radiograph).[4] Although it lacks the depth resolution of CT, tomosynthesis provides some of the benefits of CT at lower costs and radiation dosages. Furthermore, DT is less expensive than CT at approximately one-sixths of the cost of a CT.[5]

In this single-arm observational study (SOS Study), DT was used for early detection of lung cancer. The study wa approved by the Institutional Ethics Committee (approva

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Methods

- Sample size of 2,000 subjects
  - Planned on incidence and mortality data reported in Piedmont Cancer Registry
  - Current smokers or former smokers ≥20 pack-years
  - Age 45 – 75 years
  - No previous cancer in 5 years before study
- DT performed one-year later in negative baseline subjects
- In subjects with uncertain nodule >5 mm or with multiple nodules, first-line LDCT warranted

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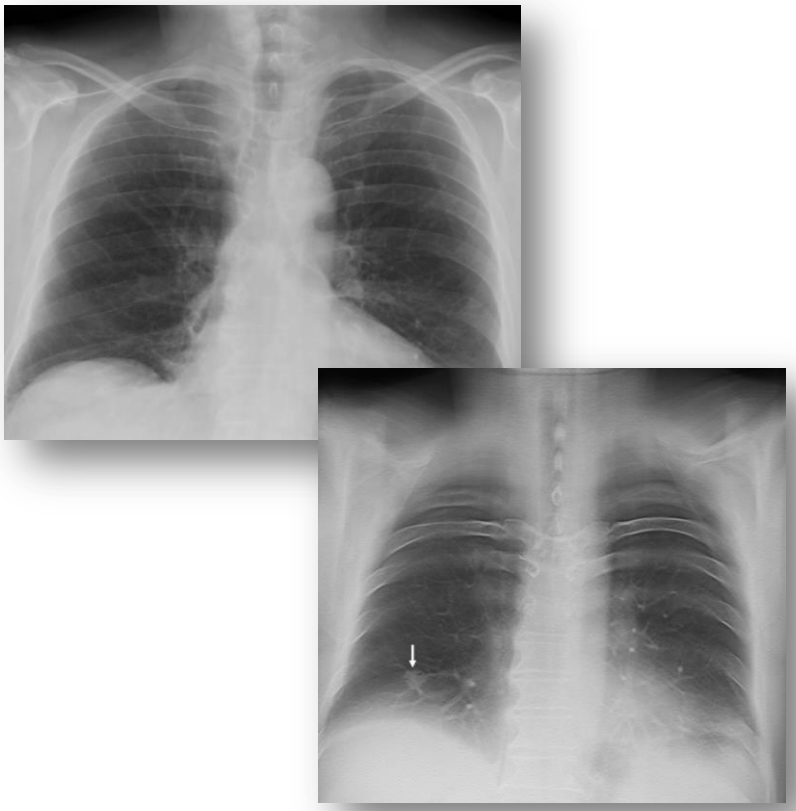
Results – 1

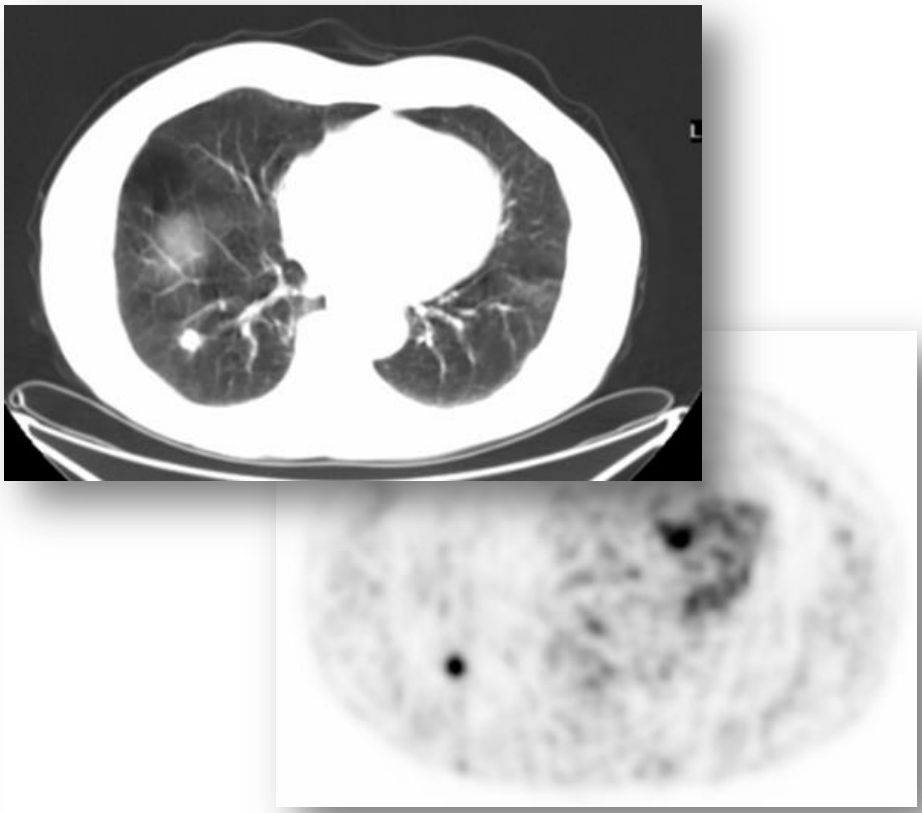
- 1,703 underwent First Round DT
  - Mean age = 60 ys
  - 92% of baseline, drop out = 0.4%
- Lung nodules >5 mm detected: 13 (0.7%)
  - No had nodules at Baseline DT
- Surgery performed in 10
  - Histology
    - Organizing pneumonia= 2
    - Tuberculosis nodule = 1
    - Intrapulmonary lymph node ⇑ in size = 1
    - Metastasis from biliary tree adenocarcinoma (operated >10 years before) = 1
  - LC diagnosed & resected by VATS lobectomy 5
- LC detection rate at First Round: 5/1703 (0.3%)

TUMOR STAGE	No. of subjects	
	Baseline	First Round
IA	6	4
IB	2	
IIA	2	1
IIB	1	
IIIA	1	
IIIB	1	
IV	5	

HISTOLOGY	No. of subjects	
	Baseline	First Round
Adenocarcinoma	10	1
Squamous cell carcinoma	7	4
Carcinoid	1	

Results – 2





- *DT showing right basal pulmonary nodule (white arrow), not visible on postero-anterior chest roentgenogram, and confirmed by CT-scan and PET*

Conclusions

- First Round results on DT in early detection of LC good as for baseline
- LC detection rate
  - Comparable to LDCT
  - Achieved at far lower costs and radiation dose
- DT possible first-line LC screening tool
  - Effective in high-risk subjects follow-up
  - Studies on larger number of subjects needed to confirm results

27PD: comments

- This study demonstrated feasibility of DTS
- Already approved for breast cancer screening in Europe
- Further study and algorithms for lung cancer screening are justified (cost, radiation savings)

28PD: background

Measure of disease burden over time

- QALY: quality adjusted life-years
- = Survival (years added) * Utility (0.0-1.0)

Comparison between treatment modalities

- ICER: incremental cost-effectiveness ratio
- = Δ Cost ($) / Δ QALY gained or lost

Measuring the Population Impact of Introducing Stereotactic Ablative Radiotherapy (SABR) for Stage I NSCLC in Canada

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European Lung Cancer Conference

March 2014

Western UNIVERSITY · CANADA

HARVARD SCHOOL OF PUBLIC HEALTH

London Health Sciences Centre
London Regional Cancer Program

Introduction/Objectives

- We used the Cancer Risk Management Model to evaluate the economic and health impact of the introduction of SABR for stage I NSCLC in Canada
- SABR was introduced into Canada in 2008 and modeled as an alternative option to surgery, conventional RT, and best supportive care
- Costs were estimated in 2013 Canadian dollars and a 10-year time horizon was used to estimate Quality adjusted life years (QALYs)
- Discounting was employed at a rate of 3%.
- For each SABR indication, a willingness to pay threshold of $100,000/QALY was used to determine cost-effectiveness

Results

- RT had lower upfront costs compared to SABR, which was offset by subsequent costs associated with recurrence.

- Costs for stage I by treatment modality were: RT ($7,646.98), SABR ($8,815.55), sublobar resection ($12,161.17), lobectomy ($16,266.12), pneumonectomy ($22,940.59), and BSC ($14.582.87).

	Mean lifetime costs per patient	Incidence (annual cases)	Total costs
Stage I NSCLC	$23,115	4,381	$98,670,810
Stage II NSCLC	$33,279	1,098	$36,234,645
Stage III NSCLC	$30,156	5,891	$88,386,602
Stage IV NSCLC	$22,364	10,621	$157,438,281
Limited SCLC	$24,895	1,135	$14,251,413
Extensive SCLC	$19,256	1,959	$30,020,783
TOTAL		25,085	$608,002,599

Conclusions

When compared to SABR, conventional RT, sublobar resection, and BSC were dominated (more expensive and lower QALYs). Lobectomy was cost-effective (more QALYs but at a higher cost) with an ICER of $55,909.06.

Scenario where SABR is introduced	Incremental Cost ($)	Incremental Life Years	Incremental QALYs	ICER ($/QALY)
RT	-5,187,816	2,510	1,693	Dominated
BSC	-9,951,612	875	660	Dominated
Sublobar resection	-3,288,656	3,385	2,353	Dominated
Lobectomy	-164,370,264	-570	-294	55,909

Implementation of SABR for the three cost-effective indications resulted in the following average annual benefits:

- $18,190,729.40 in savings
- 566.2 fewer deaths due to lung cancer
- Gain of 8663.6 life years or 5,979.6 QALYs

28PD: comments

- Relevant simulation for Canada
- Results support current practice (SABR for inoperable patients)
- Ongoing debate about QALY in Europe: ECHOUTCOME expert panel recommended against its use for decision making

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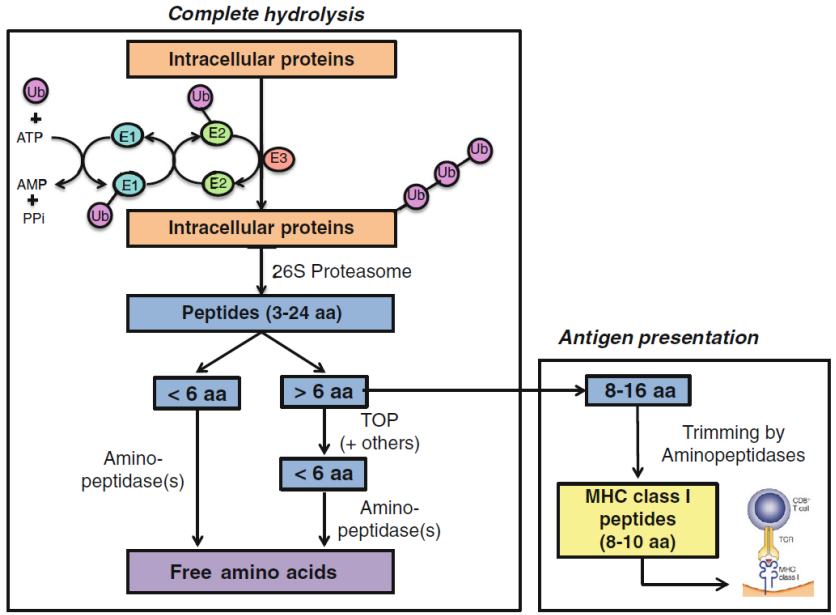
75PD: background

- Aminopeptidase N (CD13)
- Hydrolysis and antigen presentation
- Overexpression in lung cancer and stroma
- Tumor growth and metastasis



4th European Lung Cancer Conference

Efficacy by T categories of the postoperative adjuvant immunotherapy with Ubenimex on survival in patients with stage I squamous-cell lung cancer: an exploratory analysis from a randomized phase III study

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The Original study schema

P-Stage I Squamous cell carcinoma, Completely resected, age: 40-75y.o., PS; 0-2

registration

Randomization

Bestatin, 30mg/day, p.o. for 2 yrs

Placebo p.o. for 2 yrs

Follow-up: every 3 months for 2 years and every 6 months thereafter

Endpoint: Overall survival

Patients accumulation: July, 1992 - March, 1995

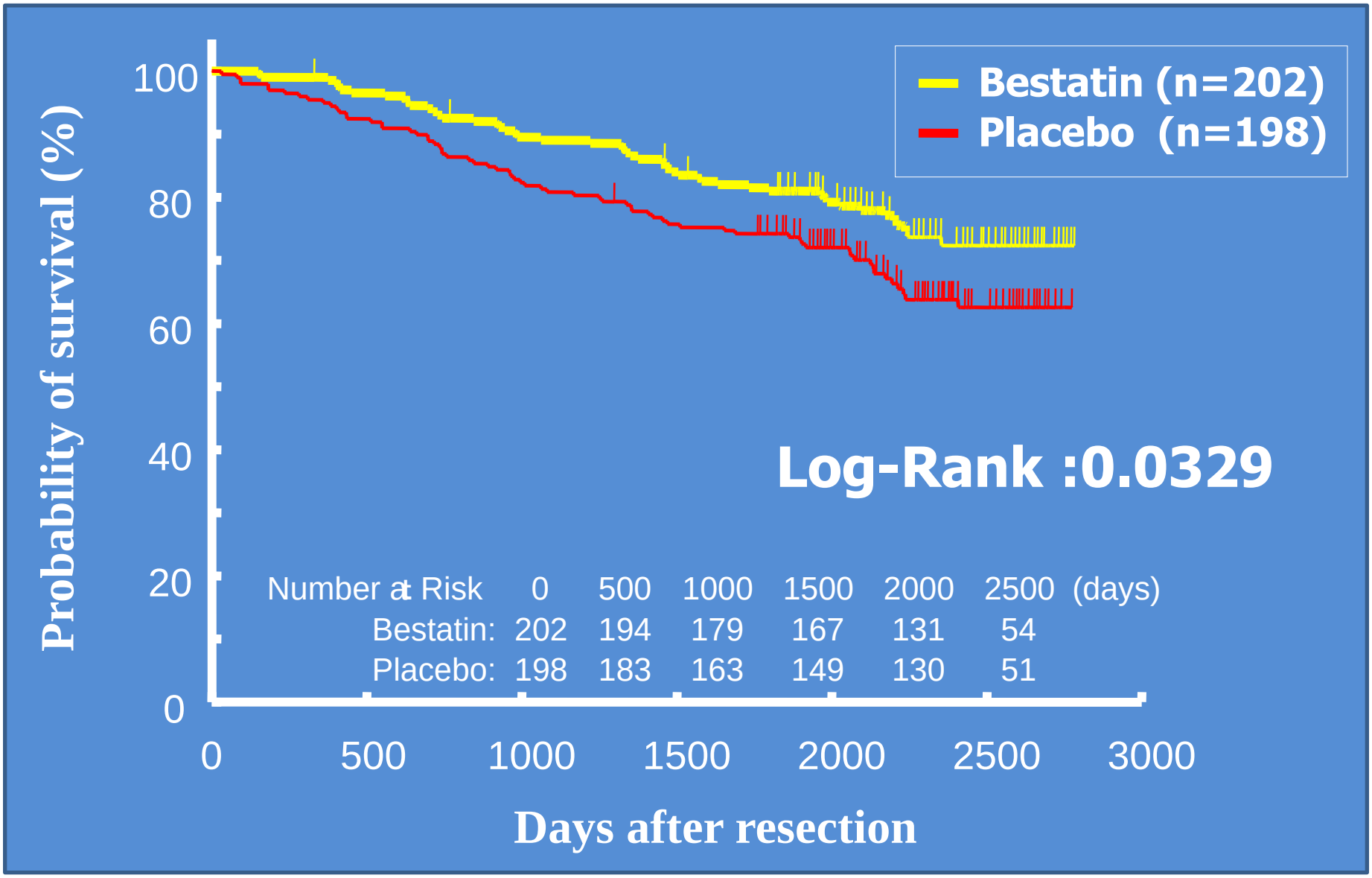
Ichinose Y, et al. JNCI 2003; 98:605-610

Patient characteristics

Characteristic		Bestatin (n=202)	Placebo (n=198)
Age	Median – yr	66	67
	Range –yr	41-76	45-75
	< 65 yr – no.(%)	83	66
	=< 65 yr	119	132
Male gender		181	180
Performance status	0	117	125
	1	81	65
	2	4	8
Tumor status	Tis	0	2
	1	99	95
	2	103	100
	3	0	1
Operation modality	Lobectomy	197	189
	Pneumonectomy	5	8
	Segmentectomy	0	1

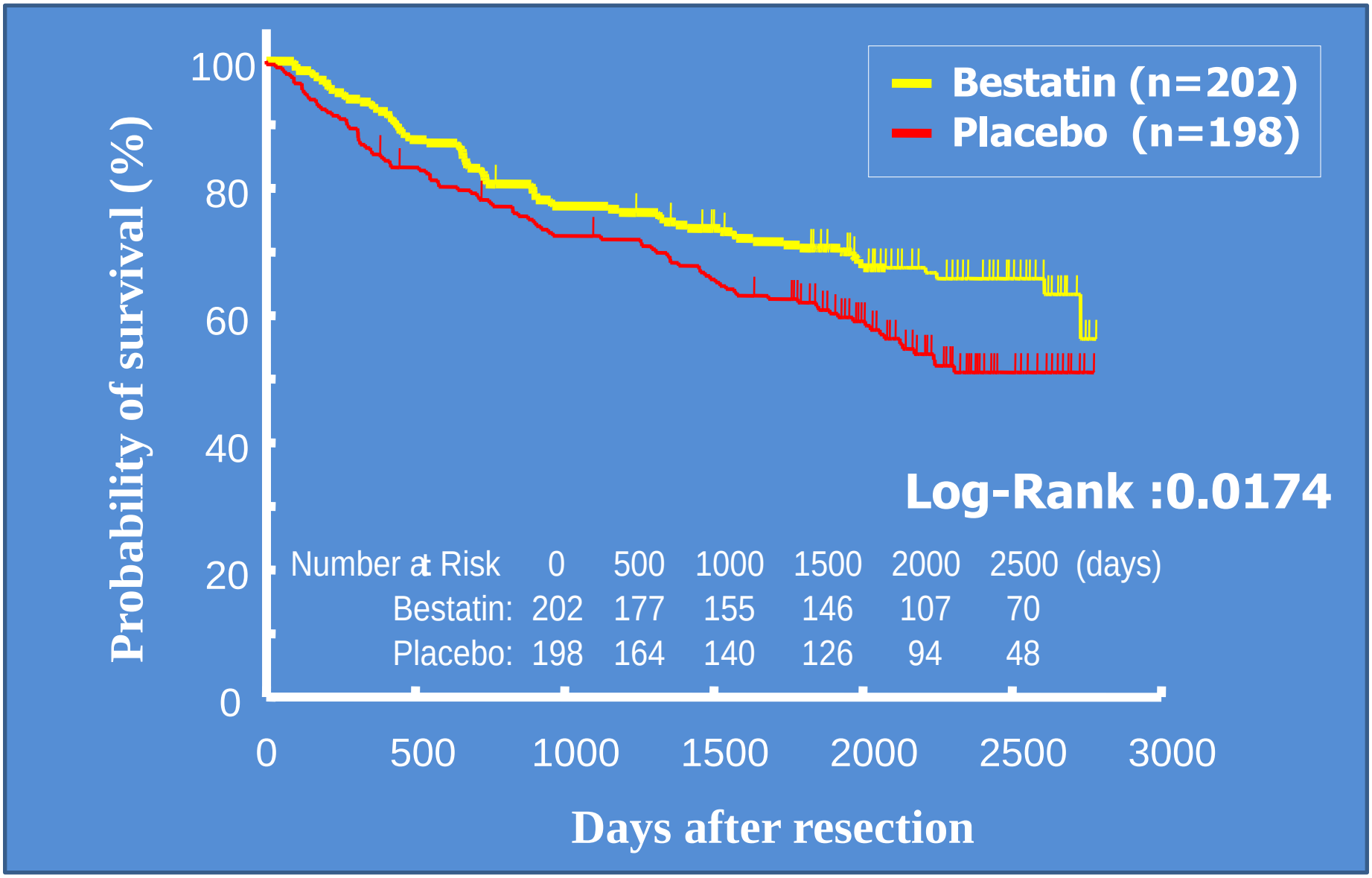
Ichinose Y, et al. JNCI 2003; 98:605-610

Overall survival



Ichinose Y, et al. JNCI 2003; 98:605-610

Disease-free survival



Ichinose Y, et al. JNCI 2003; 98:605-610

Methods of this exploratory analysis

- Data from a randomized double-blind placebo-controlled trial of Ubenimex in patients with resected stage I squamous-cell lung cancer were reanalyzed to evaluate the effectiveness of Ubenimex according to T1a, T1b and T2a tumors based on UICC7-TNM classification.

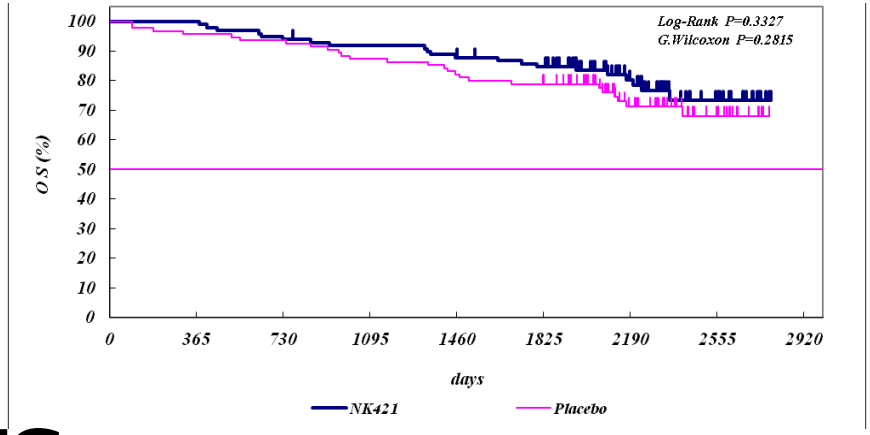
Results of this exploratory analysis

- Data from 398 patients were analyzed: 108 (27.1%) had T1a tumors, 100 (25.1%) had T1b tumors, and 190 (47.8%) had T2a tumors.
- In the surgery-alone group, overall survival rates (OS) at 5 years were 80.4% in patients with T1a tumors, 80.9% in those with T1b tumors, 68.0% in those with T2a tumors.
- In the adjuvant treatment group with Ubenimex, OS at 5 years were 88.2% in patients with T1a tumors, 79.2% in those with T1b tumors, and 77.9% in those with T2a tumors.

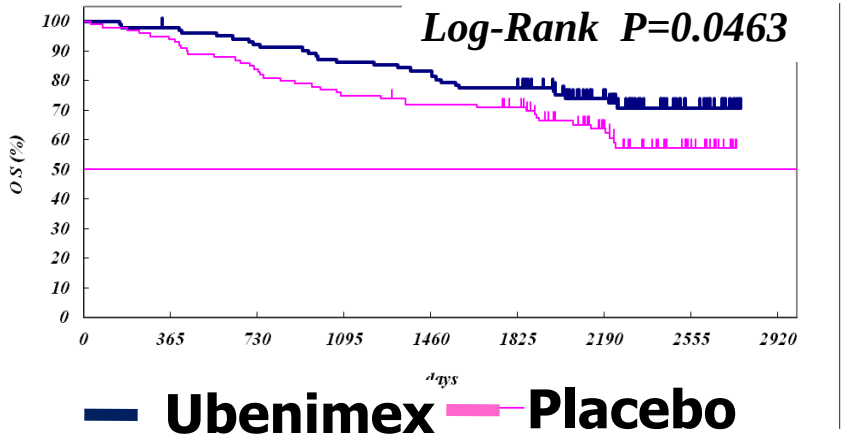
Subset analysis based on T category

OS

T1a-b



T2a



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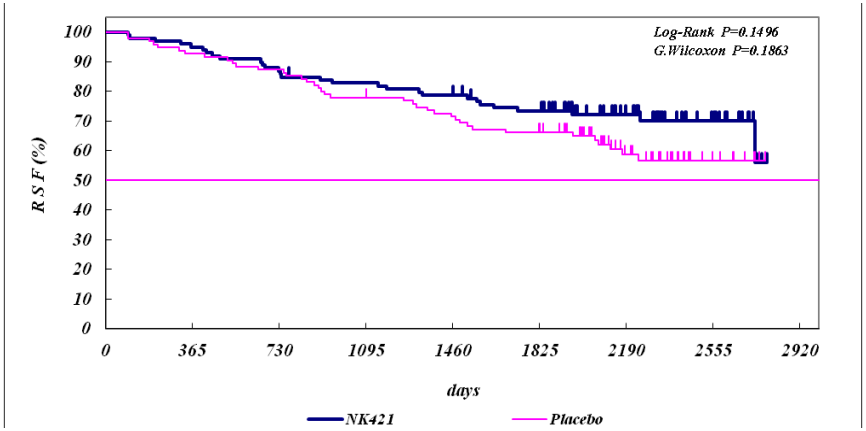
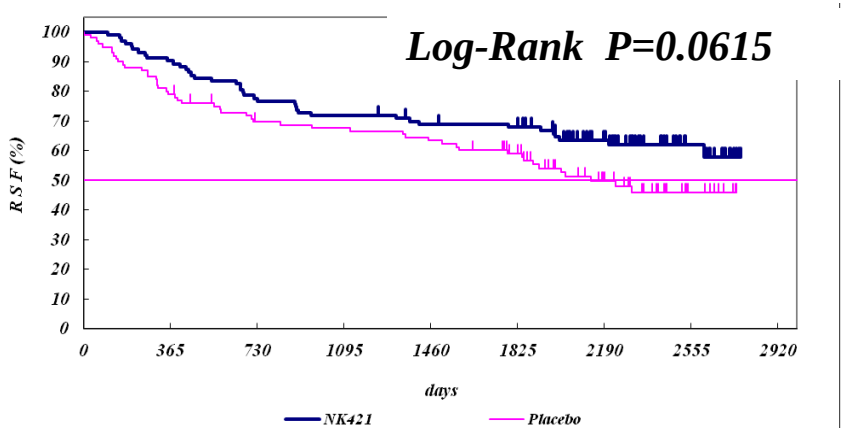
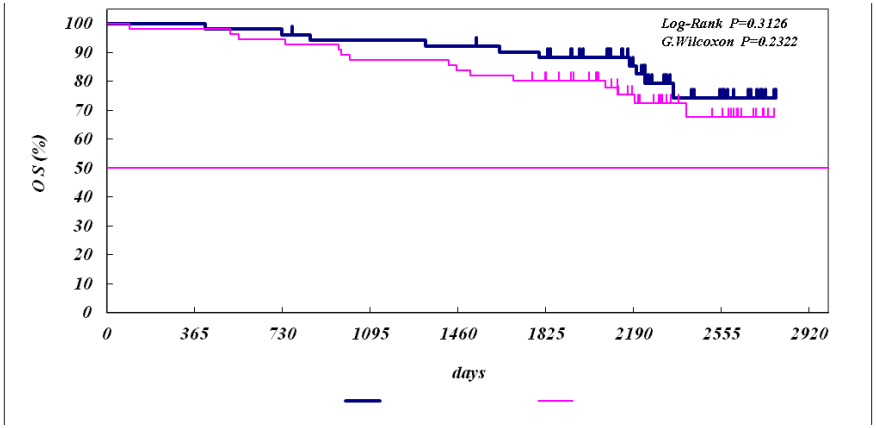




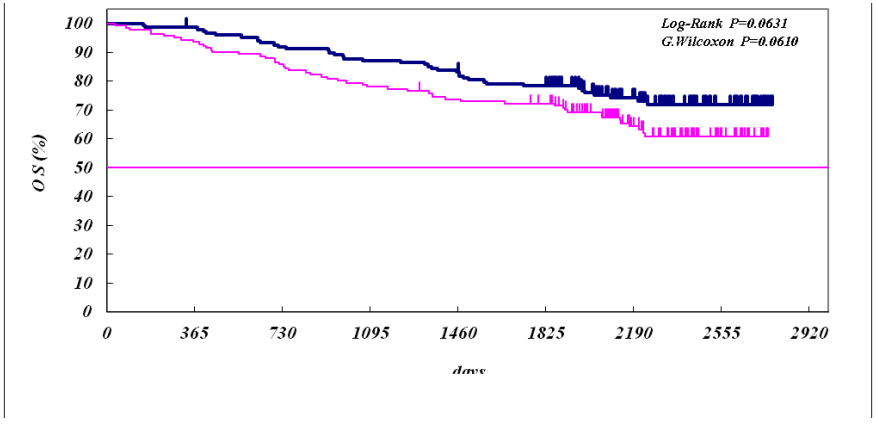
Subset analysis based on T1a and T1b

OS

T1a

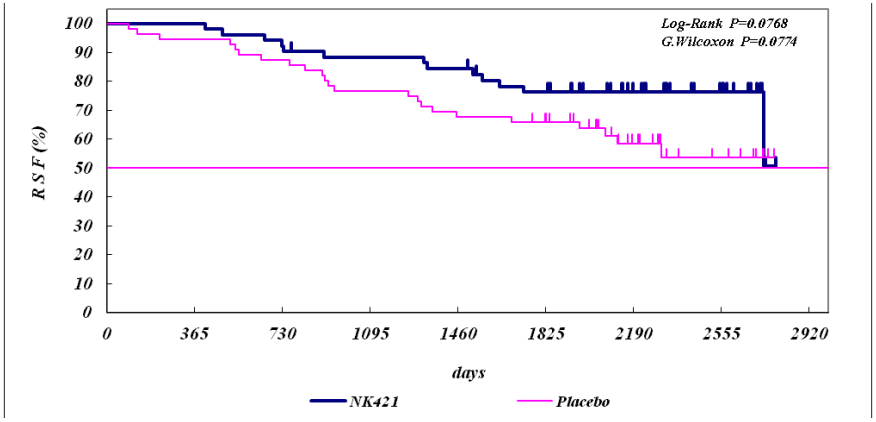


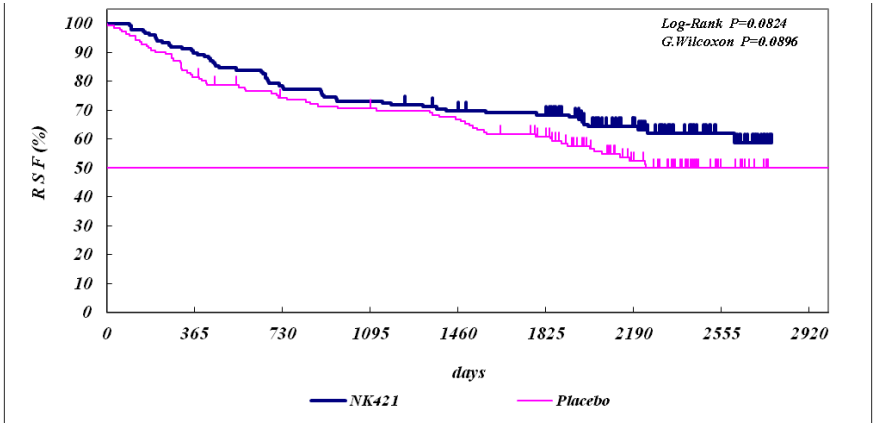
T1b



DFS

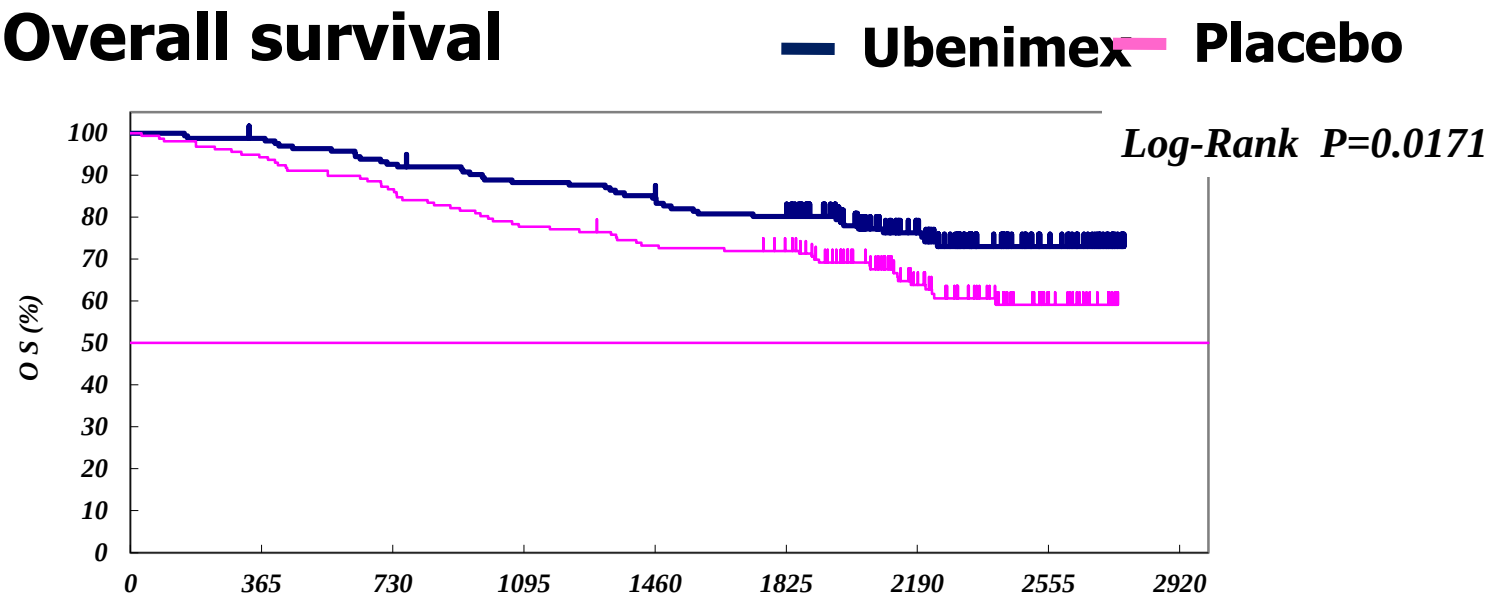
Ubenimex **Placebo**



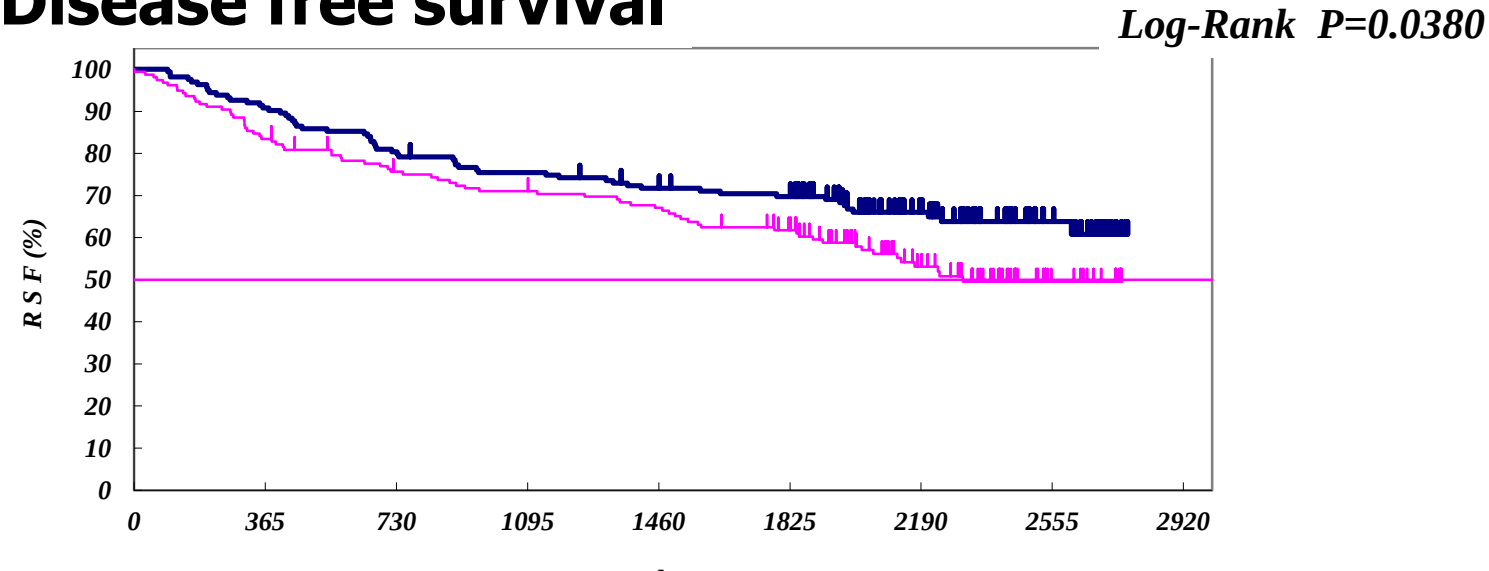


Subset analysis for T1b+T2a

Overall survival



Disease free survival



Hazard ratio

on the Ubenimex group compared with placebo

	pT	H. R.	95% confidential interval		
Overall survival	1a-b	0.754	0.424	-	1.339
	2a	0.631	0.388	-	1.026
	1b+2a	0.615	0.411	-	0.921
Disease free survival	1a-b	0.702	0.433	-	1.139
	2a	0.665	0.436	-	1.013
	1b+2a	0.693	0.490	-	0.981

In patients with T1b+T2a tumor, both the overall survival rate and the recurrence free survival were significantly higher in the Ubenimex group than in the surgery-alone group (hazard ratio = 0.62 and 0.69, log-rank p = 0.017 and 0.038, respectively)

Conclusions

- This exploratory analysis demonstrated that postoperative adjuvant therapy with Ubenimex significantly improved survival in patients with T1b-T2aN0 NSCLC compared with surgery alone.
- The confirmatory adjuvant phase III study with Ubenimex for stage I squamous-cell lung cancer is warranted.

PD75: comments

- Subgroup analysis of an earlier trial
- APN remains an interesting target
- and a potential biomarker
- Adjuvant immunotherapy is a competitive field (BLP-25, MAGE, ipilimumab, anti-PDL and others)

Summary: goals in early disease

- Early detection
- Increase cure rate
- Reduce harm
- Control cost

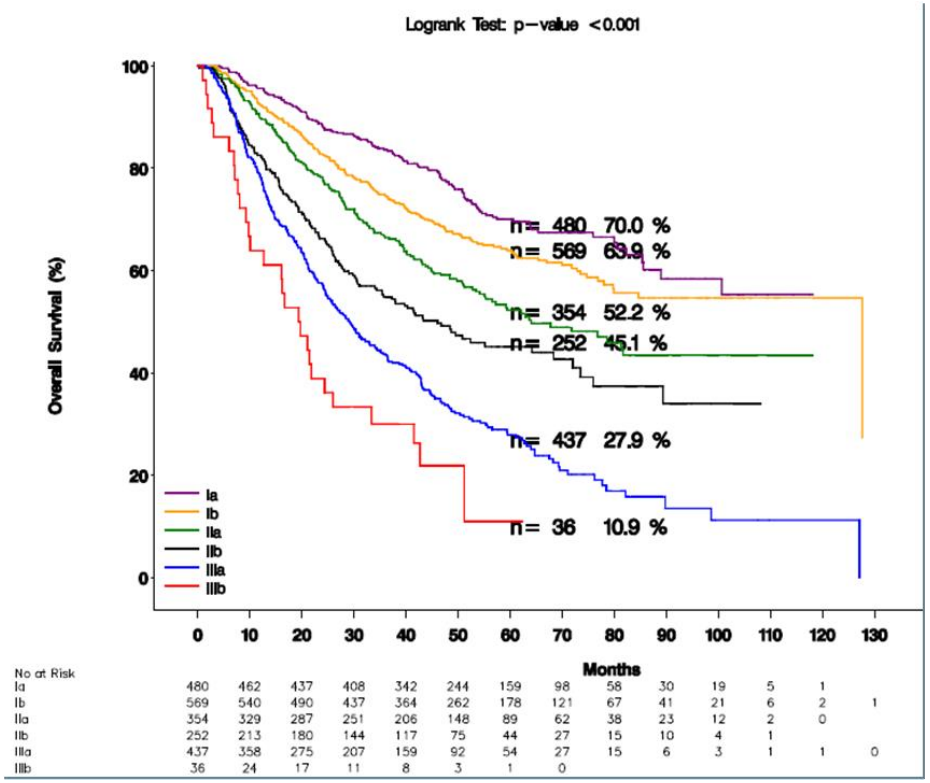


Figure:

ETOP-LUNGSCAPE

Courtesy of S. Peters