Estadios iniciales y enfermedad localmente avanzada

Carlos Gálvez

H. General Universitario Alicante

Organizado por:

GECP
lung cancer research

NSCLC – Early stage (I, II)

NELSON

- **Cirugía – Resección anatómica** (lobectomía, segmentectomía anatómica) + **linfadenectomía IASLC** **Onaitis et al.**
  - SABR (≥100Gy): I inoperables, rechazo Cx, alternativa a sublobar en no candidatos a lobectomía

- *QT adyuvante:* **IoNESCO (neoadyuvante)**
  - II-III
  - IB: >4cm, pleura visceral, invasión vascular, pobremente diferenciado, Nx, wedge
  - Esquema:
    - Dobletes platino (CisPt-VNR)
    - Osimertinib **ADAURA**
    - No targeted therapies **CTONG 1104**
    - IT en estudio **PRINCEPS (neoadyuvante)**

- *RDT adyuvante* (secuencial si QT-RDT):
  - No de rutina en R0, N0-1
  - R1-2, márgenes afectos (concomitante), pIIIA (secuencial), extracapsular, multinivel **LUNG ART**

NSCLC – Locally advanced (IIIA-B)

- **IIIA resecable**
  - Cx + QT adyuvante
  - QT neoadyuvante + Cx ± QT adyuvante **Corsini et al.**
  - CRT neoadyuvante + CX ± QT adyuvante
  - Superior sulcus, T3, T4 → CRT neoadyuvante + Cx
  - Esquema:
    - Basada en platinos (CisPt)
    - IT en estudio **SAKK 16/14** **PRINCEPS** **NADIM**
    - No targeted therapies

- **IIIA irresecable-IIIB**
  - Concomitante CRT (60-66Gy) + Durvalumab **PACIFIC**
  - Esquema:
    - Basada en platinos (CisPt)
    - No targeted therapies

The NEW ENGLAND JOURNAL of MEDICINE

LUNG CANCER SCREENING – NELSON

ORIGINAL ARTICLE

Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial

H.J. de Koning, C.M. van der Aalst, P.A. de Jong, E.T. Scholten, K. Nackaerts, M.A. Heuvelmans, J.-W.J. Lammers, C. Weenink, U. Yousaf-Khan, N. Horeweg, S. van 't Westeinde, M. Prokop, W.P. Mali, F.A.A. Mohamed Hoesein, P.M.A. van Ooijen, J.G.J.V. Aerts, M.A. den Bakker, E. Thunnissen, J. Verschakelen, R. Vliegenthart, J.E. Walter, K. ten Haaf, H.J.M. Groen, and M. Oudkerk

ABSTRACT

BACKGROUND

There are limited data from randomized trials regarding whether volume-based, low-dose computed tomographic (CT) screening can reduce lung-cancer mortality among male former and current smokers.

METHODS

A total of 13,195 men (primary analysis) and 2594 women (subgroup analyses) between the ages of 50 and 74 were randomly assigned to undergo CT screening at T0 (baseline), year 1, year 3, and year 5.5 or no screening. We obtained data on cancer diagnosis and the date and cause of death through linkages with national registries in the Netherlands and Belgium, and a review committee confirmed lung cancer as the cause of death when possible. A minimum follow-up of 10 years until December 31, 2015, was completed for all participants.

RESULTS

Among men, the average adherence to CT screening was 90.0%. On average, 9.2% of the screened participants underwent at least one additional CT scan (initially indeterminate). The overall referral rate for suspicious nodules was 2.1%. At 10 years of follow-up, the incidence of lung cancer was 5.58 cases per 1000 person-years in the screening group and 4.91 cases per 1000 person-years in the control group; lung-cancer mortality was 2.50 deaths per 1000 person-years and 3.30 deaths per 1000 person-years, respectively. The cumulative rate ratio for death from lung cancer at 10 years was 0.76 (95% confidence interval [CI], 0.61 to 0.94; P=0.01) in the screening group as compared with the control group, similar to the values at years 8 and 9. Among women, the rate ratio was 0.67 (95% CI, 0.38 to 1.14) at 10 years of follow-up, with values of 0.41 to 0.52 in years 7 through 9.

CONCLUSIONS

In this trial involving high-risk persons, lung-cancer mortality was significantly lower among those who underwent volume CT screening than among those who underwent no screening. There were low rates of follow-up procedures for results suggestive of lung cancer. (Funded by the Netherlands Organization of Health Research and Development and others; NELSON Netherlands Trial Register number, NL580.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. de Koning at the Department of Public Health, Erasmus MC–University Medical Center Rotterdam, Doctor Molewaterplein 40, 3015 GD, Rotterdam, the Netherlands, or at h.dekoning@erasmusmc.nl.

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METHODS

A total of 13,195 men (primary analysis) and 2594 women (subgroup analyses) between the ages of 50 and 74 were randomly assigned to undergo CT screening at T0 (baseline), year 1, year 3, and year 5.5 or no screening. We obtained data on cancer diagnosis and the date and cause of death through linkages with national registries in the Netherlands and Belgium, and a review committee confirmed lung cancer as the cause of death when possible. A minimum follow-up of 10 years until December 31, 2015, was completed for all participants.

50-74y

T0 (baseline) → T1 (1y) → T2 (3y) → T4 (5,5y)

Characteristic	Screening Group (N=6583)	Control Group (N=6612)
Age		
Median (IQR) — yr	58 (55–63)	58 (54–63)
Range — yr	46–76	34–89
Distribution — no./total no. (%)†		
<50 yr	3/6560 (<0.1)	6/6571 (0.1)
50–54 yr	1611/6560 (24.6)	1694/6571 (25.8)
55–59 yr	2226/6560 (33.9)	2231/6571 (34.0)
60–64 yr	1554/6560 (23.7)	1475/6571 (22.4)
65–69 yr	797/6560 (12.1)	781/6571 (11.9)
70–74 yr	329/6560 (5.0)	337/6571 (5.1)
≥75 yr	40/6560 (0.6)	47/6571 (0.7)
Pack-yr of smoking‡		
Median (IQR)	38.0 (29.7–49.5)	38.0 (29.7–49.5)
Range	0.4–159.5	1.3–156.0
Cigarettes smoked per day — no./total no. (%)		
≤10	20/6565 (0.3)	18/6596 (0.3)
11–15	1470/6565 (22.4)	1437/6596 (21.8)
16–20	1859/6565 (28.3)	1859/6596 (28.2)
21–25	1732/6565 (26.4)	1779/6596 (27.0)
26–30	669/6565 (10.2)	723/6596 (11.0)
31–40	454/6565 (6.9)	437/6596 (6.6)
>40	361/6565 (5.5)	343/6596 (5.2)
Duration of smoking — no./total no. (%)		
≤25 yr	25/6563 (0.4)	21/6594 (0.3)
26–30 yr	657/6563 (10.0)	722/6594 (10.9)
31–35 yr	1652/6563 (25.2)	1700/6594 (25.8)
36–40 yr	2030/6563 (30.9)	2105/6594 (31.9)
41–45 yr	1451/6563 (22.1)	1317/6594 (20.0)
≥45 yr	748/6563 (11.4)	729/6594 (11.1)
Age at initiation of smoking — no./total no. (%)		
<15 yr	1153/6560 (17.6)	1141/6588 (17.3)
15–29 yr	5376/6560 (82.0)	5407/6588 (82.1)
≥30 yr	31/6560 (0.5)	40/6588 (0.6)
Smoking status — no./total no. (%)		
Current	3643/6566 (55.5)	3611/6595 (54.8)
Former	2923/6566 (44.5)	2984/6595 (45.2)
Years since cessation of smoking — no./total no. (%)		
<1	489/2908 (16.8)	493/2963 (16.6)
1–5	1316/2908 (45.3)	1334/2963 (45.0)
6–10	1054/2908 (36.2)	1096/2963 (37.0)
>10	49/2908 (1.7)	40/2963 (1.3)

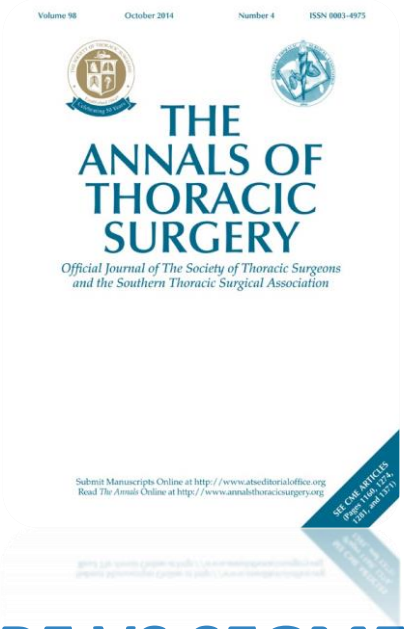
Table 3. Lung-Cancer Stage and Histologic Type of All … or on December 31, 2015.*

Variable	Screening-Detec Lung Cancer (N=203)†
Stage	
IA	95 (46.8)
IB	24 (11.8)
IIA	8 (3.9)
IIB	11 (5.4)
IIIA	20 (9.9)
IIIB	13 (6.4)
IV	19 (9.4)
Unknown	13 (6.4)
Histologic type‡	
Adenocarcinoma	123 (60.6)
Squamous-cell carcinoma	39 (19.2)
Small-cell carcinoma	13 (6.4)
NSCLC	8 (3.9)
Other	20 (9.9)

Table 4. Cause of Death of Deceased Male Participants at 10 Years of Follow-up or until the Data-Cutoff Date of December 31, 2015.*

Variable	Screening Group (N=868)	Control Group (N=860)	Total (N=1728)	Rate Ratio (95% CI)
		number (percent)		
Cause of death — no. (%)				
Lung cancer	160 (18.4)	210 (24.4)	370 (21.4)	0.76 (0.62–0.94)
No lung cancer after cause-of-death review, no other specification	6 (0.7)	11 (1.3)	17 (1.0)	0.55 (0.17–1.61)
Other neoplasm	318 (36.6)	289 (33.6)	607 (35.1)	1.10 (0.94–1.30)
Cardiovascular disease	189 (21.8)	181 (21.0)	370 (21.4)	1.05 (0.85–1.29)
Respiratory disease	42 (4.8)	43 (5.0)	85 (4.9)	0.98 (0.62–1.53)
Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	37 (4.3)	20 (2.3)	57 (3.3)	1.86 (1.05–3.37)
Diseases of the digestive system	30 (3.5)	21 (2.4)	51 (3.0)	1.43 (0.79–2.63)
External causes of illness and death	24 (2.8)	19 (2.2)	43 (2.5)	1.27 (0.67–2.45)
Endocrine, nutritional, and metabolic diseases	21 (2.4)	9 (1.0)	30 (1.7)	2.34 (1.03–5.80)
Diseases of the nervous system	9 (1.0)	19 (2.2)	28 (1.6)	0.48 (0.19–1.10)
Other cause of death	26 (3.0)	28 (3.3)	54 (3.1)	0.93 (0.52–1.65)
Unknown	6 (0.7)	10 (1.2)	16 (0.9)	0.60 (0.18–1.83)
Total person-yr at risk	62,298	62,484	124,782	
All-cause mortality — deaths per 1000 person-yr	13.93	13.76	13.85	1.01 (0.92–1.11)

Years since Randomization



LOBE VS SEGMENT

GENERAL THORACIC

RICHARD E. CLARK MEMORIAL PAPER FOR GENERAL THORACIC SURGERY

Equivalent Survival Between Lobectomy and Segmentectomy for Clinical Stage IA Lung Cancer

Mark W. Onaitis, MD, Anthony P. Furnary, MD, Andrzej S. Kosinski, PhD, Liqi Feng, MS, Daniel Boffa, MD, Betty C. Tong, MD, Patricia Cowper, PhD, Jeffrey P. Jacobs, MD, Cameron D. Wright, MD, Robert Habib, PhD, Joe B. Putnam, Jr, MD, and Felix G. Fernandez, MD, MSc

Division of Cardiothoracic Surgery, University of California San Diego, La Jolla, California; Starr-Wood Cardiac Group, Portland, Oregon; Duke Clinical Research Institute, Duke University, Durham, North Carolina; Division of Cardiothoracic Surgery, Yale University, New Haven, Connecticut; Division of Cardiothoracic Surgery, Duke University, Durham, North Carolina; Johns Hopkins All Children's Heart Institute, St Petersburg, Florida; Division of Thoracic Surgery, Massachusetts General Hospital, Boston, Massachusetts; The Society of Thoracic Surgeons, Chicago, Illinois; Baptist MD Anderson Cancer Center, Jacksonville, Florida; and Division of Cardiothoracic Surgery, Emory University, Atlanta, Georgia

Background. The oncologic efficacy of segmentectomy is controversial. We compared long-term survival in clinical stage IA (T1N0) Medicare patients undergoing lobectomy and segmentectomy in The Society of Thoracic Surgeons database.

Methods. The Society of Thoracic Surgeons General Thoracic Surgery Database was linked to Medicare data in 14,286 lung cancer patients who underwent segmentectomy (n = 1654) or lobectomy (n = 12,632) for clinical stage IA disease from 2002 to 2015. Cox regression was used to create a long-term survival model. Patients were then propensity matched on demographic and clinical variables to derive matched pairs.

Results. In Cox modeling segmentectomy was associated with survival similar to lobectomy in the entire cohort (hazard ratio, 1.04; 95% confidence interval, 0.89-1.20; P = .64) and in the matched subcohort. A subanalysis restricted to the 2009 to 2015 population (n = 11,811), when T1a tumors were specified and positron emission tomography results and mediastinal staging procedures were accurately recorded in the database, also showed that segmentectomy and lobectomy continue to have similar survival (hazard ratio, 1.00; 95% confidence interval, 0.87-1.16). Subanalysis of the pathologic N0 patients demonstrated the same results.

Conclusions. Lobectomy and segmentectomy for early-stage lung cancer are equally effective treatments with similar survival. Surgeons from The Society of Thoracic Surgeons database appear to be selecting patients appropriately for sublobar procedures.

(Ann Thorac Surg 2020;110:1882-91)

Despite the Lung Cancer Study Group setting the standard of care of lobectomy for stage IA lung cancer,[1] sublobar resection remains prevalent. Multiple studies have demonstrated conflicting survival results: no difference for selected patients[2-18] and survival improvement for lobectomy.[19-27] Thus significant controversy exists about whether segmentectomy is an adequate cancer operation for clinical stage IA patients.

Lung cancer patient records in the The Society of Thoracic Surgeons General Thoracic Surgery Database (STS-GTSD) were linked to data from the Centers for Medicare & Medicaid Services.[28] This has allowed identification of factors that predict survival in patients over age 65 years. In this analysis segmentectomy has a hazard ratio of 1.08 in the Cox model with lobectomy as the reference.[29] Our objective in the present study was to examine the long-term survival in Medicare clinical stage IA patients in the STS database. We hypothesize that the survival will be equivalent between the procedures.

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Address correspondence to Dr Onaitis, Division of Cardiothoracic Surgery, University of California San Diego, 9300 Campus Point Dr, Mail code 7892, La Jolla, CA 92037; email: monaitis@ucsd.edu.

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Patients and Methods

Population and Linkage

The STS-GTSD was queried for all patients treated with lobectomy or segmentectomy for primary clinical stage IA (American Joint Committee on Cancer, seventh edition) non-small cell lung cancer from January 1, 2002 to December 31, 2012. This study encompassed several versions of the STS-GTSD data collection instruments (v2.07, v2.081, and v2.2). The STS-GTSD has been externally audited since 2010,[30] validating the accuracy and completeness of the data. Patients were excluded if they had

STS database 2002-15

cIA

>65y

Entire population: Clinical stage IA, 2002-2015
n=14,286 Segmentectomy n=1654
Lobectomy n=12,632
11.6%

→ **Matched analysis n=2952**
Segmentectomy n=1476
Lobectomy n=1476

Restricted population: Clinical stage IA, 2009-2015
n=11,811 Segmentectomy n=1402
Lobectomy n=10,409

→ **Matched analysis n=2354**
Segmentectomy n=1177
Lobectomy n=1177

Clinical stage IA 2009-2015 cT1a n=7318
Segmentectomy n=998
Lobectomy n=6320

→ **Matched analysis n=1676**
Segmentectomy n=838
Lobectomy n=838

Clinical stage IA 2009-2015 cT1b n=4493
Segmentectomy n=404
Lobectomy n=4089

→ **Matched analysis n=678**
Segmentectomy n=339
Lobectomy n=339

Table 3. Predictors of Survival for the Entire Population

Characteristic	Univariate Hazard Ratio (95% Confidence Interval)	P	Multivariable Hazard Ratio (95% Confidence Interval)	P
American Society of Anesthesiologists group		<.001		<.001
I-II	1.00		1.00	
III	1.62 (1.40-1.86)		1.32 (1.17-1.48)	
IV-V	2.55 (2.13-3.05)		1.61 (1.39-1.86)	
Age group		<.001		<.001
65-69 y	1.00		1.00	
70-74 y	1.28 (1.18-1.38)		1.25 (1.15-1.36)	
75-79 y	1.48 (1.36-1.62)		1.50 (1.37-1.65)	
80+ y	2.01 (1.83-2.20)		2.19 (1.96-2.45)	
Gender		<.001		<.001
Male	1.00		1.00	
Female	0.66 (0.62-0.71)		0.73 (0.67-0.79)	
Body mass index group		<.001		<.001
18.5-25	1.00		1.00	
<18.5	1.48 (1.21-1.81)		1.59 (1.28-1.97)	
25-30	0.92 (0.85-1.00)		0.85 (0.79-0.93)	
30-35	0.87 (0.80-0.94)		0.83 (0.76-0.91)	
>35	0.94 (0.82-1.07)		0.90 (0.79-1.02)	
Zubrod		<.001		<.001
0	1.00		1.00	
1	1.38 (1.27-1.49)		1.22 (1.13-1.32)	
2-5	2.28 (1.98-2.64)		1.83 (1.46-1.94)	
Coronary artery disease	1.52 (1.42-1.62)	<.001	1.08 (0.99-1.18)	.072
Cardiovascular disease	1.50 (1.35-1.66)	<.001	1.16 (1.04-1.30)	<.001
Congestive heart failure	1.97 (1.69-2.29)	<.001	1.51 (1.28-1.79)	<.001
Diabetes mellitus	1.26 (1.18-1.36)	<.001	1.11 (1.03-1.19)	.004
Steroids	1.61 (1.38-1.88)	<.001	1.49 (1.27-1.76)	<.001
Hypertension	1.20 (1.12-1.30)	<.001	1.04 (0.95-1.13)	.399
Peripheral vascular disease	1.77 (1.62-1.92)	<.001	1.28 (1.17-1.41)	<.001
Chronic kidney disease	2.29 (1.86-2.81)	<.001	1.54 (1.27-1.86)	<.001
Forced expiratory volume in 1 second, % predicted		<.001		<.001
>80	1.00		1.00	
60-80	1.41 (1.30-1.53)		1.24 (1.15-1.34)	
40-60	1.70 (1.55-1.85)		1.41 (1.27-1.56)	
<40	1.73 (1.43-2.09)		1.42 (1.17-1.72)	
Smoking		<.001		<.001
Never	1.00		1.00	
Past	1.79 (1.59-2.01)		1.54 (1.35-1.75)	
Current	2.18 (1.92-2.47)		1.95 (1.68-2.26)	
Race		.227		.422
White	1.00		1.00	
Black	1.13 (0.98-1.30)		1.10 (0.95-1.26)	
Other	1.16 (0.74-1.83)		1.07 (0.64-1.76)	
Procedure		.236		.637
Lobectomy	1.00		1.00	
Segmentectomy	1.10 (0.94-1.28)		1.04 (0.89-1.20)	
Approach				
Open	1.00		1.00	
Video-assisted thoracoscopic surgery	0.77 (0.71-0.83)	<.001	0.86 (0.80-0.94)	<.001

Table 4. Demographic Characteristics of Matched Cohorts in the Entire Population

Characteristic	Lobectomy (n = 1476)	Segmentectomy (n = 1476)	Overall (N = 2952)	P
Age, y	73 (69, 78)	73 (69, 78)	73 (69, 78)	.63
Era				.999
2002-2008	205 (14)	205 (14)	410 (14)	
2009-2015	1271 (86)	1271 (86)	2,542 (86)	
Gender				.82
Male	598 (41)	604 (41)	1202 (41)	
Female	878 (59)	872 (59)	1750 (59)	
Race				.14
White	1400 (95)	1387 (94)	2787 (94)	
African American	66 (5)	84 (6)	150 (5)	
Other	10 (0.7)	5 (0.3)	15 (0.5)	
American Society of Anesthesiologists group				.40
I-II	204 (14)	195 (13)	399 (14)	
III	1-169 (79)	1-159 (79)	2328 (79)	
IV-V	103 (7)	122 (8)	225 (8)	
Forced expiratory volume in 1 second, % predicted				.87
<40	50 (3)	55 (4)	105 (4)	
40-60	285 (19)	284 (19)	569 (19)	
60-80	419 (28)	433 (29)	852 (29)	
>80	722 (49)	704 (48)	1,426 (48)	
Body mass index, kg/m^2				.97
<18.5	29 (2)	29 (2)	58 (2)	
18.5-25	470 (32)	486 (33)	956 (32)	
25-30	623 (42)	605 (41)	1228 (42)	
30-35	235 (16)	236 (16)	471 (16)	
>35	119 (8)	120 (8)	239 (8)	
Coronary artery disease	376 (25)	380 (26)	756 (26)	.87
Congestive heart failure	55 (4)	62 (4)	117 (4)	.51
Cigarette use				.86
Never	206 (14)	196 (13)	402 (14)	
Past (>1 month)	1002 (68)	1012 (69)	2014 (68)	
Current	268 (18)	268 (18)	536 (18)	
Cardiovascular disease	132 (9)	133 (9)	265 (9)	.95
Diabetes mellitus	246 (17)	255 (17)	501 (17)	.66
Hypertension	978 (66)	968 (66)	1946 (66)	.70
Peripheral vascular disease	120 (8)	144 (10)	264 (9)	.12
Chronic kidney disease	30 (2)	33 (2)	63 (2)	.70
Steroid use	42 (3)	47 (3)	89 (3)	.59
Zubrod score				.34
0	734 (50)	701 (48)	1435 (49)	
1	699 (47)	722 (49)	1421 (48)	
2-5	43 (3)	53 (4)	96 (3)	
Operative mortality	23 (1.6)	14 (1)	37 (1.2)	.14
Major respiratory morbidity	127 (8.6)	94 (6.4)	221 (7.5)	.02
Video-assisted thoracoscopic surgery	1033 (70)	1025 (69)	2058 (70)	.75
Pathologic N stage				<.001
N0	1309 (89)	1389 (94)	2698 (91)	
N1	109 (7)	52 (4)	161 (5)	
N2	58 (4)	33 (2)	91 (3)	
N3	0	2 (0.1)	2 (0.1)	

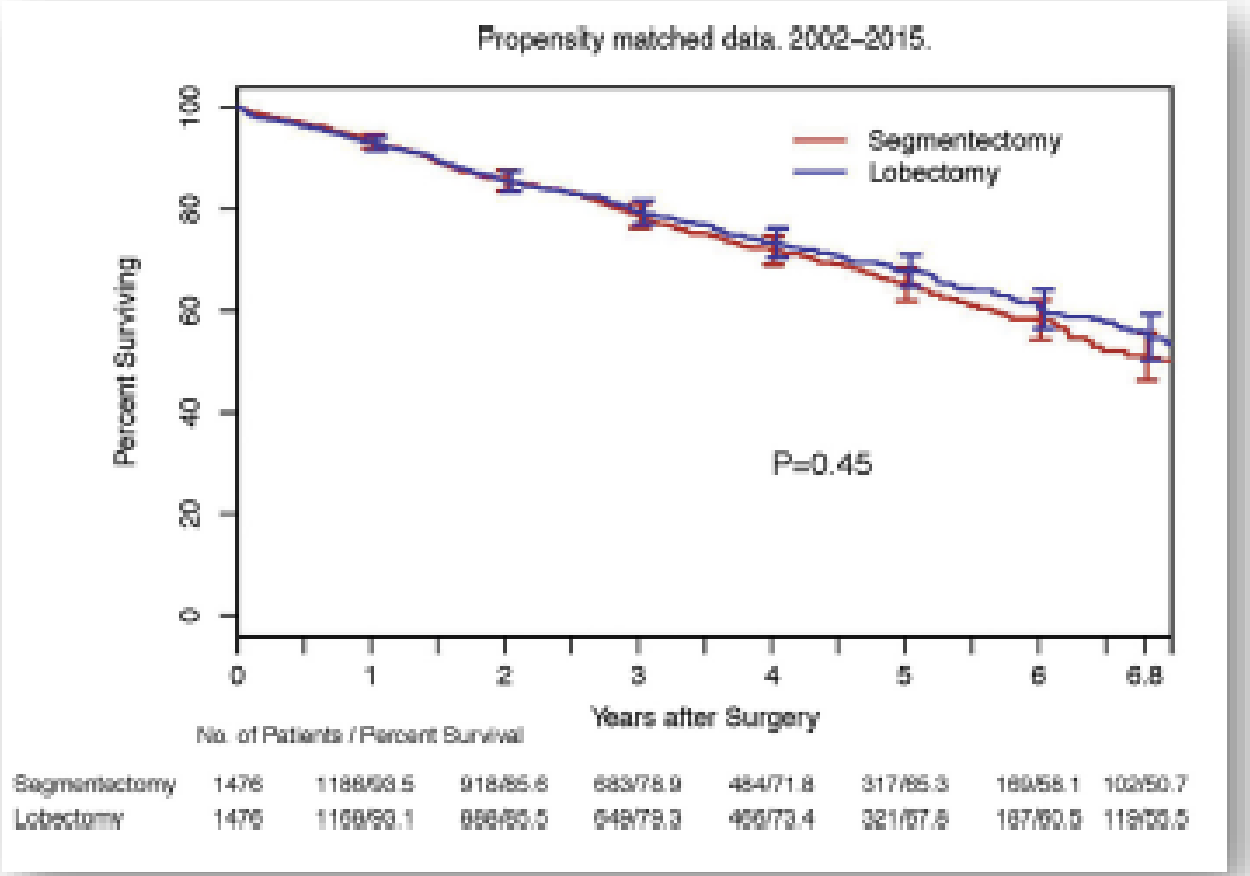
Values are n (%) or median (25th, 75th).

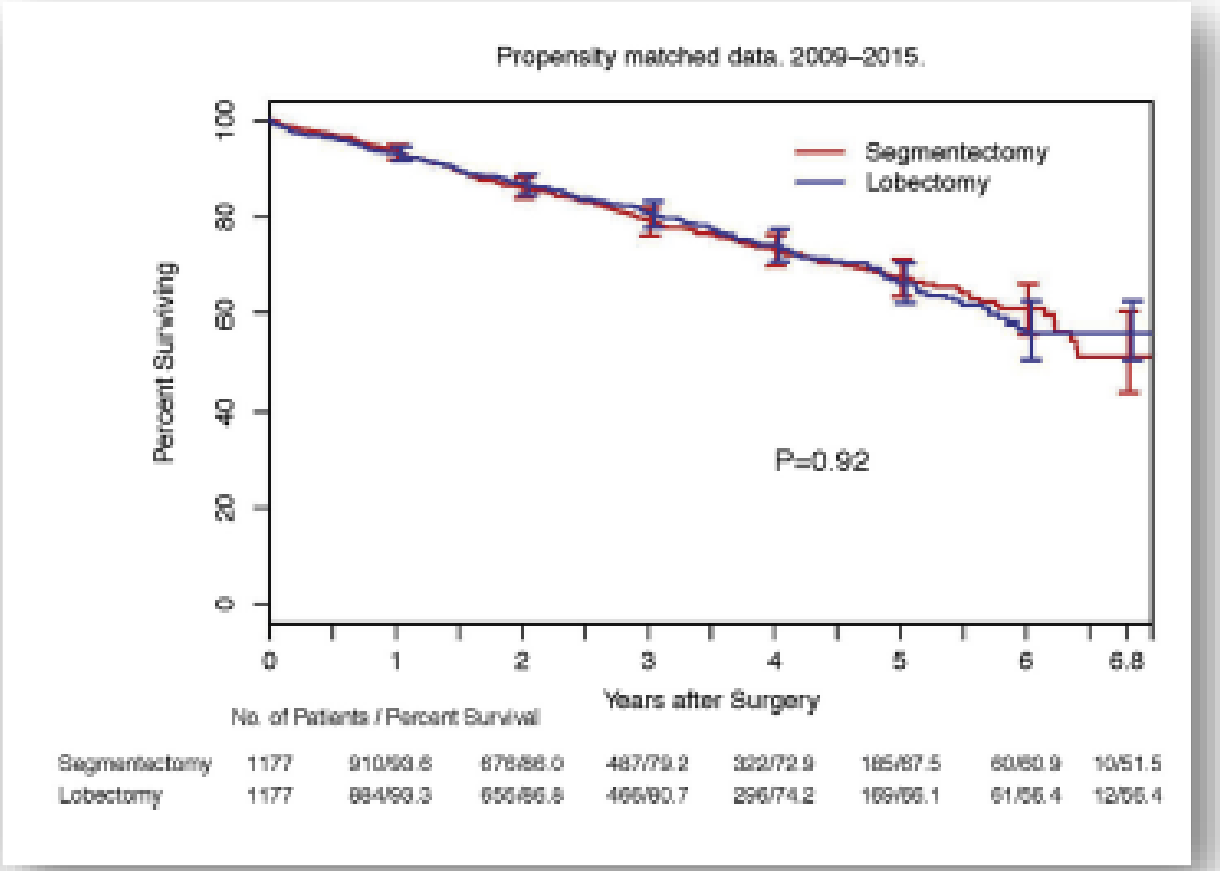
Table 5. Upstaging Rates in Matched Cohorts

Level	Entire Population (2002-2015) (n = 1476 per group)	Late Era Restricted Population (2009-2015) (n = 1177 per group)	T1a Patients (2009-2015) (n = 838 per group)	T1b Patients (2009-2015) (n = 339 per group)
N1 upstaging				
Lobectomy	7.4	6.0	5.8	8.6
Segmentectomy	3.5	3.3	2.7	4.7
N2 upstaging				
Lobectomy	3.9	4.1	3.8	4.4
Segmentectomy	2.2	1.8	1.7	2.1

Values are percents.

Mayor upstaging en Lobectomias pero no traducción en SV





No diferencias en SV ni en cohorte completa ni en periodo 2009-15

Table 6. Predictors of Survival, 2009-2015 pN0 Population

Variable	Category	Unadjusted Hazard Ratio	Unadjusted 95% Confidence Interval	Unadjusted P	Adjusted (n = 9142, c = 0.6858) Hazard Ratio	Adjusted (n = 9142, c = 0.6858) 95% Confidence Interval	Adjusted (n = 9142, c = 0.6858) P
American Society of Anesthesiologists class	I - II	1		<.001	1		<.001
	III	1.93	(1.63-2.29)		1.36	(1.15-1.61)	
	IV - V	3.23	(2.62-3.99)		1.63	(1.30-2.03)	
Age	65-69	1		<.001	1		<.001
	70-74	1.26	(1.13-1.41)		1.21	(1.07-1.37)	
	75-79	1.5	(1.32-1.70)		1.49	(1.30-1.71)	
	≥80	2.06	(1.81-2.34)		2.21	(1.88-2.59)	
Body mass index	18.5 to < 25.0	1		<.001	1		<.001
	<18.5	1.51	(1.12-2.03)		1.6	(1.15-2.21)	
	25.0 to <30.0	0.83	(0.74-0.92)		0.76	(0.68-0.85)	
	30.0 to <35.0	0.8	(0.71-0.90)		0.78	(0.68-0.89)	
	>35.0	0.83	(0.69-0.99)		0.72	(0.60-0.86)	
Cardiovascular disease	0 = No	1		<.001	1		.016
	1 = Yes	1.54	(1.33-1.78)		1.22	(1.04-1.44)	
Chronic kidney disease	0 = No	1		<.001	1		<.001
	1 = Yes	2.62	(2.03-3.37)		1.68	(1.27-2.22)	
Cigarette use	1 = Never smoked	1		<.001	1		<.001
	2 = Past smoker (stopped more than 1 month before operation)	1.98	(1.70-2.31)		1.55	(1.30-1.86)	
	3 = Current smoker	2.5	(2.11-2.97)		2.01	(1.64-2.47)	
Congestive heart failure	0 = No	1		<.001	1		<.001
	1 = Yes	2.01	(1.65-2.46)		1.48	(1.20-1.81)	
Coronary artery disease	0 = No	1		<.001	1		.009
	1 = Yes	1.65	(1.50-1.81)		1.17	(1.04-1.32)	
Diabetes mellitus	0 = No	1		<.001	1		.017
	1 = Yes	1.27	(1.15-1.41)		1.14	(1.02-1.27)	
Forced expiratory volume in 1 second Predicted	80% or more	1		<.001	1		<.001
	<40%	2.09	(1.52-2.88)		1.43	(1.01-2.02)	
	40%-60%	1.72	(1.51-1.95)		1.35	(1.15-1.59)	
	60%-80%	1.45	(1.32-1.60)		1.24	(1.12-1.39)	
Gender	1 = Male	1		<.001	1		<.001
	2 = Female	0.63	(0.59-0.69)		0.68	(0.62-0.75)	
Hypertension	0 = No	1		<.001	1		.076
	1 = Yes	1.31	(1.22-1.41)		1.08	(0.99-1.18)	
Invasive mediastinal staging	0	1		<.001	1		.012
	1	1.23	(1.10-1.37)		1.15	(1.03-1.28)	
Video-assisted thoracoscopic surgery	0 = No	1		<.001	1		.016
	1 = Yes	0.78	(0.71-0.87)		0.88	(0.80-0.98)	
Positron emission tomography or positron emission tomography/computed tomography	0	1		<.001	1		.002
	1	1.37	(1.18-1.60)		1.26	(1.08-1.46)	
Peripheral vascular disease	0 = No	1		<.001	1		<.001
	1 = Yes	1.82	(1.62-2.05)		1.29	(1.13-1.46)	
Primary procedure	Lobectomy	1		.106	1		.331
	Segmentectomy	1.12	(0.98-1.29)		1.08	(0.93-1.25)	
Race	White	1		.104	1		.177
	Black/African American	1.21	(1.02-1.45)		1.18	(0.98-1.43)	
	Other	1.07	(0.50-2.28)		0.69	(0.18-2.65)	
Steroid use	0 = No	1		<.001	1		<.001
	1 = Yes	1.83	(1.52-2.20)		1.5	(1.23-1.83)	
Zubrod	0	1		<.001	1		<.001
	1	1.45	(1.30-1.61)		1.26	(1.14-1.40)	
	2-5	2.75	(2.26-3.35)		1.95	(1.57-2.44)	

Conclusiones

- La SA no muestra diferencias en OS frente a lobectomía en estadio cIA >65 años, a pesar de un mayor upstaging ganglionar.
- La mayor proporción de pacientes fueron del periodo 2009-15 donde hay datos de PET, estadificación ganglionar invasiva.
- Limitaciones:
  - Edad >65y
  - Cirujanos torácicos de la STS
  - Ausencia de datos relevantes (diferenciación, SUVmáx, análisis genético/genómico)
  - Datos sobre recurrencia y DFS ausentes
  - Factores de confusión

IoNESCO – IFCT 1601

VIRTUAL 2020 ESMO congress

IoNESCO IFCT-1601 Study design

IFCT

Immune Neoajuvant therapy in Early Stage Non Small Cell CarcinOma

- Stage IB ≥ 4cm, II, IIIA non-N2 NSCLC
- ECOG 0 or 1
- age ≥ 18 years
- pre-therapeutic tissue required

INCLUSION

Primary Endpoint

% of complete surgical resection (R0)

Secondary Endpoints

90-day postoperative mortality, safety,

OS, DFS, RR (RECIST 1.1), MPR,

time between 1st infusion and surgery

Hypotheses

A complete resection rate (theoretical feasibility) ≤ 85% was considered unacceptable

Two-step Fleming procedure

H0 = 85%, H1 = 95% (power 90%, α=5%)

Planned Sample Size: 81 patients

(tumor + nodes) required

	N=50 (ITT)
Age (median, range)	61.0 [46 -80]
Male / female	35 (70%) / 15 (30%)
Smokers / never smokers	47 (94%) / 3 (6%)
ECOG 0 / 1	40 (80%) / 10 (20%)
Histology adenocarcinoma squamous other	 25 (50%) 21 (42%) 4 (8%)
Stage IB / IIA / IIB / IIIA	 5 (10%) / 14 (28%) / 29 (58%) / 2 (4%)
Surgical procedures lobectomy bilobectomy pneumonectomy	 32 (72.7%) 3 (6.8%) 9 (20.5%)
Number of pts receiving 3 durvalumab doses	44 (88%)

VIRTUAL 2020 ESMO congress

IFCT

Primary endpoint:
% of complete surgical resection (R0)

	N=46 (Eligible Population)
Complete resection (R0)	41 (89.1%)
Microscopically incomplete resection (R1)	2 (4.3%)
Not evaluable	3* (6.5%)

Time between 1st infusion and surgery (mean ± SD): 37 ± 4 days

* : 1 not operated (progression before surgery), 2 exploratory thoracotomies (pleural/oesophagial invasion)

IFCT

VIRTUAL 2020

Secondary endpoints : Radiographic and Pathological Response

RECIST 1.1

	N	%
CR	0	0
PR	4	8.7
SD	36	78.3
PD	6*	13
	46	100

*One patient had pseudoprogression

Major Pathologic Response (MPR)
defined as less than 10% of RVT

	N=43*
RVT (Mean±SD)	34.7% ± 22
RVT	
0%	3 (7)
0-10%	5 (11.6)
>10%	35 (81.4)

*Ongoing analysis *n=1 and n=2* not operated

Association between pathological and radiographic response

	RVT		P value
	0-10%	>10%	
PR	3 (37.5%)	1 (2.9%)	0.028
SD	4 (50%)	29 (82.9%)	
PD	1 (12.5%)*	5 (14.3%)	

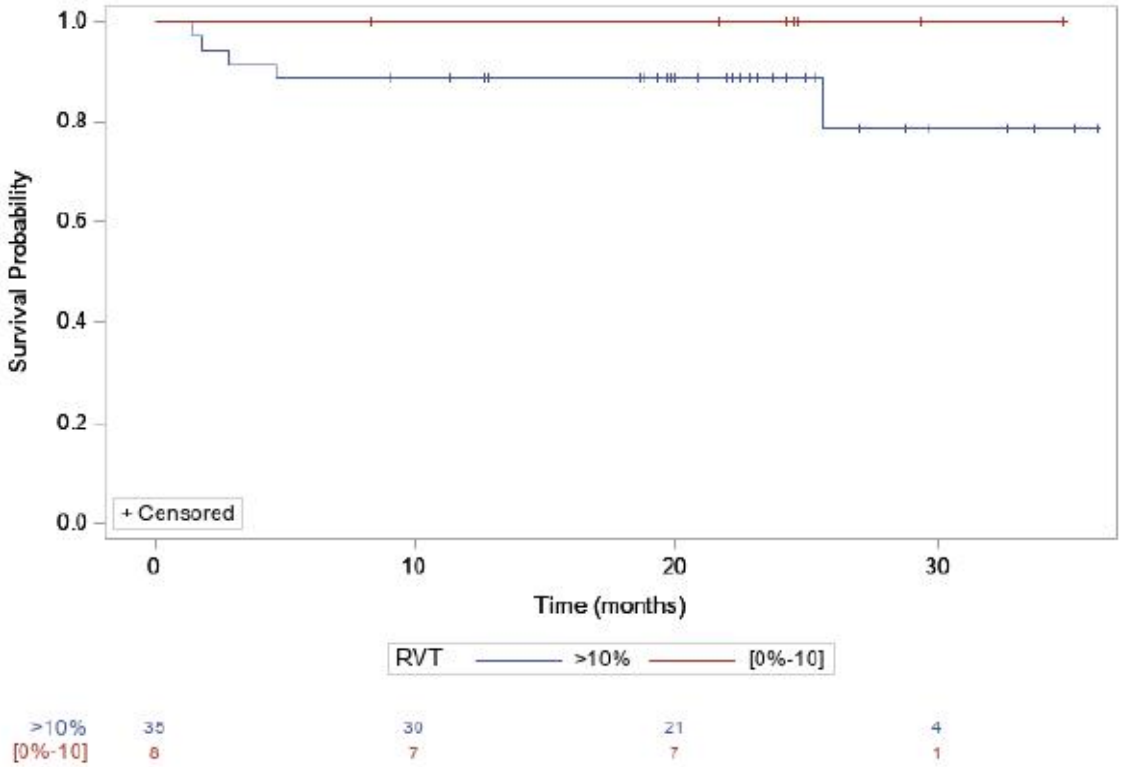
*This patient had pseudoprogression with mediastinal nodal flare-up (granulomas)

PR: 8.7%

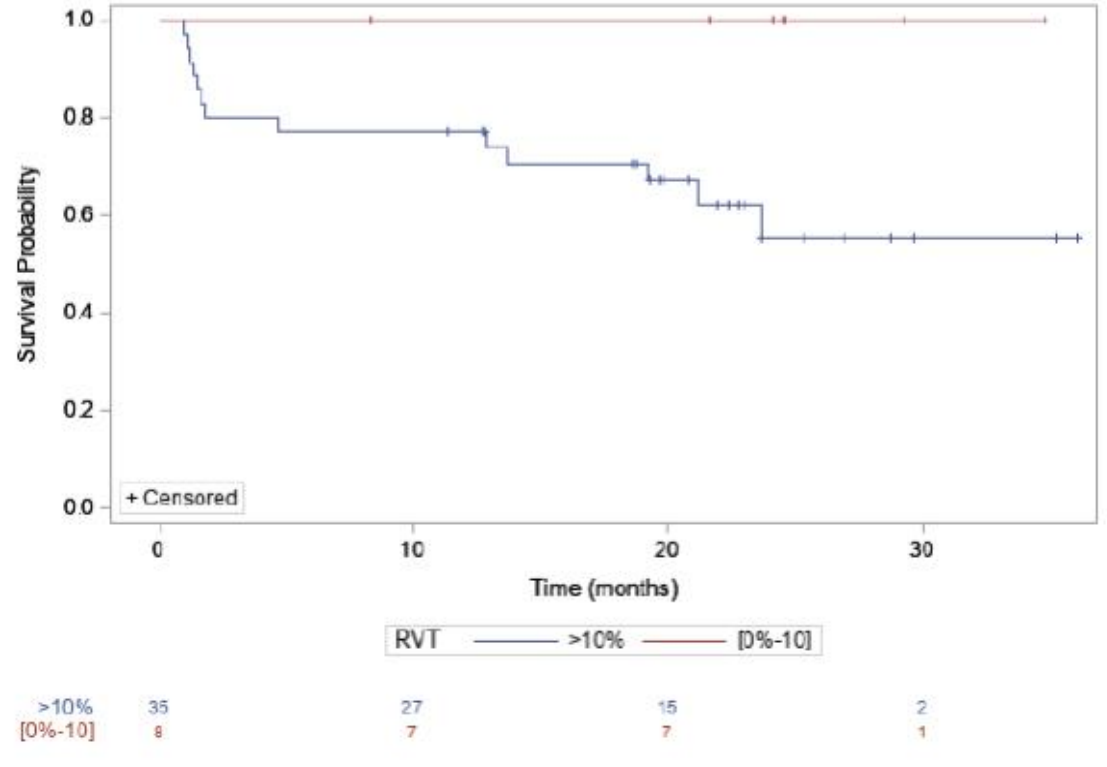
MPR: 8 (18.6%)

MPR and outcome : OS and DFS

OS



DFS



RVT	0%-10%, N=8	> 10%, N=35
Event : N (%)	0 (0)	5 (14.3%)
Median OS: mo [95% CI]	NR	NR
12-m OS: % [95% CI]	100%	88.6 [72.4-95.5]
p=0.2777		

RVT	0%-10%, N=8	> 10%, N=35
Event: N (%)	0 (0)	13 (37.1%)
Median DFS: mo [95% CI]	NR	NR
12-m DFS: % [95% CI]	100%	77.1 [59.5-87.9]
p=0.0450		

Secondary endpoints: durvalumab safety

	N=48 patients that received Durvalumab					
Adverse events	**Any Grade**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Any	**16 (33.3%)**	**11 (22.9%)**	**5 (10.4%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**
Serious	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**
General	9 (18.8%)	7 (14.6%)	2 (4.2%)	0 (0%)	0 (0%)	0 (0%)
Gastrointestinal	7 (14.6%)	6 (12.5%)	1 (2.1%)	0 (0%)	0 (0%)	0 (0%)
Skin and subcutaneous	4 (8.3%)	2 (4.2%)	2 (4.2%)	0 (0%)	0 (0%)	0 (0%)
Ear and labyrinth	2 (4.2%)	2 (4.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Thyroid	2 (4.2%)	2 (4.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Metabolism	2 (4.2%)	2 (4.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Musculoskeletal	2 (4.2%)	2 (4.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infections	1 (2.1%)	1 (2.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Reason for premature termination of trial: 90-day postoperative mortality

Study was stopped because of an excess in 90-day postoperative mortality (4 deaths, 9%)

age	gender	smoking	stage	comorbidities	surgical procedure	surgical resection / histology	RVT	cause of death* (time from surgery)
63	F	Yes	IIB	Arterial hypertension Severe COPD	Lobectomy	R0 adeno	>10%	Sudden death at home (40 days)
49	F	Yes	IIB	No	Lobectomy	R0 squamous	>10%	Surgical procedure complication (45 days)
76	M	Yes	IIA	Arterial hypertension Diabetes	Pneumonectomy	R0 squamous	>10%	Tracheal Fistula (8 days)
78	M	Yes	IIB	Arterial hypertension, Ischemic Heart disease Peripheral arterial disease	Lobectomy	R0 squamous	>10%	Respiratory Distress (21 days)

These deaths are not related to durvalumab

ADAURA

PRESENTED AT: 2020 ASCO ANNUAL MEETING

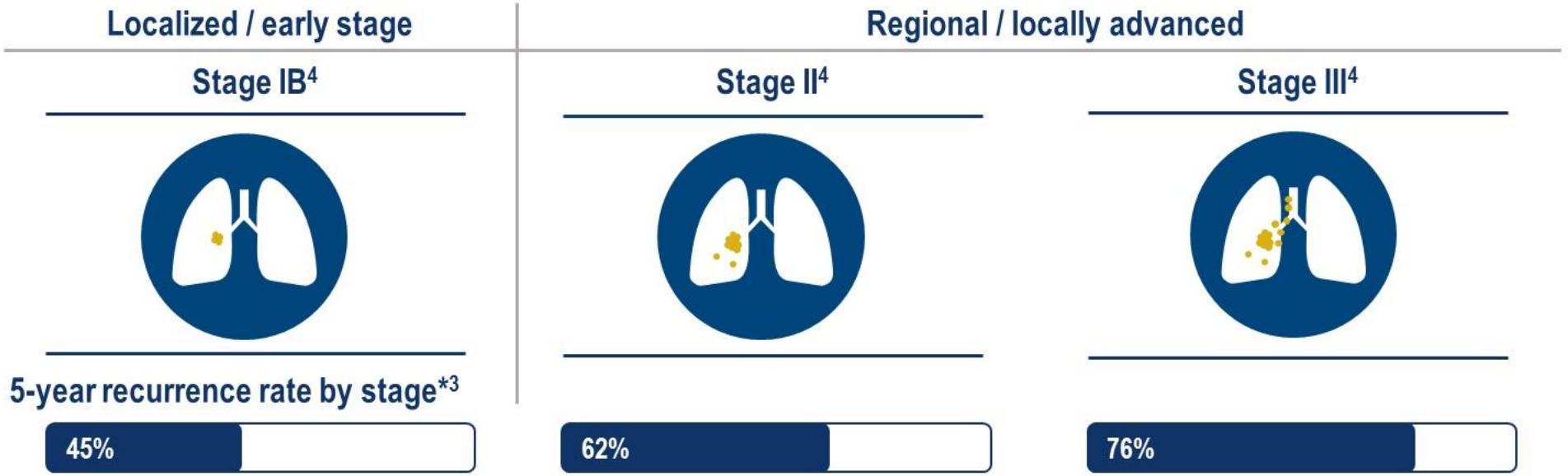
Osimertinib as adjuvant therapy in patients with stage IB–IIIA EGFR mutation positive NSCLC after complete tumor resection: ADAURA

Roy S. Herbst[1], Masahiro Tsuboi[2], Thomas John[3], Christian Grohe[4], Margarita Majem[5], Jonathan W. Goldman[6], Sang-We Kim[7], Dominika Marmol[8], Yuri Rukazenkov[8], Yi-Long Wu[9]

[1] Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA; [2] Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [3] Department of Medical Oncology, Austin Health, Melbourne, Australia; [4] Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; [5] Medical Oncology Services, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6] David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA; [7] Department of Oncology, Asan Medical Center, Seoul, South Korea; [8] Oncology Research & Development, AstraZeneca, Cambridge, United Kingdom; [9] Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China

Outcomes in early stage NSCLC need to be improved

- Surgery is the primary treatment for patients with early stage NSCLC[1]
- Adjuvant cisplatin-based chemotherapy is recommended for patients with resected stage II–IIIA NSCLC and select patients with stage IB disease[2]
  - Results from large randomized trials and meta analyses showed a 5-year OS benefit with adjuvant chemotherapy in patients with early stage NSCLC, OS HR 0.89 (95% CI 0.82, 0.96); DFS also favored adjuvant chemotherapy, DFS HR 0.84 (95% CI 0.78, 0.91)[3]
- Overall, disease recurrence or death following surgery and adjuvant chemotherapy remains high across disease stages[3]



1. Chansky et al. J Thorac Oncol 2017;12:1109–1121; 2. Kris et al. J Clin Oncol 2017;35:2960–2974; 3. Pignon et al. J Clin Oncol 2008;26:3552–3559; 4. AJCC Cancer Staging Manual. 7th edn. Springer, 2010.
*Median follow up: 5.2 years, data based on AJCC Staging Manual 6th edition.
AJCC, American Joint Committee on Cancer; CI, confidence interval; DFS, disease-free survival; HR, hazard ratio; OS, overall survival.

ADAURA Phase III double-blind study design

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
- ≥18 years (Japan / Taiwan: ≥20)
- WHO performance status 0 / 1
- Confirmed primary non-squamous NSCLC Ex19del / L858R‡
- Brain imaging, if not completed pre-operatively
- Complete resection with negative margins§
- Max. interval between surgery and randomization:
  - 10 weeks without adjuvant chemotherapy
  - 26 weeks with adjuvant chemotherapy

Stratification by:
stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
race (Asian vs non-Asian)

Randomization 1:1 (N=682)

- Osimertinib 80 mg, once daily
- Placebo, once daily

Planned treatment duration: 3 years

Treatment continues until:
- Disease recurrence
- Treatment completed
- Discontinuation criterion met

Follow up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

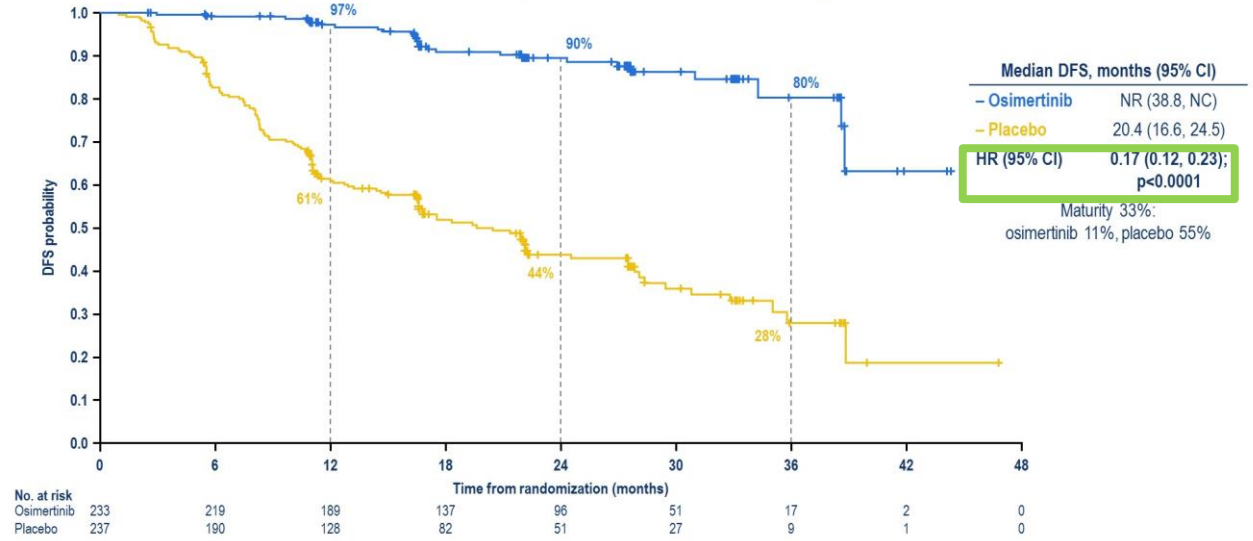
Endpoints

- **Primary**: DFS, by investigator assessment, in stage II/IIIA patients; designed for superiority under the assumed DFS HR of 0.70
- **Secondary**: DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life

- **Following IDMC recommendation, the study was unblinded early due to efficacy; here we report an unplanned interim analysis**
- **At the time of unblinding the study had completed enrollment and all patients were followed up for at least 1 year**

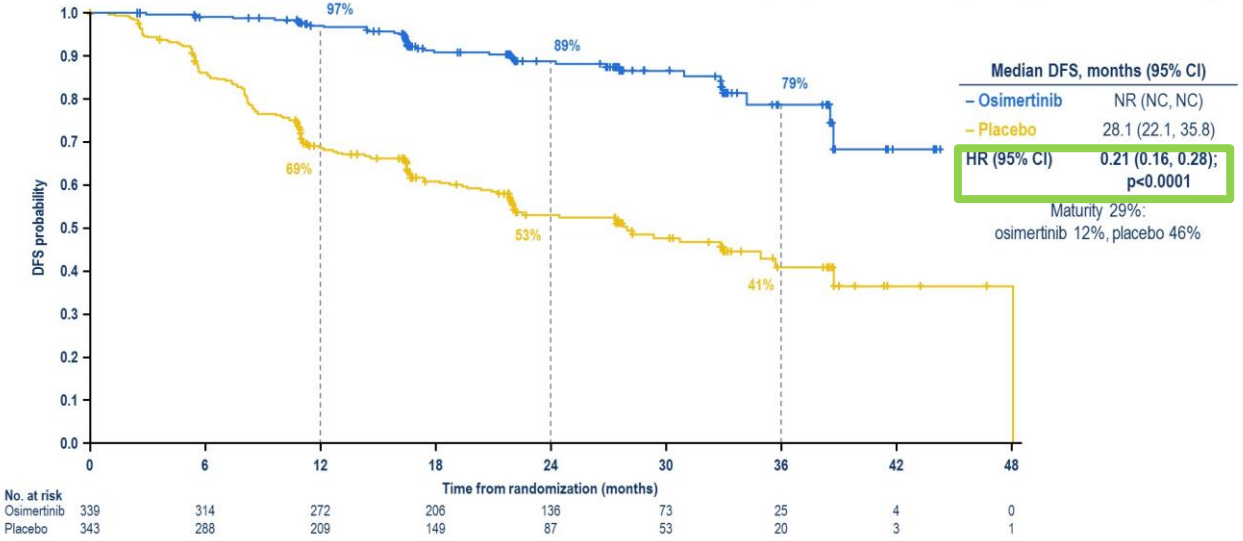
NCT02511106; ADAURA data cut-off: January 17, 2020. *AJCC 7th edition; †Prior, post, or planned radiotherapy was not allowed; ‡Centrally confirmed in tissue; §Patients received a CT scan after resection and within 28 days prior to treatment; ¶Stage IB / II / IIIA.
CT, computed tomography; Ex19del, exon 19 deletion; IDMC, Independent Data Monitoring Committee; WHO, World Health Organization.

Primary endpoint: DFS in patients with stage II/IIIA disease



ADAURA data cut-off: January 17, 2020.
Median follow-up: osimertinib 22.1, placebo 15.0 months.
DFS by investigator assessment. Tick marks indicate censored data.
NC, not calculable; NR, not reached.

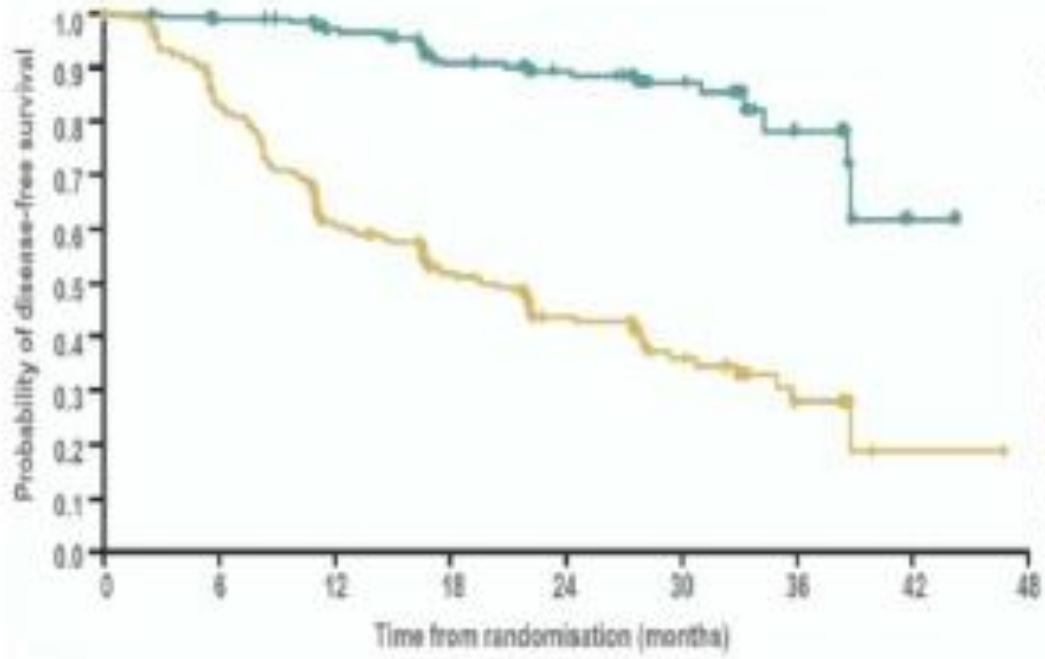
Secondary endpoint: DFS in the overall population (stage IB/II/IIIA)



ADAURA data cut-off: January 17, 2020.
Median follow-up: osimertinib 22.1, placebo 16.6 months.
DFS by investigator assessment. Tick marks indicate censored data.

ADAURA: Osimertinib improves DFS versus placebo in resected EGFRm NSCLC

Primary population: Stage II/IIIA

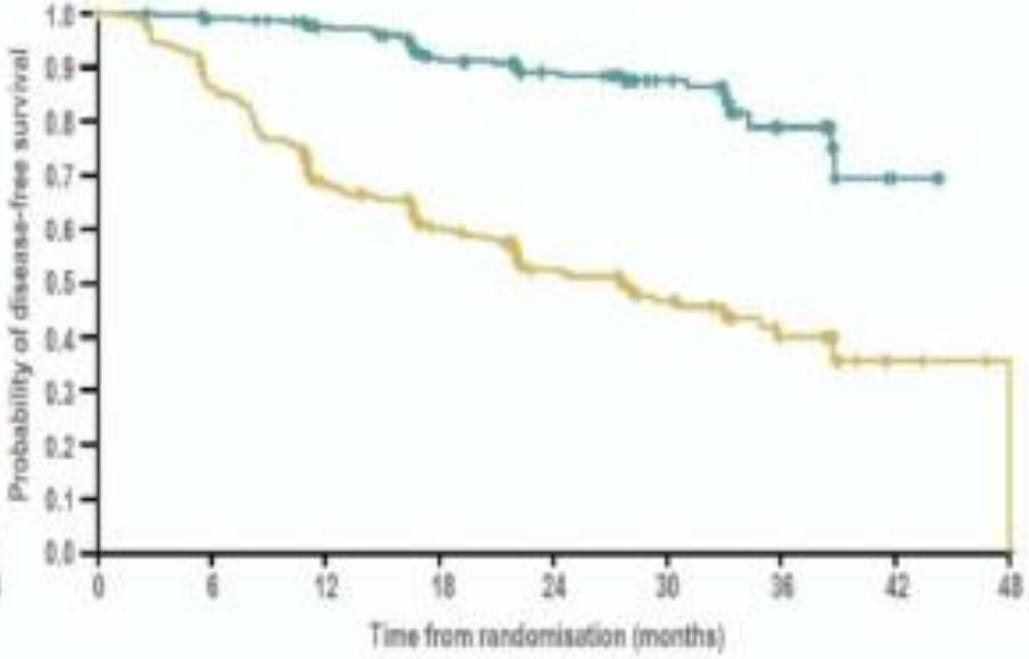


o. at risk

simertinib	233	219	189	137	97	52	18	2	0
acebo	237	190	127	82	51	27	9	1	0

	Median DFS, months (95% CI)	HR (99.06% CI)
– Osimertinib	NR (38.8, NC)	0.17 (0.11, 0.26)
– Placebo	19.6 (16.6, 24.5)	P<0.0001

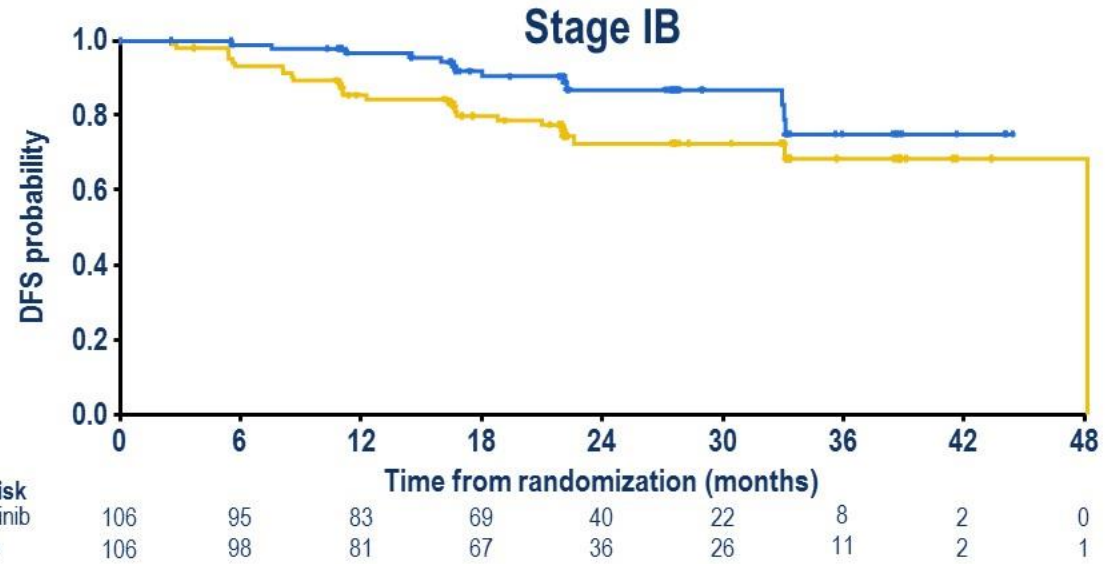
Overall population: Stage IB/II/IIIA



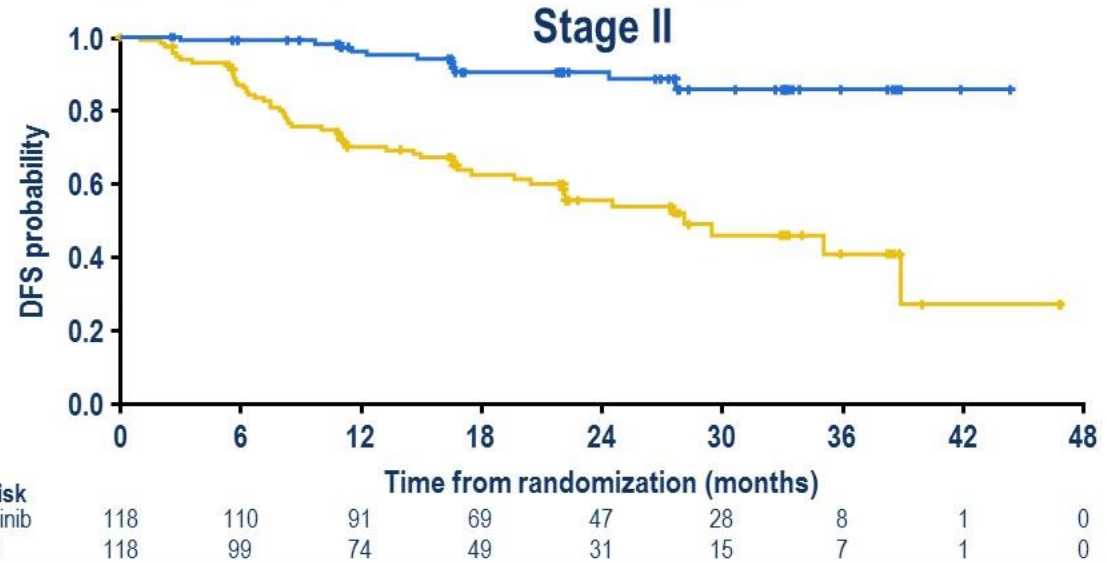
	339	313	272	208	138	74	27	5	0
	343	287	207	148	88	53	20	3	1

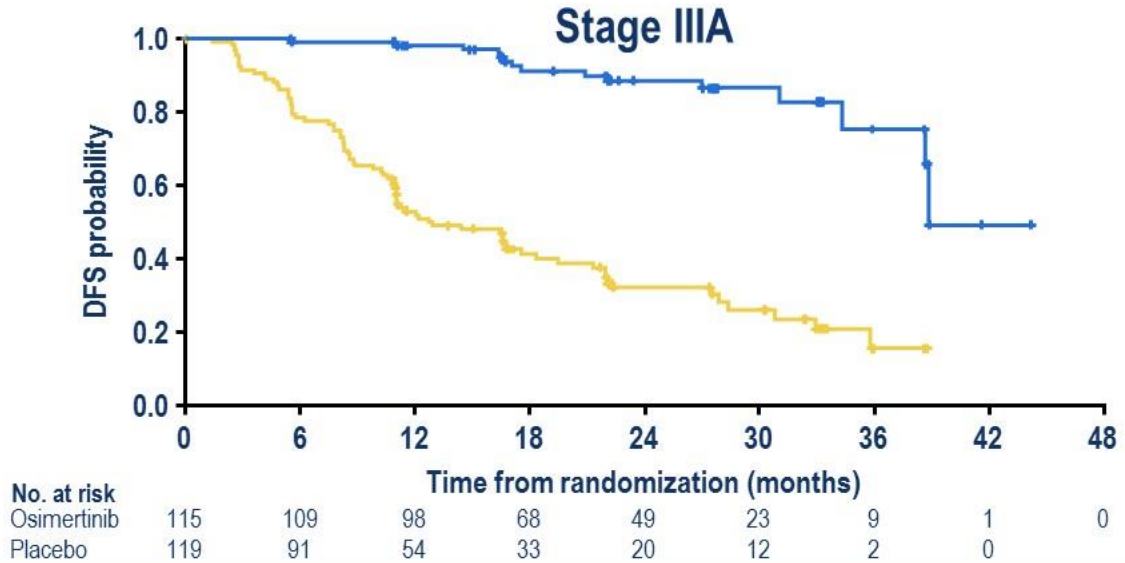
	Median DFS, months (95% CI)	HR (99.12% CI)
– Osimertinib	NR (NC, NC)	0.20 (0.14, 0.30)
– Placebo	27.5 (22.0, 35.0)	P<0.0001

DFS by stage



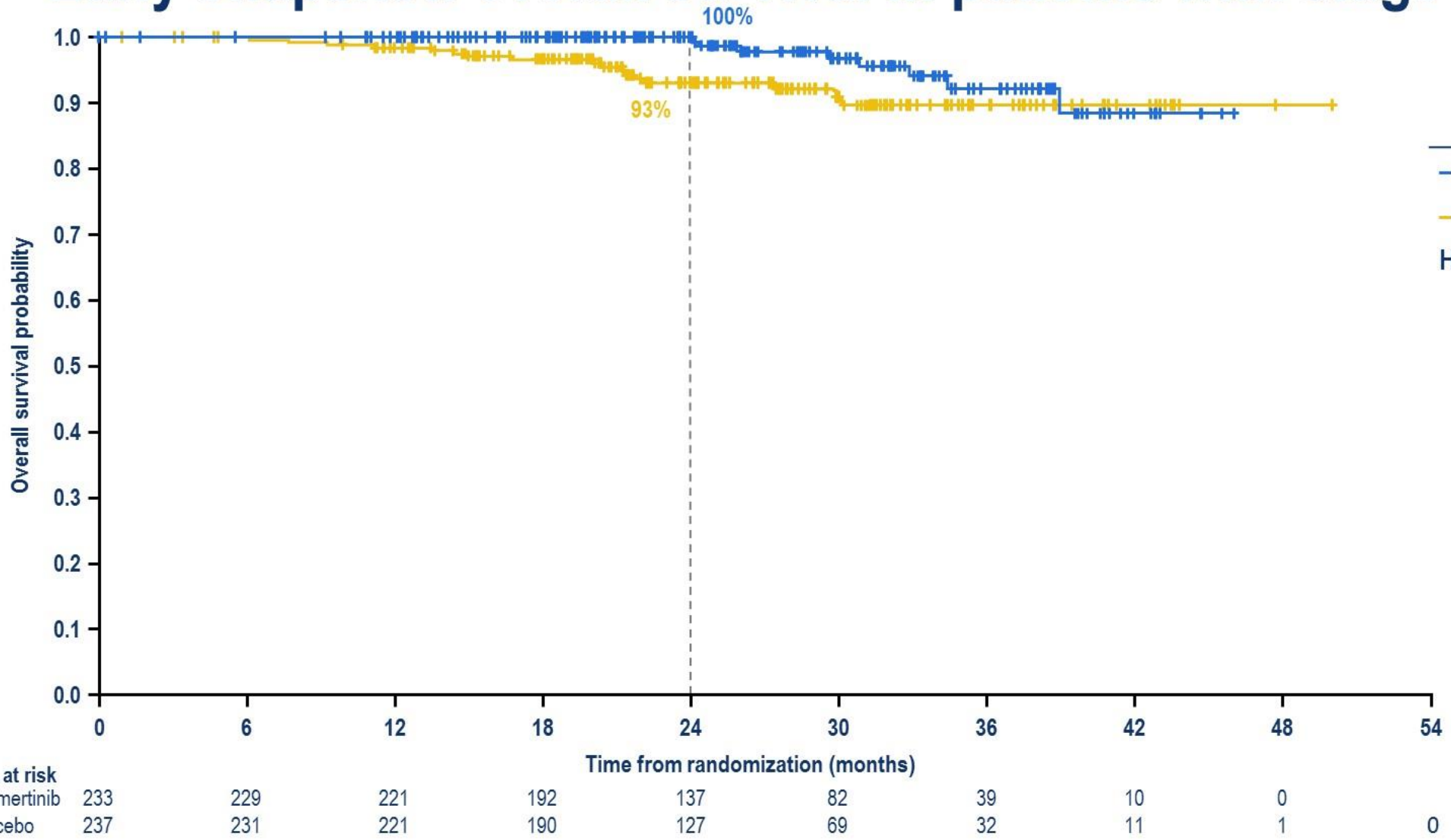
	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	**0.50 (0.25, 0.96)**	**0.17 (0.08, 0.31)**	**0.12 (0.07, 0.20)**





ADAURA data cut-off: January 17, 2020.
Tick marks indicate censored data.

Early snapshot: overall survival in patients with stage II/IIIA disease



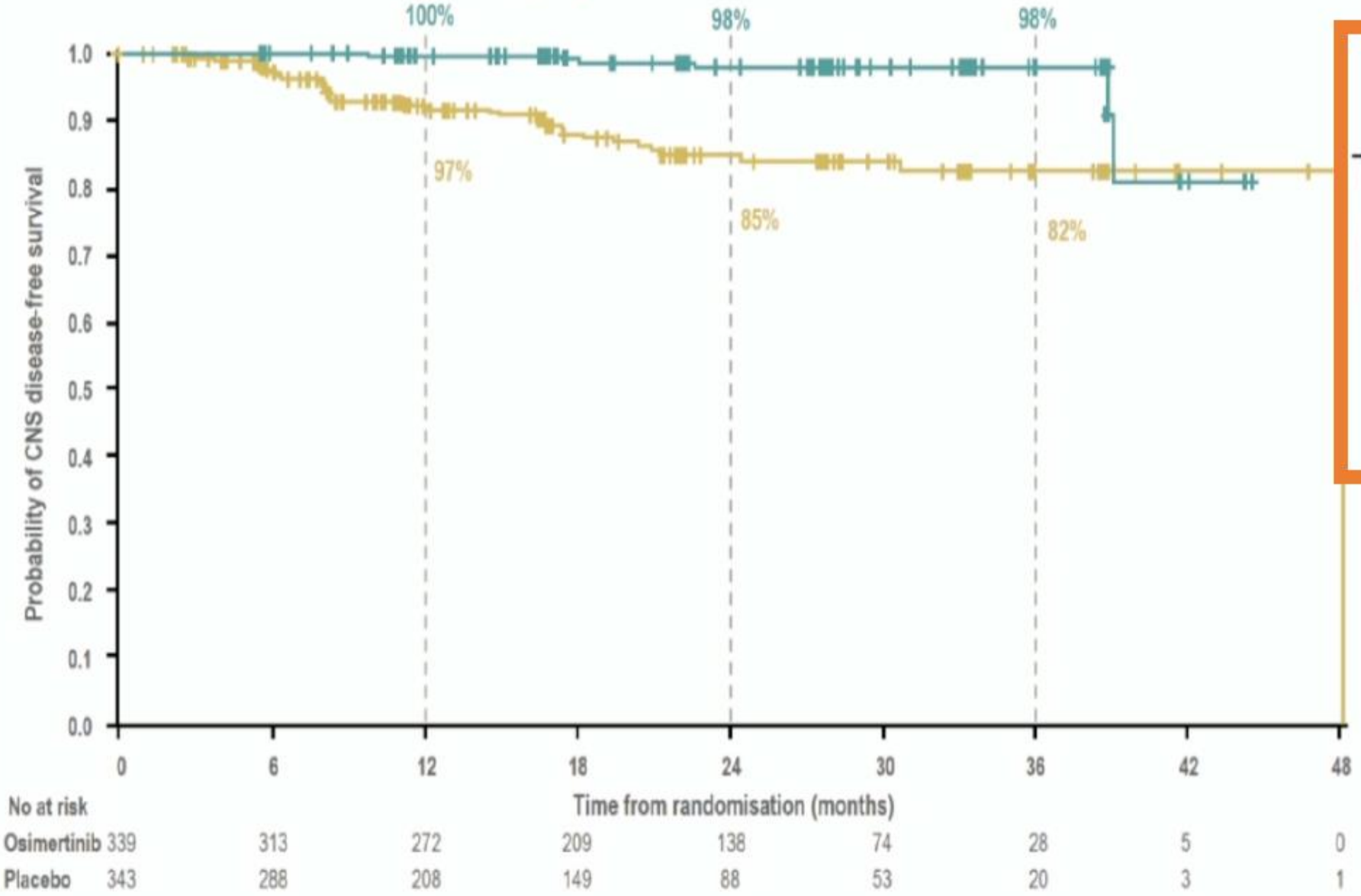
No. at risk									
Osimertinib	233	229	221	192	137	82	39	10	0
Placebo	237	231	221	190	127	69	32	11	1

Median OS, months (95% CI)	
– Osimertinib	NR (NC, NC)
– Placebo	NR (NC, NC)
HR (95% CI)	**0.40 (0.18, 0.90)**

Maturity 5%:
osimertinib 3%, placebo 7%

ADAURA data cut-off: January 17, 2020.
Median follow-up: osimertinib 26.1, placebo 24.7 months.
Tick marks indicate censored data.

CNS DFS in the overall population



Median CNS DFS, months (95% CI)	
Osimertinib	NR (39, NC)
Placebo	48.2 (NC, NC)
HR* (95% CI)	0.18 (0.10, 0.33); p<0.0001

Maturity 7%:
osimertinib 2%, placebo 11%

CTONG 1104 – NCT01405079

ADJUVANT study design (CTONG 1104 / NCT01405079)

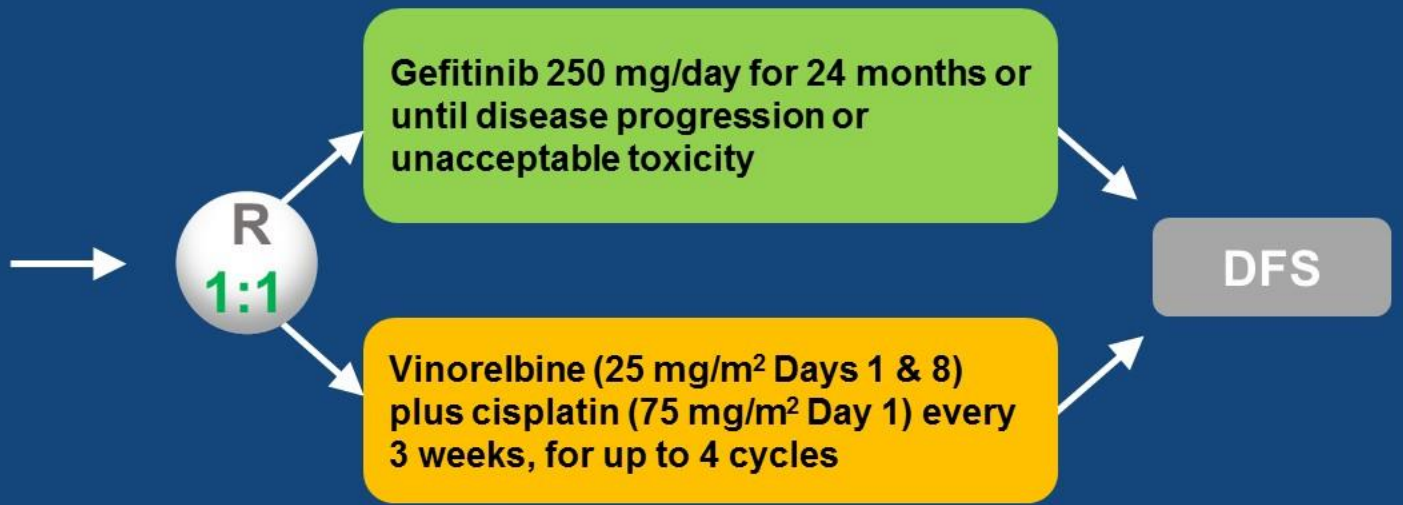
Completely resected pathological stage II-IIIA (N1-N2) NSCLC

EGFR activating mutation (exon 19 deletions or exon 21 L858R)

ECOG PS 0-1

Age ≥18 years & <75 years

n=220



Stratification factors:

- *EGFR* mutation
- N stage

Efficacy assessment:

- Every 12 weeks in 3 years
- Every 6 months after 3 year

Primary endpoint:

- DFS

Secondary endpoints:

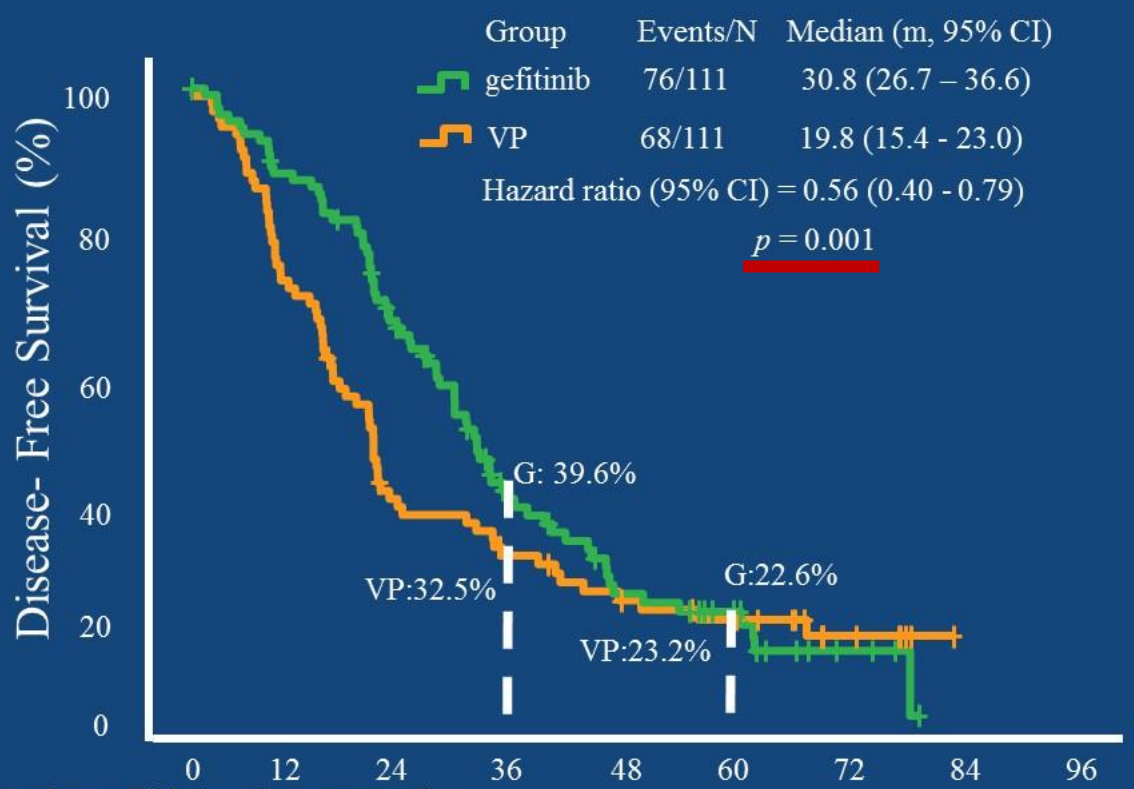
- 3-year DFS rate, 5-year DFS rate, OS, 5-year OS rate, safety, HRQoL (FACT-L, LCSS, TOI), exploratory biomarker analyses

ECOG PS: Eastern Cooperative Oncology Group Performance Status; DFS: disease-free survival; FACT-L: Functional Assessment of Cancer Therapy - Lung; HRQoL: health-related quality of life; LCSS: Lung Cancer Symptom Scale; OS: overall survival; R: randomization; TOI: Trial Outcome Index

Zhong WZ et al. Lancet Oncol 2018;19:139-148

Updated 3-year & 5-year DFS rate

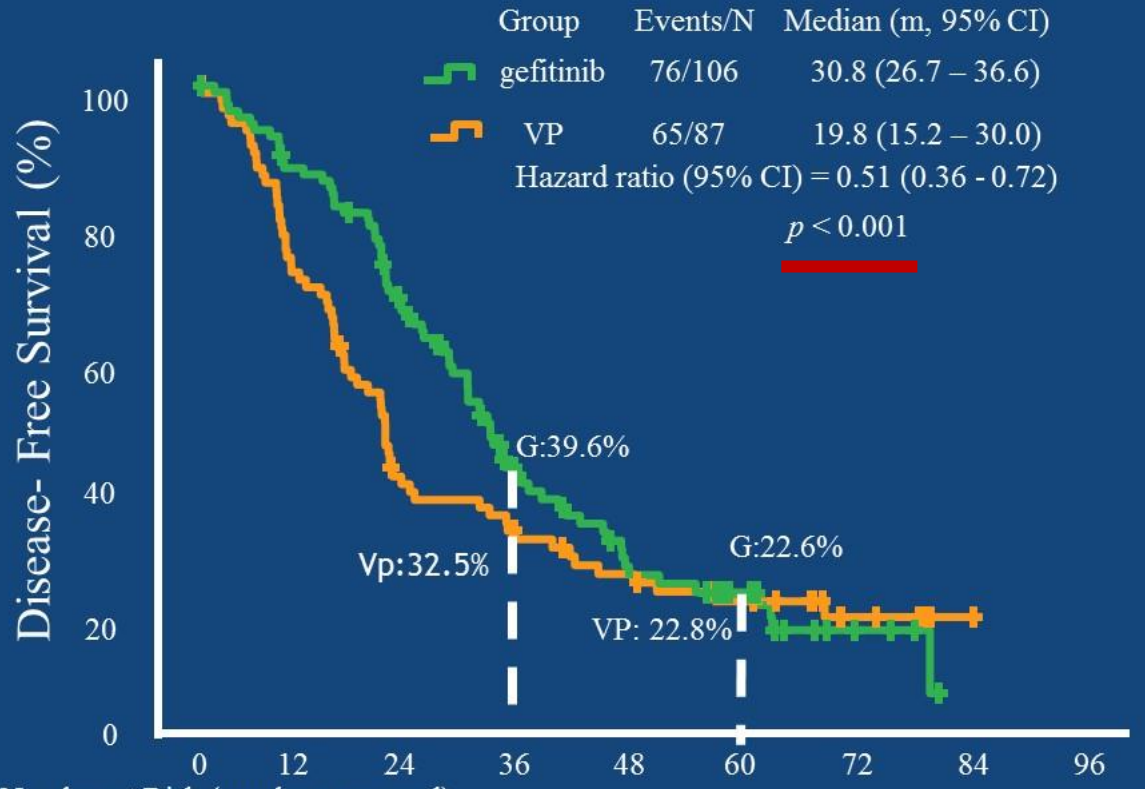
ITT population (n=222)



Number at Risk (number censored)

Gefitinib	111 (0)	91 (6)	61 (5)	33 (7)	21 (2)	12 (6)	4 (6)	0 (3)	0(0)
VP	111 (0)	63(21)	33 (2)	26 (2)	19 (2)	15 (2)	6 (8)	0 (6)	0(0)

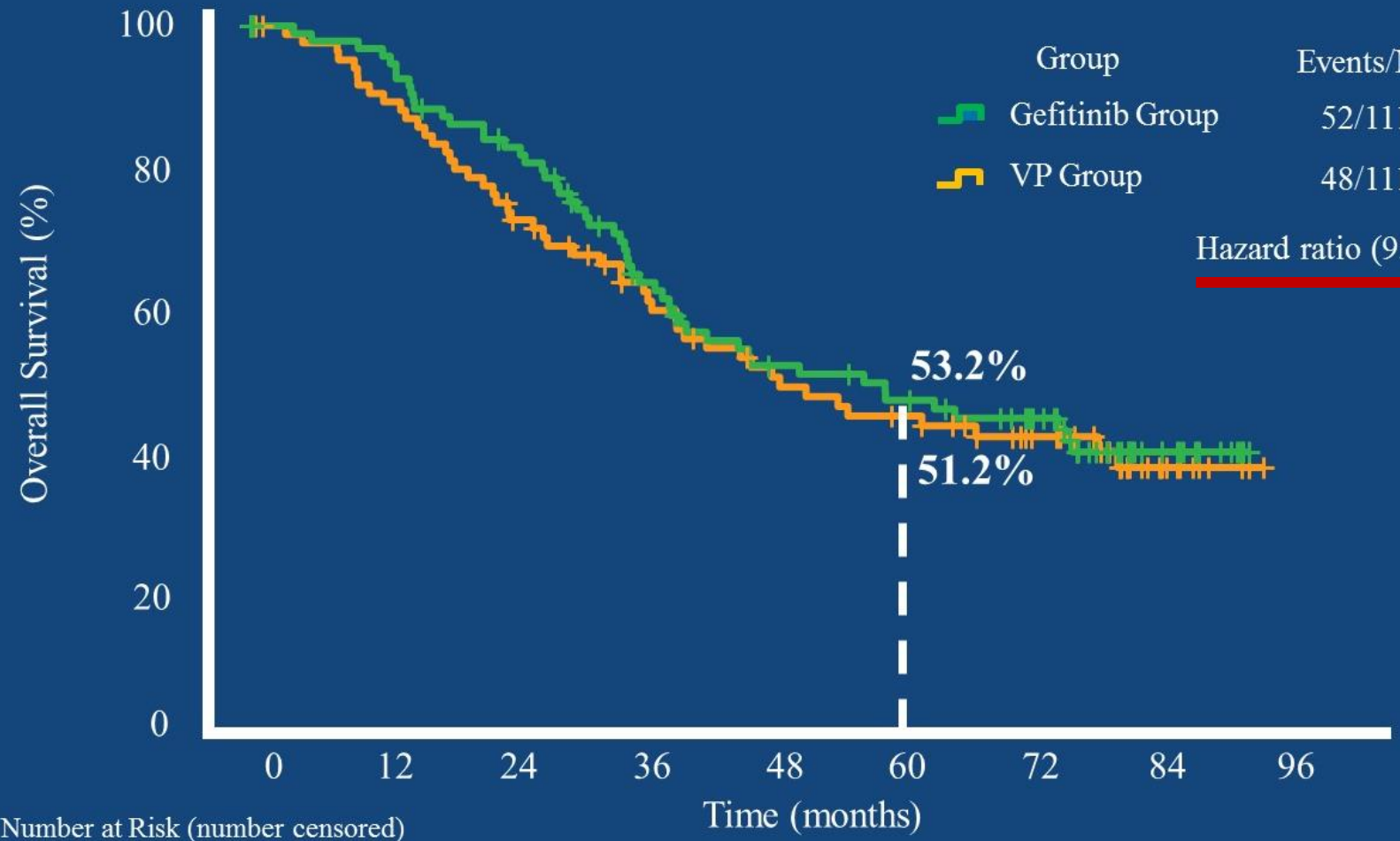
PP population (n=193)



Number at Risk (number censored)

Gefitinib	106 (0)	91 (1)	61 (5)	33 (7)	21 (2)	12 (6)	4 (6)	0 (3)	0(0)
VP	87(0)	60 (0)	32 (2)	25 (2)	18 (2)	14 (2)	6 (8)	0 (6)	0(0)

Overall survival (ITT population)



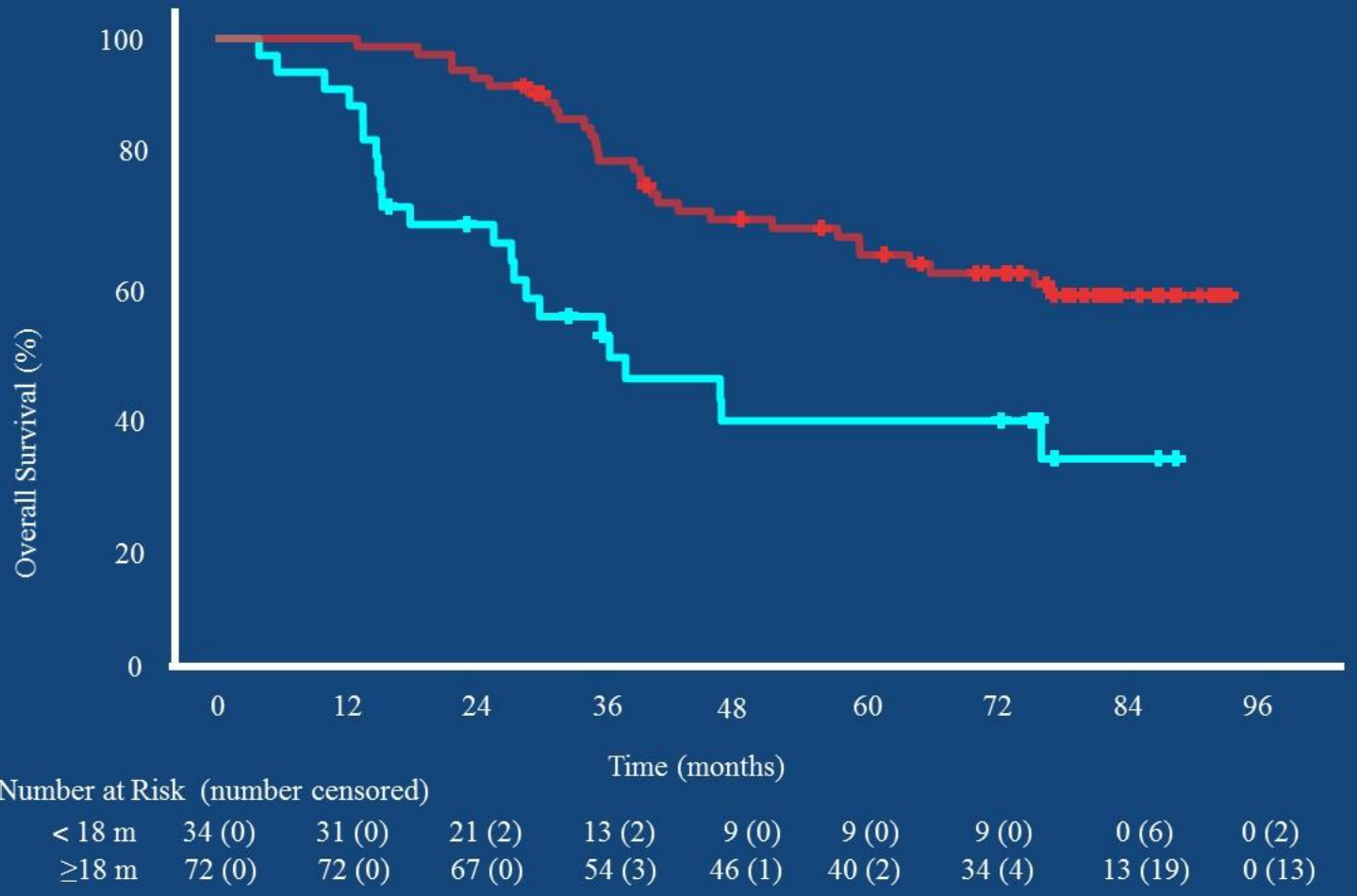
Group	Events/N	Median (m ,95% CI)
Gefitinib Group	52/111	75.5 (46.6 - NC)
VP Group	48/111	62.8 (45.8 - NC)

Hazard ratio (95% CI) = 0.92 (0.62 -1.36) $p = 0.674$

Number at Risk (number censored)

Gefitinib	111 (0)	103 (5)	88 (2)	67 (5)	55 (1)	49 (2)	43 (4)	15 (25)	0 (15)
VP	111 (0)	87 (16)	73 (1)	58 (6)	47 (2)	41 (1)	34 (5)	14 (18)	0 (14)

Post Hoc analysis: the OS for the duration of adjuvant gefitinib



The duration of gefitinib

< 18 months

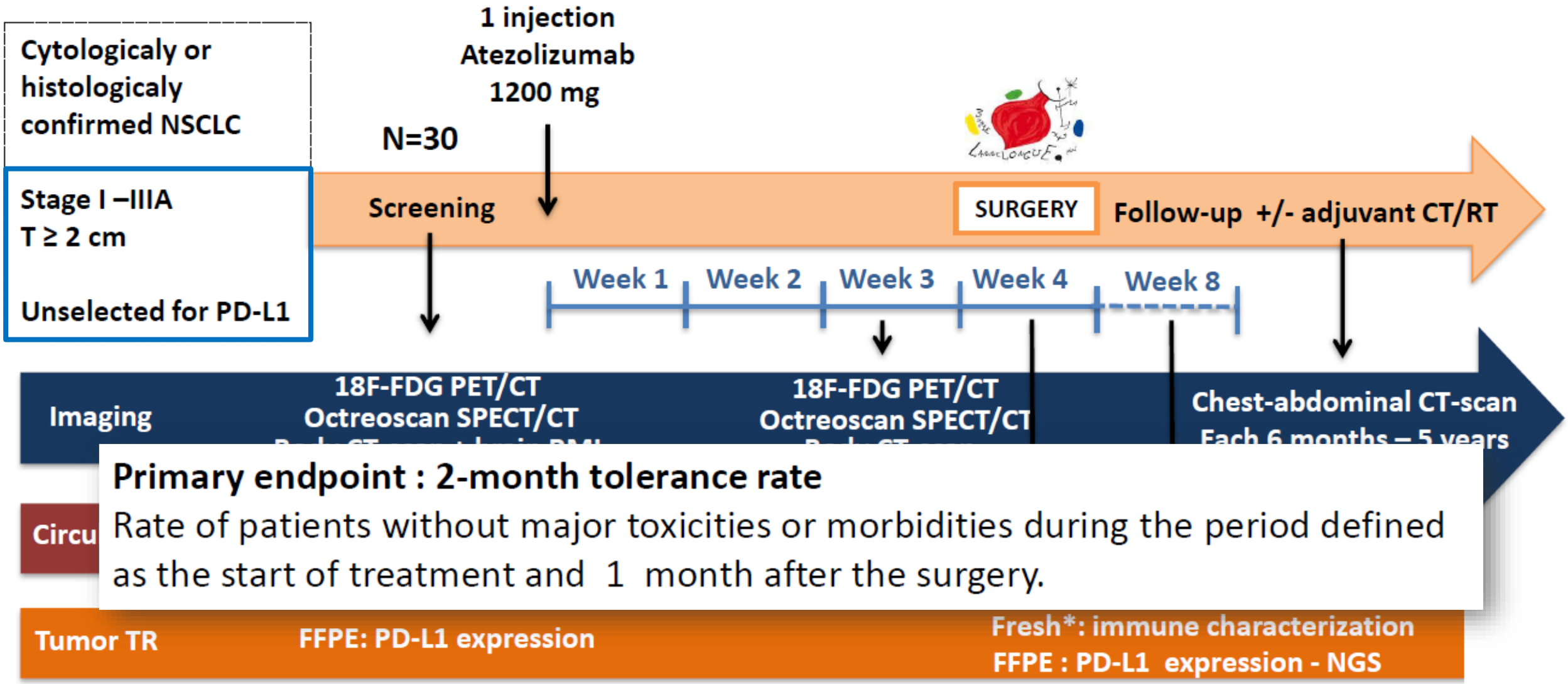
≥18 months

Events/N	Median (m ,95% CI)
22/34	35.7 (25.7 – NC)
30/72	NR (64.0 – NC)

Hazard ratio (95% CI) = 0.38 (0.22 – 0.66)

$P < 0.001$

PRINCEPS – Neoadjuvant atezolizumab



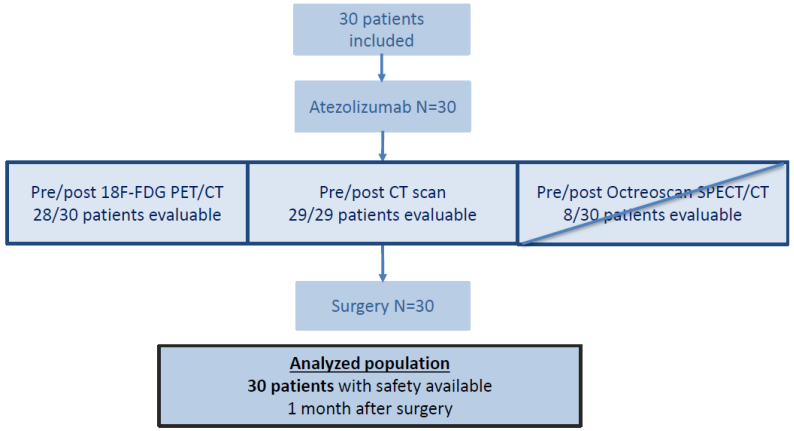
Primary endpoint : 2-month tolerance rate

Rate of patients without major toxicities or morbidities during the period defined as the start of treatment and 1 month after the surgery.

NSCLC : Non-Small Cell Lung Cancer – TR : translational research – ctDNA : circulating tumor DNA – CTCs : circulating tumor cells – CT : chemotherapy – RT : radiotherapy

* proceeded within 4 hours after surgery

Patients disposition



Patients and tumors	N=30 N (%)
Age (Years)	
Median	64
Sex	
Male	15 (50)
Female	15 (50)
ECOG performance status	
0	23 (77)
1	7 (23)
Smoking status	
Never	2 (7)
Ever	28 (93)
Pathological stage	
I	15 (50)
II	6 (20)
III	9 (30)

Mutations	N=24 N (%)
BRAF	2
EGFR	3
KRAS	8
TP53	13
PI3KCA	1
STK11	
ESR1	
WT	

Baseline PD-L1 (clone SP142)	N=29 N (%)
<1%	18 (62)
≥1%	6 (21)
≥50%	5 (17)

Treatments	N=30 N (%)
Time between atezolizumab and surgery (days)	
Median	24
Resection delayed > 15 days	0 (0)
Type of resection	
Pneumonectomy	2 (7)
Lobectomy	28 (93)
Quality of resection	
RO	29 (97)
R1	1 (3)
Adjuvant radiotherapy	19 (29.7)

Dindo Classification	N=30 Grade
Respiratory Distress* Septic Shock*	Grade III Grade III - a
Paresthesia	Grade I
Bronchial Congestion	Grade II
Atrial Fibrilation* Air leak*	Grade I Grade I
Cardiac Decomponsation secondary to Atrial Fibrilation	Grade I

Dindo D et al. Ann Surg. 2004

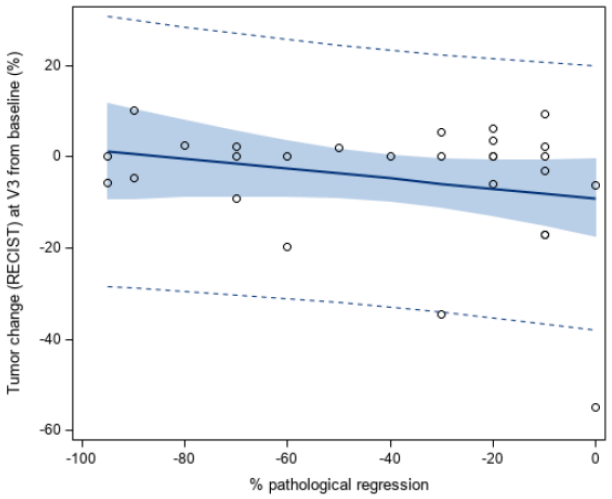
One cycle of preoperative atezolizumab was safe and did not impair surgery

- There were no grade 4-5 complications
- 7/30 patients (23%) had complication within 1 month after surgery

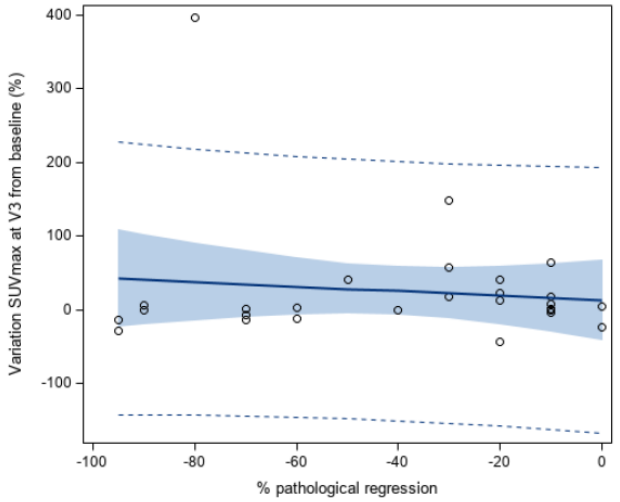
Objective response	N=29 N (%)
Complete response	0 (0)
Partial response	2 (7)
Stable disease	27 (93)
Progression	0 (0)

Pathological response	N=29 N (%)
Complete response	0 (0)
Major pathological response	4 (14)
Pathological response ≥ 50%	12 (41)

Variation of SUVmax	N=28 N (%)
+20% or more	7 (25)
Stable (between +20% and -20%)	18 (64)
-20% or more	3 (11)



- 28 patients evaluable
- Pearson correlation=-0.24
  p value=0.2
- No correlation observed between percentage of pathological regression and variation of SDM at week 3 post atezolizumab

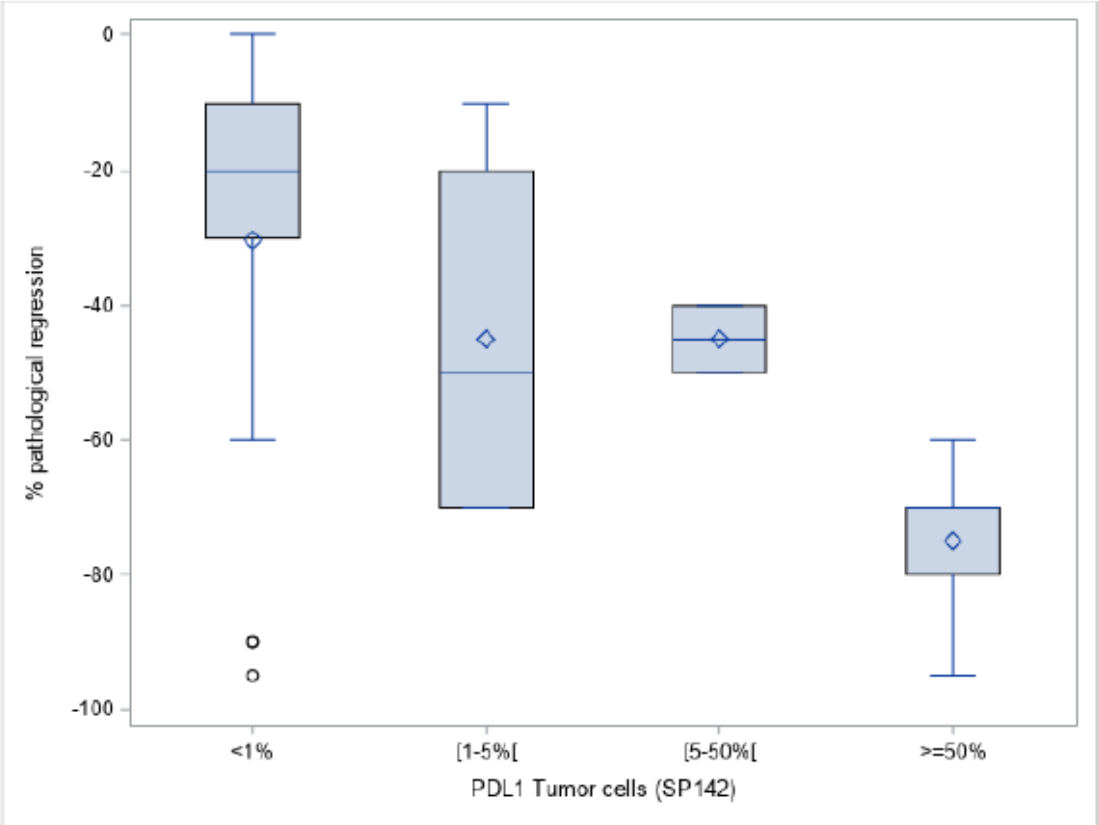


- 18F-FDG PET/CT
- 27 patients evaluable
- Pearson correlation= -0.12,
  pvalue=0.55
- No correlation observed between percentage of pathological regression and variation of SUVmax at week 3 post atezolizumab

Pathological responses were

- not correlated with RECIST 1.1 response rate
- not correlated with metabolic variations (octreoscan, 18F-FDG)

Correlation between pathological response and PD-L1 expression at baseline



- 23 patients evaluable
- PD-L1 assessed on tumor cells and considered in 4 classes (<1%, [1-5%], [5-50%], ≥ 50%)
  Spearman correlation = -0.50560 ,
  pvalue=0.0051

- Quantitative results confirmed the correlation between pathological response and PD-L1 expression

LUNG ART phase III Trial

(IFCT-0503, UK NCRI, SAKK)

Trial registry: NCT00410683

Study design

Completely resected NSCLC with N2 histo/ cytologically proven nodal involvement

Stratification factors : Center, Administration of CT (no CT vs Post-op CT vs pre-op CT alone), Histology (SCC vs other), Extent of mediastinal lymph node involvement (0 vs 1 vs 2+), use of pre-treatment PET-scan (yes/no)

Primary end-point: Disease-free survival

Secondary end-points: Overall survival, patterns of relapse, local failure, second cancers, and treatment-related toxicity

Baseline Characteristics (ITT)

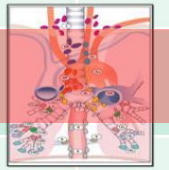
	Control arm (n = 249)	PORT arm (n = 252)
Gender male (%)	66%	66%
Age (median [min;max])	61 [38;85]	61 [36;79]
Smoking status: Current-former/ Never	90% / 10%	92%) / 8,0%
cTNM Unforeseen N2/Single St N2 / Multiple N2	41% / 34% / 25%	42%/ 35% / 23%
Histology: AdenoC / SCC	76% / 20%	70% / 23%
Adjuvant chemoT: Pre or postop/Preop	96%/12%	96%/14%
Pre-treatment PET scan	90%	92%
pTNM or ypTNM Number of N2 stations involved: 0/1/ ≥ 2	2% / 45% / 52%	4% / 45% / 52%

Stratification factors

Percents calculated on non missing data

Baseline Characteristics : Surgery

	Control arm (n = 249)	PORT arm (n = 252)
Type of surgery (n(%)) - Lobectomy - Bilobectomy - Pneumonectomy - Sublobar resection	 81% 7% 10% 2%	 78% 8% 12% 2%
Largest T size (Median [min;max],mm	34 [0;110]	33 [5;150]
pTNM pN0/pN1 (down staging after preop CT) pN2	pN0: 1% pN1: 2% pN2: 98%	pN0: 2% pN1: 1% pN2: 96%
In pN2 patients N2 stations most frequently involved on Surgical pathological exam 4R / 5 / 7	St4 R: 66% / St 5 L: 43% St7 R Tum: 66% / L Tum: 34%	St 4R: 55% / St 5 L: 31% St7 R Tum: 65% / L Tum: 35%



IASLC Nodal Map (Rusch et al, JTO 2009 TNM 7)

N=501

	PORT arm (n = 252)
Thoracic irradiation (n(%))	241 (96%)
Early termination (n(%))	7 (3%) (3 progressions, 2 toxicities)
Total received dose (in Gy) (median (min;max))	54 Gy (21;70)
Main parameters regarding Dose to lungs and Heart*	Dosimetric parameters / Median (min - max) Lungs V20: 23% (3 – 36) MLD: 12.7 Gy (2.5 – 22) Mean heart dose: 13.4Gy (0.7 – 36,2) Heart V35: 15% (0 – 50)
PORT technique	3DRT : 201 (89%) IMRT: 25 (11%) 26 Unspecified

Disease-Free Survival 1/3 (Primary Endpoint; ITT)

Main analysis (Adjusted Cox Model)

HR = 0.85
95% CI = [0.67;1.07]
p value = 0.16

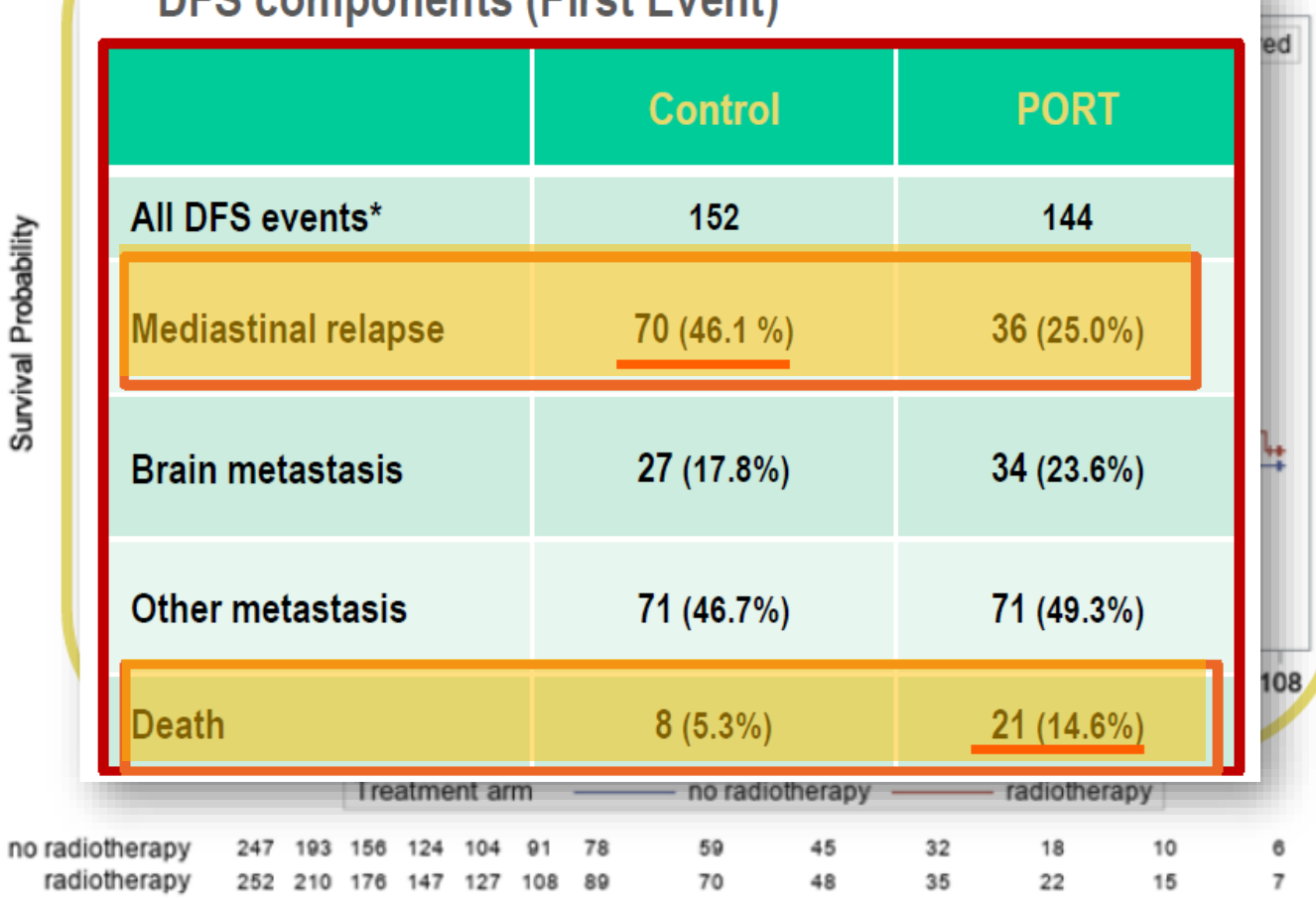
	Control	PORT
Median DFS	22.8 mo (95% CI = [17;37])	30.5 mo (95% CI = [24;49])
3-yr DFS	43.8% (95% CI = [37;51])	47.1 % (95% CI = [40;54])

95%CI = 95% bilateral Confidence Interval

DFS survival curve (Kaplan Meier method)

DFS components (First Event)

	Control	PORT
All DFS events*	152	144
Mediastinal relapse	70 (46.1 %)	36 (25.0%)
Brain metastasis	27 (17.8%)	34 (23.6%)
Other metastasis	71 (46.7%)	71 (49.3%)
Death	8 (5.3%)	21 (14.6%)



Overall Survival (Secondary Endpoint; ITT)

n_{events} = 201 ev

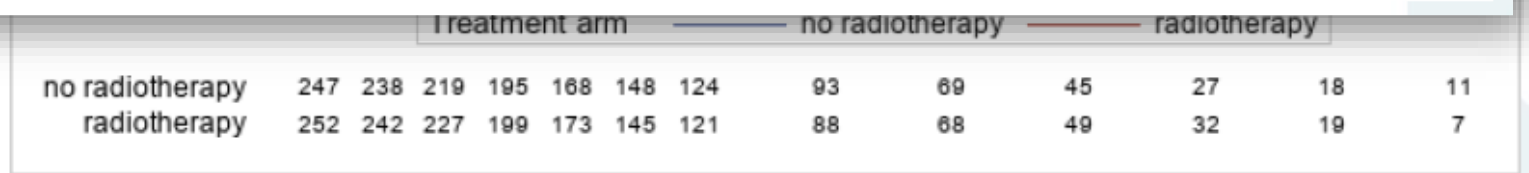
Overall Surviva

Control arm: 6

PORT arm: 66.

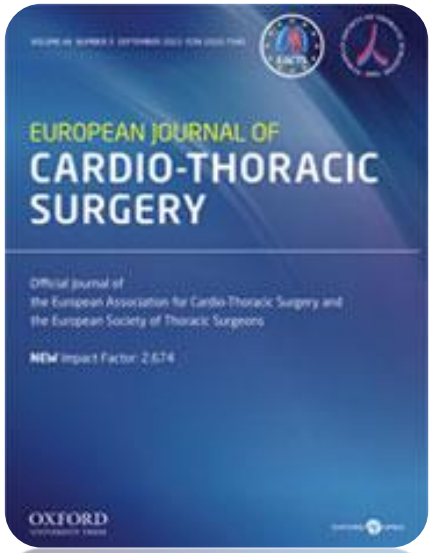
OS survival curve (Kaplan-Meier method)

	Control arm (n = 249)	PORT arm (n = 252)
Deaths	102 (41.5%)	99 (39.6%)
Cause of death		
- Progression or recurrence	87 (86.1%)	68 (69.4%)
- Cardio-pulmonary	2 (2.0%)	16 (16.2%)
- Second primary	1 (1.0%)	5 (5.1%)
- RT or CT related toxicity	0 (0%)	3 (3.0%)
- Other	11 (10.9%)	6 (6.1%)
- Unreported	1	1



n(%)	Control arm (n = 246)	PORT arm (n = 241)
At least one toxicity*	200 (81.3%)	222 (92.1%)
At least one toxicity gr 3-4	37 (15.0%) 62 events	57 (23.7%) 112 events
At least one EARLY** TOXICITY gr 3-4	19 (7,7%)	28 (11,6%)
At least one LATE TOXICITY gr 3-4	22 (8,9%)	36 (14,6%)
EARLY** TOXICITY gr 5	0 (0%)	3 (1.2%)
LATE TOXICITY gr 5	2 (0.8%)	3 (1.2%)

	Control arm (n = 249)	PORT arm (n = 252)
At least one LATE CARDIAC /PULMONARY TOXICITY gr 3-4	12 (4,9%)	26 (10,8%)
Second cancers (n(%)) - Second Lung cancers (n(% among 2nd cancers))	18 (7.2%) - 4/18 (22.2%)	28 (11.1%) - 11/28 (39.3%)



ypN AFTER INDUCTION TREATMENT

European Journal of Cardio-Thoracic Surgery 0 (2020) 1–9
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ORIGINAL ARTICLE

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Pathological nodal disease defines survival outcomes in patients with lung cancer with tumour major pathological response following neoadjuvant chemotherapy

Erin M. Corsini [a], Annikka Weissferdt [b], Apar Pataer [a], Nicolas Zhou [a], Mara B. Antonoff [a], Wayne L. Hofstetter [a], Reza J. Mehran [a], Ravi Rajaram [a], David C. Rice [a], Jack A. Roth [a], Ara A. Vaporciyan [a], Garrett L. Walsh [a], Tina Cascone [c], John V. Heymach [c], Stephen G. Swisher [a] and Boris Sepesi [a,*]

[a] Department of Thoracic and Cardiovascular Surgery, University of Texas MD Anderson Cancer Center, Houston, TX, USA
[b] Department of Pathology, University of Texas MD Anderson Cancer Center, Houston, TX, USA
[c] Department of Head and Neck Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

* Corresponding author. Department of Thoracic and Cardiovascular Surgery, University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030, USA. Tel: +1-713-745-9151; fax: +1-713-794-4901; e-mail: bsepesi@mdanderson.org (B. Sepesi).

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Key question

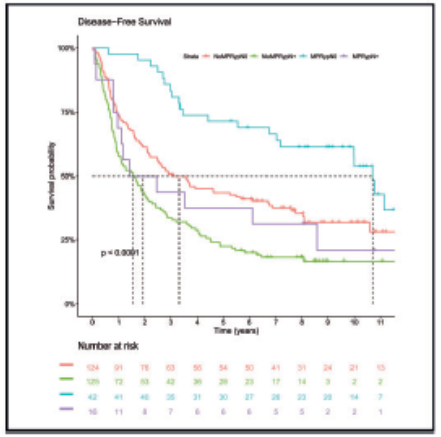
Among lung cancer patients who achieve a major pathological response in the tumour, does nodal disease impact survival?

Key finding(s)

Nodal disease is a key determinant of outcomes, even among those with an outstanding primary tumour treatment response.

Take-home message

For patients who achieve major pathological response within the tumour, only those without pathological nodal disease experience a survival benefit.



Abstract

OBJECTIVES: Major pathological response (MPR) is prognostic of outcomes for patients with non-small-cell lung cancer following neoadjuvant chemotherapy and is used as the primary end point in neoadjuvant immunotherapy trials. We studied the influence of pathological nodal disease on patterns and timing of recurrence among patients with MPR.

Accepted for presentation at the European Society of Thoracic Surgeons Annual Meeting 2020.

- *MPR in primary tumor but…what about ypN?*
- 2001-2012
- LA NSCLC QT neo + Cx

Major pathological response	58 (19)
Pathological N category	
N0	166 (54)
N1	59 (19)
N2	82 (27)
N3	0 (0)
Pathological stage	
0 (ypT0ypN0)	10 (3)
I	97 (32)
II	90 (29)
III	110 (36)
T category downstaged	79 (26)
T category upstaged	59 (19)
N category downstaged	80 (26)
N category upstaged	43 (14)
Hospital length of stay (days)	5 (4–8)

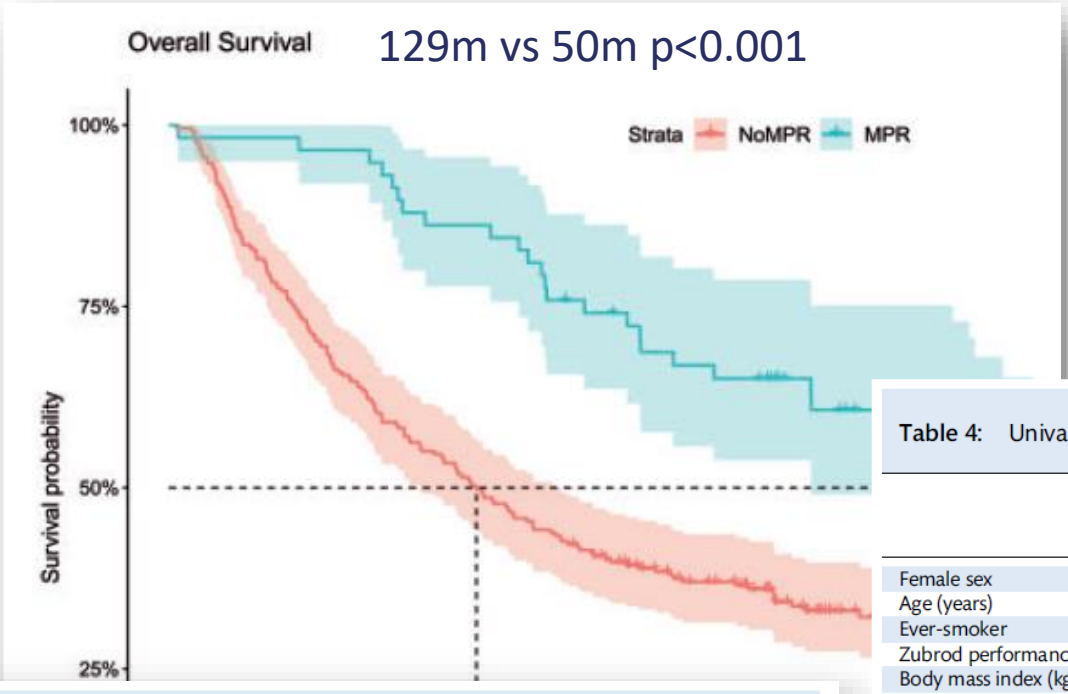
Table 1: Patient, tumour, and operative characteristics ($n = 307$)

Variable	*n* (%) or median (IQR)
Male sex	161 (52)
Age (years)	64.2 (57.1–69.6)
Ever-smoker	270 (88)
Zubrod performance status ≥1	141 (46)
Body mass index (kg/m^2)	26.2 (23.0–29.1)
Diabetes mellitus	34 (11)
Hypertension	132 (43)
Histology	
Adenocarcinoma	168 (55)
Squamous cell carcinoma	112 (36)
Others	27 (9)
Clinical T category	
T1	79 (26)
T2	146 (48)
T3	73 (24)
T4	9 (3)
Clinical N category	
N0	127 (41)
N1	58 (19)
N2	119 (39)
N3	3 (1)
Clinical stage	
I	72 (23)
II	97 (32)
III	138 (45)
Neoadjuvant chemotherapy	
Cisplatin	135 (44)
Pemetrexed	53 (17)
Paclitaxel	108 (35)
Docetaxel	123 (40)
Etoposide	4 (1)
Carboplatin	166 (54)
Others	39 (13)

Table 2: Comparison of baseline and tumour characteristics between groups

Variable	MPR, *n* (% or IQR)	NoMPR, *n* (% or IQR)	*P*-value
Male sex	41 (71)	120 (48)	0.003
Median age (years)	62.2 (55.1–69.3)	64.3 (57.4–70.0)	0.35
Ever-smoker	51 (88)	219 (88)	1.00
Zubrod performance status ≥1	23 (39)	118 (48)	0.27
Median body mass index (kg/m^2)	26.2 (24.2–28.8)	26.2 (22.8–29.2)	0.78
Histology			0.23
Adenocarcinoma	26 (44)	142 (57)	
Squamous cell carcinoma	26 (45)	86 (35)	
Others	6 (10)	21 (8)	
Clinical T category			0.45
T1	20 (34)	59 (24)	
T2	25 (43)	120 (48)	
T3	12 (20)	59 (24)	
T4	1 (2)	8 (3)	
Clinical N category			0.25
N0	18 (31)	108 (43)	
N1	12 (20)	45 (18)	
N2	28 (47)	90 (36)	
N3	0 (0)	3 (1)	
Neoadjuvant chemotherapy			
Cisplatin	27 (46)	108 (44)	0.87
Pemetrexed	6 (10)	47 (19)	0.13
Paclitaxel	28 (48)	80 (32)	0.030
Docetaxel	22 (37)	101 (41)	0.74
Etoposide	1 (2)	3 (1)	0.58
Carboplatin	33 (57)	133 (53)	0.74
Others	3 (5)	36 (15)	0.052
Pathological N category			0.006
N0	42 (72)	124 (50)	
N1	9 (15)	48 (19)	
N2	7 (12)	73 (29)	
N3	0 (0)	0 (0)	
N category downstaged	27 (47)	53 (21)	<0.001

EBL: estimated blood loss; IQR: interquartile range; MPR: major pathological response.



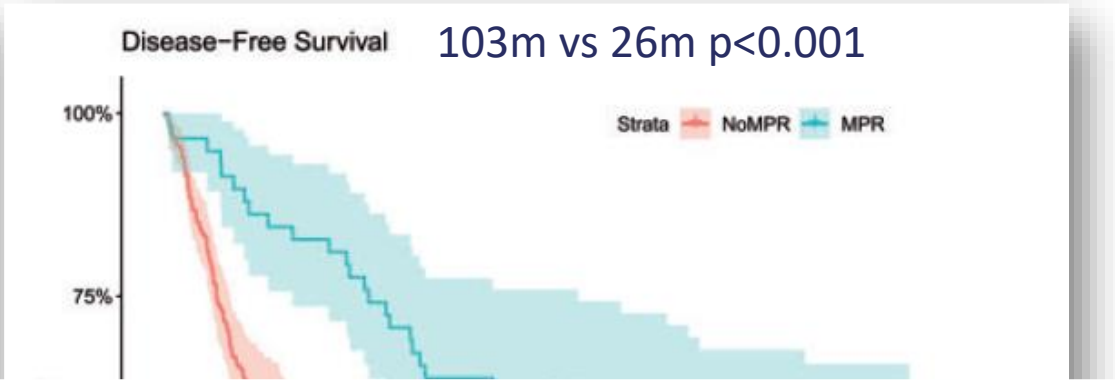


Table 3: Multivariable Cox proportional hazards model for overall survival

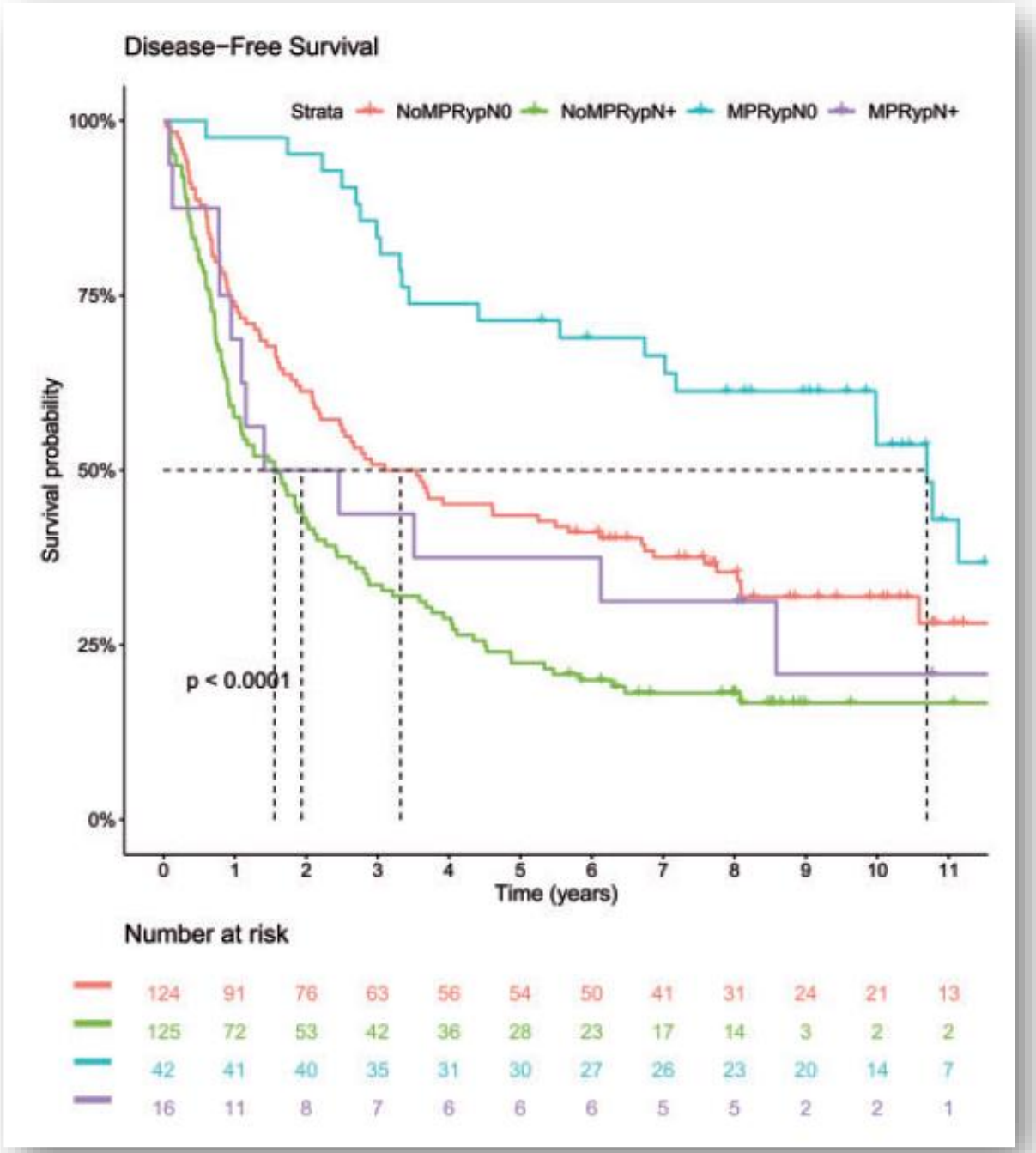
Variable	HR	95% CI	*P*-value
Age (years)	1.03	1.01–1.04	0.002
Zubrod performance status ≥1	1.52	1.15–2.01	0.004
MPR	0.57	0.39–0.84	0.005
Pathological N+ (ref: pN0)	1.77	1.32–2.36	<0.001

CI: confidence interval; HR: hazard ratio; MPR: major pathological response.

Table 4: Univariable and multivariable Cox proportional hazards model for disease-free survival

	Univariable			Multivariable		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Female sex	1.21	0.93–1.57	0.15			
Age (years)	1.01	1.00–1.03	0.090	1.02	1.00–1.03	0.024
Ever-smoker	1.38	0.91–2.12	0.13			
Zubrod performance status ≥1	1.48	1.14–1.93	0.003	1.42	1.09–1.86	0.010
Body mass index (kg/m^2)	0.99	0.98–1.01	0.52			
Diabetes mellitus	0.88	0.57–1.34	0.55			
Hypertension	0.80	0.61–1.05	0.10			
Histology						
Adenocarcinoma	Ref					
Squamous cell carcinoma	0.75	0.56–0.99	0.045			
Others	1.34	0.86–2.10	0.19			
Clinical T category						
1	Ref					
2	1.02	0.74–1.41	0.90			
3	1.27	0.88–1.85	0.21			
4	1.47	0.65–2.87	0.41			
Clinical N+ (ref: cN0)	1.02	0.78–1.33	0.88			
Minimally invasive surgery (ref: thoracotomy)	1.06	0.66–1.72	0.81			
Extent of resection						
Sublobar resection	Ref			Ref		
Lobectomy	0.44	0.25–0.80	0.007	0.41	0.21–0.78	0.006
Bilobectomy	0.50	0.23–1.08	0.079	0.45	0.20–1.02	0.056
Pneumonectomy	0.72	0.35–1.46	0.36	0.54	0.25–1.17	0.12
MPR	0.53	0.37–0.75	<0.001	0.62	0.43–0.90	0.011
Pathological N+ (ref: pN0)	1.88	1.44–2.45	<0.001	1.89	1.44–2.50	<0.001

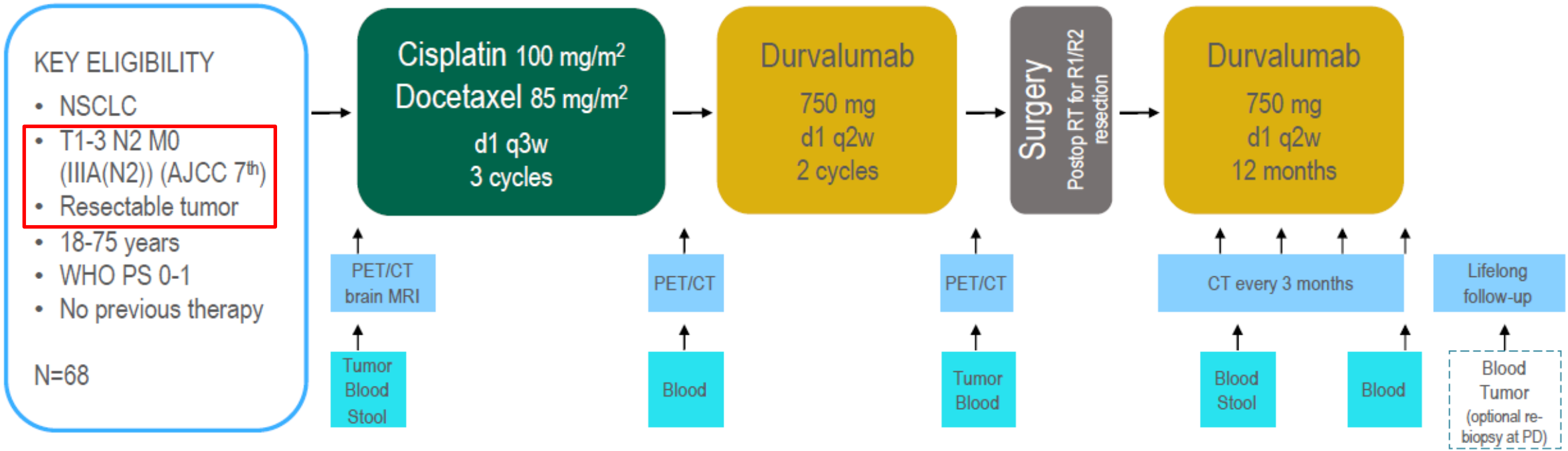
- 58 (19%) MPR
  - Multivariable OS: ypN+ HR 2.49 CI95%(1.14-5.56) p=0.022
  - Recaída a distancia ypN0 26%, ypN1 44%, ypN2 71% p=0.047
  - Mejor DFS en grupo MPRypN-
  - **Único beneficio en SV en los casos con MPR y ypN-**



SAKK 16/14

VIRTUAL 2020 ESMO congress

SAKK 16/14 – Study Design



1° endpoint: Event-free survival (EFS) at 12 months

2° endpoints: EFS, OS, ORR, pCR, MPR, nodal downstaging, complete resection, AEs

Statistical hypothesis: improve EFS at 12 months from ≤ 48% (SAKK 16/00[1]) to ≥ 65%

[1]Pless M, et al. Lancet 2015;386:1049-56

SAKK 16/14 – Radiographic and Pathologic Response

Radiographic response

Response	Total (N=62) N (%)
CR	4 (6.5%)
PR	32 (51.6%)
SD	16 (25.8%)
PD	4 (6.5%)
NE	4 (6.5%)
Missing[1]	2 (3.2%)

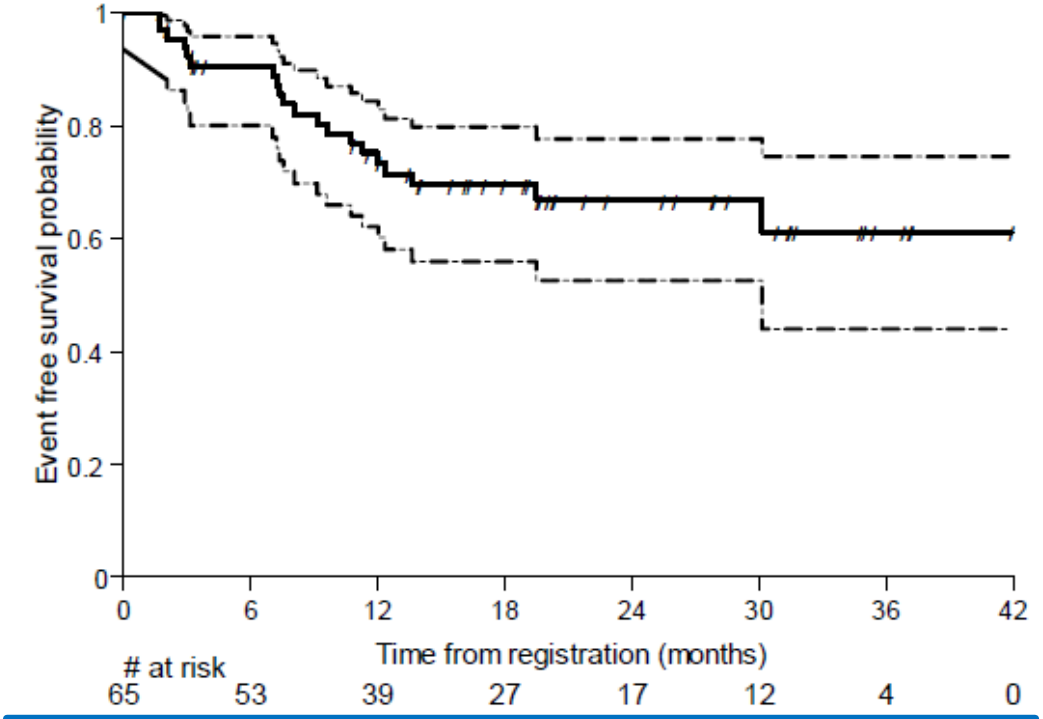
[1] Tumor assessment not done (N=2)

Pathologic response

Response	Total (N=55) N (%)
Pathological complete response (pCR)	10 (18.2%)
Major pathological response (MPR)[1]	33 (60.0%)
Nodal downstaging - ypN0 - ypN1	37 (67.3%) 26 (47.3%) 11 (20.0%)

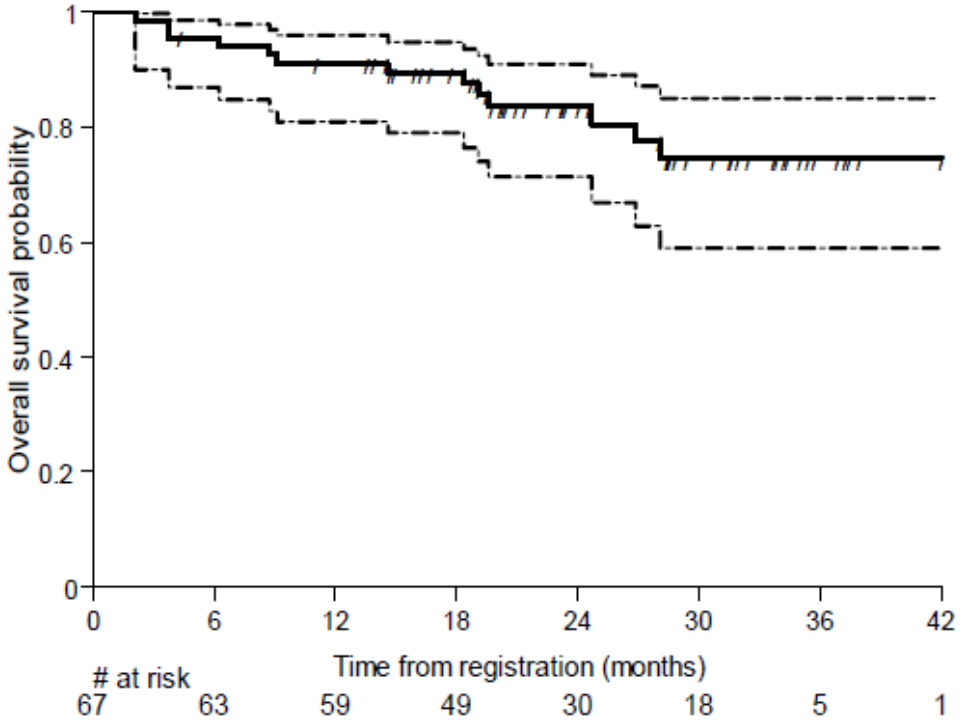
[1] Defined as ≤10% viable tumor cells
MPR significantly associated with PD-L1 positivity (> 1%), p=0.038

SAKK 16/14 – EFS and OS



EFS at 12 months: 73.4% (90% CI: 62.7 – 81.5)

Median EFS: not reached (95% CI: 27.6 – NR)



Median OS: not reached (NR) (95% CI: NR – NR)

Median follow-up: 28.6 months. Time point of analysis: July 10, 2020

SAKK 16/14 – Conclusion

- This is to our knowledge the largest cohort of patients with resectable stage IIIA(N2) NSCLC receiving perioperative immune checkpoint inhibitor therapy
- The addition of perioperative durvalumab to standard of care cisplatin/docetaxel
  - is safe
  - results in a very encouraging 1-year EFS rate that exceeds historical data of chemotherapy alone
  - leads to high major pathological response rate and rate of nodal downstaging
- Exploratory analyses of tissue and blood biomarkers are ongoing
- Perioperative PD-L1 inhibition in addition to standard neoadjuvant chemotherapy forms the backbone of our next study investigating the additional benefit of neoadjuvant immune-modulatory radiotherapy (SAKK 16/18; NCT04245514)

Neoadjuvant chemotherapy and nivolumab in resectable non-small-cell lung cancer (NADIM): an open-label, multicentre, single-arm, phase 2 trial

Mariano Provencio, Ernest Nadal, Amelia Insa, María Rosario García-Campelo, Joaquín Casal-Rubio, Manuel Dómine, Margarita Majem, Delvys Rodríguez-Abreu, Alex Martínez-Martí, Javier De Castro Carpeño, Manuel Cobo, Guillermo López Vivanco, Edel Del Barco, Reyes Bernabé Caro, Nuria Viñolas, Isidoro Barneto Aranda, Santiago Viteri, Eva Pereira, Ana Royuela, Marta Casarrubios, Clara Salas Antón, Edwin R Parra, Ignacio Wistuba, Virginia Calvo, Raquel Laza-Briviesca, Alfredo Romero, Bartomeu Massutí, Alberto Cruz-Bermúdez

Summary

Background Non-small-cell lung cancer (NSCLC) is terminal in most patients with locally advanced stage disease. We aimed to assess the antitumour activity and safety of neoadjuvant chemoimmunotherapy for resectable stage IIIA NSCLC.

Methods This was an open-label, multicentre, single-arm phase 2 trial done at 18 hospitals in Spain. Eligible patients were aged 18 years or older with histologically or cytologically documented treatment-naive American Joint Committee on Cancer-defined stage IIIA NSCLC that was deemed locally to be surgically resectable by a multidisciplinary clinical team, and an Eastern Cooperative Oncology Group performance status of 0 or 1. Patients received neoadjuvant treatment with intravenous paclitaxel (200 mg/m²) and carboplatin (area under curve 6; 6 mg/mL per min) plus nivolumab (360 mg) on day 1 of each 21-day cycle, for three cycles before surgical resection, followed by adjuvant intravenous nivolumab monotherapy for 1 year (240 mg every 2 weeks for 4 months, followed by 480 mg every 4 weeks for 8 months). The primary endpoint was progression-free survival at 24 months, assessed in the modified intention-to-treat population, which included all patients who received neoadjuvant treatment, and in the per-protocol population, which included all patients who had tumour resection and received at least one cycle of adjuvant treatment. Safety was assessed in the modified intention-to-treat population. This study is registered with ClinicalTrials.gov, NCT03081689, and is ongoing but no longer recruiting patients.

Findings Between April 26, 2017, and Aug 25, 2018, we screened 51 patients for eligibility, of whom 46 patients were enrolled and received neoadjuvant treatment. At the time of data cutoff (Jan 31, 2020), the median duration of follow-up was 24·0 months (IQR 21·4–28·1) and 35 of 41 patients who had tumour resection were progression free. At 24 months, progression-free survival was 77·1% (95% CI 59·9–87·7). 43 (93%) of 46 patients had treatment-related adverse events during neoadjuvant treatment, and 14 (30%) had treatment-related adverse events of grade 3 or worse; however, none of the adverse events were associated with surgery delays or deaths. The most common grade 3 or worse treatment-related adverse events were increased lipase (three [7%]) and febrile neutropenia (three [7%]).

Interpretation Our results support the addition of neoadjuvant nivolumab to platinum-based chemotherapy in patients with resectable stage IIIA NSCLC. Neoadjuvant chemoimmunotherapy could change the perception of locally advanced lung cancer as a potentially lethal disease to one that is curable.

Funding Bristol-Myers Squibb, Instituto de Salud Carlos III, European Union's Horizon 2020 research and innovation programme.

Introduction

Non-small-cell lung cancer (NSCLC) accounts for 80–85% of all lung cancer cases. Approximately 20% of patients with NSCLC are diagnosed with stage IIIA (N2) disease.[1] Outcomes remain poor for this subset of patients, even in patients with potentially operable tumours, with a median progression-free survival of 13 months and a 3-year overall survival of 30%, with no major treatment advances made in the past 25 years.[2]

Pathological response to neoadjuvant treatment is a potential surrogate endpoint for survival; however, considering the low proportion of patients who achieve complete pathological response with induction chemotherapy (median 4%; range 0–16%), a definitive association has been difficult to establish, and has not been validated in NSCLC.[3]

In a 2018 study, neoadjuvant administration of two doses of nivolumab was associated with major pathological response in nine (45%) of 20 evaluable patients with NSCLC tumours, with two (10%) of 20 patients achieving a complete pathological response.[4] Furthermore, in a 2020 study of neoadjuvant chemoimmunotherapy, 17 (57%) of

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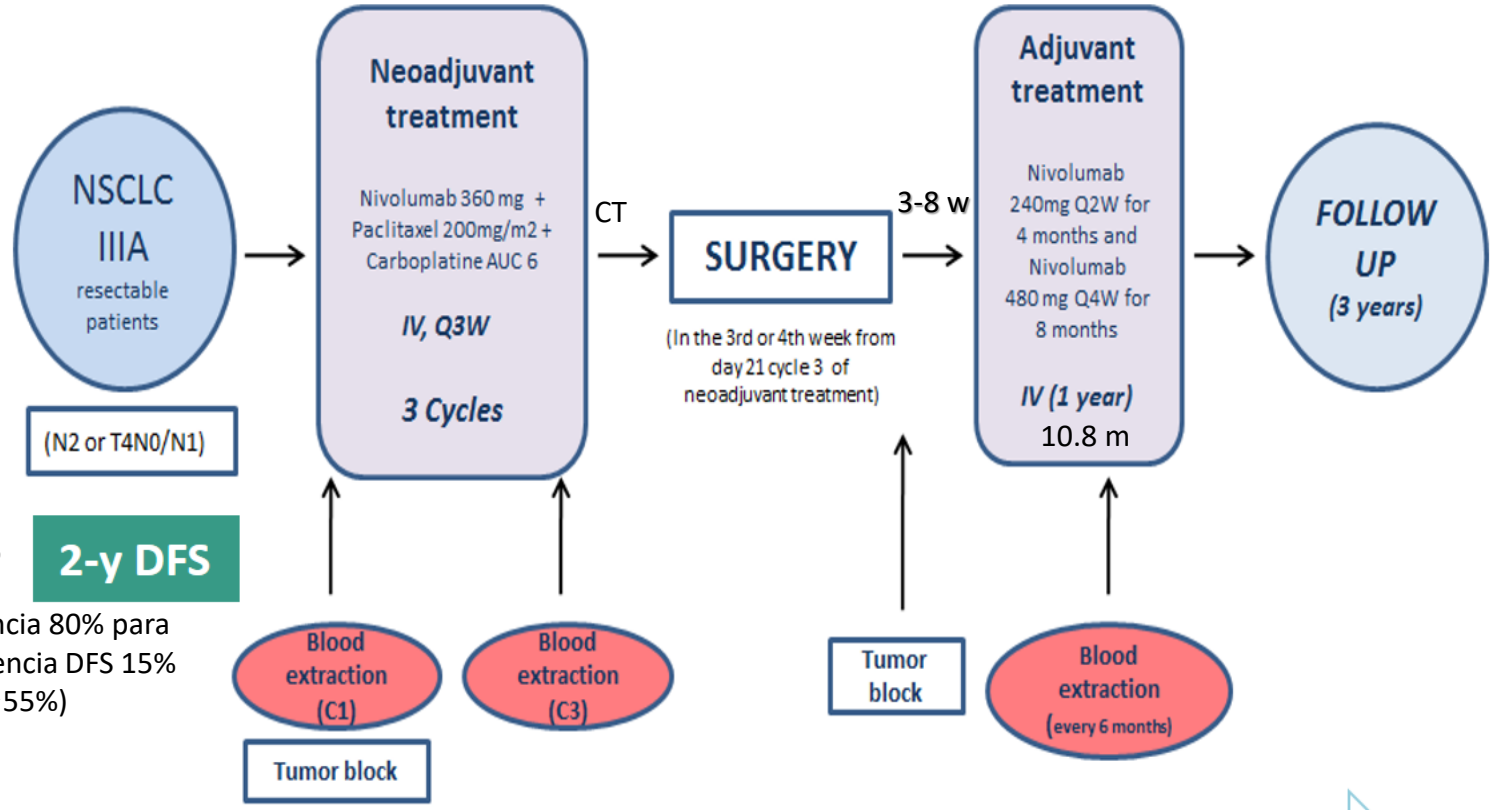
Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain (M Provencio MD, A Royuela PhD, M Casarrubios MSc, C Salas Antón MD, V Calvo MD, R Laza-Briviesca MSc, A Romero PhD, A Cruz-Bermúdez PhD); Consortium for Biomedical Research in Epidemiology and Public Health (CIBERESP), Institute of Health Carlos III, Madrid, Spain (A Royuela); Institut Català d'Oncologia, L'Hospitalet de Llobregat, Barcelona, Spain (E Nadal MD); Fundación INCLIVA, Hospital Clínico Universitario de Valencia, Valencia, Spain (A Insa MD); Hospital Universitario A Coruña, A Coruña, Spain (M R García-Campelo MD); Hospital Universitario de Vigo, Pontevedra, Spain (J Casal-Rubio MD); Instituto de Investigación Sanitaria Fundación Jiménez Díaz (IIS-FJD), Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain (M Dómine MD); Hospital de la Santa Creu I Sant Pau, Barcelona, Spain (M Majem MD); Hospital Insular de Gran Canaria, Las Palmas, Spain (D Rodríguez-Abreu MD); Hospital Universitario e Instituto de Oncología Vall d'Hebron (VHIO), Barcelona, Spain (A Martínez-Martí MD); Hospital Universitario La Paz, Madrid, Spain (J De Castro Carpeño MD); Hospital Universitario Regional de Málaga, Málaga, Spain (M Cobo MD); Hospital Universitario Cruces, Barakaldo, Spain (G López Vivanco MD); Hospital

THE LANCET Oncology

NADIM

NADIM phase II trial

18 Hospitales (Spain) Abril 2017-Agosto 2018



PEP **2-y DFS**

Potencia 80% para diferencia DFS 15% (40→55%)

N=51 **N=46** **N=41 (89%)** **N=37 (90%)**

PET-Scan

87% pN2
76% N-multisite

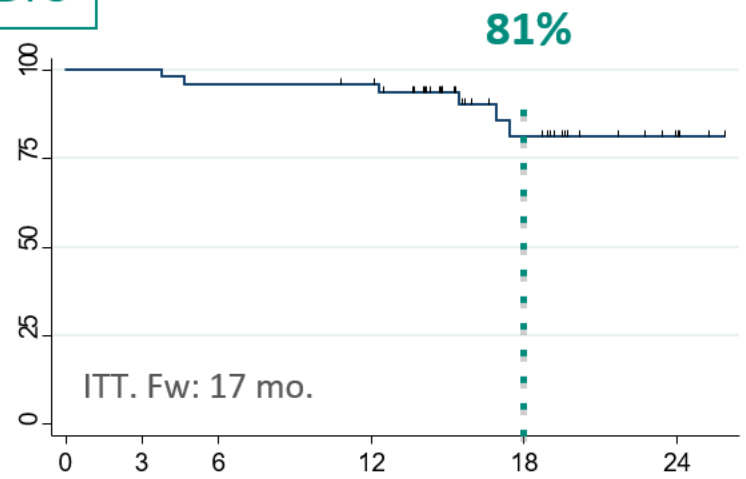
RECIST V1.1
CR 4%; PR 72%; SD 24%

MPR (≤ 10% viable cells): 83%
pCR: 59%

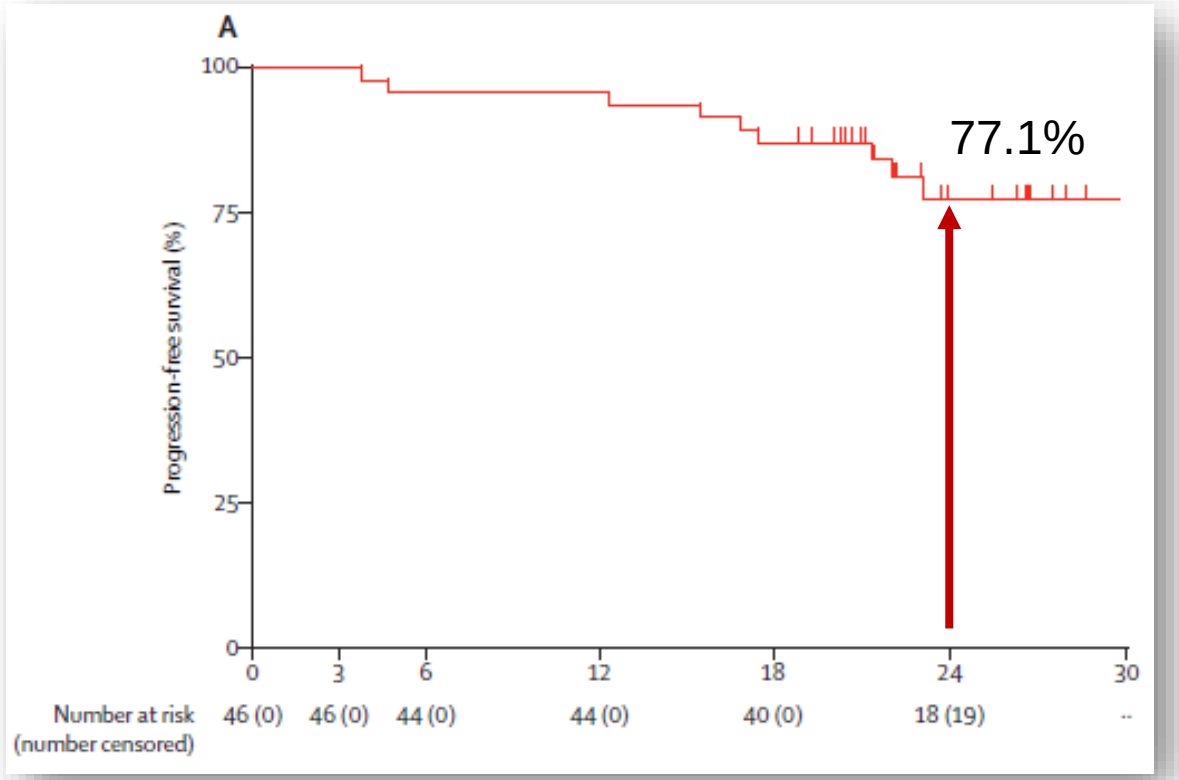
Downstaging

29 pN2 → 25 (86%) pN0
RR 74% / DownS: 90%

DFS

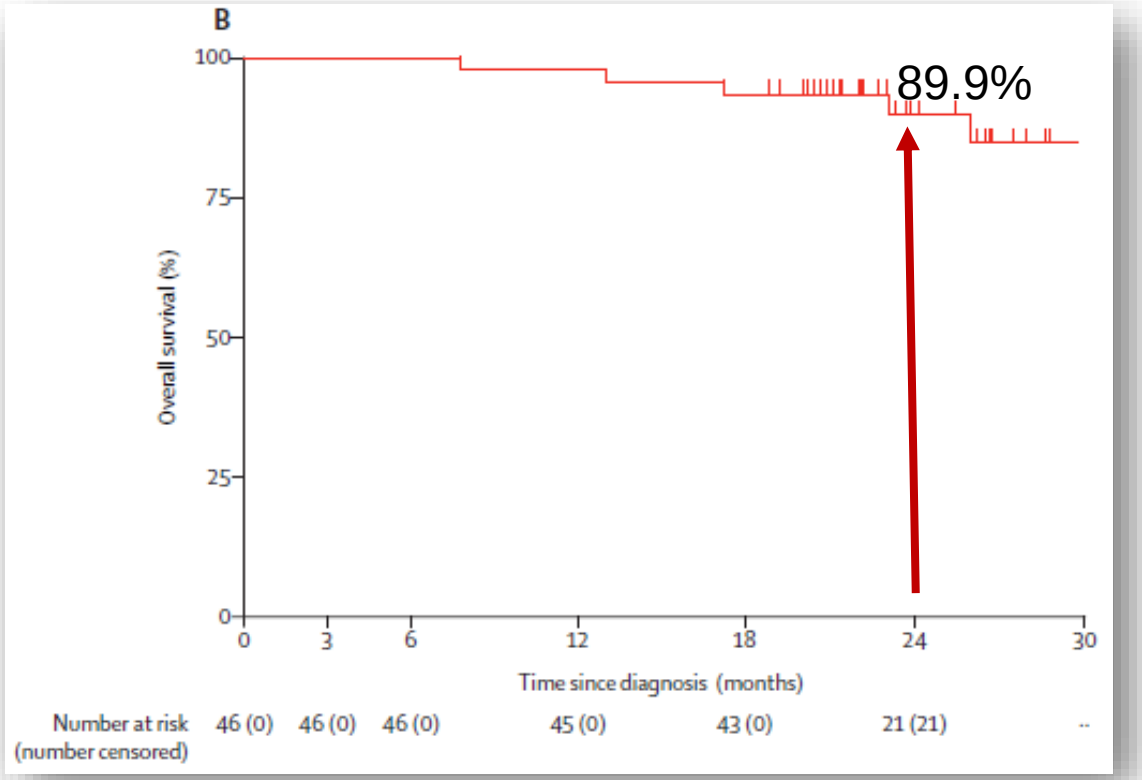


Modified ITT population



Median PFS not reached

cPR (96.2%) > iPR, MPR



Median OS not reached

cPR > iPR

	Grade 1–2	Grade 3	Grade 4
Any treatment-related adverse event	43 (93%)	14 (30%)	2 (4%)
Asthenia or fatigue	23 (50%)	1 (2%)	0
Alopecia	16 (35%)	1 (2%)	0
Nausea	15 (33%)	0	
Neurotoxicity	13 (28%)	2 (4	
Arthralgia	12 (26%)		
Diarrhoea	11 (24%)		0
Skin disorders (rash)	10 (2	)	0
Myalgia		0	0
Vomiting		0	0
Decreased appetite or anorexia	%)	1 (2%)	0
Constipation	8 (17%)	0	0
Paraesthesia	8 (17%)	0	0
Pruritus	7 (15%)	0	0
Anaemia	7 (15%)	0	0
Increased amino	4 (9%)	1 (2%)	0
Neutrope	2 (4%)	1 (2%)	1 (2%)
Incr e	1 (2%)	2 (4%)	0
Incre e	1 (2%)	2 (4%)	0
Increase pase	0	2 (4%)	1 (2%)
Febrile neutropenia	0	3 (7%)	0
Pemphigoid of the hand	0	1 (2%)	0

Data are n (%). Toxicity was monitored continuously for 100 days after the last dose of neoadjuvant nivolumab. No grade 5 treatment-related adverse events were observed.

Table 2: **Treatment-related adverse events during neoadjuvant treatment in the modified intention-to-treat population (n=46)**

No diferencias en PFS

Ningún EA ocasionó discontinuidad del tto, disminución de dosis, retraso Cx o muerte
7% no pudieron recibir Nivo adyuvante

	Grade 1–2	Grade 3	Grade 4
Any treatment-related adverse event	32 (86%)	7 (19%)	1 (3%)
Skin disorders (rash)	19 (51%)	1 (3%)	0
Asthenia or fatigue	18 (49%)	0	0
Pruritus	13 (35%)	0	0
Decreased appetite or anorexia	7 (19%)	0	0
Diarrhoea	7 (19%)	0	0
Arthralgia	7 (19%)	0	0
Myalgia	5 (14%)	0	0
Nausea	5 (14%)	0	0
Vomiting	4 (11%)	0	0
Constipation	4 (11%)	0	0
Paraesthesia	4 (11%)	0	0
Increased lipase	1 (3%)	3 (8%)	1 (3%)
Increased serum amylase	1 (3%)	3 (8%)	0
Adrenal insufficiency	0	1 (3%)	0
Pemphigoid of the hand	0	1 (3%)	0

Data are n (%). No grade 5 treatment-related adverse events were observed.

Table 3: **Treatment-related adverse events during adjuvant treatment in the per-protocol population (n=37)**

14% de pacientes con EA sufrieron discontinuidad del tto
Ningún EA ocasionó muerte

Correlación PD-L1 >25% y MPR/cPR
No correlación PD-L1 con DFS y OS

PACIFIC: 4y SV update

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PACIFIC: TRIAL DESIGN

Phase 3, Randomised, Double-blind, Placebo-controlled, Multicentre, International Trial

- Unresectable Stage III NSCLC without progression after definitive platinum-based cCRT* (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- If available, archived pre-cCRT tumour tissue for PD-L1 testing†

All-comers population (i.e. irrespective of PD-L1 status)

N=713 randomised

1–42 days post-cCRT

R

2:1 randomisation, stratified by age, sex, and smoking history

Durvalumab
10 mg/kg q2w for up to 12 months
N=476

Placebo
q2w for up to 12 months
N=237

Primary endpoints

- PFS by BICR using RECIST v1.1‡
- OS

Key secondary endpoints

- ORR, DoR, and TTDM by BICR using RECIST v1.1
- Safety
- PROs

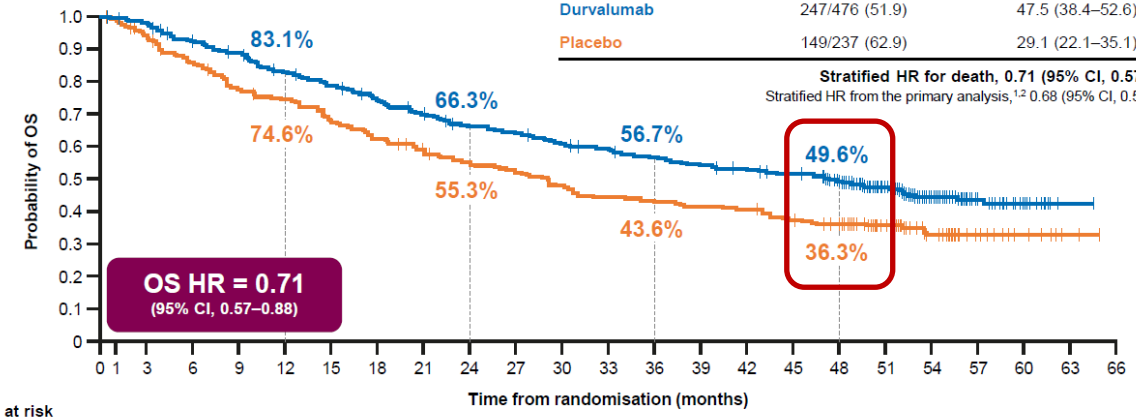
- Updated analyses of OS and PFS (~4 years after the last patient was randomised; planned exploratory update)
  - Treatment effects for the ITT population were estimated using a stratified log-rank approach (with trial stratification factors)
  - Treatment effects for patient subgroups were estimated from unstratified Cox proportional-hazards models (with treatment as the only covariate)

NCT02125461. *Radiation dosage typically 60–66 units of gray in 30–33 fractions. †Using the Ventana SP263 immunohistochemistry assay.
‡Defined as the time from randomisation (which could occur up to 6 weeks post-cCRT) to the date of objective disease progression or death by any cause in the absence of progression.
BICR, blinded independent central review; cCRT, concurrent chemoradiotherapy; DoR, duration of response; ITT, intent to treat; NSCLC, non-small-cell lung cancer; ORR, objective response rate; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival; PROs, patient-reported outcomes; PS, performance status; q2w, every 2 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; WHO, World Health Organization.

UPDATED OS (ITT)

	No. of events/ total no. of patients (%)	Median OS (95% CI), months
Durvalumab	247/476 (51.9)	47.5 (38.4–52.6)
Placebo	149/237 (62.9)	29.1 (22.1–35.1)

Stratified HR for death, 0.71 (95% CI, 0.57–0.88)
Stratified HR from the primary analysis,[1,2] 0.68 (95% CI, 0.53–0.87)



No. at risk

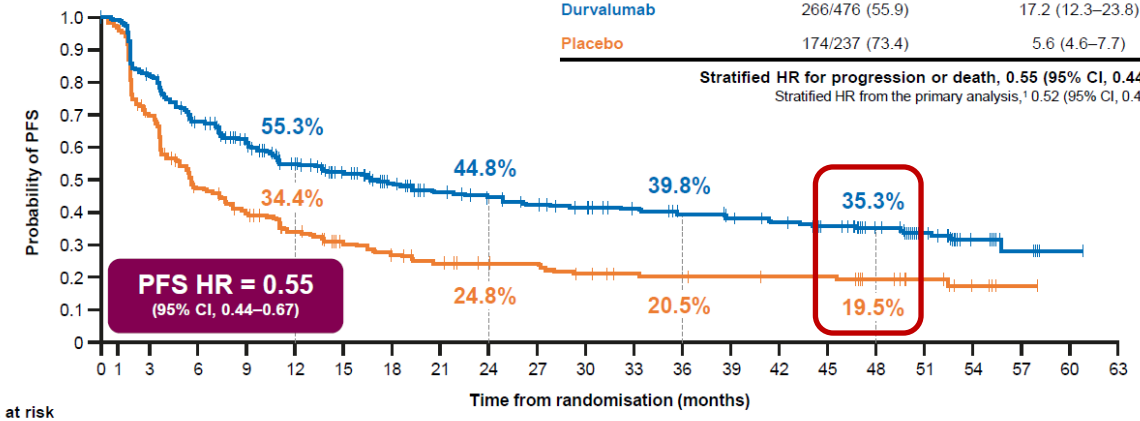
Durvalumab	476	464	431	414	385	364	343	319	299	290	274	265	252	241	235	225	195	138	75	36	15	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	75	53	29	15	7	2	0

Data cutoff: 20 March 2020 (median follow up, 34.2 months [range, 0.2–64.9]). CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival.
1. Antonia SJ, et al. New Engl J Med 2018;379:2342–50; 2. European Medicines Agency. Durvalumab (Imfinzi). Summary of product characteristics 2020 [Accessed August 2020]. Available from: https://www.ema.europa.eu/en/documents/product-information/imfinzi-epar-product-information_en.pdf.

UPDATED PFS (BICR; ITT)

	No. of events/ total no. of patients (%)	Median PFS (95% CI), months
Durvalumab	266/476 (55.9)	17.2 (12.3–23.8)
Placebo	174/237 (73.4)	5.6 (4.6–7.7)

Stratified HR for progression or death, 0.55 (95% CI, 0.44–0.67)
Stratified HR from the primary analysis,[1] 0.52 (95% CI, 0.42–0.65)



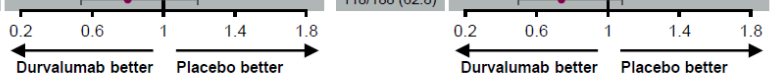
No. at risk

Durvalumab	476	377	301	266	213	189	165	146	136	127	119	110	103	97	92	80	59	37	18	8	1	0	
Placebo	237	163	105	86	67	55	47	40	36	35	29	26	25	24	23	22	16	11	5	1	0	0	

Data cutoff: 20 March 2020 (median follow up, 34.2 months [range, 0.2–64.9]). BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; PFS, progression-free survival.
1. Antonia SJ, et al. New Engl J Med 2017;377:1919–29.

UPDATED OS AND PFS IN PRE-SPECIFIED SUBGROUPS

		OS		PFS (BICR)	
		# events / # patients (%)	HR and 95% CI	# events / # patients (%)	HR and 95% CI
All patients		396/713 (55.5)		440/713 (61.7)	
Sex	Male	290/500 (58.0)		313/500 (62.6)	
	Female	106/213 (49.8)		127/213 (59.6)	
Age at randomisation	<65 years	195/391 (49.9)		235/391 (60.1)	
	≥65 years	201/322 (62.4)		205/322 (63.7)	
Smoking status	Smoker	361/649 (55.6)		401/649 (61.8)	
	Non-smoker	35/64 (54.7)		39/64 (60.9)	
NSCLC disease stage	Stage IIIA	216/377 (57.3)		223/377 (59.2)	
	Stage IIIB	170/319 (53.3)		208/319 (65.2)	
Tumour histologic type	Squamous	192/326 (58.9)		212/326 (65.0)	
	All other	204/387 (52.7)		228/387 (58.9)	
Prior definitive CT	Cisplatin	203/395 (51.4)		238/395 (60.3)	
	Carboplatin	179/301 (59.5)		189/301 (62.8)	
Best response to prior therapy	Complete response	8/16 (50.0)	NA*	9/16 (56.3)	NA*
	Partial response	177/349 (50.7)		211/349 (60.5)	
	Stable disease	203/338 (60.1)		214/338 (63.3)	
***EGFR* mutation**	Positive	24/43 (55.8)		32/43 (74.4)	
	Negative	261/482 (54.1)		290/482 (60.2)	
	Unknown	111/188 (59.0)		118/188 (62.8)	



*Hazard ratio and 95% CI not calculated if the subgroup has less than 20 events.

Data cutoff: 20 March 2020. BICR, blinded independent central review; CI, confidence interval; CT, chemotherapy; EGFR, epidermal growth factor receptor; HR, hazard ratio; ITT, intent-to-treat; NA, not applicable; OS, overall survival; PFS, progression-free survival.

UPDATED OS AND PFS IN PD-L1 SUBGROUPS

		OS		PFS (BICR)	
		# events / # patients (%)	HR and 95% CI	# events / # patients (%)	HR and 95% CI
All patients		396/713 (55.5)		440/713 (61.7)	
PD-L1 status (pre-specified)	≥25%	76/159 (47.8)		92/159 (57.9)	
	<25%	164/292 (56.2)		181/292 (62.0)	
	Unknown	156/262 (59.5)		167/262 (63.7)	
PD-L1 status (post-hoc)	1–<25%	75/144 (52.1)		85/144 (59.0)	
	≥1%	151/303 (49.8)		177/303 (58.4)	
	<1%	89/148 (60.1)		96/148 (64.9)	

- Important facts regarding PD-L1 status:
  - PD-L1 testing was not required and 37% of all randomised patients had unknown PD-L1 status
  - PD-L1 status was determined from tumour tissue obtained pre-CRT (getting a sample post-CRT medically not feasible)
  - PD-L1 expression-level cutoff of 1% was part of an unplanned post-hoc analysis requested by the EMA

Data cutoff: 20 March 2020. BICR, blinded independent central review; CRT, chemoradiotherapy; CI, confidence interval; CR, complete response; EMA, European Medicines Agency; HR, hazard ratio; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival.

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CONCLUSIONS

- The PACIFIC standard-of-care regimen, durvalumab consolidation after CRT, continues to demonstrate durable PFS and sustained OS benefit in this pre-planned exploratory update at 4 years, consistent with the significant benefit for these endpoints reported at the time of the primary analyses[1,2]
- The median OS for the durvalumab arm was reached for the first time at this update (KM estimates: durvalumab arm, 47.5 months; placebo arm, 29.1 months)
- The updated results demonstrate an estimated 4-year OS rate of 49.6% for the durvalumab arm vs 36.3% for placebo arm, and an estimated 4-year PFS rate of 35.3% vs 19.5%, respectively (KM estimates)
- Ongoing clinical trials are investigating concurrent ICI + CRT regimens and may further transform the treatment landscape for patients with unresectable Stage III NSCLC

CRT, chemoradiotherapy; ICI, immune checkpoint inhibition; KM, Kaplan–Meier; OS, overall survival; PFS, progression-free survival.

1. Antonia SJ, et al. New Engl J Med 2018;379:2342–50; 2. Antonia SJ, et al. New Engl J Med 2017;377:1919–29.

KEYNOTE 799

Conclusiones

- Screening en población de riesgo disminuye la mortalidad por CP a costa principalmente de diagnóstico en estadios iniciales potencialmente curables
    - <5% de población en riesgo en países con implementación debido a desconocimiento pacientes/médicos sobre beneficios y sobre exposición a radiación.
- Evidencia cada vez mayor sobre la equivalencia en términos de SV de la Segmentectomía anatómica frente a la lobectomía en estadios IA (falta de multicéntricos aleatorizados)
- IT neoadyuvante en estadios potencialmente resecables arroja resultados prometedores en términos de respuestas patológicas (pCR y MPR), con DFS superiores a series con QMT exclusivamente, con un perfil de EA seguro.
- El beneficio de la neoadyuvancia en términos de SV se produce principalmente cuando existe MPR unida a negativización de la afectación ganglionar.
- La RDT adyuvante en IIIA-N2 no aporta beneficio significativo en términos de DFS ni OS, con una elevada toxicidad inducida.
- En estadios III irresecables, Durvalumab de consolidación tras cCRT proporciona beneficio a 4 años en términos de DFS y OS frente a placebo.