Lung Cancer UPDATES
ASCO HIGHLIGTHS
29-31 MAYO 2020

Iniciativa científica de:
GECP lung cancer research

Cáncer de pulmón no microcítico: estadios iniciales y localmente avanzados

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De la investigación a la calidad asistencial
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IT+QT/RT neoadyuvante

Resectable NSCLC
Stage IB(≥4 cm) - IIIA
No EGFR/ALK mutation
PS 0-1

→ Induction: Nivolumab + Histology-Based Chemotherapy → Surgical Resection → Evaluation of pathologic response

Nivolumab 360 mg + Cisplatin 75 mg/m2-Pem 500 mg/m2/Gem 1250 mg/m2 d1,8
3 cycles

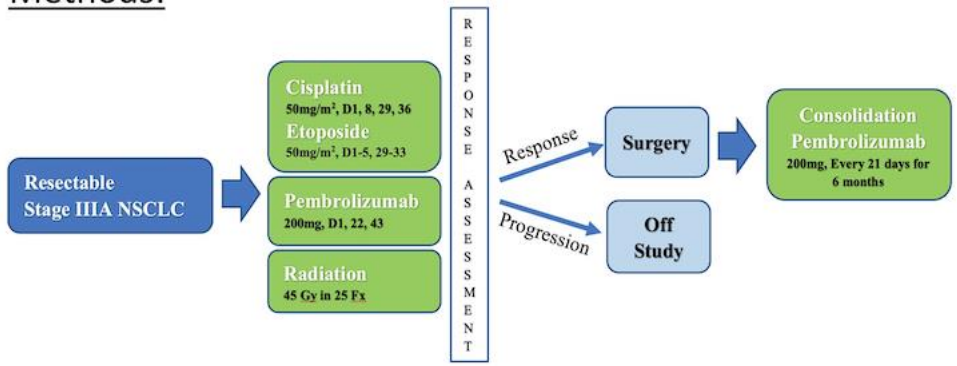
31% Non-Squamous
54% St IIIA
77% PD-L1 >1%

MPR/pCR: 11/13 (85%)
pCR: 3/13 (23%)

pt	Age	Gen	PD-L1 263 (%)	DX	Stage	stage	Path Resp	path response	CT response
1	57	M	70	sq	t1,N1	IIB	pCR	0	CR
2	69	M	30	sq	t3,N0	IIIA	MPR	8.89%	SD
3	60	W	2	sq	T4,N0	IIIA	MPR	0.01%	PR
4	49	M	60	non-sq	t4,N0	IIIA	MPR	0.50%	PR
5	56	W	>50	non-sq		IIB	pCR	0	SD
6	74	W	1	non-sq	t2a,n0	IIA	MPR	5.70%	SD
7	80	M	10	sq	t2a,n0	IIB	pCR	0%	PR
8	76	M	1	sq	t1b,n2	IIIA	MPR	<5%	SD
9	66	M	1	sq	T4,N0	IIIA	MPR	4.07%	PR
10	70	M	5	sq	T4,N0	IIIA	pCR	0	SD
11	71	W	5	sq	t4,N0	IIIA	SD	90%	PR
12	68	M	30	sq	T1,N1	IIB	pCR	0%	SD
13	70	W	<2	non-sq	t3,N0	IIB	SD	84%	SD

NADIM: 41 p
MPR: 83%
pCR: 59%

Methods:

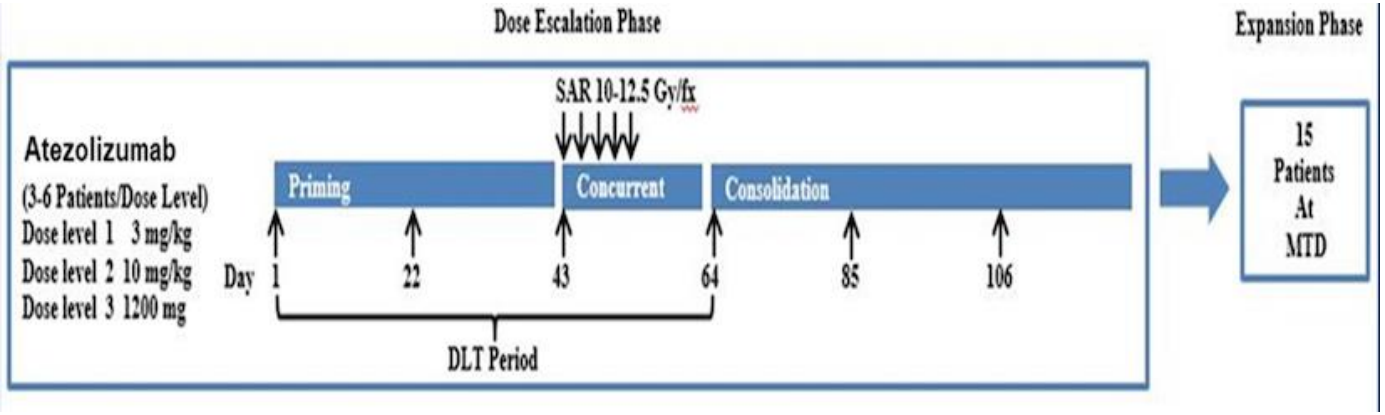


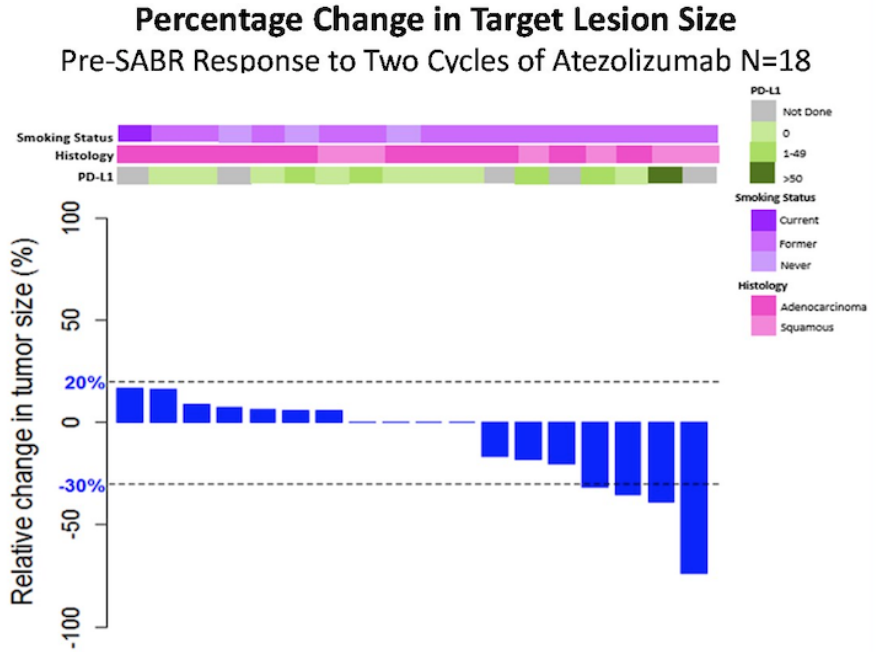
Patients	n = 9	
Completed Neoadjuvant Treatment	7	77%
Assessed for response	8	88%
Overall Response (ORR)		
Complete Response (pCR)	4/8	50%
Partial Response (PR)	1/8	13%
Stable Diseaes (SD)	1/8	13%
Progressive Disease (PD)	2/8	25%
Complete Resection	6/8	75%
Adjuvant IO	4/8	50%
Median Follow Up	19.6 months	
6 month PFS	55.6%	95% CI: 31%-99%
Median PFS	Not Reached	

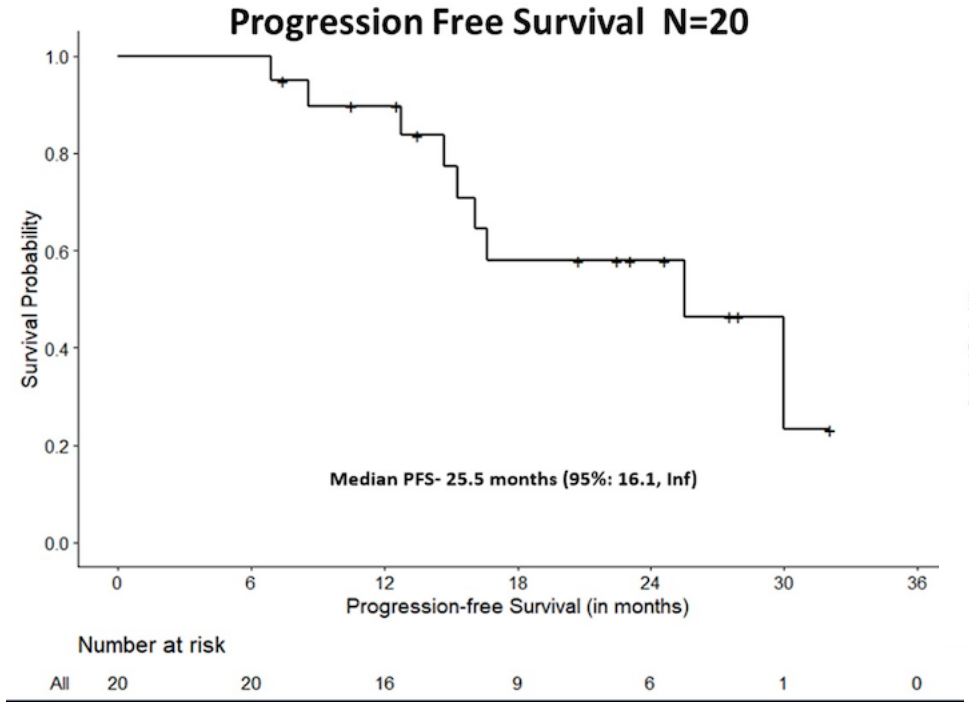
6 Surgery R0

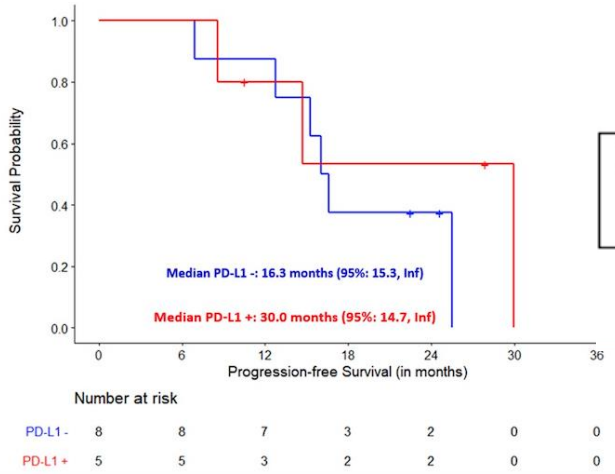
3 Complete Pembro Consolidation

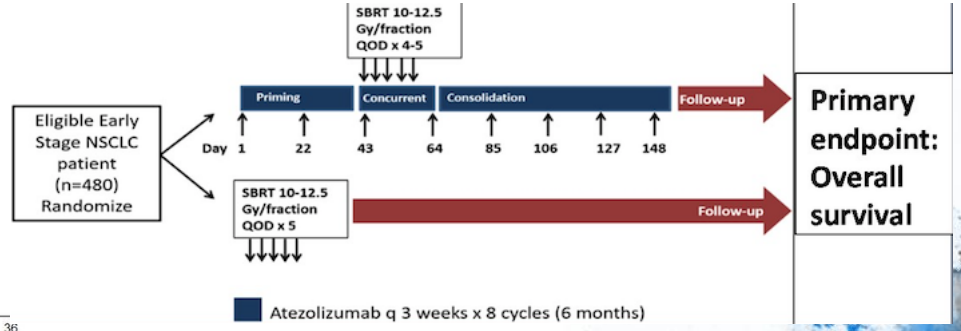
Atezolizumab + SBRT en estadios iniciales inoperables











QT adyuvante en CP Neuroendocrino Alto Grado

JOG1205/1206: Study Design

JCOG Japan Clinical Oncology Group

KEY ELIGIBILITY CRITERIA
- Completely resected HGNEC of the lung
- Pathological stage I-IIIA (7th TNM)
- ECOG PS 0-1
- Age 20-74 years
- Lobectomy or pneumonectomy with resection of N2 lymph nodes within 28-56 days

N=221

RANDOMIZED

1:1

EP arm
Etoposide (100 mg/m², days 1-3) +Cisplatin (80 mg/m², day 1) every 3 weeks, up to 4 cycles

IP arm
Irinotecan (60 mg/m², day 1, 8, 15) +Cisplatin (60 mg/m², day 1) every 4 weeks, up to 4 cycles

ENDPOINTS
- Primary
  - Relapse-free survival
- Secondary
  - Overall survival
  - Proportions of treatment completion
  - Adverse events
  - Serious adverse events
  - Second malignancies

Stratification factors:
- Sex (female vs. male)
- Pathological stage (I vs. II-IIIA)
- Histology (SCLC vs. LCNEC)
- Institution

UMIN000010298; https://www.umin.ac.jp/
jRCTs031180216; https://jrct.niph.go.jp/

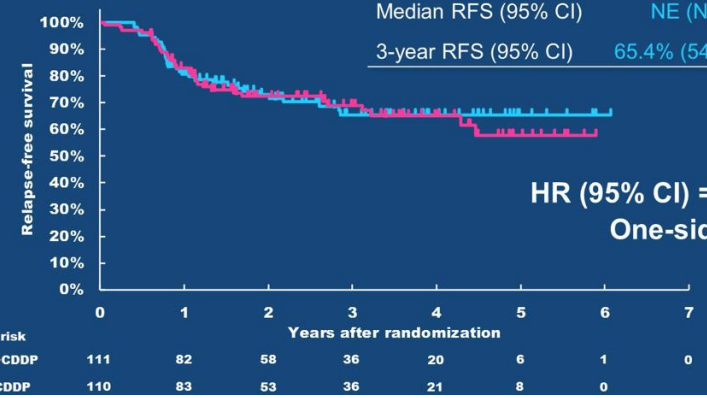
40-45% diagn postop

St IA 26%
St IIIA 17%

Primary Endpoint: RFS (ITT), assessed by investigators

	ETP+CDDP (n=111)	IRI+CDDP (n=110)
Number of events	33	34
Median RFS (95% CI)	NE (NE-NE)	NE (4.3 y- NE)
3-year RFS (95% CI)	65.4% (54.4-74.4%)	69.0% (58.4-77.5%)

Median follow up; 24.1 mo



HR (95% CI) = 1.076 (0.666-1.738)
One-sided p = 0.6185

Baseline Characteristics

JCOG Japan Clinical Oncology Group

		Etoposide + Cisplatin N=111	(%)	Irinotecan + Cisplatin N=110	(%)
Sex	Male	94	(84.7)	93	(84.5)
	Female	17	(15.3)	17	(15.5)
Age (years)	Median (Range)	65	(39 - 74)	66	(39 - 74)
ECOG-PS	0	75	(67.6)	82	(74.5)
	1	36	(32.4)	28	(25.5)
Histology	SCLC	39	(35.1)	39	(35.5)
	Combined SCLC	20	(18.0)	19	(17.3)
	LCNEC	38	(34.2)	36	(32.7)
	Combined LCNEC	14	(12.6)	16	(14.5)

ECOG-PS, Eastern Cooperative Oncology Group performance status
SCLC: Small-cell lung carcinoma, LCNEC: Large cell neuroendocrine carcinoma

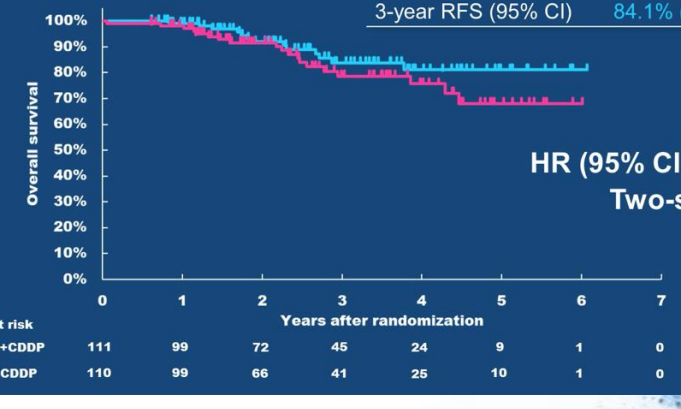
4 Cycles:
87.4% EP
vs
72.7% IP

RT ??
PCI??

Overall Survival (ITT)

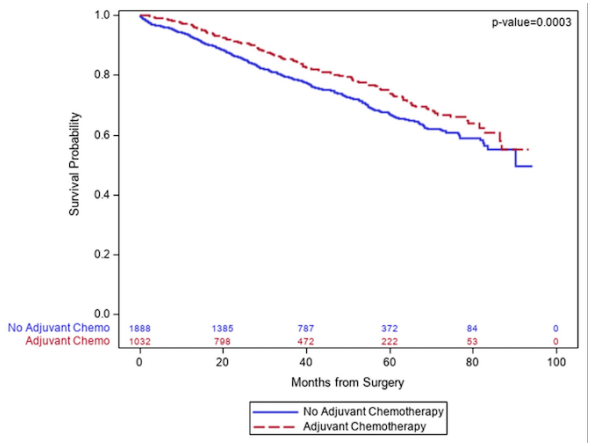
JCOG Japan Clinical Oncology Group

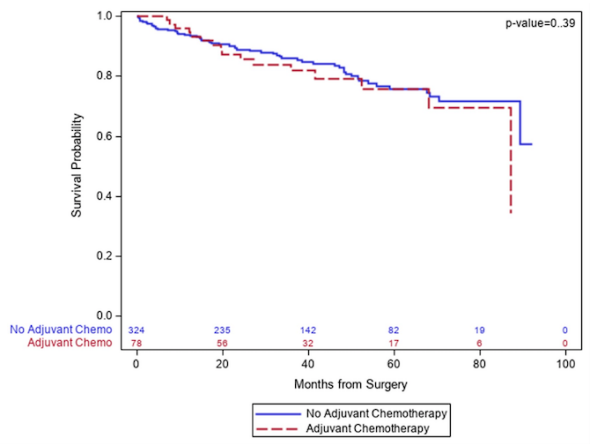
	ETP+CDDP (n=111)	IRI+CDDP (n=110)
Number of events	13	19
3-year RFS (95% CI)	84.1% (73.3-90.8%)	79.0% (67.5-86.8%)



HR (95% CI) = 1.539 (0.760-3.117)
Two-sided p = 0.2275

Tratamiento adyuvante Estadio I > 2 cm y fact. riesgo histol (inv. linfovasc/pleur)

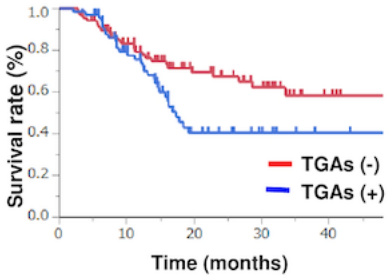




SLE tras resección o QT/RT si alteraciones genómicas

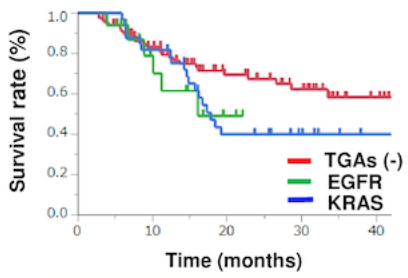
Treatment disposition	TGAs (-) n = 89	TGAs (+) n =69	p
Stage II	38	31	0.2
III	51	38	
Adjuvant therapy			
Yes	24	24	0.1
No	65	45	

Disease-free survival (DFS)



		Median DFS (m)	p
TGAs (-)	n=89	58	
TGAs (+)	n=69	17	0.03

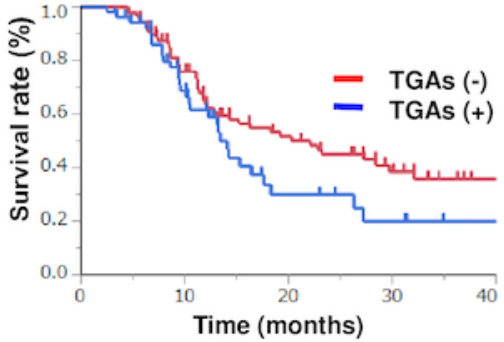
DFS according to EGFR / KRAS



		Median DFS (m)	p
TGAs (-)	n=89	58	
EGFR	n=18	16	0.2
KRAS	n=33	17	0.09

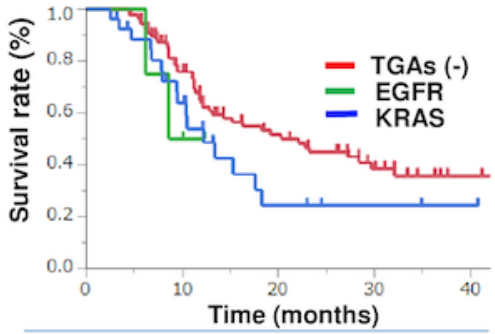
Survival analysis in patients who received chemo-radiotherapy

Progression-free survival (PFS)



		Median PFS (m)	p
TGAs (-)	n=94	22	
TGAs (+)	n=54	13	0.08

PFS according to EGFR / KRAS



		Median PFS (m)	p
TGAs (-)	n=94	22	
EGFR	n=5	9	0.3
KRAS	n=27	12	0.08

Osimertinib adyuvante en CPCNP EGFRmut+ resecado: ADAURA

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

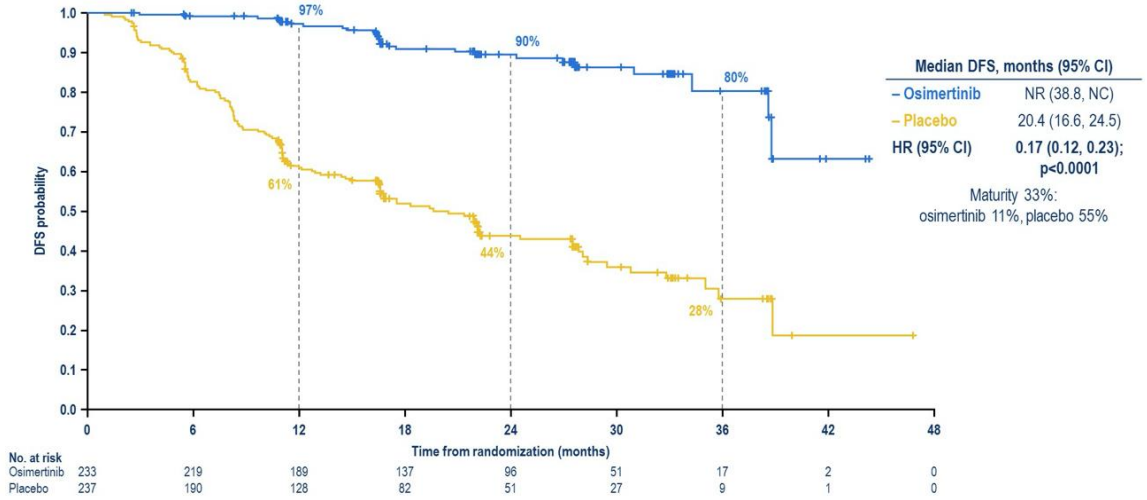
Follow up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

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

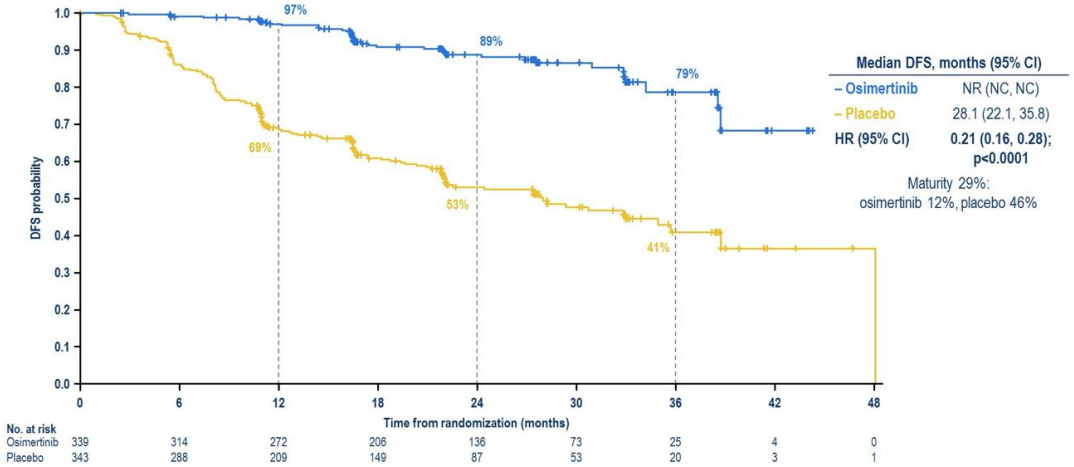
- **Following IDMC recommendation, the study was unblinded early due to efficacy; here we report an unplanned interim analysis**
- **At the time of unblinding the study had completed enrollment and all patients were followed up for at least 1 year**

Characteristic, %	Osimertinib (n=339)	Placebo (n=343)
Sex: male / female	32 / 68	28 / 72
Age, median (range), years	64 (30–86)	62 (31–82)
Smoking status: smoker* / non-smoker	32 / 68	25 / 75
Race: Asian / non-Asian	64 / 36	64 / 36
WHO performance status: 0 / 1	64 / 36	64 / 36
AJCC staging at diagnosis (7th edition): IB / II / IIIA	31 / 35 / 34	31 / 34 / 35
Histology: adenocarcinoma / other†	95 / 5	96 / 4
EGFR mutation at randomization‡: Ex19del / L858R	55 / 45	56 / 44
Adjuvant chemotherapy: yes / no	55 / 45	56 / 44

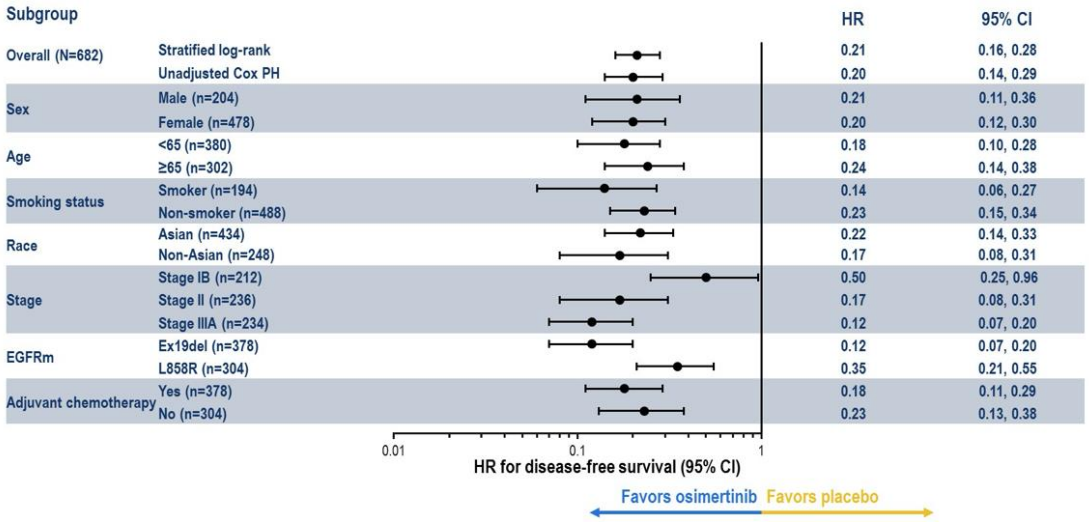
Primary endpoint: DFS in patients with stage II/IIIA disease



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

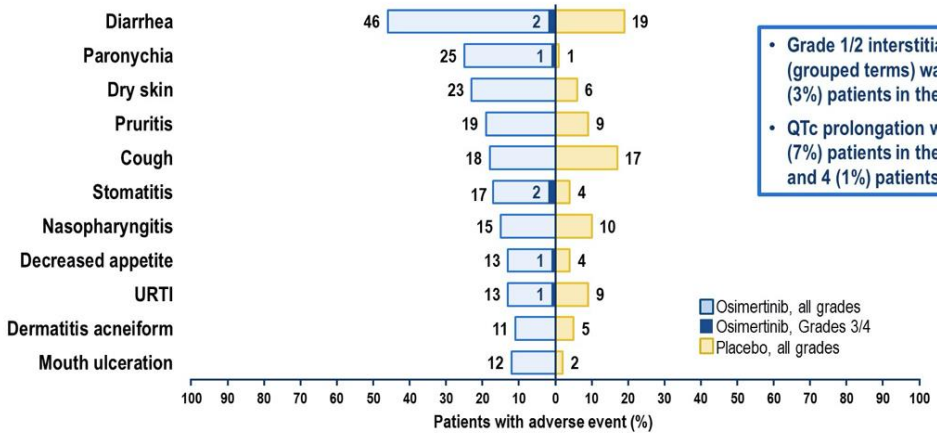


Osimertinib adyuvante en CPCNP EGFRmut+ resecado: ADAURA



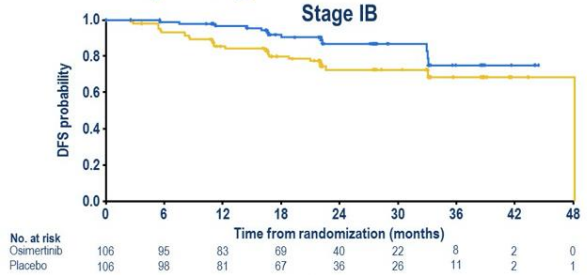
All causality adverse events (≥10% of patients)

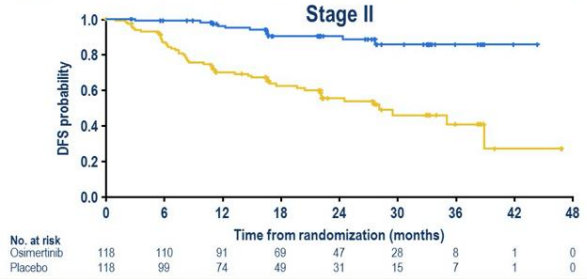
Median duration of exposure: osimertinib: 22.3 months (range 0 to 43), placebo: 18.4 months (range 0 to 48)



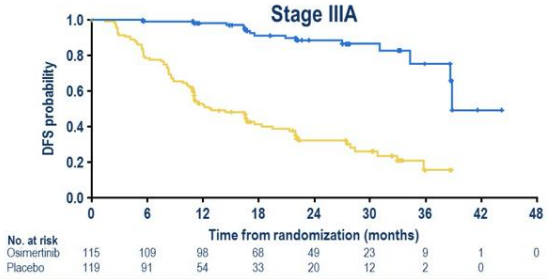
- Grade 1/2 interstitial lung disease (grouped terms) was reported in 10 (3%) patients in the osimertinib arm*
- QTc prolongation was reported in 22 (7%) patients in the osimertinib arm and 4 (1%) patients in the placebo arm†

DFS by stage

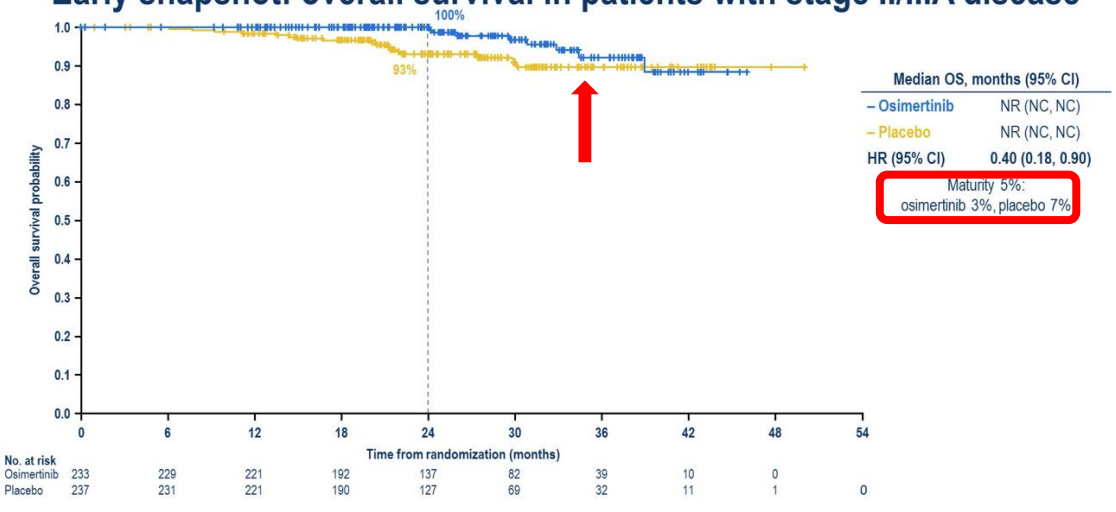




	Stage IB	Stage II	Stage IIIA
2 year DFS rate, % (95% CI)			
– Osimertinib	87 (77, 93)	91 (82, 95)	88 (79, 94)
– Placebo	73 (62, 81)	56 (45, 65)	32 (23, 42)
Overall HR (95% CI)	0.50 (0.25, 0.96)	0.17 (0.08, 0.31)	0.12 (0.07, 0.20)



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



Gefitinib adyuvante CPCNP EGFRmut+: CTONG 1104/Supervivencia

ADJUVANT study design (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

R 1:1

Gefitinib 250 mg/day for 24 months or until disease progression or unacceptable toxicity

Vinorelbine (25 mg/m² Days 1 & 8) plus cisplatin (75 mg/m² Day 1) every 3 weeks, for up to 4 cycles

DFS

Stratification factors:
- *EGFR* mutation
- N stage

Efficacy assessment:
- Every 12 weeks in 3 years
- Every 6 months after 3 year

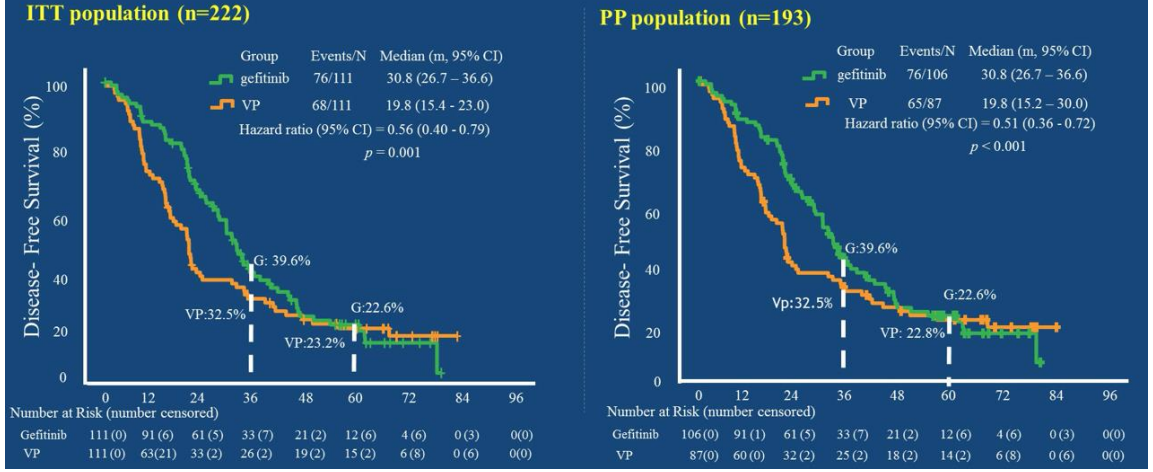
Primary endpoint:
- DFS

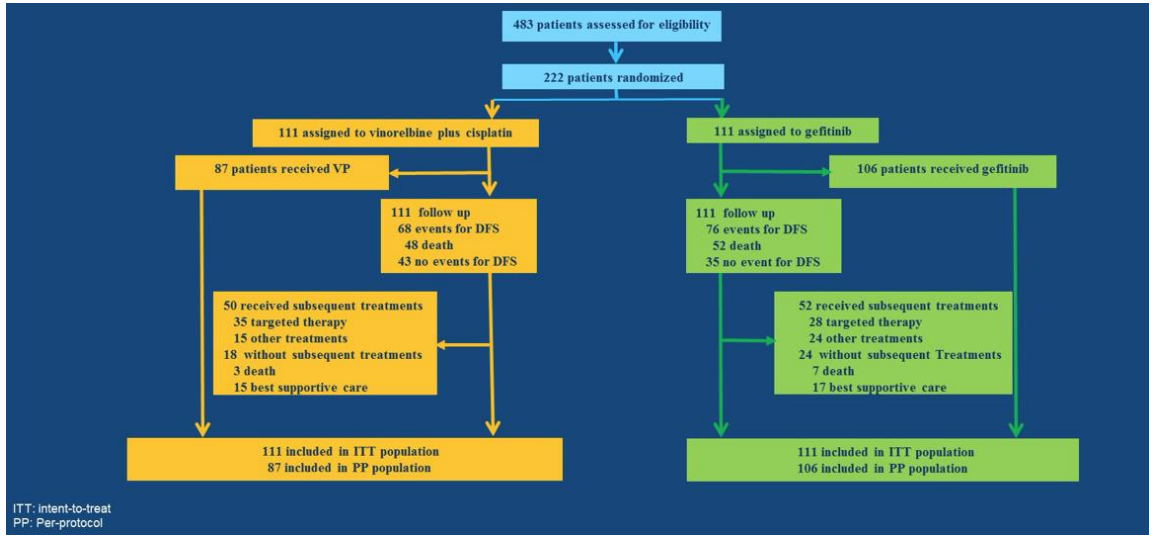
Secondary endpoints:
- 3-year DFS rate, 5-year DFS rate, OS, 5-year OS rate, safety, HRQoL (FACT-L, LCSS, TOI), exploratory biomarker analyses

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

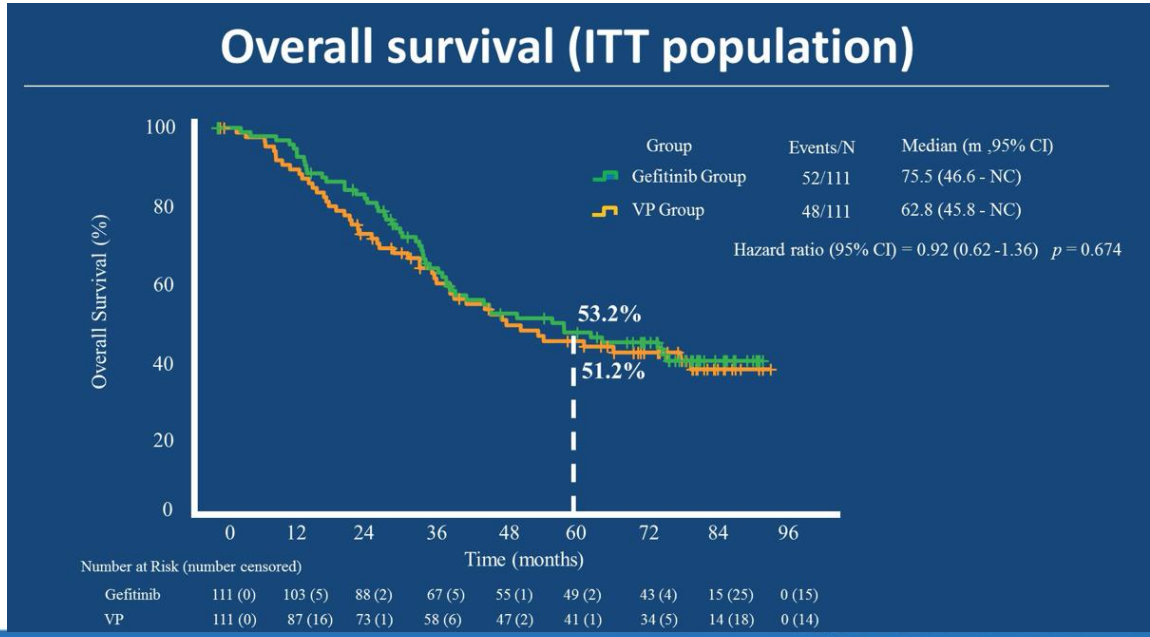
Zhong WZ et al. Lancet Oncol 2018;19:139-148

Updated 3-year & 5-year DFS rate

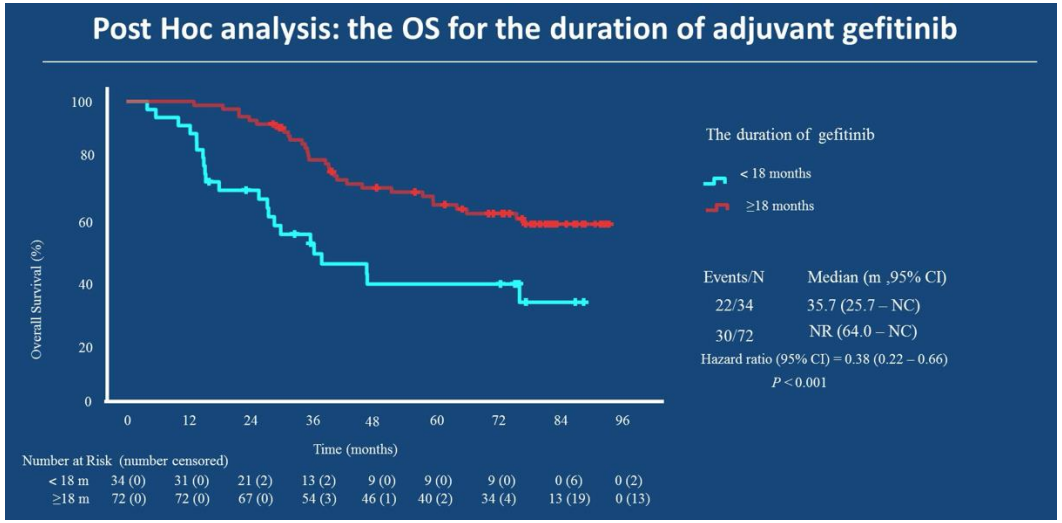




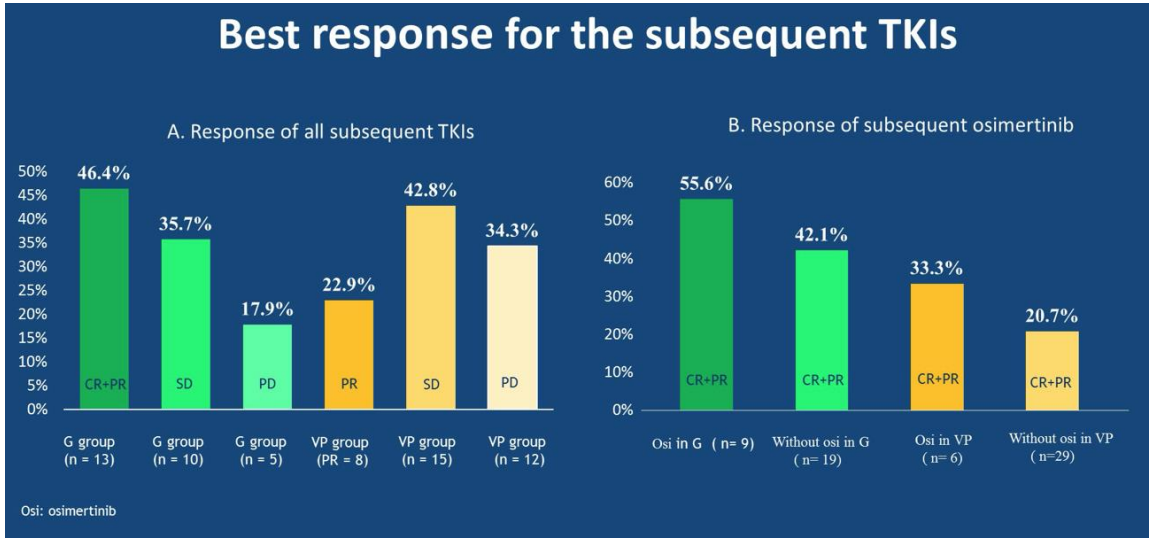
Overall survival (ITT population)



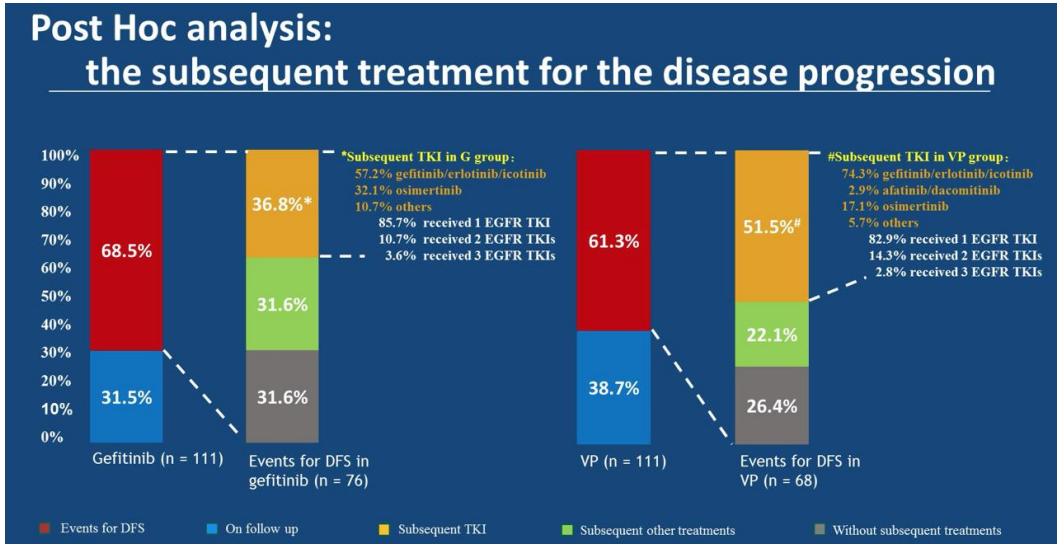
Gefitinib adyuvante CPCNP EGFRmut+: CTONG 1104/Supervivencia



Resistance mechan.?



T790M?



Intrinsic / Acquired Resistance