Lung Cancer UPDATES
IASLC HIGHLIGTHS
28-31 ENERO 2021
VIRTUAL

Iniciativa científica de:
GECP lung cancer research

CPCNP LOCALMENTE AVANZADO

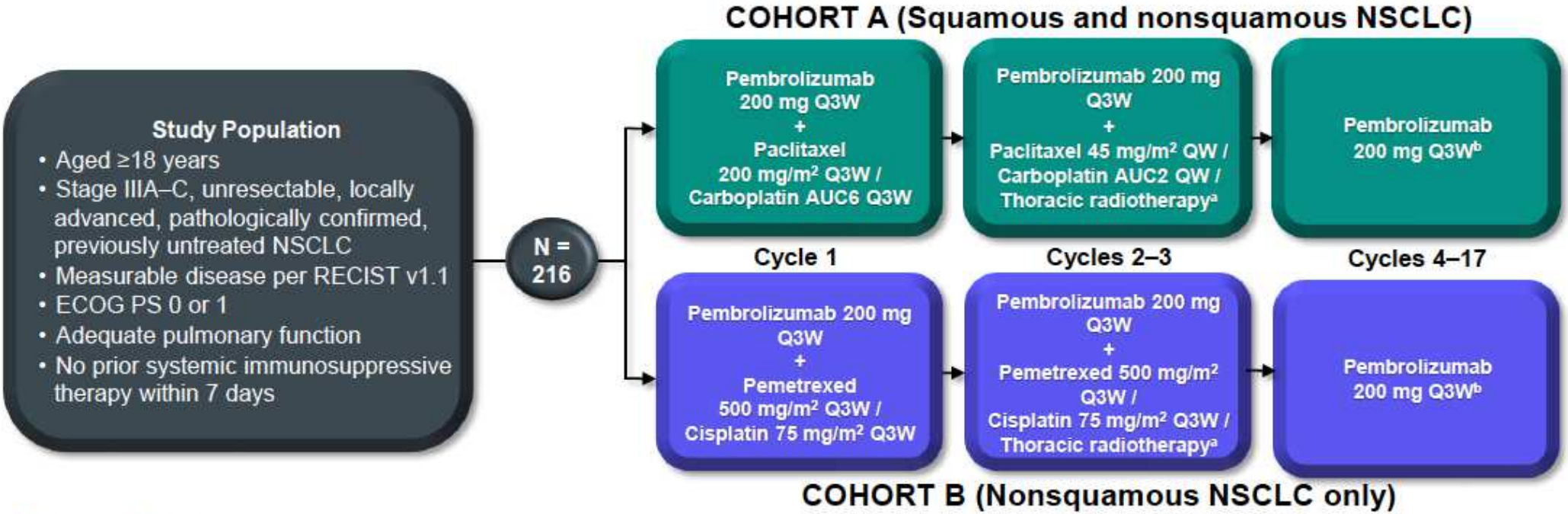
Andrés Barba Joaquín

Hospital de la Santa Creu i Sant Pau

- AGENDA

Pembrolizumab Plus Platinum Chemotherapy and Radiotherapy in Unresectable, Locally Advanced, Stage III NSCLC: KEYNOTE-799

M. Reck,[1] K.H. Lee,[2] N. Frost,[3] D.M. Kowalski,[4] V. Breder,[5] T. Pollock,[6] N. Reguart,[7] B. Houghton,[8] X. Quantin,[9] S.M. Keller,[10] H. Liu,[10] B. Piperdi,[10]



Primary Objectives

- ORR per RECIST version 1.1 by BICR
- Percentage of patients who develop grade ≥3 pneumonitis

Secondary Objectives

- PFS, OS, safety

Statistical Analysis Details

- Efficacy assessed in all patients with first study dose before or on October 31, 2019 (PE population)
- Safety assessed in all patients in the as-treated population

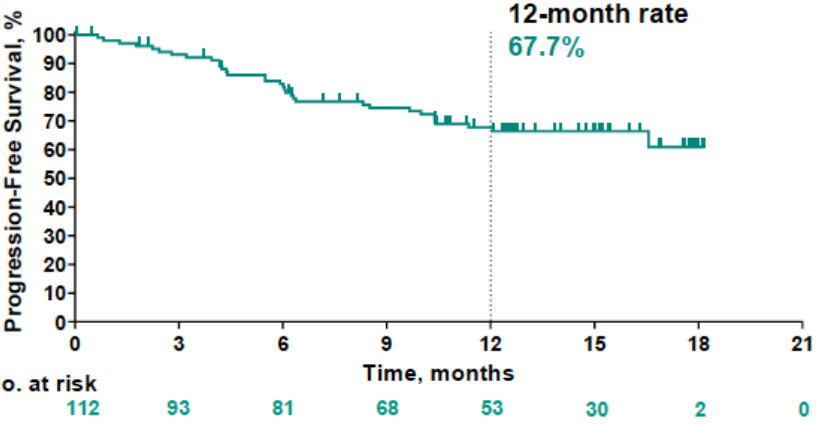
ORR and Duration of Response
By BICR per RECIST v1.1 (Primary Efficacy Population)

	Cohort A[a] n = 112		Cohort B[b] n = 61	
PE Population	**n = 112**		**n = 61**	
ORR, n (%) [95% CI]	78 (69.6) [60.2–78.0]		43 (70.5) [57.4–81.5]	
CR	4 (3.6)		3 (4.9)	
PR	74 (66.1)		40 (65.6)	
SD, n (%)	21 (18.8)		12 (19.7)	
PD, n (%)	1 (0.9)		0	
Not evaluable, n (%)	2 (1.8)		0	
No assessment, n (%)	10 (8.9)		6 (9.8)	
DOR, median (range),[c] mo	NR (1.4+ to 16.1+)		NR (2.0+ to 15.9+)	
DOR ≥12 mo,[c] n (%)	31 (82.2)		5 (72.1)	
PD-L1 Status	**TPS <1% (n = 21)**	**TPS ≥1% (n = 66)**	**TPS <1% (n = 17)**	**TPS ≥1% (n = 26)**
ORR, n (%)	14 (66.7)	49 (74.2)	11 (64.7)	18 (69.2)
Histology	**Nonsquamous (n = 39)**	**Squamous (n = 73)**	**Nonsquamous (n = 61)**	**Squamous (n = 0)**
ORR, n (%)	27 (69.2)	51 (69.9)	43 (70.5)	NA

PFS by BICR

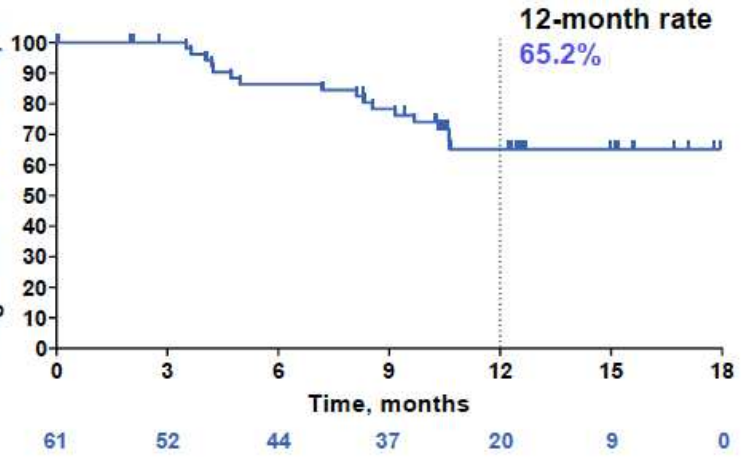
Cohort A[a]

n	Median (95% CI)
112	NR (16.6–NR)



Cohort B[b]

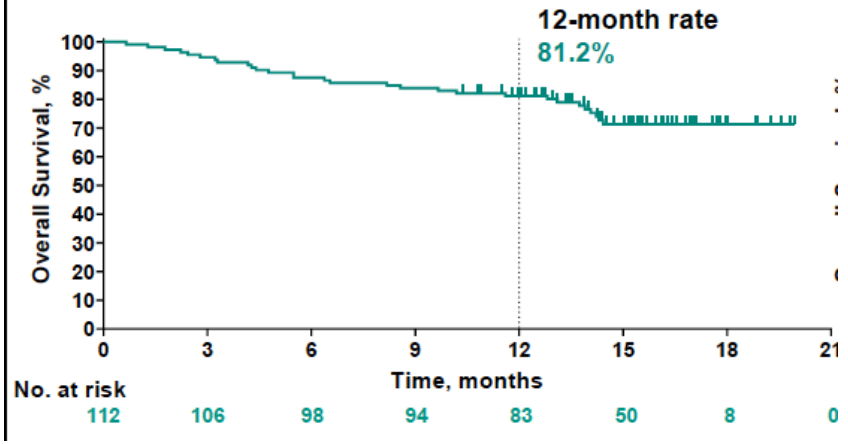
n	Median (95% CI)
61	NR (10.6–NR)



OS

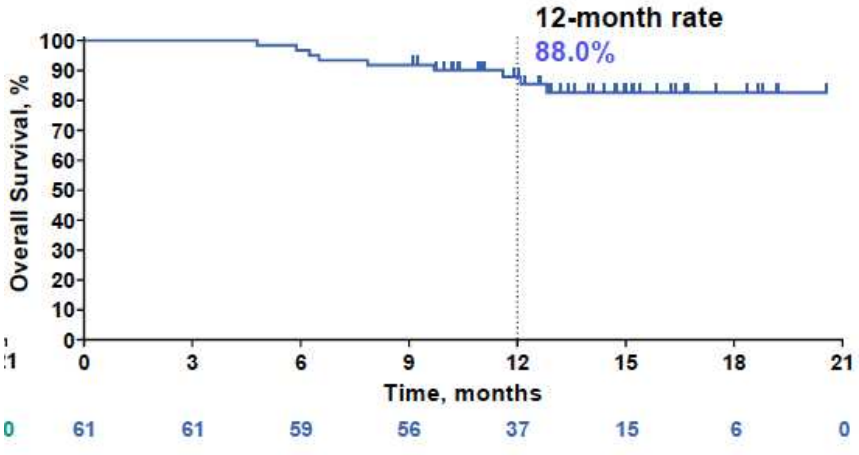
Cohort A[a]

n	Median (95% CI)
112	NR (NR–NR)



Cohort B[b]

n	Median (95% CI)
61	NR (NR–NR)



Incidence of Grade ≥3 Pneumonitis/Safet

Per NCI-CTCAE Version 4.0 (All-Treated Patients)

	Cohort A[a] (n = 112)	Cohort B[b] (n = 101)
Grade ≥3 pneumonitis (all cause),[c,d] n (%) [95% CI]	9 (8.0) [3.7–14.7]	8 (7.9) [3.5–15.0]
Treatment-related AEs, n (%)	105 (93.8)	96 (95.0)
Grades 3–5	72 (64.3)	47 (46.5)
Led to death	4[c] (3.6)	1 (1.0)
Led to discontinuation of any treatment component	38 (33.9)	16 (15.8)
Discontinued pembrolizumab	27 (24.1)	15 (14.9)
Discontinued radiotherapy	2 (1.8)	0
Discontinued any chemotherapy	18 (16.1)	3 (3.0)
Immune-mediated AEs and infusion reactions, n (%)	59 (52.7)	36 (35.6)
Grades 3–5	18 (16.1)	10 (9.9)
Led to death[d]	4 (3.6)	1 (1.0)

mous and nonsquamous. [b]Nonsquamous only. [c]Includes immune-mediated AE of "pneumonitis" and the MedDRA preferred term of "radiation pneumonitis". [d]Includes 4 pa
) with grade 5 pneumonitis in cohort A and 1 patient (1.0%) with grade 5 interstitial lung disease in cohort B. These events were classified as both treatment-related events
immune-mediated AEs and infusion reactions.
utoff date: July 30, 2020.

Results of inverse-probability of treatment weighting (IPTW) using propensity score from REFRACT: a multi-center study investigating the treatment patterns in EGFR-mutant unresectable LA- NSCLC

Nan Bi[1], Kunpeng Xu[1], Hong Ge[2], Ming Chen[3], Mingyan E[4], Li Zhang[5], Jianzhong Cao[6], Xu Zhang[7], Xiao Ding[8], Bing Xia[9], Lujun Zhao[10], Lijie Han[11], Jiancheng Li[12], Chen Hu[13], Luhua Wang[1,14]

Study design

¡RETROSPECTIVO!

NCT04304608

First-line treatment pattern

- Histologically confirmed LAC
- Unresectable IIIA/IIIB
- Age ≥18
- *EGFR* mutations +
- *ALK* gene rearrangements –
- Definitive RT

CCRT / SCRT

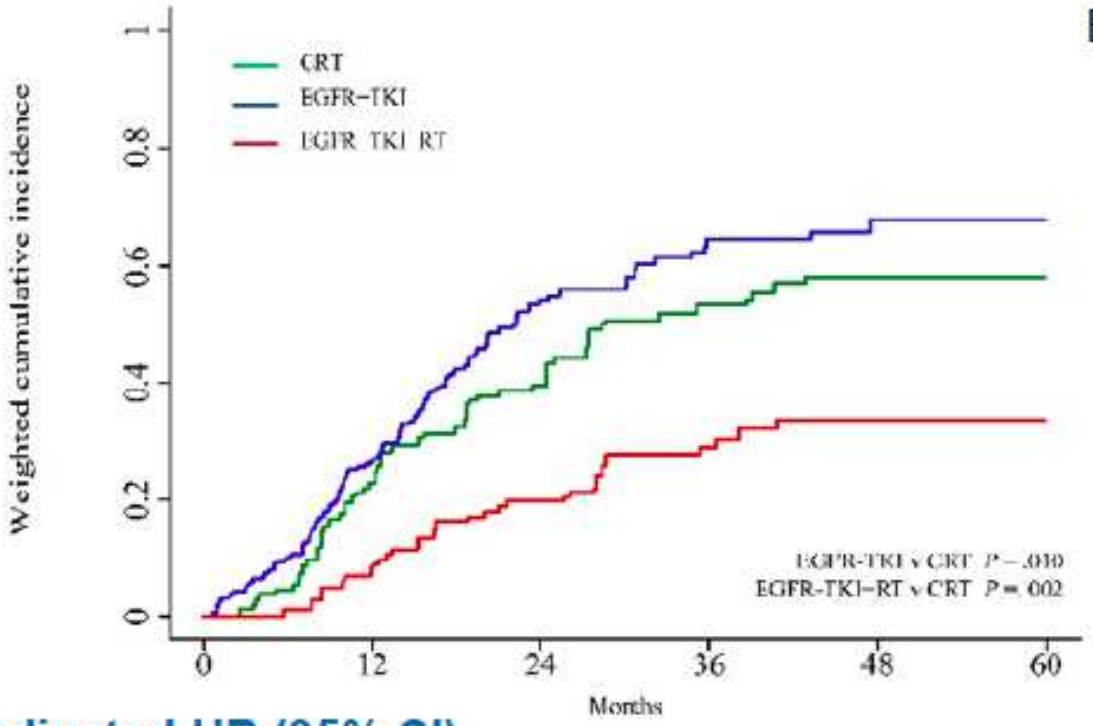
EGFR-TKI+RT+/-CT

EGFR-TKI

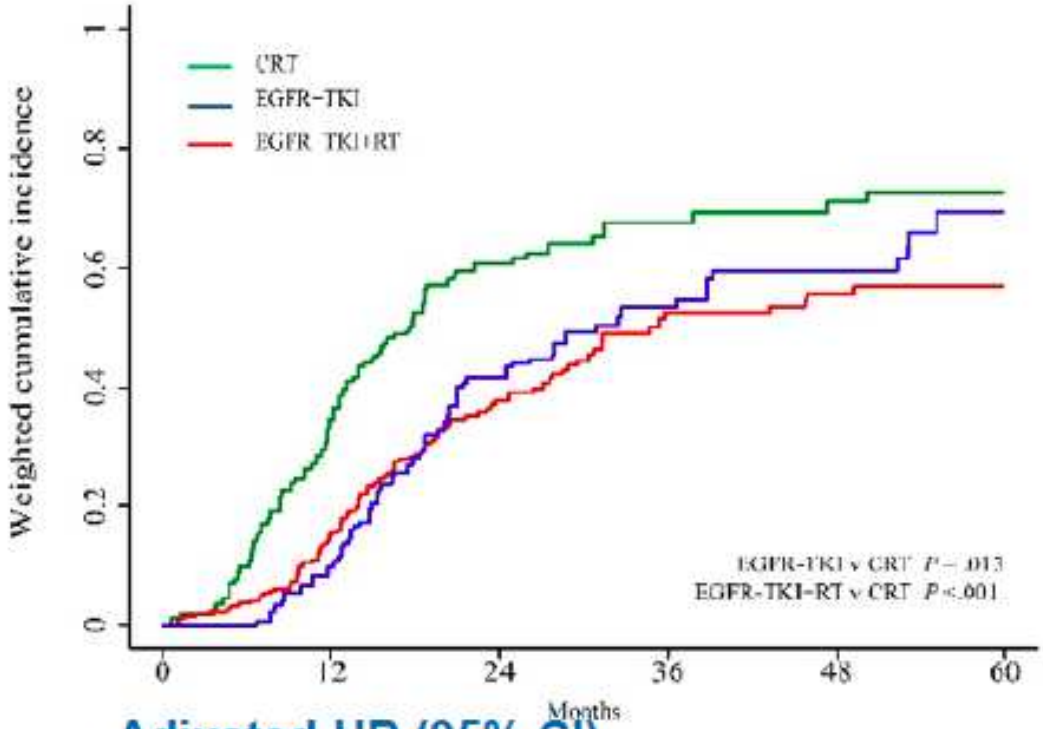
- Between Jan 2012 and Dec 2018
- 12 Chinese academic cancer institutions
- 440 patients in the efficacy analysis

- Group 1: concurrent or sequential chemoradiation.
- Group 2: combined RT and TKI with or without chemo
- Group 3: upfront TKIs alone until tumor progression

ncidence of locoregional failure (A) and distant progression (



B



Adjusted HR (95% CI)

RT+TKI vs CRT : 0.48 (0.31–0.77) *P*=.002;

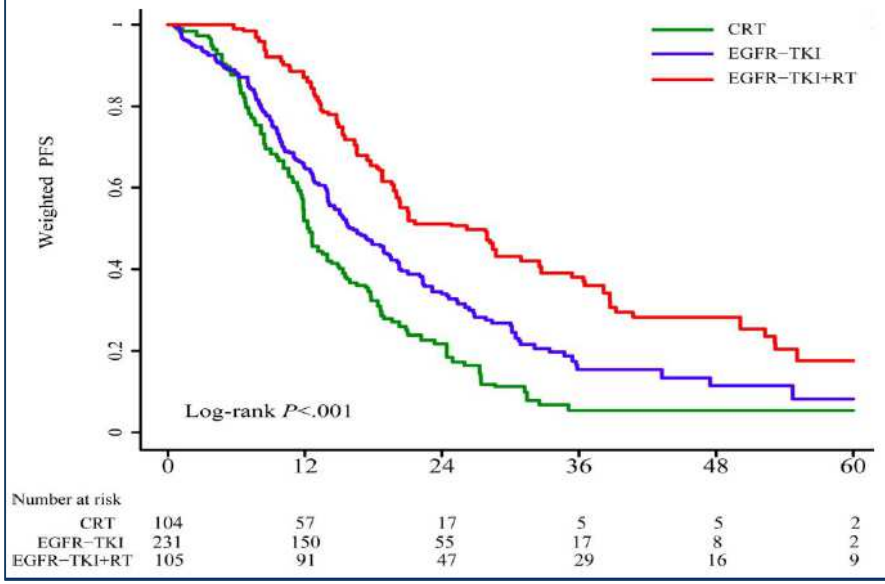
TKI vs CRT : 1.33 (0.95–1.87) *P=.10.*

Adjusted HR (95% CI)

RT+TKI vs CRT : 0.62 (0.42–0.90) *P*=.013;

TKI vs CRT : 0.56 (0.39–0.79) *P*< .001.

PFS after IPTW analysis



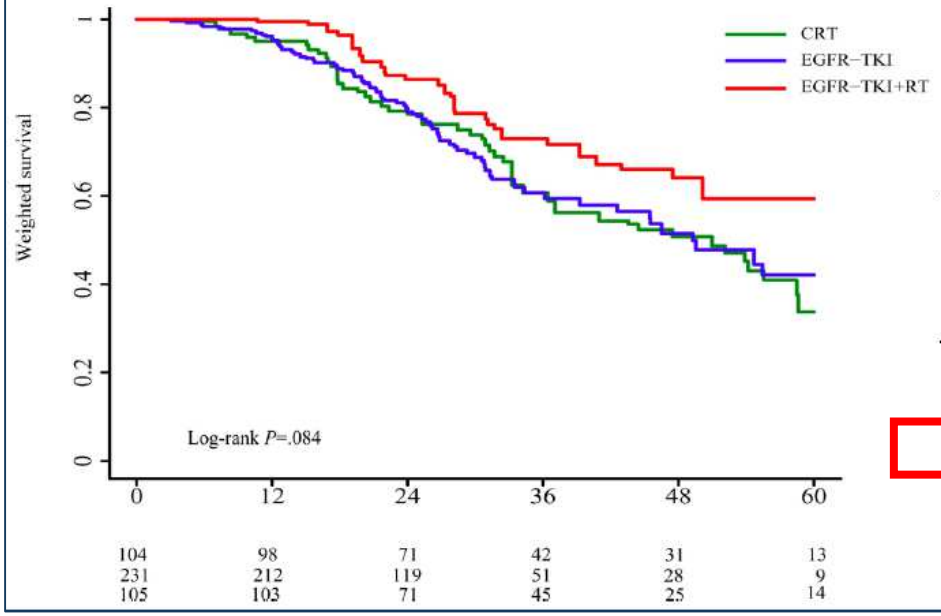
	Median PFS (months)	95% CI
CRT	12.4	11.4–15.5
RT+TKI	26.2	19.8–36.4
TKI	16.2	14.1–19.5

Adjusted HR (95% CI)

RT+TKI vs CRT : 0.40 (0.29–0.54) *P*< .001;

TKI vs CRT : 0.66 (0.50–0.87) *P*=.003.

OS after IPTW analysis



	Median OS (months)	95% CI
CRT	51.0	36.4–60.7
RT+TKI	67.4	50.1–NR
TKI	49.3	39.3–NR

Adjusted HR (95% CI)

RT+TKI vs CRT : 0.61(0.38–0.98) *P*=.039;

TKI vs CRT : 0.90 (0.62–1.32) *P=.595.*

RT adaptativa por PET-TC

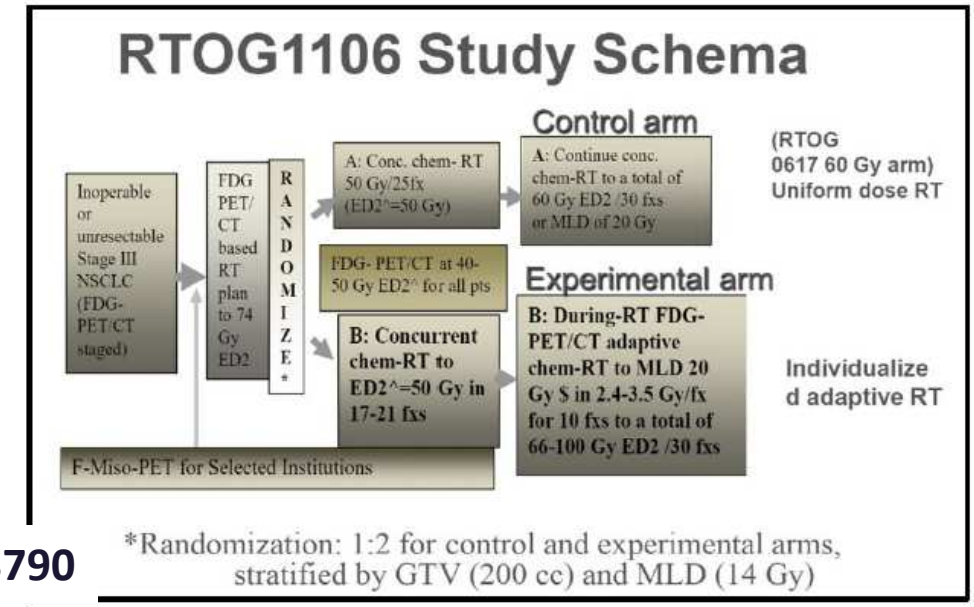
act #3790

Abstract # 2266

Similar designs of the two studies

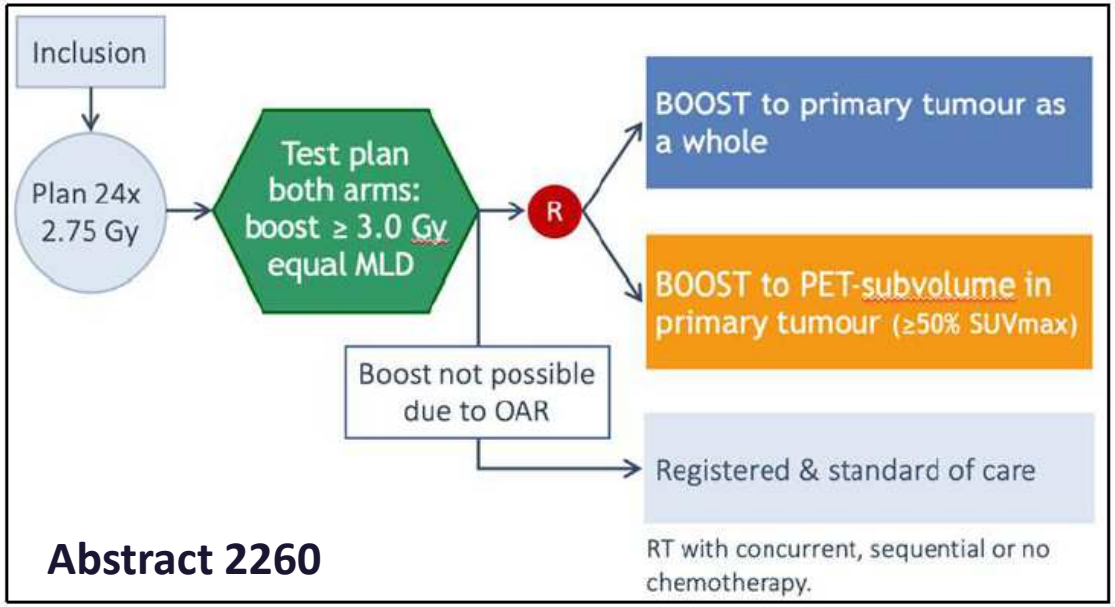
- Randomizing arms at starting radiation plan by use of Pet/CT
- Unconventional fractionation RT up to target dose prescription 80Gy or 84 Gy
- Primary endpoint: local control (1 or 2 year)

2 year local-regional control rate based on central review



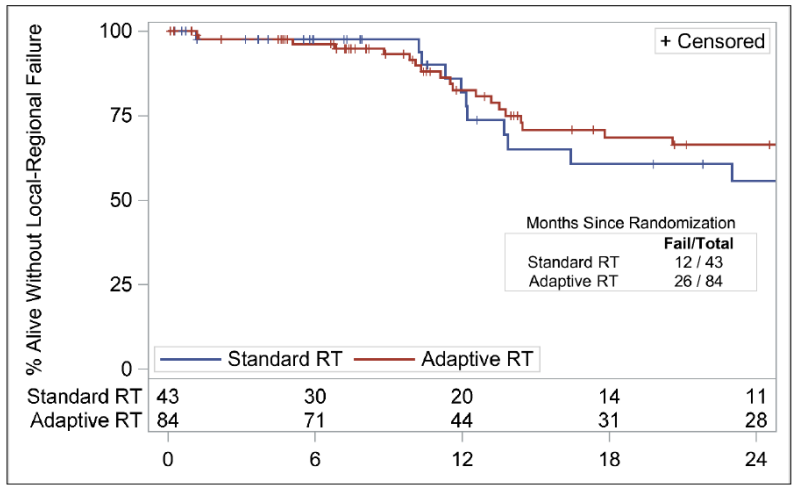
ct 3790

Freedom from local failure at **1 year** by central review of CT-sca



Abstract 2260

ults-8: Local Regional Control (Site Reported)



Abstract 3790

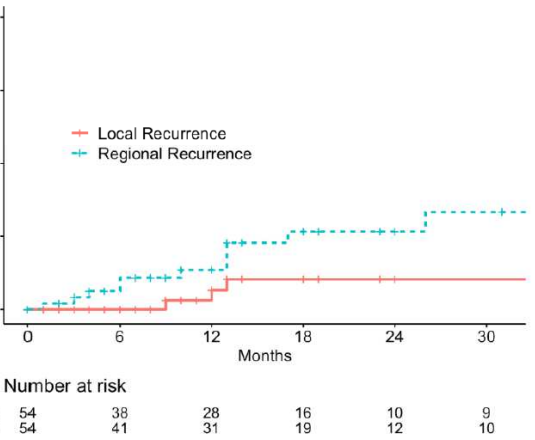
No diferencias entre RT estándar y Adapatativa

and Regional Recurrences

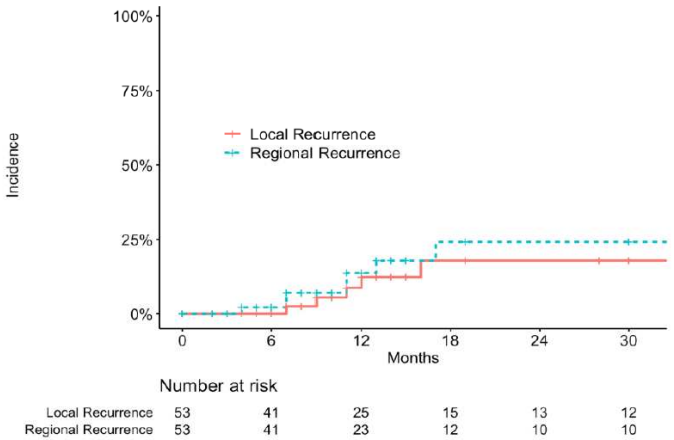
ime 12.6 months

Abstract 2260

Boost Whole Primary Tumour n=54



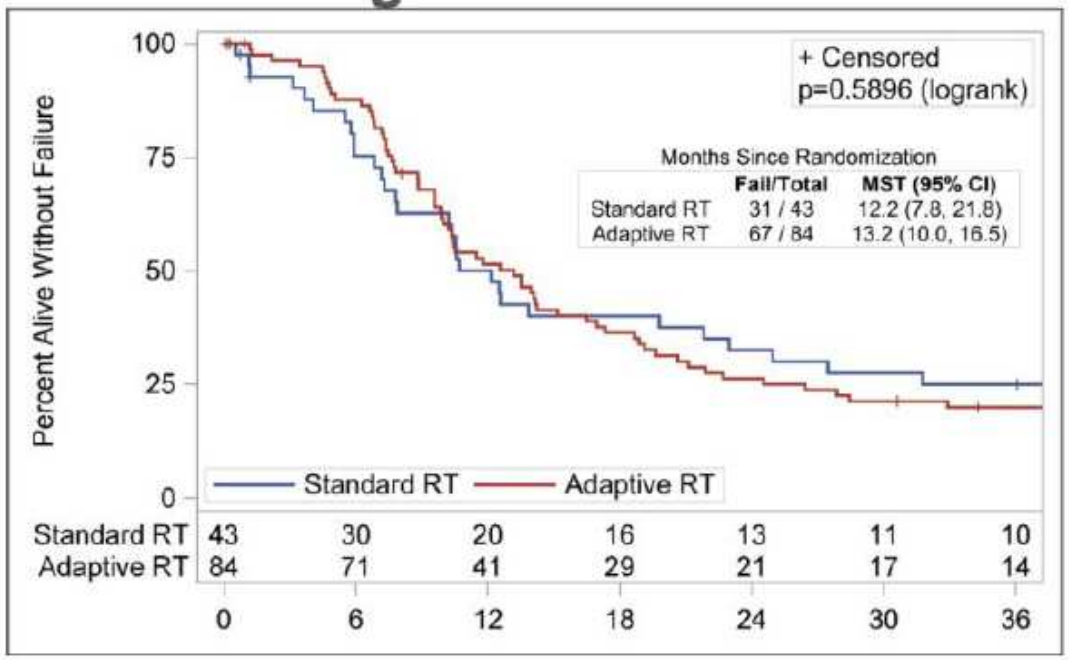
Boost PET-subvolume n=53



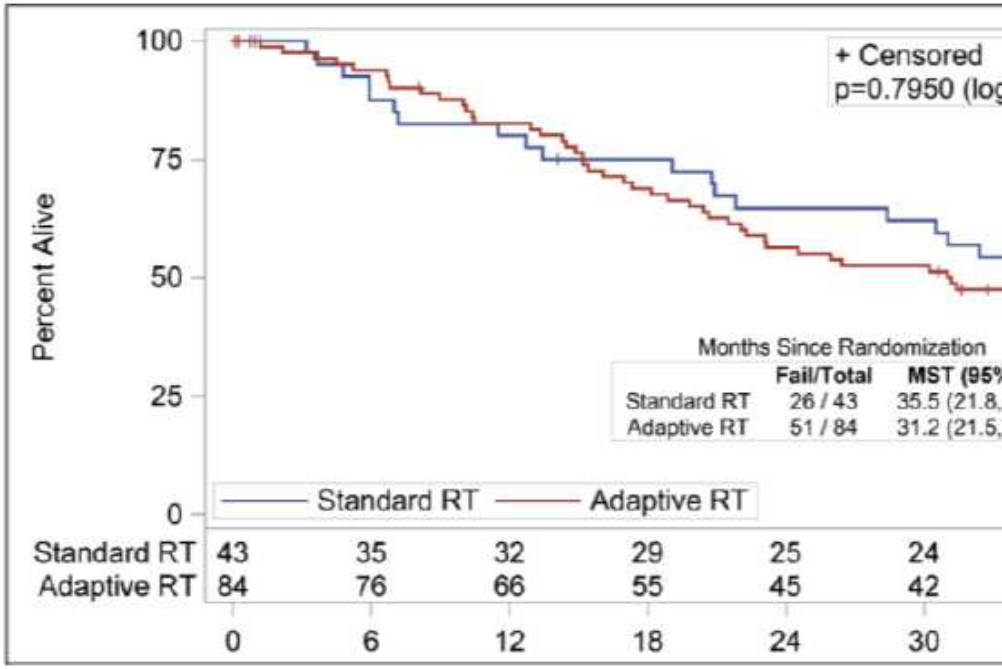
NO COMPARACIÓN ENTRE AMBOS BRAZOS (¿DIFERENCIAS?)

Abstract 3790

Results-10: Progression Free Survival



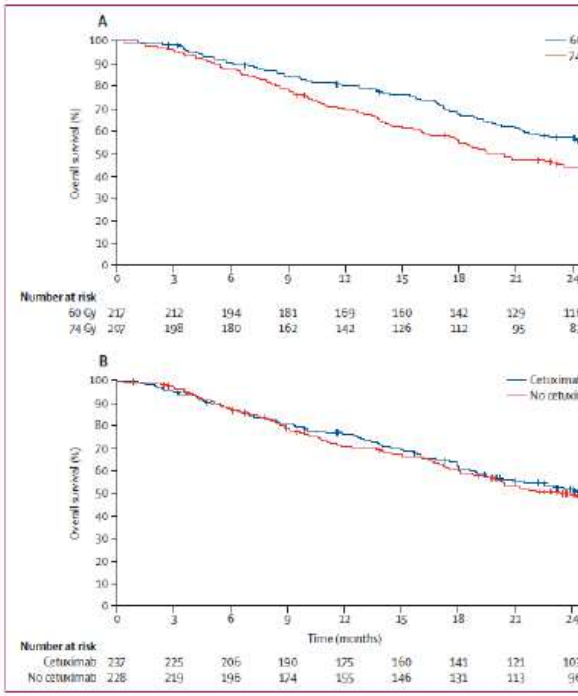
Results-11: Overall Survival



Increasing infield RT dose is important, but not the only factor involved

RTOG 0617: not targeting the high FDG-uptake region

- Negative conclusion about higher dose with 74 Gy (v.s. 60 Gy)
- Harmful higher dose with concurrent chemoradiotherapy for patients with LA-NSCLC.



Jeffrey D Bradley, et al. Lancet Oncol 201