



Enfermedad Oligometastásica

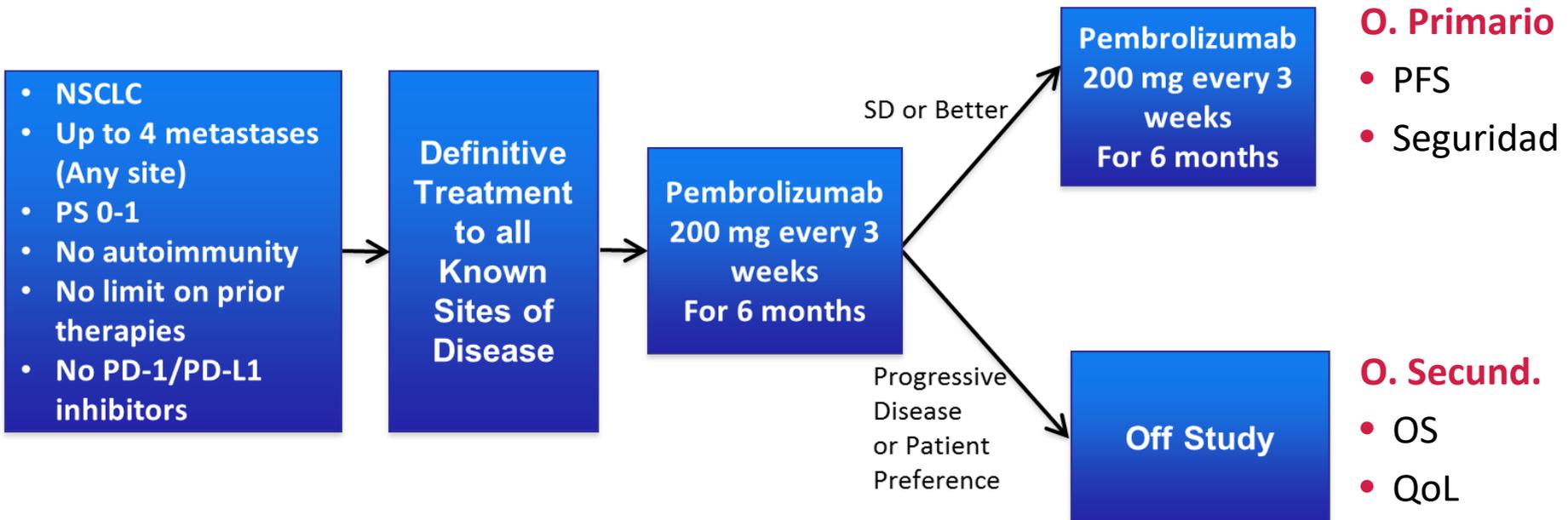
Dr. Ignacio Gil-Bazo

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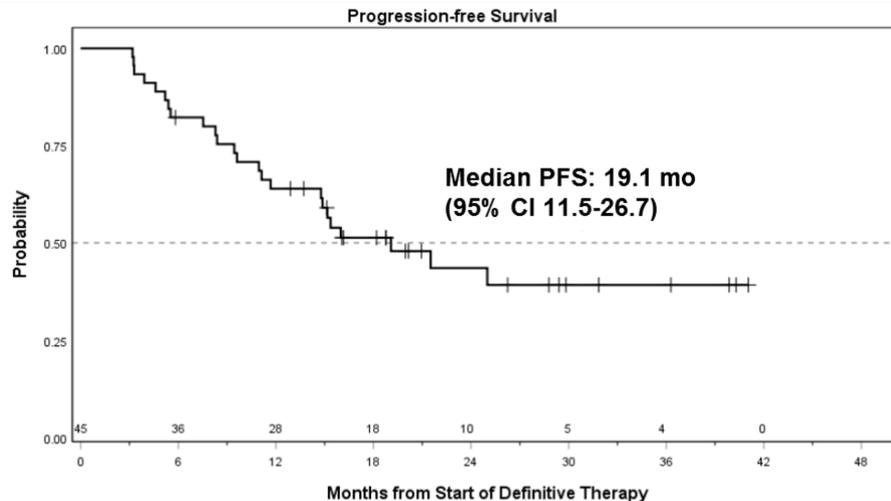


Grupo Español de Cáncer de Pulmón
Spanish Lung Cancer Group

Phase II Study of Pembrolizumab for Oligometastatic Non-Small Cell Lung Cancer (NSCLC) Following Completion of Locally Ablative Therapy (LAT)

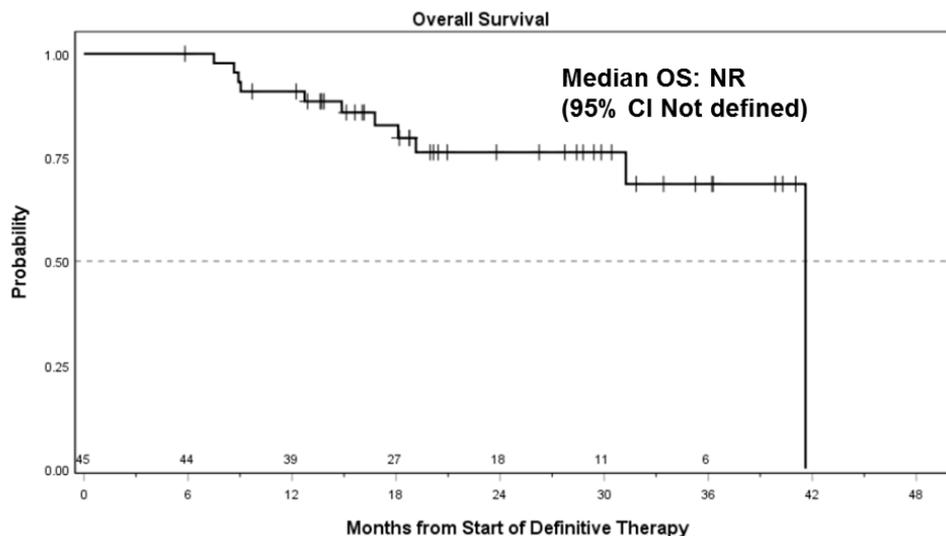


Pembrolizumab tras tratamiento local ablativo



	PFS1 (Definitive Rx)	PFS2 (Enrollment)
12 mo	64_±7.2%	63.7_±7.3%
18 mo	51.3_±7.7%	49.9_±7.9%
24 mo	43.6_±8.3%	42.1_±8.4%

Compare median PFS 19.1 mos (SE=3.9) to historical control (6.6 mos)
One sided p value= 0.00066



12 month OS	90.9_±4.3%
18 month OS	82.8_±6.0%
24 month OS	76.2_±7.1%

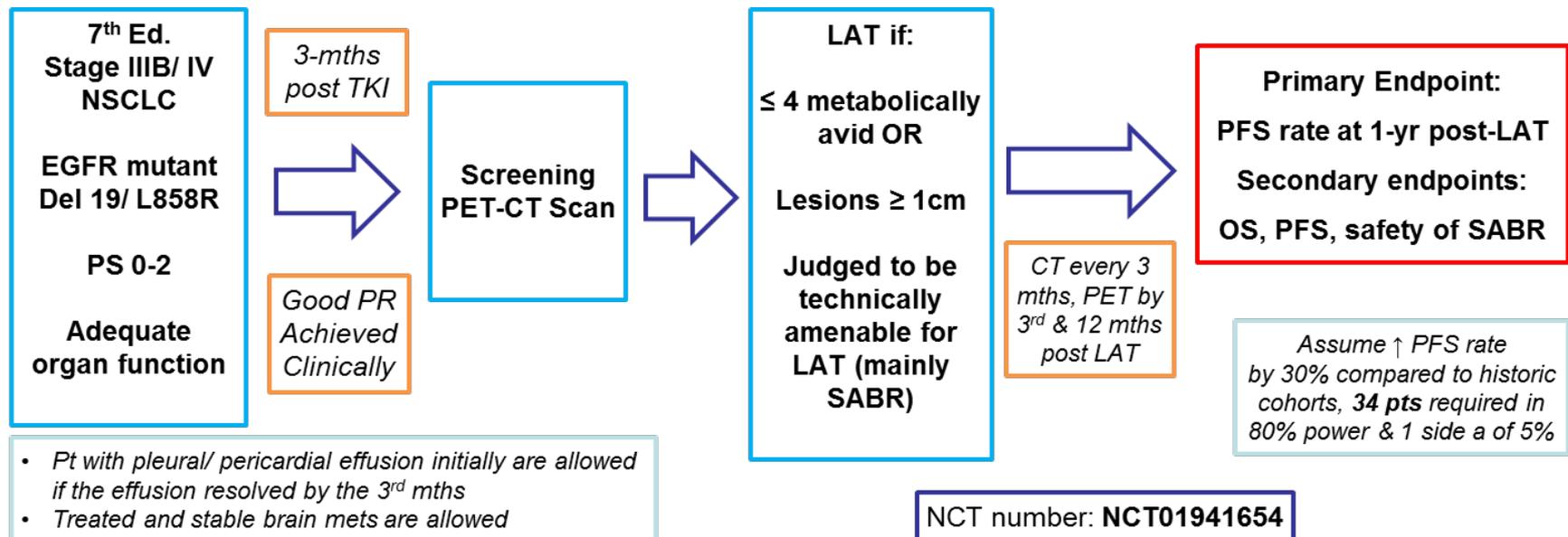
Median potential follow-up for survival
23.8 months (all patients)
20.4 months (all living patients)

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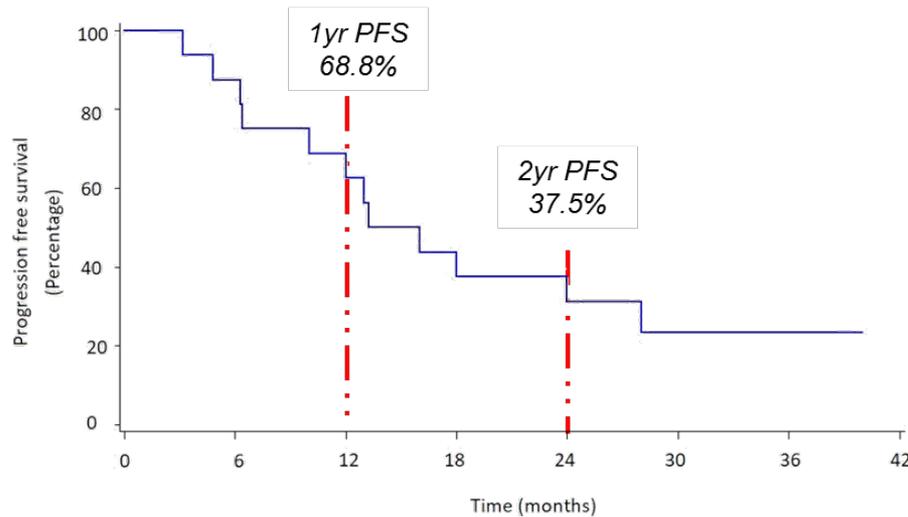


ATOM: A Phase II Study to Assess Efficacy of Preemptive Local Ablative Therapy to Residual Oligometastases After EGFR TKI

NCT01941654



ATOM: Tratamiento ablativo tras 1L EGFR TKI



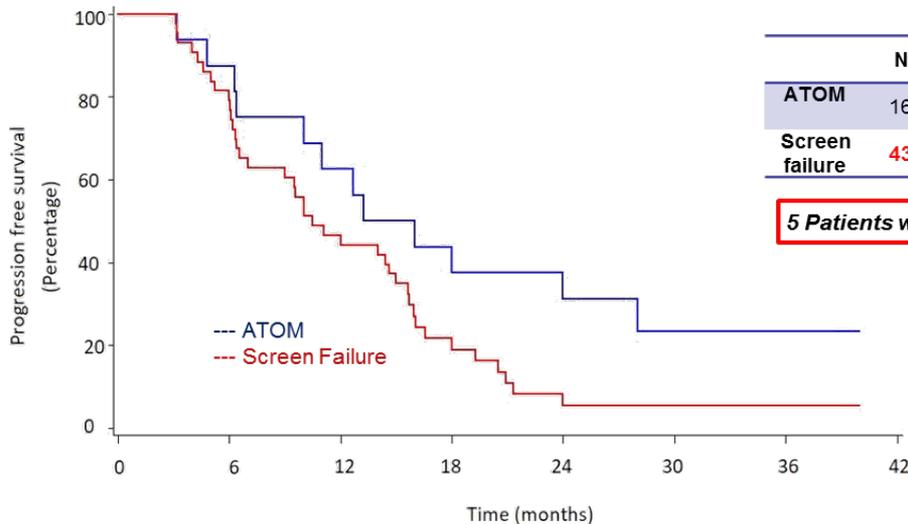
Patient characteristics:

- Median age: 57.3
- 7 male, 9 female
- All stage IV disease
- 22 lesions irradiated, 16 lung 4 bone & 2 LNs

PFS: date of screening to PD or death

1 year PFS 68.8% (75% 1year post TKI)

Median PFS: 15.2 mths (~18.2 mths post TKI)



	N	No. of event	Median PFS 95% CI	1-yr PFS (%)	2-yrs PFS (%)	p-value (log-rank)
ATOM	16	12	15.2 (8.7-29.2)	68.8	37.5	0.0433
Screen failure	43	40	11.1 (6.9-15.4)	46.5	8.1	

5 Patients with PD after PET were excluded in screen failure cohort

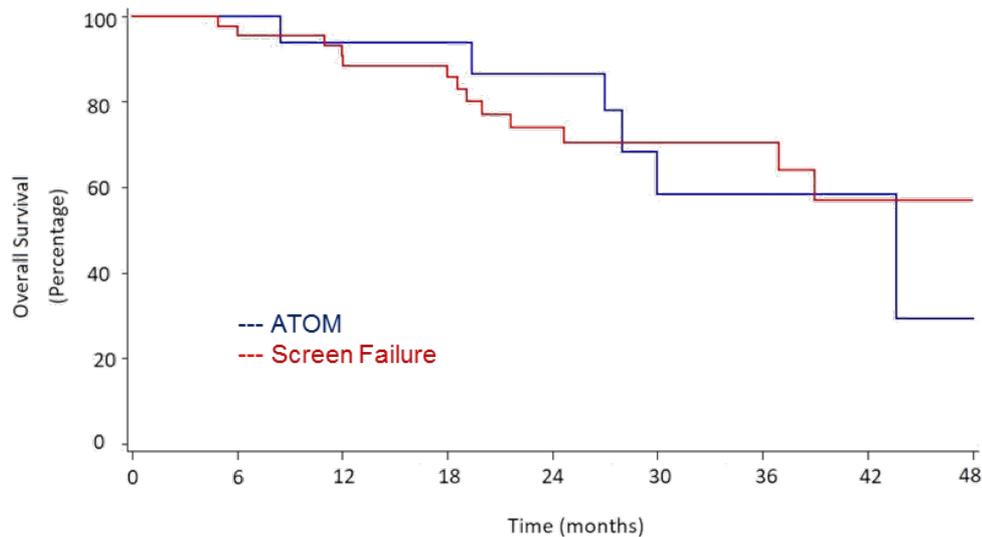
Multivariate analysis

	HR	95% CI of HR	P-value
ATOM	0.406	0.205-0.804	0.0097
AGE	0.970	0.946-0.995	0.0181

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ATOM: Tratamiento ablativo tras 1L EGFR TKI



Proportion Hazard model

	HR	95% CI of HR	P-value
ATOM	1.103	0.419-2.907	0.84

Median OS

ATOM group: 44.3m (27.1 to NR)
Screen failure group: NR (38.7 to NR)

Only Osimertinib use and number of lines of therapy after EGFR TKI are significant factors to predict survival in MV analysis.

Addition of Local Therapy to EGFR-TKI Showed Survival Benefit in EGFR-Mutant NSCLC pts with Oligometastatic or Oligoprogressive Liver Metastases

- This is a **multi-center**, retrospective study
- Time of collection: 2010.09-2017.05
- Major eligibility criteria:
 - - 1) Histological confirmation of NSCLC
 - - 2) AJCC 7th Edition Stage IV disease
 - - 3) EGFR mutations were tested by ARMS or NGS
 - - 4) Radiological confirmation of oligometastatic or oligoprogressive LM

Definition of oligometastatic LM

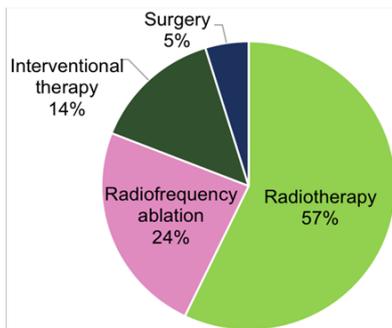
- ≤ 5 sites in liver without extrahepatic metastases at initial diagnosis

Definition of oligoprogressive LM

- ≤ 5 sites in liver progression without extrahepatic metastases during TKIs therapy.

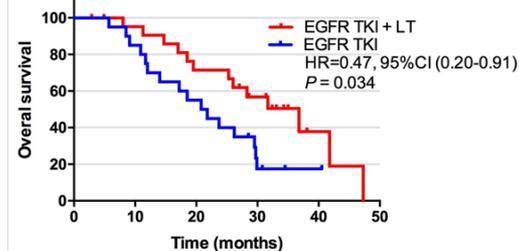
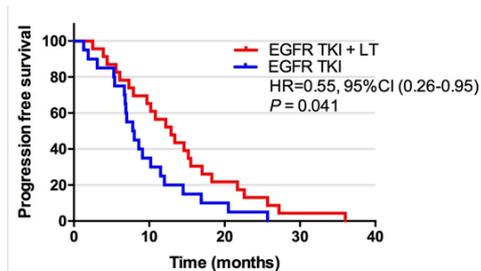
Tratamiento local más TKIs en CNMP oligom. EGFR+

• Oligometastatic cohort



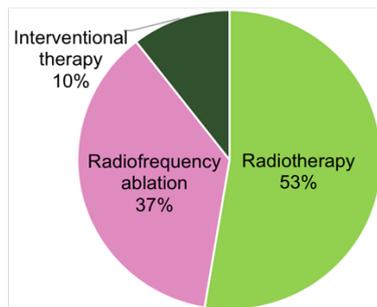
PFS

OS



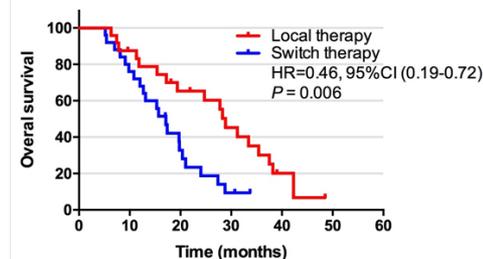
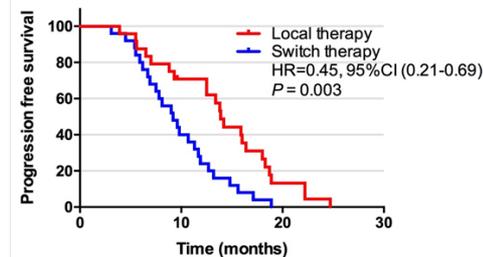
Tao Jiang, Shanghai Pulmonary Hospital, China

• Oligoprogressive cohort



PFS2

OS



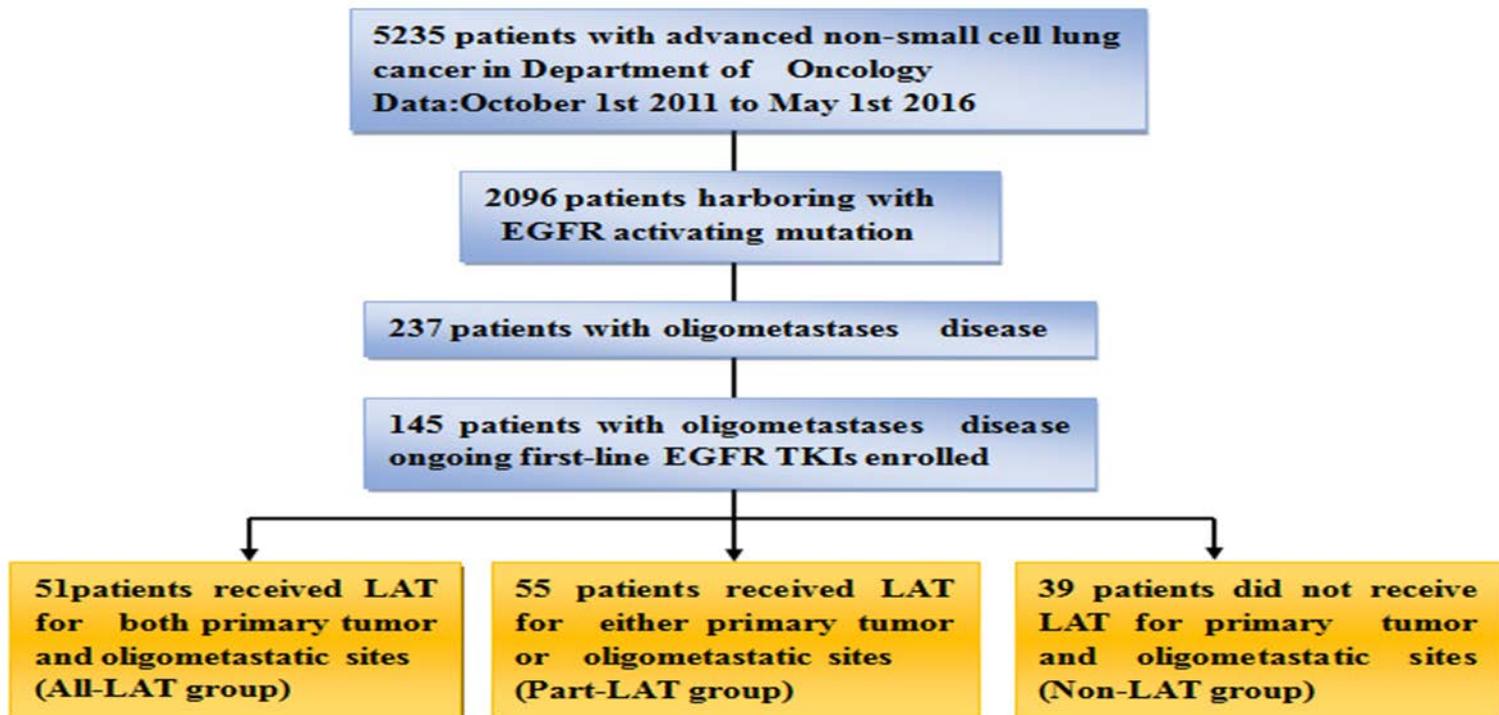
Tao Jiang, Shanghai Pulmonary Hospital, China

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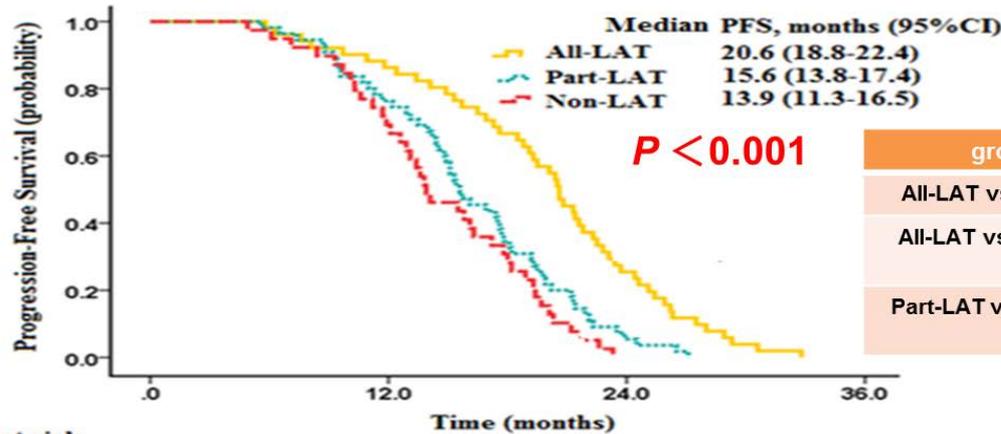


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Local Ablative Therapy Improves Survival in Patients with Synchronous Oligometastatic NSCLC Harboring EGFR Mutation Treated with EGFR-TKIs



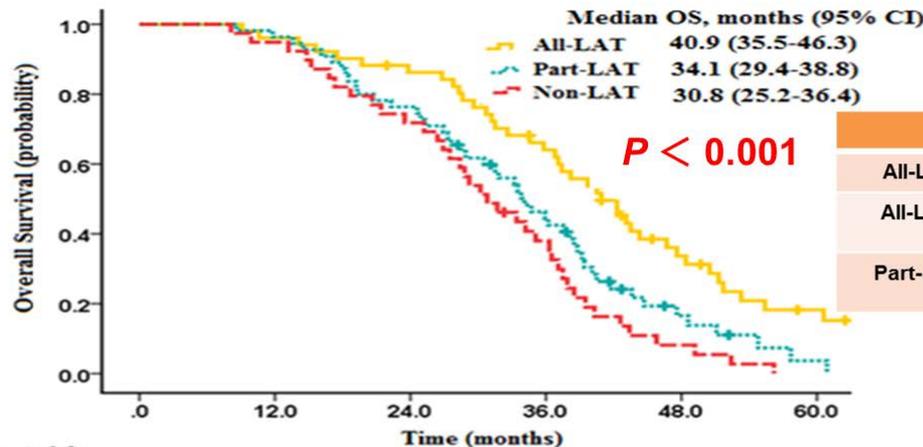
Tratamiento Local en oligometástasis sincrónicas en pacientes con tumores EGFR + tratados con TKIs



group	HR	P value
All-LAT vs. Part-LAT	0.47	< 0.001
All-LAT vs. Non-LAT	0.32	< 0.001
Part-LAT vs. Non-LAT	0.80	0.289

No. at risk

	0	12.0	24.0	36.0
All-LAT	51	44	13	0
Part-LAT	55	42	3	0
Non-LAT	39	27	0	0



group	HR	P value
All-LAT vs. Part-LAT	0.56	0.009
All-LAT vs. Non-LAT	0.42	< 0.001
Part-LAT vs. Non-LAT	0.72	0.136

No. at risk

	0	12.0	24.0	36.0	48.0	60.0
All-LAT	51	49	43	31	14	6
Part-LAT	55	53	40	23	6	1
Non-LAT	39	37	28	14	3	0

Tratamiento Local en oligometástasis sincrónicas en pacientes con tumores EGFR + tratados con TKIs

Efficacy of local consolidative therapy for oligometastatic lung adenocarcinoma patients harboring epidermal growth factor receptor mutations.

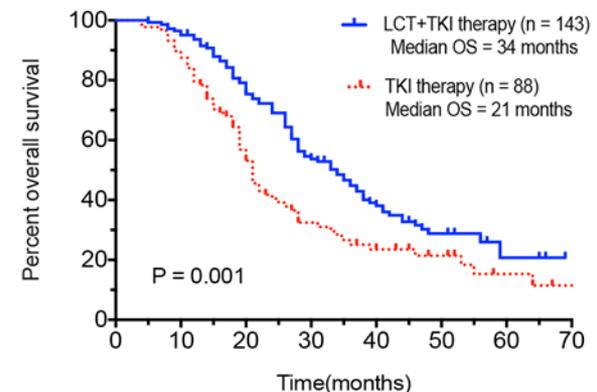
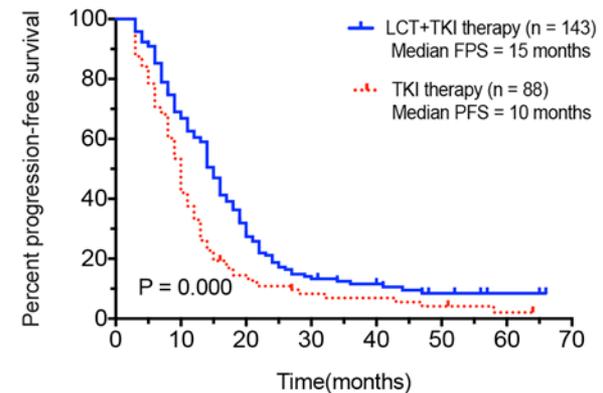
Entire cohort: The median (range) age was 59 (33-80) years old.

PFS

	Hazard Ratio	P Value
combination group	0.610 (95%CI, 0.461-0.807)	0.000
monotherapy group	1	

OS

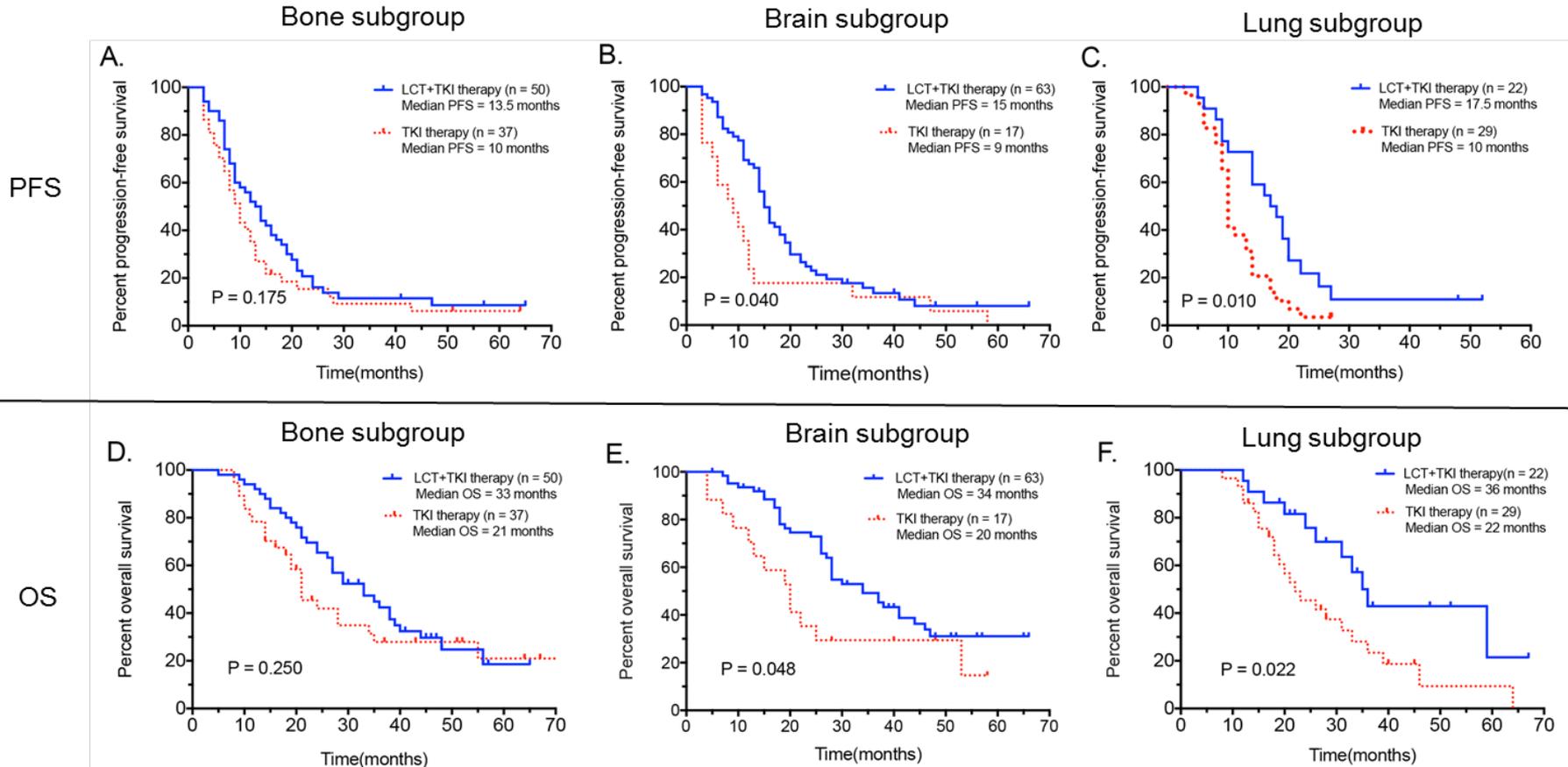
	Hazard Ratio	P Value
combination group	0.593 (95%CI, 0.430-0.817)	0.001
monotherapy group	1	



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Tratamiento Local en oligometástasis sincrónicas en pacientes con tumores EGFR + tratados con TKIs



PFS and OS Beyond 5 years of NSCLC Patients with Synchronous Oligometastases Treated in a Prospective Phase II Trial (NCT 01282450)

6-year results of a prospective, single-arm trial

- July 27, 2006 until July 23, 2010
- N=40; with one patient being ineligible
- Inclusion criteria:
 - Histologically or cytologically proven NSCLC with less than five metastases at the time of diagnosis. Whole-body FDG-PET-CT scan and CT with iv contrast or MRI brain.
 - All tumor sites (local, regional, and distant) had to be amenable for radical treatment (surgery or radiotherapy to a biological dose of at least 60 Gy in 30 daily fractions of 2 Gy, except for brain metastases in which lower radiation doses were allowed).
 - Both surgery and radiotherapy were allowed in the same patient.
 - Systemic treatment was not mandatory.
 - WHO performance status 0 to 2
 - Any other malignancy in clinical complete remission

Treatment

Surgery	0
Radiotherapy alone	2 (5.1%)
Sequential chemoradiotherapy	15 (38.5%)
Cisplatin-gemcitabine	11
Carboplatin-gemcitabine	1
Cisplatin-pemetrexed	3
Concurrent chemoradiotherapy	21 (53.8%)
Cisplatin-etoposide	7
Cisplatin-vinorelbine	14
Adjuvant after radiotherapy	1 (2.6%)
Cisplatin-gemcitabine	—
Radiotherapy dose	62.3 ± 10.1 Gy (18–79.2)
Number of fractions	35.9 ± 8.4 ³⁻⁴⁴
Overall treatment time of radiotherapy	30.56 ± 10.3 days ³⁻⁴⁴

PRO Health Status

3 mos post-treatment	
Same	6 (46.2%)
Better	4 (30.8%)
Worse	2 (15.4%)
Missing	1 (7.7%)
6 mos post-treatment	
Same	5 (38.5%)
Better	3 (23.1%)
Worse	4 (30.8%)
Missing	1 (7.7%)

Time	Overall Survival (n=39)	Progression-Free Survival (PFS)
Median	13.5 months	12.1 months
1 year	56.4 %	51.3 %
2 year	23.3 %	13.6 %
3 year	12.8 %	12.8 %
4 year	10.3 %	7.7 %
5 year	7.7 %	7.7 %
6 year	5.1 %	2.5 %