Lung Cancer UPDATES
ASCO HIGHLIGHTS
31 MAYO-04 JUNIO 2024
Chicago, USA

Iniciativa científica de:
GECP lung cancer research

# CPCNP: Estadios localmente avanzados

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# Abstract # S. Ramalinghan et al. LAURA study

2024 ASCO ANNUAL MEETING

## Osimertinib after definitive chemoradiotherapy in patients with unresectable stage III epidermal growth factor receptor-mutated (EGFRm) NSCLC: primary results of the Phase 3 LAURA study

Suresh S. Ramalingam,[1] Terufumi Kato, Xiaorong Dong, Myung-Ju Ahn, Le-Van Quang, Nopadol Soparattanapaisarn, Takako Inoue, Chih-Liang Wang, Meijuan Huang, James Chih-Hsin Yang, Manuel Cobo, Mustafa Özgüroğlu, Ignacio Casarini, Dang-Van Khiem, Virote Sriuranpong, Eduardo Cronemberger, Xiangning Huang, Toon van der Gronde, Dana Ghiorghiu, Shun Lu

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2024 ASCO ANNUAL MEETING #ASCO24 PRESENTED BY: Dr Suresh S. Ramalingam

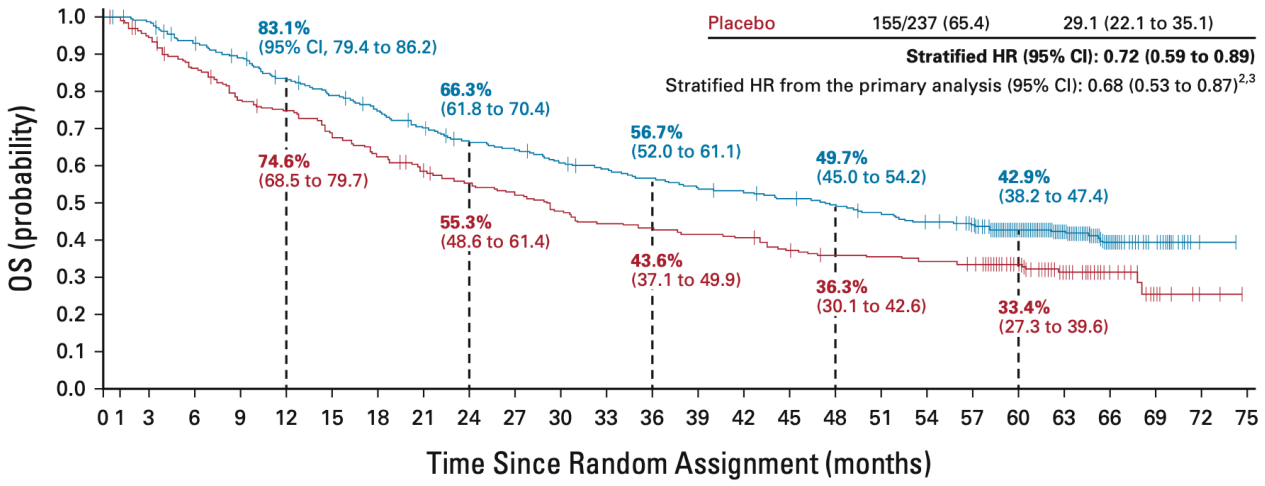


ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

| Arm | No. of Events/ Total No. of Patients (%) | Median OS (95% CI), Months |
|---|---|---|
| Durvalumab | 264/476 (55.5) | 47.5 (38.1 to 52.9) |
| Placebo | 155/237 (65.4) | 29.1 (22.1 to 35.1) |

**Stratified HR (95% CI): 0.72 (0.59 to 0.89)**

Stratified HR from the primary analysis (95% CI): 0.68 (0.53 to 0.87)[2,3]




No. at risk:

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Durvalumab | 476 | 464 | 431 | 414 | 385 | 364 | 343 | 319 | 298 | 289 | 273 | 264 | 252 | 241 | 236 | 227 | 218 | 207 | 196 | 183 | 134 | 91 | 40 | 18 | 2 | 0 |
| Placebo | 237 | 220 | 199 | 179 | 171 | 156 | 143 | 133 | 123 | 116 | 107 | 99 | 97 | 93 | 91 | 83 | 78 | 77 | 74 | 72 | 56 | 33 | 16 | 7 | 2 | 0 |

The NEW ENGLAND JOURNAL of MEDICINE

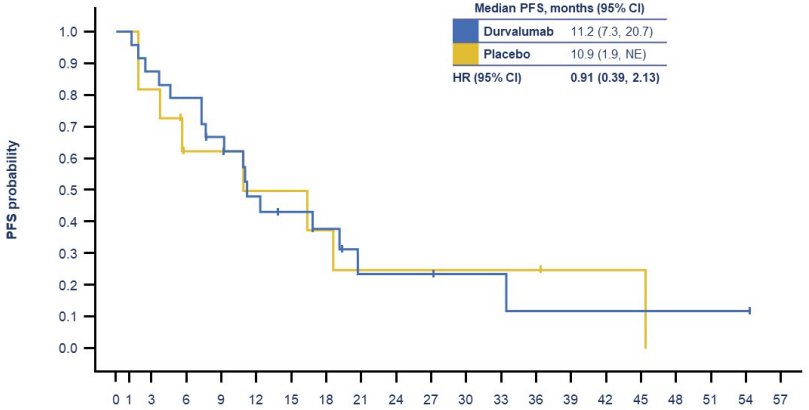
ORIGINAL ARTICLE

Iniciativa científica de: GECP lung cancer research

## Osimertinib after Chemoradiotherapy in Stage III *EGFR*-Mutated NSCLC

Shun Lu, M.D., Terufumi Kato, M.D., Xiaorong Dong, M.D., Ph.D., Myung-Ju Ahn, M.D., Le-Van Quang, M.D., Nopadol Soparattanapaisarn, M.D., Takako Inoue, M.D., Chih-Liang Wang, M.D., Meijuan Huang, M.D., James Chih-Hsin Yang, M.D., Ph.D., Manuel Cobo, M.D., Mustafa Özgüroğlu, M.D., Ignacio Casarini, M.D., Dang-Van Khiem, M.D., Virote Sriuranpong, M.D., Ph.D., Eduardo Cronemberger, M.D., Toshiaki Takahashi, M.D., Ph.D., Yotsawaj Runglodvatana, M.D., Ming Chen, M.D., Ph.D., Xiangning Huang, Ph.D., Ellie Grainger, M.Sc., Dana Ghiorghiu, M.D., Ph.D., Toon van der Gronde, Pharm.D., Ph.D., and Suresh S. Ramalingam, M.D., for the LAURA Trial Investigators*

### PACIFIC EGFRm *post-hoc* subgroup analysis




No. at risk

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Durvalumab | 24 | 21 | 19 | 15 | 10 | 8 | 6 | 3 | 3 | 3 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| Placebo | 11 | 9 | 5 | 5 | 4 | 4 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 0 | 0 | 0 |

856–1384; Remon et al. Ann Oncol 2021;32:1637–1642; Naidoo et al. J Thorac Oncol 2023;18:657–663; Xing et al. Int J Rad Oncol Biol Phys 2021;109:1349–1358; Sun et al. BMC Cancer 2020;20:646;

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**Patients with locally advanced, unresectable stage III* EGFRm NSCLC with no progression during / following definitive CRT† treatment**

Key inclusion criteria:
- ≥18 years (Japan: ≥20)
- WHO PS 0 / 1
- Confirmed locally advanced, unresectable stage III* NSCLC
- Ex19del / L858R‡
- Maximum interval between last dose of CRT and randomization: 6 weeks

**Osimertinib 80 mg, once daily**

**Randomization 2:1 (N=216)**

**Stratification by:**
**Concurrent vs sequential CRT**
**Stage IIIA vs stage IIIB/IIIC**
**China vs non-China**

**Placebo, once daily**

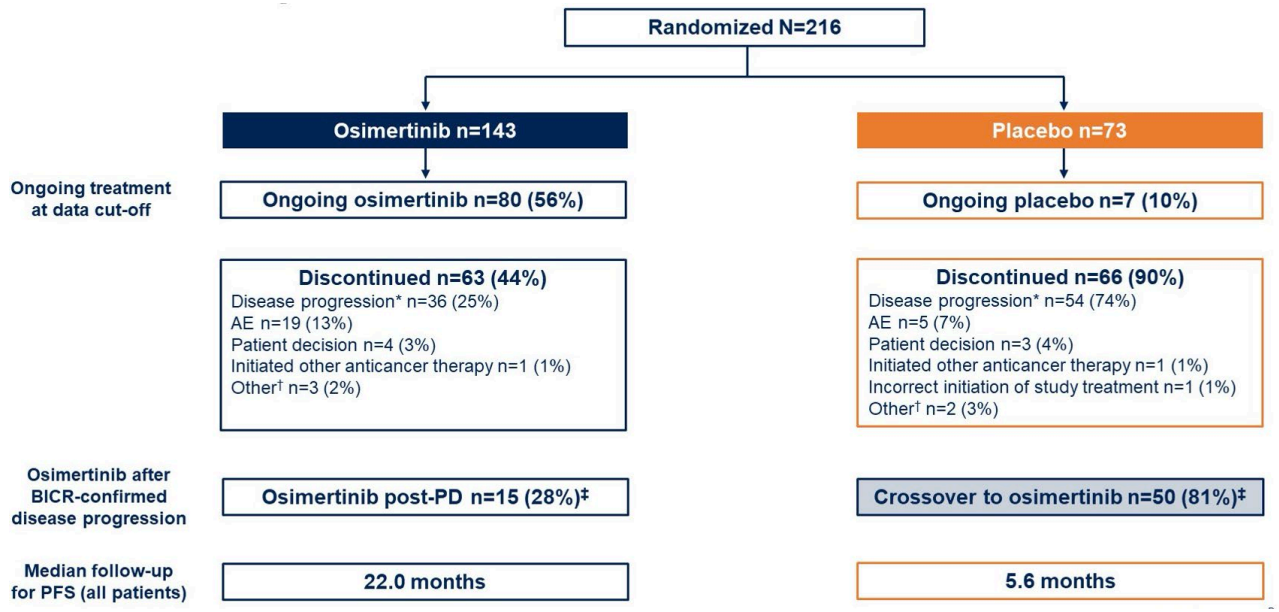
Treatment duration until BICR-assessed progression (per RECIST v1.1), toxicity, or other discontinuation criteria

**Open-label osimertinib after BICR-confirmed progression offered to both treatment arms§**

**Tumor assessments:**
- Chest CT / MRI and brain MRI
- At baseline, every 8 weeks to Week 48, then every 12 weeks until BICR-assessed progression

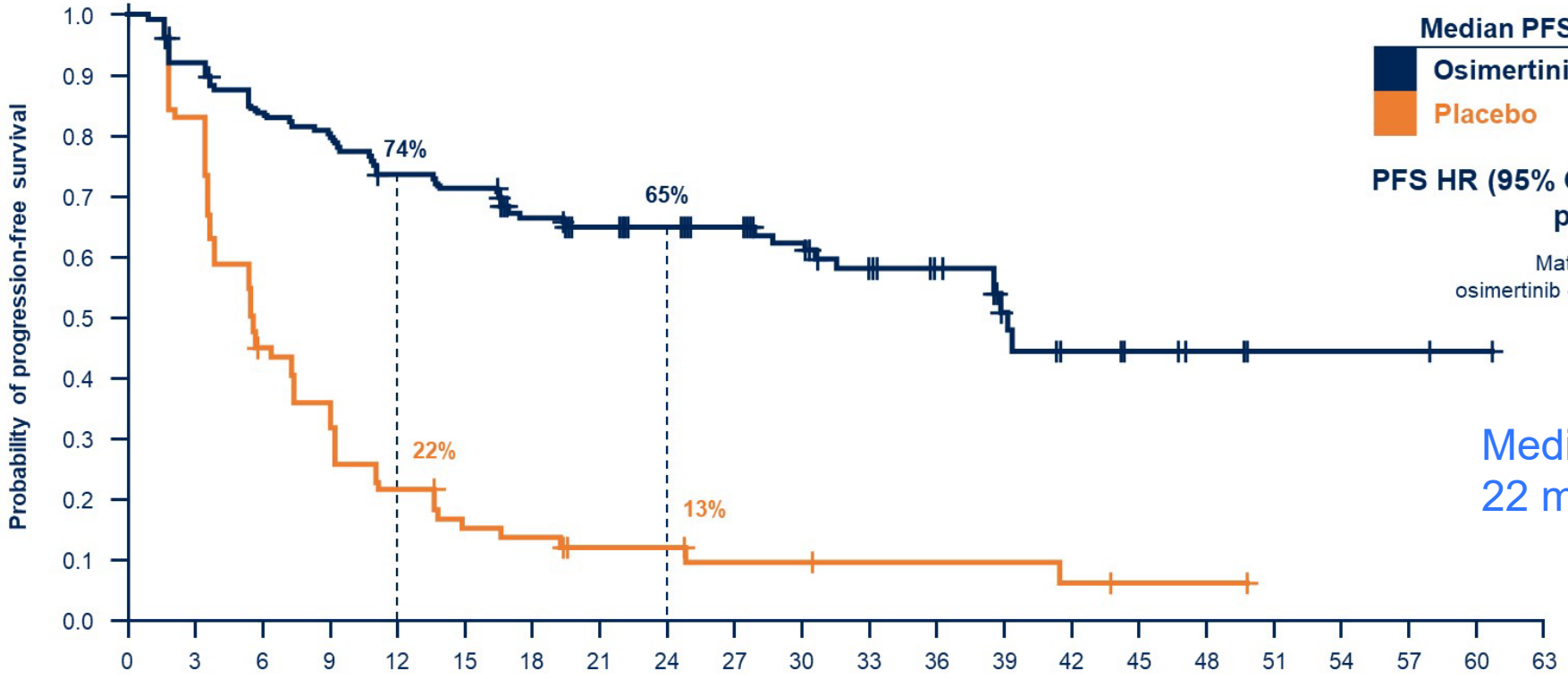
Objetivo primario: PFS
Objetivos secundarios: OS, Seguridad; Superv sin metastatis cerebrales

HR 0.53
Mediana PFS 8 → 15 m




| Characteristics, % | Osimertinib (n=143) | Placebo (n=73) |
|---|---|---|
| Sex: male / female | 37 / 63 | 42 / 58 |
| Age: median (range), years | 62 (36–84) | 64 (37–83) |
| Smoking history: formerly / currently / never | 26 / 3 / 71 | 32 / 1 / 67 |
| Race: Asian / non-Asian | 81 / 19 | 85 / 15 |
| WHO PS: 0 / 1 | 56 / 44 | 42 / 58 |
| AJCC / UICC staging (8th edition) at diagnosis: IIIA / IIIB / IIIC | 36 / 47 / 17 | 33 / 52 / 15 |
| Histology: adenocarcinoma / other | 97 / 3 | 95 / 5 |
| EGFR mutation at randomization:* Ex19del / L858R | 52 / 48† | 59 / 41 |
| Type of CRT: concurrent CRT / sequential CRT | 92 / 8 | 85 / 15 |
| Response to prior CRT: CR / PR / SD / PD / NE | 3 / 47 / 43 / 0 / 8 | 4 / 37 / 51 / 0 / 8 |
| Target lesion size by BICR:‡ mean (SD), mm | 33 (18) | 36 (17) |

# Progression-free survival by BICR




**Median PFS, months (95% CI)**

| | |
|---|---|
| Osimertinib | 39.1 (31.5, NC) |
| Placebo | 5.6 (3.7, 7.4) |

**PFS HR (95% CI): 0.16 (0.10, 0.24), p<0.001**

Maturity 56%:
osimertinib 40%, placebo 86%

Mediana seguimiento
22 meses

**No. at risk**

| | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Osimertinib | 143 | 127 | 114 | 109 | 99 | 96 | 83 | 76 | 69 | 61 | 49 | 37 | 28 | 16 | 9 | 6 | 4 | 2 | 2 | 2 | 1 | 0 |
| Placebo | 73 | 59 | 31 | 25 | 15 | 10 | 9 | 6 | 6 | 4 | 4 | 3 | 3 | 3 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |

Data cut-off: January 5, 2024.

Tick marks indicate censored data. Median follow-up for PFS (all patients): osimertinib 22.0 months, placebo 5.6 months. Median follow-up for PFS (censored patients): osimertinib 27.7 months, placebo 19.5 months.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; NC, not calculable; PFS, progression-free survival

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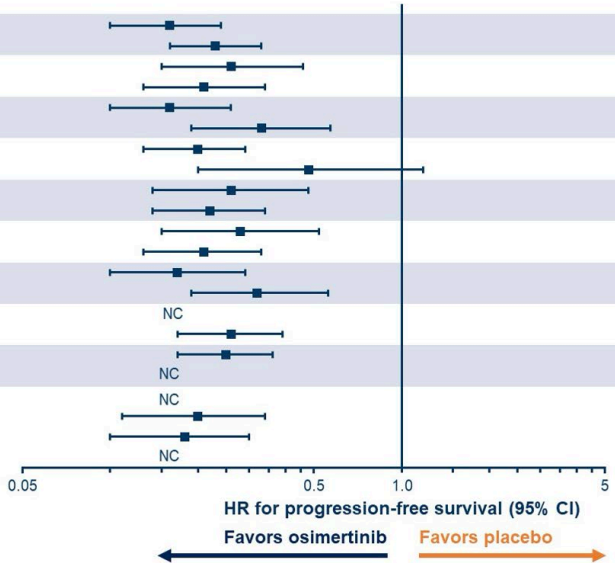
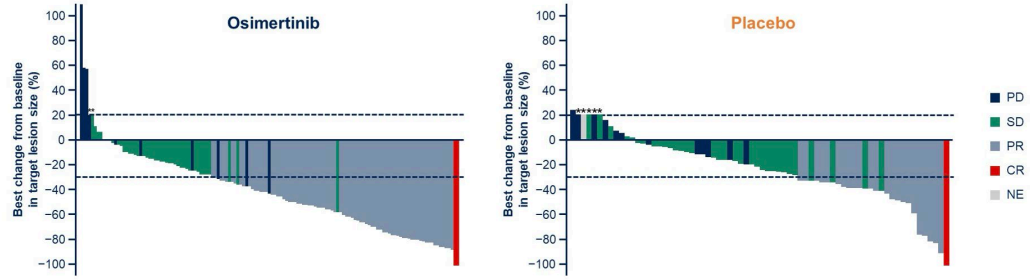
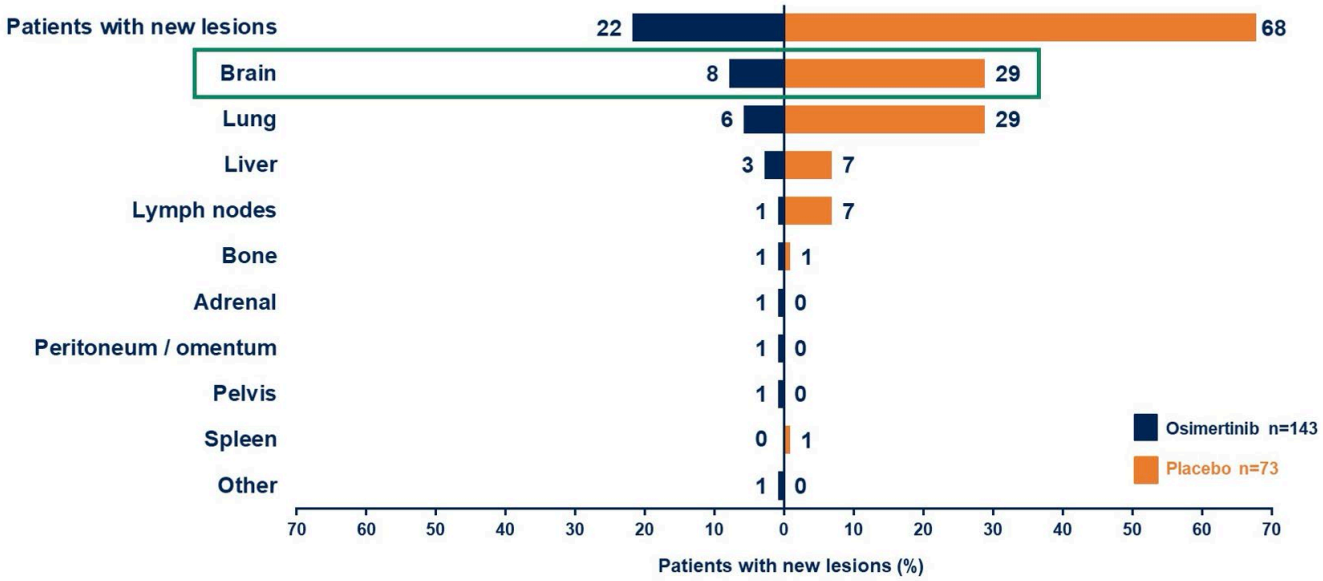
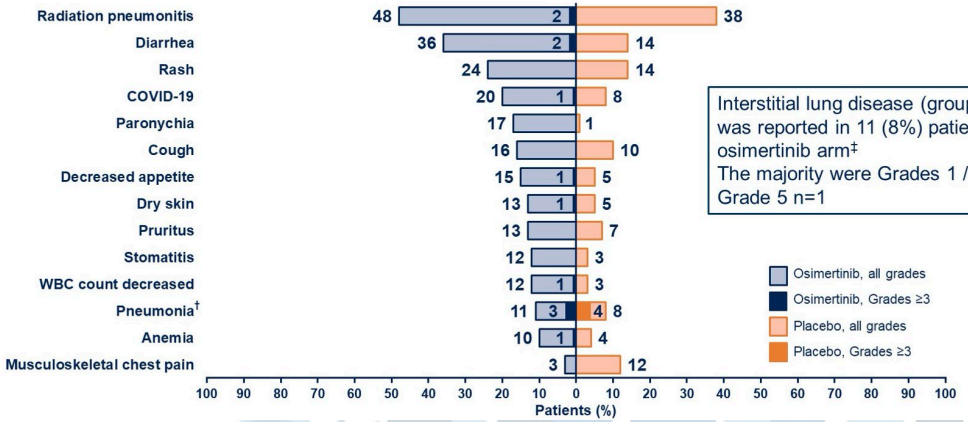
| Subgroup | | No. of events / patients | HR | 95% CI |
|---|---|---|---|---|
| Overall (N=216) | Stratified log-rank | 120 / 216 | 0.16 | 0.10, 0.24 |
| | Unadjusted Cox PH | 120 / 216 | 0.23 | 0.16, 0.33 |
| Sex | Male | 50 / 84 | 0.26 | 0.15, 0.46 |
| | Female | 70 / 132 | 0.21 | 0.13, 0.34 |
| Age | <65 years | 67 / 120 | 0.16 | 0.10, 0.26 |
| | ≥65 years | 53 / 96 | 0.33 | 0.19, 0.57 |
| Race | Asian | 98 / 178 | 0.20 | 0.13, 0.29 |
| | Non-Asian | 22 / 38 | 0.48 | 0.20, 1.19 |
| Smoking history | Current / former (yes) | 42 / 65 | 0.26 | 0.14, 0.48 |
| | Never (no) | 78 / 151 | 0.22 | 0.14, 0.34 |
| Stage* | IIIA | 42 / 76 | 0.28 | 0.15, 0.52 |
| | IIIB / IIIC | 78 / 140 | 0.21 | 0.13, 0.33 |
| EGFR mutation† | Ex19del | 65 / 117 | 0.17 | 0.10, 0.29 |
| | L858R | 55 / 98 | 0.32 | 0.19, 0.56 |
| China cohort | Chinese | 18 / 40 | NC | NC, NC |
| | Non-Chinese | 102 / 176 | 0.26 | 0.17, 0.39 |
| Chemoradiotherapy | Concurrent | 107 / 193 | 0.25 | 0.17, 0.36 |
| | Sequential | 13 / 23 | NC | NC, NC |
| Response to prior CRT | Complete response | 3 / 7 | NC | NC, NC |
| | Partial response | 53 / 94 | 0.20 | 0.11, 0.34 |
| | Stable disease | 58 / 98 | 0.18 | 0.10, 0.30 |
| | Non-evaluable | 6 / 17 | NC | NC, NC |




| | Osimertinib (n=143) | Placebo (n=73) |
|---|---|---|
| Objective response rate, % (95% CI) | 57 (49, 66) | 33 (22, 45) |
| Disease control rate, % (95% CI) | 89 (83, 94) | 79 (68, 88) |
| Median duration of response, months (95% CI) | 36.9 (30.1, NC) | 6.5 (3.6, 8.3) |




Interstitial lung disease (grouped term) was reported in 11 (8%) patients in the osimertinib arm‡
The majority were Grades 1 / 2; Grade 5 n=1

# Abstract # H. Liu et al. CA109-7AL

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**Key eligibility criteria**
- Unresectable, stage III NSCLC (per AJCC 8th edition)
- No prior anti-cancer treatment
- age 18 to 75 years
- ECOG 0-1

→ NIVO 360 mg Q3W + Chemo[b] Q3W (2 cycles) → Split-Course Hypo-RT (54~64Gy) + Concurrent chemo[c] (weekly) → R 1:1 → NIVO 360 mg Q3W (1 year) / Observation (1 year)

Follow-up

Stratified by age, sex, smoking history and EGFR mutation status

**Primary endpoint**
- PFS

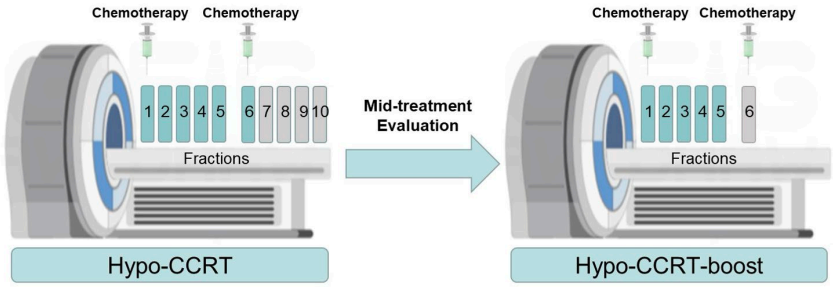
**Secondary endpoints**
- OS
- ORR
- Safety
- QOL

**Exploratory analyses**
- Cytokine levels in plasma
- Peripheral lymphocyte subsets

- **Hypo-CCRT and hypo-CCRT-boost** [1,2]

  Hypo-CCRT: 40Gy/10fr or 30Gy/6fr; Hypo-CCRT-boost: 24~30Gy/6fr; Total dose: 60~64Gy
- **Concurrent chemotherapy**

  Docetaxel 25 mg/ m², d1 plus cisplatin 25 mg/ m², d1, every week




**264 enrolled patients**

**Received neoadjuvant therapy 264 (100%)**
Completed neoadjuvant therapy 235 (89.0%)

29 discontinued neoadjuvant therapy

| | |
|---|---|
| Toxicity | 18 (6.8%) |
| Patient refusal | 10 (3.8%) |
| Disease progression | 1 (0.4%) |

**Received hypo-CCRT 242 (91.7%)**
Completed hypo-CCRT 228 (86.4%)

22 cancelled hypo-CCRT

| | |
|---|---|
| Toxicity | 9 (3.4%) |
| Patient refusal | 8 (3.0%) |
| Disease progression | 4 (1.5%) |
| Mis-staging | 1 (0.4%) |

14 discontinued hypo-CCRT

| | |
|---|---|
| Toxicity | 5 (1.9%) |
| Patient refusal | 5 (1.9%) |
| Disease progression | 2 (0.8%) |
| Covid 19 | 2 (0.8%) |

**Randomized population 172 (65.2%)**

56 excluded from randomization

| | |
|---|---|
| Disease progression | 22 (8.3%) |
| Toxicity | 19 (7.2%) |
| Covid19 | 10 (3.8%) |
| Patient refusal | 3 (1.1%) |
| Other | 2 (0.8%) |

**Randomized population 172 （65.2%）**

**86 assigned to consolidation group 86 received consolidative NIVO**

23 completed NIVO
43 discontinued NIVO
- 23 toxicity
- 7 disease progression
- 3 patient decision
- 10 covid19

20 still receiving NIVO at data cutoff

86 included in the survival analysis

**86 assigned to observation group 86 received observation**

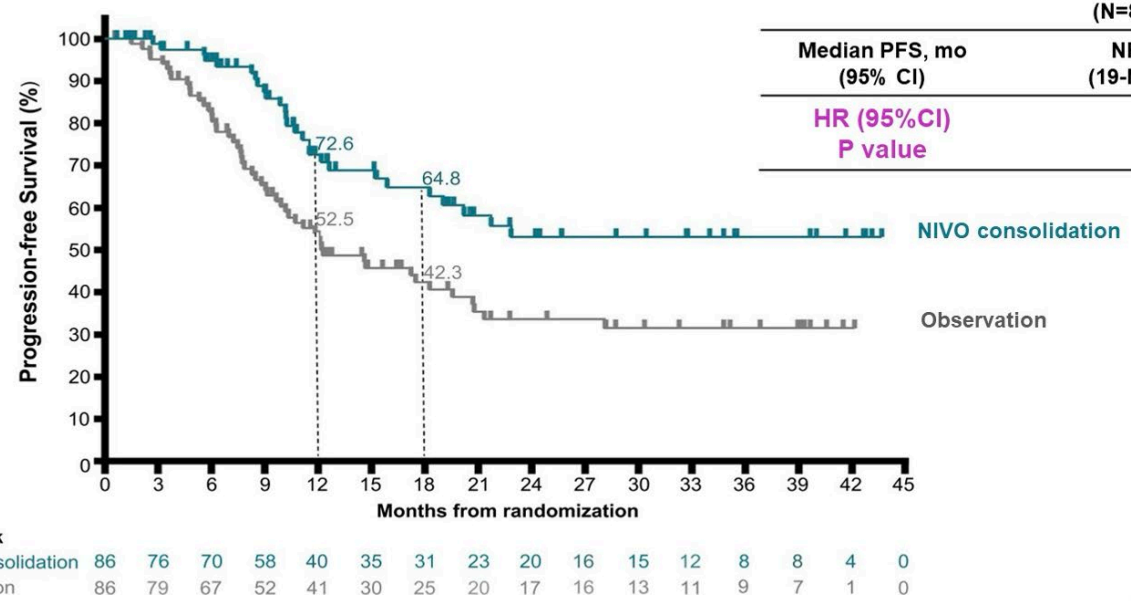
33 completed observation
36 discontinued observation
- 31 disease progression
- 5 died

17 still receiving observation at data cutoff

86 included in the survival analysis

| Objective response | Patients (N=264) |
|---|---|
| Partial response | 173 (65.5%) |
| Stable disease | 70 (26.5%) |
| Progressive disease | 4 (1.5%) |
| Could not be evaluated | 17 (6.4%) |
| **Objective response rate** | **65.5%** |
| **Relative change in tumor volume, median (IQR)** | **61.1% (36.3~76.4)** |

| Objective response | Patients (N=242) |
|---|---|
| Complete response | 55 (22.7%) |
| Partial response | 149 (61.6%) |
| Stable disease | 5 (2.1%) |
| Progressive disease | 20 (8.3%) |
| Could not be evaluated | 13 (5.4%) |
| **Objective response rate** | **84.3%** |
| **Relative change in tumor volume, median (IQR)** | **93.5% (84.4~100)** |




| | NIVO consolidation (N=86) | Observation (N=86) |
|---|---|---|
| Median PFS, mo (95% CI) | NR (19-NR) | 12.2 (10.2-20.8) |
| HR (95%CI) | 0.49 (0.30-0.79) | |
| P value | p=0.003 | |

| | Consolidation group (N=86) | Observation group (N=86) |
|---|---|---|
| **Best overall response** | | |
| Complete response | 43 (50.0%) | 24 (27.9%) |
| Partial response | 42 (48.8%) | 60 (69.8%) |
| Stable disease | 1 (1.2%) | 2 (2.3%) |
| **Objective response rate** | **98.8%** | **97.7%** |

Mediana seguimiento
22.8 meses

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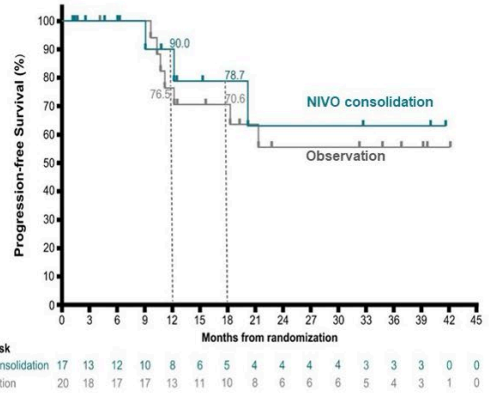
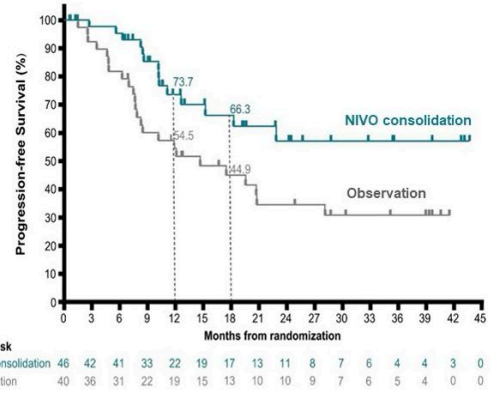
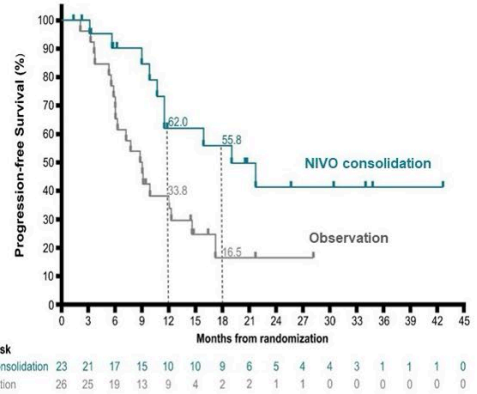
| Stage IIIA | NIVO consolidation (N=17) | Observation (N=20) |
|---|---|---|
| Median PFS, mo (95% CI) | NR (20.2-NR) | NR (18.3-NR) |
| HR (95%CI) | 0.76 (0.20-2.95) | |
| P value | P=0.694 | |




| Stage IIIB | NIVO consolidation (N=46) | Observation (N=40) |
|---|---|---|
| Median PFS, mo (95% CI) | NR (18.3-NR) | 14.7 (8.3-NR) |
| HR (95%CI) | 0.46 (0.24-0.89) | |
| P value | P=0.018 | |




| Stage IIIC | NIVO consolidation (N=23) | Observation (N=26) |
|---|---|---|
| Median PFS, mo (95% CI) | 19.0 (11.5-NR) | 8.9 (6.1-14.6) |
| HR (95%CI) | 0.38 (0.18-0.84) | |
| P value | P=0.013 | |




Correlación significativa con PFS:

- PS
- IL-6
- CD3+

| Recaída (%) | Consolidación | Observación |
|---|---|---|
| Total | 17.4 % | 47.7 % |
| Locoregional. | 12.8% | 24.4% |
| Distancia | 9.3% | 17.9% |
| Cerebral | 25% | |
| Oligomet. | 7% | 19.8% |

| Neumonitis | Cualquier grado | Grado > 3 | Discontinuación x EAs |
|---|---|---|---|
| Inducción | 4.2% | 1.1% | 11% |
| RT hipofrac. | 54.5% | 2.5% | 13.6% |
| Nivolumab consolid. | 29.1% vs 14% | 3.5% vs 2.3% | 26.7% |

# Abstract # Y Puneeth et al. NRG-LU002

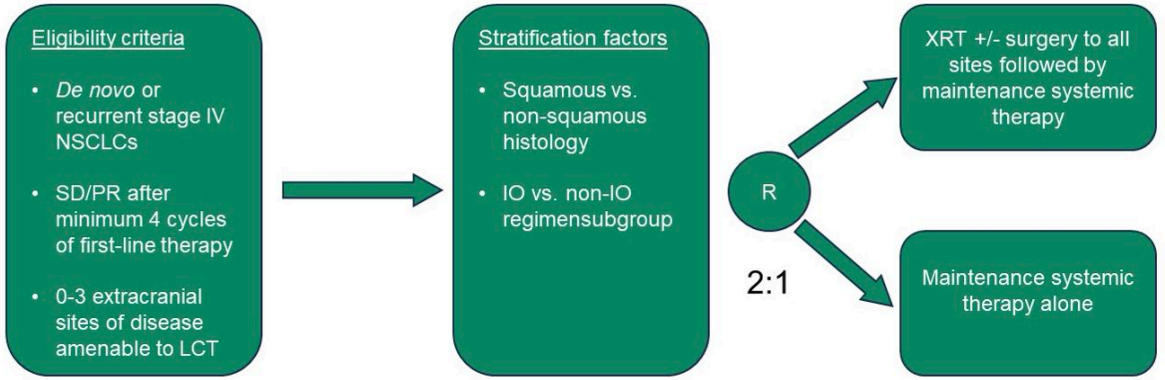
| | | | | |
|---|---|---|---|---|
| Patients with metastatic NSCLC having completed at least 4 cycles or courses* of first-line/induction systemic therapy<br><br>Restaging studies reveal no evidence of progression and limited metastatic disease (0-3 discrete extracranial sites), all of which must be amenable to SBRT/ radiation +/- Surgery<br><br>A minimum of one disease site (metastasis or primary) needs to be present after first-line/induction systemic therapy and treatable with local consolidative therapy | **STRATIFY** | **Histology:**<br><br>Squamous vs. Non-squamous<br><br>**Systemic Therapy:**<br>Immunotherapy-containing Induction Regimens vs. Cytotoxic Chemotherapy Only Induction Regimens** | **RANDOMIZE** | **Arm 1**:<br>Maintenance systemic therapy alone**<br><br>**Arm 2:**<br>SBRT/radiation or SBRT/ radiation and Surgery to all sites of metastases (0-3 discrete sites) and/or irradiation (SBRT or hypofractionated RT) of the primary site followed by maintenance systemic therapy. All Arm 2 patients, even if treated with Surgery, must have one site of disease (metastasis or primary) treated with radiation***<br><br>If a metastatic site is best treated with hypofractionated radiation, this will be permitted if SBRT or surgery not indicated<br><br>*** **As noted in Section 5** |

Aleatorización: 2:1
90% con tto QT-IT
85% con 1-2 lesiones
RT de lesión primaria 31%
Objetivo primario:
- Fase 2: PFS
- Fase 3: OS

Objetivos secundarios:
- Calidad de vida
- ct-DNA

Finaliza tras Fase 2:
- 218 pacientes
- HR objetivo 0.60

HR mínima para Fase 3: 0.83



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## PTV Dosimetry Compliance for SBRT

| Name of Structure | Dosimetric parameter | Per Protocol | Variation Acceptable | Fractions |
|---|---|---|---|---|
| PTVXY_2400 | D95%[Gy] | 24 | 16-27 | 1 |
| PTVXY_3000 | D95%[Gy] | 30 | 24.5-33 | 3 |
| PTVXY_3400 | D95%[Gy] | 34 | 28-37.5 | 5 |

## PTV Dosimetry Compliance for Primary Site (45 Gy Acceptable)

| Name of Structure | Dosimetric parameter | Per Protocol | Variation Acceptable | Fractions |
|---|---|---|---|---|
| PTV_4500 | D95%[Gy] | 45 | 42-48 (excluding 45) | 15 |

Tratamiento mantenimiento:

- Pemetrexed
- Gemcitabina
- Pembrolizumab-Pemetrexed
- Nivolumab-Ipilimumab
- Atezolizumab

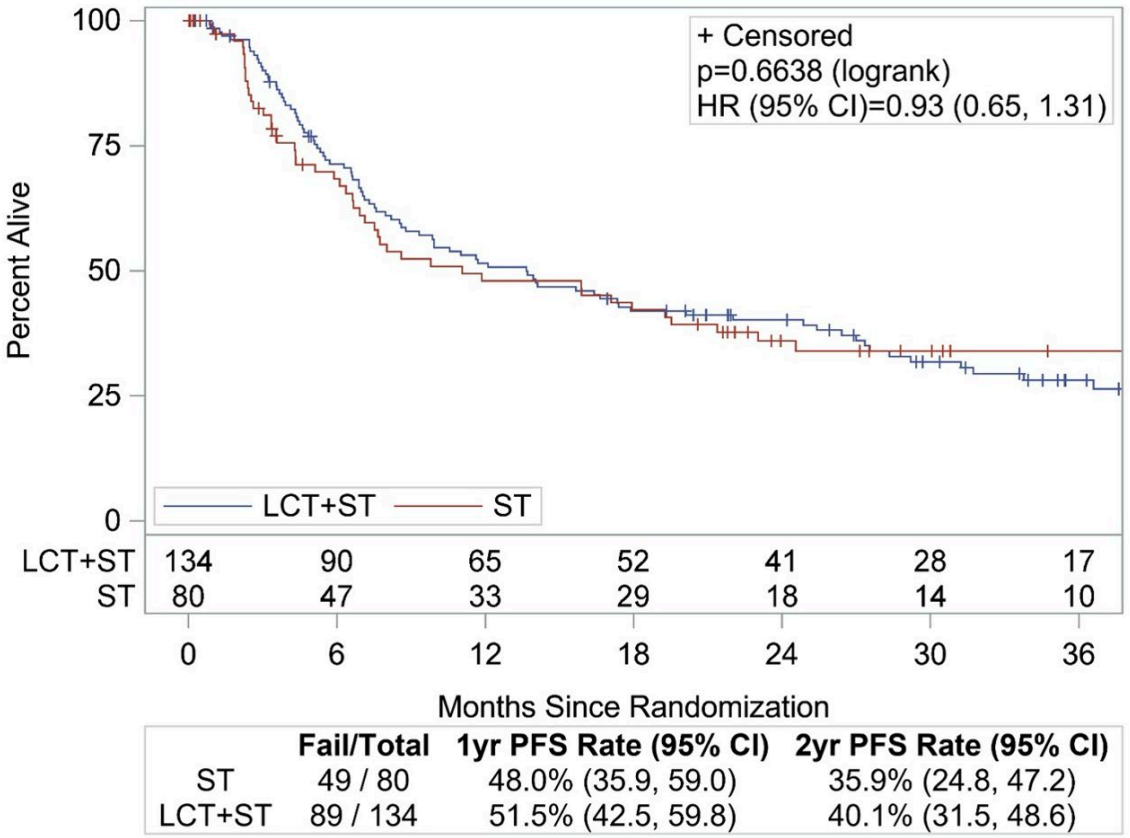
Se inicia en 2 semanas desde inclusión o en las 2 semanas tras tratamiento local

185/215 pacientes incluidos recibieron tratamiento con IT/QT o IT

| | | | |
|---|---|---|---|
| Histology* | | | |
| Non-Squamous cell carcinoma | 64 ( 79.0%) | 103 ( 76.9%) | 167 ( 77.7%) |
| Squamous cell carcinoma | 17 ( 21.0%) | 31 ( 23.1%) | 48 ( 22.3%) |
| Systemic Therapy Type*† | (n=75) | (n=129) | (n=204) |
| Cytotoxic Chemotherapy | 8 ( 10.7%) | 11 ( 8.5%) | 19 ( 9.3%) |
| Immunotherapy | 67 ( 89.3%) | 118 ( 91.5%) | 185 ( 90.7%) |
| Number of Lesions | | | |
| 1 | 49 ( 60.5%) | 77 ( 57.5%) | 126 ( 58.6%) |
| 2 | 20 ( 24.7%) | 37 ( 27.6%) | 57 ( 26.5%) |
| 3 | 12 ( 14.8%) | 18 ( 13.4%) | 30 ( 14.0%) |
| 4 | 0 ( 0.0%) | 1 ( 0.7%) | 1 ( 0.5%) |
| 5 | 0 ( 0.0%) | 1 ( 0.7%) | 1 ( 0.5%) |
| Consented to tissue/blood collection | | | |
| No | 13 ( 16.0%) | 26 ( 19.4%) | 39 ( 18.1%) |
| Yes | 68 ( 84.0%) | 108 ( 80.6%) | 176 ( 81.9%) |

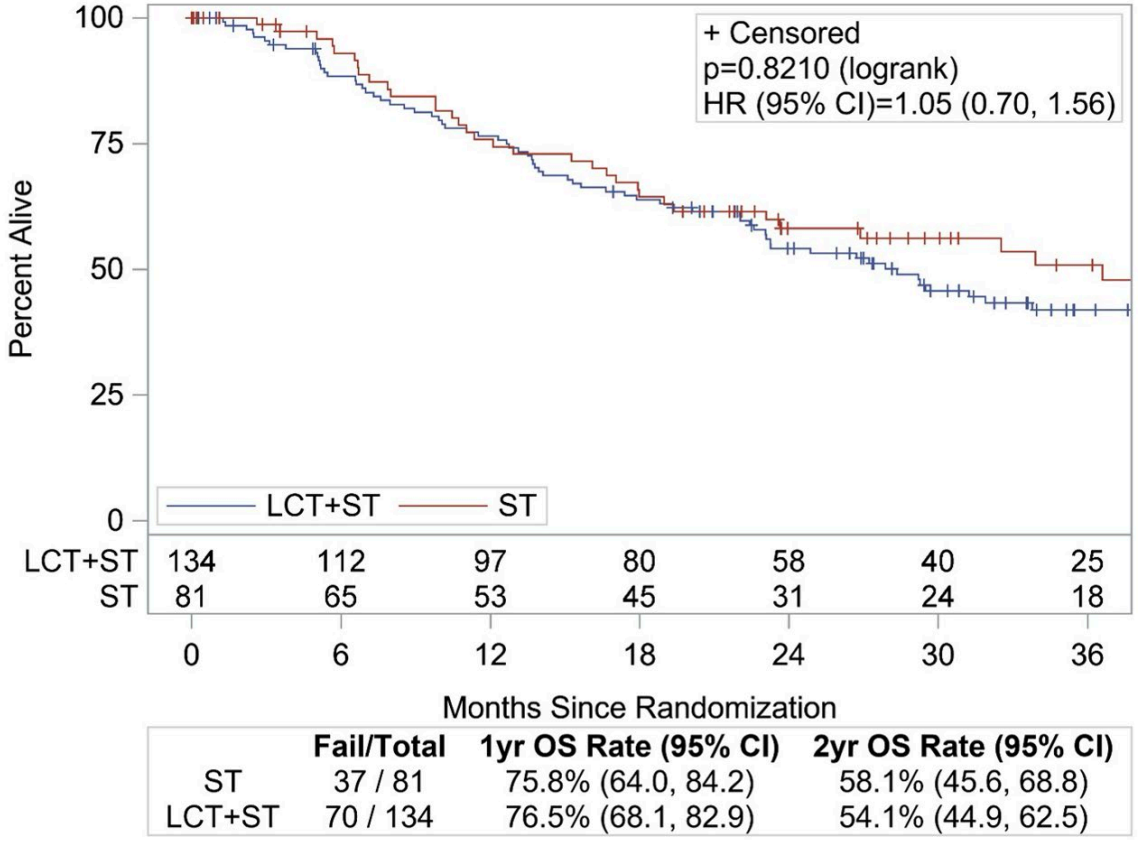
| | Systemic Therapy (n=81) | LCT + Systemic Therapy (n=134) | Total (n=215) |
|---|---|---|---|
| Primary Tumor Response at Baseline | | | |
| Stable Disease | 46 (59.0%) | 69 (57.0%) | 115 (57.8%) |
| Partial Response | 25 (32.1%) | 40 (33.1%) | 65 (32.7%) |
| Not evaluable | 6 (7.7%) | 6 (5.0%) | 12 (6.0%) |
| Complete Response | 1 (1.3%) | 6 (5.0%) | 7 (3.5%) |
| Number of Lesions at Baseline | | | |
| Median | 2 | 2 | 2 |
| Min - Max | 1 - 5 | 1 - 25 | 1 - 25 |
| Q1 - Q3 | 2 - 3 | 2 - 4 | 2 - 3 |

## PFS




| | Fail/Total | 1yr PFS Rate (95% CI) | 2yr PFS Rate (95% CI) |
|---|---|---|---|
| ST | 49 / 80 | 48.0% (35.9, 59.0) | 35.9% (24.8, 47.2) |
| LCT+ST | 89 / 134 | 51.5% (42.5, 59.8) | 40.1% (31.5, 48.6) |

## OS




| | Fail/Total | 1yr OS Rate (95% CI) | 2yr OS Rate (95% CI) |
|---|---|---|---|
| ST | 37 / 81 | 75.8% (64.0, 84.2) | 58.1% (45.6, 68.8) |
| LCT+ST | 70 / 134 | 76.5% (68.1, 82.9) | 54.1% (44.9, 62.5) |

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Mediana seguimiento 21.9 meses

| EAs | Grado > 2 | Grado 4 | Grado 5 | Neumonitis |
|---|---|---|---|---|
| Tto Sistemico | 73% | 15% | 6% | 1 % |
| Tto sist.+local | 84% | 15% | 8% | 10% |

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