



CNMP ESTADIOS TEMPRANOS

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Unidad de Oncología Hospital Universitario Fundación Alcorcón



OUTLINE

ASCO 2024 Lung Cancer Updates GECP



Perioperative immunotherapy

Perioperative targeted therapy

ctDNA – MRD

Operability parameters changes



CHECKMATE-77T: EXPLORATORY ANALYSYS BY NODAL STATUS (N2 vs not-N2)





#LBA 8007

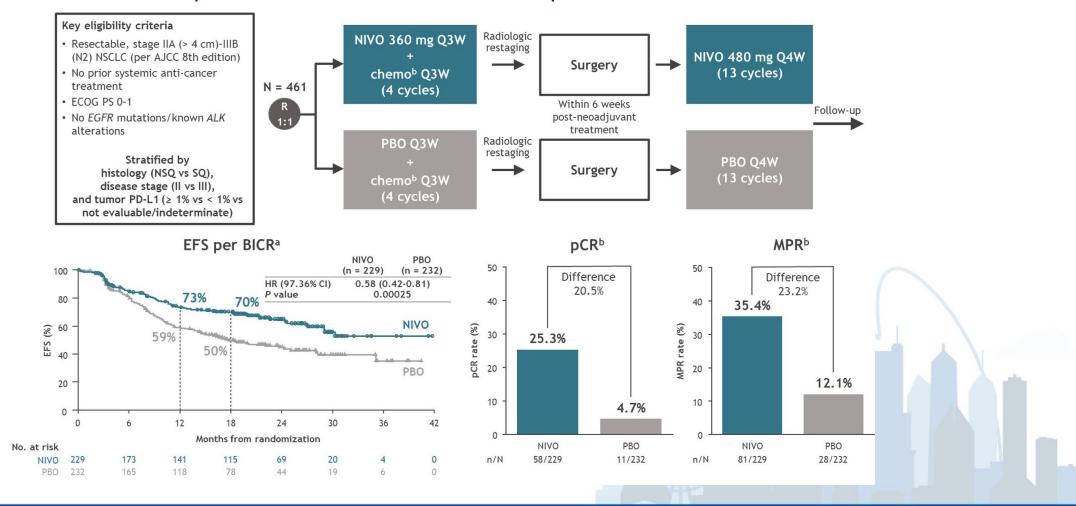
Clinical outcomes with perioperative nivolumab by nodal status among patients with stage III resectable NSCLC: results from the phase 3 CheckMate 77T study

Mariano Provencio Pulla,¹ Mark M. Awad,² Jonathan D. Spicer,³ Annelies Janssens,⁴ Fedor Moiseyenko,⁵ Yang Gao,⁶ Yasutaka Watanabe,⁷ Aurelia Alexandru,⁸ Florian Guisier,⁹ Nikolaj Frost,¹⁰ Fabio Franke,¹¹ T. Jeroen Nicolaas Hiltermann,¹² Jie He,¹³ Fumihiro Tanaka,¹⁴ Shun Lu,¹⁵ Cinthya Coronado Erdmann,¹⁶ Padma Sathyanarayana,¹⁶ Phuong Tran,¹⁶ Vipul Devas,¹⁶ <u>Tina Cascone</u>¹⁷



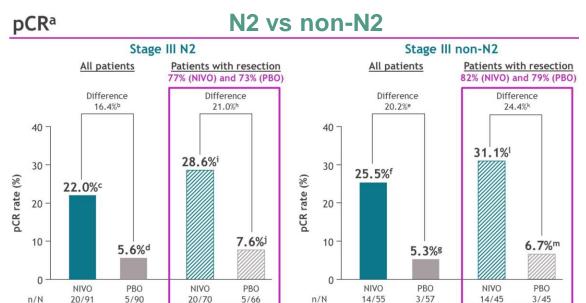
CHECKMATE-77T: EXPLORATORY ANALYSYS BY NODAL STATUS (N2 vs not-N2)

In phase III CM-77T trial, perioperative Nivolumab showed significant EFS improvement vs PBO in pts with stage II-IIIB resectable NSCLC. pCR and MPR rates were also improved



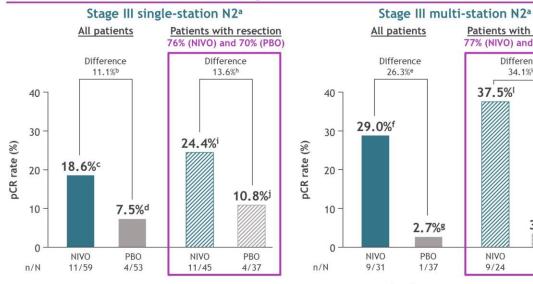
Iniciativa científica de:

CHECKMATE-77T: EXPLORATORY ANALYSIS BY NODAL STATUS (N2 vs not-N2)



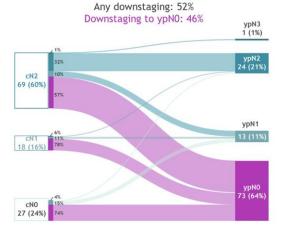
N Downstaging





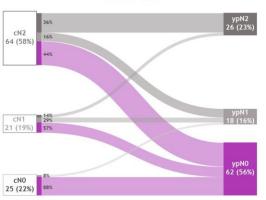
Patients with resection 77% (NIVO) and 78% (PBO) Difference 34.1%k 37.5% 3.4%m 2.7%g NIVO PBO **PBO** 1/37 9/24 1/29

NIVO $(n = 115)^a$



PBO $(n = 111)^a$

Any downstaging: 45% Downstaging to ypN0: 36%



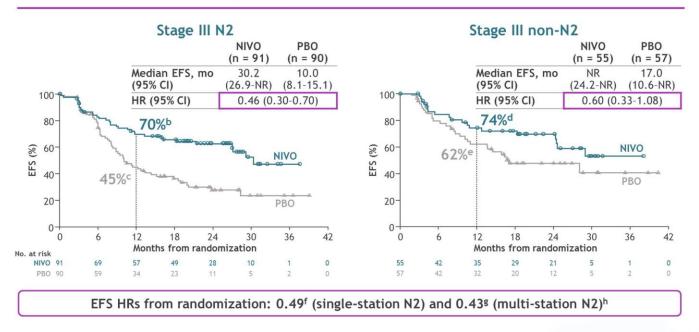
N2

- 67% downstaging
- 57% to NO

CHECKMATE-77T: EXPLORATORY ANALYSYS BY NODAL STATUS (N2 vs not-N2)



EFS from randomization^a

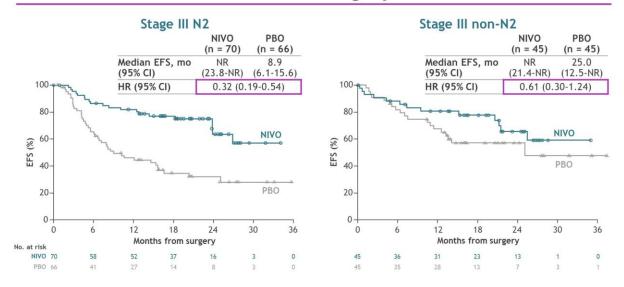


- Beneficio clínico con nivolumab perioperatorio vs placebo tanto en pacientes estadio III N2 como no-N2
- Mejora pCR, downstaging
- Mejora la EFS:
 - HR 0.46 (N2); HR 0.6 (non-N2)
 - HR 0.43 (multi-N2); HR 0.49 (single N2)

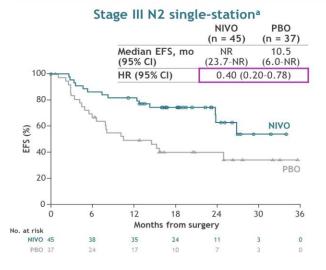
CHECKMATE-77T: EXPLORATORY ANALYSYS BY NODAL STATUS (N2 vs not-N2)

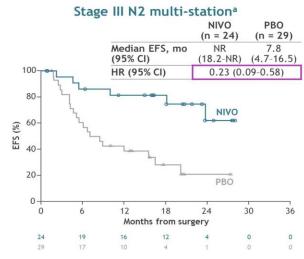


Landmark EFS from definitive surgery

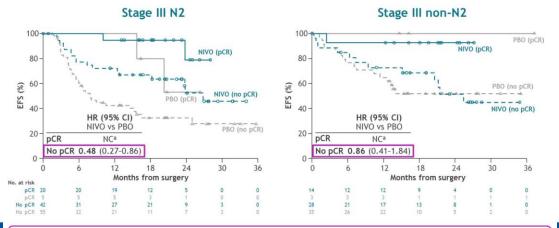


Landmark EFS from definitive surgery





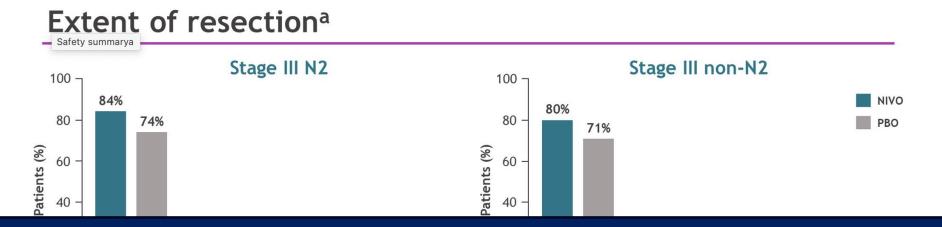
Landmark EFS from definitive surgery by pCR status



- Mejoría de la EFS desde la cirugía con mayor reducción de riesgo a más N
 - HR 0.32 N2
 - HR 0.23 multi-N2
- Mejoría de la EFS en pacientes N2 sin pCR
 - HR 0.48



CHECKMATE-77T: EXPLORATORY ANALYSYS BY NODAL STATUS (N2 vs not-N2)



Estos resultados avalan el uso de Nivolumab perioperatorio en pacientes con CNMP resecable, también en el subgrupo de peor pronóstico estadio III N2

 Complete resection (R0), %
 86c
 86d
 84e
 87f

- La viabilidad quirúrgica fue similar en los pacientes N2 respecto a los no-N2 tras quimio-inmuno neoadyuvante con nivolumab
- 86% de las cirugías fue R0, comparable e incluso mayor numéricamente que en los no-N2

CHECKMATE-816: 4-year update





#LBA 8010

Neoadjuvant nivolumab plus chemotherapy vs chemotherapy in patients with resectable NSCLC: 4-year update from CheckMate 816

<u>Jonathan D. Spicer</u>, ¹ Nicolas Girard, ² Mariano Provencio Pulla, ³ Changli Wang, ⁴ Tetsuya Mitsudomi, ⁵ Mark M. Awad, ⁶ Everett E. Vokes, ⁷ Janis M. Taube, ⁸ Lorena Lupinacci, ⁹ Gene B. Saylors, ¹⁰ Fumihiro Tanaka, ¹¹ Moishe Liberman, ¹² Sung Yong Lee, ¹³ Aurelia Alexandru, ¹⁴ Manolo D'Arcangelo, ¹⁵ Phuong Tran, ¹⁶ Javed Mahmood, ¹⁶ Vishwanath Gharpure, ¹⁶ Apurva Bhingare, ¹⁶ Patrick M. Forde⁸

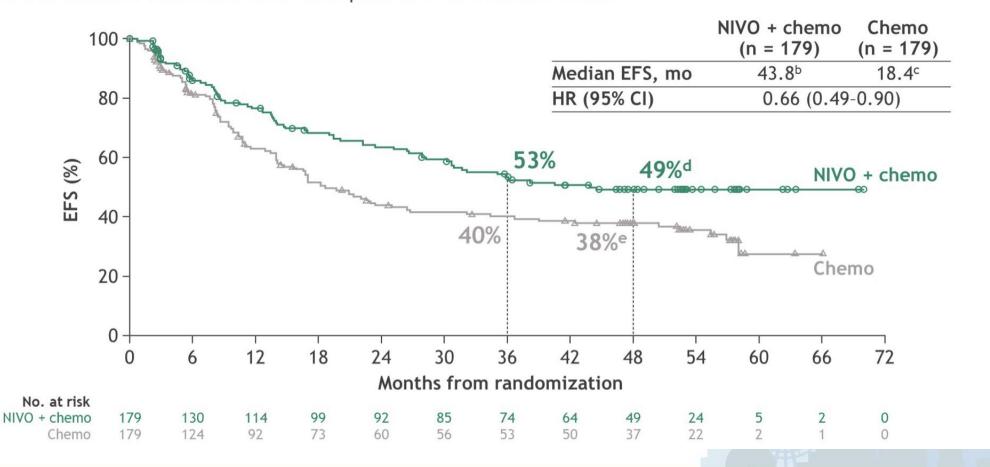
¹McGill University Health Centre, Montreal, Quebec, Canada; ²Institut du Thorax Curie-Montsouris, Institut Curie, Paris, France; ³Hospital Universitario Puerta de Hierro, Madrid, Spain; ⁴Tianjin Lung Cancer Center, Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; ⁵Kindai University Faculty of Medicine, Ohno-Higashi, Osaka-Sayama, Japan; ⁶Dana-Farber Cancer Institute, Boston, MA; ⁷University of Chicago Medicine, Chicago, IL; ⁸The Bloomberg-Kimmel Institute for Cancer Immunotherapy, Johns Hopkins Medicine, The Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; ⁹Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; ¹⁰Charleston Oncology, Charleston, SC; ¹¹University of Occupational and Environmental Health, Kitakyushu, Japan; ¹²Centre Hospitalier de l'Universite de Montreal, Montreal, Quebec, Canada; ¹³Korea University Guro Hospital, Korea University College of Medicine, Seoul, Republic of Korea; ¹⁴Institutul Oncologic București Prof. Dr. Alexandru Trestioreanu, Bucharest, Romania; ¹⁵Azienda Unita Sanitaria Locale della Romagna, Ravenna, Italy; ¹⁶Bristol Myers Squibb, Princeton, NJ



CHECKMATE-816: 4-year update EFS

EFS: 4-year update^a

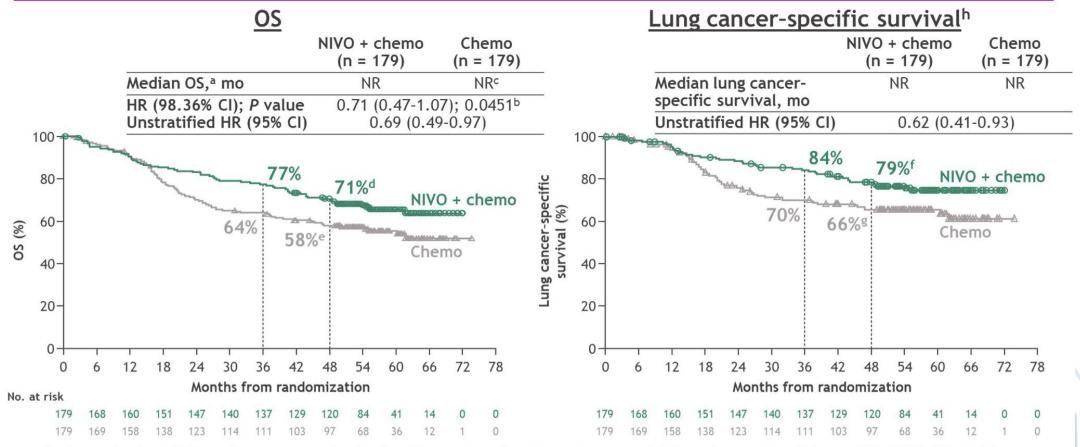
• In CheckMate 816, neoadjuvant NIVO + chemo significantly improved the primary endpoints of EFS and pCR vs chemo and demonstrated a favorable OS trend in patients with resectable NSCLC^{1,2}





CHECKMATE-816: 4-year update OS and lung cancer-specific survival





• Patients in the NIVO + chemo arm who had pCR continued to have improved OS vs those who did not (HR [95% CI], 0.08 [0.02-0.34]; 4-year OS rates, 95% vs 63%)

CHECKMATE-816: 4-year update

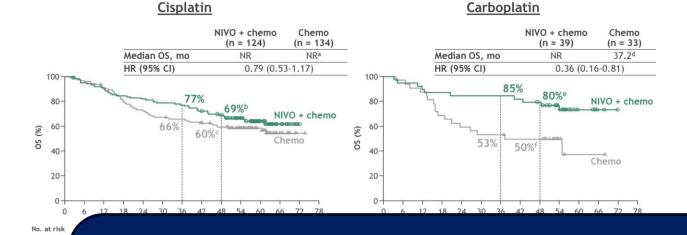
ctD

 Amo level

80



NΑ



 Tendencia a mejor OS independientemente del tipo de platino utilizado (carboplatino HR 0.36) o de la extensión de la cirugía

Estos resultados refuerzan el uso de quimio-inmunoterapia neoadyuvante con nivolumab como SoC de los pacientes con CNMP resecable y nos aporta más conocimiento del beneficio a largo plazo de la QTIO neoadyuvante

| NIVO + chemo | Chemo | n/N | 24/43 | 15/43 | 15/43 | 15/43 | 15/43 | No ctDNA clearance | N

El aclaramiento de ctDNA precirugía fue un factor pronóstico de OS

actectable

AEGEAN: N2 subgroup analysis





#8011

Outcomes with Perioperative Durvalumab in Patients with Resectable NSCLC and Baseline N2 Lymph Node Involvement (N2 R-NSCLC)

An Exploratory Subgroup Analysis of AEGEAN

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¹Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA; ²Lung Clinic Grosshansdorf, Airway Research Center North, German Center for Lung Research, Grosshansdorf, Germany; ³Division of Thoracic Surgery, Department of Surgery, Kindai University Faculty of Medicine, Osaka-Sayama, Japan; ⁴Bloomberg–Kimmel Institute for Cancer Immunotherapy, Johns Hopkins Kimmel Cancer Center, Baltimore, MD, USA; ⁵Virginia Cancer Specialists Research Institute, Fairfax, VA, & US Oncology Research, The Woodlands, TX, USA; ⁶Memorial Sloan-Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA; ⁷AstraZeneca, Cambridge, UK; ⁸AstraZeneca, New York, NY, USA; ⁹Department of Surgery, Duke University Medical Center, Durham, NC, USA

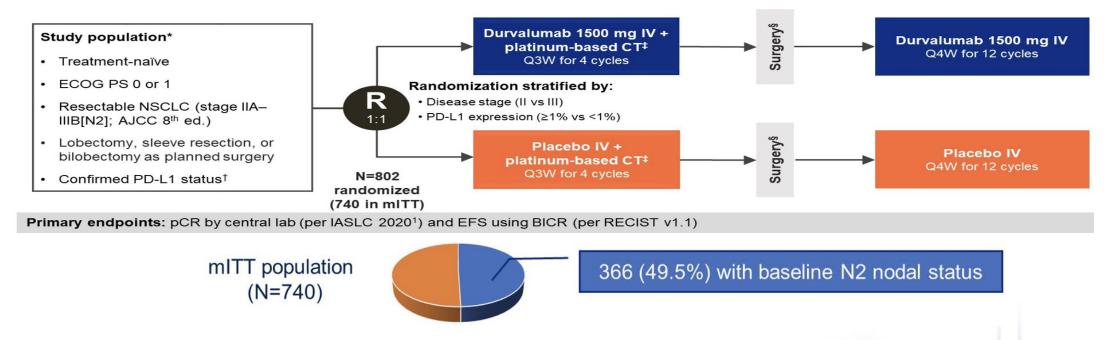






AEGEAN: N2 subgroup analysis



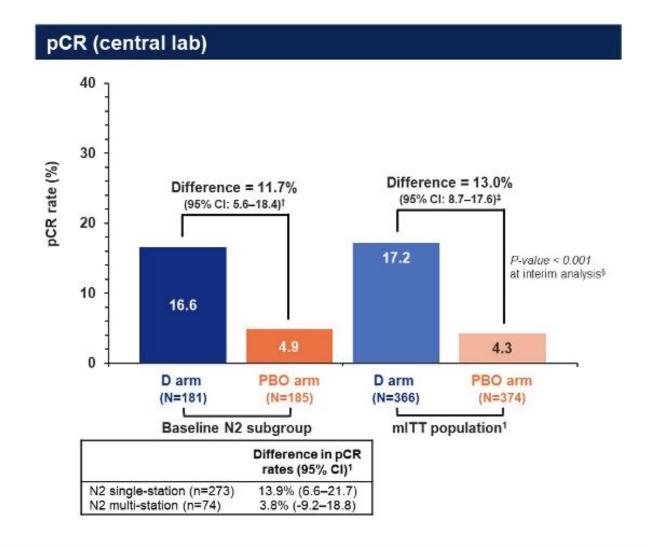


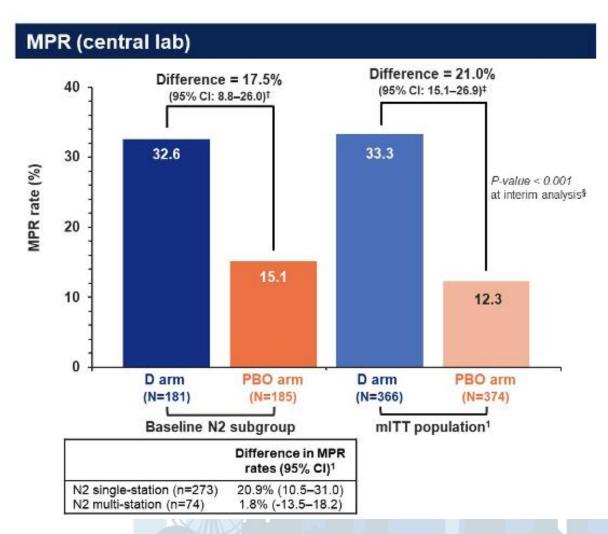
N2 vs mITT

- % 4 ciclos completos neoadyuvancia: similar
- % cirugía de resección ligeramente menor (73,5% N2 vs 77,6% mITT)
- % resección R0 similar (94,7% en ambos) y numéricamente superior que en los que no recibieron durva
- Procedimiento quirúrgico: similar porcentaje cirugía abierta
- Extensión de la cirugía: similar porcentaje de neumonectomías y lobectomías
- % retraso de cirugía similar: 19,9% N2 vs 17,3% mITT

AEGEAN: N2 vs mITT







AEGEAN: N2 vs mITT



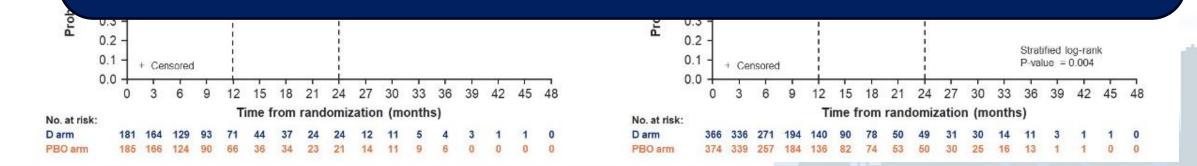
EFS using RECIST v1.1 (BICR) (baseline N2 subgroup and mITT)*

- EFS benefit in this subgroup was consistent with the mITT population and similar among patients with single- and multi-station N2 disease
 - N2 single-station (n=273) HR[†] (95% CI): 0.61 (0.39–0.94)¹
 - N2 multi-station (n=74) HR[†] (95% CI): 0.69 (0.33–1.38)¹

HR 0.63 in N2 patients

Baseline N2 subgroup D arm PBO arm mITT population¹ D arm PBO arm

Estos resultados avalan el posible uso de durvalumab perioperatorio en pacientes con CNMP resecable N2 con mejoría estadística y clínicamente significativa de la eficicacia y sin un impacto negativo en los resultado quirúrgicos



KEYNOTE-671: HRQoL





#8012

Health-Related Quality of Life Outcomes From the Randomized, Double-Blind Phase 3 KEYNOTE-671 Study of Perioperative Pembrolizumab for Early-Stage NSCLC

Marina C Garassino, Heather Wakelee, Jonathan D Spicer, Moishe Liberman, Terufumi Kato, Masahiro Tsuboi, Se-Hoon Lee, Ke-Neng Chen, Christophe Dooms, Margarita Majem, Ekkehard Eigendorff, Gastón L Martinengo, Olivier Bylicki, Delvys Rodríguez-Abreu, Jamie Chaft, Jing Yang, Ashwini Arunachalam, Josephine M Norquist, Steven M Keller, Shugeng Gao

Presented by Marina C Garassino of the University of Chicago School of Medicine and Biological Sciences, Chicago, IL, USA



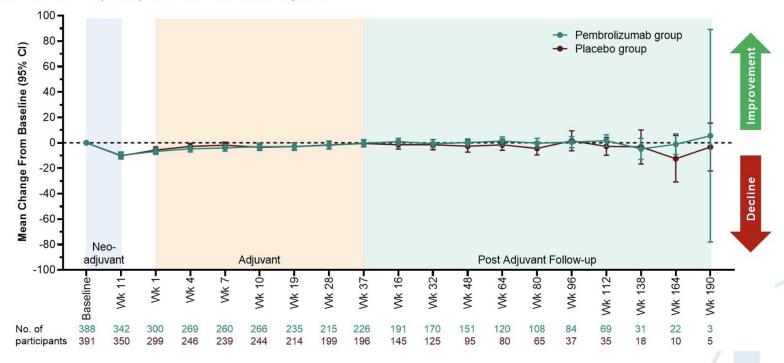




KEYNOTE-671: HRQoL



Empirical Mean Change From Baseline Over Time EORTC QLQ-C30 GHS/QoL



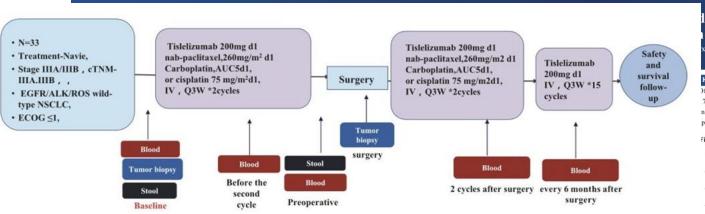
- El uso de pembrolizumab perioperatorio no deterioró la calidad de vida relacionada con la salud en comparación con la QT neoadyuvante en pacientes con CNMP estadio II-IIIB (N2) resecable
- La calidad de vida empeoró durante el periodo neoadyuvante y posteriormente se restauró hasta la situación basal durante la fase adyuvante en ambos brazos

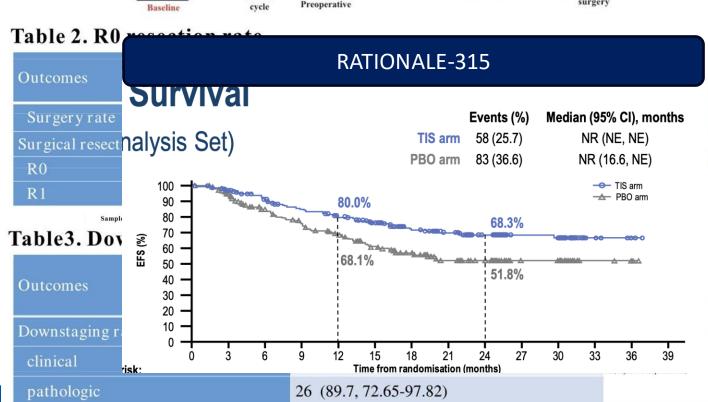
#8024

GECP

research

PH. II TISLELIZUMAB + CT PRE AND POST





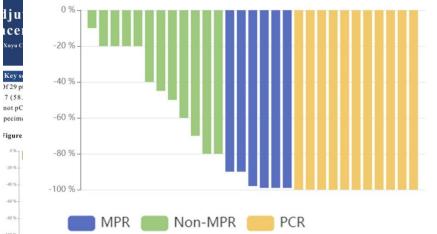


Table 5. Pathologic response

Outcome		· · · · · · · · · · · · · · · · · · ·		
MPR PCR	Outcomes	Results, n (%, 95% CI); n = 29		
Non-MP	MPR	17 (58.6, 38.94-76.48)		
Con	PCR	11 (38.0, 20.69-57.74)		
Neoadji	Non-MPR	12 (41.4, 23.52-61.06)		
advanced stag	e IIIA/IIIB NSCLC			

Clinical trial identification Clinical trial information: NCT04865705

Table 6. EFS rate

Outcomes (n = 31)	Results, (%, 95% CI);
12-month EFS rate	82.3 (68.1-96.4)
24-month EFS rate	64.0 (41.8-85.7)

PREOPERATIVE IMMUNOTHERAPY + RT

#8054

PHASE IB NEOADJUVANT HYPOFRACTIONATED RT + PEMBRO + CT





Neoadjuvant hypofractioned radiotherapy combined with pembrolizumab plus chemotherapy for potentially resectable non-small cell lung cancer: A phase Ib study

Naixin Ding¹, Lijun Zhao¹, Shuai Zhang², Ninglei Qiu², Xue Song¹, Cheng Kong¹, Ning Jiang¹, Yang Zhao², Jianfeng Huang², Feng Jiang², Ming Jiang², Zihao Zhu¹, Rong Yin⁴, Binhui Ren², Xiangzhi Zhu¹, Ming Li²

1 Department of Radiation Oncology. The Affiliated Cancer Hospital of Nanjing Medical University, Jiangsu Cancer Hospital, Jiangsu

Background and Objective

Background

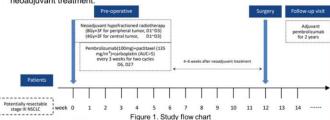
- Lung cancer is the malignant tumor with the highest incidence rate and mortality in the world[1],and non small cell lung cancer (NSCLC) accounts for approximately 85% of lung cancer[2].
- Neoadjuvant immune checkpoint inhibitors(ICIs) plus chemotherapy in resectable nonsmall cell lung cancer (NSCLC) has become a standard of care[3, 4].
- More effective neoadjuvant therapy is required for potentially resectable stage III NSCLC to improve surgical resection rate.
- · Therefore, there is a need to explore safer and more effective treatment schedules.

Objective:

 To evaluate the safety and feasibility of neoadjuvant hypofractioned radiotherapy (HFRT) with pembrolizumab plus chemotherapy followed by radical resection of lung cancer in patients (pts) with potentially resectable stage III NSCLC with negative driver oncogene.

Methods

- Study design: A single center, single arm exploratory phase lb trial (Figure1)
- Neoadjuvant Treatment:
- Radiotherapy: 24Gy / 3 fractions for peripheral primary tumor, D1~D3. 12Gy / 3 fractions for central primary tumor, D1~D3.
- Pembrolizumab(100mg) + paclitaxel (135 mg/m²) + carboplatin (AUC=5) on D6, D27
- Individualized target volume delineation: discussed and determined by both radiation oncologists and thoracic surgeons.
- Radical surgery of lung cancer: within a 4–6 week period after the completion of neoadjuvant treatment.



- Primary endpoint: Safety.
- Secondary endpoint: Feasibility, pathological complete response (pCR),major pathological response(MPR),objective response rate(ORR),progression free survival (PFS),overall survival(OS).
- Study population: cT4N0M0/cT3-4N1M0/cT1-4N2M0 histopathologically confirmed NSCLC patients who were potentially resectable with negative driver oncogene.
- Radiographic response: 64-row spiral CT was used to evaluate the primary tumor regression.
- Pathological response: All surgical specimens were evaluated by two expert oncopathologist (JY Zhang and YN Wu) independently.

Combining HFRT with pembrolizumab and chemotherapy is feasible and effective in patients with potentially resectable NSCLC.

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Results



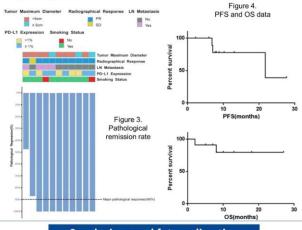
- · Study enrollment:
- From Apr 2021 to Nov 2023, 36 pts were screened and 17 pts met the inclusion criteria (Figure 2).
- ➤ 11 pts (64.7%) underwent surgery after the completion of preoperative treatment. The remaining 6 patients were transitioned to definitive chemoradiotherapy.
- General information of patients:
- Median age was 66 years old(range 54-74) and 15 (88.2%) patients had squamous cell lung cancer. 10 (58.8%) patients had central primary lesion.
- Figure 2. Study enrollment status The majority of them were diagnosed with clinical stage of cT3-T4 (64.7%), cN1-2 (100%), and cTNM IIIB(N2) (70.6%).
- Safety:
- All 17 pts received HFRT and at least one cycle of immunochemotherapy. Only two pts received chemotherapy alone in the second cycle due to grade 1 nephrotoxicity and grade 2 pulmonary toxicity, respectively.
- Only one patient died from intraoperative bleeding, and the remaining patients were followed up.
 Grade1~4 Ats
 NO. 55
- ➤ The patient with Grade 5 intraoperative AE had coronary heart disease and hypertension as comorbidities, and a history of intracoronary stent implantation. Bleeding occurred at the suturing nail of the pulmonary artery during lymph node traction, resulting in a sudden cardiac arrest. The patient had normal myocardial enzymes, cardiac troponin T, and electrocardiogram performance, so it was uncertain whether his cardiac arrest was related to neoadjuvant therapy.
- ➤ The most common adverse events (AEs) included abnormal hemagglutination(n=10, 58.8%), alopecia (n=10, 58.8%), anemia(n=9, 52.9%), neutropenia(n=8, 47.1%) and hyperlipidemia (n=8, 47.1%).(Table 1)
- No grade 3 or higher AEs were observed in 17 pts during neoadjuvant therapy.



Table 1. AEs during neoadjuvant therapy

Results

- Efficacy:
- Among the 11 pts, 8 (72.7%) achieved R0 resection, 6 (54.5%) achieved complete pathologic responses in both primary lesions and lymph nodes. 3 (27.3%) achieved pCR in only primary tumor. The primary lesions of the remaining 2 pts did not achieve pCR, including one with remission rate of 87%, the other with remission rate of 47.5% accompanied by residual lymph nodes (Figure 3).
- No progression was observed during preoperative treatment period. Objective response rate (ORR) was 94.1%.
- The median PFS was 21.7 months, median OS were not reached, and the 2year OS rate was 85.6% (Figure 4). The study was terminated early due to slow recruitment.



Conclusions and future direction

Combining HFRT with pembrolizumab and chemotherapy in neoadjuvant therapy was safe and achieved a pCR rate of 54.5% in pts with potentially resectable NSCLC. We are conducting a phase II trial with an expanded sample size in resectable stage IIA-IIIA NSCLC for further research.

Reference

- [1] Freddie Bray, et al. CA Cancer J. Clin. 2024:1-35.
- [2] Erin L Schenk, et al. [J]. Oncologist, 2021, 26(3): e454-e472.
- [3] Patrick M Forde, et al.N Engl J Med, 2022, 386(21): 1973-1985.
- [4] Heather Wakelee, et al. [J], N Engl J Med, 2023, 389(6):491-503.

- 72,7% R0
- 54,5% pCR
- mPFS 21,7 mo
- 2-y-OS 85,6%

2024 ASCO Poster Session: Lung Cancer

ADJUVANT IMMUNOTHERAPY (ATEZOLIZUMAB)

LBA 8035

IMpower 010: updated DFS and OS analysis after ≥ 5 year follow up



IMpower010: Disease-Free Survival Final Analysis and Second Overall Survival Interim Analysis Results After ≥5 years of Follow-up of a Phase III Study of Adjuvant Atezolizumab vs Best Supportive Care in Resected Stage IB-IIIA Non-Small Cell Lung Cancer

Heather A., Wakelee, 1 Nasser Altoriki, 2 Caicum Zhou, 4 Tibor Csöszi, 1 Ihor O. Vynnychenko, 2 Oleksandr Goloborodko, 4 Achim Rittmeyer, 7 Martin Reck, 1 Alex Martinez-Marti, 1 Hirotsugu Kenmotsu, 1 Yuh-Min Chen, 1 Antonio Chella, 1 Shunichi Sugawara, 1 Chenqi Fu, 1 Marcus Ballinger, 1 Yu Deng, 1 Minu K. Srivastava, 1 Elizabeth Bennett, 1 Barbara J. Gitlitz, 1 Enriqueta Felip 1 Stanford University School of Medicine, Stanford, CA, USA; NewYork-Presbyterian Hospital, Welli Cornell Medicine, New York, NY, USA: Tongji University Affiliated Shanghai, China; "Jasz-Nagykun-Szolnok Megyei Hetenyi Geza Korhaz-Rend Int., Szolnok, Hungary; "Regional Municipal Institution Sumy Regional Clinical Oncology Dispersary, Sumy, Ukraine,

BACKGROUND

- . The use of cancer immunotherapy has transformed the treatment of early-stage resectable non-small cell lung cancer (NSCLC)1-4
- Adjuvant cancer immunotherapy treatment options include atezolizumab (anti–PD-L1) and pembrolizumab (anti–PD-1) based on results from the Phase III IMpower010 (NCT02486718) and KEYNOTE-091/PEARLS (NCT02504372)
- ver010 was the first Phase III cancer immunotherapy study to show statistically significant disease-free survival (DFS) improvement in the adjuvant setting after chemotherapy in patients with resected NSCLC1
- At the DFS interim analysis (clinical cutoff, January 21, 2021), the study met its. primary endpoint, showing a statistically significant improvement in DFS with adjuvant atezolizumab vs best supportive care (BSC) after resection and chemotherapy in the stage II-IIIA PD-L1 tumor cell (TC) ≥1% (stratified HR, 0.66; 95% CI: 0.50, 0.88) and all-randomized stage II-IIIA (stratified HR, 0.79; 95% CI: 0.64, 0.96) populations but not in the ITT population; DFS benefit with atezolizumab vs BSC was also seen in the subpopulation with stage II-IIIA PD-L1 TC ≥50% disease (unstratified HR, 0.43;
- These DFS outcomes led to global approvals of adjuvant atezolizumab afte complete resection and platinum-based chemotherapy for stage II-IIIA PD-L1 TC ≥1% NSCLC and stage II-IIIA PD-L1 TC ≥50% NSCLC (excluding EGFR/ALK alterations in the EU)
- At the first overall survival (OS) interim analysis (clinical cutoff, April 18, 2022) although OS data were immature and not formally tested, there was a trend toward OS improvement in favor of atezolizumab vs BSC in the stage II-IIIA PD-L1 TC ≥1% (stratified HR, 0.71; 95% CI: 0.49, 1.03) and stage II-IIIA PD-L1 TC ≥50% (unstratified HR, 0.43; 95% CI: 0.24, 0.78) populations¹
- No OS improvement in favor of atezolizumab vs BSC was seen in the all-randomized
- Here we report updated efficacy and safety results from the IMpower010 DFS fina analysis and second OS interim analysis, with a minimum follow-up of 60 months

METHODS

- IMpower010 is a global, multicenter, open-label, randomized, Phase III study of adjuvant atezolizumab vs BSC in patients with stage IB-IIIA NSCLC after complete resection and platinum-based chemotherapy (Figure 1)
- Investigator-assessed DFS, the primary endpoint, was hierarchically tested:
 1) stage II-IIIA PD-L1 TC ≥1% population, 2) all-randomized stage II-IIIA population and 3) ITT (stage IB-IIIA) population
- OS in the ITT population, a key secondary endpoint, could be formally tested only when the statistical significance boundary for DFS was crossed in all 3
- . The DFS final analysis and second OS interim analysis were conducted at the same

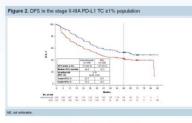
Figure 1. IMpower010 study design and endpoint testing hierarchy ELOS in the ITT population (stage IB-IBA Key secondary endpoints OS in ITT | DPS in PD-L1 TC 250% stage II-IIIA | 3- and 5-year DPS

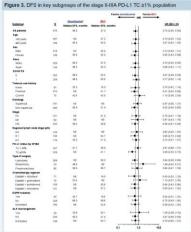
RESULTS

- The ITT population included 1005 patients (stage IB-IIIA; atezolizumab, n=507 BSC, n=498), the all-randomized stage II-IIIA population included 882 patients mab, n=442; BSC, n=440) and the stage II-IIIA PD-L1 TC ≥1% population included 476 patients (atezolizumab, n=248; BSC, n=228)
- Demographics and baseline characteristics were generally balanced between arms across the 3 primary populations, as previously reported
- The median duration of follow-up was 65.0 months (range, 0.0-94.4) in the ITT population, 64.8 months (range, 0.0-93.3) in the all-randomized stage II-IIIA population and 65.2 months (range, 0.1-93.3) in the stage II-IIIA PD-L1 TC
- As of the clinical cutoff date (January 26, 2024), in the ITT population, 59.4% (n=301) and 56.6% (n=282) of patients in the atezolizumab and BSC arms, respectively,
- Of the 206 (40.6%) and 216 (43.4%) patients in the respective treatment arms who discontinued from the study, the most common reasons for discontinuation were death (atezolizumab, n=154 [30.4%]; BSC, n=155 [31.1%]) and patient withdrawal (atezolizumab n=44 (8 7%): BSC n=47 (9 4%))

DFS and OS in the ITT, all-randomized stage II-IIIA and stage II-IIIA PD-L1 TC ≥1% populations

- DFS events in the atezolizumab and BSC arms, respectively, occurred in
- 47.1% (n=239) and 52.2% (n=260) of the patients in the ITT population 49.5% (n=219) and 54.5% (n=240) of the patients in the all-randomized stage
- (stratified HR, 0.85; 95% CI: 0.71, 1.01; P=0.07) Median DFS was 65.6 months in the atezolizumab arm and 47.8 months in the
- The 3-year DFS rates were 61.4% and 55.5%, and the 5-year DFS rates were 52.0% and 46.5%, respectively
- The stratified DFS HR in the all-randomized stage II-IIIA population was 0.83 (95% CI: 0.69, 1.00)
- Median DFS was 57.4 months in the atezolizumab arm and 40.8 months in the
- The 3-year DFS rates were 59.3 % and 52.6%, and the 5-year DFS rates were
- DFS in the stage II-IIIA PD-L1 TC ≥1% population is shown in Figure 2.
- DFS in key subgroups in the stage II-IIIA PD-L1 TC ≥1% population generally favored atezolizumab vs BSC (Figure 3)



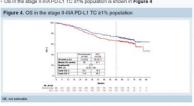




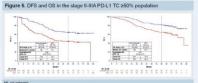
OS events in the atezolizumab and BSC arms, respectively, occurred in: - 31.4% (n=159) and 31.5% (n=157) of patients in the ITT population

- 32.4% (n=143) and 33.0% (n=143) of patients in the all-randomized stage II-IIIA population Median OS was NE in either treatment arm in the ITT and all-randomized stag II-IIIA populations, with stratified HRs of 0.97 (95% CI: 0.78, 1.22) and 0.94 (95% CI: 0.75, 1.19), respectively
- In the ITT population, the 3-year OS rates were 79.3% and 81.1%, and the 5-year OS rates were 70.9% and 69.8% respectively
- in the all-randomized stage II-IIIA population, the 3-year OS rates were 78.7% and 79.7%, and the 5-year OS rates were 69.8% and 68.6%, respe

OS in the stage II-IIIA PD-L1 TC ≥1% population is shown in Figure 4



DFS and OS in the stage II-IIIA PD-L1 TC ≥50% population DFS and OS in the stage II-IIIA PD-L1 TC ≥50% population are shown in Figure 5



When the 20 patients with known EGFR mutations or ALK rearrangements were

excluded from the analysis, DFS and OS data remained similar (Figure 6) In general, DFS favored atezolizumab vs BSC in key subgroups of the stage II-IIIA

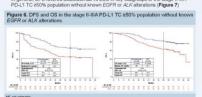
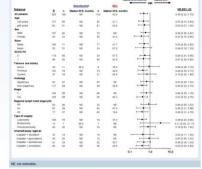


Figure 7. DFS in key subgroups of the stage II-IIIA PD-L1 TC ≥50% population without known EGFR or ALK alterations



- Atezolizumab exposure data have not changed since the clinical cutoff for the DFS treatment at that time
- Overall, 156 patients (31.5%) in the atezolizumab arm and 157 patients (31.7%) in the
- In the respective treatment arms, 91 (18.4%) and 118 (23.8%) patients died due to disease relapse, 9 (1.8%) and 3 (0.6%) died due to AEs and 56 (11.3%) and 36 (7.3%) died due to other reasons (i.e., COVID-19 related death, medical causes unrelated to the study treatment or NSCLC that occurred outside the AE reporting period, death information from public records or death due to unknown causes)
- Since the previous report (clinical cutoff, April 18, 2022) 5 there have been minima updates to the safety findings, and no new or unexpected signals have been identified
- The incidences of Grade 3/4 and Grade 5 adverse events of special interest (AESIs) remained unchanged in the atezolizumab arm since the previous report.5 Grade 3/4 AESIs were reported in 4 patients (0.8%) and Grade 5 AESIs in 1 patient (0.2%) in the
- No new medical concept categories developed

CONCLUSIONS

- The data from this DFS final analysis and second OS interim analysis provide the first Phase III cancer immunotherapy data in resectable NSCLC with ≥5 years of follow-up and were consistent with the previous reported analyses11
- This analysis showed that DFS benefit continues to translate into positive OS outcome in the stage II-IIIA PD-L1 TC ≥1% and the stage II-IIIA PD-L1 TC ≥50% populations
- In the stage II-IIIA PD-L1 TC ≥1% population, median DFS in the atezolizumab arm was >30 months longer than in the BSC arm
- The significance boundary for DFS was not crossed in the ITT population, and OS outcomes in the atezolizumab and BSC arms were similar, although OS data were not mature
- In general, atezolizumab's safety profile remained consistent with previous analyses; no new or unexpected safety signals or AESI medical concept categories were reported^{1,5}
- After 5 years of follow-up, the updated survival outcomes with atezolizumab in PD-L1-selected populations continue to support the use of adjuvant atezolizumab for stage II-IIIA PD-L1 TC ≥1% and stage II-IIIA PD-L1 TC ≥50% NSCLC

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- 2. O'Brien M, et al. Lancet Oncol 2022;23:1274-86
- Wakelee H, et al. N Engl J Med 2023;389:491-503.
- Mountzios G. et al. Nat Rev 2023:20:664-77. Felip E. et al. Ann Oncol 2023:34:907-19.

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- Editorial support for this poster was provided by Kia C. E. Walcott, PhD, of Nucleus Global, an Inizio Company, funded by F. Hoffmann-La Roche Ltd

DISCLOSURES

- Dr. Heather Wakelee has received consulting fees from IOBiotech and Miratt, is an unpaid advisor for Bristol Meyers Squibb, Genentech/Roche, Merck, and AstraZenoca, has received institutional support for the conduct of clinical trials from AstraZenoca/Medimmune, Bayer, Bristol Meyers Squibb, Genentech/Roche, Helson, Merck, SaaGen, and Xcovery, and received writing support for this poster from F. Helfman-La Roche Lid
- Please see published abstract for disclosures of coauthors

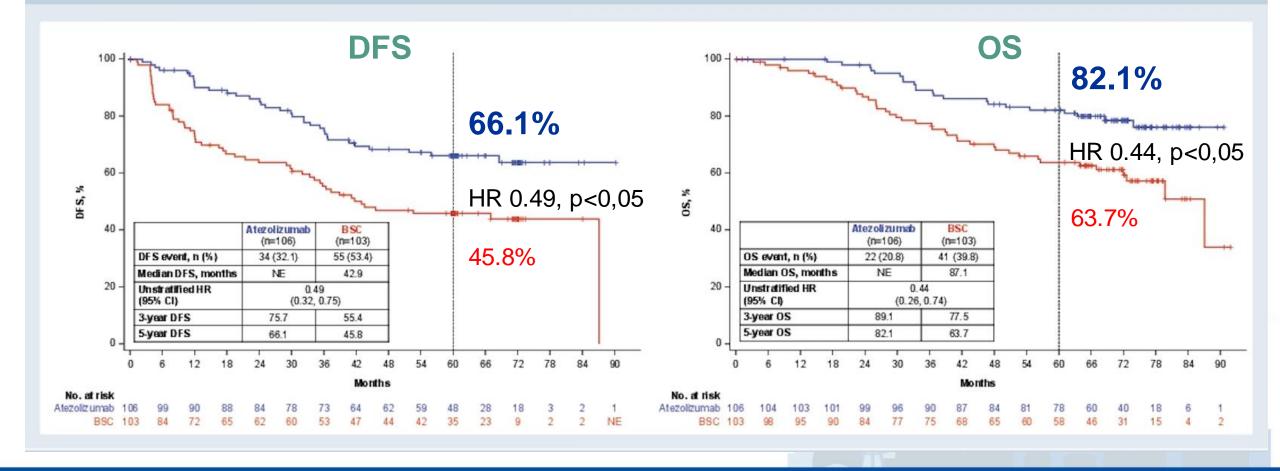


ADJUVANT IMMUNOTHERAPY (ATEZOLIZUMAB)

IMpower 010: updated DFS and OS análisis after ≥ 5 year follow up



Figure 6. DFS and OS in the stage II-IIIA PD-L1 TC ≥50% population without known *EGFR* or *ALK* alterations



ICTAN, GASTO1002 STUDY: ADJUVANT ICOTINIB 12 or 6 mo





#8004

Adjuvant icotinib of 12 months or 6 months versus observation following adjuvant chemotherapy for resected EGFR-mutated stage II–IIIA non-small-cell lung cancer (ICTAN, GASTO1002): a randomized phase 3 trial

Authors: **Si-Yu Wang**, ¹, Hao Long¹, Ning Li¹, Chao Cheng², Wei Ou¹, Lin Yang³, Jian You⁴, Yi Liang⁵, Bao-Xiao Wang⁶, on behalf of the ICTAN study investigators

1 Sun Yat-sen University Cancer Center, Guangzhou, China; 2 The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; 3 Shenzhen People's Hospital, Shenzhen, China; 4 Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; 5 Zhongshan city people's hospital, Zhongshan, China; 6 Sun Yat-Sen Memorial Hospital, Guangzhou, China.

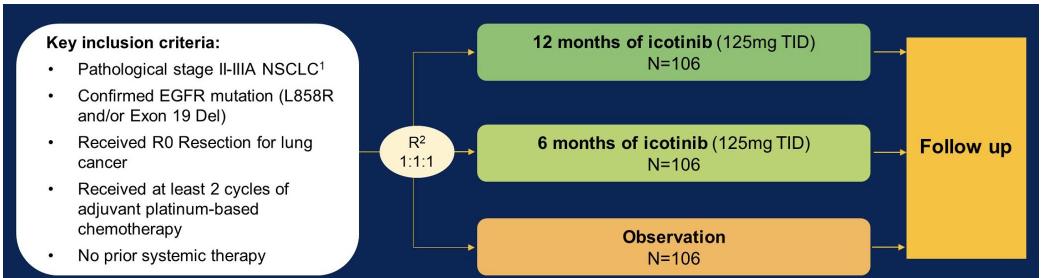






ICTAN, GASTO1002 STUDY: ADJUVANT ICOTINIB 12 or 6 mo





Primary endpoint:

- DFS

Secondary endpoints:

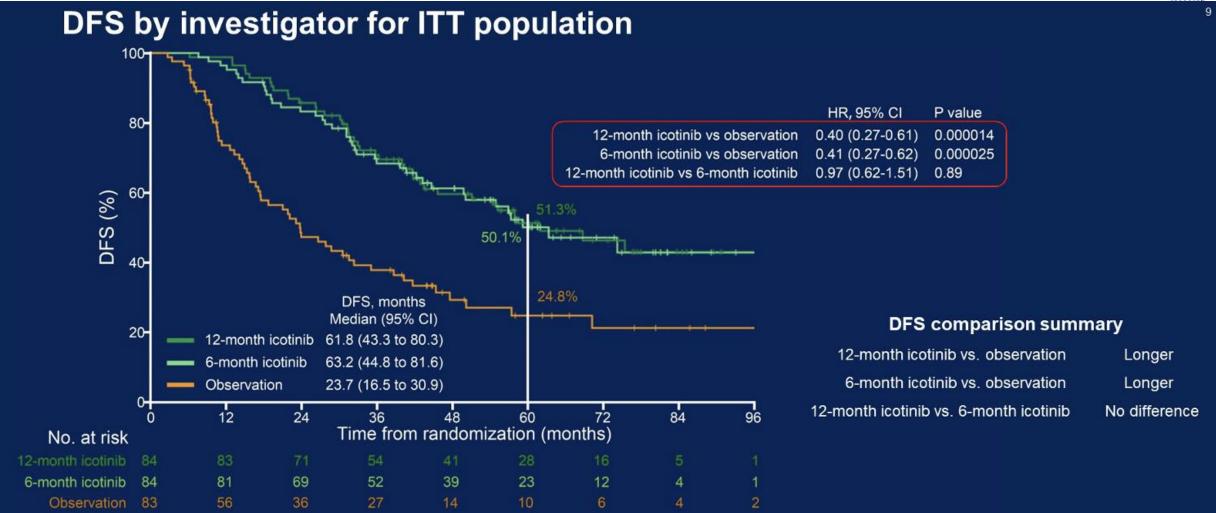
- OS
- Safety

- En torno al 80% completaron 4 ciclos de QT adyuvante
- Siendo carboplatino + pemetrexed el régimen mayoritario (70%)



ICTAN, GASTO1002 STUDY: ADJUVANT ICOTINIB 12 or 6 mo



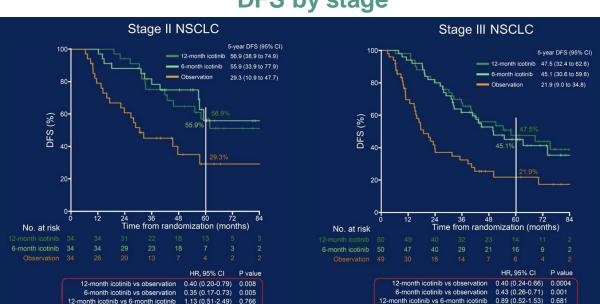


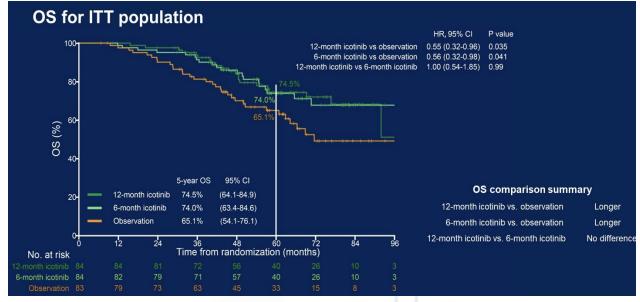
Adjuvant icotinib for 12 months or 6 months provide a significant DFS benefit compared with observation. 12 months of icotinib had no DFS benefit compared with 6 months.

ICTAN, GASTO1002 STUDY: ADJUVANT ICOTINIB 12 or 6 mo



DFS by stage





OS

First subsequent treatments	lcotinib of 12 months (n=40)		Icotinib of 6 months (n=39)		Observation (n=56)	
1st generation EGFR-TKI	5	(12.5%)	10	(25.6%)	31	(55.4%)
2nd generation EGFR-TKI	1	(2.5%)	4	(10.3%)	3	(5.4%)
3rd generation EGFR-TKI	17	(42.5%)	12	(30.8%)	9	(16.1%)
Other treatments without EGFR-TKI	6	(15.0%)	3	(7.7%)	1	(1.8%)
No subsequent treatments	11	(27.5%)	10	(25.6%)	12	(21.4%)

AEs leading to discontinuation

- 12 mo: 4,8%

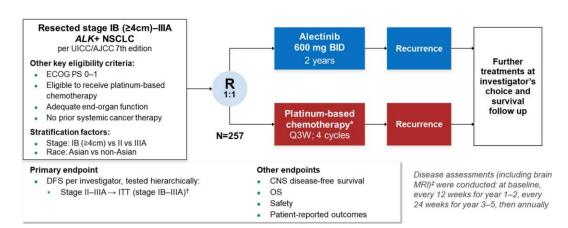
- 6 mo: 3,6%

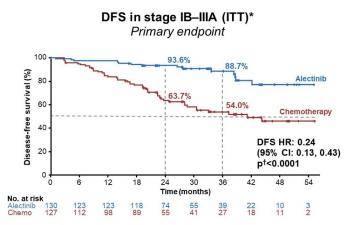
NO dose reduction NO fatal events

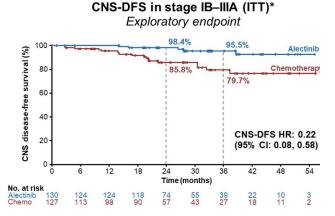
#8006

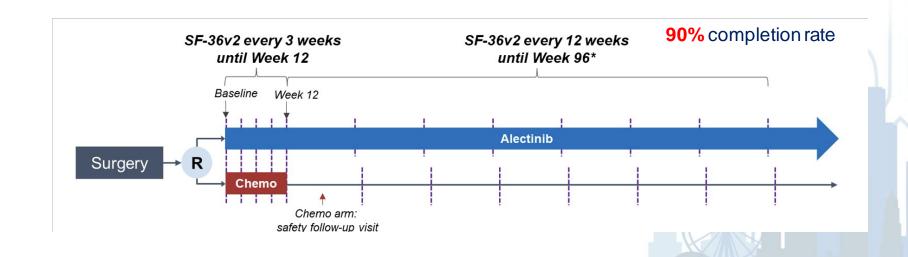


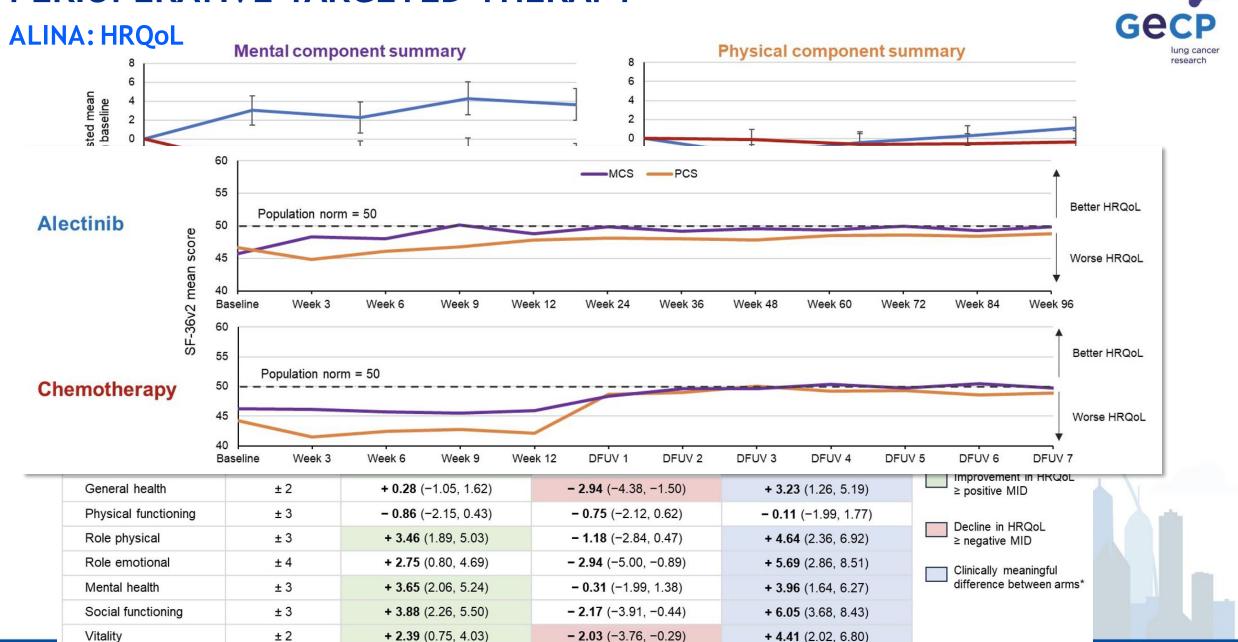
ALINA: HRQoL











Iniciativa científica de:

MRD analysis from ADAURA





#8005

Molecular residual disease analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated stage IB-IIIA non-small cell lung cancer

<u>Thomas John.</u>¹ Christian Grohé, Jonathan Goldman, Terufumi Kato, Konstantin Laktionov, Laura Bonanno, Marcello Tiseo, Margarita Majem, Manuel Dómine, Myung-Ju Ahn, Maurice Pérol, Ryan Hartmaier, Jacqulyne Robichaux, Preetida Bhetariya, Aleksandra Markovets, Yuri Rukazenkov, Caitlin Muldoon, Roy S. Herbst, Masahiro Tsuboi, Yi-Long Wu

¹Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia







MRD analysis from ADAURA



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

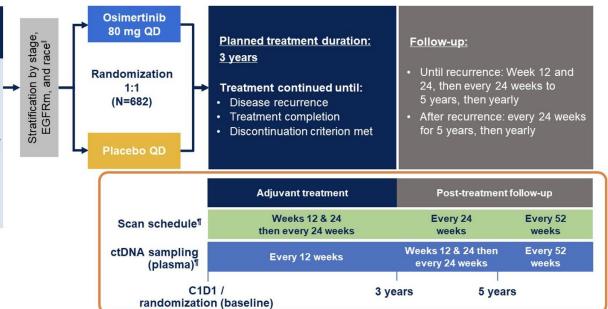
Key inclusion criteria:

≥18 years (Japan / Taiwan: ≥20 years) WHO performance status 0 / 1

Confirmed primary non-squamous NSCLC Ex19del / L858R‡

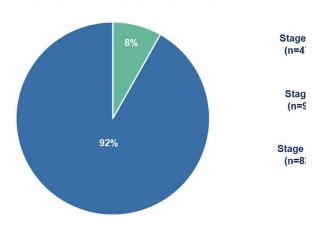
Brain imaging, if not completed pre-operatively Complete resection with negative margins§ Maximum interval between surgery and randomization:

- 10 weeks without adjuvant chemotherapy
- · 26 weeks with adjuvant chemotherapy



Exploratory endpoint: Evaluate the feasibility of ctDNA-based MRD detection to predict disease recurrence during adjuvant osimertinib treatment and post-treatment follow-up

Baseline MRD status (MRD analysis set)



■ Baseline MRD undetected (n=202) ■ Baseline MRD detected (n=18)



36 months

86 (78, 92)

36 (27, 45)

DFS and MRD event-free rate

24 months

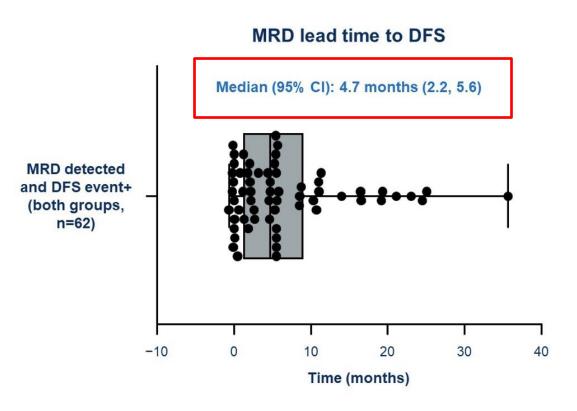
91 (84, 95)

46 (36, 55)

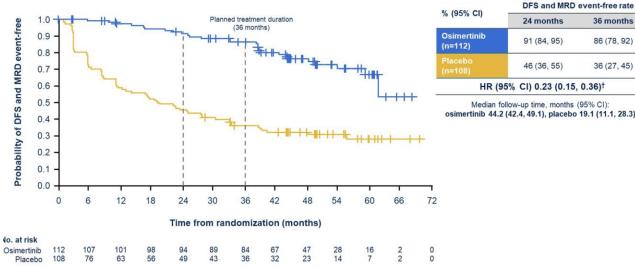
HR (95% CI) 0.23 (0.15, 0.36)†

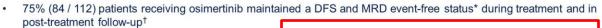
Median follow-up time, months (95% CI):

MRD analysis from ADAURA



La mayoría de eventos de MRD-DFS en el brazo de osimertinib se dan tras su suspensión, el 58% en el primer año post









OPERABILITY PARAMETER CHANGES AFTER NEOADJUVANT CTIO

#8055 Sereno M et al.

Abstract 8055#: Operability changes in NSCLC patients after neoadjuvant chemotherapy and anti-PD-1/PD-L1

Authors: Garitaonaindia Y 1/2 Baena J 2/2, Aquado C 3/2, Cruz P 4/2, López-Castro R 5/2, Rubio J 6/3, Gomez A 7/2, López-Martin A 8/2, Traseira C 9/2, Mielgo Rubio X 1/2, Romano I 1/3, Campo-cañayeral JL 1/4, Gómez de Antonio D 1/4, Falagan S 1/3, Rubio G 1/3, Montoro FJ 1/4, López-Castro R 5/2, Rubio G 1/3, Rubio G 1/3, Montoro FJ 1/4, López-Castro R 5/2, Rubio G 1/3, Rubio G 1/3, Rubio G 1/3, Montoro FJ 1/4, López-Castro R 5/2, Rubio G 1/3, Rubio G 1/3, Montoro FJ 1/4, López-Castro R 5/2, Rubio G 1/4, Rub HierroUniversity Hospital, Majadahonda, Madrid, Spain; (2) Hospital Universitario 12 De Octubre, Madrid, Spain; (3)Hospital Clínico Universitario de Valladolid, Valladolid, Spain; Hospital Universitario de Cuidad Real, Quidad Real, Spain; Medical Oncology Department. (5) Hospital Universitario de Valladolid, Valladolid, Valladolid, Valladolid, Spain (6) University Hospital Fundación Jiménez Díaz, Madrid, Spain; (7) Ramon y Cajal University Hospital, Madrid, Spain; (8) Hospital Severo Ochoa, Madrid, Spain; (9)Hospital de Henares, Coslada, Madrid, Spain; (10) Hospital Fundación Alcorcon, Madrid, Spain; (11) Hospital Universitario de Fuenlabrada,

Background:

- Neoadiuvant (NA) treatment for non-small cell lung cancer (NSCLC) has evolved with the emergence of chemotherapy (CT) and immunotherapy (IO) combinations
- However, limited data exist on the impact of these treatments on respiratory function

Methods:

NSCLC

IB-IIIB

Operable

- We conducted a multicenter study of NSCLC pts who underwent NA (CT or CT-IO) and pre- and post-NA respiratory tests from Jan 2021 to Dec 2023.
- · Clinical, pathological and surgical variables were also collected (Figure 1).
- DLCO (Diffusing Capacity for Carbon Monoxide), FEV1 (Forced Espiratory Volumein first second) and FVC (Forced Vital Capacity) pre- and post-NA in CT/CT-IO subgroups were compared.
- A regression univariate analysis with variables influencing DLCO, FEV1 and FVC variations was also performed

COMORBIDITIES

TUMOR

BOARD

FRT pre-NA:

FEV1, FCV,

DLCO

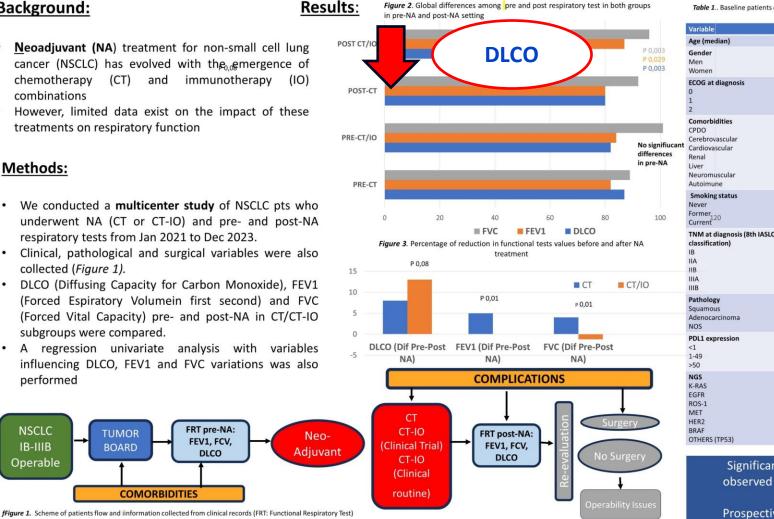


Table 2.. Comparative analysis of surgical events between both gropus Table 1.. Baseline patients characteristics

70

107 (67.3

52 (32.7)

98 (61.6)

59 (37,1)

2 (1,2)

10 (6,2)

17 (10,6)

6 (3,7)

7 (4,4)

2 (1,2)

12 (7,5)

11 (6,9)

86 (54)

62 (38,9)

1 (0,6)

1 (0,6) 33 (20,6)

113 (71) 11 (6,9)

80 (50.3)

70 (44,5)

9 (5,2)

23 (38)

19 (31)

19 (30)

11 (44)

7 (28)

2 (8)

1(4)

1 (4)

1(4)

Variable	CT N 39 (%)	CT-IO N 117 (%)	P
Surgery No Yes	6 (15,4) 33 (84,6)	12 (10,4) 103 (89,6)	0,39
Downstaging	20 (51)	72 (62,1)	0,23
Pathological responses CPR MPR	6 (18,1) 4(12,1)	53 (51,4) 36 (34,9)	0,006
VATS-thoracotomy conversion	6 (17,6)	7 (6,7)	0,08
ICU admission	2 (6,1)	6 (5,8)	1,00
Complications after surgery Respiratory Cardiovascular Others	5(15,2) 2 (6,1) 1 (3)	23 (22,1) 5 (4,8) 6 (5,8)	0,38 0,67 1,00
Re-operation within 90 days	1 (3)	5 (4,8)	1,00
Re-admission within 90 days	2 (6,1)	6 (5,8)	1,00
Inoperability rate	3 (7,7)	6 (5,2)	0,69
Exitus No Yes	30 (76,9) 9 (23,1)	108 (92,3) 9 (7,7)	0,017

Conclusions:

Significant differences in post-NA functional variables were observed between CT-IO and CT subgroups, including lower DLCO and higher FEV1/FVC in the CT-IO group. Prospective validation is essential to confirm these findings

KEY-HOME MESSAGES

ASCO 2024 Lung Cancer Updates GECP



Perioperative immunotherapy

Perioperative targeted therapy

ctDNA – MRD

Operability parameters changes



ASCO 2024

• GECP LUNG CANCER UPDATES

