Lung Cancer UPDATES
ESMO HIGHLIGTHS
09-13 SEPTIEMBRE 2022
Paris, France

Iniciativa científica de:
GECP lung cancer research

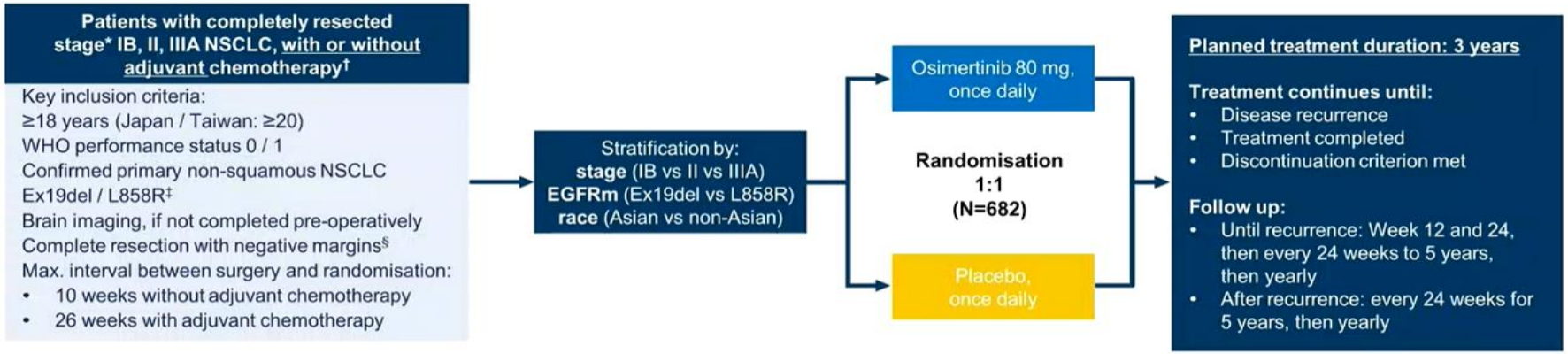
Cáncer de Pulmón: enfermedad localizada y microcítico

Sergio Vázquez Estévez

Hospital Unniversitario Lucus Augusti. Lugo

ENFERMEDAD LOCALIZADA: ADYUVANCIA

PHASE III ADAURA STUDY DESIGN



Endpoints

- **Primary endpoint:** DFS by investigator assessment in stage II / IIIA patients, designed for superiority under the assumed DFS HR of 0.70
- **Key secondary endpoints:** DFS in the overall population¶, DFS at 2, 3, 4, and 5 years, OS, safety, health-related quality of life
- **Pre-specified exploratory endpoints:** Patterns of recurrence, time to CNS disease recurrence or death (CNS DFS)

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Masahiro Tsuboi, MD

*At the time of recruitment, staging was determined by the AJCC / UICC 7th edition staging manual. †Prior, post, or planned radiotherapy was not allowed; ‡Centrally confirmed in tissue. §Patients received a CT scan after resection and within 28 days prior to treatment. ¶Stage IB / II / IIIA.

AJCC / UICC, American Joint Committee on Cancer / Union for International Cancer Control; CNS, central nervous system; CT, computerized tomography; DFS, disease-free survival; EGFRm, epidermal growth factor receptor-mutated; Ex19del, exon 19 deletion; HR, hazard ratio; NSCLC, non-small cell lung cancer; OS, overall survival; WHO, World Health Organization

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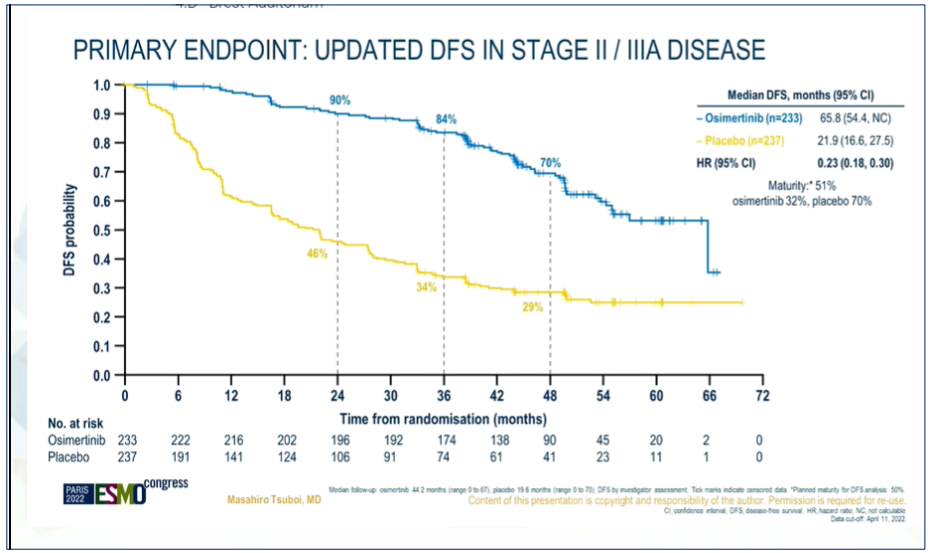

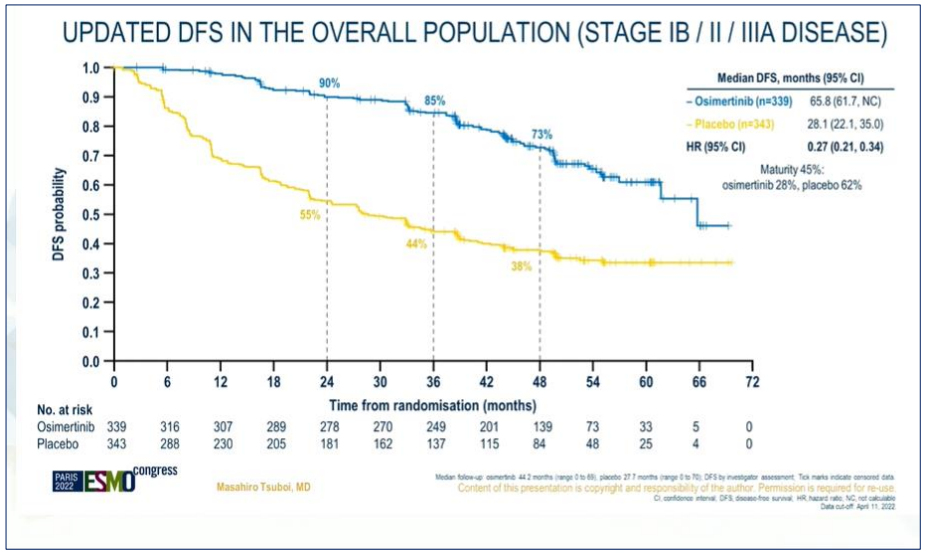

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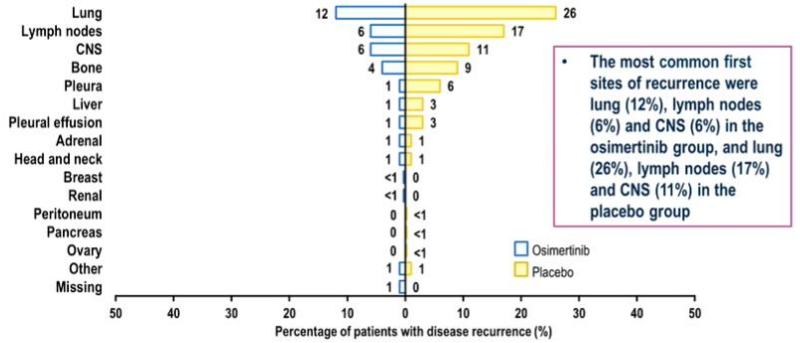
PATTERNS OF DISEASE RECURRENCE (OVERALL POPULATION)

- In the overall population, fewer patients treated with osimertinib had disease recurrence (93/339; 27%) compared with placebo (205/343; 60%)*



- The most common first sites of recurrence were lung (12%), lymph nodes (6%) and CNS (6%) in the osimertinib group, and lung (26%), lymph nodes (17%) and CNS (11%) in the placebo group

*Distant recurrence only: osimertinib 45/339 (13%), placebo 107/343 (31%); local/regional only: osimertinib 42/339 (12%), placebo 78/343 (23%); local/regional and distant: osimertinib 6/339 (2%), placebo 20/343 (6%).
CNS, central nervous system.
Data cut-off: April 11, 2022.

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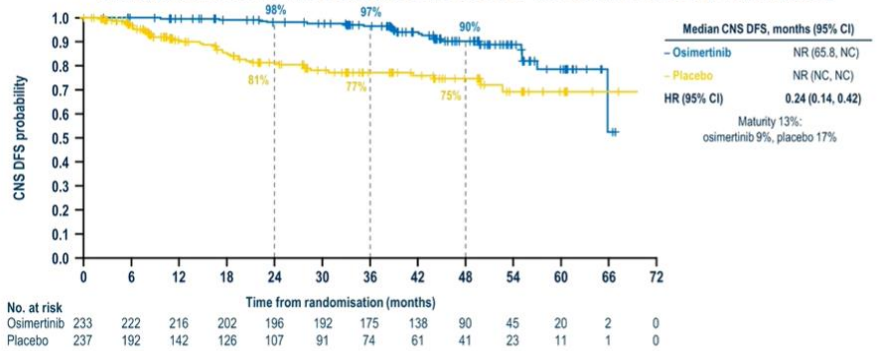
UPDATED CNS DFS IN PATIENTS WITH STAGE II / IIIA DISEASE

- Overall, 63 patients (osimertinib n=22, placebo n=41) had CNS DFS events:*
  - 3 (14%) patients were on treatment at the time of CNS recurrence with osimertinib, versus 29 (71%) with placebo



No. at risk												
Osimertinib	233	222	216	202	196	192	175	138	90	45	20	2	0
Placebo	237	192	142	126	107	91	74	61	41	23	11	1	0

Median follow-up: osimertinib 44.2 months, placebo 20.4 months; DFS by investigator assessment. Tick marks indicate censored data.
*Defined as CNS as the first site of disease recurrence, or death without any disease recurrence.
CI, confidence interval; CNS, central nervous system; DFS, disease-free survival; HR, hazard ratio; NC, not calculable; NR, not reached.
Data cut-off: April 11, 2022.

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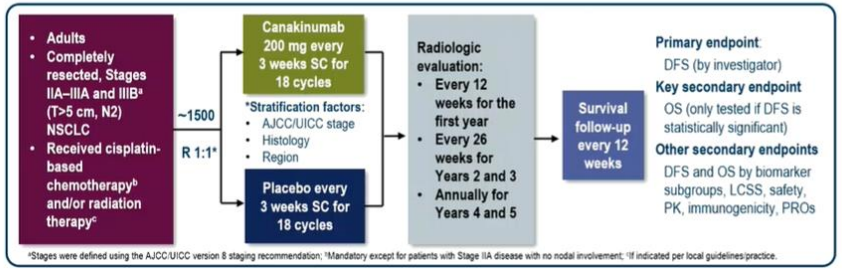
CANOPY-A study design



[a]Stages were defined using the AJCC/UICC version 8 staging recommendation; [b]Mandatory except for patients with Stage IIA disease with no nodal involvement; [c]If indicated per local guidelines/practice.

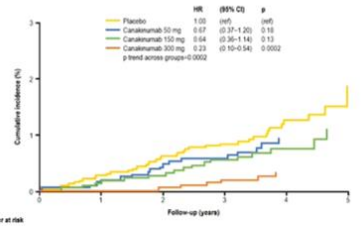
- A total of 1382 patients were randomized (1:1) between April 2018 and December 2021 to receive canakinumab (n=693) or placebo (n=689)

AJCC, American Joint Committee on Cancer; DFS, disease-free survival; LCSS, lung cancer-specific survival; N, node; NSCLC, non-small cell lung cancer; OS, overall survival; PK, pharmacokinetics; PRO, patient-reported outcome; R, randomization; SC, subcutaneous; T, tumor; UICC, Union for International Cancer Control.

Background: Canakinumab and lung cancer

- The role of inflammation in lung cancer has been well studied[1]
- Targeting inflammation in lung cancer has not been therapeutically harnessed[1]
- Canakinumab is a high-affinity, anti–IL-1β monoclonal antibody[2]
- Exploratory analysis of the CANTOS (Phase III cardiovascular) study showed reductions in NSCLC incidence and mortality[3]
  - The majority of patients diagnosed with lung cancer during the CANTOS trial had detectable ctDNA at baseline[4]
- This led to the launch of the CANOPY-A study

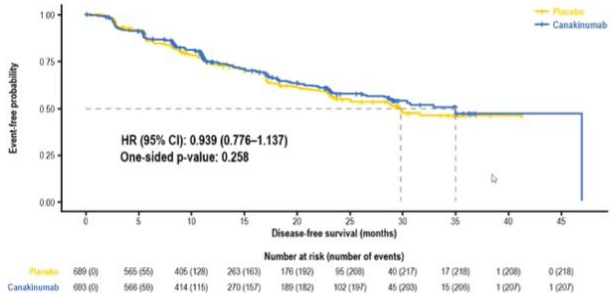
Cumulative incidence of fatal lung cancer cases among CANTOS participants[3]



Reprinted from The Lancet, 390, Ridker PM, MacFadyen JG, Thuren T, Everett BM, Libby P, Glynn RJ, Effect of interleukin-1β inhibition with canakinumab on incident lung cancer in patients with atherosclerosis: exploratory results from a randomised, double-blind, placebo-controlled trial, 1833–1842, 2017, with permission from Elsevier

1. Garon EB, *et al. JTO Clin Res Rep* 2020;1:100001. 2. Data on file, 2020, Novartis Pharmaceuticals Corporation. 3. Ridker PM, *et al. Lancet* 2017;390:1833–1842. 4. Wong CC, *et al. Cancer Res* 2020;80:5597–5605.
CI, confidence interval; ctDNA, circulating tumor DNA; HR, hazard ratio; IL-1β, interleukin-1 beta; NSCLC, non-small cell lung cancer.

DFS (primary endpoint)



- DFS was not significantly improved with canakinumab versus placebo (median 35.0 months and 29.7 months, respectively; HR 0.94; 95% CI 0.78–1.14; one-sided p=0.258)

CI, confidence interval; DFS, disease-free survival; HR, hazard ratio.

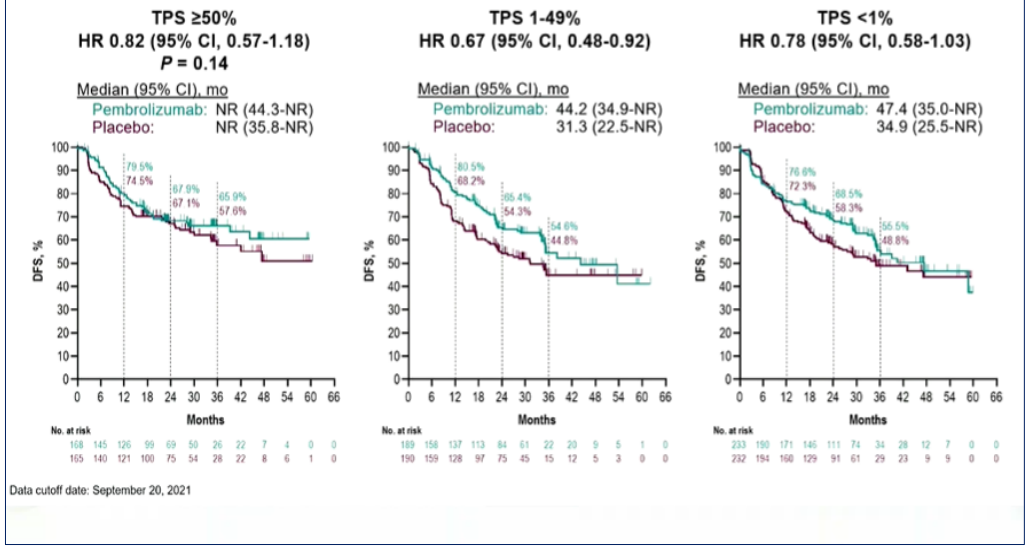
Garon EB, et al. ESMO 2022

PD-L1 Expression and Outcomes of Pembrolizumab and Placebo in Completely Resected Stage IB-IIIA NSCLC: Subgroup Analysis of PEARLS/KEYNOTE-091

Solange Peters,[1] Benjamin Besse,[2] Sandrine Marreaud,[3] Urania Dafni,[4] Kersti Oselin,[5] Libor Havel,[6] Emilio Esteban,[7] Dolores Isla,[8] Alex Martinez-Marti,[9] Martin Faehling,[10] Masahiro Tsuboi,[11] Jong-Seok Lee,[12] Kazuhiko Nakagawa,[13] Jing Yang,[14] Steven M Keller,[14] Murielle Mauer,[3] Nitish Jha,[3] Rolf Stahel,[15] Luis Paz-Ares,[16] Mary O'Brien[17]

[1]Lausanne University Hospital, Lausanne, Switzerland; [2]Institut Gustave Roussy, Villejuif, France; [3]European Organisation for Research and Treatment of Cancer, Headquarters Brussels, Belgium; [4]National and Kapodistrian University of Athens and Frontier Science Foundation Hellas; [5]North Estonia Medical Centre, Tallinn, Estonia; [6]Charles University and Thomayer Hospital, Prague, Czech Republic; [7]Hospital Universitario Central de Asturias, Oviedo, Spain; [8]University Hospital Lozano Blesa, IIS Aragon, Zaragoza, Spain; [9]Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, Barcelona, Spain; [10]Klinikum Esslingen, Esslingen, Germany; [11]National Cancer Center Hospital East, Kashiwa, Japan; [12]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, South Korea; [13]Kindai University Faculty of Medicine, Osaka, Japan; [14]Merck & Co., Inc., Rahway, NJ, USA; [15]European Thoracic Oncology Platform, Bern, Switzerland; [16]Hospital Universitario 12 de Octubre, CNIO, Ciberonc & Universidad Complutense, Madrid, Spain; [17]Royal Marsden Hospital, London, UK

DFS: Pembrolizumab vs Placebo by PD-L1 TPS



Data cutoff date: September 20, 2021

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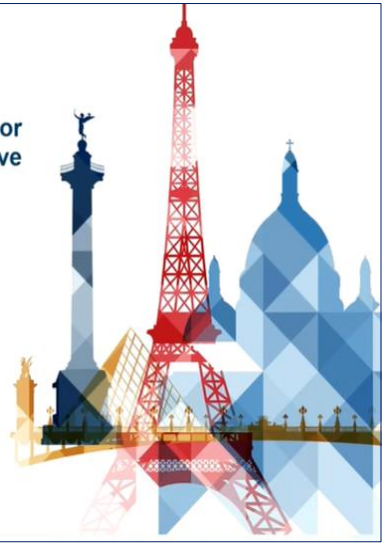
Longitudinal Monitoring of Circulating Tumor DNA from Plasma in Patients with Curative Resected Stage IA-IIIA *EGFR* mutant Non-small Cell Lung Cancer



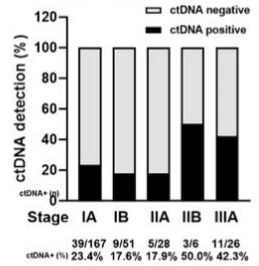
Myung-Ju Ahn, Hyun-Ae Jung, Bo Mi Ku, Yeon Jeong Kim, Sehhoon Park, Jong-Mu Sun, Se-Hoon Lee, Jin Seok Ahn, Jong Ho Cho, Hong Kwan Kim, Yong Soo Choi, Jhingook Kim

Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

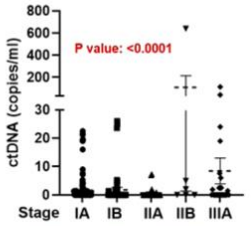
Results

- Among 278 patients, baseline ctDNA was detected in 67 (24.1%) patients: 23.4% (stage IA), 17.6% (IB), 17.9% (IIA), 50.0% (IIB), and 42.3% (IIIA) (P=0.06), Baseline ctDNA copy numbers are increasing according to stage
- Among 67 patients with baseline ctDNA+, 76.1% (51/67) showed ctDNA clearance 4 weeks after surgery
- No difference in ctDNA detection rate (24% vs 24.3%) or clearance rate (75% vs 77.8%) between exon 19 del and L858R

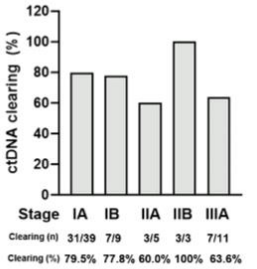
Baseline ctDNA detection rate



Baseline ctDNA copy numbers



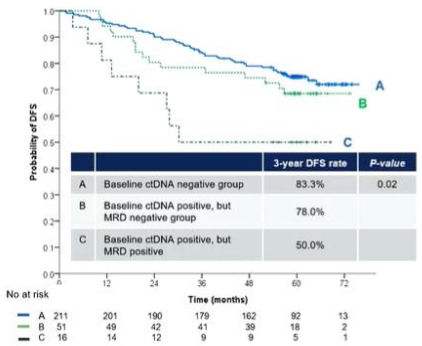
ctDNA clearance after surgery



Myung-Ju Ahn, M.D.

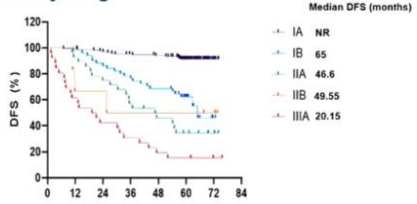
DFS by ctDNA status

Recurrence 78/278 (28.1%)



		3-year DFS rate	P-value
A	Baseline ctDNA negative group	83.3%	0.02
B	Baseline ctDNA positive, but MRD negative group	78.0%	
C	Baseline ctDNA positive, but MRD positive	50.0%	

DFS by Stage



Multivariate Analysis for DFS

Variable	HR (95% CI)	P-value
Sex (Female vs. Male)	0.70 (0.31-1.58)	0.39
Smoking status (Never vs. Ever)	1.55 (0.67-3.55)	0.31
EGFR mutation (Del19 vs. L858R)	0.68 (0.42-1.11)	0.12
ECOG PS (0 vs.1)	0.91 (0.21-4.01)	0.91
Stage (I vs II-III)	3.84 (2.91-5.06)	<0.001
ctDNA group	1.27 (1.03-1.57)	0.03

MRD: minimal residual disease

Ahn M-J, et al. ESMO 2022

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Final overall survival analysis of phase III study of pemetrexed/cisplatin versus vinorelbine/cisplatin for completely resected non-squamous non-small-cell lung cancer: the JIPANG Study

jRCTs041180023

On the behalf of JIPANG investigators

Kiyotaka Yoh, Hirotsugu Kenmotsu, Nobuyuki Yamamoto, Toshihiro Misumi, Toshiaki Takahashi, Haruhiro Saito, Shunichi Sugawara, Koji Yamazaki, Kazuhiko Nakagawa, Kenji Sugio, Takashi Seto, Shinichi Toyooka, Hiroshi Date, Tetsuya Mitsudomi, Isamu Okamoto, Kohei Yokoi, Hideo Saka, Hiroaki Okamoto, Yuichi Takiguchi, Masahiro Tsuboi

JIPANG: Study Design

The JIPANG study has demonstrated pemetrexed/cisplatin had a similar efficacy on recurrence-free survival to vinorelbine/cisplatin with a better tolerability as postoperative adjuvant chemotherapy for patients with completely resected non-squamous non-small-cell lung cancer (Kenmotsu H, et al. J Clin Oncol 2020; 38: 2187-2196).

KEY ELIGILITY

- Completely resected non-Sq NSCLC
- Pathological stage II-IIIA (7th TNM)
- ECOG PS 0-1
- Age 20-75 years
- Lobectomy or pneumonectomy with resection of N2 lymph nodes within 3–8 weeks

N=804

RANDOMIZED 1:1

- **Vinorelbine (25 mg/m2, days 1, 8) +Cisplatin (80 mg/m2, day 1) every 3 weeks, up to 4 cycles**
- **Pemetrexed (500 mg/m2, day 1) +Cisplatin (75 mg/m2, day 1) every 3 weeks, up to 4 cycles**

ENDPOINTS

Primary
- Recurrence-free survival

Secondary
- Overall survival
- Rate of treatment completion
- Toxicity

Stratification factors: Gender (female vs. male), Age (<70 years vs. ≥70 years), Pathological stage (II vs. IIIA), EGFR mutation (mutant vs. wild), Institution

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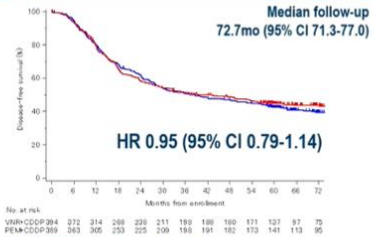
National Cancer Center Hospital East

RFS and OS: 5-year follow-up

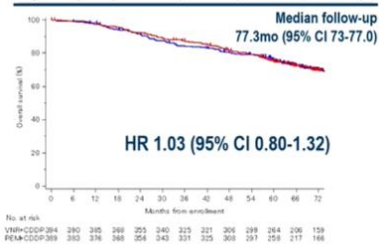
RFS assessed by investigators

	VNR+CDDP (n=394)	PEM+CDDP (n=389)
Number of events	236	220
Median RFS (95%CI)	37.5 mo (28.9-52.6)	43.4 mo (29.0-59.7)
3-year RFS (95%CI)	51.0% (49.5-74.9%)	51.6% (46.5-56.4%)
5-year RFS (95%CI)	42.6% (37.7-47.5 %)	44.9% (39.8-49.8%)



Overall survival

	VNR+CDDP (n=394)	PEM+CDDP (n=389)
Number of events	119	123
Median OS (95%CI)	Not reached (NR-NR)	Not reached (NR-NR)
3-year OS (95%CI)	84.1% (80.0-87.3%)	87.0% (83.2-90.0%)
5-year OS (95%CI)	75.6% (71.0-79.6%)	75.0% (70.3-79.0%)



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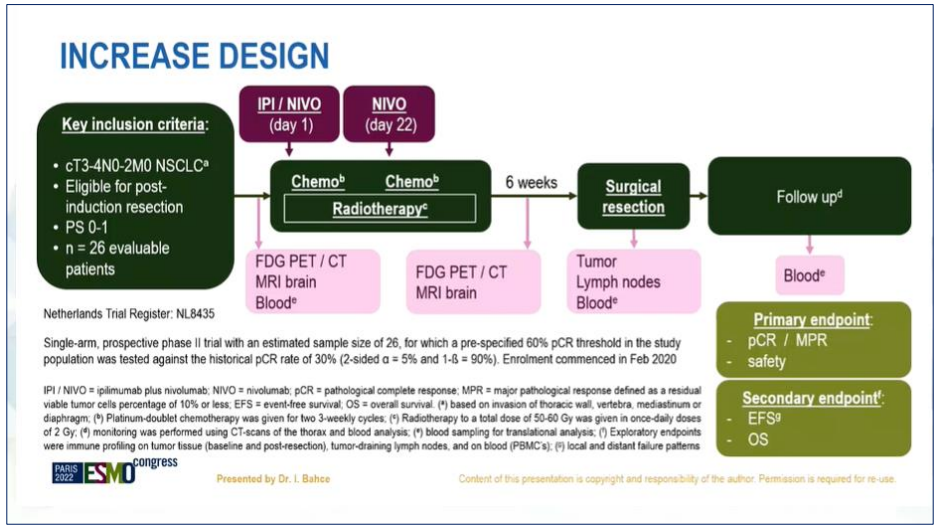
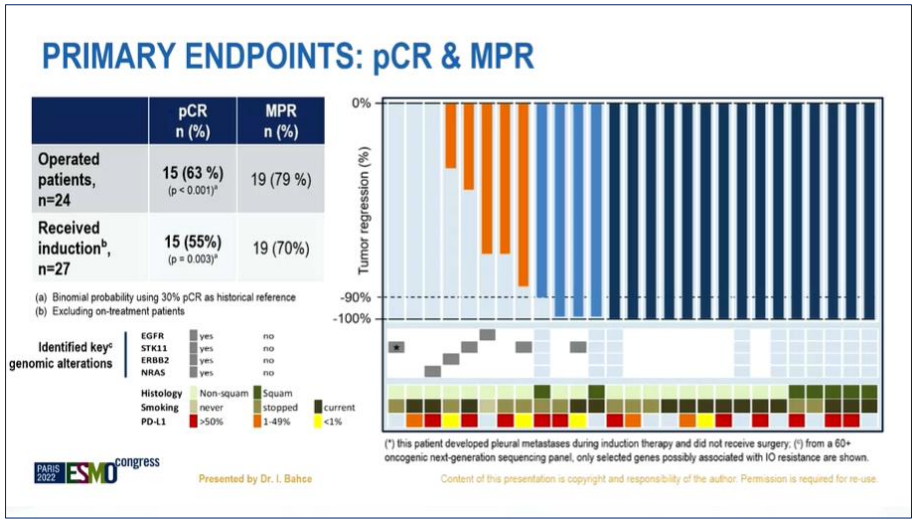
ENFERMEDAD LOCALIZADA: NEOADYUVANCIA





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AE'S IN 27 PATIENTS WHO UNDERWENT IO-THERAPY

	n (%)
Any TEAE	27 (100%)
• Grade 3-4	22 (81%)
• Serious adverse events	10 (37%)
• Grade 5	1[a] (4%)
Any TRAE	21 (78%)
• Grade 3-4	18 (67%)
• irAE Grade 3-4	5 (19%)
• Grade 5	0 (0%)
• Leading to IO discontinuation	2 (7%)
• Leading to failure to surgery	0 (0%)

Key irAE[c]	Any grade n (%)	Grade 1-2	Grade 3-4
Dermatitis	11 (41%)	9	2
Thyroid disorders	9 (33%)	9	0
Pneumonitis	3 (11%)	2	1
Hepatitis	2 (7%)	0	2
Pancreatitis	1 (4%)	0	1
Allergic reaction	1 (4%)	1	0

Median follow-up: 14 (range 4-26) months[b]
Grade 3-4 ITT: 56%

IO = immune oncology drugs; TEAE = treatment-emergent adverse events; TRAE = treatment-related adverse events; irAE= immune-related adverse events. (a) death from COVID-19 in 1 patient was not considered as treatment related; (b) from the first cycle of immunotherapy to data cut-off at 3-May-2022 (abstract deadline); (c) within the 90-days post-surgery timeframe.

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Presented by Dr. I. Bahce

Bahce I, et al. ESMO 2022

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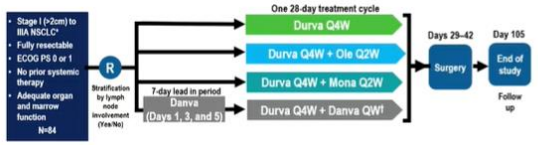
Platform study of neoadjuvant durvalumab (anti-PD-L1) alone or combined with oleclumab (anti-CD73), monalizumab (anti-NKG2A), or danvatirsen (anti-STAT3) in patients with resectable, early-stage non-small-cell lung cancer: pharmacodynamic correlates and ctDNA dynamics in the NeoCOAST study

Jonathan Spicer[1], Tina Cascone[2], Gozde Kar[3], Ying Zheng[4], Jorge Blando[4], Tze Heng Tan[5], Lin-Yang Cheng[4], Ray Mager[4], Oday Hamid[4], Yee Soo-Hoo[6], Patrick Forde[7], Walter Weder[8], Rosario Garcia-Campelo[9], Italia Grenga[10], Rakesh Kumar[4], and Lara McGrath[10]

[1]McGill University, Montreal, QC, Canada; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]AstraZeneca, Cambridge, UK; [4]AstraZeneca, Gaithersburg, MD, USA; [5]AstraZeneca, Munich, Germany; [6]AstraZeneca, Wilmington, DE, USA; [7]Bloomberg–Kimmel Institute for Cancer Immunotherapy, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD, USA; [8]Thoracic surgery, Clinic Bethanien, Zurich, Switzerland; [9]Medical Oncology Unit, University Hospital A Coruña, A Coruña, Spain; [10]AstraZeneca, Waltham, MA, USA.

NeoCOAST: Neoadjuvant durvalumab +/– novel agents in resectable, early-stage (I [>2cm] to IIIA) NSCLC



	Durva (n=27)	Durva + Ole (n=21)	Durva + Mona (n=20)	Durva + Danva (n=16)
Overall MPR (n/N, %)	3/27 (11%)	4/21 (19%)	6/20 (30%)	5/16 (31%)
PD-L1+	0/6 (0%)	2/5 (40%)	3/6 (50%)	0/2 (0%)
PD-L1–	0/3 (0%)	1/6 (16.7%)	0/2 (0%)	0/5 (0%)
PD-L1 NE	3/18 (17%)	1/10 (10%)	3/12 (25%)	5/9 (56%)

- Primary endpoint: MPR rate (proportion of patients with ≤10% residual viable tumour cells in resected tumour specimen and sampled nodes at surgery) per investigator assessment.
- A **single cycle of** neoadjuvant durva combined with ole, mona, or danva produced numerically improved MPR rates (19–31.3%) compared with durva alone (11.1%).[1]
- MPR was associated with baseline tumour PD-L1 expression in durva + ole and durva + mona arms.

*Per American Joint Committee on Cancer Staging, 8th edition. †Danvatirsen arm was stopped early as the program was discontinued.
ctDNA, circulating tumour DNA; ECOG, Eastern Cooperative Oncology Group; MPR, major pathological response; NE, not evaluable; NSCLC, non-small-cell lung cancer; PD-L1, programmed cell death ligand-1; PS, performance status; QRW, once every 4 weeks; Q2W, once every 2 weeks; Q3W, every week; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TMB, tumour mutational burden.
1. Cascone T, et al. AACR 2022 (presentation CT011).

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Summary and conclusions

- A single cycle of neoadjuvant durva combined with ole, mona, or danva produced numerically improved MPR rates (19–31.3%) compared with durva alone (11.1%).
- Pathological regressions were not associated with TMB.
- Molecular responses by ctDNA were observed in 25–60% of patients per arm after treatment, and 75–100% of patients post-surgery, including those without an MPR.
- Pharmacodynamic responses by intratumoural mRNA show greater increases in immune activation genes with durva + ole and durva + mona than with durva alone.
- Further translational analyses of durva combined with ole or mona will be carried out as part of NeoCOAST-2 (NCT05061550), a Phase 2 study of neoadjuvant durva combined with chemotherapy and either ole or mona, followed by surgery and adjuvant durva plus ole or mona, in patients with resectable, Stage IIA–IIIA NSCLC.[1]

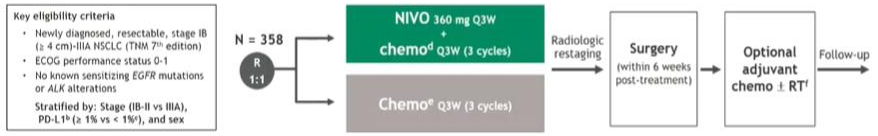
PARIS 2022 ESMO congress NeoCOAST-2

ctDNA, circulating tumour DNA; MPR, major pathological response; TMB, tumour mutational burden.
1. Cascone T, et al. AACR 2022 (poster CT124).

Spicer J, et al. ESMO 2022

CheckMate 816[a] study design and HRQoL assessments

- In CheckMate 816, neoadjuvant NIVO + chemo significantly improved the primary endpoints of EFS and pCR vs chemo alone in patients with resectable NSCLC[1]
- NIVO + chemo is approved in the United States and other countries as a neoadjuvant treatment for adult patients with resectable NSCLC (tumors ≥ 4 cm or node positive)[2]



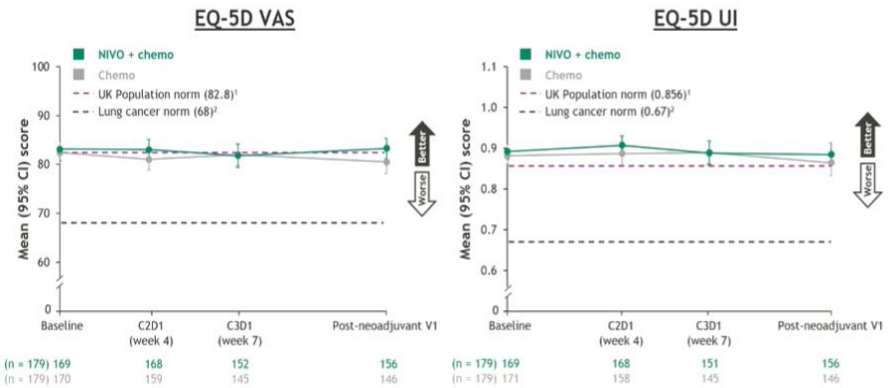
Primary endpoints
- pCR by BIPR
- EFS by BICR

HRQoL, assessed by prespecified PRO exploratory endpoints[g]
- **EQ-5D VAS:** overall health status based on a visual analog scale (VAS); range: 0 (worst imaginable health state) to 100 (best imaginable health state)
- **EQ-5D UI:** health status utility index (UI) score calculated from 5 dimensions[h]; range: < 0 (worse than death), 0 (same as death), 1 (full health)

Database lock: October 20, 2021

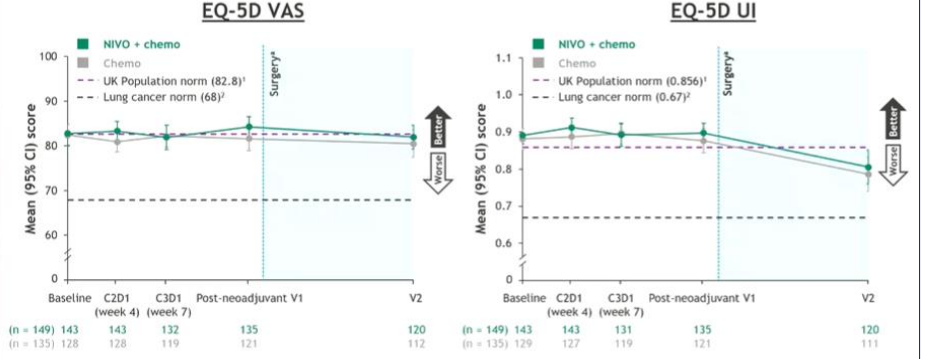
[a]NCT02998528. [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako). [c]Included patients with PD-L1 expression status not evaluable and indeterminate. [d]NSQ: pemetrexed + cisplatin or paclitaxel + carboplatin; SQ: gemcitabine + cisplatin or paclitaxel + carboplatin. [e]Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (SQ only), pemetrexed + cisplatin (NSQ only), or paclitaxel + carboplatin. [f]Per healthcare professional choice. [g]Evaluated by the 3-level version of the EQ-5D questionnaire. [h]Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. [i]Forde PM, et al. *N Engl J Med.* 2022;386:1973-85. [j]OPDIVO® (nivolumab) [package insert]. Princeton, NJ: Bristol Myers Squibb; March 2022.

EQ-5D VAS and UI scores during the neoadjuvant period: all randomized patients



VAS, visual analog scale; UI, utility index. EQ-5D VAS ranges from 0 to 100, with higher scores indicating better functioning. EQ-5D UI UK ranges from −0.594 to 1, with higher scores indicating better functioning. 1. Szende A, et al. Self-Reported Population Health: An International Perspective based on EQ-5D. Dordrecht, The Netherlands: Springer; 2014. 2. Pickard AS, et al. *Health Qual Life Outcomes* 2007;5:70.

EQ-5D VAS and UI scores during the neoadjuvant period and post-surgery: patients who received surgery



- Similar patterns of EQ-5D VAS and UI scores were seen in all randomized patients at post-neoadjuvant Visit 2

VAS, visual analog scale; UI, utility index. [a]Median (IQR) time from last neoadjuvant dose to definitive surgery was 5.3 (4.6-6.0) weeks with NIVO + chemo and 5.0 (4.6-5.9) weeks with chemo for all patients with definitive surgery; EQ-5D VAS ranges from 0 to 100, with higher scores indicating better functioning. EQ-5D UI UK ranges from −0.594 to 1, with higher scores indicating better functioning. 1. Szende A, et al. Self-Reported Population Health: An International Perspective based on EQ-5D. Dordrecht, The Netherlands: Springer; 2014. 2. Pickard AS, et al. *Health Qual Life Outcomes* 2007;5:70.

Summary

- In CheckMate 816, HRQoL as measured by EQ-5D was preserved from baseline during the neoadjuvant treatment period with neoadjuvant NIVO + chemo, similar to chemo alone, in patients with resectable NSCLC
- Among patients who received surgery, NIVO + chemo did not impact post-operative PROs in comparison with chemo only
  - Similar postoperative declines in EQ-5D VAS and UI scores were observed (approximately 2 months after surgery) in both treatment arms
  - This decrease is consistent with previous reports of HRQoL impacts following surgical resection[1-3]
  - Continued follow-up is required to assess post-operative recovery of HRQoL
- No notable differences were seen in EQ-5D VAS and UI scores between treatment arms across patient subgroups
- These patient-reported HRQoL results, along with previously reported efficacy and safety data, support the use of NIVO + chemo as neoadjuvant treatment for resectable NSCLC

VAS, visual analog scale; UI, utility index. 1. Balduyck B, et al. *Lung Cancer* 2007;56:423-431; 2. Ichimura H, et al. *Thoracic Cancer* 2021;12:835-844; 3. Poghosyan H, et al. *Lung Cancer* 2013;81:11-26.

Felip E, et al. ESMO 2022

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Analysis of pathological features and efficacy outcomes with neoadjuvant nivolumab plus platinum-doublet chemotherapy for resectable non-small cell lung cancer in CheckMate 816

Julie Stein Deutsch,[1] Ashley Cimino-Mathews,[1] Elizabeth D. Thompson,[1] Daphne Wang,[1] Robert A. Anders,[1] Edward Gabrielson,[1] Peter Illei,[1] Jaroslaw Jedrych,[1] Ludmila Danilova,[1] Jonathan D. Spicer,[2] Mariano Provencio,[3] Patrick M. Forde,[1] Dimple Pandya,[4] Mia Tran,[4] Joseph Fiore,[4] Vipul Devas,[4] Tricia R. Cottrell,[1] Alex S. Baras,[1] Janis M. Taube[1]

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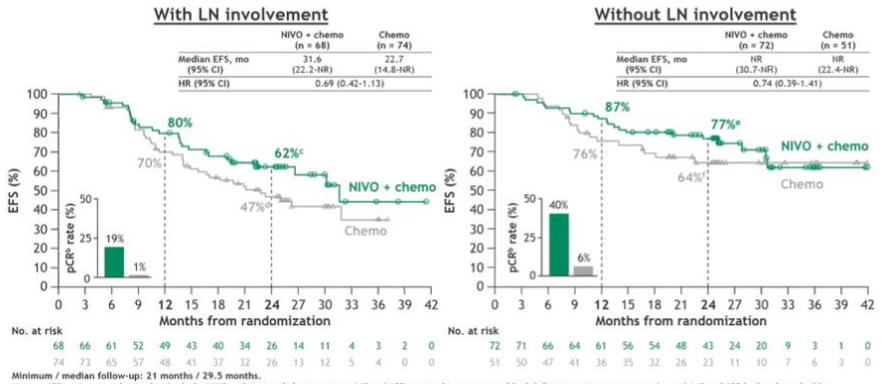
Presentation number LBA50

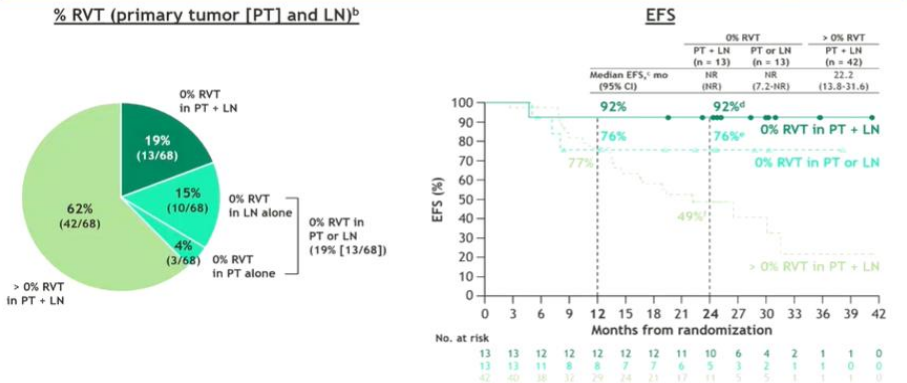
Efficacy in patients with or without pathologic evidence of LN involvement[a]



Minimum / median follow-up: 21 months / 29.5 months.

[a]Among 179 patients randomized to both the NIVO + chemo and chemo groups, 149 and 135 received treatment and had definitive surgery, respectively, and 140 and 125 had path-evaluable samples from both primary tumor and LN; LN involvement refers to pathologic evidence of LN disease at resection that had or had not fully regressed after neoadjuvant treatment (0% or > 0% RVT in the resected LN). [b]0% RVT in both the primary tumor and LN; MPR (≤ 10% RVT in both primary tumor and LN) with NIVO + chemo vs chemo: 29% vs 5% (patients with LN involvement) and 62% vs 24% (patients without LN involvement). 95% CI: [c]49-73, [d]34-58, [e]65-85, [f]49-76.

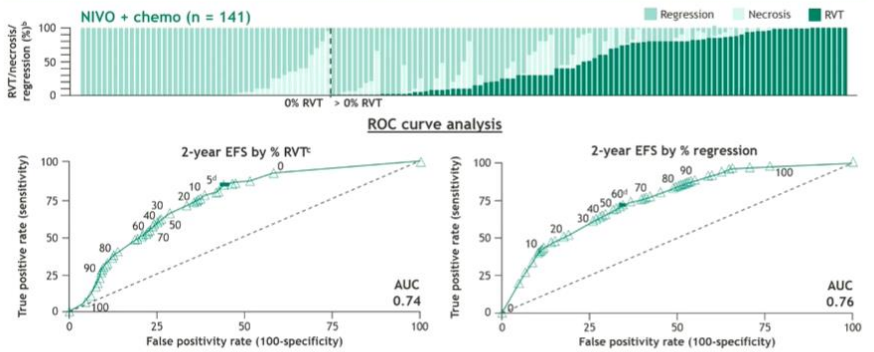
EFS by % RVT in patients with LN involvement[a]: NIVO + chemo



Minimum / median follow-up: 21 months / 29.5 months.

[a]LN involvement refers to pathologic evidence of LN disease at resection that had or had not fully regressed after neoadjuvant treatment (0% or > 0% RVT in the resected LN). [b]Patients in the chemo arm with 0% RVT in both PT + LN, 1% (1/74); PT alone, 1% (1/74); LN alone, 4% (3/74); either PT or LN, 5% (4/74); > 0% RVT in PT + LN, 93% (69/74). [c]HRs were not computed because of the low number of events in the 0% RVT subgroups. 95% CI: [d]57-99, [e]42-91, [f]32-64.

Association of % RVT and % regression in the primary tumor with EFS[a]



- Similar AUCs for % RVT and % regression were observed with NIVO + chemo in both patients with or without LN involvement[e]

[a]In patients who underwent surgery and had path-evaluable primary tumor samples. [b]In individual patients. [c]Adapted with permission from Provencio-Pulla M, et al. Poster presentation at the ASCO Annual Meeting; June 3-7, 2022; Chicago, IL & online. Abstract LBA8511. [d]The solid square is the optimal cutoff, which is the difference between the true positive rate and false positive rate over all possible cutoff values. [e]LN involvement refers to pathologic evidence of LN disease at resection that had or had not fully regressed after neoadjuvant treatment (0% or > 0% RVT in the resected LN).

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The genomic landscape of small cell lung cancer in never smoking patients

Michael S Oh[1], Alex Barrett[2], Arya Ashok[2], Elizabeth Mauer[2], Edward B Garon[1], Aaron E Lisberg[1], Amy L Cummings[1], Jonathan W Goldman[1]

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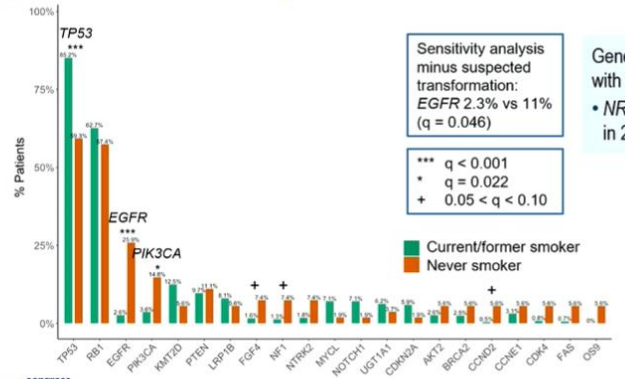
[2]Tempus Labs, Inc, Chicago IL, USA

NS patients exhibit unique somatic variant landscape



Sensitivity analysis minus suspected transformation: *EGFR* 2.3% vs 11% (q = 0.046)

*** q < 0.001
* q = 0.022
\+ 0.05 < q < 0.10

Gene fusions infrequent with no differences
- *NRG1* fusions found in 2 NS patients

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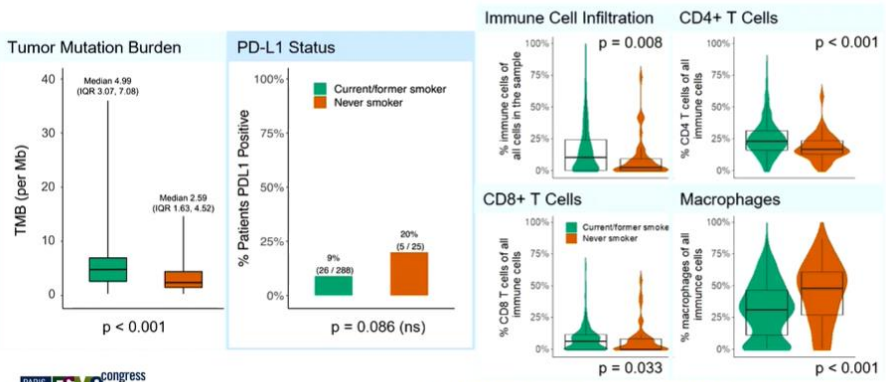
Immune microenvironment by smoking status



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Conclusions

- Mutational landscape of SCLC differs based on smoking status
- Tumors of NS more likely to harbor variants in *EGFR* and *PIK3CA*
- Potential differences seen in the immune microenvironment
- Future need to explore possible treatment implications

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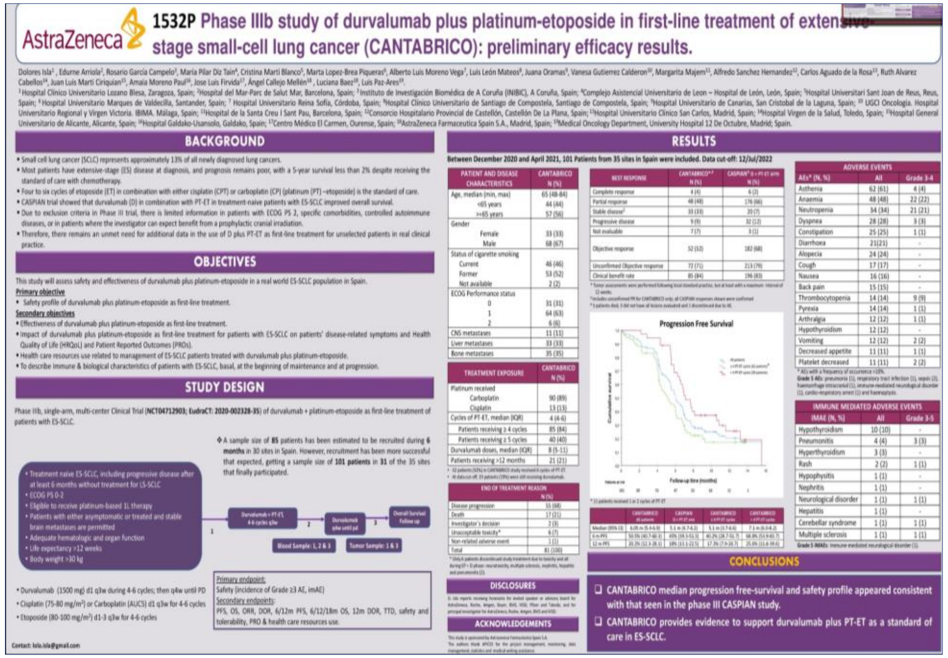

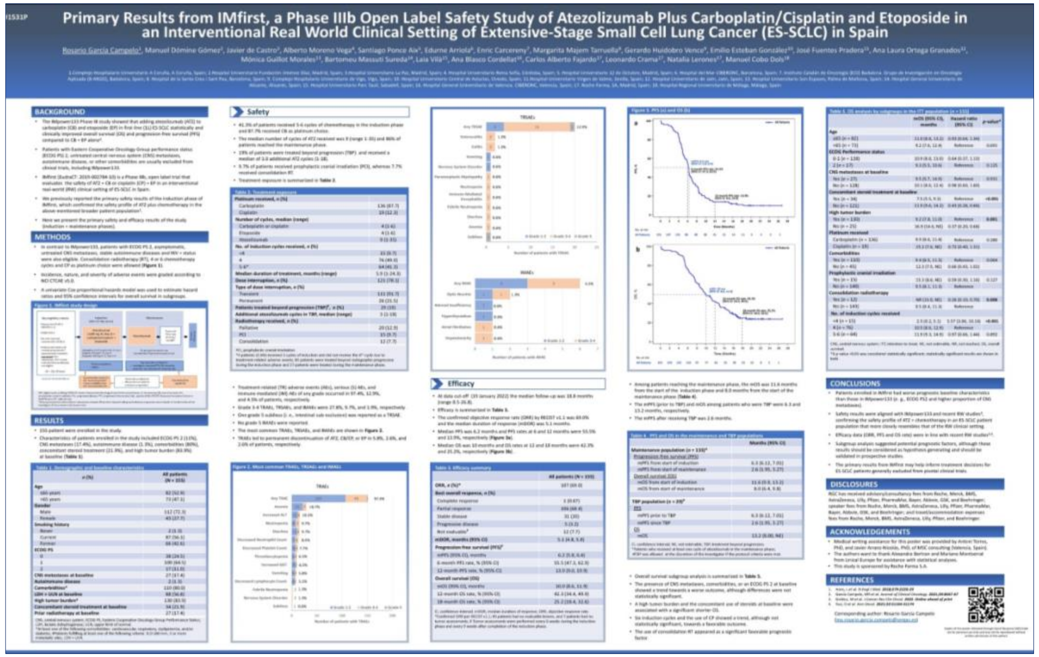

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García Campelo R, et al. ESMO 2022

543P

A retrospective cross-sectional study of treatment patterns in small-cell lung cancer (SCLC) in Europe 2018–2021

Noemi Reguart, MD, PhD;[1] Stephen Puntis, DPhil;[2] Katarina Öhrling, MD, PhD;[3] Ali Abbasi MD, PhD;[2]* Karly S Louie, PhD;[2]* Martin Sebastian, MD[4]

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INTRODUCTION

SCLC is an aggressive malignancy with a poor prognosis that represents ~15% of all lung cancer cases[1,2]

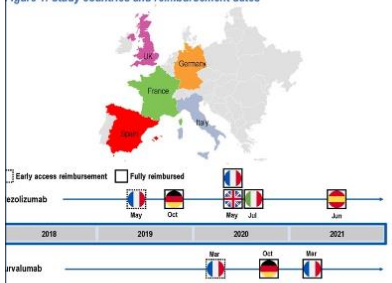
Development of new effective treatments for SCLC was limited until anti–PD-L1 therapies, atezolizumab and durvalumab, received EU approval for 1st-line (1L) treatment of extensive stage SCLC (ES-SCLC) in 2019[3] and 2020,[4] respectively (reimbursement dates are shown in Figure 1)

Previous studies of treatment patterns in patients with SCLC in Europe described single countries and were limited to specific settings (e.g. hospital database)[5] or were conducted prior to the approval of the anti–PD-L1 therapies[6]

Updated information on real-world treatment patterns in Europe is important to understand the therapeutic landscape in the context of new regimen approvals and to identify potential unmet needs for patients with SCLC

Here we report demographics, clinical characteristics and treatment patterns for patients with ES-SCLC in France, Germany, Spain, Italy and the UK

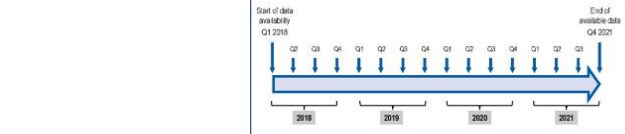
Figure 1. Study countries and reimbursement dates



METHODS

IQVIA Oncology Dynamics dataset

- A repeated quarterly, cross-sectional, retrospective study of drug-treated patients with cancer in Europe and the UK
- A network of physicians from general hospitals, specialist cancer hospitals, academic centres and office-based cancer facilities collect individual-level information from patient medical records into an anonymised survey form



The study included adults ≥18 years of age who were diagnosed with ES-SCLC and received any systemic treatment between Q1 2018 and Q4 2021

The primary objectives were to describe clinical characteristics, demographics and treatment patterns of patients with ES-SCLC in France, Germany, Italy, Spain and the UK

RESULTS

Baseline characteristics

- Overall, data for 5,832 patients with ES-SCLC were included in the analysis; n=4,898 1L, n=804 2nd-line (2L) and n=130 3rd-line or greater. Baseline demographics and characteristics are shown in Table 1
- Specialist cancer hospitals treated the greatest number of patients (n=2,419, 41.5%), followed by academic cancer hospitals (n=2,041, 34.9%), office-based practitioners (n=849, 14.6%) and general hospitals (n=519, 8.9%), and n=4 (0.1%) unknown (data not shown)

Table 1. Characteristics of ES-SCLC patients (n=5,832)

	EU5 (N=5,832)	France (n=544)	Germany (n=1,919)	Spain (n=771)	Italy (n=1,850)	UK (n=1,149)
Male, n (%)	**3,843 (65.9)**	394 (72.4)	975 (64.2)	561 (72.8)	1,277 (69.0)	636 (55.4)
Median age (Q1, Q3)	**66 (58, 72)**	63 (58, 68)	63 (58, 68)	63 (58, 71.8)	67.7 (58, 72.8)	67 (58, 72.4)
Stage at primary diagnosis, n (%)						
I/II	**50 (0.9)**	11 (2.0)	14 (0.9)	8 (1.0)	10 (0.5)	7 (0.6)
III	**304 (5.2)**	30 (5.5)	66 (4.3)	53 (6.9)	78 (4.2)	77 (6.7)
IV	**5,158 (88.4)**	503 (92.5)	1,438 (94.7)	709 (91.9)	1,443 (78.0)	1,065 (92.7)
Unknown	**320 (5.5)**	-	-	1 (0.1)	319 (17.2)	-
Current[a] ECOG score, n (%)						
0–1	**4,350 (74.6)**	394 (72.4)	1,054 (69.4)	572 (74.2)	1,567 (84.7)	763 (66.4)
2+	**1,482 (24.9)**	150 (27.6)	464 (30.6)	199 (25.8)	253 (13.7)	386 (33.6)
Unknown	**30 (0.5)**	-	-	-	30 (1.6)	-
Current[a] smoking status, n (%)[b]	**(n=4,425)**	(n=374)	(n=1,142)	(n=594)	(n=1,454)	(n=861)
Current	**2,316 (52.3)**	234 (62.6)	649 (56.8)	303 (51.0)	670 (46.1)	460 (53.4)
Former	**1,684 (38.1)**	113 (30.2)	405 (35.5)	226 (38.0)	613 (42.2)	327 (38.0)
Never	**364 (8.2)**	23 (6.1)	78 (6.8)	65 (10.9)	133 (9.1)	65 (7.5)
Unknown	**61 (1.4)**	4 (1.1)	10 (0.9)	0 (0.0)	38 (2.6)	9 (1.0)

[a]At time of survey. [b]Smoking status from 2018–2020; data on smoking status were not collected in 2021
ECOG, Eastern Cooperative Oncology Group; ES-SCLC, extensive stage small cell lung cancer

Treatment regimens by year in EU5

- The most common 1L regimens during 2018–2021 were platinum + etoposide combination chemotherapies (91.8%, 85.9%, 62.8%, 42.3% in each year, respectively; Figure 2, left panel)
- By 2021, the overall extent of 1L atezolizumab + platinum chemotherapy combination use was similar to use of the platinum + etoposide combination (41.2% and 42.3%, respectively)
- The most common 2L treatment during 2018–2021 was topotecan with its use decreasing slightly during this period (59.8%, 57.7%, 57.3%, 50.3% in each year, respectively; Figure 2, right panel)
- Anti–PD-(L)1 / anti–CTLA-4 use in 2L treatment increased during 2018–2021 (2.2%–9.2%) despite no approval for SCLC 2L (data not shown)

1L platinum + atezolizumab

- Platinum chemotherapy + atezolizumab 1L treatment has increased across Europe during 2018–2021, and in 2021 was the most common 1L regimen in Germany (54.8%), France (48.5%) and the UK (43.7%) (Figure 3, left panel)

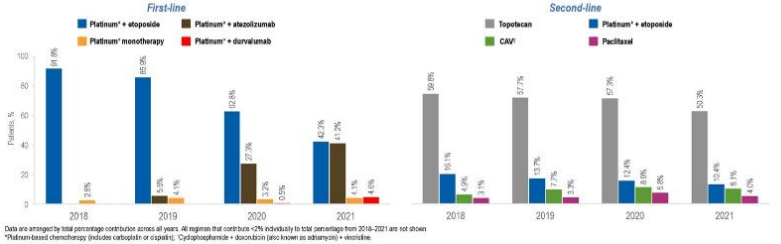
1L platinum + durvalumab

- In 2021, platinum chemotherapy + durvalumab combination 1L use represented 31.8% of all 1L treatment in France, but <3% of all 1L use in the other European countries examined (Germany [2.7%], Spain [2.0%], the UK [0.4%] and Italy [0.3%]; Figure 3, right panel)

2L treatment by platinum status

- Topotecan was the most used 2L treatment irrespective of platinum sensitivity status, with carboplatin / etoposide the second most used treatment in platinum-sensitive patients (Table 2)

Figure 2. Most frequent regimens by line of therapy (EU5) from 2018–2021



Data are arranged by total percentage contribution across all years. All regimens that contribute <2% individually to total percentage from 2018–2021 are not shown
*Platinum-based chemotherapy (includes carboplatin or cisplatin); †Cyclophosphamide + doxorubicin (also known as adriamycin) + vincristine.

Figure 3. Use of platinum chemotherapy + atezolizumab or durvalumab, as a percentage of all 1L treatment from 2018–2021

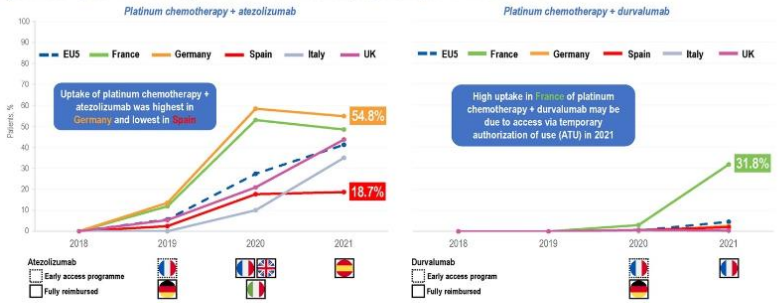


Table 2. Top 3 systemic 2L ES-SCLC regimens by platinum status (EU5)

	2018		2019		2020		2021	
Platinum status	**Regimen**	**n (%)**	**Regimen**	**n (%)**	**Regimen**	**n (%)**	**Regimen**	**n (%)**
Resistant		N=63		N=47		N=44		N=45
	Topotecan	46 (68.3)	Topotecan	31 (65.9)	Topotecan	31 (70.5)	Topotecan	25 (55.5)
	Carboplatin / paclitaxel	4 (6.3)	CAV†	7 (14.9)	CAV†	7 (15.9)	Carboplatin / etoposide	5 (11.1)
	Nivolumab*, paclitaxel*, CAV*†	3 (4.8)	Carboplatin / irinotecan	2 (4.3)	Carboplatin / vinorelbine	2 (4.5)	CAV†	4 (8.8)
Sensitive		N=133		N=98		N=126		N=91
	Topotecan	71 (53.4)	Topotecan	53 (54.1)	Topotecan	56 (51.9)	Topotecan	35 (57.4)
	Carboplatin / etoposide	30 (22.6)	Carboplatin / etoposide	17 (17.3)	Carboplatin / etoposide	24 (22.2)	Carboplatin / etoposide	6 (9.8)
	CAV†	8 (6.0)	CAV†	5 (5.1)	CAV†	9 (8.3)	CAV*†, lurbinectedin*	3 (4.9)
Unknown		N=28		N=37		N=73		N=67
	Topotecan	17 (60.7)	Topotecan	21 (56.8)	Topotecan	47 (64.4)	Topotecan	27 (40.3)
	Paclitaxel	2 (7.1)	Paclitaxel	3 (8.1)	Paclitaxel	6 (8.2)	Atezolizumab	8 (11.9)
	Irinotecan	2 (7.1)	CAV*†, gemcitabine / irinotecan*	2 (5.4)	CAV†	4 (5.5)	CAV†	7 (10.4)

Percentages do not add up to 100% as only the top 3 regimens are shown
*Equal number of patients on regimen; †Cyclophosphamide + doxorubicin (also known as adriamycin) + vincristine. ES-SCLC, extensive stage small cell lung cancer

CONCLUSIONS

- Use of platinum-based chemothera**anti–PD-L1 inhibitor therapy** as a of ES-SCLC in Europe has **increas** period from 2018–2021
- **Extent of uptake of platinum-bas chemotherapy + anti–PD-L1 inhib for 1L treatment varied** between t
  - Overall greatest in France, which to an early access programme for and lowest in Spain, which may b delay in reimbursement of atezoli
- Topotecan continues to be the mos treatment overall in EU5 regardless sensitivity

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ACKNOWLEDGEMENTS

- Medical writing support for this presentation was funded by Amg by Thomas Owens, PhD, and Josh Lilly, PhD, of Aspire Scientifi
- This study was sponsored by Amgen Ltd

DISCLOSURES

- Noemi Reguart has received honoraria for speaker / advisory bo AstraZeneca, Bayer, BMS, Boehringer, Guardant, Janssen, MS Sanofi and Takeda
- Stephen Puntis and Katarina Öhrling are employed by and hold
- Ali Abbasi reports contract work with Amgen
- Karly S Louie is a former employee of and holds stocks in Amge and holds stock options / shares in BioMarin Pharmaceutical Inc
- Martin Sebastian has received grants from AstraZeneca, person AstraZeneca, BioNTech, BMS, Boehringer Ingelheim, CureVac, Serono, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis and Take support from BMS, Pfizer and Takeda

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CONCLUSIONES

- Se confirman los resultados del ADAURA a 4 años. No datos de SG.
- El beneficio de pembrolizumab en el escenario adyuvante es independiente de la expresión de PD-L1.
- Papel de la combinación de inmunoterapia y quimioterapia en el escenario neoadyuvante.
- Posible relación entre ctDNA en CPNCP EGFR M+ resecado y SLE.
- Extrapolación de los datos de inmunoterapia + quimioterapia en CPCP al mundo real.

GRACIAS

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