ASCO Updates: Lung Cancer

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Iowa Oncology Society

Disclosures

- None

Outline

Peri-operative NSCLC
Abstract 8500: Surgical outcomes with resectable NSCLC receiving neoadjuvant nivolumab +/- relatlimab
Abstract 8501: NEOTORCH: Peri-operative toripalimab with chemotherapy in resectable stage II-III NSCLC
Adjuvant NSCLC with EGFR mutation
Abstract LBA3: ADAURA: Adjuvant Osimertinib with resected EGFR-mutated stage I-III NSCLC
Metastatic NSCLC without targetable genomic alterations
1st line
Abstract 9004: Tropion-LUNG02: DATO-DxD with pembrolizumab with or without platinum for advanced NSCLC
2nd line
Abstract 9005: LUNAR study: Tumor treating fields with standard of care chemotherapy for advanced NSCLC
Metastatic NSCLC with EGFR Exon 20 insertion
Abstract 9002: Sunvozertinib for exon 20 mutations
Small cell lung cancer
1st line
Abstract 8504: Maintenance atezolizumab and talazoparib in SLFN11 positive ES-SCLC
≥ 2nd line
Abstract 8502: DLL-3 bispecific T-cell engager (BI 764563) in previously-treated SCLC

2023 ASCO ANNUAL MEETING

Surgical outcomes of patients with resectable NSCLC receiving neoadjuvant immunotherapy with nivolumab plus relatlimab or nivolumab

Findings from the prospective, randomized, multicentric phase II study NEOpredict-Lung

Clemens Aigner[1], Bert Du Pont[2], Koen Hartemink[3], Marcel Wiesweg[1], Michel Vanbockrijck[2], Kaid Darwiche[1], Balazs Hegedus[1], Alexander Schramm[1], Hubertus Hautzel[1], Brigitte Maes[2], Dirk Theegarten[1], Hans-Ulrich Schildhaus[1], Paul Baas[3], Kristof Cuppens[2], Martin Schuler[1] and Till Plönes[1]

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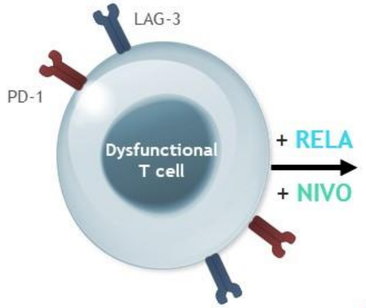
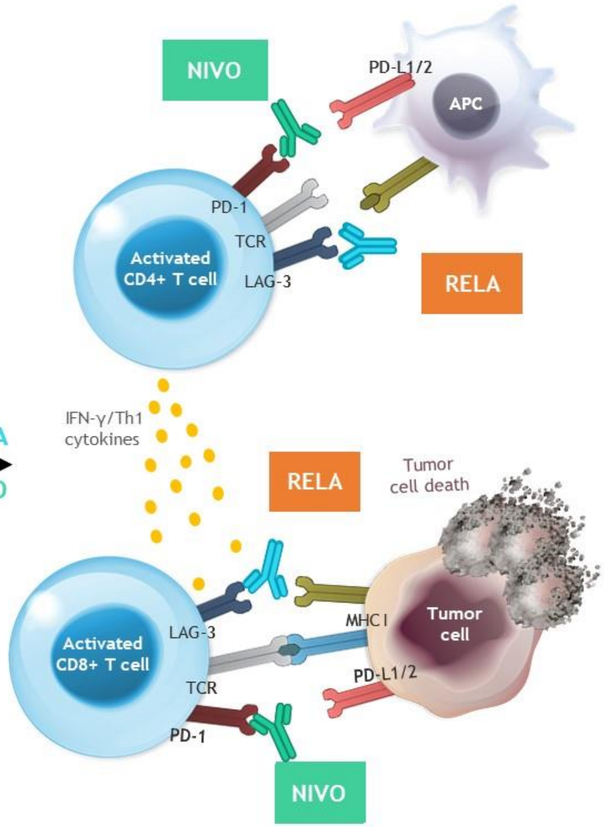
[2]Jessa Hospital, Hasselt, Belgium

[3]Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

Study design

- Randomized phase II study in patients with resectable NSCLC exploring the feasibility, safety and early efficacy of combined preoperative treatment with nivolumab and relatlimab, a monoclonal antibody targeting LAG-3
- Reference arm with nivolumab monotherapy
- Primary study endpoint: Feasibility of curatively intended surgery within 43 days (continuously assessed)
- Secondary endpoints (selected): Radiological and histopathological response rates, DFS and OS at 12 months, safety, R0 resection rate





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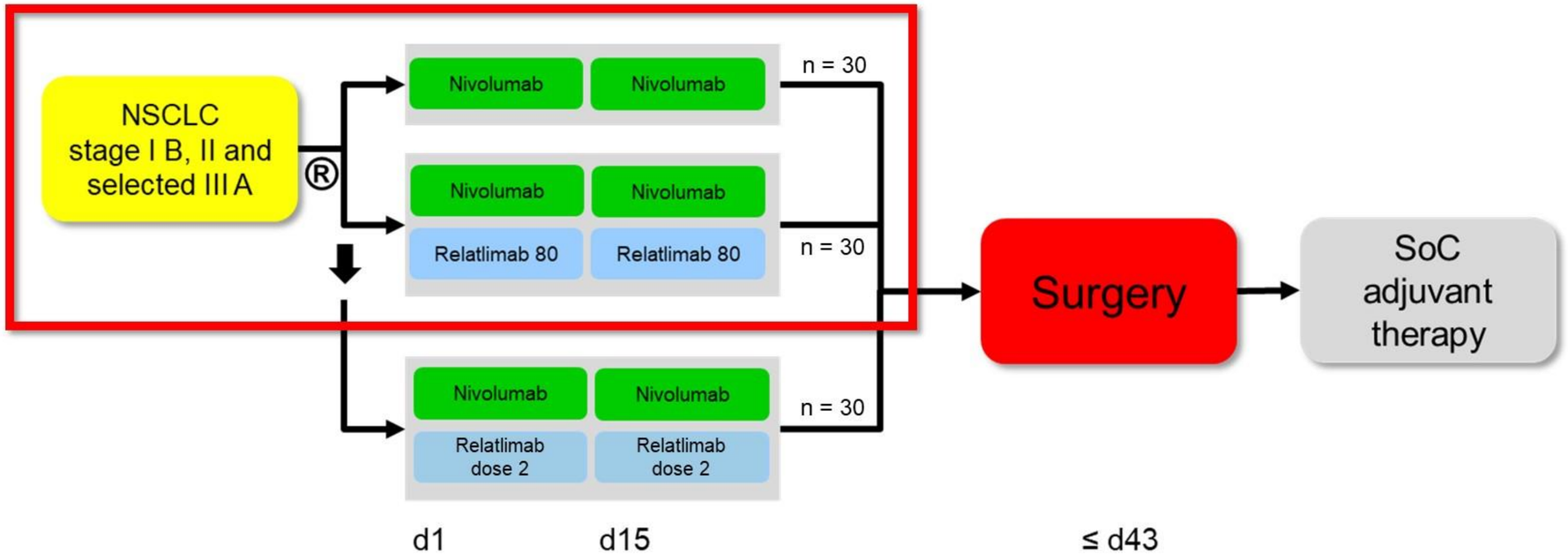
Study design, NCT 04205552



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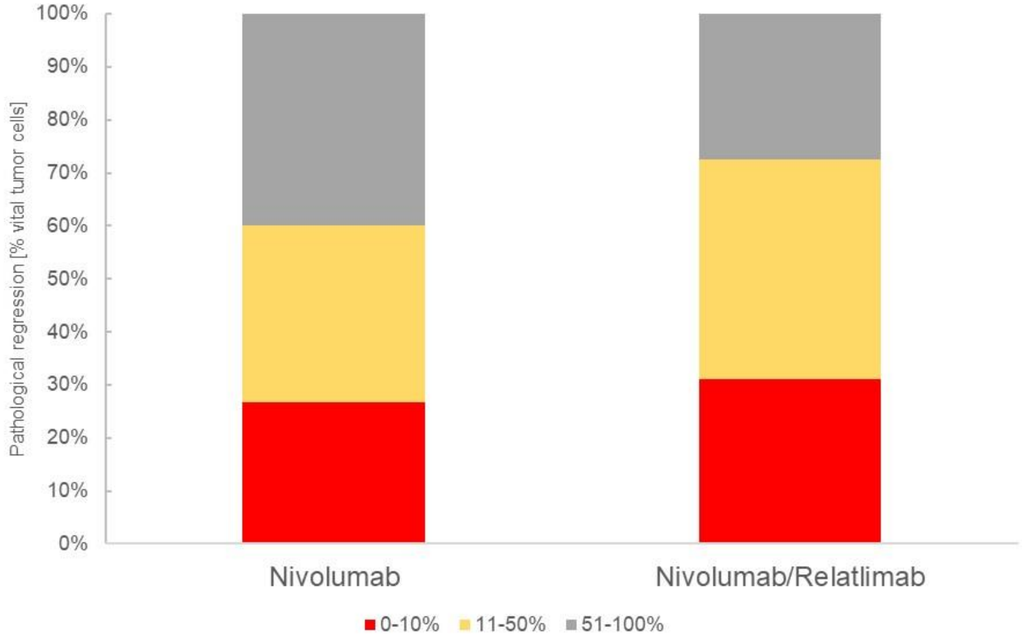
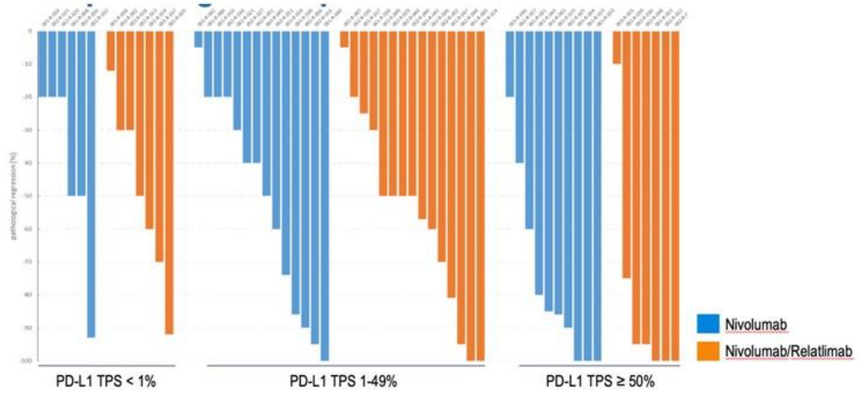
Histopathological response



Protocol definition: Vital tumor cells

0-10%	major pathological response
11-50%	pathological response
51-100%	no pathological response



	pCR	MPR
Nivolumab	13.3%	27%
Nivolumab + Relatlimab	16.7%	30%

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Perioperative outcome and follow-up

	Nivolumab (240 mg)	Nivolumab (240 mg)/Relatlimab (80 mg)
30 day mortality	0%	0%
Adjuvant therapy (guideline based according to pathological staging)	n=14	n=14
12 months OS	96 % (95% CI: 83-99%)	
12 months DFS	91% (95% CI: 78-97%)	

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IO treatment related adverse events

	Nivolumab (240 mg)		Nivolumab (240 mg)/ Relatlimab (80 mg)	
	all	grade ≥ 3	all	grade ≥ 3
Anemia	2 (7%)	-	-	-
Atrial fibrillation	1 (3%)	1 (3%)	-	-
Hyperthyroidism	5 (17%)	1 (3%)	4 (13%)	-
Hypothyroidism	2 (7%)	-	3 (10%)	-
Gastrointestinal	1 (3%)	-	2 (7%)	-
Hepatic	1 (3%)	1 (3%)	1 (3%)	1 (3%)
Proteinuria	1 (3%)	-	-	-
Pneumonitis	-	-	2 (7%)	-
Chills/fever	2 (3%)	-	-	-
Rash	1 (3%)	-	-	-

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Conclusions

- Primary study endpoint was met by all patients in both treatment arms.
- Minimally invasive and open techniques are safely possible. There seems to be no increased risk for complications in bronchial and/or vascular sleeve resections.
- Perioperative course, morbidity and mortality rates are comparable to other neoadjuvant regimens. Standard adjuvant therapies can be safely administered in this setting.
- Comprehensive correlative studies and biomarker analyses are ongoing
- Protocol has been amended to explore a higher dose of relatlimab for increased LAG-3 target occupancy

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Perioperative Toripalimab + Platinum-Doublet Chemotherapy vs Chemotherapy in Resectable Stage II/III Non-small Cell Lung Cancer: Interim Event-Free Survival Analysis of the Phase III Neotorch Study

Shun Lu,[1] Lin Wu,[2] Wei Zhang, [3] Peng Zhang,[4] Wenxiang Wang,[2] Wentao Fang,[1] Wenqun Xing,[5] Qixun Chen,[6] Jiandong Mei,[7] Lin Yang,[8] Lijie Tan,[9] Xiaohong Sun,[10] Shidong Xu,[11] Xiaohua Hu,[12] Guohua Yu,[13] Dongliang Yu, [14]Jinlu Shan,[15] Nong Yang,[2] Yuping Chen,[16] Hui Tian,[17]Weihua Wang,[18] Wenbo Yu [18]

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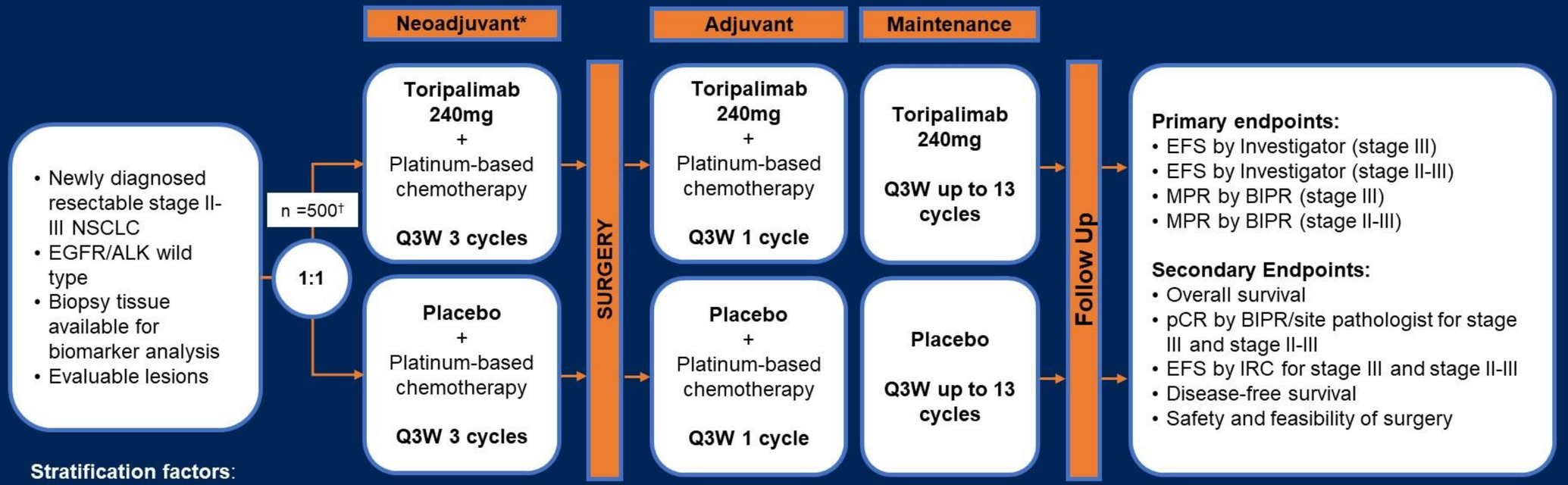
Neotorch Study Design



Stratification factors:
- II vs IIIA vs IIIB
- Lobectomy vs pneumonectomy
- Non-squamous vs squamous
- PD-L1 TC expression: ≥ 1% vs < 1% or non-evaluable

*3 cycles of neoadjuvant chemotherapy with 4 cycles of peri-operative chemotherapy in total were required with in Neotorch study, meanwhile, surgeons were allowed to determine the most appropriate timing for surgery based on the patient's condition
†About 400 patients with Stage III NSCLC and ~100 patients with Stage II NSCLC patients would be enrolled

EFS: Event-Free Survival
MPR: Major Pathologic Response
BIPR: Blinded Independent Pathologic Review
pCR: Pathological Complete Response
IRC: Independent Review Committee

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Treatment Summary - Surgery

	Toripalimab + chemo n = 202	Placebo + chemo n = 202
No surgery performed, n(%)	36 (17.8)	54 (26.7)
Disease progression	5(2.5)	31(15.3)
Patient refusal	18 (8.9)	13 (6.4)
Adverse event#	6 (3.0)	0
Other*	7 (3.5)	10 (5.0)
Patient underwent surgery, n(%)	166 (82.2)	148 (73.3)
R0 resection n(% of underwent surgery)	159 (95.8)	137 (92.6)
Type of surgery(% of underwent surgery)		
Lobectomy	134 (80.7)	123 (83.1)
Sleeve lobectomy	15 (9.0)	11 (7.5)
Pneumonectomy	15(9.0)	14 (9.5)
Other^	2 (1.2)	0

In toripalimab arm, 6 patients canceled surgery due to AE, 3 were judged as not related to toripalimab, the AEs were aggravation of cirrhosis, pneumonia and cerebral infarction, 3 were judged as related to toripalimab, the AEs were Immune-mediated hepatitis, hypophysitis and pneumonitis.

* Other reasons were unresectable at the baseline in 3 patients in toripalimab arm and 5 in placebo arm, unresectability during intraoperative exploration in 1 patient in toripalimab arm and 2 in placebo arm, unfit for surgery due to poor lung function in 1 patients in toripalimab arm and intolerate to anesthetic in 1 patient in placebo arm, high risk of surgery due to tumor enclosing the blood vessels or unremarkable shrinkage in each patient in toripalimab arm, and high risk of surgery due to lower limbs edema and ventricular premature and lost to follow up in each patient in placebo arm.

^ 2 patients were R2 resection and underwent the regional lymph node dissection in toripalimab arm .

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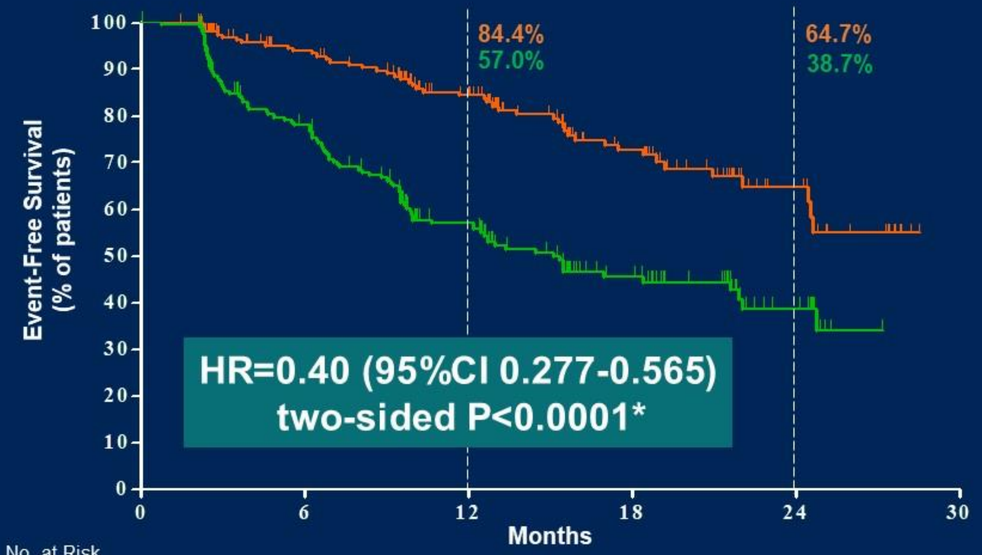
Event-Free Survival Analysis

Intent-to-treat Stage III patients assessed by investigator per RECIST v1.1

EFS by investigator

	No. of Events/ No. of Patients	Median EFS *mos.* (95% CI)
Toripalimab + chemo	47/202	NE (24.4, NE)
Placebo + chemo	97/202	15.1 (10.6, 21.9)

Median follow-up: 18.25 months



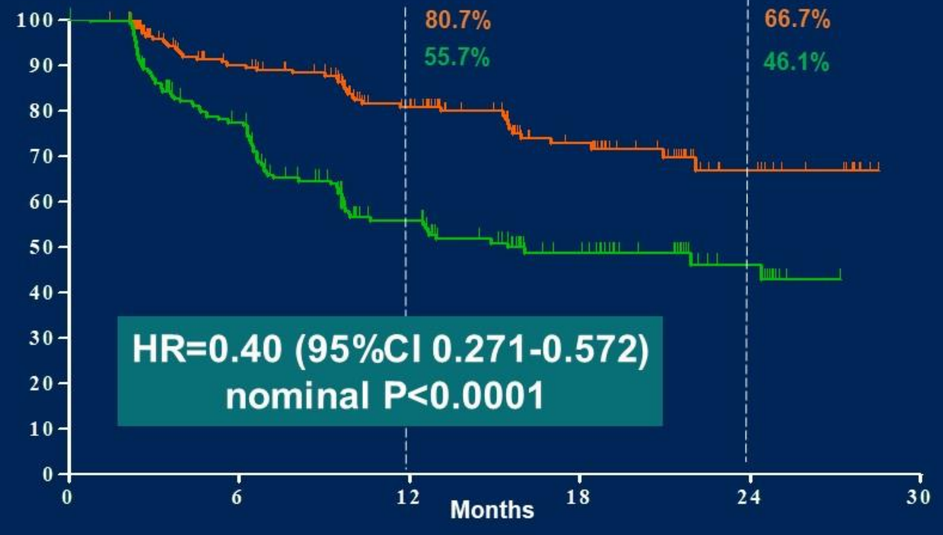
No. at Risk						
Toripalimab + chemo	202	156	116	66	23	0
Placebo + chemo	202	139	86	43	15	0

*2-sided efficacy boundary: 0.01683

EFS by IRC

	No. of Events/ No. of Patients	Median EFS *mos.* (95% CI)
Toripalimab + chemo	43/202	NE (NE, NE)
Placebo + chemo	87/202	15.5 (9.9, NE)

Median follow-up: 18.25 months



	202	150	107	60	17	0
	202	134	74	38	14	0

NE: not evaluable
HR; Hazard ratio
CI: confidence interval
Data cutoff date: Nov. 30, 2022

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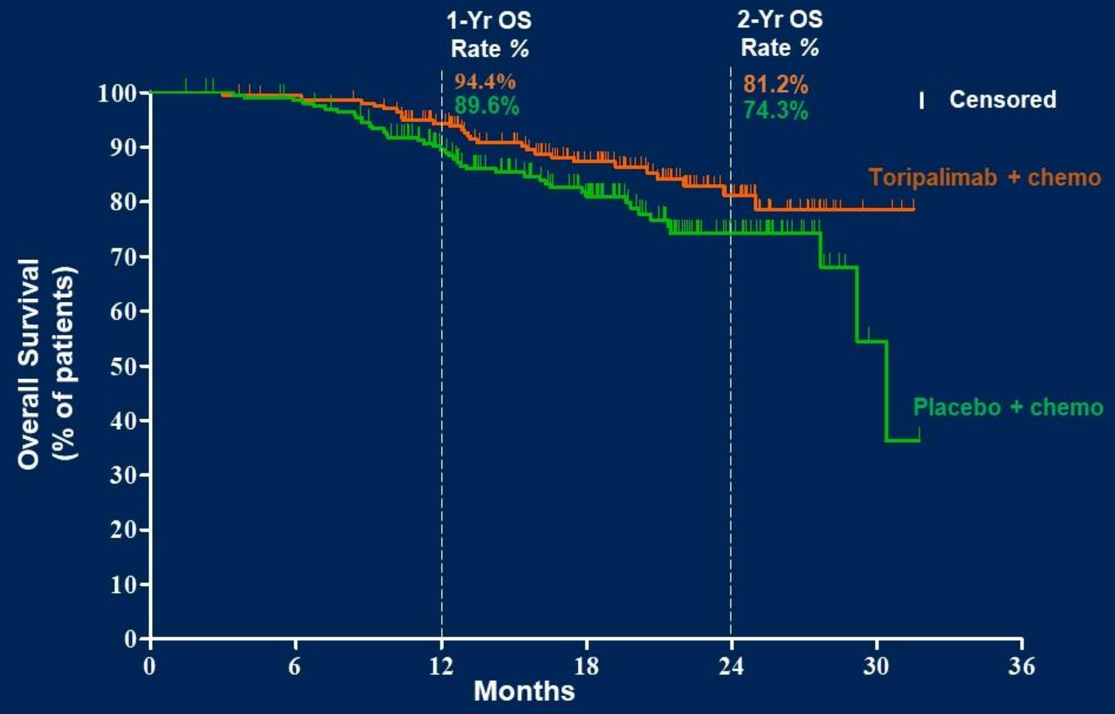
Overall Survival Analysis

Median follow-up: 18.25 months
Intent-to-treat Stage III patients



No. at Risk							
Toripalimab + chemo	202	198	169	107	45	3	0
Placebo + chemo	202	194	156	101	37	3	0

	No. of Events/ No. of Patients	Median OS *mo* (95% CI)
Toripalimab + chemo	28/202	NE (NE, NE)
Placebo + chemo	48/202	30.4 (29.2, NE)

HR=0.62 (95% CI 0.38-0.999)

P=0.0502

Data cutoff date: Nov. 30, 2022
NE: not evaluable
HR; Hazard ratio
CI: confidence interval

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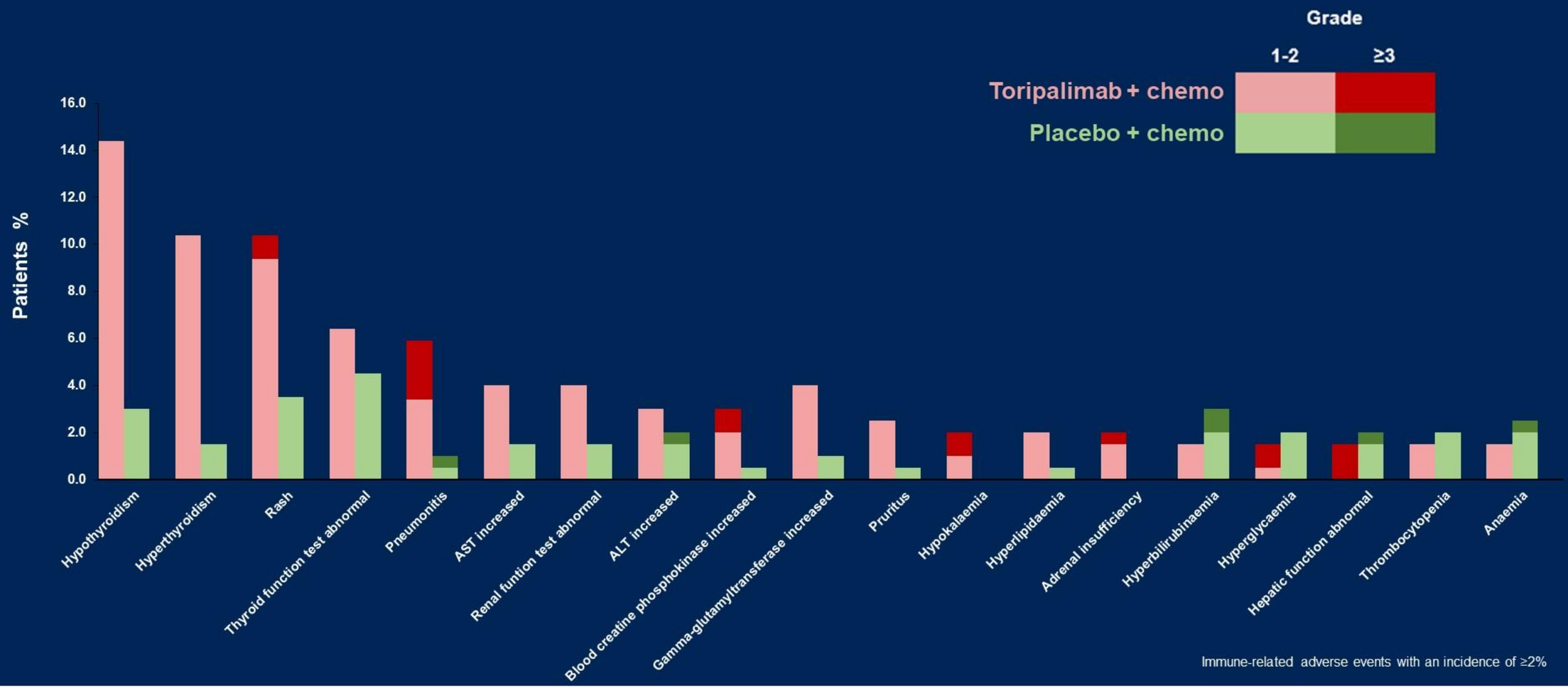
Immune-related Adverse Events



Immune-related adverse events with an incidence of ≥2%

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Summary and Conclusions

- Toripalimab plus chemotherapy significantly improved EFS (NE vs. 15.1 months) and had higher MPR and pCR rates (48.5% vs. 8.4%; 24.8% vs. 1.0%) compared to chemotherapy alone in stage III NSCLC patients, with a survival trend favoring toripalimab. The combination regimen was well-tolerated with no new safety signals.
- Improvement in EFS was consistent across all key subgroups:
  - ❑Benefits in all PD-L1 subgroups: the HRs were 0.59, 0.31 and 0.31 in PD-L1<1%,1-49% and ≥ 50%, respectively
  - ❑Benefits in both non-squamous and squamous subtypes: the HRs were 0.54 and 0.35, respectively
- The results from Neotorch study, as well as other studies, indicated that perioperative immunotherapy plus chemotherapy should be a standard of care for stage III NSCLC patients.

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Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC)

Roy S. Herbst[1], Masahiro Tsuboi[2], Thomas John[3], Terufumi Kato[4], Margarita Majem[5], Christian Grohé[6], Jie Wang[7], Jonathan Goldman[8], Shun Lu[9], Wu-Chou Su[10], Filippo de Marinis[11], Frances A. Shepherd[12], Ki Hyeong Lee[13], Nhieu Thi Le[14], Arunee Dechaphunkul[15], Dariusz Kowalski[16], Lynne Poole[17], Marta Stachowiak[18], Yuri Rukazenkov[19], Yi-Long Wu[20]

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ADAURA Phase III study design

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

Key inclusion criteria:
≥18 years (Japan / Taiwan: ≥20)
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

Stratification by:
Stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
Race (Asian vs non-Asian)

Randomization 1:1 (N=682)

Osimertinib 80 mg, once daily

Placebo, once daily

Planned treatment duration: 3 years

Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

Endpoints
- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

*At the time of recruitment, staging was determined by the AJCC / UICC Staging Manual 7th edition. Patients with stage IB disease were not eligible in Japan. †Pre-operative, post-operative, or planned radiotherapy was not allowed. ‡Centrally confirmed in tissue. §Patients received a CT scan after resection and within 28 days prior to treatment.

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

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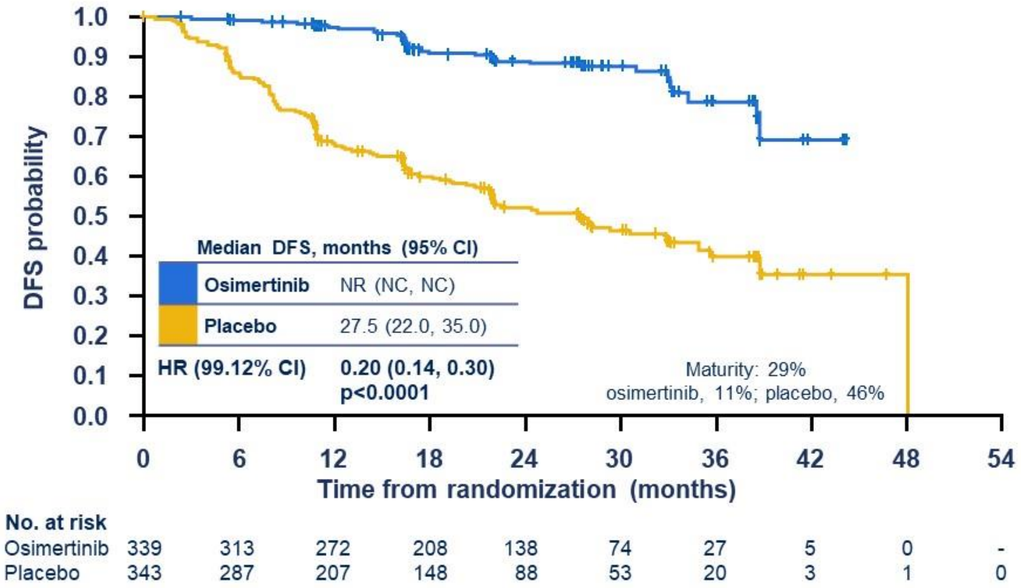
Adjuvant osimertinib has significantly improved DFS

- Adjuvant osimertinib demonstrated highly statistically significant[1,2] and clinically meaningful improvement in DFS in completely resected EGFRm NSCLC vs placebo in both the primary (stage II–IIIA) and overall (IB–IIIA) populations, along with a tolerable safety profile[1–4]

ADAURA primary DFS analysis[1,2] (stage IB–IIIA)*

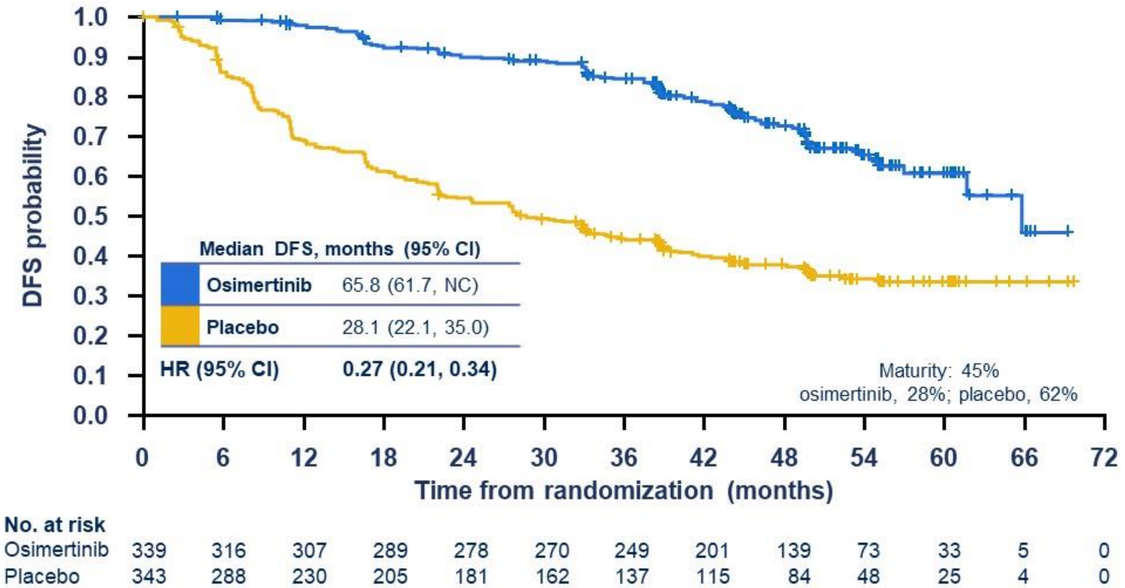
NEJM October 2020



No. at risk										
Osimertinib	339	313	272	208	138	74	27	5	0	-
Placebo	343	287	207	148	88	53	20	3	1	0

ADAURA updated DFS analysis[3,4] (stage IB–IIIA)†

JCO January 2023



No. at risk													
Osimertinib	339	316	307	289	278	270	249	201	139	73	33	5	0
Placebo	343	288	230	205	181	162	137	115	84	48	25	4	0

*Data cut-off: January 17, 2020. †Data cut-off: April 11, 2022.

1. Wu et al. N Engl J Med 2020;383:1711–1723; 2. Herbst et al. J Clin Oncol 2020;38(Suppl 18): abstract / oral LBA5; 3. Herbst et al. J Clin Oncol 2023;41:1830–1840; 4. Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract / oral LBA47.

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CI, confidence interval; DFS, disease-free survival; EGFRm, epidermal growth factor receptor-mutated; HR, hazard ratio; NC, not calculable; NR, not reached; NSCLC, non-small cell lung cancer

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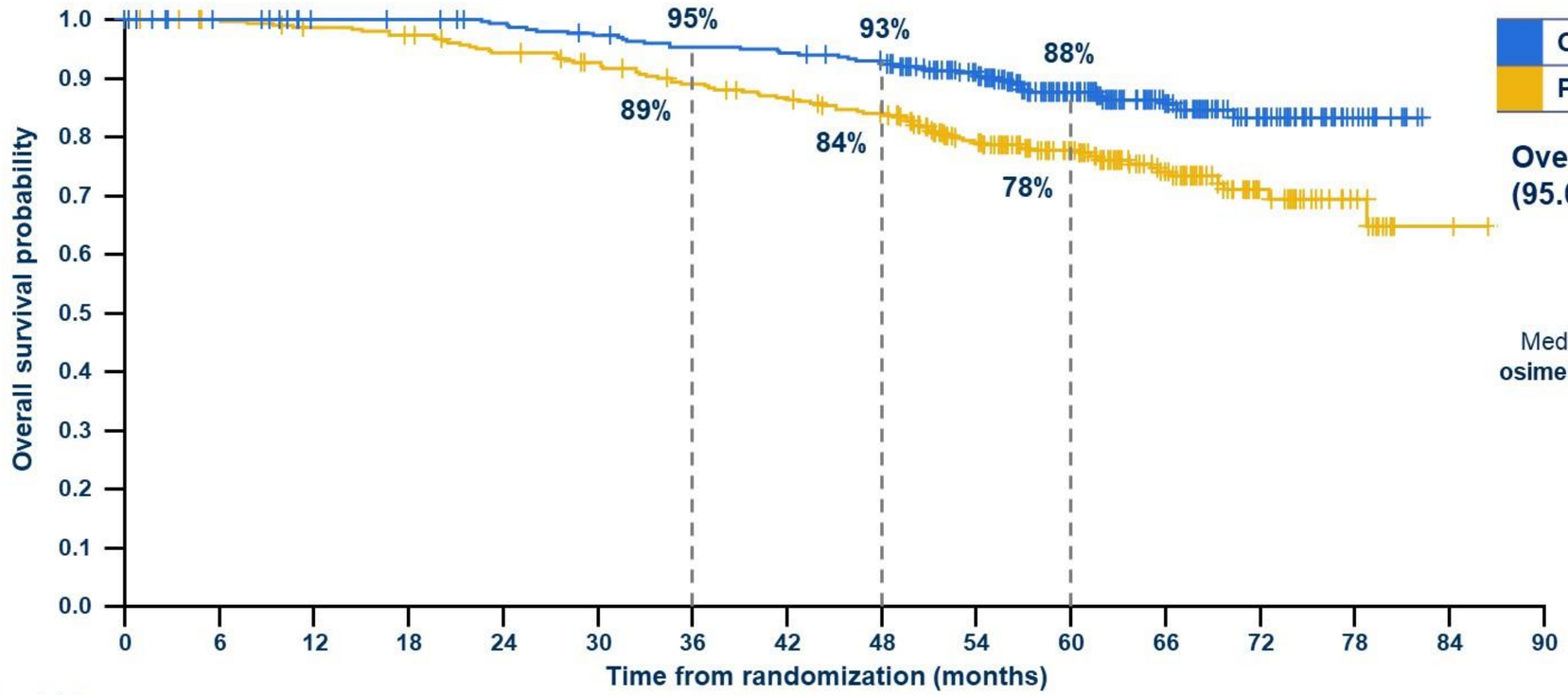
Overall survival: patients with stage IB / II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the overall population of stage IB–IIIA disease



5-year OS rate, % (95% CI)	
Osimertinib (n=339)	88 (83, 91)
Placebo (n=343)	78 (73, 82)

Overall OS HR (95.03% CI) **0.49 (0.34, 0.70); p<0.0001**

Maturity: 18%
osimertinib 12%, placebo 24%

Median follow-up for OS* (censored patients):
osimertinib 61.5 months, placebo 61.5 months

No. at risk

Osimertinib	339	332	325	324	319	311	304	301	294	252	176	108	50	15	0	-
Placebo	343	338	332	326	314	304	290	281	267	223	164	97	44	17	3	0

Data cut-off: January 27, 2023.
Tick marks indicate censored data. Alpha allocation of 0.0497. *Median follow-up for OS (all patients): osimertinib 60.4 months, placebo 59.4 months.

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CI, confidence interval; HR, hazard ratio; OS, overall survival

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Safety summary

- At the final DFS analysis (data cut-off: April 11, 2022), all patients had completed or discontinued study treatment; the safety profile of adjuvant osimertinib with extended follow-up[1,2] was consistent with the ADAURA primary analysis[3]

AE, any cause*, n (%)	Osimertinib (n=337)	Placebo (n=343)
Any AE	330 (98)	309 (90)
Any AE Grade ≥3	79 (23)	48 (14)
Any AE leading to death	1 (<1)	2 (1)
Any serious AE	68 (20)	47 (14)
Any AE leading to discontinuation	43 (13)	9 (3)
Any AE leading to dose reduction	42 (12)	3 (1)
Any AE leading to dose interruption	91 (27)	43 (13)
AE, possibly causally related*†, n (%)		
Any AE	308 (91)	199 (58)
Any AE Grade ≥3	36 (11)	7 (2)
Any AE leading to death	0	0
Any serious AE	10 (3)	2 (1)

- At the time of the current data cut-off for OS (January 27, 2023), one additional serious AE (COVID-19 pneumonia) had been reported, which occurred >28 days after treatment discontinuation; the investigator determined that this was not treatment related and the patient made a full recovery

*Data cut-off: April 11, 2022. Patients with multiple events in the same category counted only once in that category. Patients with events in more than one category counted once in each of those categories. Includes AEs with an onset date on or after the date of first dose and up to and including 28 days following the discontinuation of study treatment and before starting subsequent cancer therapy. †As assessed by the investigator.

1. Herbst et al. J Clin Oncol 2023;41:1830–1840; 2. John et al. J Thorac Oncol 2023; online ahead of print; 3. Wu et al. N Engl J Med 2020;383:1711–1723.

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AE, adverse event; DFS, disease-free survival; COVID-19, coronavirus disease 2019; OS, overall survival

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Conclusions

- In the ADAURA primary analysis, adjuvant osimertinib demonstrated a statistically significant[1] and clinically meaningful DFS benefit vs placebo in resected EGFRm stage IB–IIIA NSCLC, along with improved CNS DFS and a tolerable safety profile[1,2]
- **DFS benefit in ADAURA has translated into a statistically significant OS benefit with adjuvant osimertinib vs placebo**
  - **Primary (stage II–IIIA) population, OS HR 0.49; 95.03% CI 0.33, 0.73; p=0.0004**
  - **Overall (stage IB–IIIA) population, OS HR 0.49; 95.03% CI 0.34, 0.70; p<0.0001**
- OS benefit with adjuvant osimertinib vs placebo was generally consistent across subgroups, including by disease stage (IB / II / IIIA) and prior adjuvant chemotherapy use (yes / no)

ADAURA is the first global Phase III study to demonstrate statistically significant and clinically meaningful OS benefit with targeted treatment in this patient population, reinforcing adjuvant osimertinib as the standard of care for patients with resected EGFRm stage IB–IIIA NSCLC

Data cut-off: January 27, 2023.

1. Wu et al. N Engl J Med 2020;383:1711–1723; 2. Herbst et al. J Clin Oncol 2023;41:1830–1840.

CNS, central nervous system; DFS, disease-free survival; EGFRm, epidermal growth factor receptor-mutated; HR, hazard ratio; NSCLC, non-small cell lung cancer; OS, overall survival

Herbst, R., et al. ASCO Annual Meeting 2023.

2023 ASCO ANNUAL MEETING

TROPION-Lung02: Datopotamab Deruxtecan (Dato-DXd) Plus Pembrolizumab With or Without Platinum Chemotherapy in Advanced Non-Small Cell Lung Cancer

Yasushi Goto, MD, PhD,[1] Wu Chou Su, MD,[2] Benjamin Levy, MD,[3] Olivier Rixe, MD, PhD,[4,5] Tsung Ying Yang, MD, PhD,[6] Anthony Tolcher, MD,[7] Yanyan Lou, MD, PhD,[8] Yoshitaka Zenke, MD, PhD,[9] Panayiotis Savvides, MD,[10] Enriqueta Felip, MD, PhD,[11] Manuel Domine, MD, PhD,[12] Konstantinos Leventakos, MD, PhD,[13] Mariano Provencio Pulla, MD, PhD,[14] Atsushi Horiike, MD, PhD,[15] Edward Pan, MD,[5] Daisy Lin, PhD,[5] Jessie Gu, PhD, MS,[5] Priyanka Basak, MD, MBE,[5] Michael Chisamore, PhD,[16] Luis Paz-Ares, MD, PhD[17]

[1]National Cancer Center Hospital, Tokyo, Japan; [2]Department of Oncology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [3]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD; [4]Quantum Santa Fe, Santa Fe, NM; [5]Daiichi Sankyo, Inc, Basking Ridge, NJ; [6]Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [7]NEXT Oncology, San Antonio, TX; [8]Mayo Clinic, Jacksonville, FL; [9]Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [10]Mayo Clinic, Phoenix, AZ; [11]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology, Barcelona, Spain; [12]Department of Oncology, Hospital Universitario Fundación Jiménez Díaz (IIS-FJD), Madrid, Spain; [13]Mayo Clinic, Rochester, MN; [14]Department of Medical Oncology, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain; [15]Division of Medical Oncology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan; [16]Merck & Co, Inc, Rahway, NJ; [17]Hospital Universitario 12 de Octubre, CNIO-H12O Lung Cancer Unit, Universidad Complutense and CIBERONC, Madrid, Spain

Introduction

- Dato-DXd is an antibody-drug conjugate composed of a TROP2-directed monoclonal antibody covalently linked to a highly potent cytotoxic payload via a plasma-stable, tumor-selective, tetrapeptide-based cleavable linker[1-5]
- Dato-DXd 6-mg/kg monotherapy demonstrated encouraging antitumor activity, with an ORR of 28% and a median DOR of 10.5 months, in patients with heavily pretreated advanced/metastatic NSCLC[6]

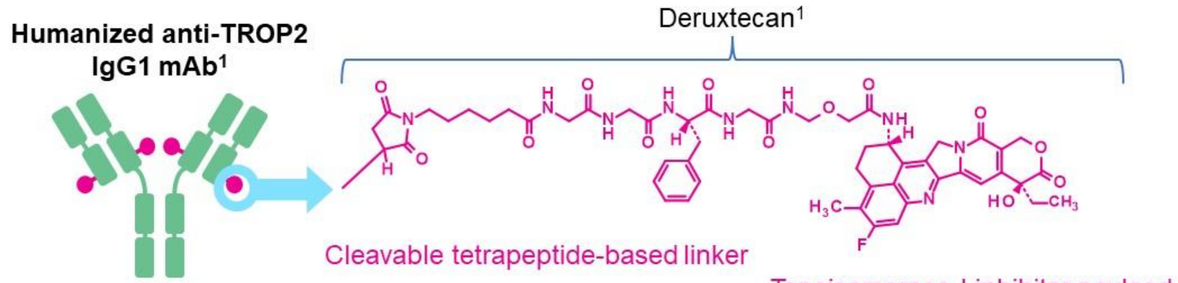


Image is for illustrative purposes only; actual drug positions may vary.

Dato-DXd, datopotamab deruxtecan; DOR, duration of response; IgG1, immunoglobulin G1; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; ORR, objective response rate; TROP2, trophoblast cell-surface antigen 2.

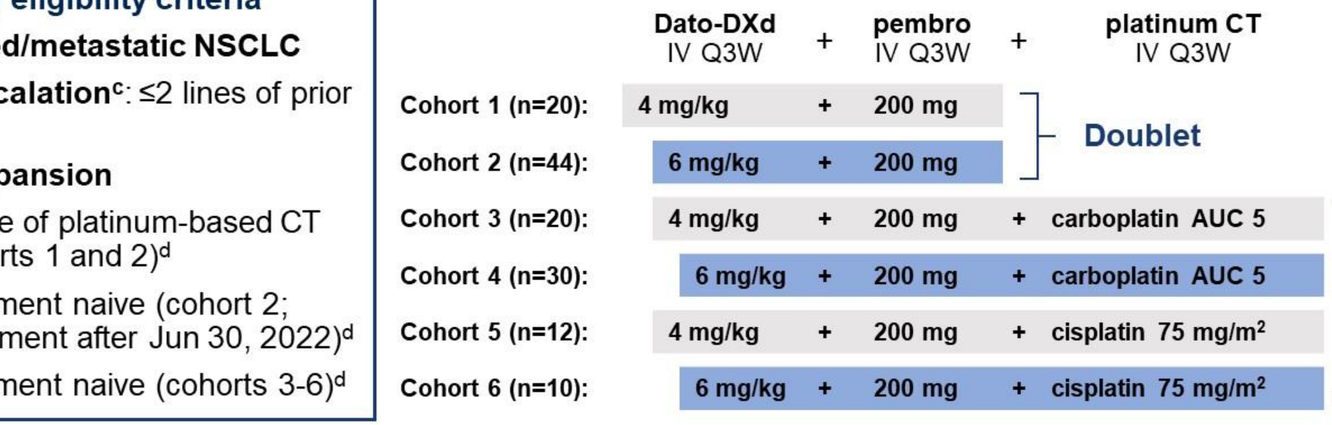
1. Okajima D, et al. *Mol Cancer Ther*. 2021;20(12):2329-2340. **2.** Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173-185. **3.** Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. **4.** Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046. **5.** Shiose Y, et al. *Biol Pharm Bull*. 2007;30(12):2365-2370. **6.** Garon EB, et al. IASLC WCLC 2021. Abstract MA03.02.

TROPION-Lung02: Phase 1b Study

- TROPION-Lung02 is the first study evaluating Dato-DXd + pembrolizumab ± platinum CT[a] in advanced NSCLC without actionable genomic alterations[b] (NCT04526691)
  - The safety of the Dato-DXd + pembrolizumab doublet was established prior to evaluation of the platinum-containing triplet
  - The safety of Dato-DXd 4-mg/kg combinations was established prior to evaluation of 6-mg/kg combinations

Key eligibility criteria

- **Advanced/metastatic NSCLC**
- **Dose escalation**[c]: ≤2 lines of prior therapy[d]
- **Dose expansion**
  - ≤1 line of platinum-based CT (cohorts 1 and 2)[d]
  - Treatment naive (cohort 2; enrollment after Jun 30, 2022)[d]
  - Treatment naive (cohorts 3-6)[d]



- **Primary objectives:** safety and tolerability
- **Secondary objectives:** efficacy, pharmacokinetics, and antidrug antibodies

Data cutoff: April 7, 2023.
AUC, area under the curve; CT, chemotherapy; Dato-DXd, datopotamab deruxtecan; DLT, dose-limiting toxicity; IV, intravenous; NSCLC, non-small cell lung cancer; pembro, pembrolizumab; Q3W, every 3 weeks.
[a] Administered sequentially at the same visit. [b] Patients with known actionable *EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *RET*, or *MET* mutations or alterations in other actionable oncogenic driver kinases were not eligible for this study. Testing for *EGFR* and *ALK* alterations was not required for patients with squamous histology who were smokers or ≥40 years of age. [c] The first 3 to 6 patients in each cohort were enrolled to confirm acceptable safety/DLT rate; the remaining patients are considered part of dose expansion (for which enrollment was ongoing at the time of data cutoff). [d] Prior therapy requirements are for treatment in the advanced/metastatic setting.

PRESENTED BY: Yasushi Goto, MD, PhD

Goto, Y., et al. ASCO Annual Meeting 2023.

Antitumor Activity

Response[a]	All patients: Doublet (n=61)[b]	All patients: Triplet (n=71)[b]	Patients in 1L: Doublet (n=34)[b]	Patients in 1L: Triplet (n=53)[b]
Confirmed + pending ORR, n (%)[c,d]	23 (38)	35 (49)	17 (50)	30 (57)
[95% CI]	[26-51]	[37-61]	[32-68]	[42-70]
Confirmed + pending BOR, n (%)[d,e]				
Confirmed CR	0	1 (1)	0	1 (2)
Pending CR[d]	0	0	0	0
Confirmed PR	21 (34)	34 (48)	15 (44)	29 (55)
Pending PR[d]	2 (3)	0	2 (6)	0
SD, n (%)[f]	30 (49)	27 (38)	16 (47)	18 (34)
DCR, n (%)[g]	51 (84)	62 (87)	31 (91)	48 (91)
Median DOR, months	NE	NE	NE	NE
[95% CI]	[8.8-NE]	[5.8-NE]	[5.5-NE]	[5.7-NE]

- In the 1L setting, the ORR (confirmed and pending)[d] was 50% in patients receiving doublet therapy and 57% in those receiving triplet therapy
- Among all patients, the DCR was 84% (doublet) and 87% (triplet); in the 1L setting, the DCR was 91% in both therapy subgroups

Preliminary PFS in all patients, median (95% CI), months: doublet, 8.3 (6.8-11.8); triplet 7.8 (5.6-11.1)[h]

Data cutoff: April 7, 2023.

1L, first line; 2L+, second line and later; BOR, best overall response; CR, complete response; DCR, disease control rate; DOR, duration of response; NE, not estimable; ORR, objective response rate; PFS, progression-free survival; PR, partial response; SD, stable disease.

[a] By investigator. [b] Response-evaluable patients, which includes patients with ≥1 postbaseline overall response and those who discontinued without a postbaseline overall response. [c] ORR defined as BOR of CR + PR. [d] Responses pending confirmation. [e] BOR was determined using tumor assessments at different evaluation time points from the date of the first dose of study treatment until documented disease progression or the start of the next line of nonpalliative anticancer therapy (inclusive), whichever was earlier. [f] SD defined as ≥1 SD assessment (or better) ≥5 weeks after starting treatment and before progression without qualification for CR or PR (includes pending responses). [g] DCR defined as BOR of confirmed CR + confirmed PR + SD. [h] Preliminary PFS is limited by immature duration of follow-up.

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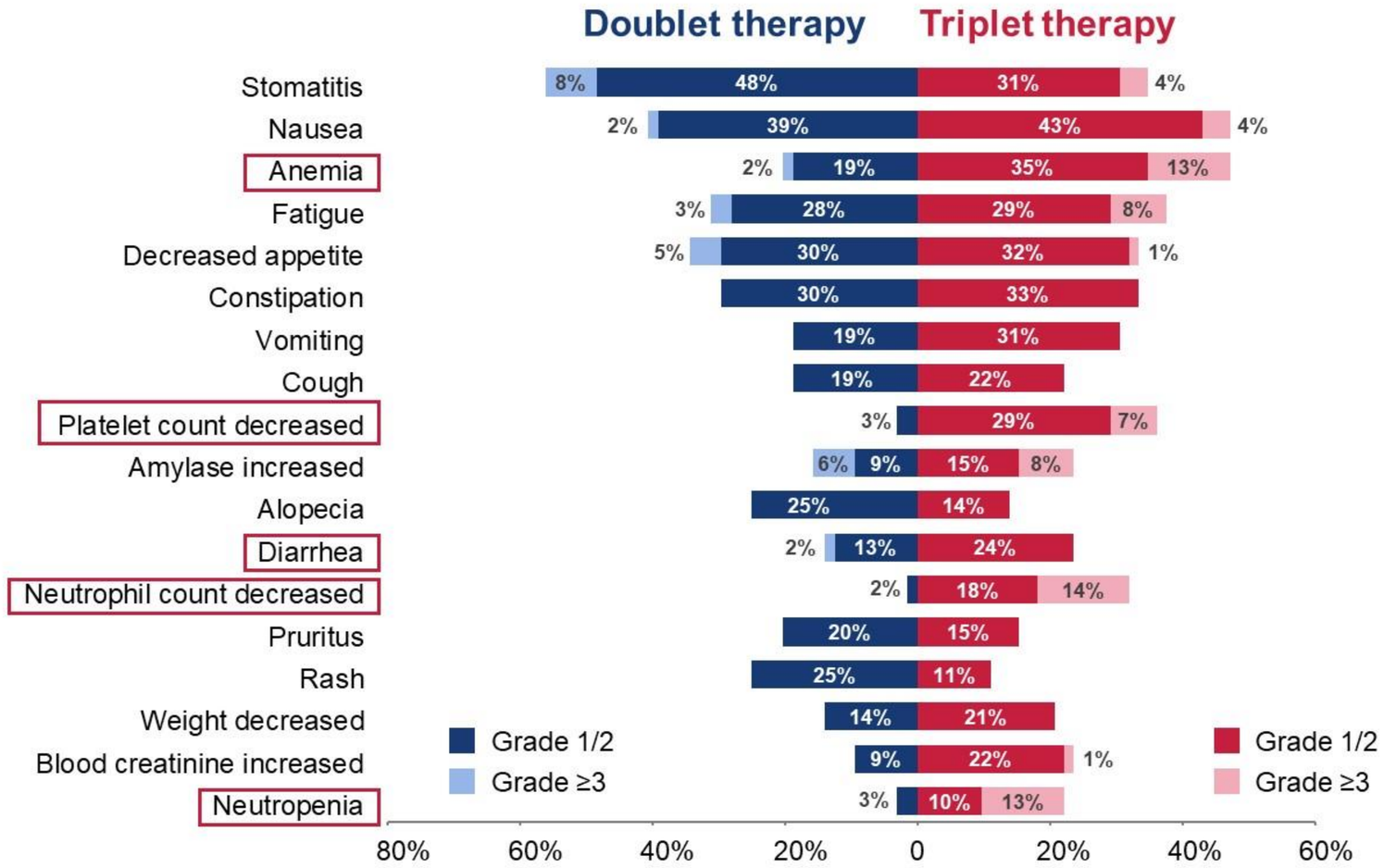
TEAEs Occurring in ≥20% of Patients

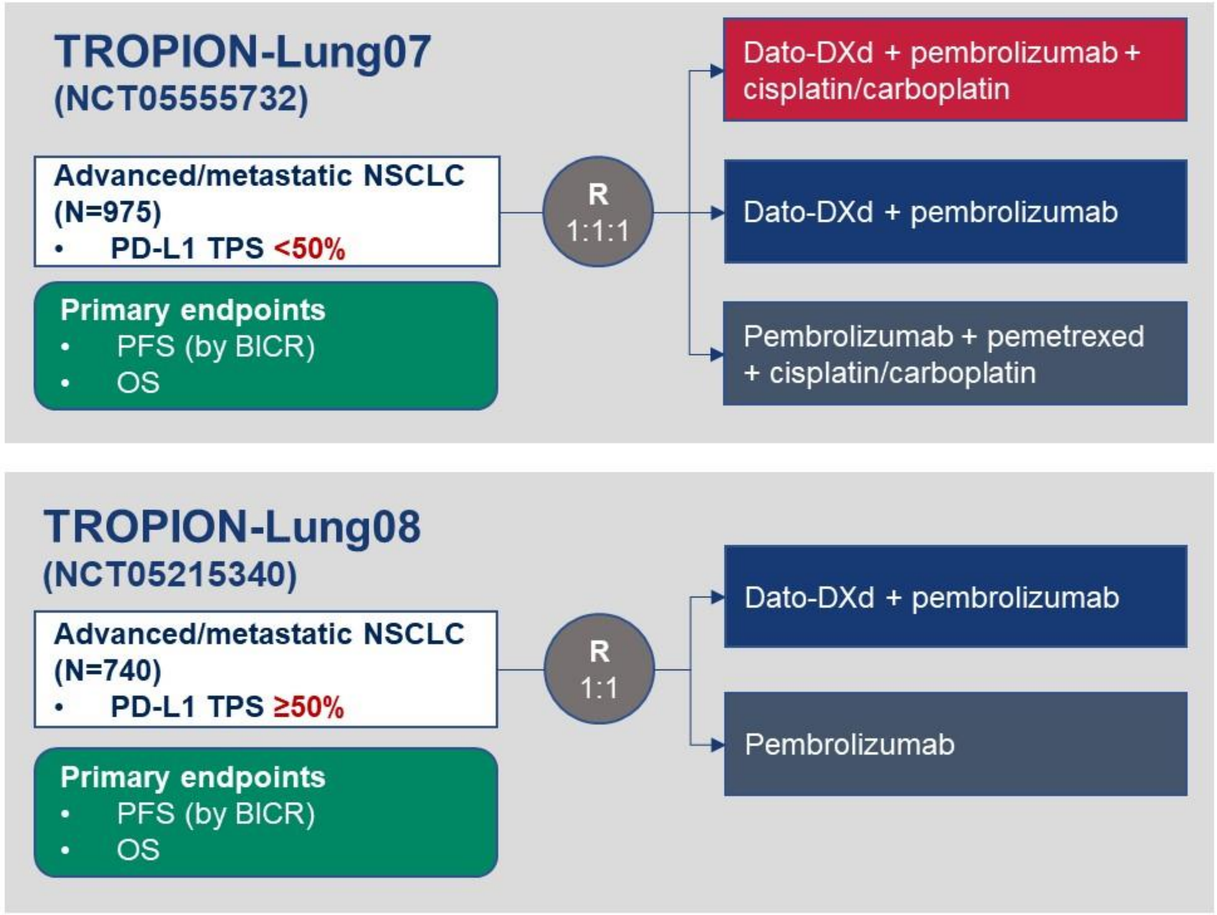


Data cutoff: April 7, 2023.
TEAE, treatment-emergent adverse event.

- The most frequent TEAEs of any grade were stomatitis, nausea, anemia, and fatigue
- In general, hematologic TEAEs, particularly those of grade ≥3, were more frequently observed with triplet therapy than with doublet therapy

Conclusions and Ongoing Studies With Pembrolizumab

- In this study, Dato-DXd + pembrolizumab ± platinum chemotherapy demonstrated encouraging antitumor activity in patients with NSCLC in the 1L and 2L+ settings
- No new safety signals were observed
  - The most frequent TEAEs of any grade were stomatitis, nausea, anemia, and fatigue
- Dato-DXd + pembrolizumab ± chemotherapy is being compared with SOC therapies in the 1L setting in the pivotal phase 3 TROPION-Lung07 and TROPION-Lung08 studies



1L, first line; 2L+, second line and later; BICR, blinded independent central review; Dato-DXd, datopotamab deruxtecan; NSCLC, non-small cell lung cancer; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; R, randomized; SOC, standard of care; TEAE, treatment-emergent adverse event; TPS, tumor proportion score.

LBA9005. Session Date: Tuesday, June 6, 2023. Time: 9:45 AM–12:45 PM

2023 ASCO ANNUAL MEETING

Tumor Treating Fields (TTFields) Therapy with Standard of Care (SOC) in Metastatic Non-Small Cell Lung Cancer (mNSCLC) After Platinum-based Therapies: Randomized, Phase 3 LUNAR Study

Ticiana Leal[1], Rupesh Kotecha[2], Rodryg Ramlau[3], Li Zhang[4], Janusz Milanowski[5], Manuel Cobo[6], Jaromir Roubec[7], Lubos Petruzelka[8], Libor Havel[9], Sujith Kalmadi[10], Jeffrey Ward[11], Zoran Andric[12], Thierry Berghmans[13], David E. Gerber[14], Goetz Kloecker[15], Rajiv Panikkar[16], Joachim Aerts[17], Angelo Delmonte[18], Miklos Pless[19], Richard Greil[20], Christian Rolfo[21], Wallace Akerley[22], Michael Eaton[23], Mussawar Iqbal[24], and Corey Langer[25]; *on behalf of the LUNAR study investigators*

[1]Winship Cancer Institute at Emory University, Atlanta, GA, USA; [2]Miami Cancer Institute, Baptist Health South Florida, Miami, FL, USA; [3]Rodryg Ramlau, Poznan University of Medical Sciences, Poznan, Poland; [4]Sun Yat-sen University Cancer Center (SYSUCC), Guangzhou, China; [5]Medical University of Lublin, Lublin, Poland; [6]Medical Oncology Intercenter Unit, Regional and Virgen de la Victoria University Hospitals, IBIMA, Málaga, Spain; [7]Nemocnice AGEL Ostrava-Vítkovice, Ostrava, Czech Republic; [8]General University Hospital in Prague, Prague, Czech Republic; [9]Thomayer Hospital, Prague, Czech Republic; [10]Ironwood Cancer & Research Centers, Chandler, AZ, USA; [11]Washington University School of Medicine, St. Louis, MO, USA; [12]Clinical Hospital Centre Bezanijska Kosa, Belgrade, Serbia; [13]Jules Bordet Institute, Hôpitaux Universitaires de Bruxelles, Université Libre de Bruxelles, Brussels, Belgium; [14]Harold C. Simmons Comprehensive Cancer Center, UT Texas Southwestern Medical Center, Dallas, TX, USA; [15]University of Louisville, Louisville, KY, USA; [16]Geisinger Cancer Institute, Danville, PA, USA; [17]Erasmus University Medical Center, Erasmus MC Cancer Institute, Rotterdam, The Netherlands; [18]IRCCS Istituto Romagnolo per lo Studio dei Tumori "Dino Amadori" (IRST), Meldola, Italy, Meldola, Italy; [19]Kantonsspital Winterthur, Winterthur, Switzerland; [20]Salzburg Cancer Research Institute-Center for Clinical Cancer and Immunology Trials (SCRI-CCCIT); Paracelsus Medical University Salzburg; Cancer Cluster, Salzburg, Austria; [21]Center for Thoracic Oncology, Tisch Cancer Institute at Icahn School of Medicine, Mount Sinai, New York, NY, USA; [22]Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; [23]St Francis Hospital, Indianapolis, IN, USA; [24]College of Medicine, University of Saskatchewan, Saskatoon, Canada; [25]Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, PA, USA

PRESENTED BY: Ticiana Leal, MD, Winship Cancer Institute - Emory University

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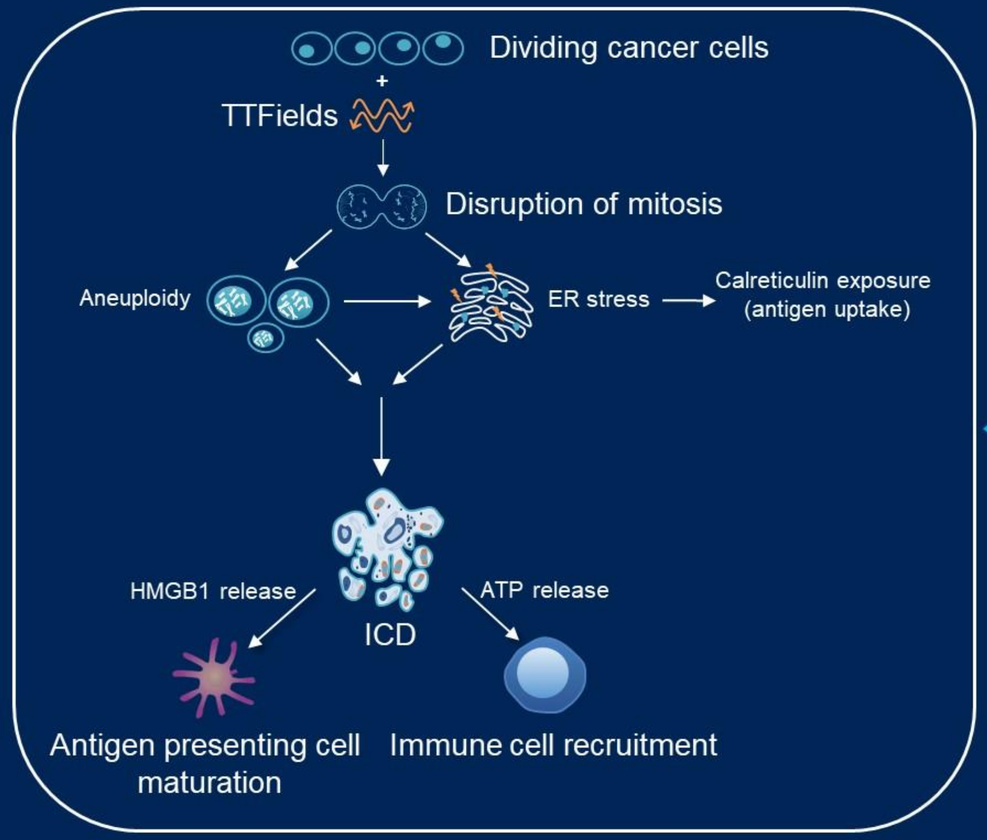
Tumor Treating Fields (TTFields) Mechanism of Action



- TTFields are electric fields that exert physical forces on electrically charged components in dividing cancer cells, leading to an antimitotic effect[1,2]

- Downstream effects include cell stress-induced immunogenic cell death (ICD), triggering a systemic anti-tumor immune response[3,4]

ATP, adenosine triphosphate; ER, endoplasmic reticulum; HMGB1, high mobility group box 1 protein; ICD, immunogenic cell death; TTFields, Tumor Treating Fields.

1. Mun EJ et al. *Clin Cancer Res.* 2018;24(2):266–275; **2.** Giladi M et al. *Sci Rep.* 2015;5:18046; **3.** Voloshin T et al. *Cancer Immunol Immunother.* 2020;69(7):1191–1204; **4.** Barsheshet Y et al. *Int J Mol Sci.* 2022;23(22):14073. Figure adapted from: Shteingauz A et al. *Cell Death Dis.* 2018;9(11):1074.

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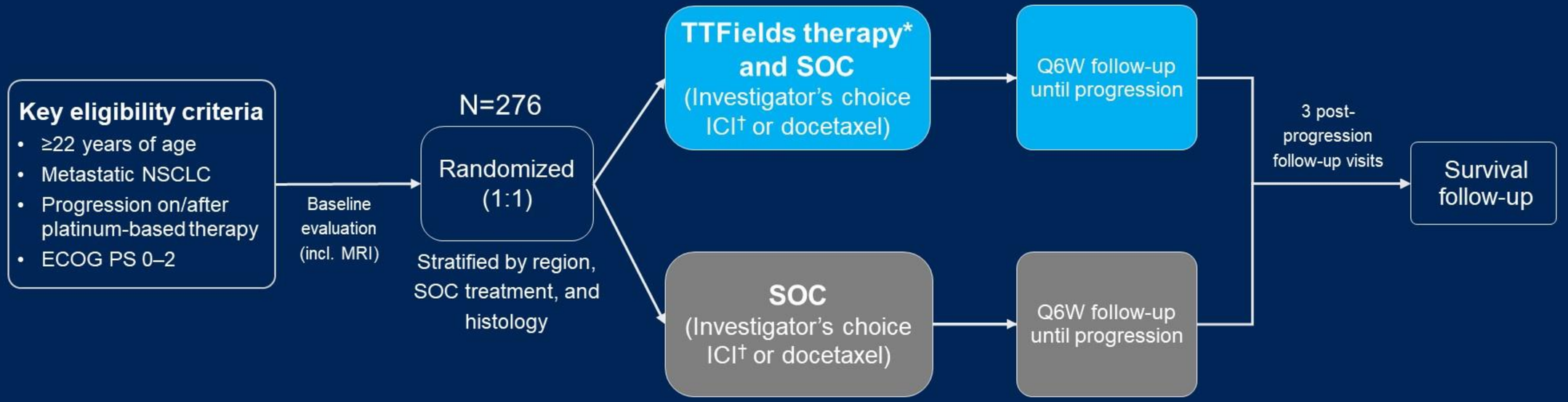
LUNAR Phase 3 Study Design

Objective: To evaluate safety and efficacy of TTFields therapy with standard of care (SOC) compared to SOC alone in metastatic NSCLC progressing on or after platinum-based therapy



Data cut-off: November 26, 2022
Study sites: 124 in 17 countries (North America, Europe, Asia)

*150 kHz; ≥18 h/day; †pembrolizumab, nivolumab, or atezolizumab.
ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; MRI, magnetic resonance imaging; NSCLC, non-small cell lung cancer; Q6W, every 6 weeks; SOC, standard of care; TTFields, Tumor Treating Fields.

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Response Rates in the ITT Population

	TTFields + SOC (n=137)	SOC (n=139)
Patients with a follow-up scan	n=122	n=127
ORR, % (95% CI)	20% (14–28)	17% (11–25)
Difference in ORR, % (95% CI)	3% (-8.5–15.0) *P*=0.5	
Best overall response, %		
Complete response	3%	1%
Partial response	18%	17%
Stable disease	49%	47%
Progressive disease	18%	26%
Not evaluable	2%	1%

- All 5 complete responses occurred in patients receiving an ICI
  - 4 with TTFields therapy
  - 1 with ICI alone
- Analysis of patterns of progression (infield* vs outfield) is ongoing

*Infield=thorax and upper abdomen
CI, confidence interval; ICI, immune checkpoint inhibitor; ITT, intent-to-treat; ORR, overall response rate; SOC, standard of care; TTFields, Tumor Treating Fields.

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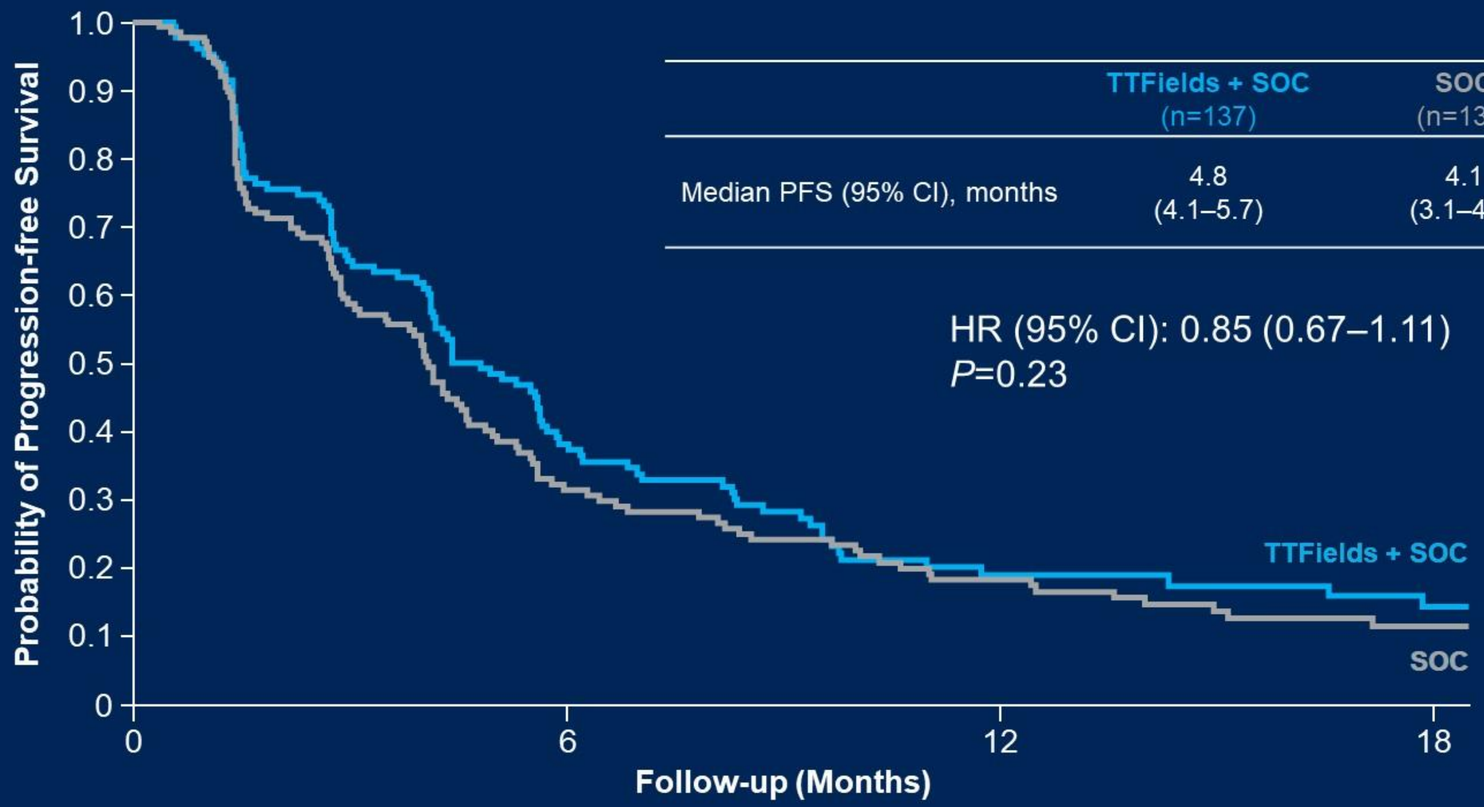
Progression-free Survival in the ITT Population



	TTFields + SOC (n=137)	SOC (n=139)
Median PFS (95% CI), months	4.8 (4.1–5.7)	4.1 (3.1–4.6)

HR (95% CI): 0.85 (0.67–1.11)
P=0.23

No. at risk:				
TTFields + SOC	137	44	17	9
SOC	139	40	21	9

PFS was defined as the time from date of randomization until date of disease progression, or death by any cause.
CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; PFS, progression-free survival; SOC, standard of care; TTFields, Tumor Treating Fields.

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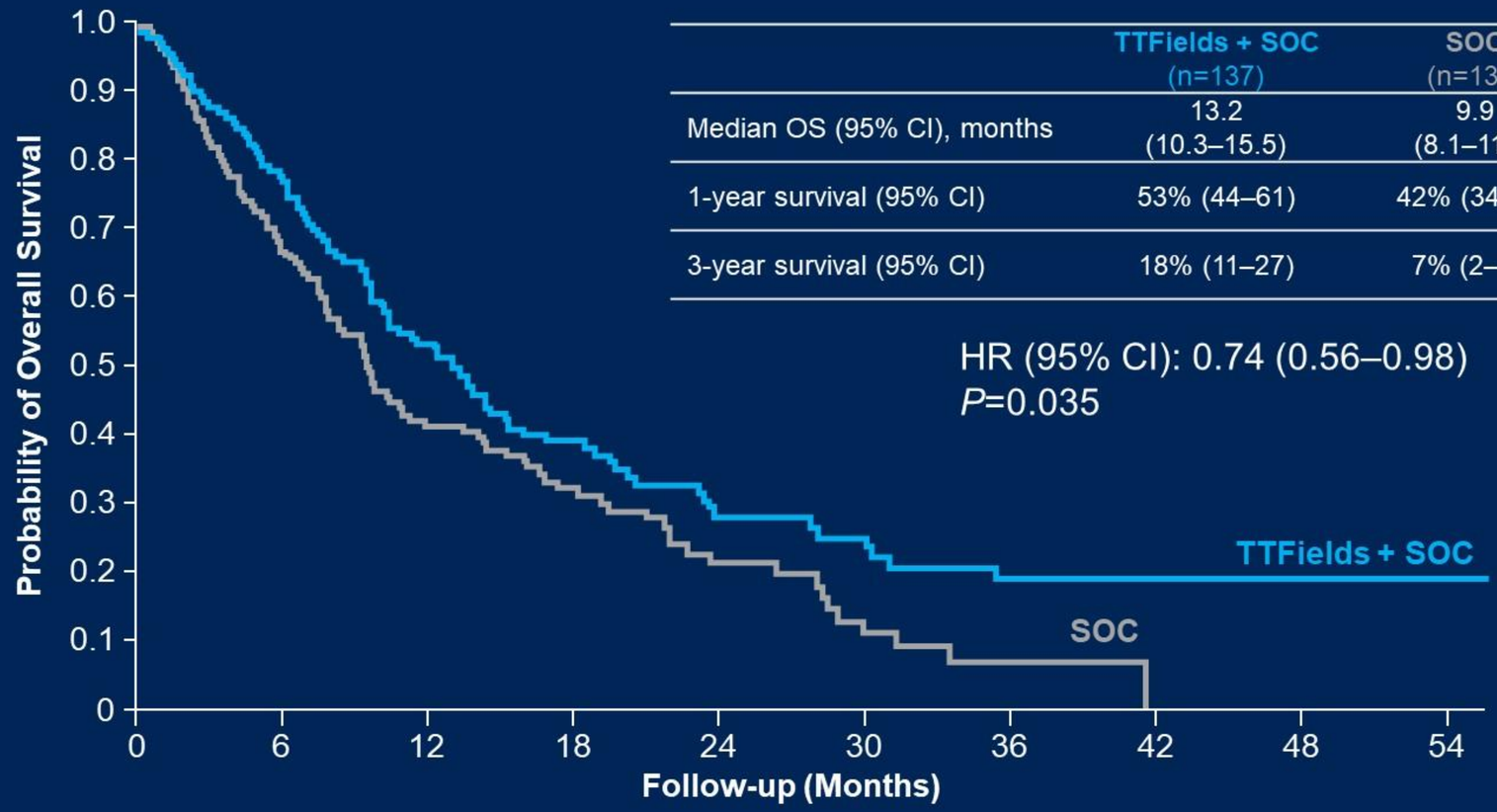
Overall Survival in the ITT Population



	TTFields + SOC (n=137)	SOC (n=139)
Median OS (95% CI), months	13.2 (10.3–15.5)	9.9 (8.1–11.5)
1-year survival (95% CI)	53% (44–61)	42% (34–50)
3-year survival (95% CI)	18% (11–27)	7% (2–15)

HR (95% CI): 0.74 (0.56–0.98)
P=0.035

No. at Risk:										
TTFields + SOC	137	100	62	36	22	16	11	9	5	3
SOC	139	96	54	32	16	7	3	0	0	0

CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat; OS, overall survival; SOC, standard of care; TTFields, Tumor Treating Fields.

Median (range) follow-up: 10.0 (0.03–58.7) months

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Safety and Tolerability

	TTFields + SOC (n=133)		SOC (n=134)	
	All grades	Grade ≥3	All grades	Grade ≥3
Any AE*	97%	59%	91%	56%
Most frequent AEs				
Dermatitis	**43%**	**2%**	**2%**	**0%**
Fatigue	28%	4%	37%	8%
Musculoskeletal pain	36%	3%	27%	4%
Dyspnea	20%	7%	25%	3%
Anemia	23%	8%	22%	8%
Diarrhea	19%	2%	19%	0%
Cough	18%	0%	19%	1%
Nausea	19%	0%	16%	1%
Leukopenia	17%	14%	18%	14%
Pneumonia	15%	11%	17%	11%
Alopecia	10%	0%	17%	1%
Respiratory tract infection	15%	3%	16%	0%
Localized edema	15%	1%	16%	2%
Any serious AE	53%		38%	
Any AE leading to discontinuation	36%		20%	
Any AE leading to death	10%		8%	

*Any AE; not necessarily related to treatment.
AE, adverse event; SOC, standard of care; HRQoL. Health-related quality of life; TTFields, Tumor Treating Fields.

- Majority of patients (94%) had ≥1 AE
- Comparable incidence of grade ≥3 AEs between arms
- No difference in rate of pneumonitis or other immune-related AEs
- No notable differences in HRQoL when TTFields therapy was added to SOC (detailed analysis ongoing)

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Conclusions

- Pivotal, phase 3 LUNAR study met its primary endpoint
- TTFields therapy with SOC provided a statistically significant and clinically meaningful 3-month improvement in median OS vs SOC (HR: 0.74, *P*=0.035) with no added systemic toxicities
  - Statistically significant ~8-month increase in median OS (from 10.8 to 18.5 months) was demonstrated with TTFields therapy and an ICI (HR: 0.63, *P*=0.030)
  - There was a 2.4-month difference in median OS (from 8.7 to 11.1) for TTFields therapy and docetaxel vs docetaxel alone (HR: 0.81, *P*=0.28)
- TTFields therapy should be considered part of SOC for metastatic NSCLC following progression on or after platinum-based therapy
- Additional studies evaluating TTFields therapy with current SOC for first-line metastatic and locally advanced NSCLC are underway
- TTFields therapy is a potentially paradigm shifting new treatment modality

HR, hazard ratio; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; OS, overall survival; SOC, standard of care; TTFields; Tumor Treating Fields.

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PRESENTED BY: Ticiana Leal, MD, Winship Cancer Institute - Emory University

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2023 ASCO ANNUAL MEETING

Sunvozertinib for the Treatment of NSCLC with *EGFR* Exon20 Insertion Mutations: the First Pivotal Study Results

Mengzhao Wang[1], Yun Fan[2], Meili Sun[3], Yongsheng Wang[4], Yanqiu Zhao[5], Bo Jin[6] Ying Hu[7], Zhigang Han[8], Xia Song[9], Anwen Liu[10], Kejing Tang[11], Cuimin Ding[12], Li Liang[13], Lin Wu[14], Junzhen Gao[15], Jianghong Wang[16], Ying Cheng[17], Jianying Zhou[18] Yong He[19], Li Zheng[20]

[1]Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, CN; [2]Zhejiang Cancer Hospital, Hangzhou, CN; [3]Central Hospital Affiliated to Shandong First Medical University, Jinan, CN; [4]Clinical Trial Center, National Medical Products Administration Key Laboratory for Clinical Research and Evaluation of Innovative Drugs, West China Hospital, Sichuan University, Chengdu, CN; [5]Respiratory Department of Internal Medicine, The Affiliated Cancer Hospital of Zhengzhou University, Zhengzhou, CN; [6]The First Hospital of China Medical University, Shenyang, CN; [7]Beijing Chest Hospital, Capital Medical University, Beijing, CN; [8]The Affiliated Cancer Hospital of Xinjiang Medical University, Wulumuqi, CN; [9]Shanxi Cancer Hospital, Taiyuan, CN; [10]Second Affiliated Hospital of Nanchang University, Nanchang, CN; [11]The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, CN; [12]The Fourth Hospital of Hebei Medical University, Shijiazhuang, CN; [13]Peking University Third Hospital, Beijing, CN; [14]Hunan Cancer Hospital, Changsha, CN; [15]The Affiliated Hospital of Inner Mongolia Medical University, Huhehaote, CN; [16]Chongqing Cancer Hospital, Chongqing, CN; [17]Jilin Cancer Hospital, Changchun, CN; [18]The First Affiliated Hospital, Zhejiang University School of Medicine, Zhejiang University, Hang Zhou, CN; [19]Army Medical Center of PLA, Chongqing, China; [20]Dizal Pharmaceutical, Shanghai, CN.

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PRESENTED BY: Mengzhao Wang, MD, Ph.D

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WU-KONG6 Study Design

Key inclusion criteria:

- Locally advanced or metastatic NSCLC
- Confirmed EGFR exon20ins in tumor tissues
- Received 1 – 3 lines of prior systemic therapies
- Disease progressed on or after platinum-based chemotherapy

DZD9008

300 mg, QD

Primary endpoint:

- IRC assessed† ORR

Secondary end point:

- IRC assessed† DoR
- ORR (investigator assessed), PFS, DCR, tumor size changes
- OS
- Safety and tolerability
- Pharmacokinetics

† According to RECIST 1.1. Tumor assessment every 6 weeks

IRC, independent review committee; ORR, objective response rate; DoR, duration of response; PFS, progression free survival; DCR, disease control rate; OS, overall survival.

Data cut-off for analysis: October 17, 2022

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Anti-tumor Efficacy of Sunvozertinib by IRC Assessment

Anti-tumor Efficacy	N = 97
Tumor Response, n (%)	
Partial response (confirmed)	59 (60.8)
Stable disease	26 (26.8)
Progression disease	6 (6.2)
Not evaluable	6 (6.2)
Objective Response Rate (ORR), n (%)	59 (60.8)
(95% CI)	(50.4, 70.6)
P value	< 0.0001
Disease Control Rate (DCR), n (%)	85 (87.6)
(95% CI)	(79.4%, 93.4%)

- The IRC assessed ORR (primary endpoint) was 60.8%, which met its pre-defined target with statistical significance.

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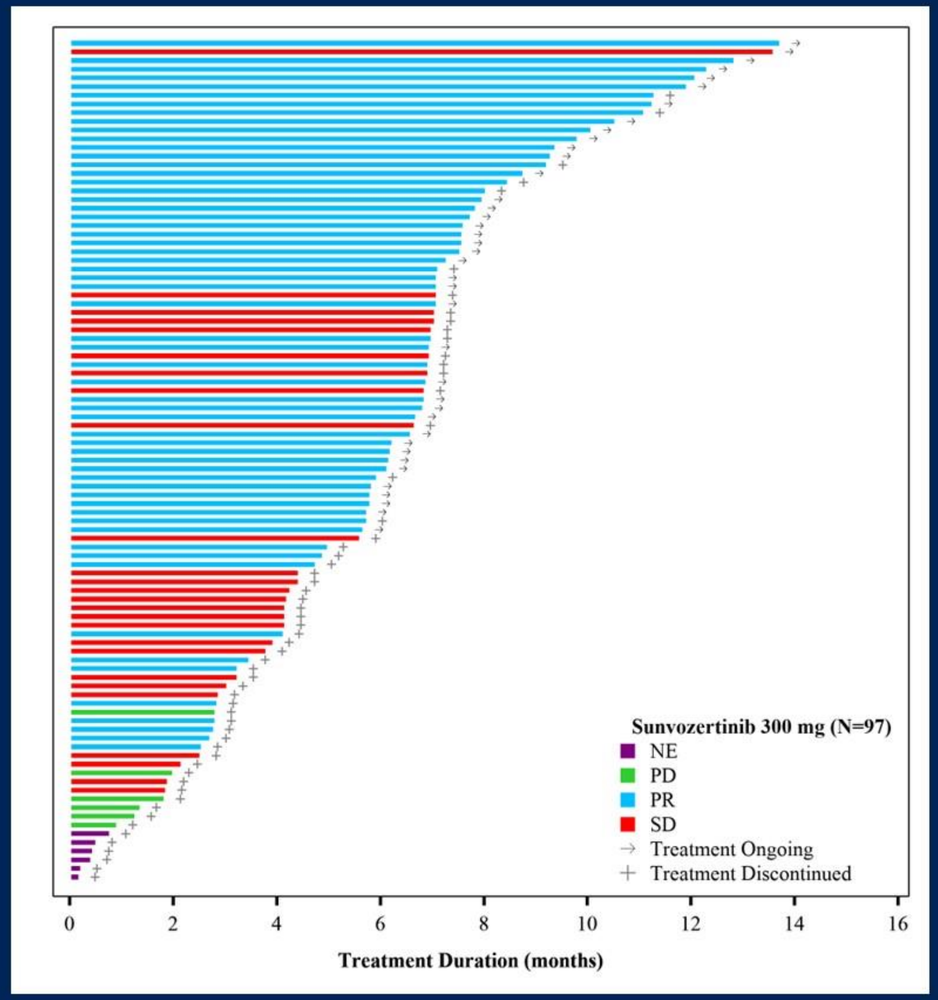
Duration on Treatment

- At the data cut-off date, median duration on treatment (DoT) was 7.0 months, and the longest DoT was 19.2 months.
- With median follow-up of 5.6 months after documented response, 38 of 59 responders (64.4%) were still responding. Median DoR was not reached. The longest DoR was > 11.2 months and the patient was still responding.



Tumor response was assessed by IRC
Data cut-off: Oct 17, 2022

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Safety Profile of Sunvozertinib

Common TEAE by PT	N = 104 All Grade	N = 104 ≥ Grade 3
Diarrhea	70（67.3）	8（7.7）
Blood CPK increase	60（57.7）	18（17.3）
Rash	56（53.8）	1（1.0）
Anemia	51（49.0）	6（5.8）
Blood creatinine increase	39（37.5）	0（0.0）
Paronychia	34（32.7）	2（1.9）
Body weight decrease	30（28.8）	1（1.0）
White blood cell decrease	27（26.0）	0（0.0）
Lipase increase	27（26.0）	2（1.9）
Vomiting	25（24.0）	1（1.0）
Decreased appetite	25（24.0）	2（1.9）
Mouth ulceration	24（23.1）	0（0.0）

- Safety profile of sunvozertinib was similar to other EGFR TKIs. Majorities of the AEs were grade 1 or 2.

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Conclusion

- In WU-KONG6 pivotal study, sunvozertinib demonstrated significant anti-tumor efficacy and well-tolerated safety profile in platinum-based chemotherapy pretreated NSCLC with EGFR exon20ins.
  - The confirmed ORR at 300 mg QD was 60.8% assessed by IRC.
  - Anti-tumor efficacy was observed across a variety of EGFR exon20ins subtypes and regardless of insertion locations.
  - Anti-tumor efficacy was observed in patients with baseline brain metastasis and who failed amivantamab treatment.
  - Sunvozertinib demonstrated comparable safety profile to other EGFR TKIs.
- Sunvozertinib can be a potential treatment option for NSCLC with EGFR exon20ins.
- A phase III, randomized, multinational study (WU-KONG28, NCT05668988) is ongoing to assess sunvozertinib versus platinum-based chemotherapy in the 1st line EGFR exon20ins NSCLC.

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2023 ASCO ANNUAL MEETING

Phase II randomized study of maintenance atezolizumab (A) versus atezolizumab + talazoparib (AT) in patients with SLFN11 positive extensive stage small cell lung cancer SWOG S1929

Authors: **Nagla Fawzy Abdel Karim,** Jieling Miao, Karen L. Reckamp, Carl Michael Gay, Lauren Averett Byers, Yingqi Zhao, Mary Weber Redman, Daniel R. Carrizosa, Wei-Lien Wang, William J. Petty, Kathan Mehta, Bryan A. Faller, Edem S. Agamah, Samer S. Kasbari, Rajini Katipamula Malisetti, Atul Kumar, John Schallenkamp, Krishna Chaitanya Alluri, Jhanelle Elaine Gray, Karen Kelly.

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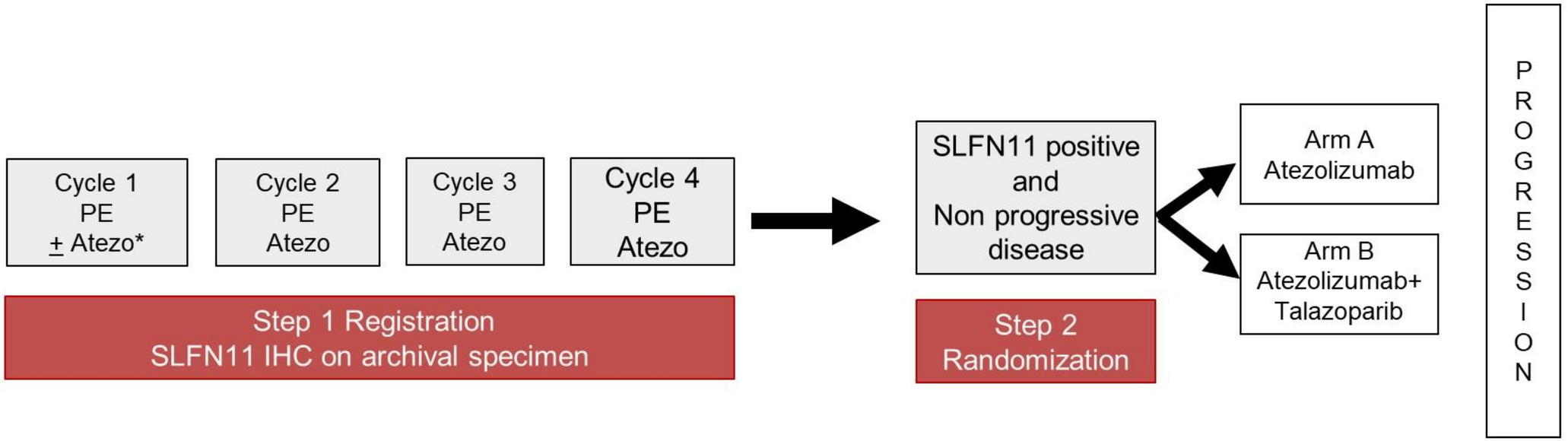
PRESENTED BY: Nagla Abdel Karim, MD

S1929: Phase II Study of Maintenance Atezolizumab Versus Atezolizumab in Combination with Talazoparib in Patients with SLFN11 Positive Extensive Stage Small Cell Lung Cancer (ES-SCLC) NCT04334941



Hypothesis: The addition of talazoparib to maintenance atezolizumab will improve PFS in SLFN11+ SCLC.

Primary Endpoint: PFS

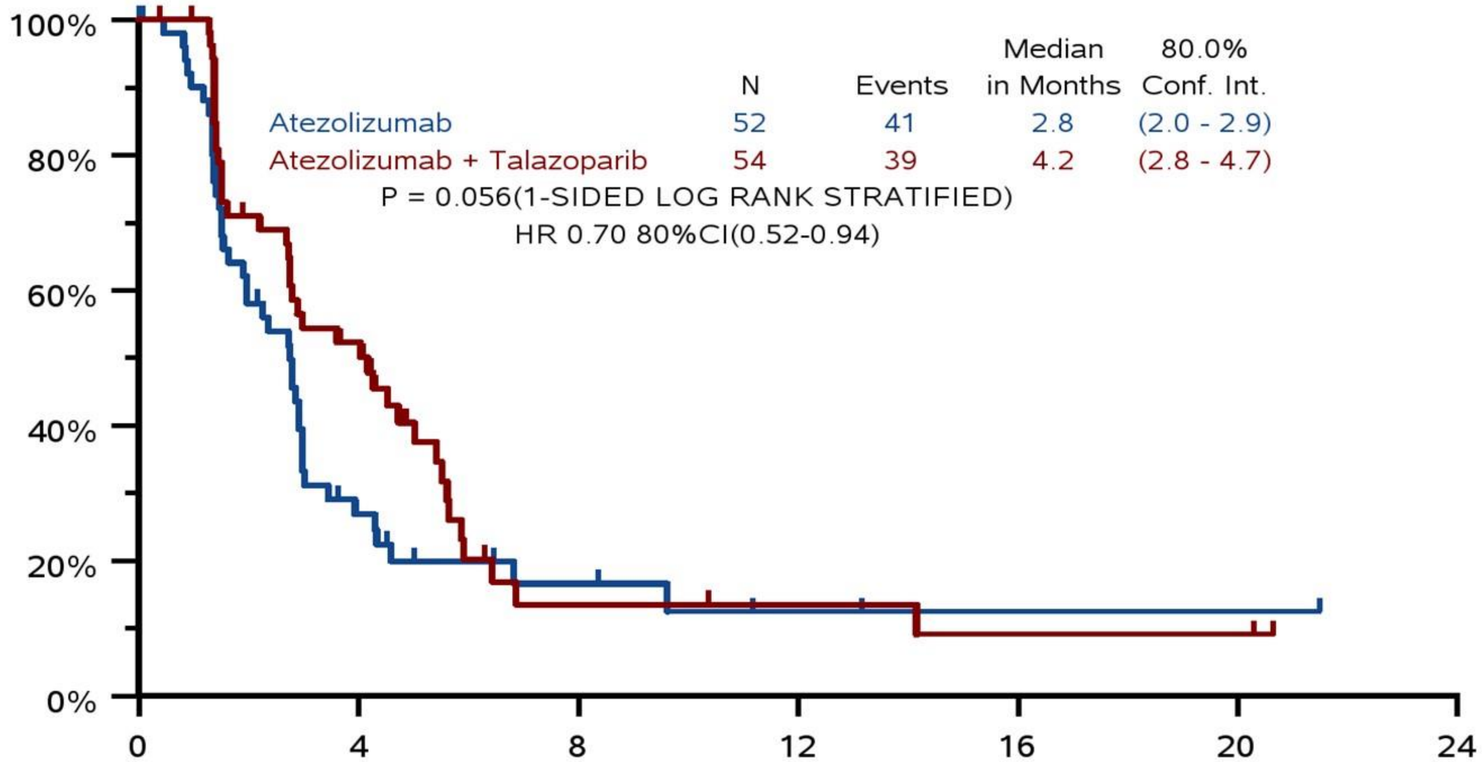
Secondary endpoints: OS, ORR, AE.

TM Objective: To bank specimens for future correlative studies.

**Atezolizumab was optional if the patient is hospitalized for cycle 1*

A maximum of 9 weeks after the end of cycle 4 was allowed prior to randomization

Progression Free Survival



Median FU time among patients who are alive is 5 months with a range of (0, 21.5M)

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SWOG CANCER RESEARCH NETWORK | NCI National Clinical Trials Network | NCI Community Oncology Research Program

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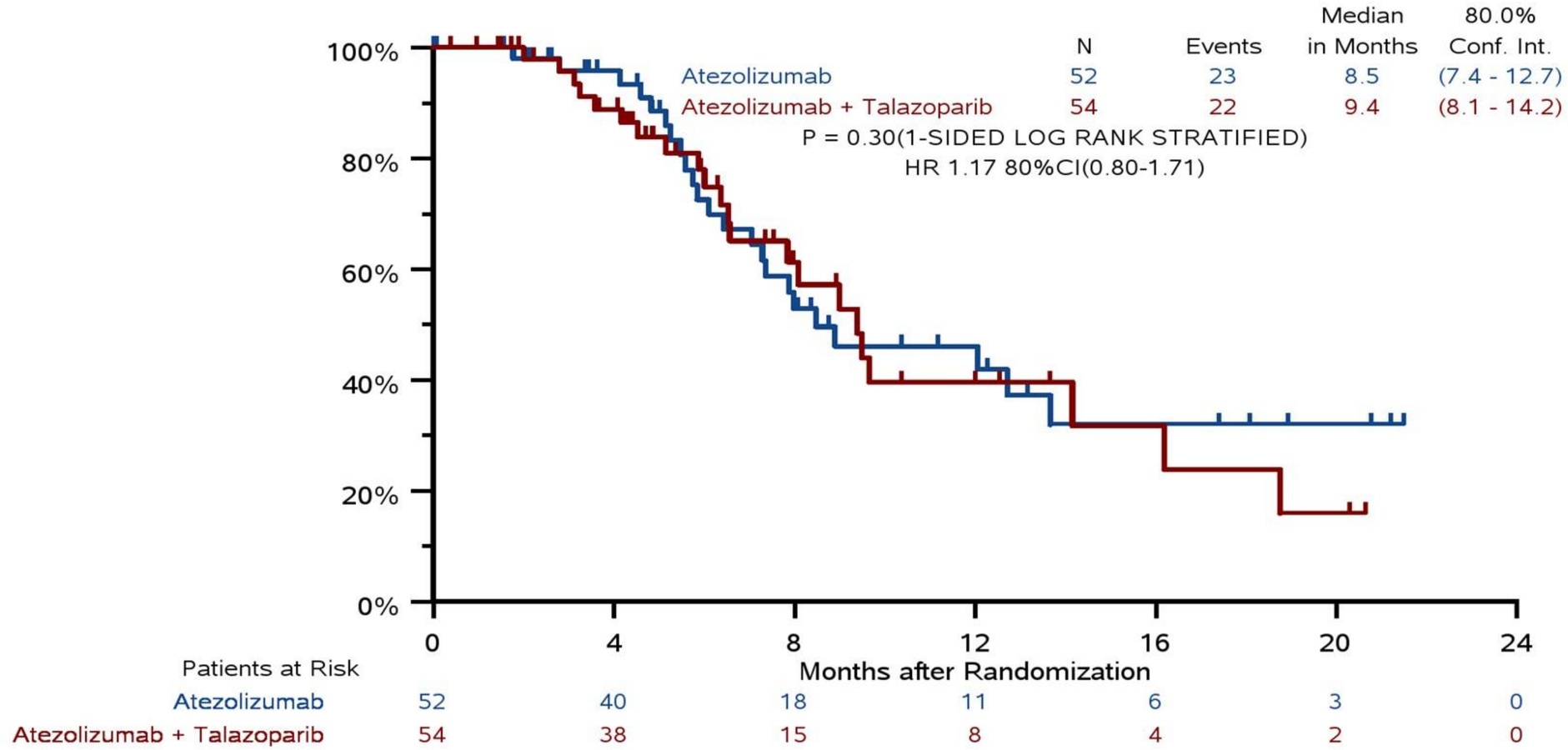
Preliminary OS



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Toxicity

- Grade 3 or higher treatment related non-hematological adverse events (AEs) occurred in 13% pts in A and 15% in AT.
- Hematological AEs occurred 4% in A compared to 50% pts in AT (Expected for T) ($p < 0.001$).
- Only three pts discontinued treatment due to toxicity (2 in A and 1 in AT).

Conclusion

- S1929 met its primary endpoint demonstrating that maintenance AT improved PFS in SLFN11-positive patients with ES-SCLC.
- Hematologic toxicity was increased with AT as expected, mainly grade 3 anemia.
- This study demonstrates the feasibility of conducting biomarker selected trials in SCLC, paving the way for future evaluation of novel therapies in selected SCLC populations.
- We are currently analyzing the association of SLFN11 expression levels to the clinical outcomes.

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First-in-human dose-escalation trial of BI 764532, a delta-like ligand 3/CD3 IgG-like T-cell engager, in patients with DLL3-positive small-cell lung cancer and neuroendocrine carcinoma

Martin Wermke[1], Enriqueta Felip[2], Yasutoshi Kuboki[3], Olatunji B. Alese[4], Daniel Morgensztern[5], Cyrus Sayehli[6], Miguel F Sanmamed[7], Edurne Arriola[8], Zohra Oum' Hamed[9], Eric Song[10], Matus Studeny[11], Valentina Gambardella[12]

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Dr Martin Wermke

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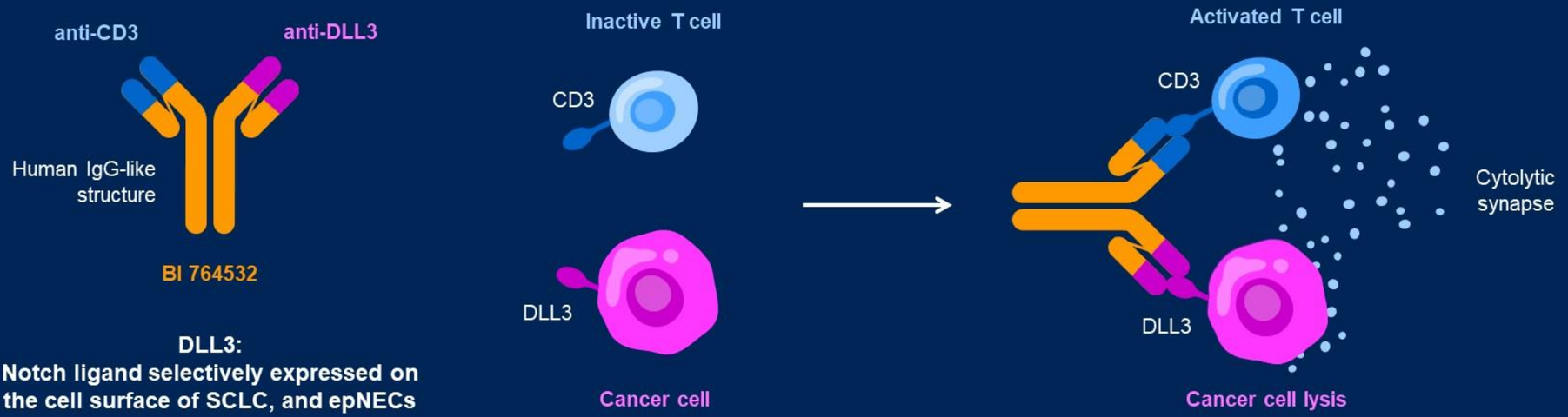
BI 764532: a novel DLL3-targeting T cell engager



- BI 764532 redirects the patient's own T cells to lyse DLL3-expressing cancer cells
- Potent preclinical antitumor activity in DLL3-positive cells and xenograft models[1]

DLL3, delta-like canonical Notch ligand 3; epNECs, extrapulmonary neuroendocrine carcinomas; SCLC, small-cell lung cancer

1. Hipp S, et al. Clin Cancer Res 2020;26(19):5258–68

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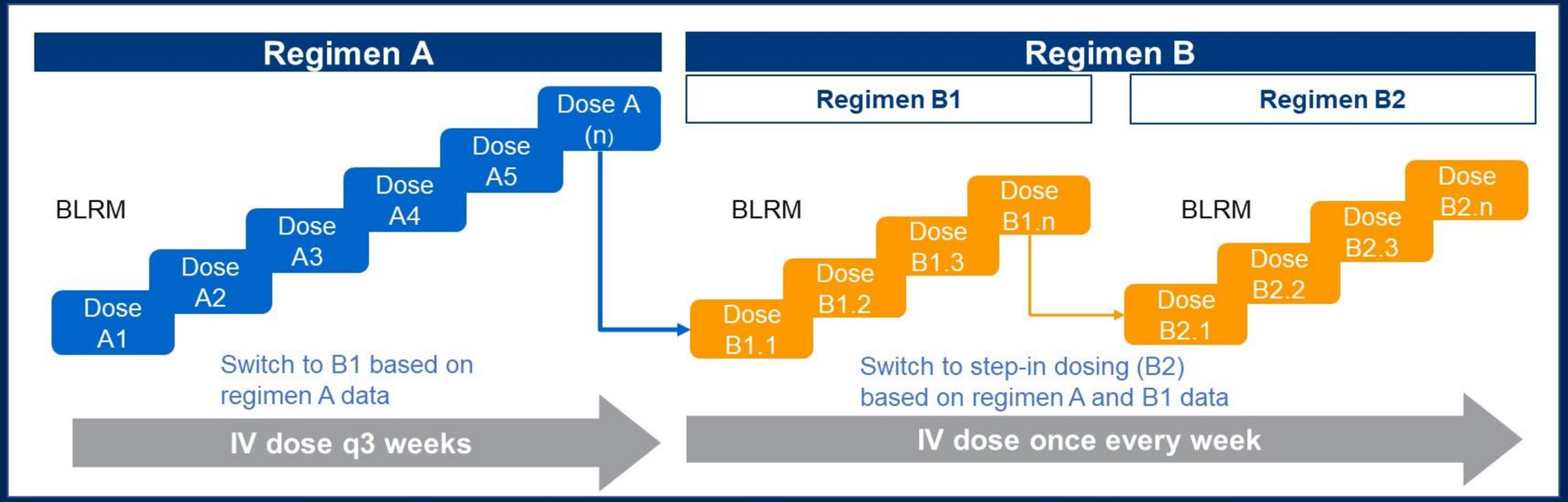
First-in-human dose escalation trial of BI 764532 in patients with SCLC or NECs: NCT04429087



Primary endpoints	Secondary endpoints
• MTD • DLTs in the MTD evaluation period	• Objective response (RECIST 1.1) • PK parameters

- **Patients are treated until disease worsening or a maximum duration of 36 months**

BLRM, Bayesian Logistic Regression Model with overdose control; DLTs, dose-limiting toxicities; IV, intravenous; MTD, maximum tolerated dose; PK, pharmacokinetic; RECIST, Response Evaluation Criteria In Solid Tumors version 1.1

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Inclusion criteria and patient baseline characteristics

Key inclusion criteria

- Advanced SCLC, LCNEC, or epNEC
- DLL3 positive (archived tissue or in-study biopsy) according to central* review
- Failed/ineligible for available standard therapies (≥1 line of platinum-based chemotherapy)
- Adequate liver, bone marrow and renal function
- ECOG PS 0/1

As of March 2023†	N=107‡
Median age, years (range)	60.0 (32–79)
Male, n (%)	61 (57)
Prior lines of therapy, n (%)	
1–2	72 (67)
≥3	33 (31)
ECOG PS 0/1, n (%)	28 (26)/78 (73)
Prior PD-1/PD-L1, n (%)	52 (49)
Brain/liver metastases, n (%)	41 (38)/60 (56)

*Ventana DLL3 (SP347) assay at the Roche CDx CAP/CLIA laboratory

†Data snapshot: 26th March 2023

‡Safety population: ≥1 dose of BI 764532

CAP/CLIA, College of American Pathologists & Clinical Laboratory Improvement Amendment; ECOG PS, Eastern Cooperative Oncology Group performance status; epNEC, extrapulmonary neuroendocrine carcinoma; LCNEC, large cell neuroendocrine lung carcinoma; PD-1, programmed cell death protein -1; PD-L1, programmed death-ligand 1; SCLC, small cell lung cancer

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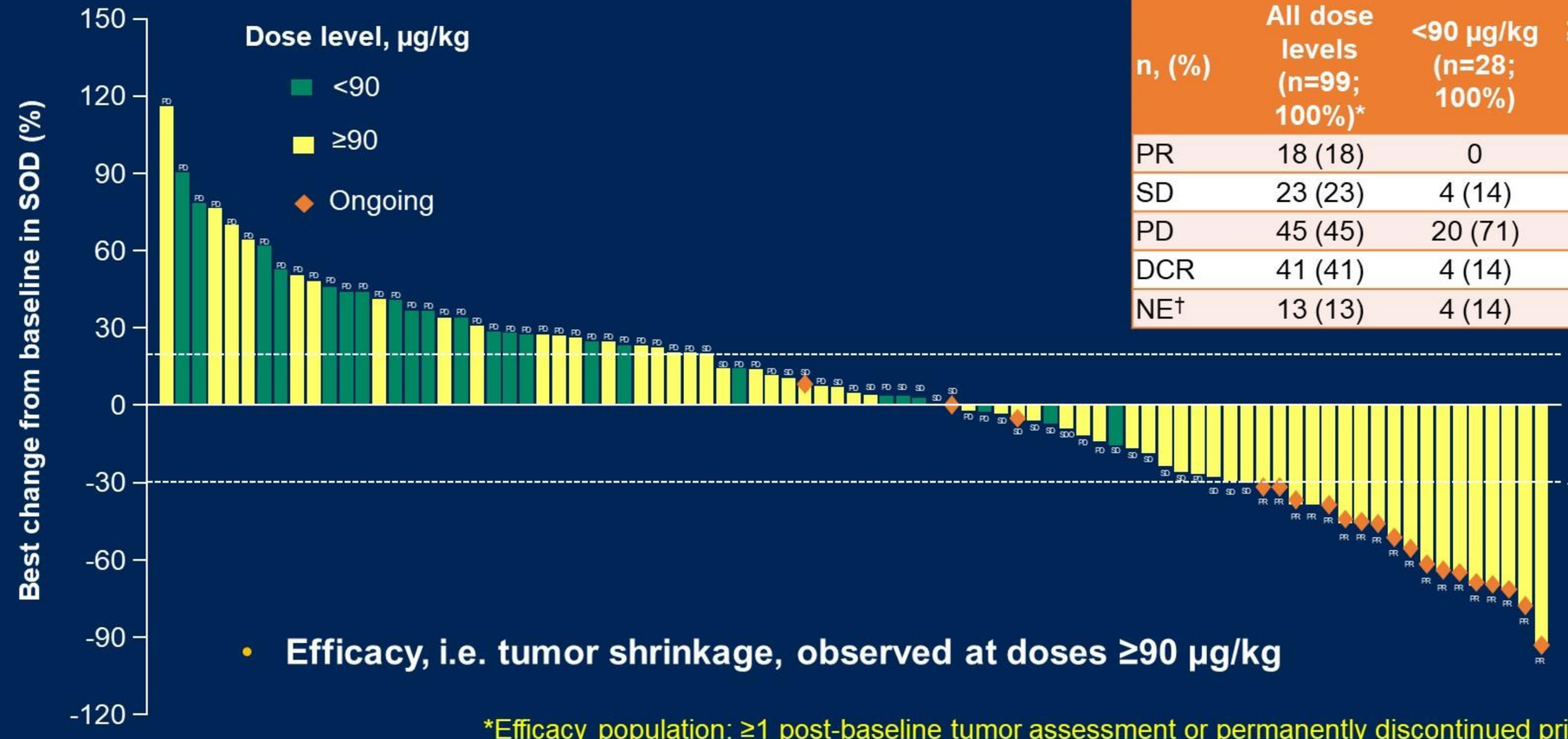
Overall efficacy



n, (%)	All dose levels (n=99; 100%)*	<90 µg/kg (n=28; 100%)	≥90 µg/kg (n=71; 100%)
PR	18 (18)	0	18 (25)
SD	23 (23)	4 (14)	19 (27)
PD	45 (45)	20 (71)	25 (35)
DCR	41 (41)	4 (14)	37 (52)
NE†	13 (13)	4 (14)	9 (13)

- **Efficacy, i.e. tumor shrinkage, observed at doses ≥90 µg/kg**

*Efficacy population: ≥1 post-baseline tumor assessment or permanently discontinued prior to tumor assessment; responses evaluated per RECIST v1.1 criteria; †Discontinued prior to tumor assessment

DCR, disease control rate; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SOD, sum of diameters

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Most common treatment-related AEs (>10% patients)

TRAE, n (%)	Total (N=107; 100%)* All grade	Grade 1–2	Grade 3–5
Number of pts with ≥1 TRAE	**92 (86)**	**63 (59)**	**29 (27)**
CRS	63 (59)	61 (57)	2 (2)
Lymphocyte count decreased	21 (20)	4 (4)	17 (16)
Dysgeusia	21 (20)	21 (20)	0
Asthenia	20 (19)	19 (18)	1 (<1)
Pyrexia	19 (18)	19 (18)	0
AST increased	15 (14)	13 (12)	2 (2)
Fatigue	15 (14)	14 (13)	1 (<1)
Nausea	13 (12)	13 (12)	0

- **CRS managed with supportive care, corticosteroids, and/or anti-IL-6R antibodies**
- **Patients with AEs/TRAEs leading to discontinuation: 13%/4%**

*Safety population: ≥1 dose of BI 764532

AST, aspartate aminotransferase; CRS, cytokine release syndrome; IL-6R, interleukin 6 receptor; TRAEs, treatment-related AEs

Summary and conclusions

- At clinically efficacious BI 764532 dose levels, safety is clinically acceptable and manageable
- The drug discontinuation rate due to TRAEs was low: 4%
- CRS was reported in 59% of patients; cases were mostly Grade 1–2, occurred during initial drug administrations, and were manageable with standard supportive care
- Promising efficacy (at doses ≥90 µg/kg):
  - Overall ORR: 25%
  - SCLC: 26%
  - epNEC: 19%
  - LCNEC: 60%
- Responses appeared to be durable
- Further dose optimization is ongoing

epNEC, extrapulmonary neuroendocrine carcinoma; ORR, overall response rate; SCLC, small-cell lung cancer; TRAE, treatment-related adverse event

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Questions?