XXIV SPOTKANIE Po ASCO

Zaawansowany rak płuca

Anna Wrona

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Plan prezentacji

- Opcja leczenia 1L zNDRP NGS(-) – ADC+IM+/-CHT
- Opcja leczenia bez udziału CHT – po niepowodzeniu IM w 1L – ram+pembro
- Opcja leczenia 2L w EGFRins20 zNDRP
- Opcja leczenia po progresji na EGFRi, METamp(+)
- Dwie opcje leczenia po progresji na iEGFR 3 gen
- Opcja leczenia 1L anty-KRAS
- Opcja leczenia anty-HER2
- Opcja leczenia podtrzymującego w ED DRP
- Opcja leczenia 2L w ED DRP
- Opcja leczenia immunokompetentnego w neo grasicy

2025 ASCO ANNUAL MEETING

TROPION-Lung02: Datopotamab deruxtecan (Dato-DXd) plus pembrolizumab (pembro) with or without platinum chemotherapy (Pt-CT) as first-line (1L) therapy for advanced non-small cell lung cancer (aNSCLC)

Benjamin P. Levy,[1] Luis G. Paz-Ares,[2] Chien-Chung Lin,[3] Scott Herbert,[4] Tsung-Ying Yang,[5] Anthony W. Tolcher,[6] Yanyan Lou,[7] Yoshitaka Zenke,[8] Diego Cortinovis,[9] Enriqueta Felip,[10] Manuel Domine Sr.,[11] Konstantinos Leventakos,[12] Emiliano Calvo,[13] Atsushi Horiike,[14] Edward Pan,[15] Keisuke Matsubara,[16] Xiaoyu Jia,[15] Rachel A. Chiaverelli,[15] Michael J. Chisamore,[17] Yasushi Goto[18]

[1]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins Medicine, Baltimore, MD, USA; [2]Hospital Universitario 12 de Octubre, CNIO-H12O Lung Cancer Unit, Universidad Complutense & CiberOnc, Madrid, Spain; [3]Department of Internal Medicine, National Cheng Kung University Hospital and Tainan Hospital, Ministry of Health & Welfare, Tainan City, Taiwan; [4]Quantum, Santa Fe, NM, USA; [5]Department of Chest Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [6]NEXT Oncology, San Antonio, TX, USA; [7]Mayo Clinic, Jacksonville, FL, USA; [8]Department of Thoracic Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [9]Fondazione IRCCS San Gerardo dei Tintori, Monza, Italy; [10]Vall d'Hebron Hospital Campus, Vall d'Hebron Institute of Oncology, Universitat Autònoma de Barcelona, Spain; [11]Department of Oncology, Hospital Universitario Fundación Jiménez Díaz (IIS-FJD), Madrid, Spain; [12]Mayo Clinic, Rochester, MN, USA; [13]START Madrid-CIOCC, Centro Integral Oncológico Clara Campal, Madrid, Spain; [14]Division of Medical Oncology, Department of Medicine, Showa University School of Medicine, Tokyo, Japan; [15]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [16]Daiichi Sankyo Co, Ltd., Tokyo, Japan; [17]Merck & Co., Inc., Rahway, NJ, USA; [18]National Cancer Center Hospital, Tokyo, Japan.

PRESENTED BY: Benjamin P. Levy, MD, FASCO

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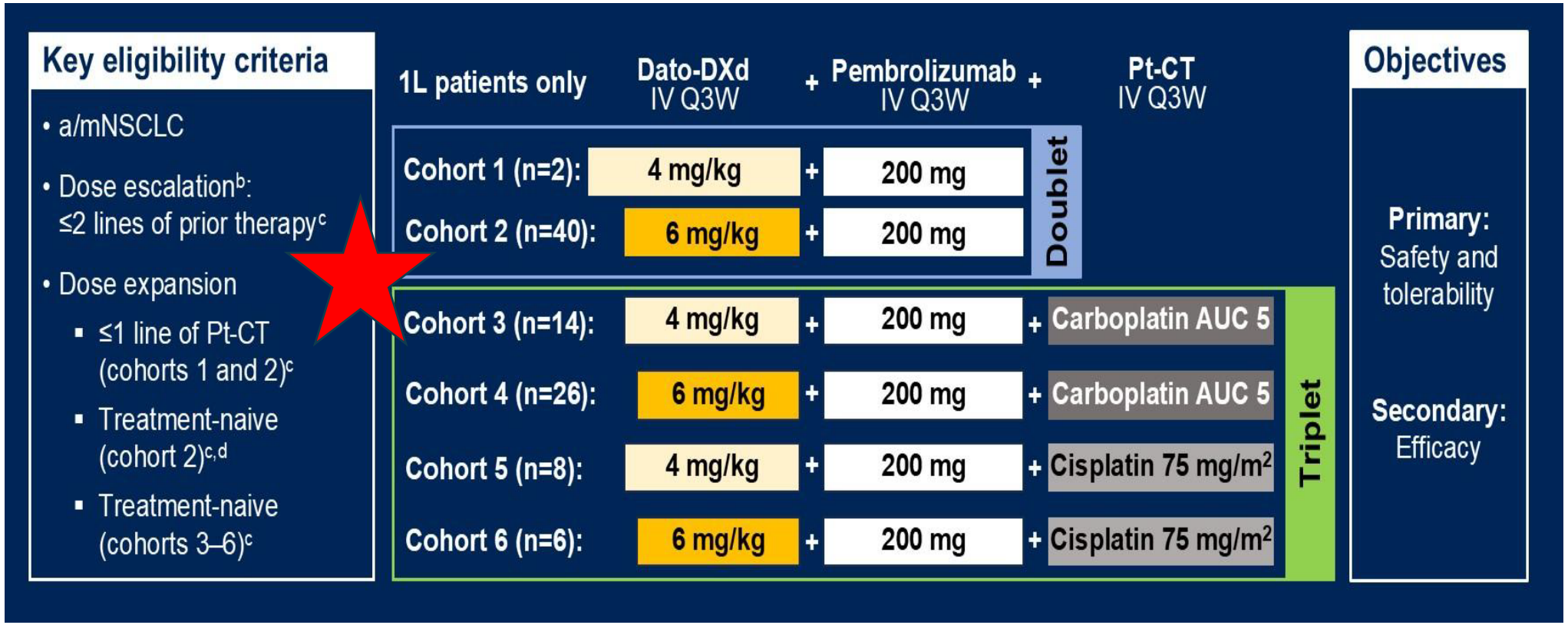
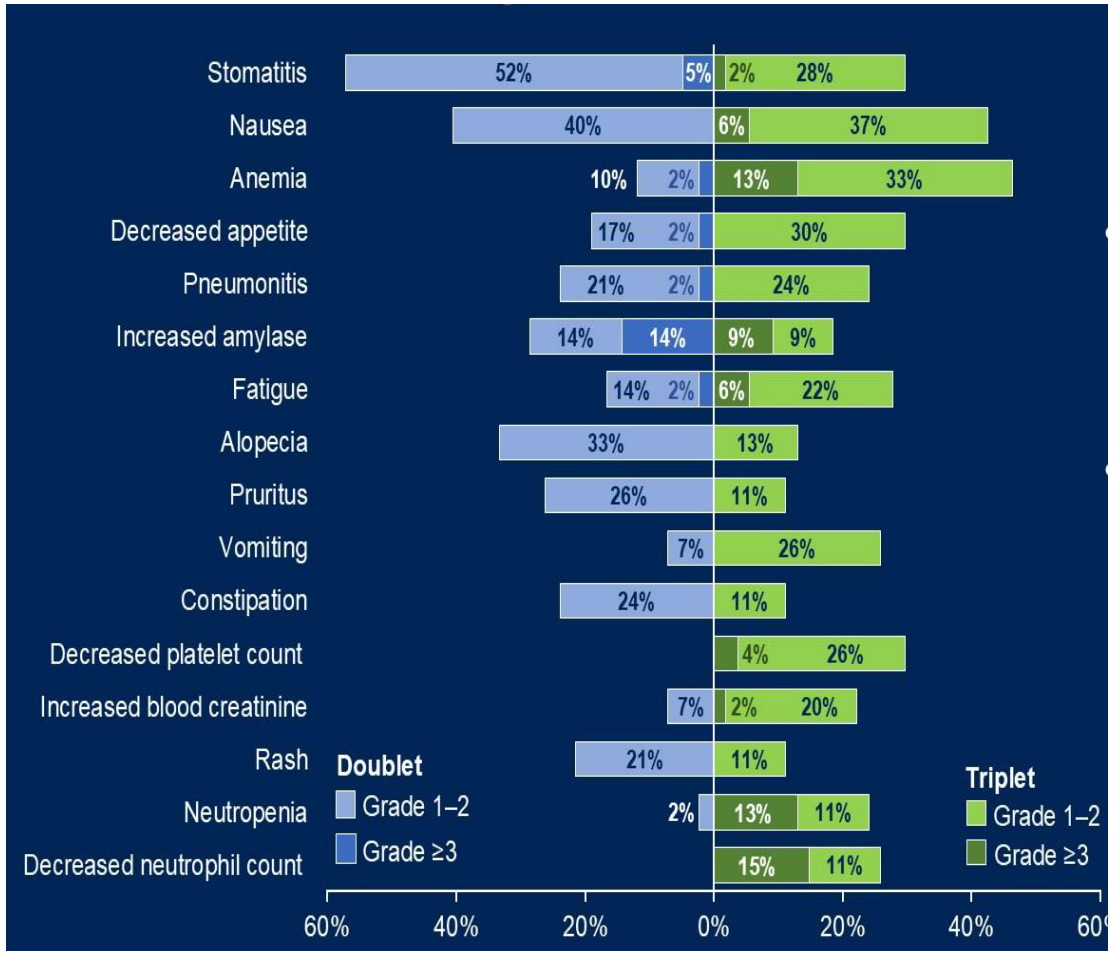
TROPION-Lung02 – BK non-R fazy 1b, 1L datopotamab DXd (ADC a/TROP2) +pembro+\-CHT w zNDRP , bez wiodących zaburzeń molekularnych



Charakterystyka chorych

	All 1L (N=96)	
	Doublet (n=42)	Triplet (n=54)
Age, median (range), years	65 (48–83)	64 (33–78)
Male, n (%)	32 (76.2)	34 (63.0)
Asian race, n (%)	31 (73.8)	23 (42.6)
Histology, n (%)		
Nonsquamous	32 (76.2)	40 (74.1)
Squamous	10 (23.8)	14 (25.9)
History of brain metastases, n (%)	4 (9.5)	10 (18.5)
ECOG PS 1, n (%)	24 (57.1)	33 (61.1)
Dato-DXd dosing, n (%)		
4 mg/kg	2 (4.8)	22 (40.7)
6 mg/kg	40 (95.2)	32 (59.3)
PD-L1 expression[a], n (%)		
<50%	30 (71.4)	40 (74.1)
≥50%	5 (11.9)	10 (18.5)
NE	7 (16.7)	4 (7.4)

Najczęściej występujące TRAE: zapalenie błony śluzowej jamy ustnej, nudności, niedokrwistość, spadek apetytu, bez AESI st. 4 i 5



Event, n (%)	All 1L (N=96) Doublet (n=42)	Triplet (n=54)
TRAEs	39 (92.9)	54 (100)
Grade ≥3	17 (40.5)	30 (55.6)
Associated with death	0	0
TRAEs associated with dose modifications		
Dose reduction of any drug	8 (19.0)	14 (25.9)
Dose reduction of Dato-DXd	8 (19.0)	7 (13.0)
Discontinuation of any drug	14 (33.3)	20 (37.0)
Discontinuation of Dato-DXd	13 (31.0)	16 (29.6)
Serious TRAEs	5 (11.9)	12 (22.2)
Grade ≥3	4 (9.5)	9 (16.7)
AESIs		
Oral mucositis/stomatitis	26 (61.9)	22 (40.7)
Grade 3	2 (4.8)	1 (1.9)
Adjudicated drug-related ILD/pneumonitis	11 (26.2)	14 (25.9)
Grade 3	2 (4.8)	1 (1.9)
Ocular surface events	9 (21.4)	18 (33.3)
Grade 3	1 (2.4)	2 (3.7)

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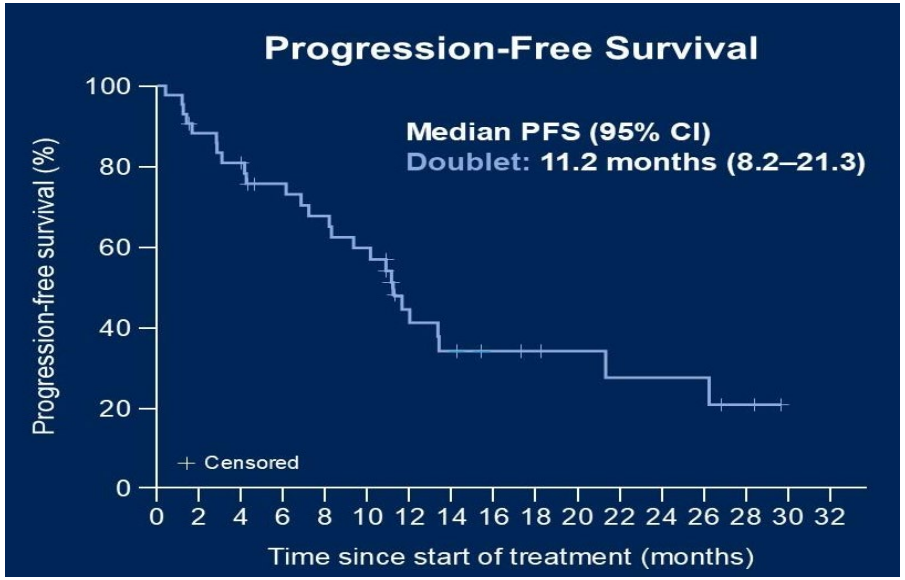
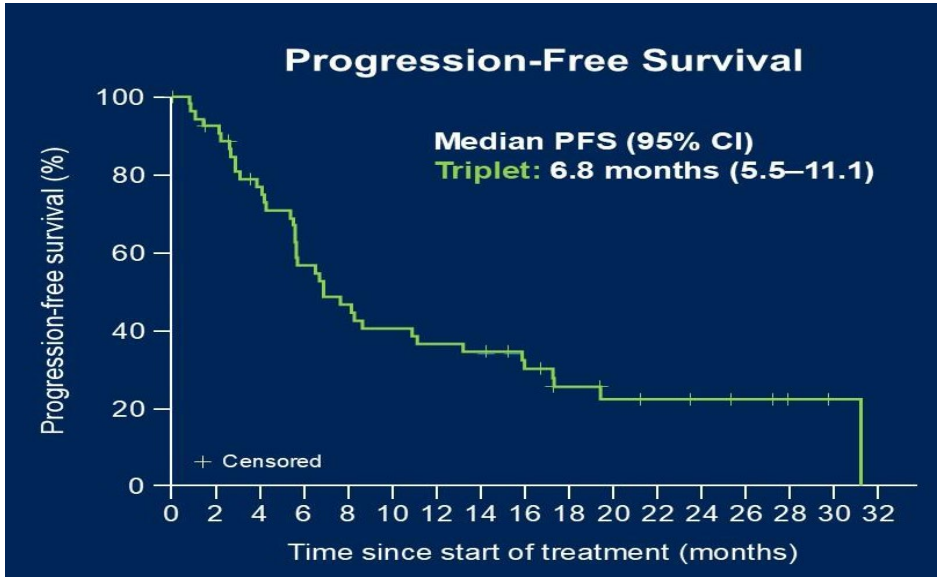
Skuteczność dubletu (mPFS=11, ORR=55) i tripletu (mPFS=7, ORR=55) z DatoDXd





	Doublet (n=42)
Confirmed ORR*, n (%)	**23 (54.8)**
95% CI	38.7–70.2
Median DOR, months	**20.1**
95% CI	9.7–NE
DCR, n (%)	**37 (88.1)**
95% CI	74.4–96.0
Median TTR, months	**1.4**
Range	1.2–7.0
Median PFS, months	**11.2**
95% CI	8.2–21.3
Median OS, months	**NE**
95% CI	19.2–NE

	Triplet (n=54)
Confirmed ORR*, n (%)	**30 (55.6)**
95% CI	41.4–69.1
Median DOR, months	**13.7**
95% CI	5.7–NE
DCR, n (%)	**48 (88.9)**
95% CI	77.4–95.8
Median TTR, months	**1.4**
Range	1.2–9.6
Median PFS, months	**6.8**
95% CI	5.5–11.1
Median OS, months	**17.4**
95% CI	9.1–NE

DatoDXd skuteczny w NDRP o wysokiej i niskiej immunoekspresji PD-L1

	Doublet		Triplet	
	PD-L1 <50%	PD-L1 ≥50%	PD-L1 <50%	PD-L1 ≥50%
N	30	5	40	10
ORR,% (95% CI)	**53.3%** (34.3–71.7)	**100%** (47.8–100)	**55.0%** (38.5-70.7)	**60.0%** (26.2–87.8)
BoR (%)				
CR	3.3%	0	2.5%	10.0%
PR	50%	100%	52.5%	50.0%
DOR, months (95% CI)	**12.0** (8.0–NE)	**NE** (5.5–NE)	**14.6** (5.3–NE)	**NE** 4.1–NE
DCR (%) (95% CI)	**96.7** (82.8–99.9)	**100** (47.8–100)	**87.5** (73.2–95.8)	**90.0** (55.5–99.7)
Median PFS, months (95% CI)	**11.1** (7.2–13.3)	**NE** (8.3–NE)	**6.4** (5.5–13.2)	**6.8** (0.8–NE)
Median OS, months (95% CI)	**NE** (19.2-NE)	**NE** (12.6-NE)	**13.3** (7.7-NE)	**NE** (0.8-NE)

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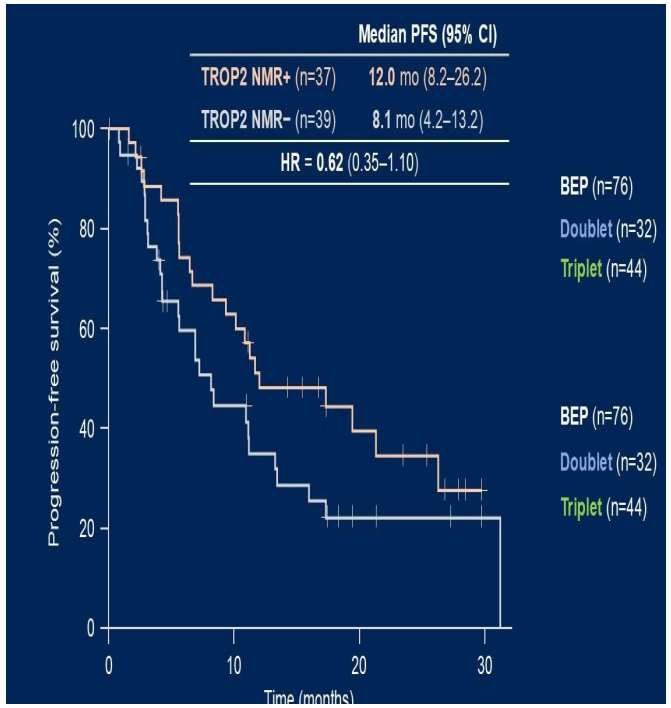
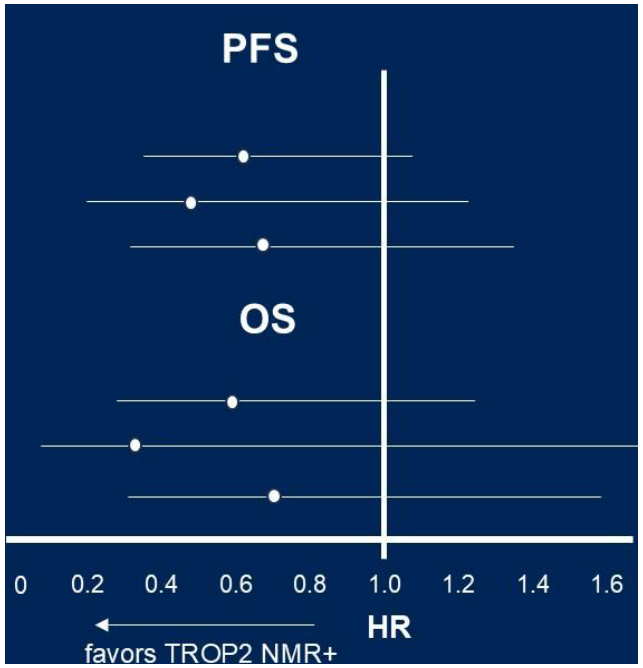
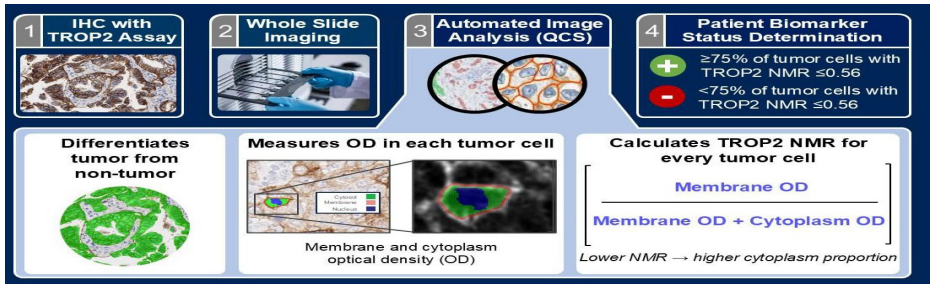
Znormalizowany wskaźnik błonowy (NMR) potencjalnym czynnikiem predykcyjnym

		TROP2 NMR biomarker evaluable, 1L (n=76)[a]	
	All 1L (N=96)	TROP2 NMR+ (n=37)	TROP2 NMR- (n=39)
Age, median (range), years	64 (33–83)	61 (33–76)	65 (48–82)
Male, n (%)	66 (68.8)	24 (64.9)	27 (69.2)
Asian race, n (%)	54 (56.3)	23 (62.2)	21 (53.8)
Histology, n (%)			
Nonsquamous	72 (75.0)	32 (86.5)	27 (69.2)
Squamous	24 (25.0)	5 (13.5)	12 (30.8)
History of brain metastases, n (%)	14 (14.6)	5 (13.5)	6 (15.4)
ECOG PS 1, n (%)	57 (59.4)	19 (51.4)	26 (66.7)
PD-L1 expression[b], n (%)			
<50%	70 (72.9)	26 (70.3)	31 (79.5)
≥50%	15 (15.6)	8 (21.6)	6 (15.4)
NE	11 (11.5)	3 (8.1)	2 (5.1)







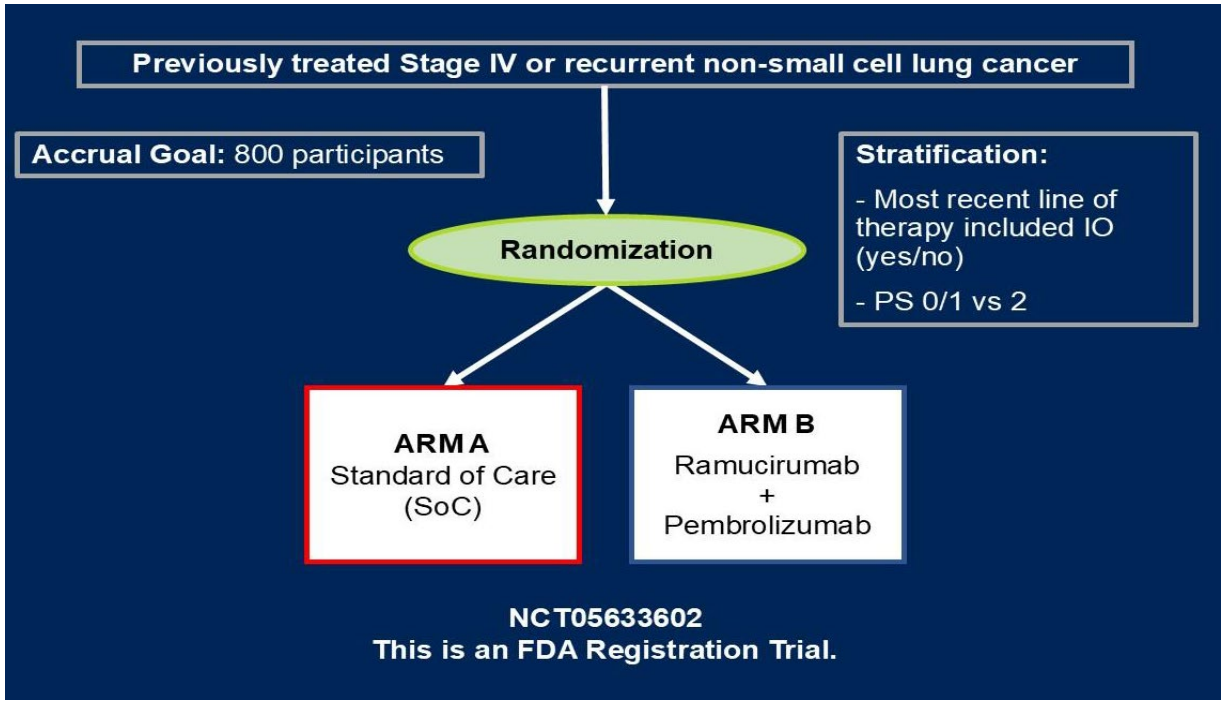
2025 ASCO ANNUAL MEETING

PRAGMATICA-LUNG (SWOG S2302): A prospective pragmatic randomized study of ramucirumab plus pembrolizumab versus standard of care for participants previously treated with immunotherapy for stage IV or recurrent non-small cell lung cancer

Konstantin H. Dragnev, MD[1], Mary Redman, PhD[2,3], Karen L. Reckamp, MD, MS[4], Maya Khalil, MD[5], Brian S. Henick, MD[6], James Moon, MS[2,3], Pasarlai Ahmadzai[2,3], Michael LeBlanc, PhD[2,3], Daniel R. Carrizosa, MD, MS[7], Paul J. Hesketh, MD[8], Ellen V. Sigal, PhD[9], Jeff Allen, PhD[9], Andreas N. Saltos, MD[10], Bryan A. Faller, MD[11], Roy S. Herbst, MD, PhD[12], Charles D. Blanke, MD[13], Jhanelle E. Gray, MD[10]

[1]Dartmouth Cancer Center, Lebanon, NH; [2]SWOG Statistics and Data Management Center, Seattle, WA; [3]Fred Hutchinson Cancer Center, Seattle, WA; [4]Cedars-Sinai Medical Center, Los Angeles, CA; [5]The University of Alabama, Birmingham, Birmingham, AL; [6]Columbia University/Herbert Irving Comprehensive Cancer Center, New York, NY; [7]Levine Cancer Institute/ Wake Forest Baptist Comprehensive Cancer Center, Charlotte, NC; [8]Lahey Hospital and Medical Center, Burlington, MA; [9]Friends of Cancer Research, Washington, DC [10]Moffitt Cancer Center, Tampa, FL; [11]Heartland NCORP/Missouri Baptist Medical Center, St. Louis, MO, [12]Yale University, New Haven, CT; [13]SWOG Network Operations Center/Oregon Health & Science University, Portland, OR; [10]Moffitt Cancer Center, Tampa, FL

Pragmatyczny protokół badania z R – NDRP po niepowodzeniu IM – dla sprawnej rekrutacji i uzyskania szybkich wyników



	Standard of Care		Ramucirumab + Pembrolizumab	
	(n=419)		(n=419)	
Age (median)	68.7	34.7-88.2	67.7	33.8-87
Female Sex	170	41%	197	47%
Race/Ethnicity				
White	317	76%	335	80%
Black	62	15%	50	12%
Asian	17	4%	15	4%
Hispanic	17	4%	15	4%
Most recent therapy I/O Yes	339	81%	336	80%
No	80	19%	83	20%
PS 0-1	365	87%	361	86%
PS 2	54	13%	58	14%
Squamous cell carcinoma	120	29%	122	29%
Non-squamous cell carcinoma	296	71%	292	71%
PD-L1 Negative,<1%	133	36%	144	38%
Positive,>=1%	235	65%	232	63%
Positive,>=50%	98	27%	66	18%
Number of prior lines 0	36	9%	36	9%
1	233	56%	221	53%
2	95	23%	106	25%
3+	54	13%	53	13%

- Pierwotny punkt końcowy: OS
- Wtórne punkty końcowe:
  profil bezpieczeństwa,
  OS w zależności od HP

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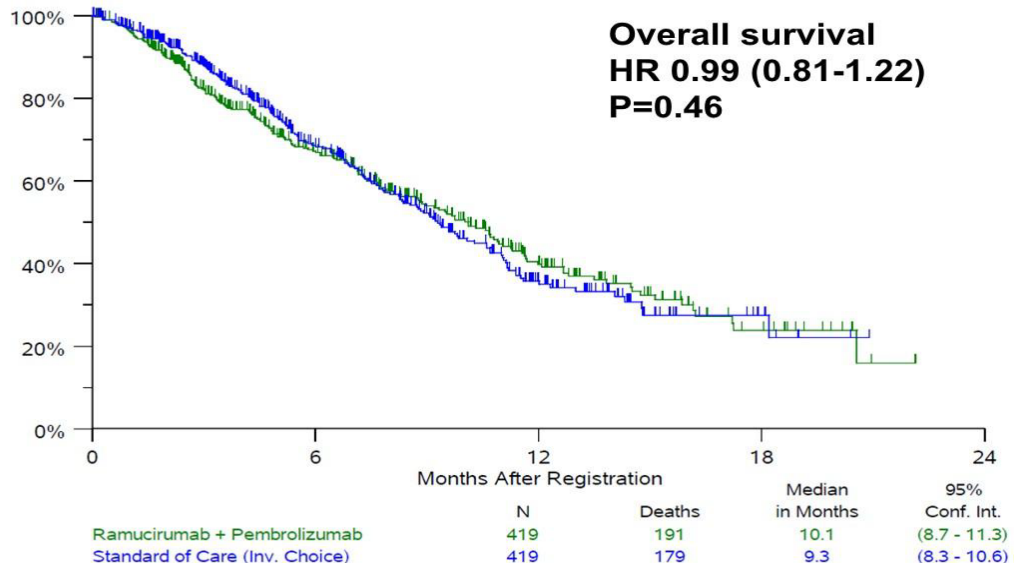
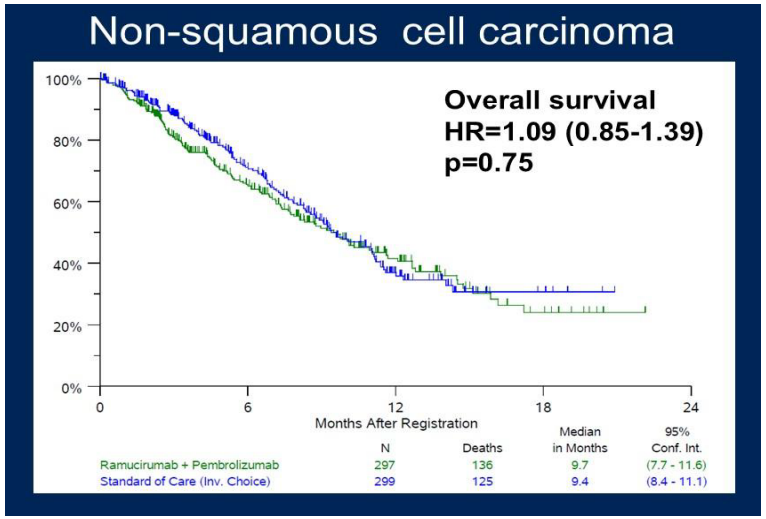
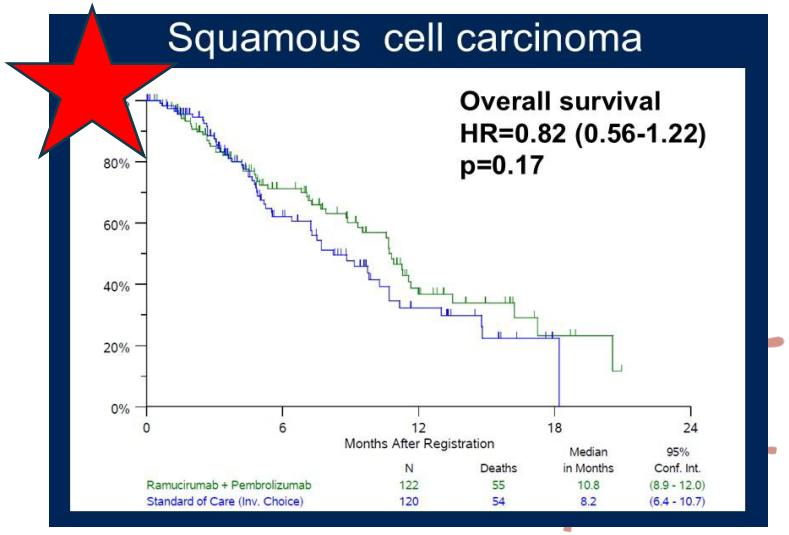
OS: dla ram+pembro zbliżony do SoC (gł. ram+DXL), mniej AEs







	Standard of Care	Ramucirumab + Pembrolizumab
Adverse Event or side effects	41	29
Refusal unrelated to adverse event	48	24
Progression/relapse	171	187
Death	39	36

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2025 ASCO ANNUAL MEETING

Efficacy of zipalertinib in NSCLC patients with EGFR exon 20 insertion mutations who received prior platinum-based chemotherapy with or without amivantamab

Helena Alexandra Yu,[1] Danny Nguyen,[2] Gerrina Ruiter,[3] Victor Ho-Fun Lee,[4] Ross A. Soo,[5] Se Hyun Kim,[6] Daniel Shao-Weng Tan,[7] Se-Hoon Lee,[8] Haruko Daga,[9] Vamsidhar Velcheti,[10] James Chih-Hsin Yang,[11] Antonio Passaro,[12] Gonzalo Fernandez-Hinojal,[13] Alexander I. Spira,[14] Oscar Juan-Vidal,[15] Sang-We Kim,[16] Shengting Li,[17] Zhiying Cindy Xu,[17] Jeffrey Alan Jones,[17] Zofia Piotrowska[18]

[1]Memorial Sloan Kettering Cancer Center, New York, NY; [2]City of Hope- Long Beach Elm, Long Beach, CA; [3]Departments of Clinical Pharmacology and Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; Department of Clinical Oncology, [4]The University of Hong Kong, Hong Kong, Hong Kong; [5]National University Hospital Singapore, Singapore, Singapore; [6]Division of Hematology-Oncology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea; [7]Division of Medical Oncology, National Cancer Centre Singapore, Duke-NUS Medical School, Singapore, Singapore; [8]Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [9]Osaka City General Hospital, Osaka, Japan; [10]Laura and Isaac Perlmutter Cancer Center, New York, NY; [11]Department of Oncology, National Taiwan University Hospital and Graduate Institute of Oncology, National Taiwan University, Taipei, Taiwan; [12]European Institute of Oncology, Division of Thoracic Oncology, Milan, Italy; [13]Clinica Universidad de Navarra, Madrid, Spain; [14]Virginia Cancer Specialists, Fairfax, VA; [15]Hospital Universitario y Politécnico La Fe, Valencia, Spain; [16]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [17]Cullinan Therapeutics Inc, Cambridge, MA; [18]Massachusetts General Hospital, Boston, MA

Helena Alexandra Yu, MD
Memorial Sloan Kettering Cancer Center, New York, NY

Rezilient1 BK faza 1/2

Key eligibility criteria

- Age ≥18 years
- Locally advanced or metastatic NSCLC
- Documented EGFR exon 20 insertion
- ECOG PS 0 or 1
- Stable/asymptomatic CNS metastases allowed

Zipalertinib
100 mg PO BID

- **Prior platinum-based chemotherapy without prior ex20ins-targeted therapy**
- **Prior platinum-based chemotherapy with prior amivantamab ± other ex20ins-targeted therapy**

Primary endpoint:

- **ORR and DOR as assessed by blinded ICR per RECIST v1.1**

Secondary endpoints:

- ORR and DOR by investigator
- DCR
- CBR
- PFS by ICR and investigator
- OS
- Antitumor activity in patients with CNS disease
- Safety

Charakterystyka chorych

Characteristic	Platinum-based chemotherapy without ex20ins-targeted therapy (n=143)	Prior ex20ins-targeted therapy (n=101)	Safety population (N=244)
Age, y, median (range)	66 (36–86)	62 (31–85)	65 (31–86)
Aged <65 y / ≥65 y, No. (%)	61 (43) / 82 (57)	60 (59) / 41 (41)	121 (50) / 123 (50)
Female, No. (%)	87 (61)	70 (69)	157 (64)
Race, No. (%)[a]			
White	51 (36)	47 (47)	98 (40)
Black or African American	5 (4)	7 (7)	12 (5)
Asian	77 (54)	45 (45)	122 (50)
Disease stage III / IV, No. (%)	7 (5) / 136 (95)	2 (2) / 99 (98)	9 (4) / 235 (96)
Cell type, No. (%)[b]			
Adenocarcinoma	140 (98)	96 (95)	236 (97)
Squamous cell carcinoma	1 (1)	1 (1)	2 (1)
Large cell carcinoma	0	1 (1)	1 (1)
ECOG PS 0 / 1, No. (%)	45 (32) / 98 (69)	33 (33) / 68 (67)	78 (32) / 166 (68)
Smoking history, No. (%)[c]			
Former	55 (39)	32 (32)	87 (36)
Current	1 (1)	3 (3)	4 (2)
None	86 (60)	66 (65)	152 (62)
CNS/brain metastases, No. (%)	48 (34)	55 (55)	103 (42)

Charakterystyka zastosowanego leczenia

Characteristic	Platinum-based chemotherapy without ex20ins-targeted therapy (n=143)	Prior ex20ins-targeted therapy (n=101)	Safety population (N=244)
Median number of prior systemic regimens, No. (range)	1 (0–6)	2 (1–7)	2 (0–7)
Prior chemotherapy, No. (%)	132 (92)	96 (95)	228 (93)
Prior anti–PD-(L)1, No. (%)	67 (47)	46 (46)	113 (46)
Prior targeted therapy, No. (%)	37 (26)	101 (100)	138 (57)
Amivantamab	0	84 (83)	84 (34)
Mobocertinib	0	40 (40)	40 (16)
Bevacizumab	14 (10)	16 (16)	30 (12)
Osimertinib	13 (9)	7 (7)	20 (8)
BLU-451	0	5 (5)	5 (2)
Cetuximab	4 (3)	0	4 (2)
Poziotinib	0	3 (3)	3 (1)
Sunvozertinib	0	3 (3)	3 (1)
Other[a]	17 (12)	9 (9)	26 (11)
Prior brain radiation, No. (%)	18 (13)	15 (15)	33 (14)
Brain metastasis untreated, No. (%)	30 (21)	40 (40)	70 (29)

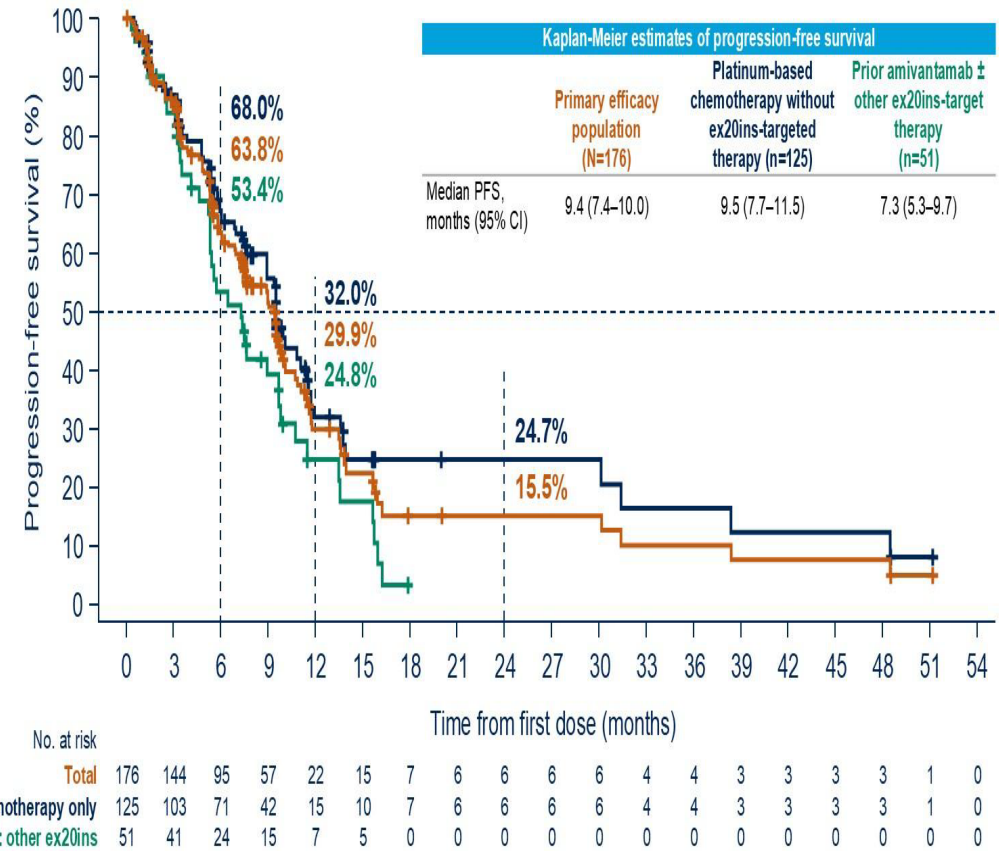
Skuteczność zipalertynibu

Outcome	Primary efficacy population (N=176)	Platinum-based chemotherapy without ex20ins-targeted therapy (n=125)	Prior amivantamab ± other ex20ins-target therapy (n=51)[a]
BOR, No. (%)[b]			
CR	1 (1)	0	1 (2)
PR	61 (35)	50 (40)	11 (22)
Unconfirmed PR[c]	7 (4)	6 (5)	1 (2)
SD	88 (50)	55 (44)	33 (65)
PD	11 (6)	8 (6)	3 (6)
Not evaluable[d]	8 (5)	6 (5)	0
Confirmed ORR, No. (%) [95% CI][e]	62 (35) [28–43]	50 (40) [31–49]	12 (24) [13–38]
DCR, No. (%) [95% CI][f]	157 (89) [84–93]	111 (89) [82–94]	46 (90) [79–97]
CBR, No. (%) [95% CI][g]	113 (64) [57–71]	85 (68) [59–76]	28 (55) [40–69]
Median time to response, days (range)	44 (31–295)	44 (39–232)	44 (39–232)
Median DOR, months (95% CI)	8.8 (8.3–12.7)	8.8 (8.3–12.7)	8.5 (4.2–14.8)

Skuteczność wewnątrzczaszkowa zipalertynibu

Outcome	Primary efficacy population (N=176)	Patients with brain metastases[a] (n=68)
BOR, No. (%)[b]		
CR	1 (1)	1 (2)
PR	61 (35)	20 (29)
Unconfirmed PR[c]	7 (4)	2 (3)
SD	88 (50)	37 (54)
PD	11 (6)	5 (7)
Not evaluable[d]	8 (5)	3 (4)
Confirmed ORR, No. (%) [95% CI][e]	62 (35) [28–43]	21 (31) [20–43]
DCR, No. (%) [95% CI][f]	157 (89) [84–93]	60 (88) [78–95]
CBR, No. (%) [95% CI][g]	113 (64) [57–71]	38 (56) [43–68]
Median time to response, days (range)	44 (31–295)	98 (35–232)
Median DOR, months (95% CI)	8.8 (8.3–12.7)	8.3 (4.2–9.9)

Skuteczność zipalertynibu: mPFS=9,5 m-cy(CHT)/7,3 m-cy (amiv, skuteczność sekwencyjnego leczenia anty-EGFRinsEx20)



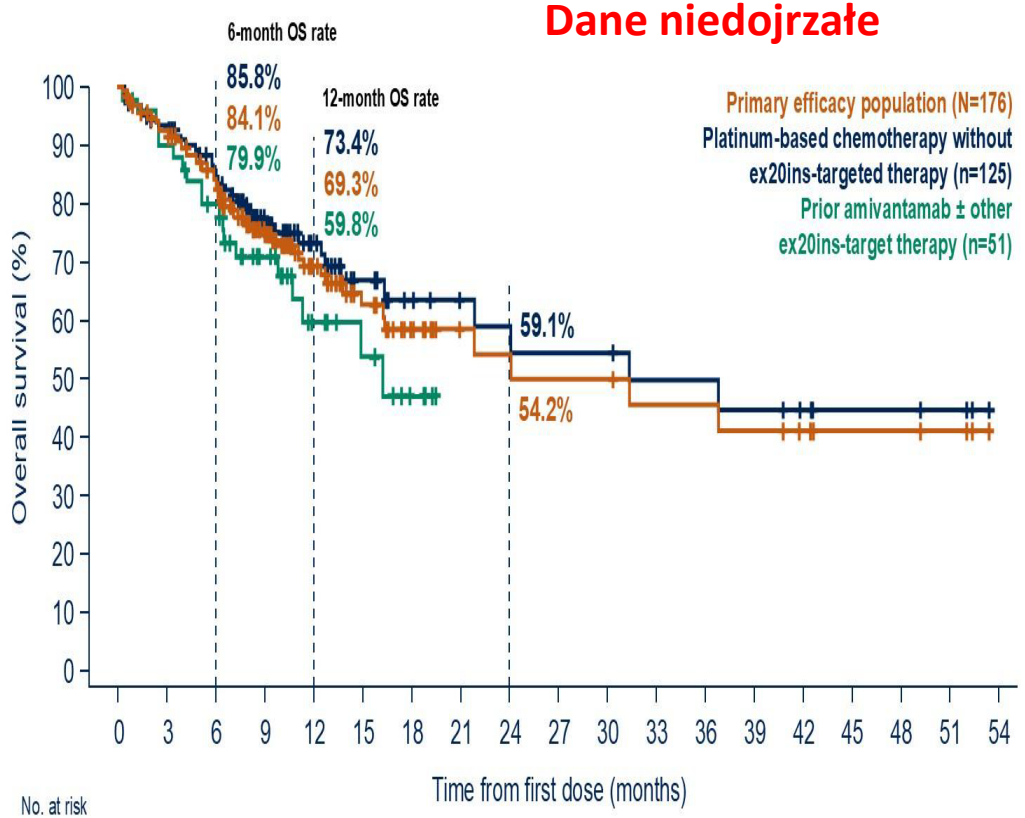
Kaplan-Meier estimates of progression-free survival

	Primary efficacy population (N=176)	Platinum-based chemotherapy without ex20ins-targeted therapy (n=125)	Prior amivantamab ± other ex20ins-target therapy (n=51)
Median PFS, months (95% CI)	9.4 (7.4–10.0)	9.5 (7.7–11.5)	7.3 (5.3–9.7)

No. at risk

Total	176	144	95	57	22	15	7	6	6	6	6	4	4	3	3	3	3	1	0
Platinum-based chemotherapy only	125	103	71	42	15	10	7	6	6	6	6	4	4	3	3	3	3	1	0
Prior amivantamab ± other ex20ins	51	41	24	15	7	5	0	0	0	0	0	0	0	0	0	0	0	0	0

Dane niedojrzałe



No. at risk

Total	176	158	137	88	51	32	21	14	13	12	12	10	10	9	7	5	5	3	0
Platinum-based chemotherapy only	125	113	99	64	38	23	17	14	13	12	12	10	10	9	7	5	5	3	0
Prior amivantamab ± other ex20ins	51	15	38	24	13	9	4	0	0	0	0	0	0	0	0	0	0	0	0

Profil bezpieczeństwa

AE, No. (%)	Safety population (N=244)
TEAEs	
Any TEAE	242 (99.2)
Grade ≥3 TEAE	137 (56.1)
TRAEs	
Any TRAE	223 (91.4)
Grade ≥3 TRAE	72 (29.5)
TRAE leading to treatment modification	
Dose reduction	35 (14.3)
Dose interruption	96 (39.3)
Treatment discontinuation[a]	20 (8.2)
TRAE leading to death	2 (0.8)

Any-grade TRAEs reported in ≥10% of patients, No. (%)	Any grade	Grade 3
Paronychia	94 (38.5)	0
Rash	74 (30.3)	6 (2.5)
Dermatitis acneiform	60 (24.6)	1 (0.4)
Dry skin	60 (24.6)	0
Diarrhea	53 (21.7)	5 (2.0)
Stomatitis	49 (20.1)	4 (1.6)
Anemia	48 (19.7)	17 (7.0)
Pruritus	44 (18.0)	1 (0.4)
Nausea	35 (14.3)	2 (0.8)
Rash maculopapular	34 (13.9)	3 (1.2)
Fatigue	29 (11.9)	0

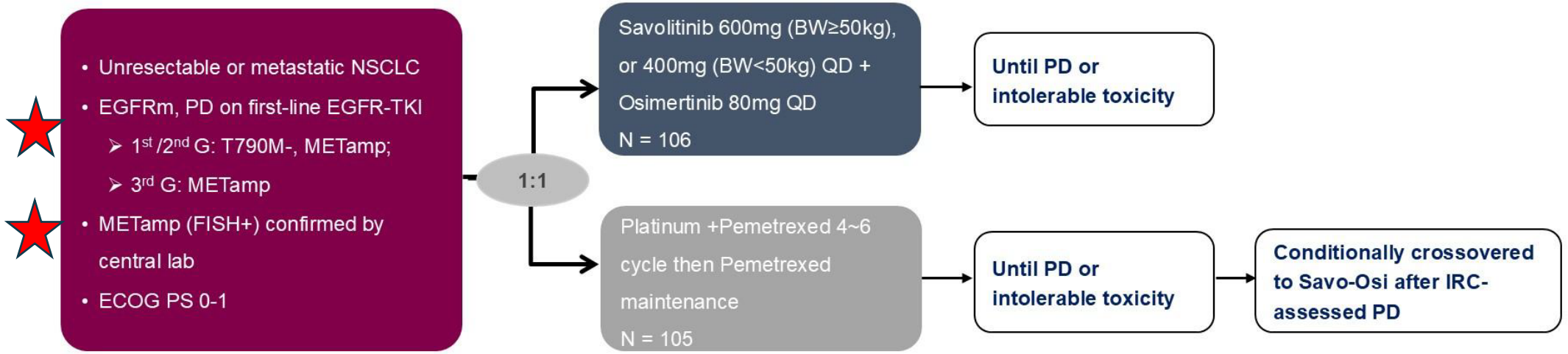
2025 ASCO ANNUAL MEETING

Savolitinib combined with osimertinib versus chemotherapy in EGFR-mutant and MET-amplified advanced NSCLC after disease progression on EGFR tyrosine kinase inhibitor: results from a randomized phase 3 SACHI study

Shun Lu[1], Jie Wang[2], Nong Yang[3], Dongqing Lv[4], Lijuan Chen[5], Lin Wu[3], Xingya Li[6], Longhua Sun[7], Yongfeng Yu[1], Bo Jin[8], Lin Yang[9], Yubiao Guo[10], Haipeng Xu[11], Tienan Yi[12], Aiping Zeng[13], Xiaorong Dong[14], Jianhua Chen[3], Ziping Wang[15], Tony Mok[16], Weiguo Su[17]

1. Shanghai Chest Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; 2. Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China: 3. Hunan Cancer Hospital, Changsha, China; 4. Taizhou Hospital of Zhejiang Province, Taizhou, China; 5. Henan Cancer Hospital, Zhengzhou, China; 6. First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; 7. First Affiliated Hospital of Nanchang University, Nanchang, China; 8. The First Hospital of China Medical University, Shenyang, China; 9. Shenzhen People's Hospital, Shenzhen, China; 10. The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China; 11. Fujian Provincial Cancer Hospital, Fuzhou, China; 12. Xiangyang Central Hospital, Xiangyang, China; 13. The Cancer Hospital Affiliated to Guangxi Medical University, Nanning, China; 14. Union Hospital Tongji Medical College Huazhong University of Science and Technology, Wuhan, China; 15. Beijing Cancer Hospital, Beijing, China; 16. Department of Clinical Oncology, Faculty of Medicine, The Chinese University of Hong Kong, Hongkong, China; 17. HUTCHMED, Shanghai, China

Sachi BK 3 fazy, EGFRmNSCLC, PD po 1L EGFR TKI, METamp(+)



METamp:

- **Post 1st /2nd G:** MET copy number ≥5 or MET/CEP7 ≥2
- **Post 3rd G:** MET copy number ≥ 10

Stratification factors:

- **Brain metastasis**: (yes or no)
- **Prior 3rd G EGFR-TKI**: (yes or no)
- **EGFR mutation**: (ex19del vs L858R vs others)

Primary endpoint: PFS by investigator

Secondary endpoints: PFS by IRC, ORR, DCR, DoR, TTR, OS, safety

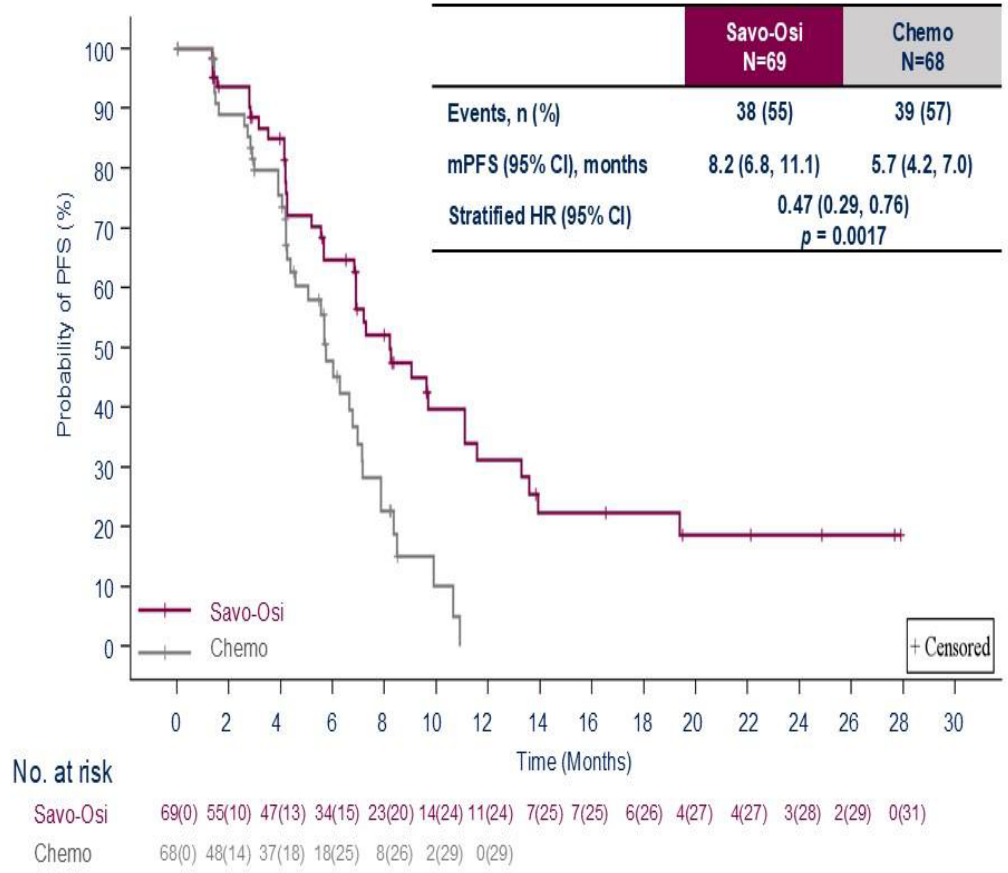
Charakterystyka chorych

Characteristics	Savo-Osi N=106	Chemo N=105
Age		
Median (range), year	59.4 (34.1–75.8)	61.9 (36.8–75.8)
Sex, n (%)		
Male	44 (42)	50 (48)
Female	62 (58)	55 (52)
ECOG PS, n (%)		
0	28 (26)	27 (26)
1	78 (74)	78 (74)
Body weight		
Median (range), kg	60.0 (40.0–92.3)	60.0 (41.0–90.0)
<50 kg, n (%)	19 (18)	8 (8)
≥50 kg, n (%)	87 (82)	97 (92)

Characteristics	Savo-Osi N=106	Chemo N=105
Pathological diagnosis, n (%)		
Adenocarcinoma	105 (99)	105 (100)
Other*	1 (1)	0
Brain metastases, n (%)		
Yes	39 (37)	41 (39)
No	67 (63)	64 (61)
Previous first-line EGFR-TKI, n (%)		
1st /2nd generation	69 (65)	68 (65)
3rd generation	37 (35)	37 (35)
Type of *EGFR* mutation, n (%)		
Exon 19 deletion	40 (38)	40 (38)
L858R	55 (52)	53 (50)
Other#	11 (10)	12 (11)

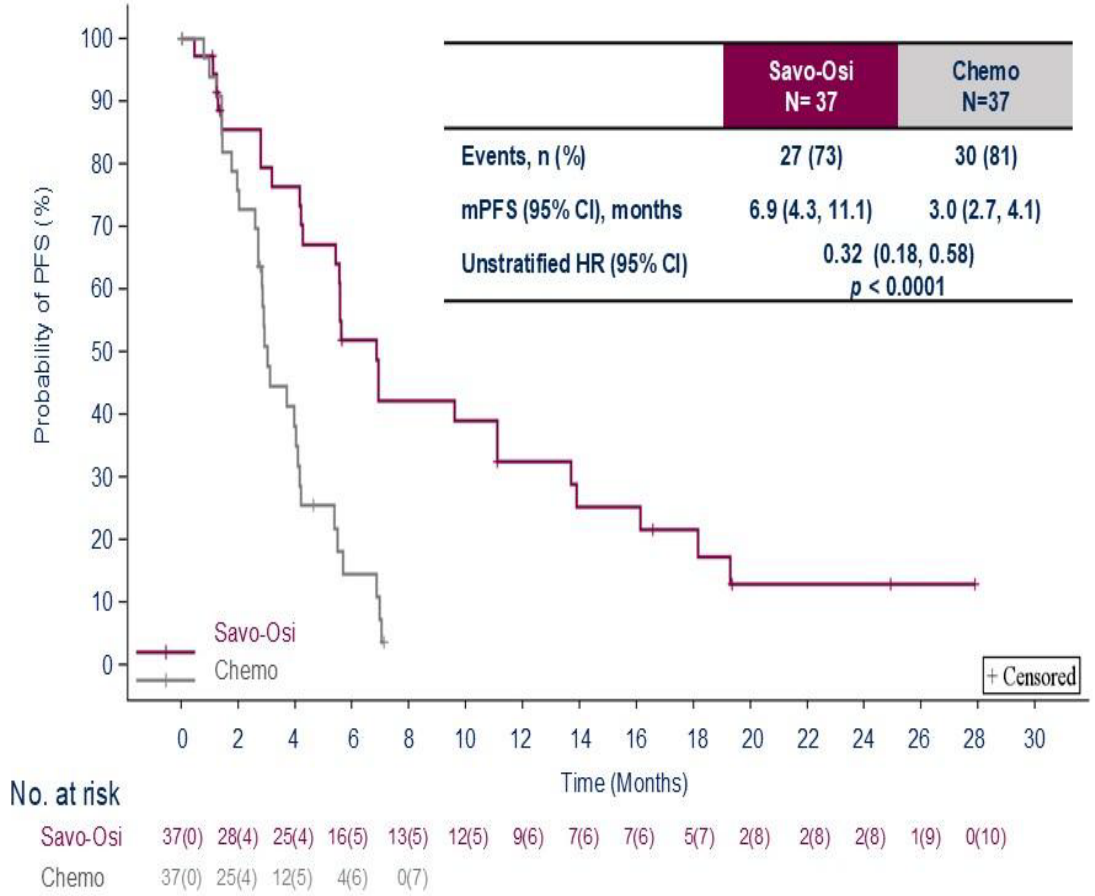
Kombinacja savo+ozi skuteczniejsza od CHT – mPFS dłuższa po leczeniu iEGFR 1/2gen (8,2 vs 7 m-cy)

po EGFR 1/2 gen



	Savo-Osi N=69	Chemo N=68
Events, n (%)	38 (55)	39 (57)
mPFS (95% CI), months	8.2 (6.8, 11.1)	5.7 (4.2, 7.0)
Stratified HR (95% CI)	0.47 (0.29, 0.76) $p = 0.0017$	

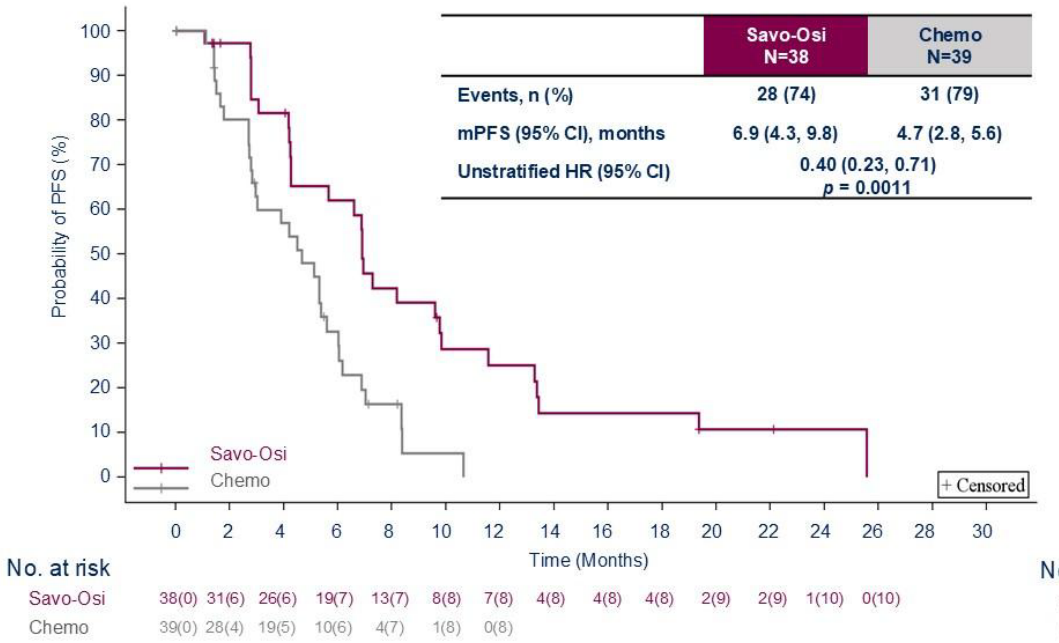
po EGFR 3 gen



	Savo-Osi N= 37	Chemo N=37
Events, n (%)	27 (73)	30 (81)
mPFS (95% CI), months	6.9 (4.3, 11.1)	3.0 (2.7, 4.1)
Unstratified HR (95% CI)	0.32 (0.18, 0.58) $p < 0.0001$	

Kombinacja savo+ozi skuteczniejsza wewnątrzczaszkowo od CHT

With history of brain metastases

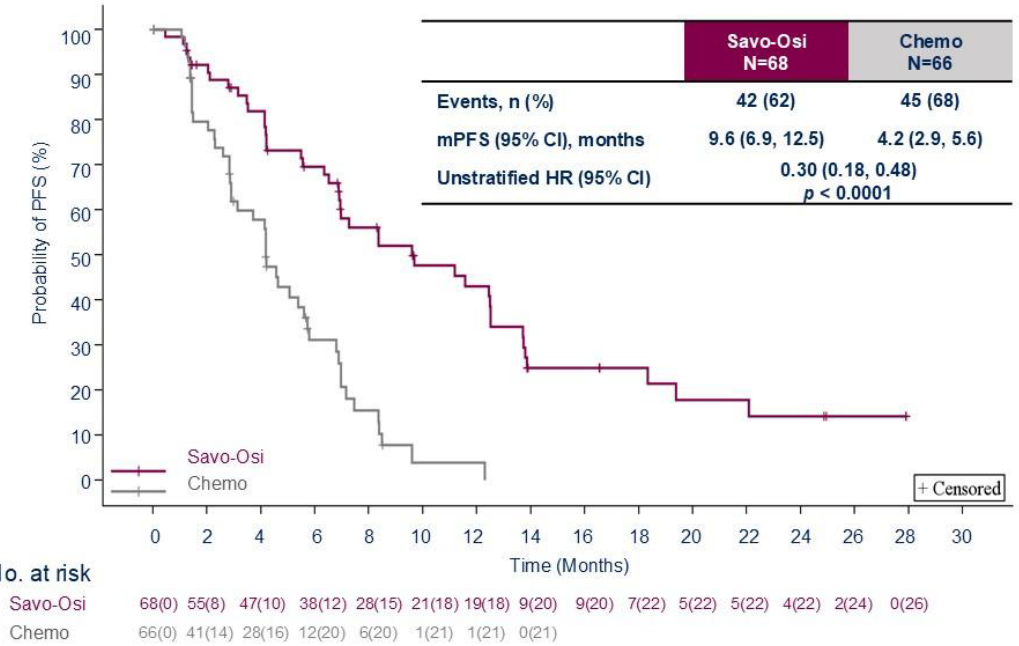


	Savo-Osi N=38	Chemo N=39
Events, n (%)	28 (74)	31 (79)
mPFS (95% CI), months	6.9 (4.3, 9.8)	4.7 (2.8, 5.6)
Unstratified HR (95% CI)	0.40 (0.23, 0.71) $p = 0.0011$	

No. at risk

Savo-Osi	38(0)	31(6)	26(6)	19(7)	13(7)	8(8)	7(8)	4(8)	4(8)	4(8)	2(9)	2(9)	1(10)	0(10)
Chemo	39(0)	28(4)	19(5)	10(6)	4(7)	1(8)	0(8)							

Without history of brain metastases

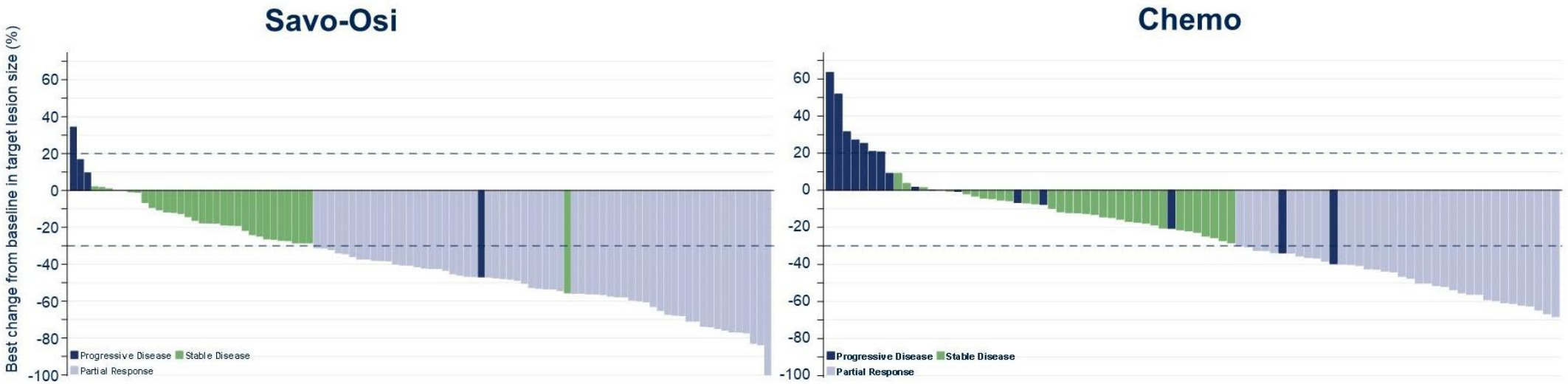


	Savo-Osi N=68	Chemo N=66
Events, n (%)	42 (62)	45 (68)
mPFS (95% CI), months	9.6 (6.9, 12.5)	4.2 (2.9, 5.6)
Unstratified HR (95% CI)	0.30 (0.18, 0.48) $p < 0.0001$	

No. at risk

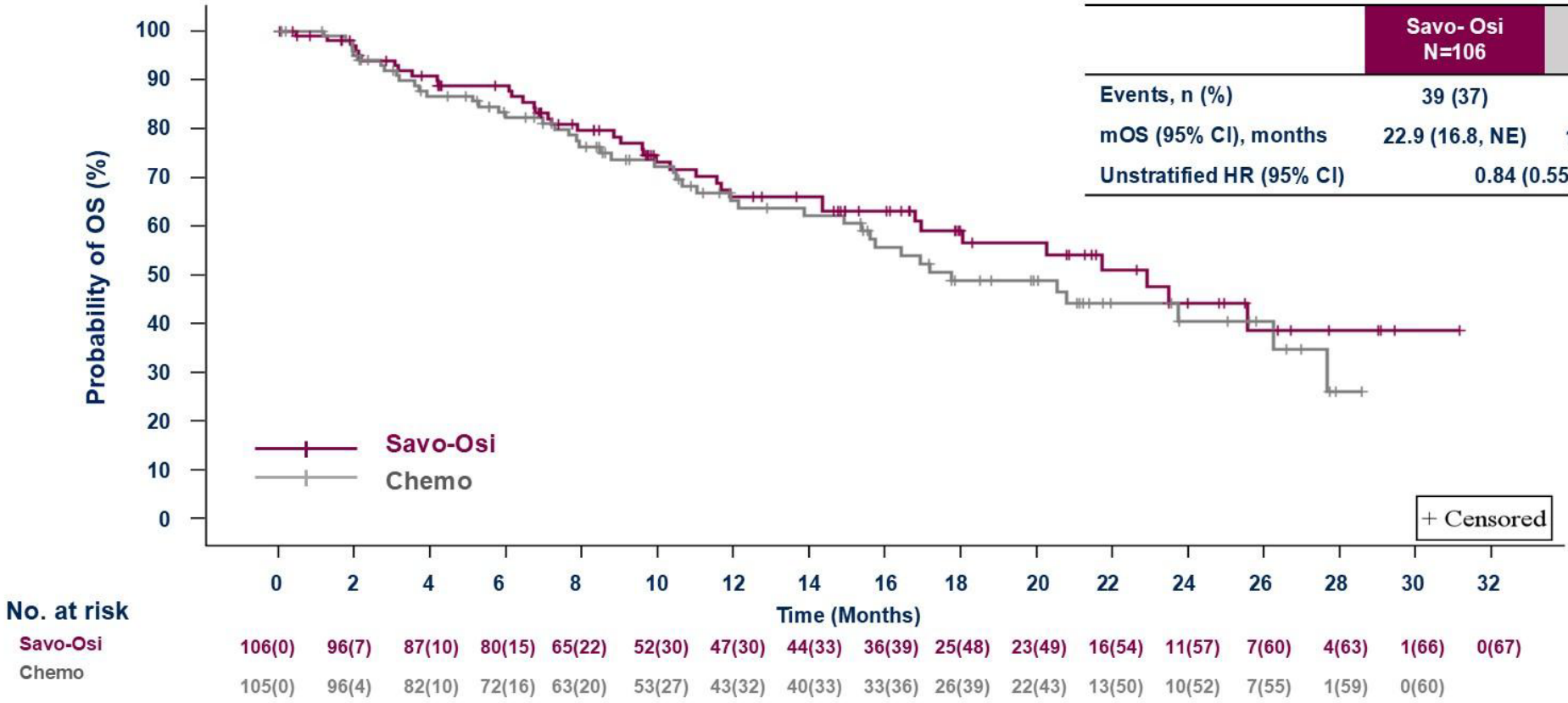
Savo-Osi	68(0)	55(8)	47(10)	38(12)	28(15)	21(18)	19(18)	9(20)	9(20)	7(22)	5(22)	5(22)	4(22)	2(24)	0(26)
Chemo	66(0)	41(14)	28(16)	12(20)	6(20)	1(21)	1(21)	0(21)							

ORR savo+ozi istotnie wyższy od CHT (58% vs34%)



	Savo-Osi N=106	Chemo N=105	Stratified OR (95% CI)
ORR, % (95% CI)	58 (49-68)	34 (25-44)	2.74 (1.50-4.98) *p*=0.0004
DCR, % (95% CI)	89 (81-94)	67 (57-76)	3.98 (1.81-8.82) *p*=0.0001
Median DoR, month (95% CI)	8.4 (5.9-11.1)	3.2 (2.8-4.2)	-

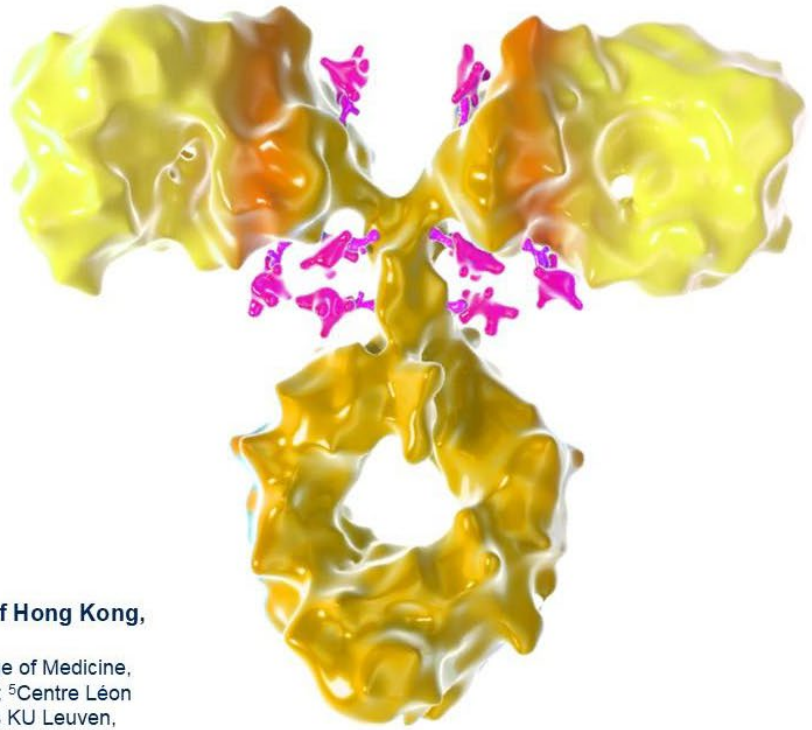
Savo+ozi – dane dotyczące OS – niedojrzałe, c-over dozwolony



	Savo- Osi N=106	Chemo N=105
Events, n (%)	39 (37)	45 (43)
mOS (95% CI), months	22.9 (16.8, NE)	17.7 (14.9, 26.3)
Unstratified HR (95% CI)	0.84 (0.55, 1.29)	

2025 ASCO ANNUAL MEETING

Patritumab Deruxtecan (HER3-DXd) in Resistant *EGFR*-Mutated Advanced NSCLC After a Third-Generation EGFR TKI: The Phase 3 HERTHENA-Lung02 Study



Tony S. K. Mok, MD, FRCPC, FASCO[1]

Helena A. Yu, MD,[2] Sun Min Lim, MD, PhD,[3] Isamu Okamoto, MD, PhD,[4] Maurice Pérol, MD,[5] Silvia Novello, MD, PhD,[6] Christophe Dooms, MD, PhD,[7] Jong-Mu Sun, PhD,[8] Steven Kao, BHB, MBChB, PhD, FRACP,[9] Pasi A. Jänne, MD, PhD,[10] Martin Reck, MD, PhD,[11] Conor Steuer, MD,[12] Makoto Nishio, MD, PhD,[13] Yi-Long Wu, MD,[14] Ronan Fougeray, MS,[15] Ragini Kudchadkar, MD,[15] Jian Yu Wu,[16] Stephen Esker, PharmD,[15] Antonio Passaro, MD, PhD[17]

[1]Department of Clinical Oncology, State Key Laboratory of Translational Oncology and The Chinese University of Hong Kong, Hong Kong, Hong Kong PRC

[2]Department of Medicine, Medical Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Yonsei University College of Medicine, Seoul, South Korea; [4]Department of Respiratory Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; [5]Centre Léon Bérard, Lyon, France; [6]Oncology Department at San Luigi Hospital in Orbassano, University of Turin, Turin, Italy; [7]University Hospitals KU Leuven, Leuven, Belgium; [8]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [9]Chris O'Brien Lifehouse, Camperdown, NSW, Australia; [10]Dana-Farber Cancer Institute, Boston, MA, USA; [11]Department of Thoracic Oncology, Airway Research Center North, German Center for Lung Research, LungenClinic Grosshansdorf, Grosshansdorf, Germany; [12]Winship Cancer Institute of Emory University, Atlanta, GA, USA; [13]The Cancer Institute Hospital of JFCR, Tokyo, Japan; [14]Guangdong Lung Cancer Institute, Guangdong Province People's Hospital, Southern Medical University, Guangzhou, China; [15]Daiichi Sankyo, Inc, Basking Ridge, NJ, USA; [16]Merck & Co, Inc, Rahway, NJ, USA; [17]Division of Thoracic Oncology, European Institute of Oncology, Milan, Italy

Study design

HERTHENA-Lung02: A phase 3, global, multi-center, randomized, open-label study[1]

586 patients; study start date, 08 July 2022

Select Eligibility Criteria

- Advanced nonsquamous NSCLC with an *EGFR*-activating mutation (exon 19 deletion or L858R)
- 1 or 2 prior line(s) of an approved EGFR TKI (must include a third-generation EGFR TKI)
  - Non-osimertinib third-generation TKIs ≤20% in each arm
- Disease progression while or after receiving a third-generation EGFR TKI
- Stable brain metastases (asymptomatic and not requiring corticosteroids or anticonvulsants) were permitted

Randomized 1:1

HER3-DXd (N=293)
Patritumab deruxtecan
5.6 mg/kg IV Q3W

No crossover

PBC (N=293)
Cisplatin 75 mg/m^2
or carboplatin AUC5
Q3W (× 4 cycles)
+ Pemetrexed 500 mg/m^2 Q3W[a]

Primary analysis of PFS (primary endpoint)

2nd interim analysis for OS

3rd interim analysis for OS

End of study

Primary Endpoint

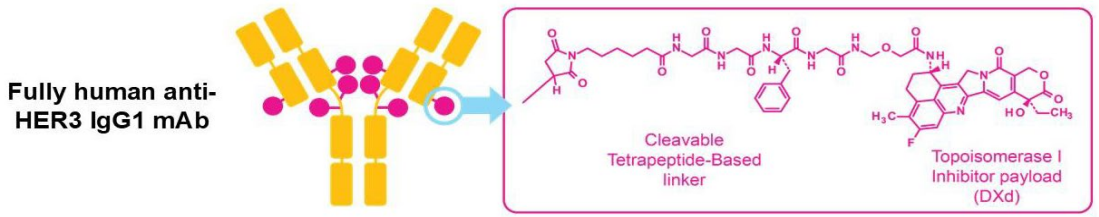
PFS (by BICR per RECIST version 1.1)

Secondary Endpoints

- Key secondary: OS
- Other Secondary:
  - Safety
  - Intracranial PFS in patients with baseline brain metastases (by CNS BICR per CNS RECIST)[b]
  - HER3 protein expression and its relationship with efficacy
    - Analysis of the potential role of HER3 expression by IHC as a predictive biomarker of response to HER3-DXd in HERTHENA-Lung02 is ongoing

Stratification

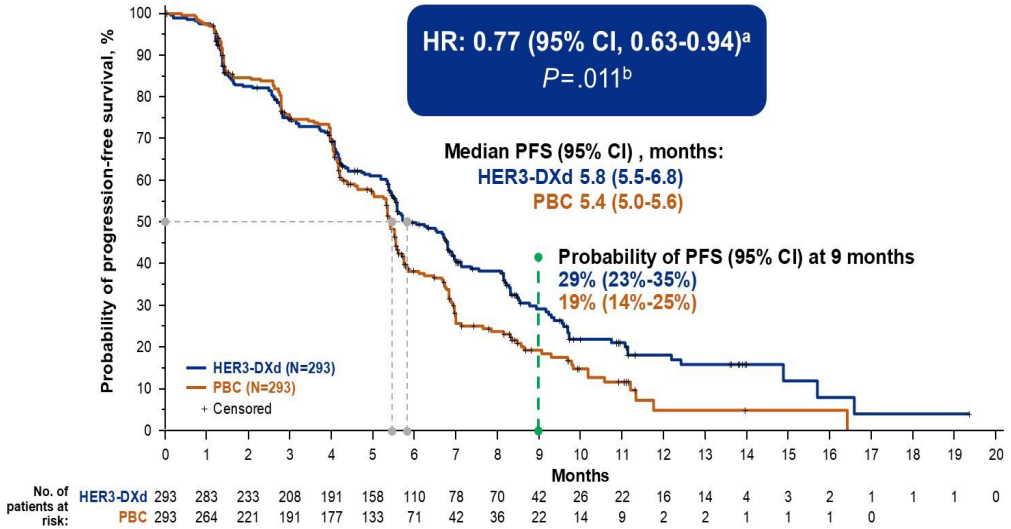
- Third generation EGFR TKI (osimertinib, other)
- Line of third generation EGFR TKI (first, second)
- Region (Asia, Non-Asia)
- Presence of stable brain metastases (yes, no)

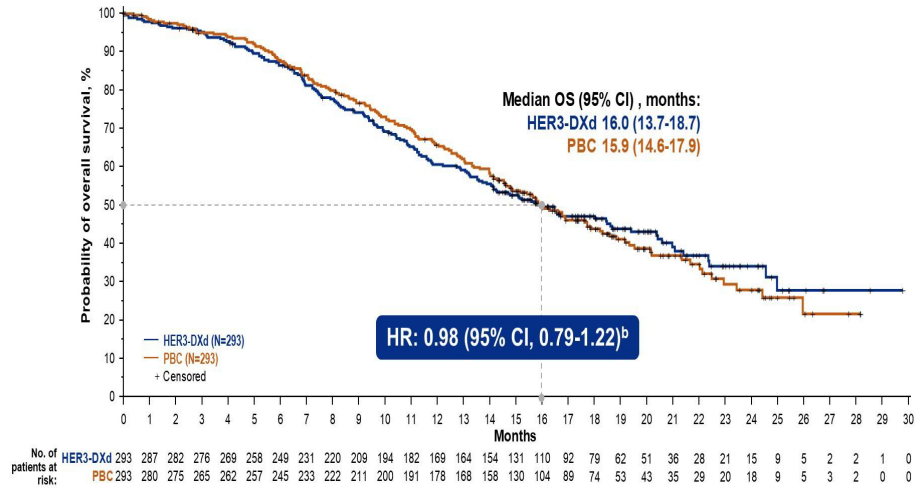


Charakterystyka chorych

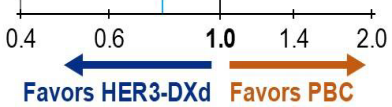
Baseline characteristics		HER3-DXd (N=293)	PBC (N=293)
Age, median (range), years		64 (35-82)	64 (34-86)
Female, n (%)		184 (62.8)	175 (59.7)
Asian, n (%)		176 (60.1)	178 (60.8)
Smoking history, n (%)	Never	187 (63.8)	185 (63.1)
	Ever	106 (36.2)	108 (36.9)
Time since initial NSCLC diagnosis, median (range), months		24.2 (2.5-121.1)	24.1 (3.2-146.1)
ECOG PS at baseline, n (%)	0	110 (37.5)	102 (34.8)
	1	183 (62.5)	190 (64.8)
	2[a]	0	1 (0.3)
History of brain metastasis, n (%)[b]		127 (43.3)	132 (45.1)
Brain metastasis at baseline (by CNS BICR per CNS RECIST), n (%)[c]		105 (35.8)	95 (32.4)
EGFR activating mutations, n (%)	Ex19del	177 (60.4)	178 (60.8)
	L858R	113 (38.6)	112 (38.2)
	Dual Ex19del and L858R	3 (1.0)	3 (1.0)
Prior EGFR TKI, n (%)	Only 3rd-generation	225 (76.8)	223 (76.1)
	3rd- and 1st/2nd-generation	68 (23.2)	70 (23.9)
Line of treatment for prior 3rd-generation EGFR TKI, n (%)	First line	226 (77.1)	227 (77.5)
	Second line	67 (22.9)	66 (22.5)
Type of prior 3rd-generation EGFR TKI, n (%)	Osimertinib	266 (90.8)	263 (89.8)
	Other 3rd-generation[d]	27 (9.2)	30 (10.2)

Korzyść w mPFS dla HER3-DXd vs CHT, OS bez różnic



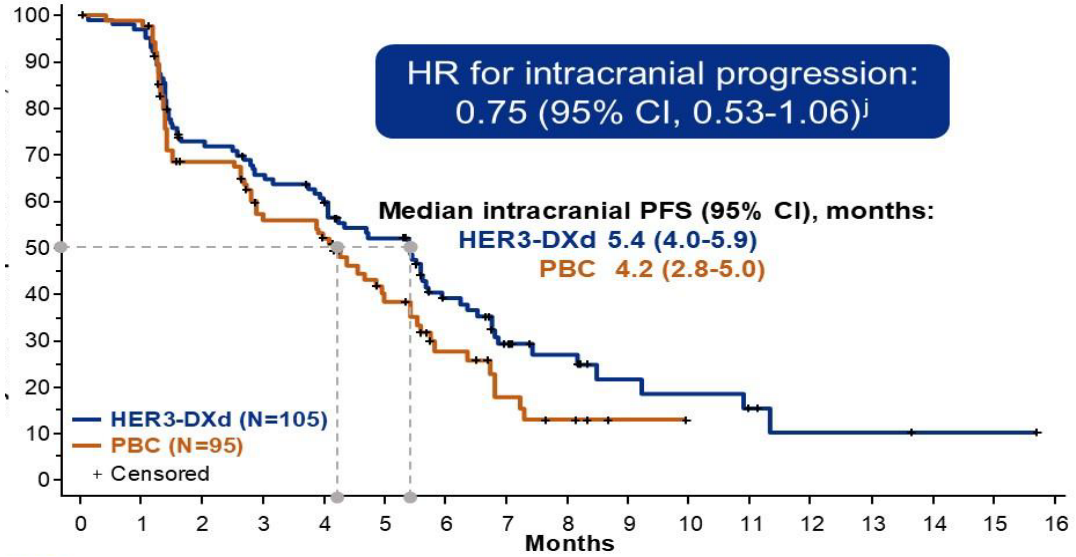


Subgroup		No. of events/n HER3-DXd	PBC	HR
Overall		194/293	195/293	0.77
Age	<65 y	105/153	108/149	0.86
	≥65 y	89/140	87/144	0.71
Sex	Female	117/184	116/175	0.73
	Male	77/109	79/118	0.87
Region	Asia	105/160	107/160	0.82
	Non-Asia	89/133	88/133	0.69
EGFR activating mutation	Ex19del	113/177	124/178	0.69
	L858R	79/113	69/112	0.94
Brain metastasis at baseline (by BICR per RECIST)	Yes	78/98	69/91	0.83
	No	116/195	126/202	0.72
Smoking status	Ever	76/106	73/108	0.86
	Never	118/187	122/185	0.74
ECOG PS at screening	0	69/111	65/103	0.68
	1	125/182	130/190	0.86



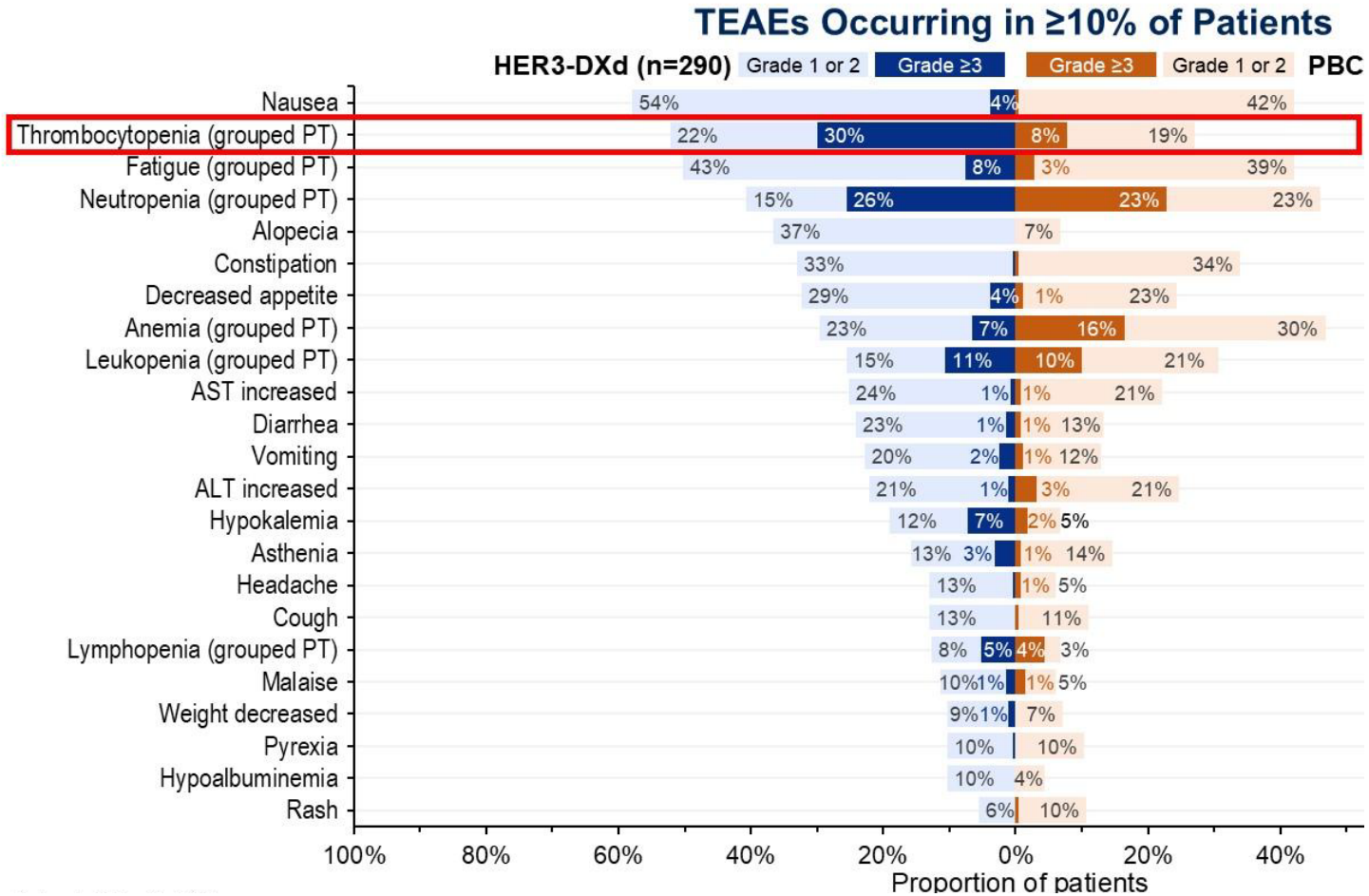
Skuteczność pozaczaszkowa (ORR=35%) i wewnątrzczaszkowa (ICORR=19%) HER3-DXd

Responses by BICR per RECIST		HER3-DXd (N=293)	PBC (N=293)
Confirmed ORR (95% CI), %		**35.2 (29.7-40.9)**	**25.3 (20.4-30.6)**
Best overall response, n (%)	CR	1 (0.3)	3 (1.0)
	PR	102 (34.8)	71 (24.2)
	SD[a]	133 (45.4)	148 (50.5)
	PD	40 (13.7)	35 (11.9)
	NE	17 (5.8)[b]	36 (12.3)[c]
BOR to be confirmed, n (%)		2 (0.7)[d]	2 (0.7)[d]
DCR (95% CI), %		80.5 (75.5-84.9)	75.8 (70.4-80.6)
Median TTR (range), mo		1.5 (0.3-8.1)	1.5 (1.2-6.9)
Median DOR (95% CI), mo		5.7 (5.1-7.3)	5.4 (4.1-5.6)



Intracranial response by CNS BICR per CNS RECIST[a]		Patients with ≥1 CNS lesion (target or non-target) at baseline (CNS BICR) HER3-DXd (N=105)[b]	PBC (N=95)[c]
Confirmed intracranial ORR (95% CI), %		**19.0 (12.0-27.9)**	**11.6 (5.9-19.8)**
Best overall intracranial response, n (%)	CR	13 (12.4)[d]	4 (4.2)[e]
	PR	7 (6.7)	7 (7.4)
	SD[f]	52 (49.5)	47 (49.5)
	PD	27 (25.7)	26 (27.4)
	NE	6 (5.7)[g]	11 (11.6)[h]
BOR to be confirmed, n (%)		2 (1.9)[i]	0
Intracranial DCR (95% CI), %		68.6 (58.8-77.3)	61.1 (50.5-70.9)
Median intracranial TTR (range), mo		2.1 (1.2-6.9)	2.6 (1.2-4.7)
Median intracranial DOR (95% CI), mo		4.5 (4.1-NE)	4.2 (2.4-NE)
Prior radiation to the brain, n (%)		39 (37.1)	36 (37.9)

Profil bezpieczeństwa HER3-DXd



- **AE ≥3 HER3-DXd: 72% vs 57% PBC**
- Gł. Tox. **Hematologiczne** – wczesne, przemijające oraz **żołądkowo-jelitowe**
- W każdym z ramion – 1 epizod krwawienia G≥3
- **ILD – 5%, gł. G1-2, mediana czasu do wystąpienia – 126 dni, u 5% → przerwanie leczenia**

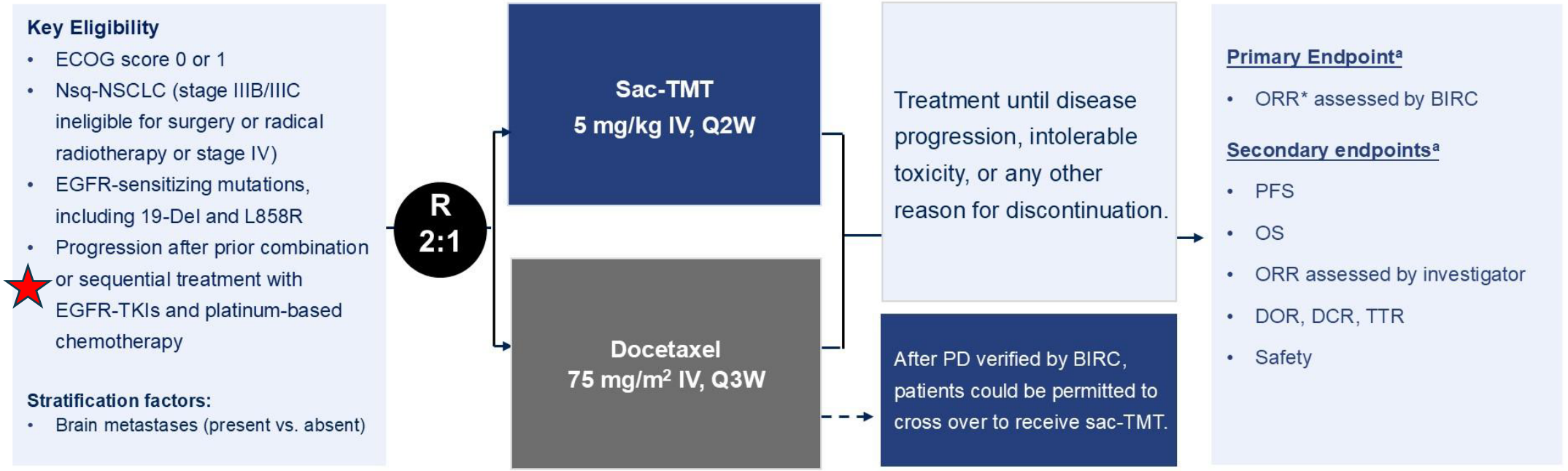
2025 ASCO ANNUAL MEETING

Sacituzumab tirumotecan (sac-TMT) in patients (pts) with previously treated advanced EGFR-mutated non-small cell lung cancer (NSCLC): results from the randomized OptiTROP-Lung03 study

Li Zhang[1], Wenfeng Fang[1], Xingya Li[2], Qiming Wang[3], Xiangjiao Meng[4], Wei Zheng[5], Longhua Sun[6], Wenxiu Yao[7], Wu Zhuang[8], Yun Fan[9], Minglei Zhuo[10], Yongzhong Luo[11], Zhiye Zhang[12], Xia Song[13], Runxiang Yang[14], Jiacheng Yang[15], Yina Diao[15], Junyou Ge[15]

[1]Sun Yat-sen University Cancer Center, Guangzhou, China; [2]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [3]The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China; [4]Shandong Cancer Hospital and Institute, Shandong First Medical University, Jinan, China; [5]Shengjing Hospital of China Medical University, Shenyang, China; [6]The First Affiliated Hospital of Nanchang University, Nanchang, China; [7]Sichuan Cancer Hospital, Chengdu, China; [8]Fujian Cancer Hospital, Fuzhou, China; [9]Zhejiang Cancer Hospital, Hangzhou, China; [10]Beijing Cancer Hospital, Beijing, China; [11]Hunan Cancer Hospital, Changsha, China; [12]The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, China; [13]Shanxi Cancer Hospital, Taiyuan, China; [14]Yunnan Cancer Hospital, Kunming, China; [15]Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China

Schemat badania OptiTROP-Lung03

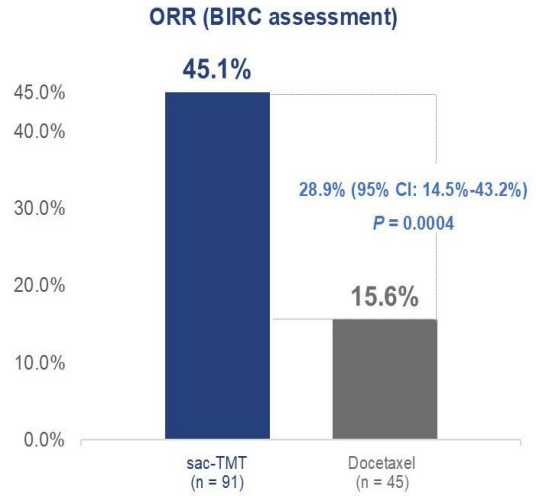


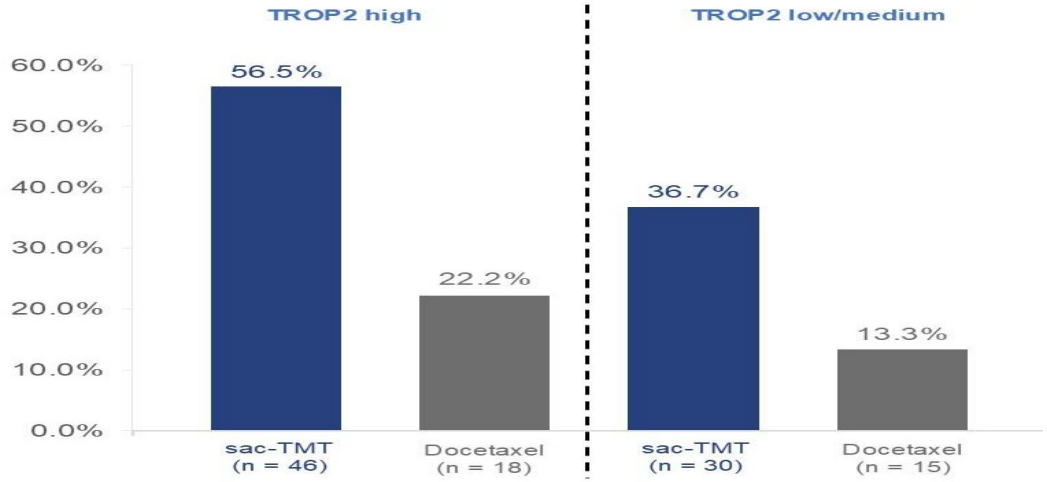
Charakterystyka chorych

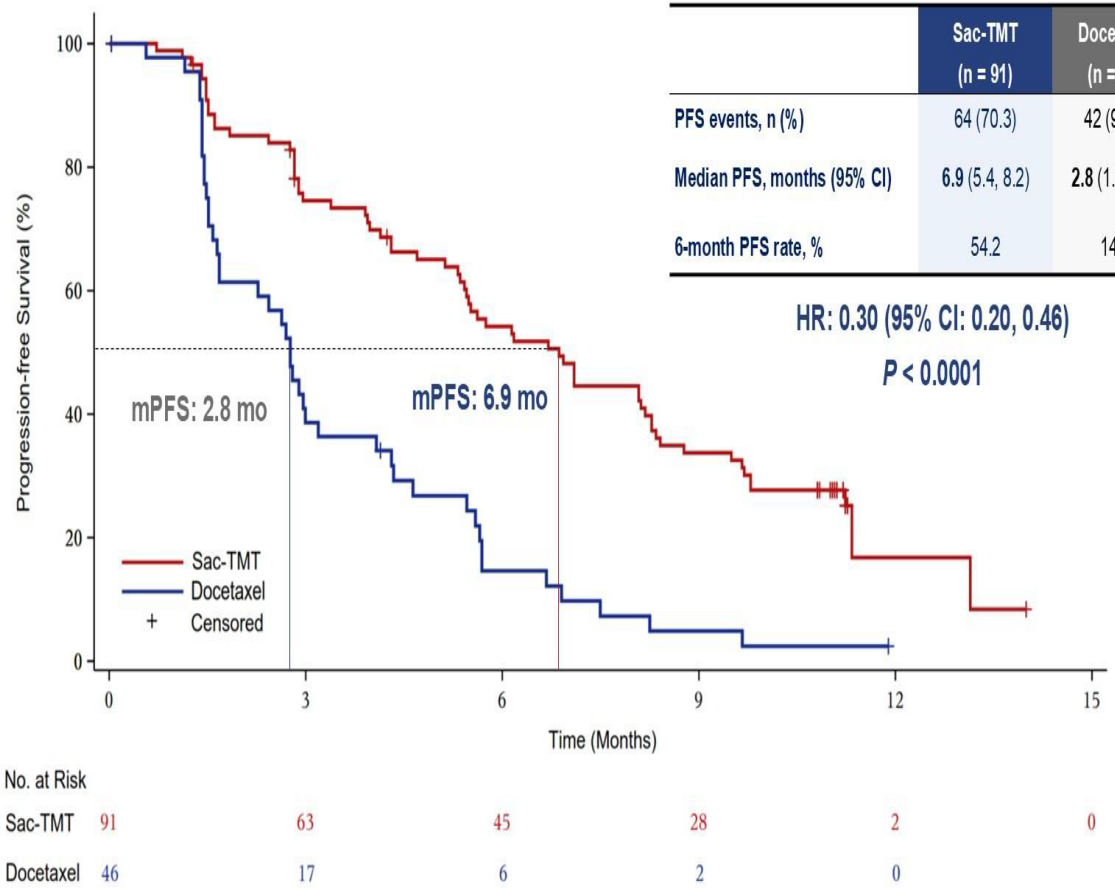
	Sac-TMT (n = 91)	Docetaxel (n = 46)
Median age (range)	57.0 (37, 75)	55.0 (34, 74)
≥65 years, n (%)	19 (20.9)	8 (17.4)
Male, n (%)	38 (41.8)	22 (47.8)
Histologic type: adenocarcinoma, n (%)	91 (100)	46 (100)
Clinical stage at enrollment, n (%)		
Stage IIIb	2 (2.2)	1 (2.2)
Stage IV	89 (97.8)	45 (97.8)
ECOG PS 1, n (%)	76 (83.5)	37 (80.4)
Brain metastases, n (%)	18 (19.8)	10 (21.7)
Liver metastases, n (%)	18 (19.8)	7 (15.2)
EGFR mutation type#, n (%)		
19-Del	43 (47.3)	32 (69.6)
L858R	48 (52.7)	14 (30.4)

	Sac-TMT (n = 91)	Docetaxel (n = 46)
T790M gene status, n (%)		
Positive	19 (20.9)	10 (21.7)
Negative	32 (35.2)	13 (28.3)
Unknown	40 (44.0)	23 (50.0)
Prior anti-tumor therapy lines (Including EGFR-TKI), n (%)		
1*	9 (9.9)	5 (10.9)
2	52 (57.1)	20 (43.5)
>2	30 (33.0)	21 (45.7)
Prior EGFR-TKI therapy, n (%)		
3rd generation EGFR-TKI in 1st line	54 (59.3)	26 (56.5)
3rd generation EGFR-TKI in 2nd line	30 (33.0)	18 (39.1)
No 3rd generation EGFR-TKI used	7 (7.7)	2 (4.3)
Prior antiangiogenic therapy, n (%)	60 (65.9)	33 (71.7)
Prior immunotherapy, n (%)	15 (16.5)	6 (13.0)

Skuteczność Sac-TMT: ORR 45% (3x↑vs CHT), w TROP2(+) – 56%, mPFS (2x↑ vs CHT)





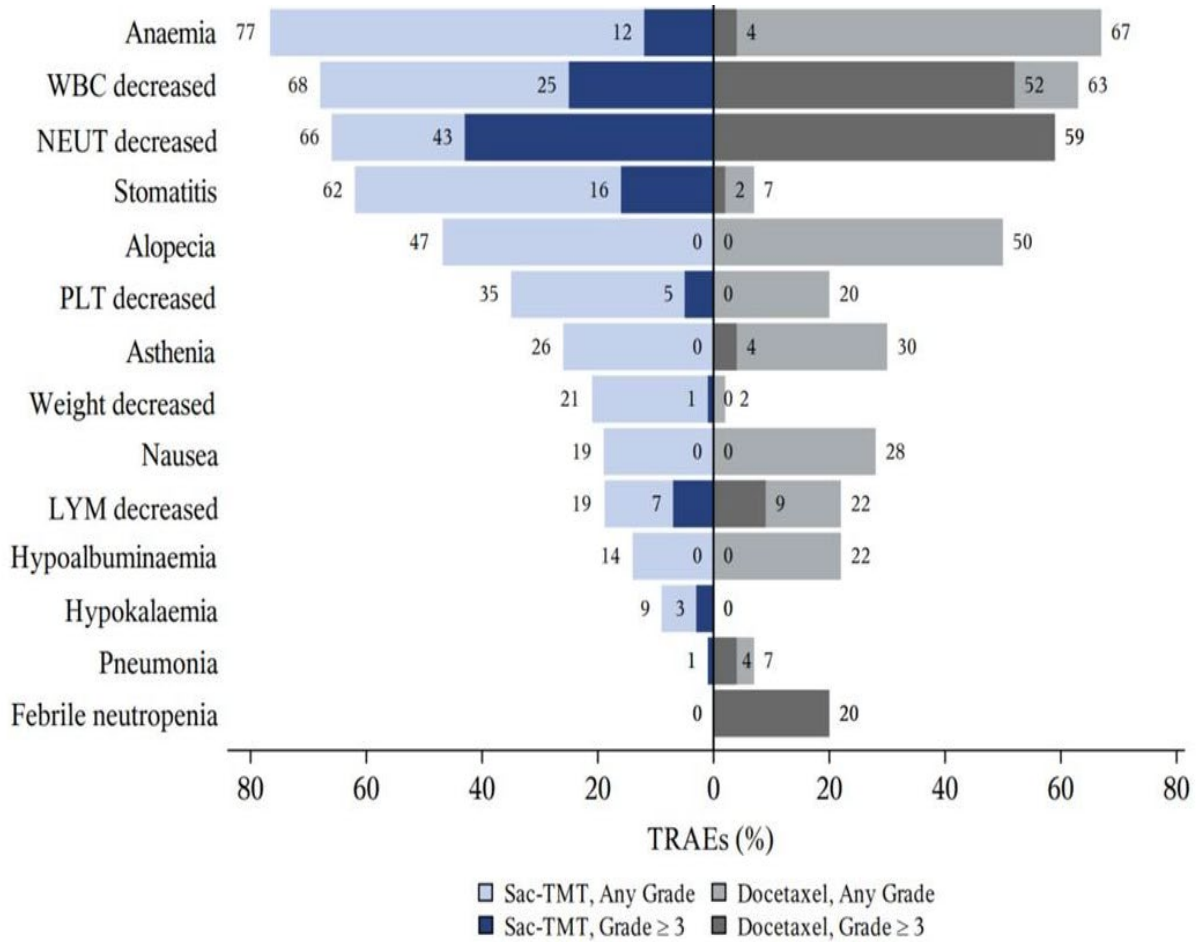


	Sac-TMT (n = 91)	Docetaxel (n = 46)
PFS events, n (%)	64 (70.3)	42 (91.3)
Median PFS, months (95% CI)	6.9 (5.4, 8.2)	2.8 (1.6, 4.1)
6-month PFS rate, %	54.2	14.6

HR: 0.30 (95% CI: 0.20, 0.46)

P < 0.0001

Profil bezpieczeństwa



- **Głównie tox. hematologiczne w obu ramionach**
- **G≥ 3 i SAE – rzadziej w ramieniu z saci (56 vs 71%, 16% vs 41%)**
- nie obserwoano ILD
- Zaburzenia widzenia i ból gałek ocznych – 1 chory, G1

2025 ASCO ANNUAL MEETING

First-line adagrasib (ADA) with pembrolizumab (PEMBRO) in patients with advanced/metastatic *KRAS*^{G12C}-mutated non-small cell lung cancer (NSCLC) from the phase 2 portion of the KRYSTAL-7 study

Pasi A. Jänne,[1] Willemijn S.M.E. Theelen,[2] Marina C. Garassino,[3] Alexander I. Spira,[4-6] Janessa Laskin,[7] Filippo de Marinis,[8] Firas B. Badin,[9] Lisenka N. Boom,[10] Carlos Aguado,[11] Izabela Chmielewska,[12] Enriqueta Felip,[13] Gyula Ostoros,[14] Lauren Jimenez-Kurlander,[15] Cassie M. Lane,[15] Archie Sachdeva,[15] Laura J. Eccles,[15*] Shun Lu[16]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]The Netherlands Cancer Institute, Amsterdam, The Netherlands; [3]The University of Chicago, Chicago, IL, USA; [4]Virginia Cancer Specialists, Fairfax, VA, USA; [5]US Oncology Research, The Woodlands, TX, USA; [6]NEXT Oncology, Fairfax, VA, USA; [7]BC Cancer Vancouver Centre, Vancouver, BC, Canada; [8]Istituto Europeo di Oncologia, IRCCS, Milan, Italy; [9]Baptist Health Medical Group, Lexington, KY, USA; [10]Ziekenhuis St Jansdal, Harderwijk, The Netherlands; [11]Hospital Clinico Universitario San Carlos, Madrid, Spain; [12]Medical University of Lublin, Lublin, Poland; [13]Vall d'Hebron Institute of Oncology, Vall d'Hebron Barcelona Hospital Campus, Universitat Autònoma de Barcelona, Barcelona, Spain; [14]National Korányi Institute of Pulmonology, Budapest, Hungary; [15]Bristol Myers Squibb, Princeton, NJ, USA; [16]Shanghai Chest Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai, China

KRYSTAL-7[a] phase 2

Key eligibility criteria

- Advanced, unresectable or metastatic NSCLC with *KRAS*^{G12C} mutation[b]
- No prior systemic therapy for locally advanced/metastatic disease[c]
- Known PD-L1 TPS (local or central testing)[d]
- Treated, neurologically stable brain metastases allowed

ADA 400 mg PO BID +
PEMBRO 200 mg IV Q3W[e,f]

Primary endpoint

- ORR per investigator assessment (RECIST v1.1)

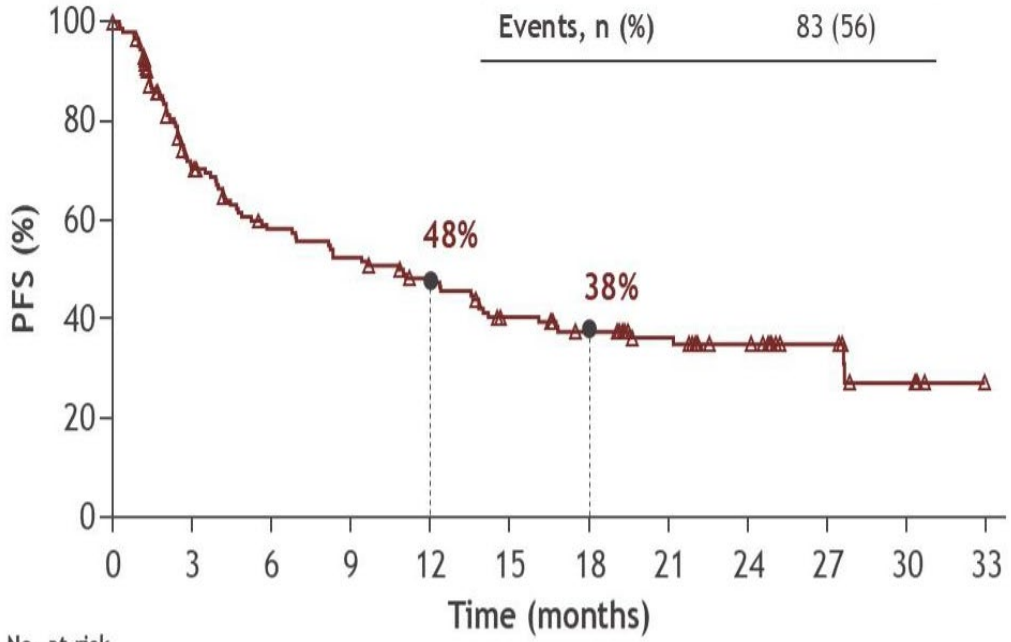
Secondary endpoints

- DOR and PFS per investigator assessment
- OS
- Safety

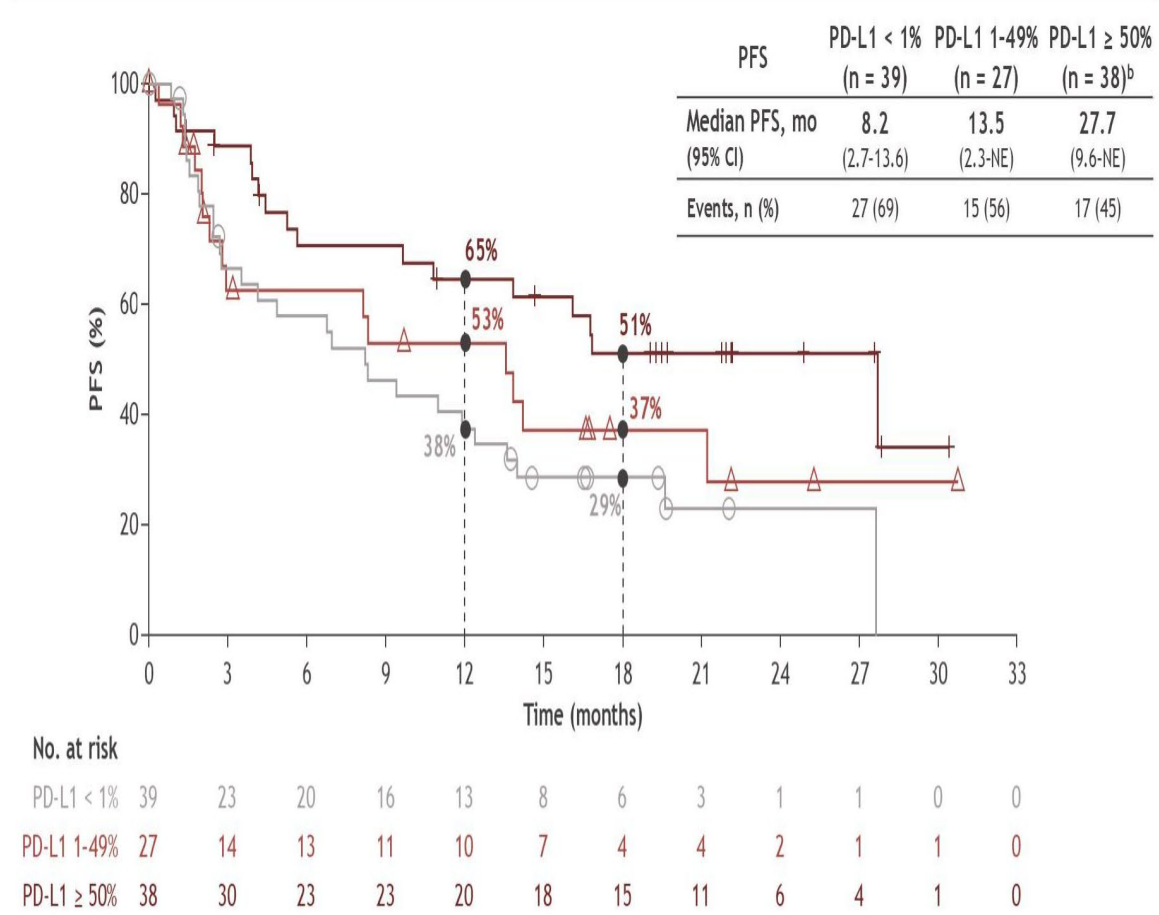
	All patients (N = 149)
Median age, years (range)	67 (40-90)
Female, n (%)	71 (48)
Race, n (%)	
Asian	23 (15)
Black or African American	5 (3)
White	113 (76)
Other or not reported	8 (5)
Ethnicity,[a] n (%)	
Hispanic or Latino / Non-Hispanic or Latino	5 (3) / 139 (93)
Histology, n (%)	
Adenocarcinoma / Other[b]	143 (96) / 6 (4)
Smoking status, n (%)	
Current or former smoker / never smoker	146 (98) / 3 (2)
ECOG PS, n (%)	
0 / 1	57 (38) / 92 (62)
Baseline metastases, n (%)	
Adrenal / Bone / CNS / Liver	28 (19) / 46 (31) / 24 (16) / 25 (17)
PD-L1 TPS, n (%)[c]	
< 1%	39 (26)
1-49%	27 (18)
≥ 50%	38 (26)[d]

Skuteczność ada+pembro: mPFS=11 m-cy, 28 m-cy!!! dla NDRP z PD-L1≥50%

PFS	All patients (N = 149)
Median PFS, mo (95% CI)	11.0 (5.8-14.0)
Events, n (%)	83 (56)

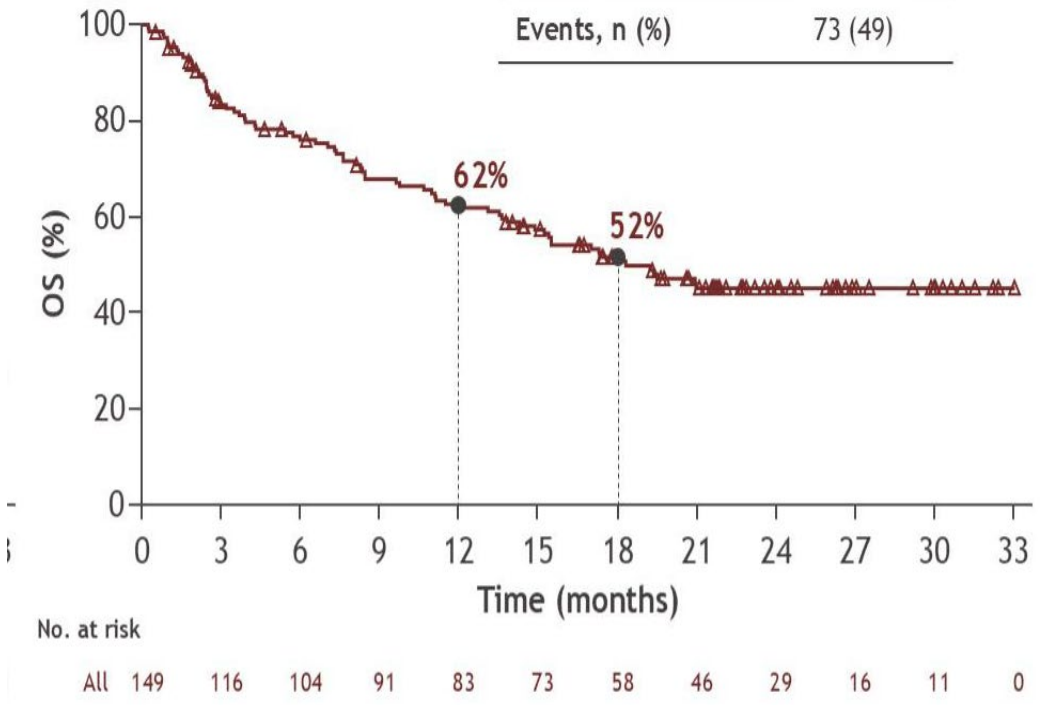


PFS	PD-L1 < 1% (n = 39)	PD-L1 1-49% (n = 27)	PD-L1 ≥ 50% (n = 38)[b]
Median PFS, mo (95% CI)	8.2 (2.7-13.6)	13.5 (2.3-NE)	27.7 (9.6-NE)
Events, n (%)	27 (69)	15 (56)	17 (45)

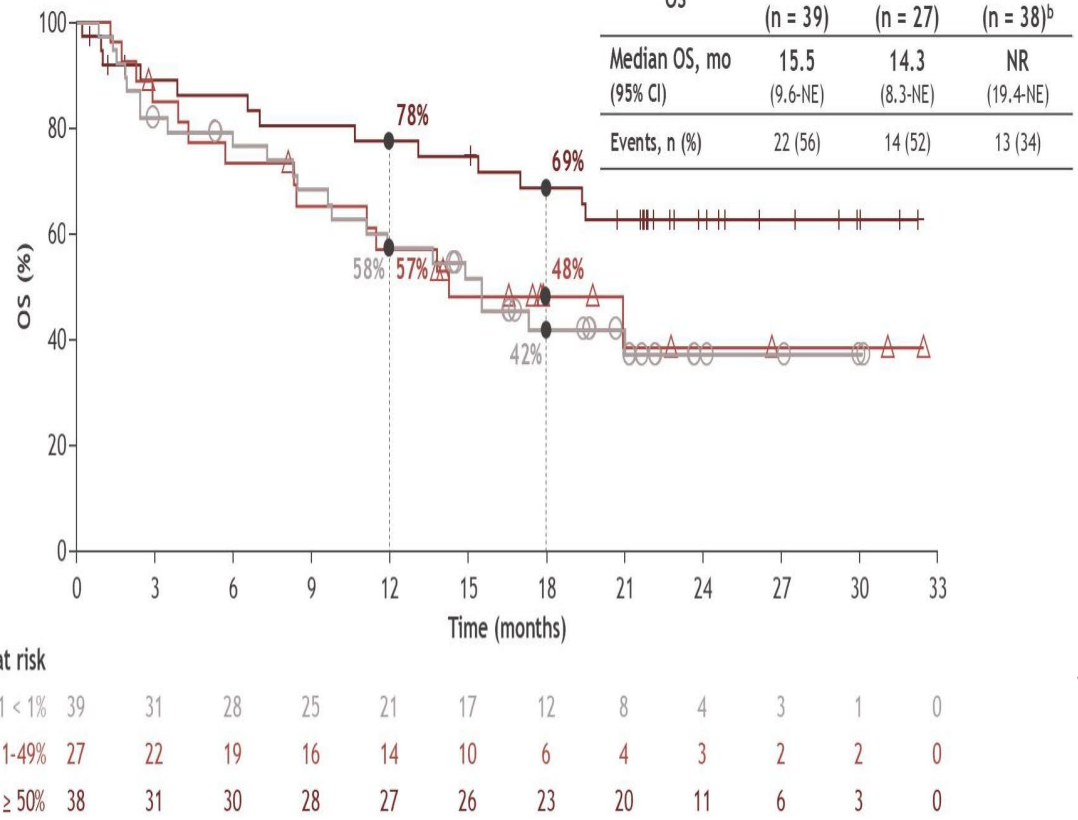


Skuteczność ada+pembro: mOS=18 m-cy, NR!!! dla NDRP z PD-L1≥50%

OS	All patients (N = 149)
Median OS, mo (95% CI)	18.3 (14.3-NE)
Events, n (%)	73 (49)



OS	PD-L1 < 1% (n = 39)	PD-L1 1-49% (n = 27)	PD-L1 ≥ 50% (n = 38)[b]
Median OS, mo (95% CI)	15.5 (9.6-NE)	14.3 (8.3-NE)	NR (19.4-NE)
Events, n (%)	22 (56)	14 (52)	13 (34)



Profil bezpieczeństwa kombinacji ada+pembro

Patients, n (%)	PD-L1 < 50% (n = 95)	PD-L1 ≥ 50% (n = 54)	All patients (N = 149)
TRAEs			
Any grade	91 (96)	50 (93)	141 (95)
Grade 3	54 (57)	32 (59)	86 (58)
Grade 4	13 (14)	3 (6)	16 (11)
Grade 5	3 (3)	0	3 (2)[b]
TRAEs leading to			
ADA dose interruption	65 (68)	35 (65)	100 (67)
ADA dose reduction[c]	50 (53)	22 (41)	72 (48)
ADA discontinuation only	5 (5)	5 (9)	10 (7)
PEMBRO discontinuation only	19 (20)	6 (11)	25 (17)
ADA and PEMBRO discontinuation[d]	7 (7)	3 (6)	10 (7)
Any grade immune-related AEs	23 (24)	10 (19)	33 (22)

- **Najczęstsze działania niepożądane: nudności, biegunka, ↑ Aspat i Alat, gł. G1-2**
- **Najczęstsze AE ≥3: ↑ Aspat, lipaza, Alat**
- **irAE: ILD (12%), niedoczynność tarczycy (7%),** zapalenie wątroby (4%),

2025 ASCO ANNUAL MEETING

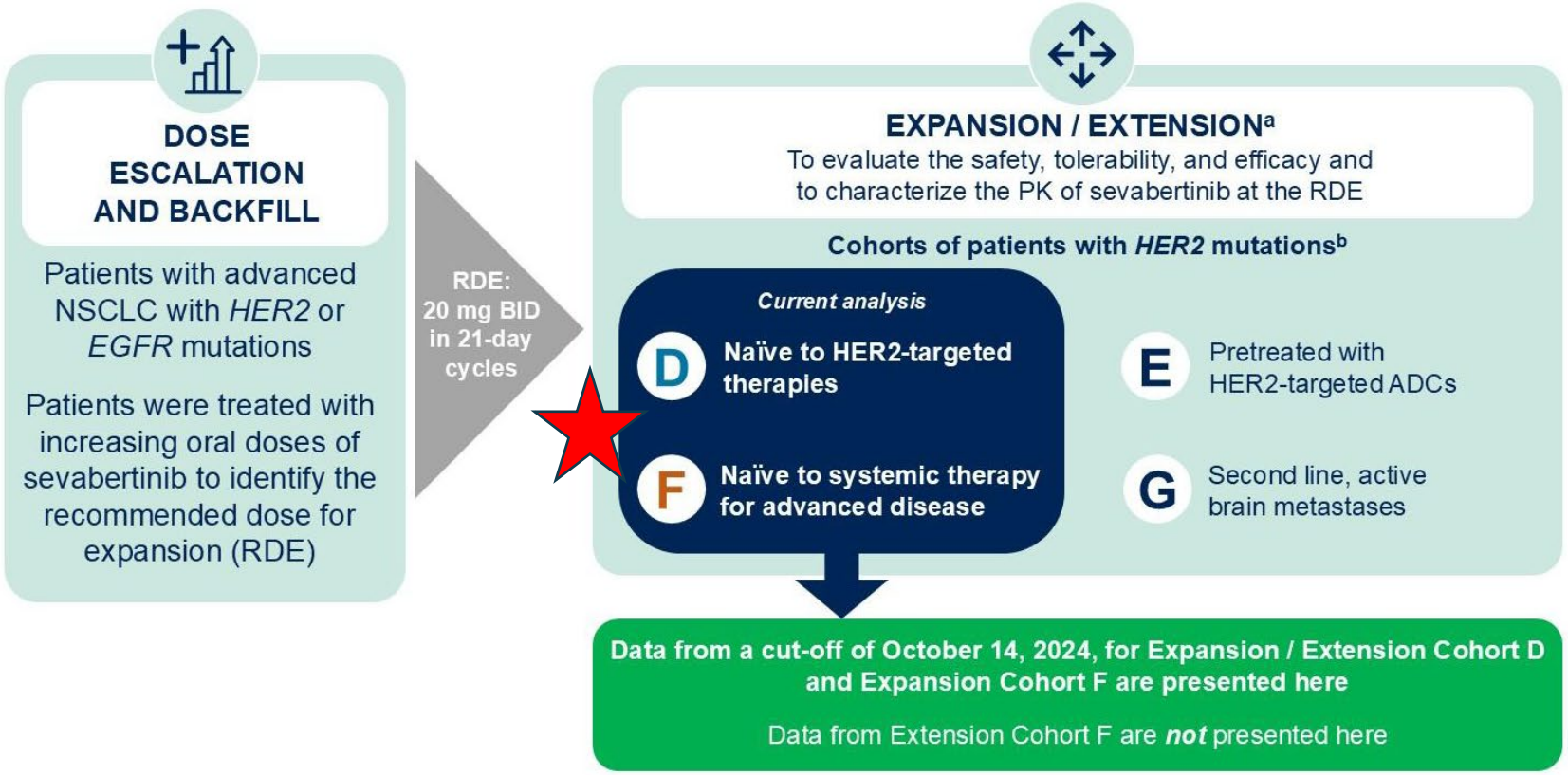
SOHO-01: Safety and efficacy of sevabertinib (BAY 2927088) in patients with advanced *HER2*-mutant non-small cell lung cancer (NSCLC) who were pretreated but naïve to HER2-targeted therapy or had not received any treatment for advanced disease

Herbert H. Loong,[1] Lin Li,[2] Lin Wu,[3] Tae Min Kim,[4] Arsela Prelaj,[5] Xiaorong Dong,[6] Hye Ryun Kim,[7] Tsung-Ying Yang,[8] Gennaro Daniele,[9] Shun Lu,[10] Yong Fang,[11] Yuki Shinno,[12] Liyun Miao,[13] Nicolas Girard,[14] Jun Zhao,[15] Gerrina Ruiter,[16] Virginie Aris,[17] Rui Li,[17] Paolo Grassi,[18] Xiuning Le[19]

June 1, 2025

[1]The Chinese University of Hong Kong, Hong Kong SAR, China; [2]Department of Medical Oncology, Beijing Hospital, National Center of Gerontology, Institute of Geriatric Medicine, Chinese Academy of Medical Sciences, Beijing, China; [3]Department of Thoracic Medical Oncology, Hunan Cancer Hospital, The Affiliated Cancer Hospital of Xiangya School of Medicine, Central South University, Changsha, China; [4]Seoul National University Hospital, Seoul, South Korea; [5]Oncologia Medica Toracica Dept., Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy; [6]Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [7]Yonsei Cancer Center, Seoul, South Korea; [8]Department of Chest Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [9]Phase 1 Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy; [10]Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [11]Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China; [12]National Cancer Center Hospital, Chuo-ku, Tokyo, Japan; [13]Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing, China; [14]Institut Curie, Paris, France; [15]Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department I of Thoracic Oncology, Peking University Cancer Hospital & Institute, Beijing, China; [16]Departments of Clinical Pharmacology and Thoracic Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands; [17]Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ, USA; [18]Bayer S.p.A., Milan, Italy; [19]MD Anderson Cancer Center, Houston, TX, USA

SOHO-01 study design (NCT05099172)



PRIMARY ENDPOINTS

- Safety and tolerability
- PK

SECONDARY ENDPOINTS

- ORR (per investigator assessment and BICR) by RECIST v1.1
- DoR, DCR, and PFS (per investigator assessment and BICR)

[a]Patients from dose escalation / backfill treated with 20 mg BID and who met the same eligibility criteria were combined for statistical analysis; [b]Cohorts of patients with *EGFR* mutations are not shown

Charakterystyka chorych

	Cohort D[a] (*n*=81)	Cohort F[b] (*n*=39)
Female, *n* (%)	50 (61.7)	25 (64.1)
Race, *n* (%)		
White	18 (22.2)	10 (25.6)
Black or African American	1 (1.2)	0
Asian	57 (70.4)	28 (71.8)
Not reported	5 (6.2)	1 (2.6)
Median age, years (range)	60.0 (29-82)	65.0 (31-80)
Baseline ECOG PS, *n* (%)		
0	31 (38.3)	9 (23.1)
1	50 (61.7)	30 (76.9)
Smoking habits at informed consent, *n* (%)		
Never	50 (61.7)	31 (79.5)
Former	27 (33.3)	6 (15.4)
Current	4 (4.9)	2 (5.1)
NSCLC histology, *n* (%)		
Adenocarcinoma, mixed, or NOS[c]	77 (95.1)	39 (100)
Squamous cell carcinoma, other	4 (4.9)	0
Activating *HER2* mutations, *n* (%)		
HER2 ex20ins	68 (84.0)	37 (94.9)
HER2 point mutation	13 (16.0)	1 (2.6)
Other	0	1 (2.6)

	Cohort D[a] (*n*=81)	Cohort F[b] (*n*=39)
***HER2* TKD mutation, *n* (%)**		
Yes	72 (88.9)	38 (97.4)
No	8 (9.9)	1 (2.6)
Not applicable[d]	1 (1.2)	0
Median time since most recent progression / relapse to first administration of study treatment, months (range)[e]	1.2 (0-14)	1.4 (0-3)
Brain metastases at baseline,[f] *n* (%)		
Yes	17 (21.0)	2 (5.1)
No	64 (79.0)	37 (94.9)
Number of prior systemic anti-cancer therapies, *n* (%)		
0	0	37 (94.9)
1	46 (56.8)	0
2	16 (19.8)	2 (5.1)
≥3	19 (23.5)	0
Prior anti-cancer therapies, *n* (%)		
Chemotherapy	78 (96.3)	2 (5.1)
Platinum and no immunotherapy	20 (24.7)	0
Platinum and immunotherapy	56 (69.1)	2 (5.1)
Trastuzumab deruxtecan[g]	2 (2.5)	0

Skuteczność sewabertinibu: niezależnie od linii leczenia oraz obecności przerzutów w OUN

Cohort D (*n*=81), naïve to HER2-targeted therapy

Median follow-up: 7.3 months[a]

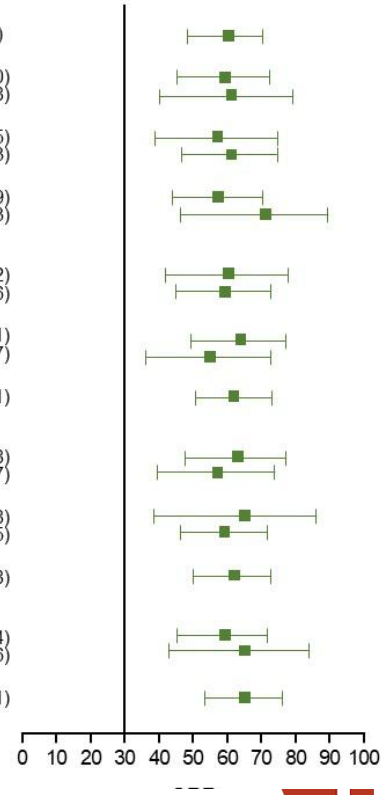
n (%)	INV	BICR
CR	1 (1.2)	1 (1.2)
PR	47 (58.0)	48 (59.3)
SD	22 (27.2)	22 (27.2)
PD	10 (12.3)	7 (8.6)
Not evaluable[b]	1 (1.2)	3 (3.7)
ORR[c] [95% CI]	**48 (59.3)** [47.8, 70.1]	**49 (60.5)** [49.0, 71.2]
DCR[d] [95% CI]	**68 (84.0)** [74.1, 91.2]	**66 (81.5)** [71.3, 89.2]

Cohort F (*n*=39): naïve to systemic therapy for advanced disease

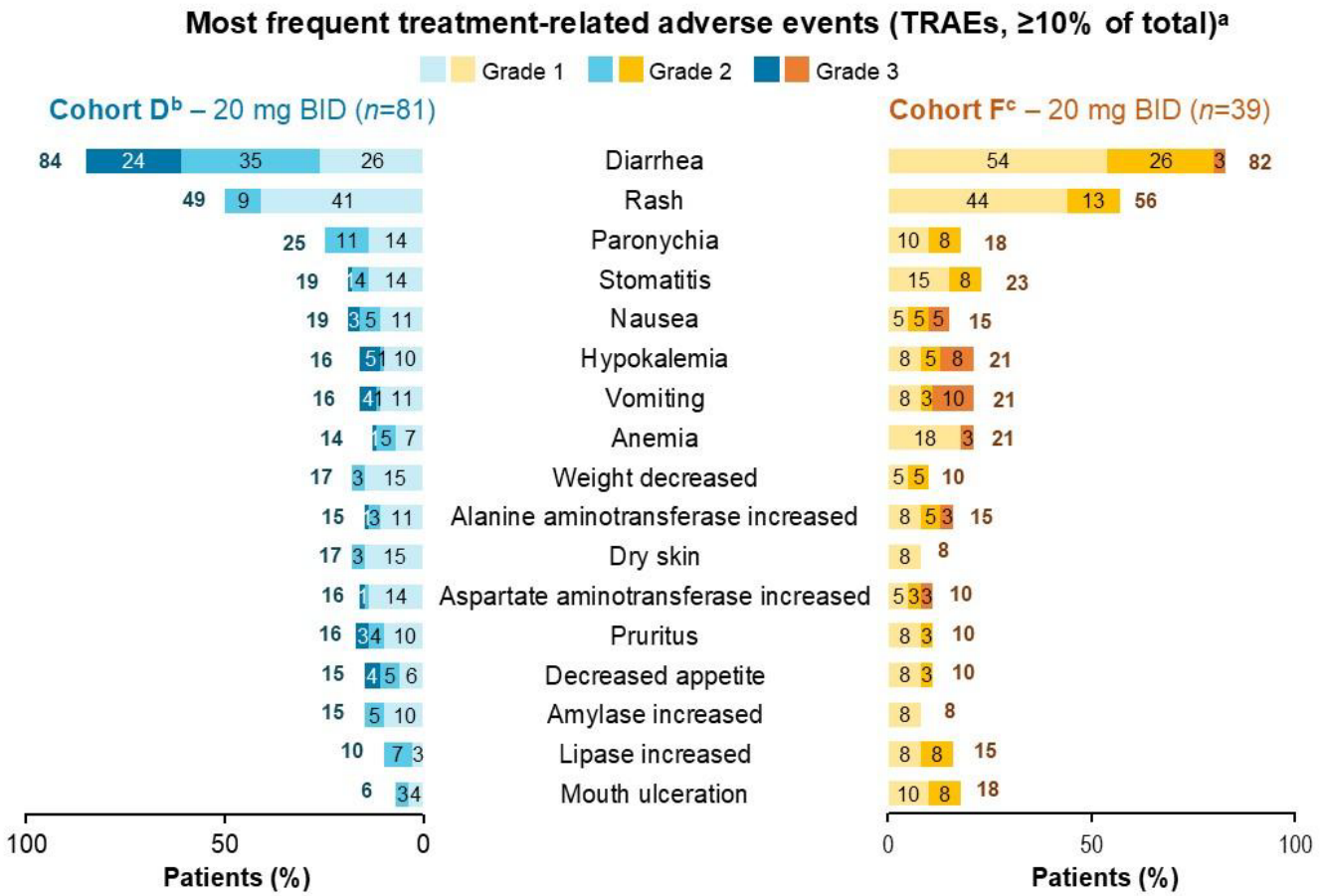
Median follow-up: 5.6 months[a]

n (%)	INV
CR	0
PR	23 (59.0)
SD	12 (30.8)
PD	3 (7.7)
NA[b]	1 (2.6)
ORR[c] [95% CI]	**23 (59.0)** [42.1, 74.4]
DCR[d] [95% CI]	**33 (84.6)** [69.5, 94.1]

	Participants, *n*	CR / PR, *n*	ORR (95% CI)
All participants			
Overall	81	49	60.5 (49, 71.2)
Age group			
<65	55	33	60.0 (45.9, 73.0)
≥65	26	16	61.5 (40.6, 79.8)
Sex			
Male	31	18	58.1 (39.1, 75.5)
Female	50	31	62.0 (47.2, 75.3)
Race			
Asian	57	33	57.9 (44.1, 70.9)
White	18	13	72.2 (46.5, 90.3)
Other	6	3	NC
ECOG PS at baseline			
0 – FULLY ACTIVE	31	19	61.3 (42.2, 78.2)
1 – RESTRICTED ACTIVE	50	30	60.0 (45.2, 73.6)
Smoking status			
Never	50	32	64.0 (49.2, 77.1)
Former / current	31	17	54.8 (36.0, 72.7)
Histology adenocarcinoma			
Yes	77	48	62.3 (50.6, 73.1)
No	4	1	NC
Number of prior systemic anti-cancer therapies			
<2	46	29	63.0 (47.5, 76.8)
≥2	35	20	57.1 (39.4, 73.7)
Brain metastases at baseline			
Yes	17	11	64.7 (38.3, 85.8)
No	64	38	59.4 (46.4, 71.5)
Prior platinum therapy			
Yes	76	47	61.8 (50.0, 72.8)
No	5	2	NC
Prior anti-PD(L)1 therapy			
Yes	58	34	58.6 (44.9, 71.4)
No	23	15	65.2 (42.7, 83.6)
***HER2* TKD mutation status at baseline**			
Yes	72	47	65.3 (53.1, 76.1)
No	8	2	NC



Profil bezpieczeństwa sewabertinibu: gł. toksyczność żołądkowo-jelitowa



XXIV SPOTKANIE Po ASCO

2025 ASCO ANNUAL MEETING

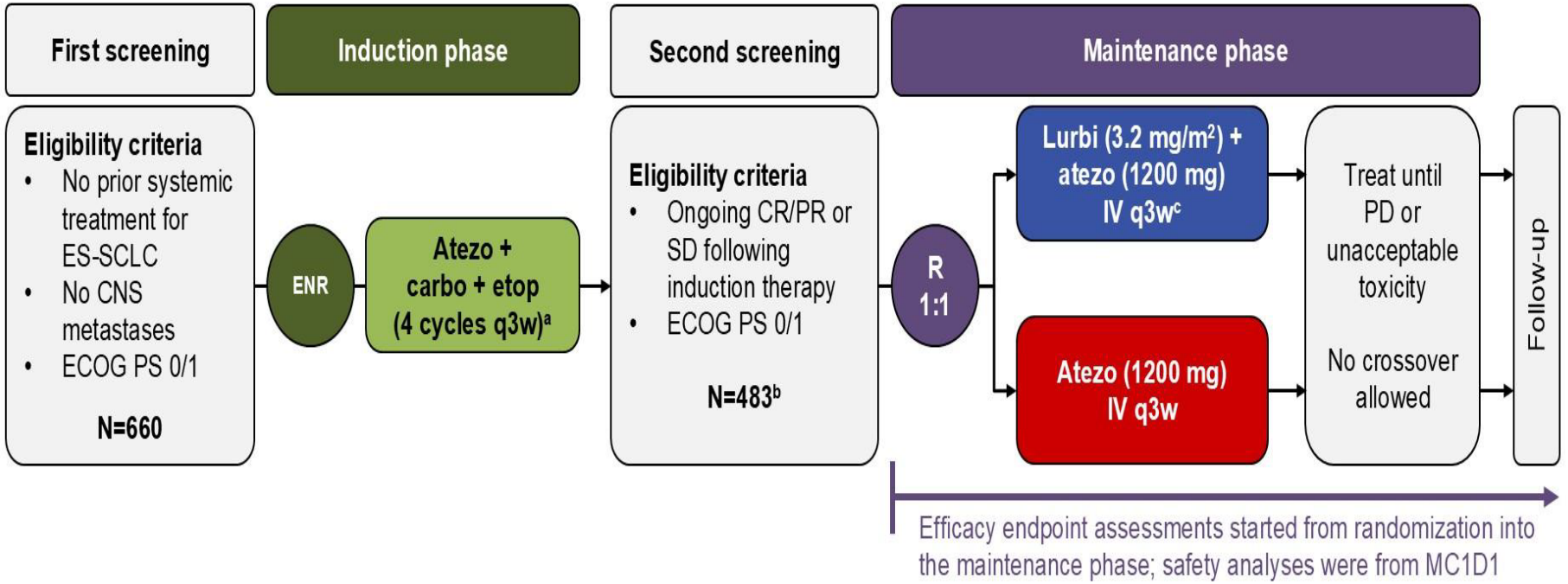
Lurbinectedin + atezolizumab as first-line maintenance treatment in patients with extensive-stage small cell lung cancer: Primary results of the Phase 3 IMforte trial

Luis Paz-Ares,[1] Hossein Borghaei,[2] Stephen V. Liu,[3] Solange Peters,[4] Roy S. Herbst,[5] Katarzyna Stencel,[6] Margarita Majem,[7] Grzegorz Czyżewicz,[8] Reyes Bernabé Caro,[9] Ki Hyeong Lee,[10] Melissa L. Johnson,[11] Nuri Karadurmuş,[12] Christian Grohé,[13] Vaikunth Cuchelkar,[14] Vilma Graupner,[15] Monika Kaul,[14] Ya-Chen Lin,[14] Debasis Chakrabarti,[16] Kamalnayan Bhatt,[16] Martin Reck[17]

[1]Hospital Universitario 12 de Octubre, H12O-CNIO Lung Cancer Unit, Universidad Complutense and Ciberonc, Madrid, Spain; [2]Fox Chase Cancer Center, Philadelphia, PA, USA; [3]Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; [4]University Hospital CHUV, Lausanne, Switzerland; [5]Yale School of Medicine, New Haven, CT, USA; [6]Wielkopolska Center of Pulmonology and Thoracic Surgery of Eugenia and Janusz Zeyland, Poznan, Poland; [7]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [8]The John Paul II Specialist Hospital, Kraków, Poland; [9]Hospital Universitario Virgen del Rocío, Seville, Spain; [10]Chungbuk National University Hospital, Cheongju, South Korea; [11]Tennessee Oncology, Sarah Cannon Research Institute, Nashville, TN, USA; [12]University of Health Sciences, Gülhane Training and Research Hospital, Ankara, Türkiye; [13]Klinik für Pneumologie, Evangelische Lungenklinik Berlin, Berlin, Germany; [14]Genentech Inc, South San Francisco, CA, USA; [15]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]Jazz Pharmaceuticals plc, Dublin, Ireland; [17]Lung Clinic Grosshansdorf, Airway Research Center North, German Center of Lung Research, Grosshansdorf, Germany

XXIV SPOTKANIE Po ASCO

BK Imforte – leczenie podtrzymujące atezo vs atezo+lurbi w ED SCLC odpowiadających na atezo+karbo+etop



Last patient randomized: April 30, 2024
Clinical cutoff: July 29, 2024

Stratification factors for randomization
- ECOG PS (0/1)
- LDH (≤ULN/>ULN)
- Presence of liver metastases (Y/N) at induction BL
- Prior receipt of PCI (Y/N)

Primary endpoints
IRF-PFS and OS

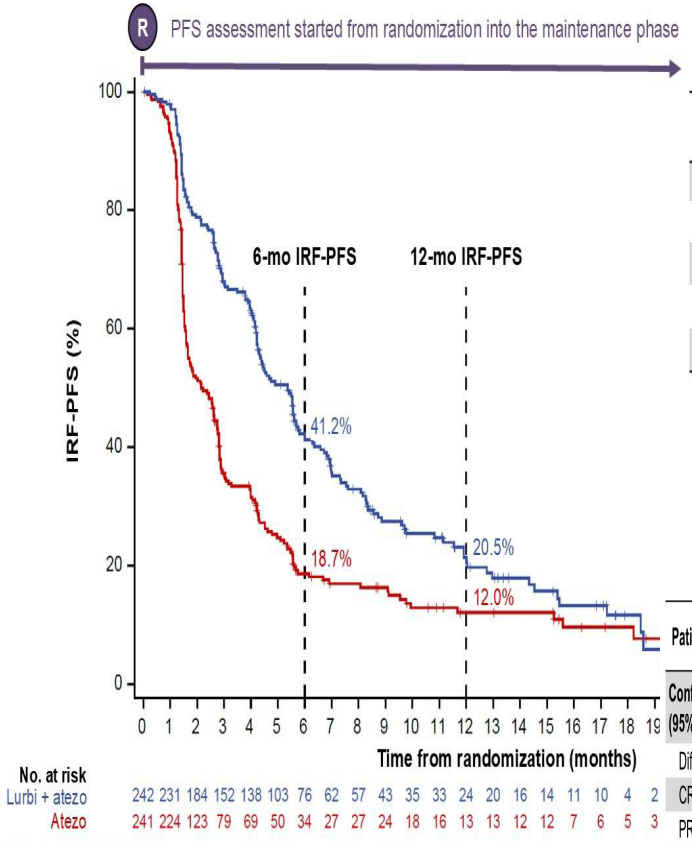
Secondary endpoints included
INV-PFS, ORR, DOR, and safety

Charakterystyka chorych

Characteristic	Lurbi + atezo (n=242)	Atezo (n=241)
Age, median (range), years	65.0 (38-85)	67.0 (35-85)
<65 years, n (%)	118 (48.8)	90 (37.3)
Sex, male, n (%)	151 (62.4)	151 (62.7)
Race, n (%)		
White	195 (80.6)	199 (82.6)
Asian	31 (12.8)	31 (12.9)
Other[a]	16 (6.6)	11 (4.6)
Current or previous tobacco use history, n (%)	235 (97.1)	236 (97.9)
Liver metastases at induction BL, n (%)[b]	100 (41.3)	94 (39.0)
Prior PCI, n (%)[b]	34 (14.0)	37 (15.4)
ECOG PS 0 at maintenance BL, n (%)[b]	105 (43.4)	102 (42.3)
LDH ≤ULN at maintenance BL, n (%)[b]	176 (72.7)	179 (74.3)
Time from induction Cycle 1 Day 1 to randomization, median (range), mo	3.2 (2.6-4.6)	3.2 (2.7-5.2)
Response to induction therapy, n (%)[c]		
CR/PR	206 (87.3)	213 (88.8)
SD	28 (11.9)	25 (10.4)
PD[d]	2 (0.8)	2 (0.8)

XXIV SPOTKANIE Po ASCO

Kombinacja lurbi+atezo skuteczniejsza od atezo: mPFS: 5,4 vs 2 m-ce, ORR2x↑ (20vs10%), mOS: 13 vs 10 m-cy

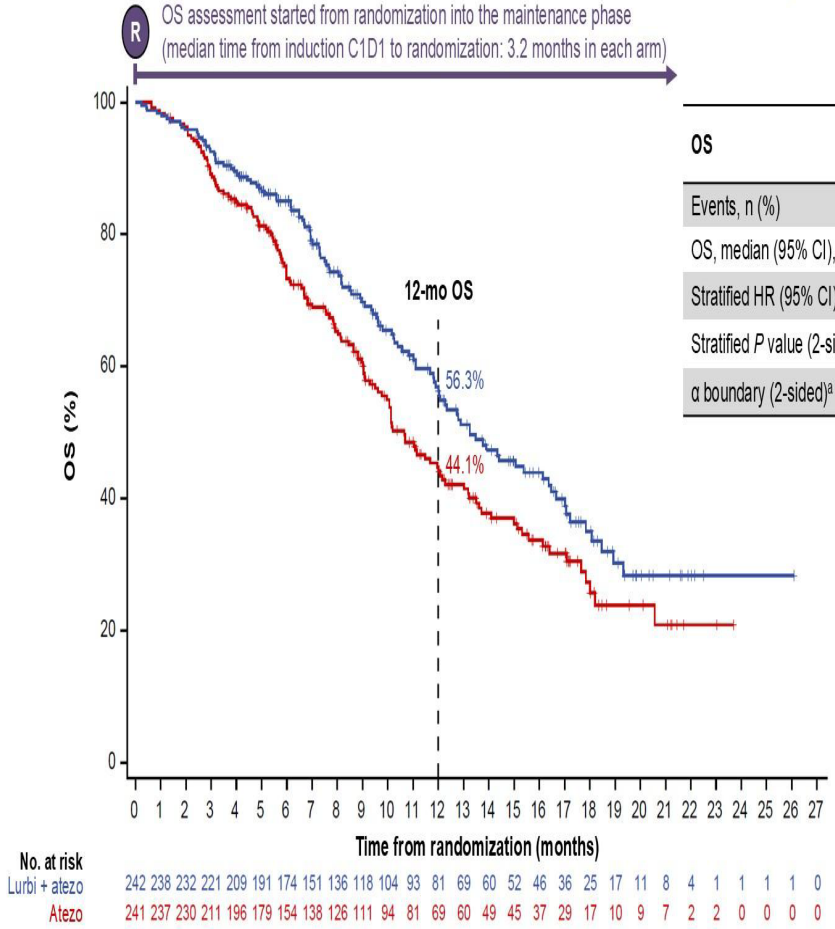


IRF-PFS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	174 (71.9)	202 (83.8)
PFS, median (95% CI), mo	5.4 (4.2, 5.8)	2.1 (1.6, 2.7)
Stratified HR (95% CI)	**0.54 (0.43, 0.67)**	
Stratified *P* value (2-sided)	<0.0001	
α boundary (2-sided)	0.001	

Investigator-assessed PFS was consistent with IRF-PFS

- Median: 5.4 mo with lurbi + atezo and 2.7 mo with atezo (stratified HR, 0.55 [95% CI: 0.45, 0.68])

Patients with measurable disease[a]	Lurbi + atezo (n=175)	Atezo (n=182)
Confirmed objective response, n (%) (95% CI)[b]	34 (19.4) (13.9, 26.1)	19 (10.4) (6.4, 15.8)
Difference in ORR (95% CI), %	9.0 (1.1, 16.9)	
CR, n (%)	4 (2.3)	1 (0.5)
PR, n (%)	30 (17.1)	18 (9.9)
SD, n (%)	96 (54.9)	68 (37.4)
PD, n (%)	34 (19.4)	87 (47.8)



OS	Lurbi + atezo (n=242)	Atezo (n=241)
Events, n (%)	113 (46.7)	136 (56.4)
OS, median (95% CI), mo	13.2 (11.9, 16.4)	10.6 (9.5, 12.2)
Stratified HR (95% CI)	**0.73 (0.57, 0.95)**	
Stratified *P* value (2-sided)	0.0174	
α boundary (2-sided)[a]	0.0313	

XXIV SPOTKANIE Po ASCO

Profil bezpieczeństwa: lurbi+atezo – gł.nudności i niedokrwistość

Patients with ≥1 AE, n (%)	Lurbi + atezo (n=242)	Atezo (n=240)
All-cause AEs	235 (97.1)	194 (80.8)
Grade 3/4 AEs	92 (38.0)	53 (22.1)
Treatment-related Grade 3/4 AEs	62 (25.6)	14.0 (5.8)
Grade 5 AEs	12 (5.0)	6 (2.5)
Treatment-related Grade 5 AEs	2 (0.8)[a]	1 (0.4)[b]
Serious AEs	75 (31.0)	41 (17.1)
AEs leading to discontinuation of any study drug	15 (6.2)	8 (3.3)
AEs leading to dose interruption/ modification of any study drug[c]	92 (38.0)	33 (13.8)

Patients with ≥1 AE, n (%)	Lurbi + atezo (n=242)	Atezo (n=240)
Lurbinectedin AESI[d]	93 (38.4)	62 (25.8)
Grade 5 AESI	7 (2.9)	4 (1.7)
Atezolizumab AESI[d]	76 (31.4)	54 (22.5)
Grade 5 AESI	0	0
Atezolizumab AESI requiring corticosteroids	40 (16.5)	18 (7.5)
Median treatment duration, mo	4.1 (lurbi)/ 4.2 (atezo)	2.1
Median number of doses received	6.5 (lurbi)/ 7.0 (atezo)	4.0

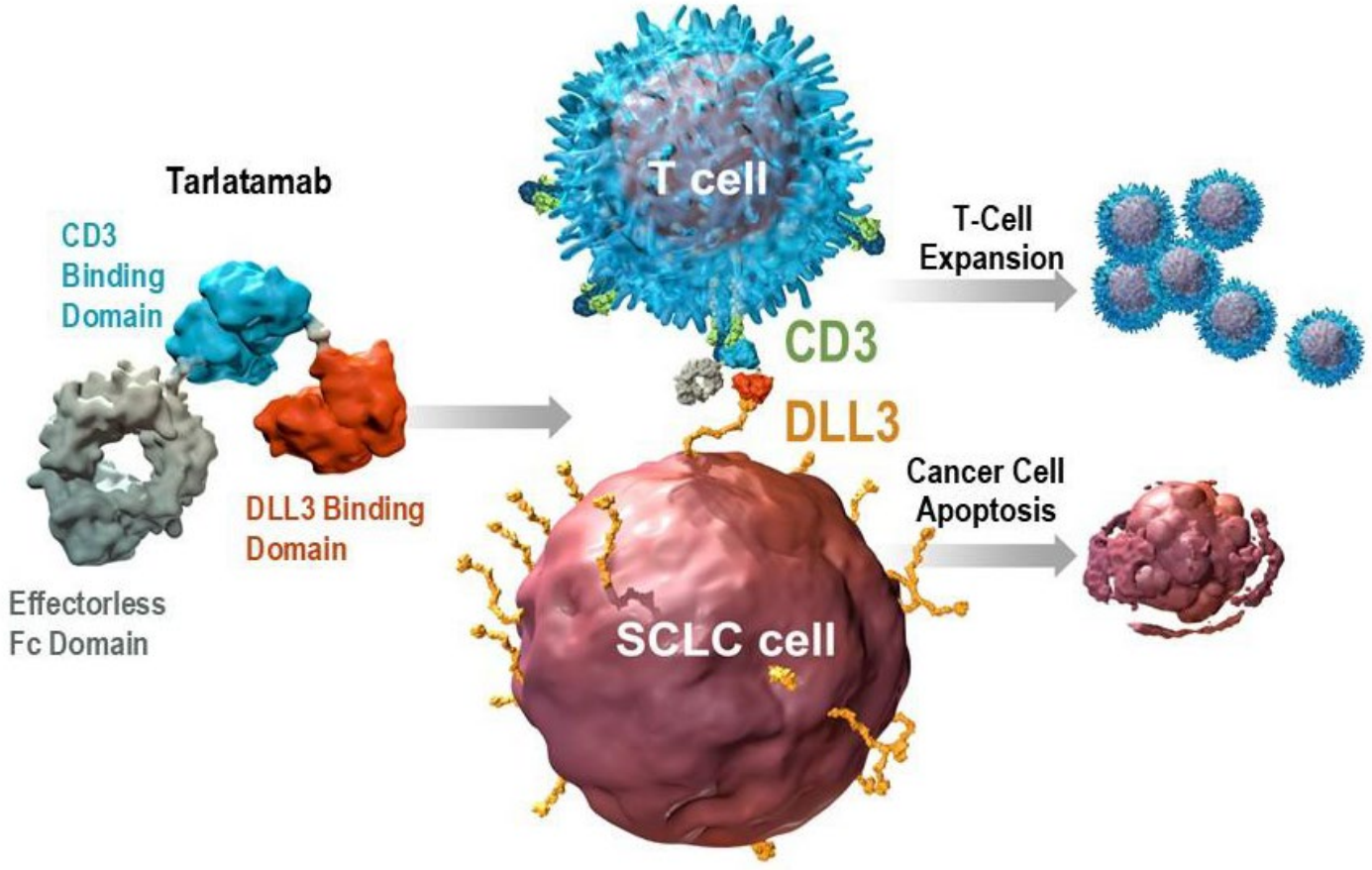
2025 ASCO ANNUAL MEETING

Tarlatamab versus chemotherapy as second-line treatment for small cell lung cancer (SCLC): primary analysis of the phase 3 DeLLphi-304 study

Charles M. Rudin, Giannis S. Mountzios, Longhua Sun, Byoung Chul Cho, Umut Demirci, Sofia Baka, Mahmut Gumus, Antonio Lugini, Tudor-Eliade Ciuleanu, Myung-Ju Ahn, Pedro Rocha, Bo Zhu, Fiona Blackhall, Tatsuya Yoshida, Taofeek K. Owonikoko, Luis Paz-Ares, Shuang Huang, Diana Gauto, Gonzalo Recondo, Martin Schuler

Speaker: **Charles M. Rudin, MD, PhD,** Fiona and Stanley Druckenmiller Center for Lung Cancer Research, Memorial Sloan Kettering Cancer Center, New York, USA.

Tarlatamab – bispecyficzny lek immunokompetentny – rec CD3 na limfocycie T i liganda DLL3 na komórce DRP



Randomized, controlled, phase 3 DeLLphi-304 study (NCT05740566)

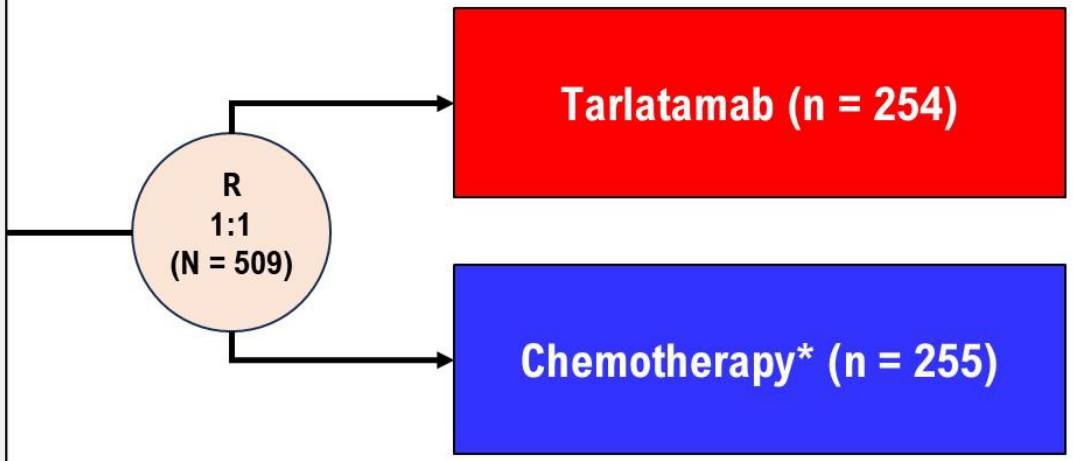
DeLLphi 304

Key inclusion criteria

- Histologically or cytologically confirmed SCLC
- Progression after 1L platinum-based chemotherapy +/- anti-PD-(L)1
- ECOG PS 0 or 1
- Asymptomatic, treated or untreated brain metastases

Randomization stratified by

- Prior anti-PD-(L)1 exposure (yes/no)
- Chemotherapy-free interval (< 90 days vs ≥ 90 to < 180 days vs ≥ 180 days)
- Presence of (previous/current) brain metastases (yes/no)
- Intended chemotherapy (topotecan/amrubicin vs lurbinectedin)



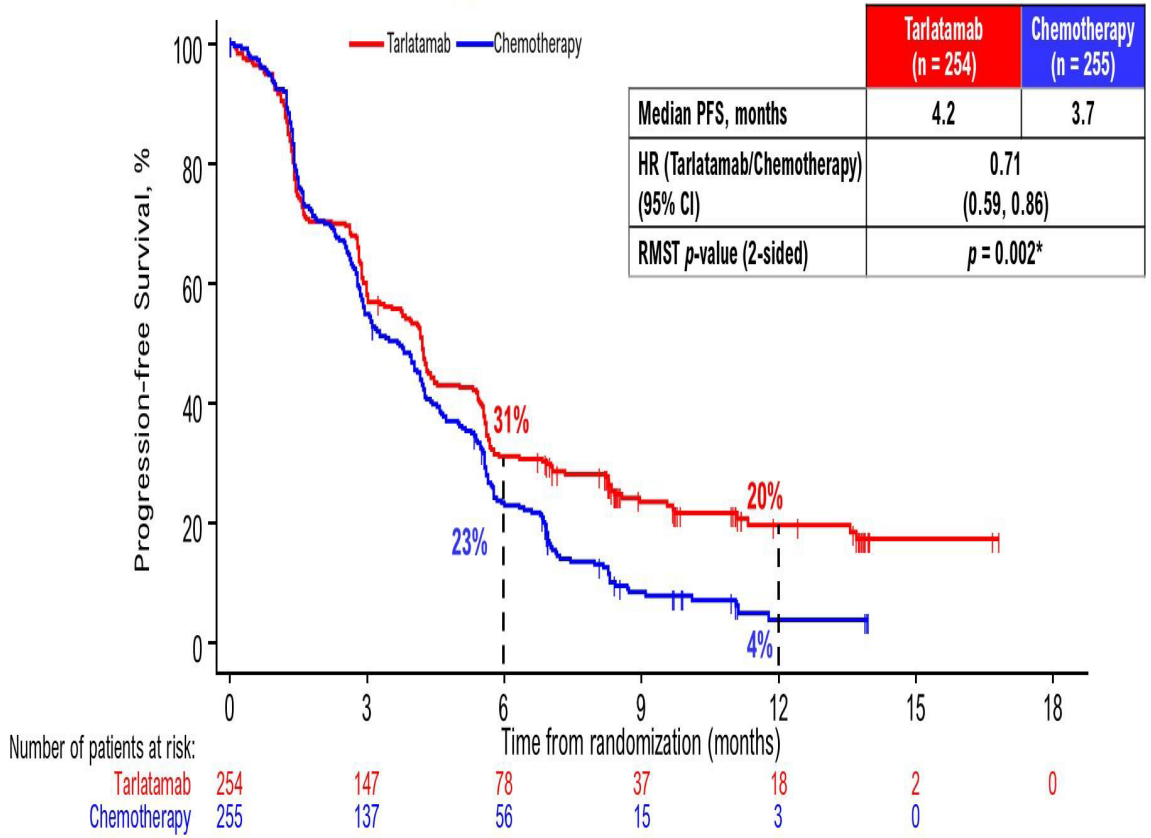
Topotecan (n = 185); Lurbinectedin (n = 47); Amrubicin (n = 23)

Primary Endpoint: Overall survival
Key Secondary Endpoints: Progression-free survival, patient-reported outcomes
Other Secondary Endpoints: Objective response, disease control, duration of response, safety

Charakterystyka chorych

	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median age, years (range)	64 (20 – 86)	66 (26 – 84)
Male / Female, %	72 / 28	66 / 34
Race Asian / Black / White, %	38 / 1 / 60	42 / 1 / 55
Smoking history Current or former smokers / Never smokers, %	91 / 9	88 / 12
ECOG performance status, 0 / 1, %	33 / 67	31 / 68
Prior anti-PD-(L)1 therapy, %	71	71
Prior radiotherapy for current malignancy*, %	63	63
Chemotherapy-free interval,% < 90 days ≥ 90 to < 180 days ≥ 180 days	 43 33 24	 45 31 25
Presence of brain / liver metastases, %	44 / 33	45 / 37
DLL3 expression, %, (n/N†)	95 (207/217)	93 (198/214)

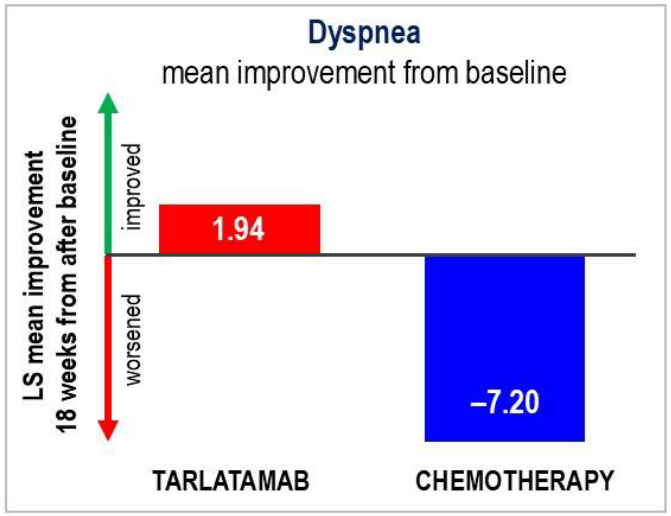
Tarlatamab skuteczniejszy od CHT – ORR 35 vs 20%, ↑ mPFS i mOS



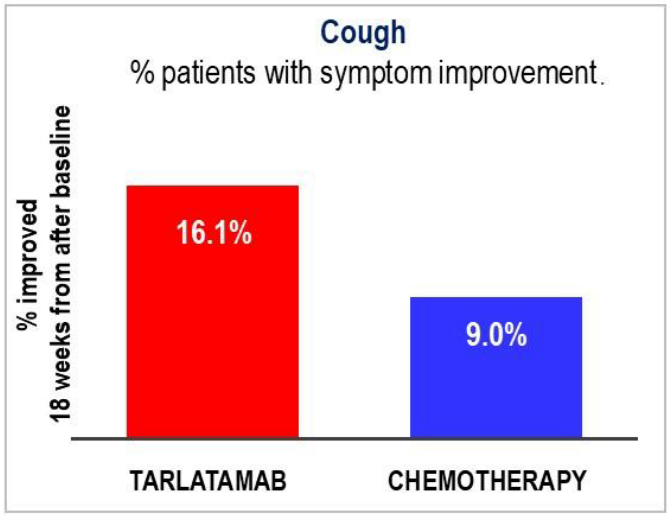
	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median PFS, months	4.2	3.7
HR (Tarlatamab/Chemotherapy) (95% CI)	0.71 (0.59, 0.86)	
RMST *p*-value (2-sided)	*p* = 0.002*	

	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Best overall response[*†], n (%)		
Complete response	3 (1)	0 (0)
Partial response	86 (34)	52 (20)
Stable disease	84 (33)	112 (44)
Progressive disease	56 (22)	50 (20)
Not evaluable/no post-baseline scan	25 (10)	41 (16)
Objective response rate[‡], % (95% CI)	35 (29–41)	20 (16–26)
Median duration of response, months	6.9	5.5
Median time to objective response, months	1.5	1.4
Ongoing response at data cutoff, n[§] (%)	42 (47)	8 (15)

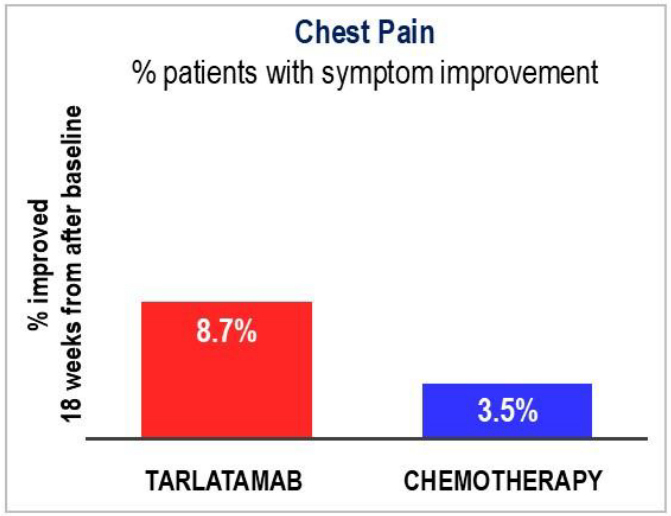
Tarlatamab skuteczniejszy od CHT w kontrolowaniu objawów NDRP – duszność i kaszel



LS mean difference = -9.14*
95% CI (-12.64, -5.64)
$p < 0.001$



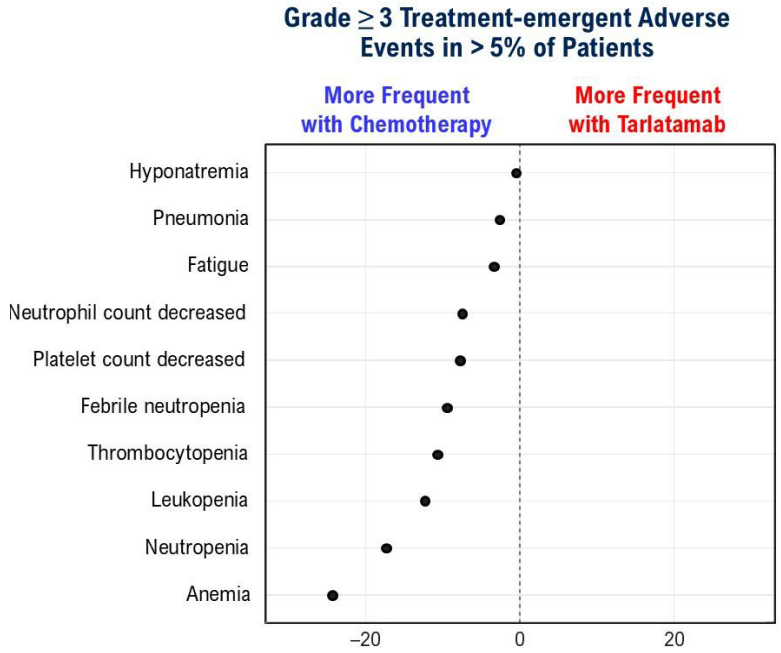
Odds ratio = 2.04*
95% CI (1.17, 3.55)
$p = 0.012$

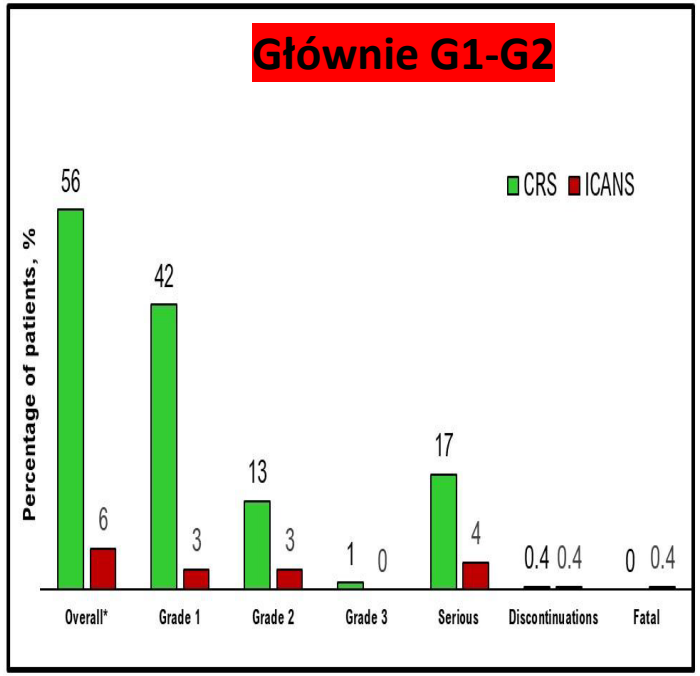


Odds ratio = 1.84*
95% CI (0.89, 3.81)
$p = 0.1$
(Did not meet statistical significance)

Tarlatamab – mniej poważnych działań niepożądanych

	Tarlatamab (n = 252)*	Chemotherapy (n = 244)*
Median duration of treatment, months, (range)	4.2 (< 1–17)	2.5 (< 1–15)
All grade, TEAEs, n (%)	249 (99)	243 (100)
All grade, TRAEs n (%)	235 (93)	223 (91)
Grade ≥ 3 TRAEs, n (%)	67 (27)	152 (62)
Serious TRAEs, n (%)	70 (28)	75 (31)
TRAEs leading to dose interruption and/or dose reduction, n (%)	48 (19)	134 (55)
TRAEs leading to discontinuation, n (%)	7 (3)	15 (6)
Treatment-related grade 5 events†, n (%)	1 (0.4)	4 (2)





2025 ASCO ANNUAL MEETING

ETOP·IBCSG PARTNERS FOUNDATION

EORTC

Efficacy and safety of nivolumab plus ipilimumab for patients with pre-treated type B3 thymoma and thymic carcinoma: Results from the EORTC-ETOP NIVOTHYM phase II trial

Nicolas Girard[1], Benjamin Besse[2], Michaël Duruisseaux[3], Laurent Greillier[4], Thierry Berghmans[5], Nuria Pardo[6], Sanjay Popat[7], Radj Gervais[8], Santiago Ponce Aix[9], Annelies Janssens[10], Sjaak Burgers[11], Joachim Aerts[12], Julien Mazières[13], Yvonne J. Summers[14], Anne-Claire Toffart[15], Anne-Sophie Govaerts[16], Eleni Xenophontos[16], Luc Boone[16], Rolf Stahel[17], Solange Peters[18]

[1] Institut Curie, Paris, and UVSQ, Paris Saclay University, Versailles, France; [2] Gustave Roussy, Paris Saclay University, Paris, France; [3] Hospices Civils de Lyon Cancer Institute, Lyon, France; [4] APHM, Hôpital Nord, Marseille, France; [5] Institut Jules Bordet, Hôpital Universitaire de Bruxelles, Brussels, Belgium; [6] Vall d´Hebron Institute of Oncology (VHIO), Barcelona, Spain; [7] The Royal Marsden NHS Foundation Trust, London, United Kingdom; [8] Centre Francois Baclesse, Caen, France; [9] Hospital Universitario 12 de Octubre, Madrid, Spain; [10] Antwerp University Hospital, Edegem, Belgium; [11] The Netherlands Cancer Institute, Amsterdam, Netherlands; [12] Erasmus University Medical Center, Rotterdam, Netherlands; [13] CHU de Toulouse, Université Paul Sabatier, Toulouse, France; [14] Christie NHS Foundation Trust, Manchester, United Kingdom; [15] Grenoble-Alpes University Hospital, Grenoble, France; [16] EORTC Headquarters, Brussels, Belgium; EORTC HQ, Sint-Lambrechts-Woluwe, Belgium; [17] ETOP-IBCSG, Bern, Switzerland; [18] Lausanne University Hospital, Lausanne, Switzerland

NIVOTHYM BK Ph2, 2-kohortowe, jednoramienne

Advanced/relapsed thymic tumor

Type B3 thymoma or thymic carcinoma

No more than one line of platinum-based chemotherapy

No autoimmune disorder

Cohort 1:

Nivolumab
(240 mg IV Q2 weeks)

n=55

Previously published

Cohort 2:
Nivolumab
(240 mg IV Q2 weeks)
+ Ipilimumab
(1 mg/kg IV Q6 weeks)
n=56

Imaging at week 8 and then every 6 weeks

Primary endpoint :
PFS rate at 6 months per BICR (RECIST 1.1)

H0: PFSR-6 ≤ 40%
H1: PFSR-6 = 60%

Alpha = 0.1 (one-sided)
Power = 94%

Secondary endpoints: PFSR-6 per local investigator, PFS, Response, OS, Safety

Charakterystyka chorych

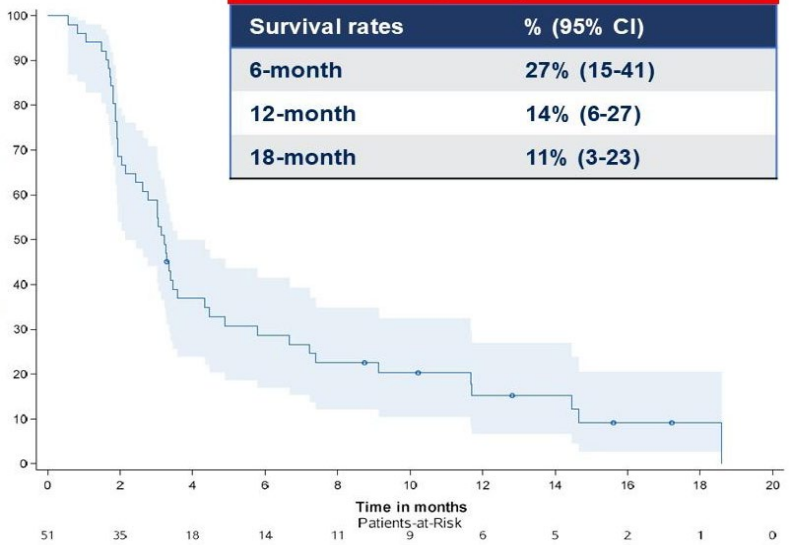
	Cohort 2 (n=56) n (%)
Median age (range)	64y (34-82)
Gender	
Male	37 (66)
Female	19 (34)
Performance status	
0-1	54 (96)
2	2 (4)
Histological type	
Thymoma (type B3)	8 (14)
Thymic carcinoma	48 (86)
Previous primary tumor resection	33 (59)
Previous chemotherapy for locally-advanced disease	3 (5)

	Cohort 2 (n=56) n (%)
Metastatic sites	
Brain	0 (0)
Lymph nodes	30 (54)
Liver	26 (46)
Lung	26 (46)
Pleura	24 (43)
Bone	26 (46)
Type of progression on last line of treatment	
Locoregional	16 (29)
Distant	25 (45)
Both	14 (25)
Unknown	1 (2)

Skuteczność ograniczona….mPFS=3 m-ce, PR=16%..., 30% AE≥G3

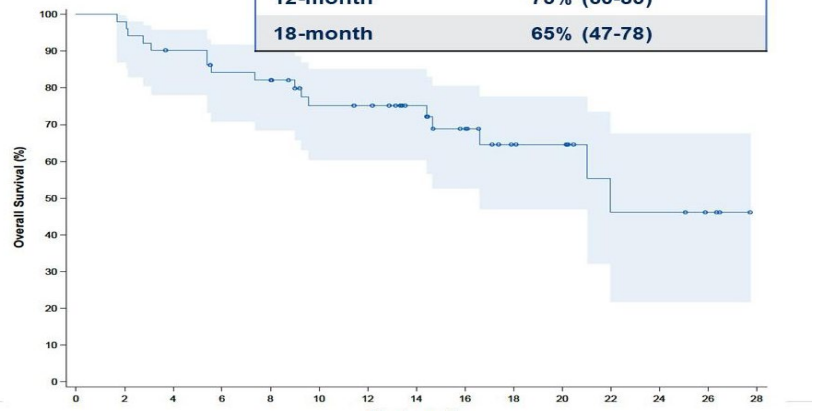
Median Follow-up 16.1 months

Median PFS: 3.1 (2.0-3.6) months	
Survival rates	% (95% CI)
6-month	27% (15-41)
12-month	14% (6-27)
18-month	11% (3-23)



Overall survival

Median OS: 22.0 (16.6-NE) months	
Survival rates	% (95% CI)
6-month	84% (71-92)
12-month	75% (60-85)
18-month	65% (47-78)



Objective response

	Nivolumab + Ipilimumab (n=51) n (%)
Partial response	8 (16)
Stable disease	22 (43)
Disease control rate	59%
Progressive disease	18 (35)
NE	3 (6)

	Cohort 2 (n=56) n (%)
Maximal grade of adverse events	
1-2	29 (52)
3-4	27 (48)
Grade ≥3 Treatment-Related Adverse Events	16 (29)
Myocarditis	2 (4)
Colitis	4 (8)
Infusion-related reaction/allergy	2 (4)
Skin rash	2 (4)
Other: heart failure, immune-related hepatitis, arthritis, myositis, hypophysitis, Gougerot-Sjögren syndrome, pharyngitis, fatigue, fever, infusion-related reaction	1 patient each
Death related to Treatment-Related Adverse Events	0 (0)

Podsumowanie

- **Opcja leczenia 1L zNDRP NGS(-) – ADC+IM+/-CHT – skuteczna, TROP2 NMR potencjalnym czynnikiem predykcyjnym**
- **Opcja leczenia bez udziału CHT – po niepowodzeniu IM w 1L – ramu+pembro – OS zbliżony do CHT, mniejsza toksyczność**
- **Opcja leczenia 2L w EGFRins20 zNDRP – zipalertynib – skuteczny u przeleczonych chorych, także po amiwantamabie, badanie 3 fazy w toku**
- **Opcja leczenia po progresji na EGFRi, METamp(+) – savo+ozi – skuteczniejszy od CHT – PFS i ORR**
- **Dwie opcje leczenia po progresji na iEGFR 3 gen – sacituzumab tirumotecan skuteczniejszy od DXL (ORR, PFS i OS), patritumab deruxtecan skuteczniejszy od CHT – PFS, ale nie w OS**
- **Opcja leczenia 1L anty-KRAS – ada+pembro – skuteczna kombinacja (ORR, PFS), szczególna korzyść PD-L1≥50%**
- **Opcja leczenia anty-HER2 – sevabertinib skuteczny, BK 3fazy 1L w toku**
- **Opcja leczenia podtrzymującego w ED DRP – lurbi+atezo skuteczniejsza (PFS, OS) od atezo**
- **Opcja leczenia 2L w ED DRP – tarlatamab skuteczniejszy od CHT (PFS, OS)**
- **Opcja leczenia immunokompetentnego w neo grasicy – podwójna IM – słaba skuteczność, dodanie ipi nie poprawia wyników leczenia**

XXIV SPOTKANIE Po ASCO

Dziękuję