XXIV SPOTKANIE Po ASCO

Rak płuca – omówienie doniesień

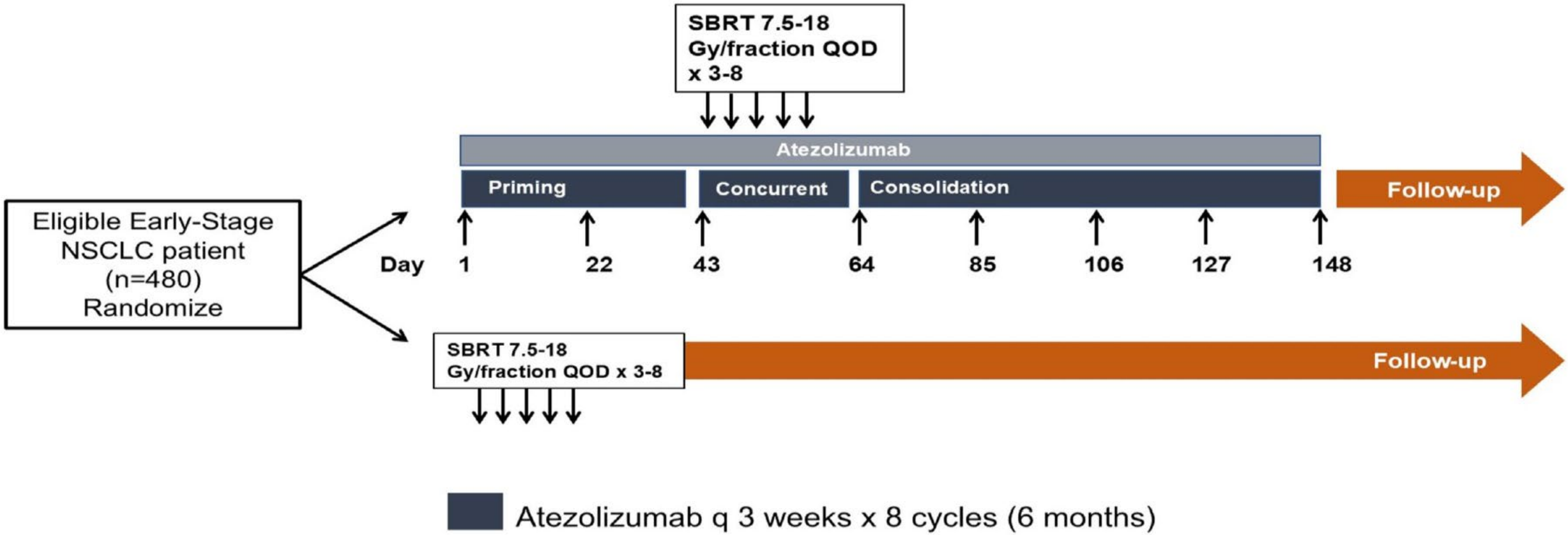
Rafał Dziadziuszko

XXIV SPOTKANIE Po ASCO

Wczesny rak płuca

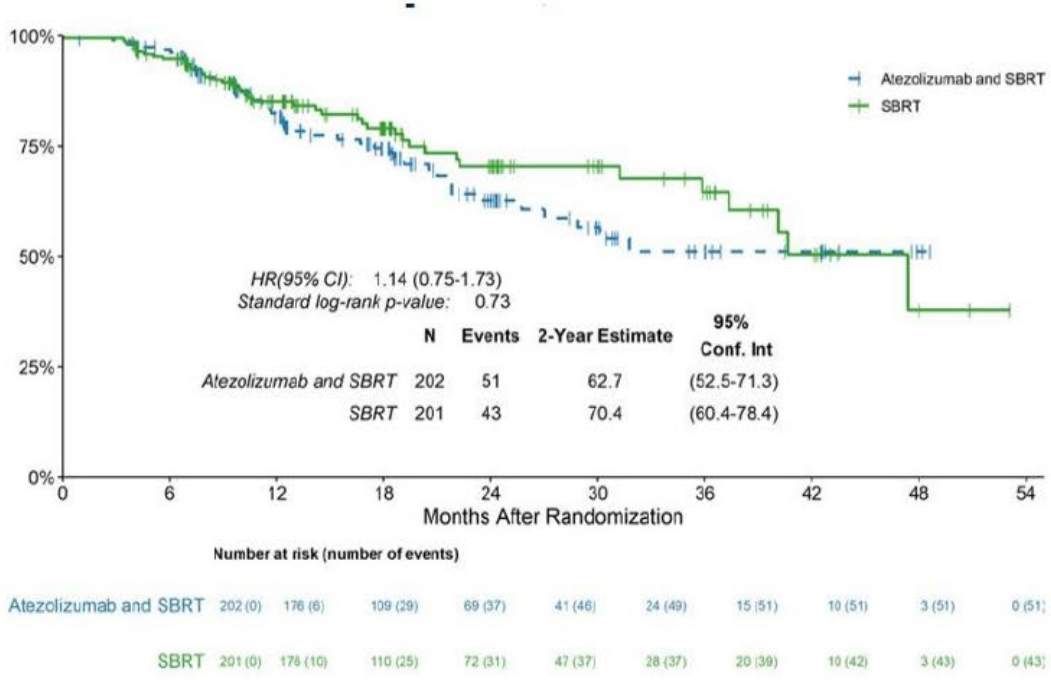
SWOG/NRG S1914

SCHEMAT BADANIA



SWOG/NRG S1914

PFS



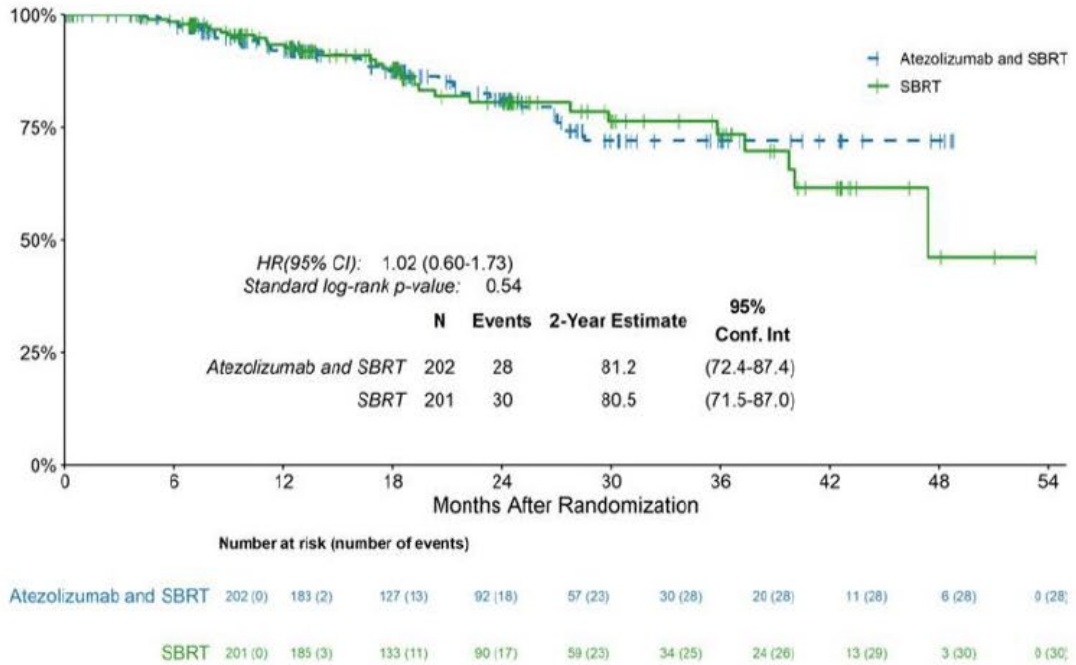
Analysis on 94 PFS events

* If continued to full information, primary analysis at 225 PFS events

FU (in months) 345 for alive pts:

Median: 13.8 months, IQR: 9.4-24.6, Range: 0.1-53.3

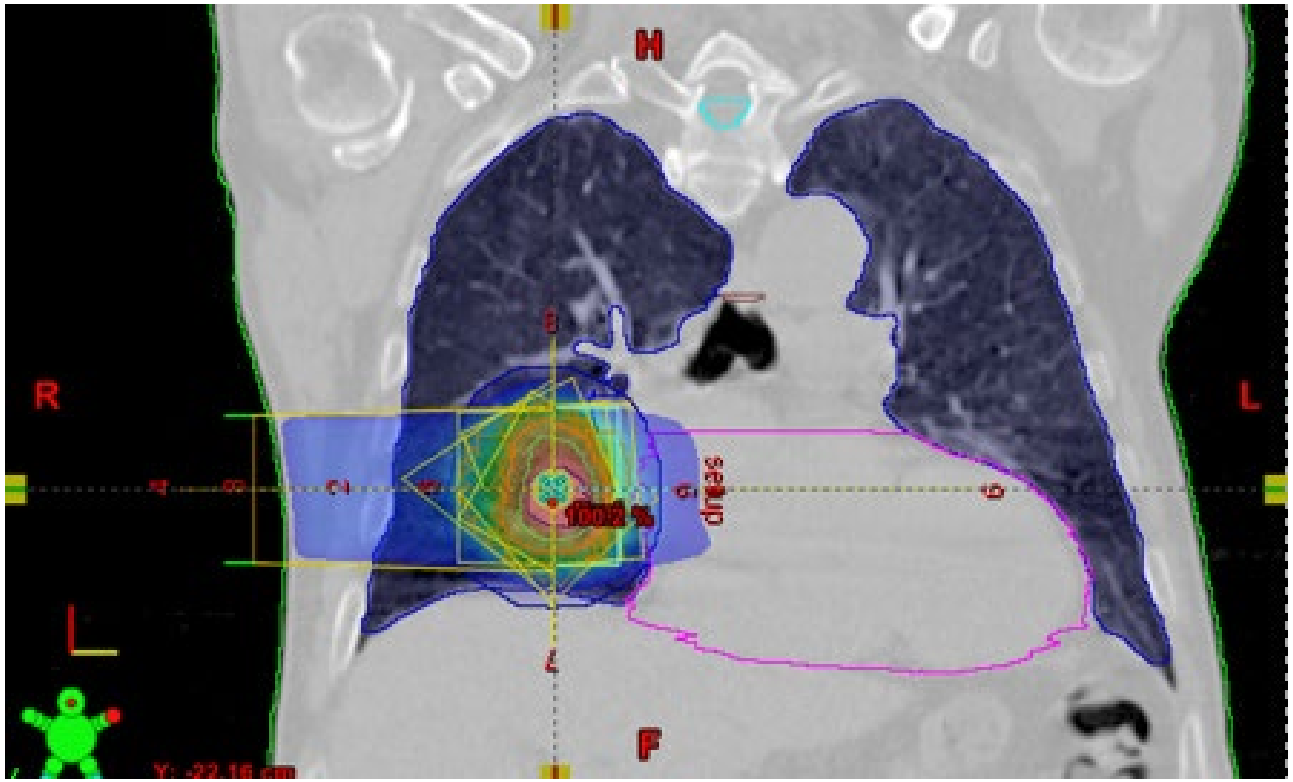
OS



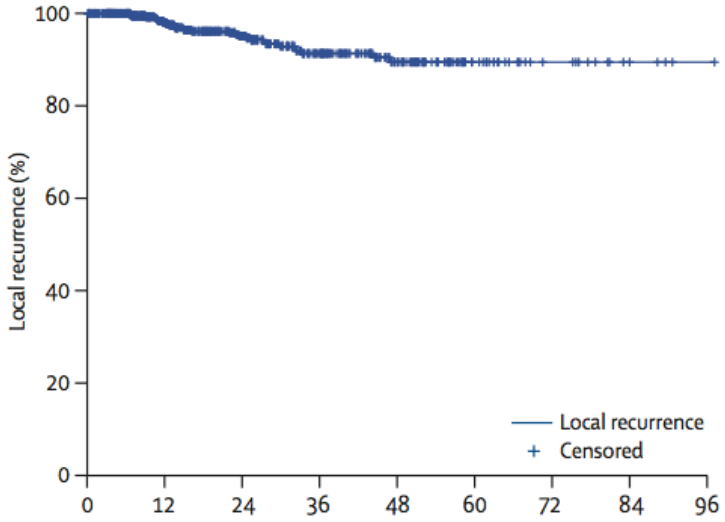
Analysis on 58 deaths

* If continued to full information, primary analysis at 245 deaths or 36 months of follow-up

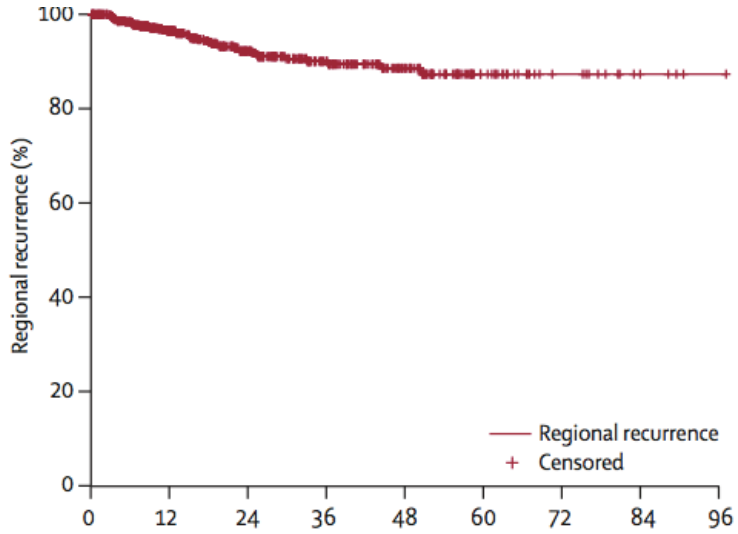
60Gy/8fx.



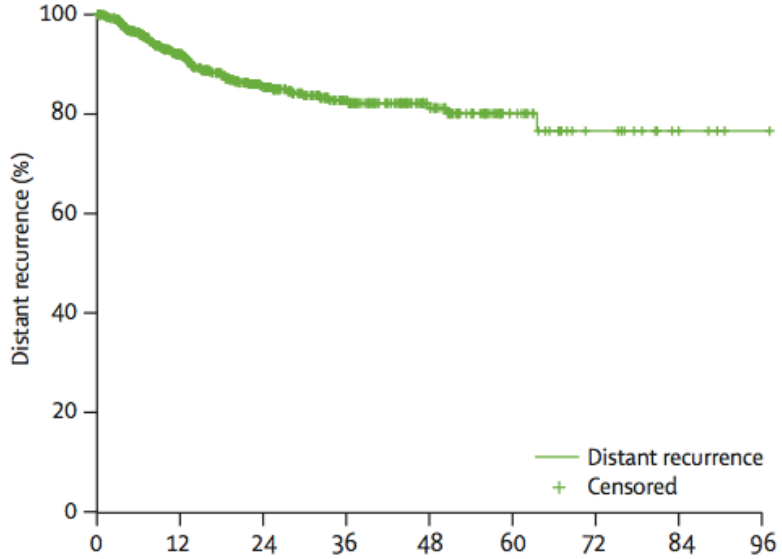
Local relapse-free survival



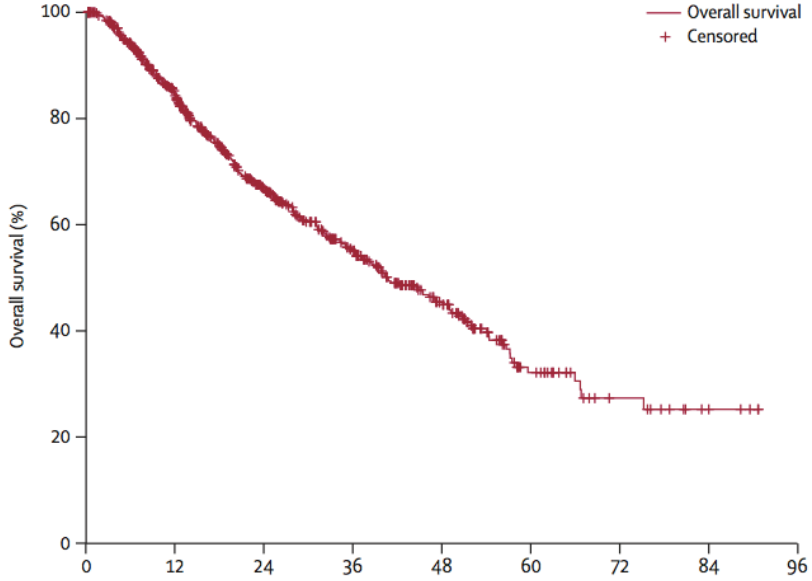
Regional relapse-free survival



Metastasis-free survival



Overall survival



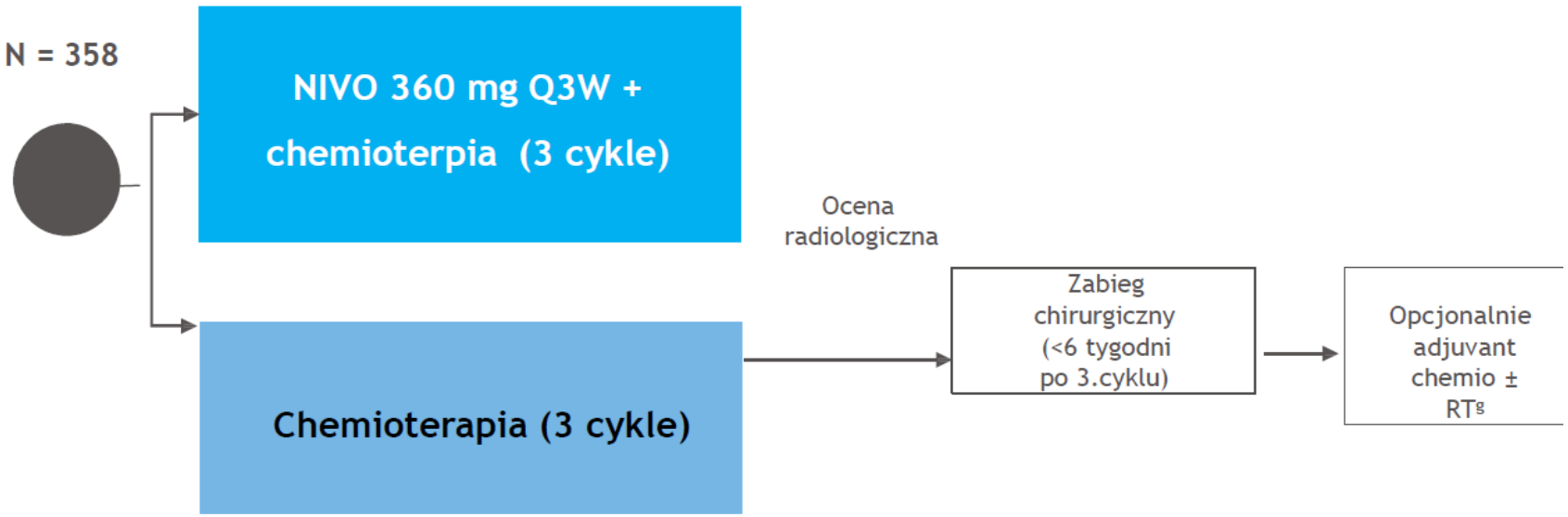
Senti et al., 2013

CheckMate 816

Niwolumab w połączeniu z chemioterapią w leczeniu przedoperacyjnym

Kluczowe kryteria włączenia

- CS IB (≥ 4 cm)-IIIA NDRP
- ECOG PS 0-1
- EGFR/ALK (-)
- Stratyfikacja wg CS (IB-II vs IIIA), PD-L1[c] (≥ 1% vs < 1%[d]), i płci



Pierwszorzędowe punkty końcowe
- pCR by BIPR
- EFS by BICR

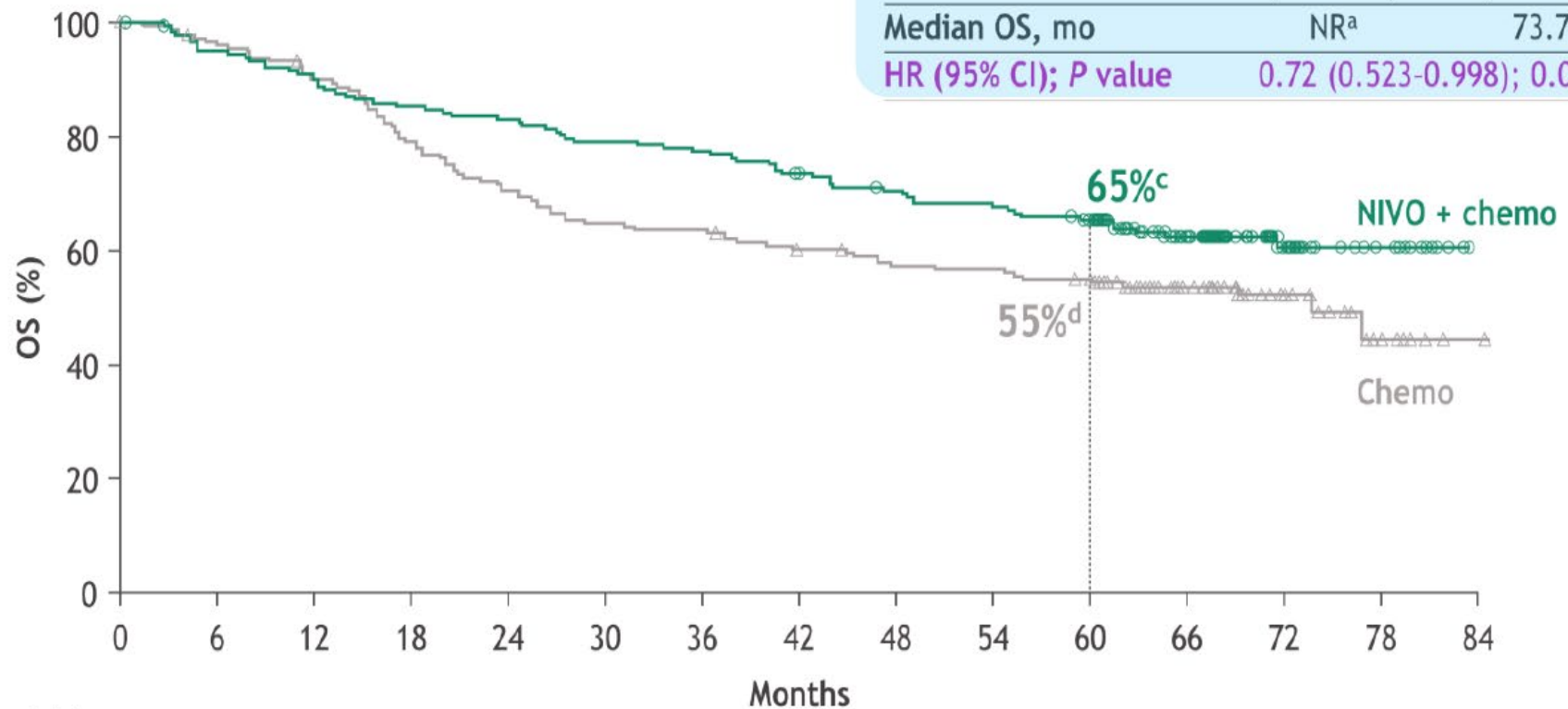
Drugorzędowe punkty końcowe
- MPR by BIPR
- OS
- Czas do zgonu lub rozsiewu

Analiza eksploracyjna
- EFS wg remisji patologicznej

CheckMate 816

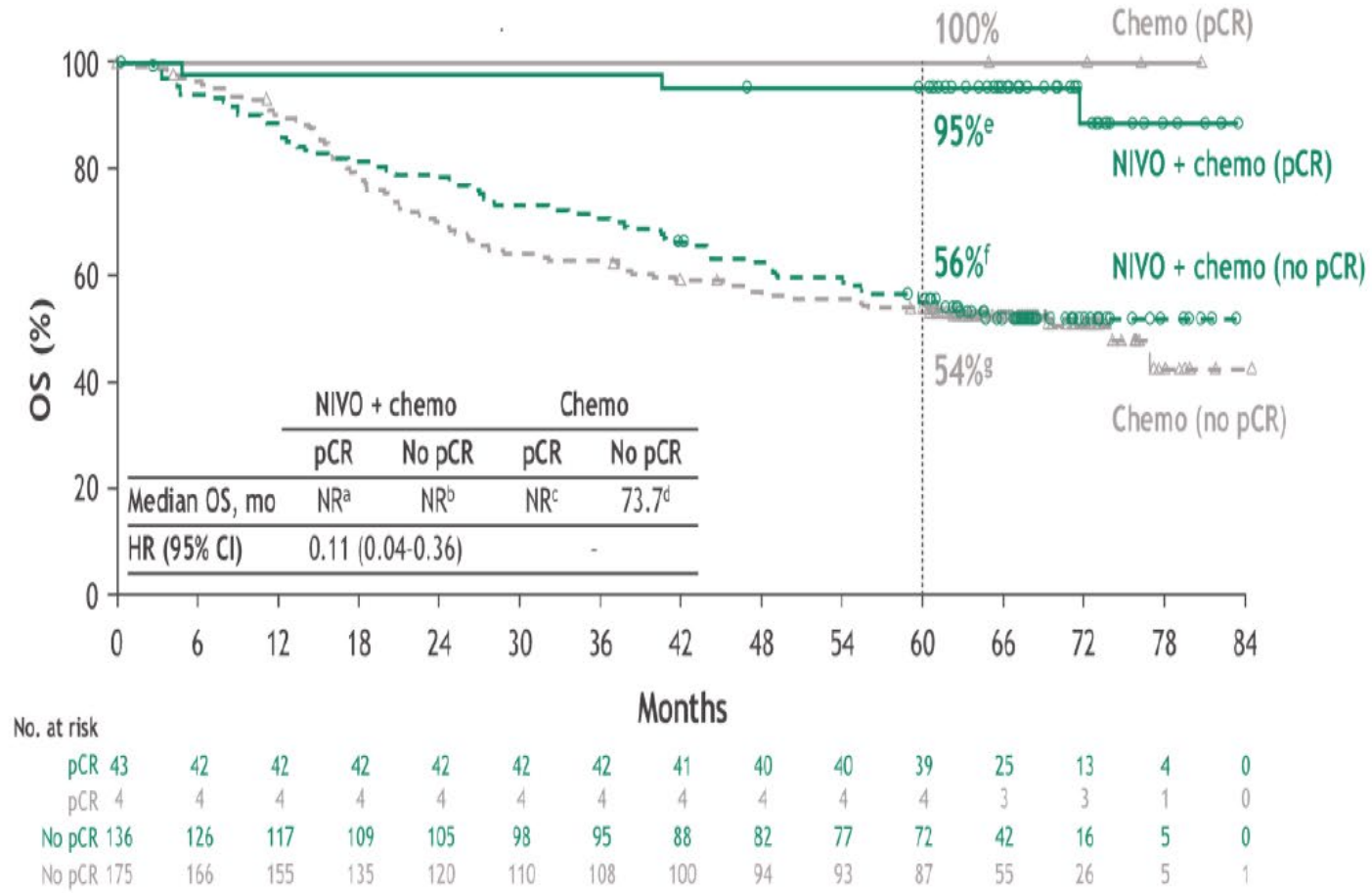
CZAS PRZEŻYCIA CAŁKOWITEGO

	NIVO + chemo (n = 179)	Chemo (n = 179)
Median OS, mo	NR[a]	73.7[b]
HR (95% CI); *P* value	0.72 (0.523-0.998); 0.0479	



CheckMate 816

CZAS PRZEŻYCIA CAŁKOWITEGO WOBEC pCR

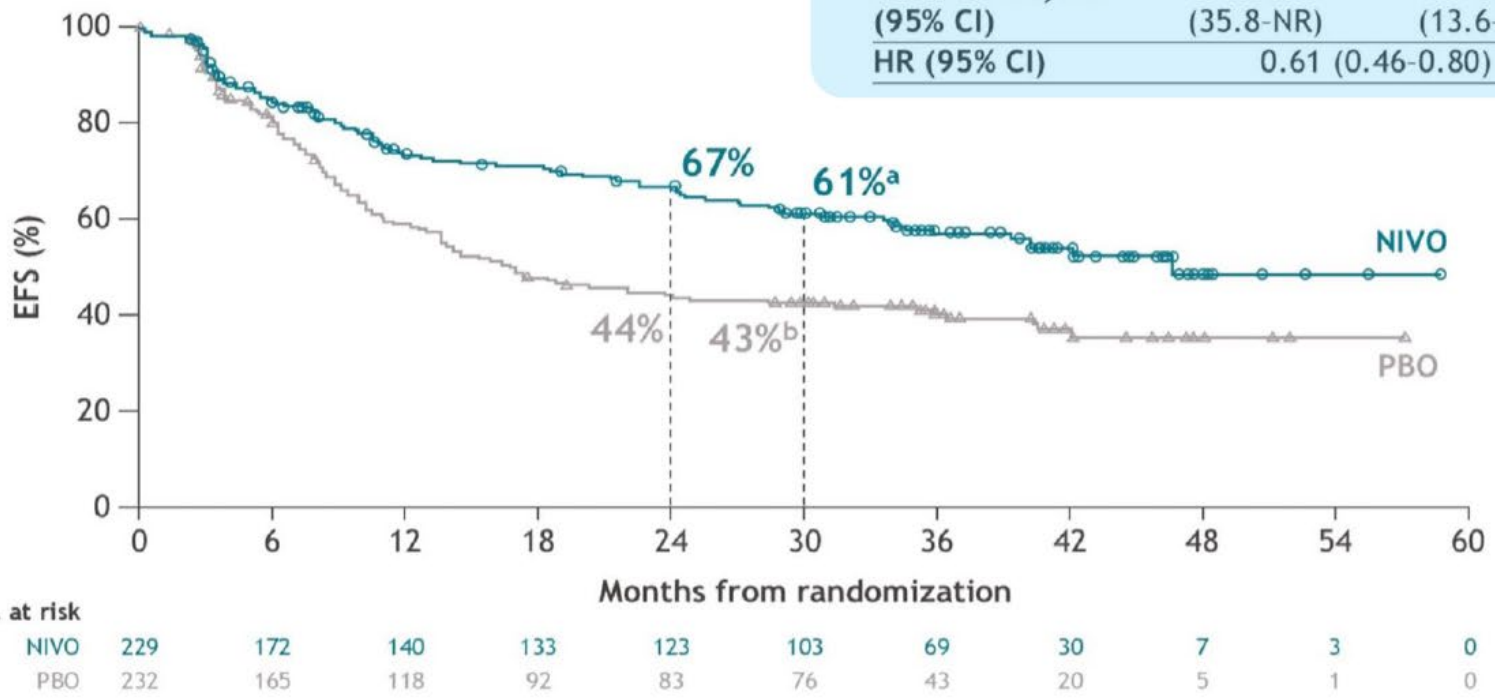


CheckMate 77T

Niwolumab w połączeniu z chemioterapią w leczeniu okołooperacyjnym

EFS CSII-IIIB

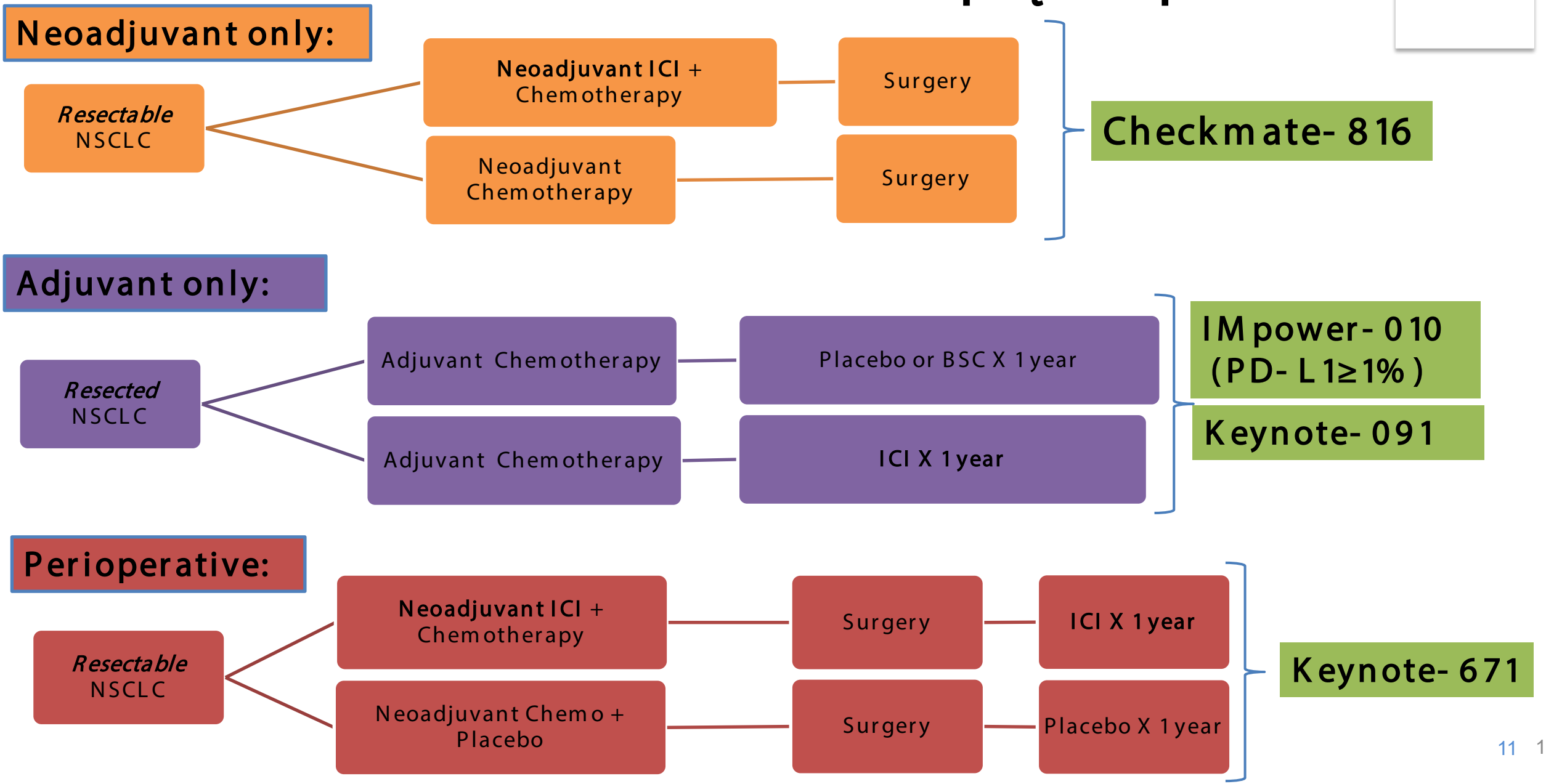
	NIVO (n = 229)	PBO (n = 232)
Median EFS, mo (95% CI)	46.6 (35.8-NR)	16.9 (13.6-28.2)
HR (95% CI)	0.61 (0.46-0.80)	



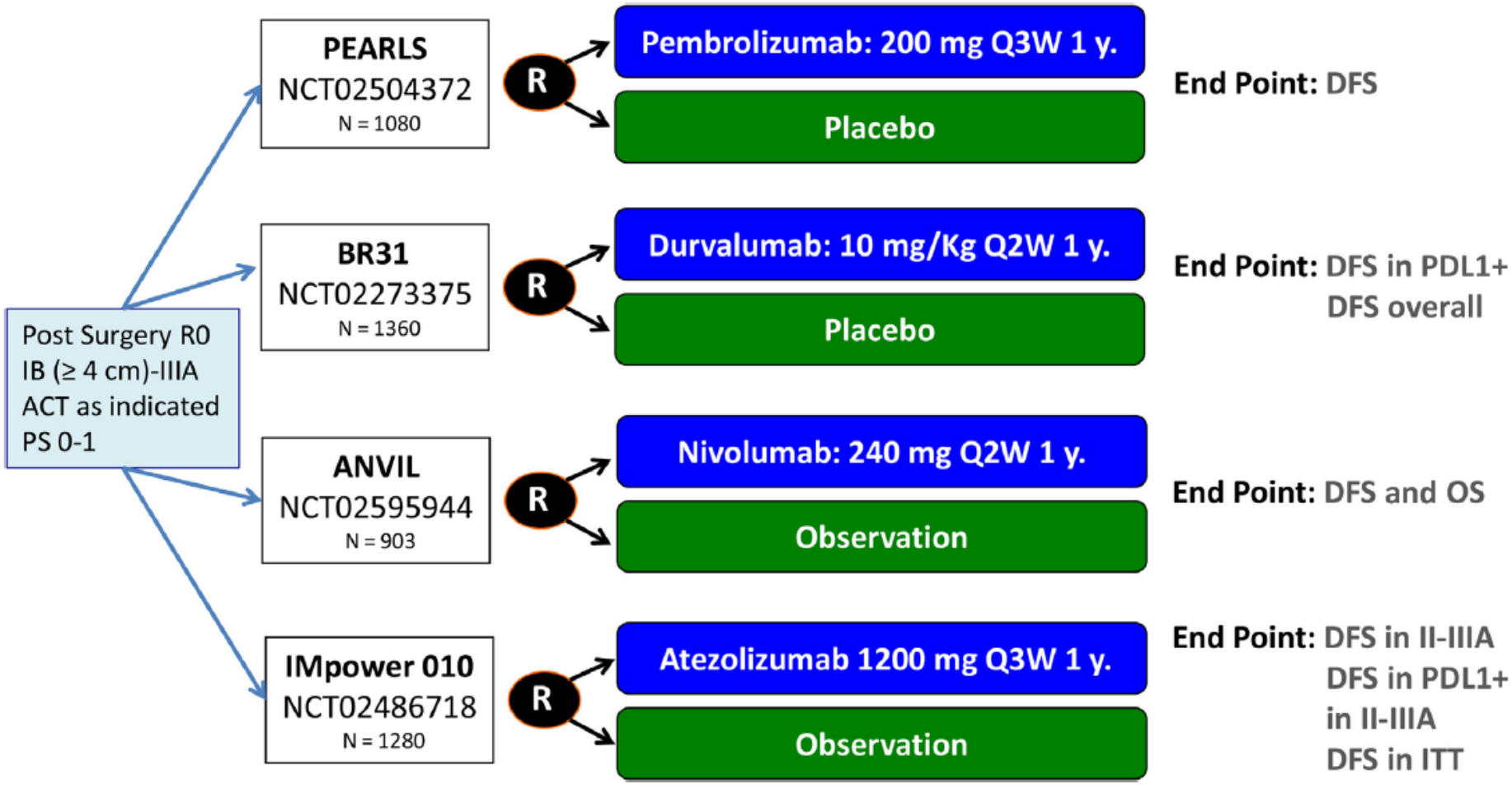
Database lock date: December 16, 2024; median follow-up (range): 41.0 months (31.3-59.8).

a,b95% CI: a54-68; b36-50.

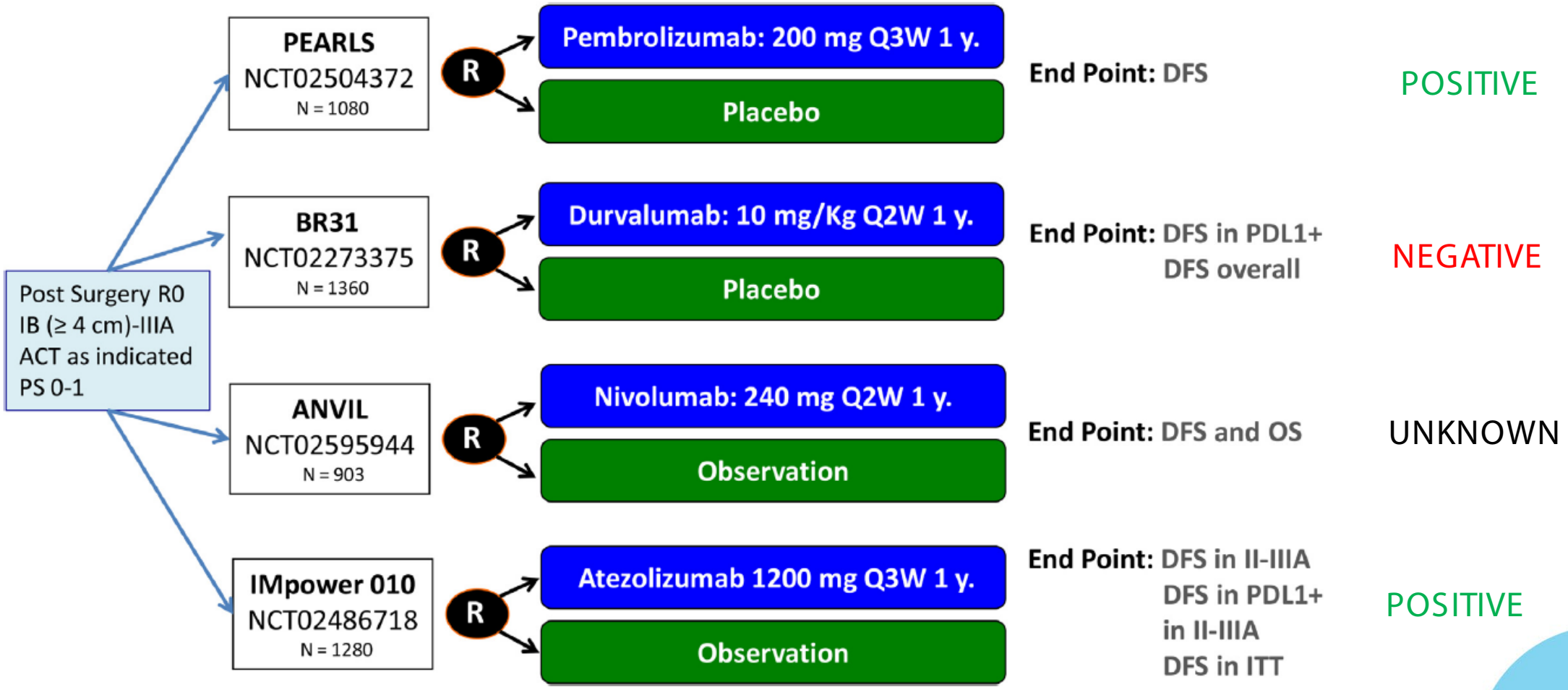
Badania z immunoterapią w op. NDRP



Phase III clinical trials with adjuvant immunotherapy in NSCLC

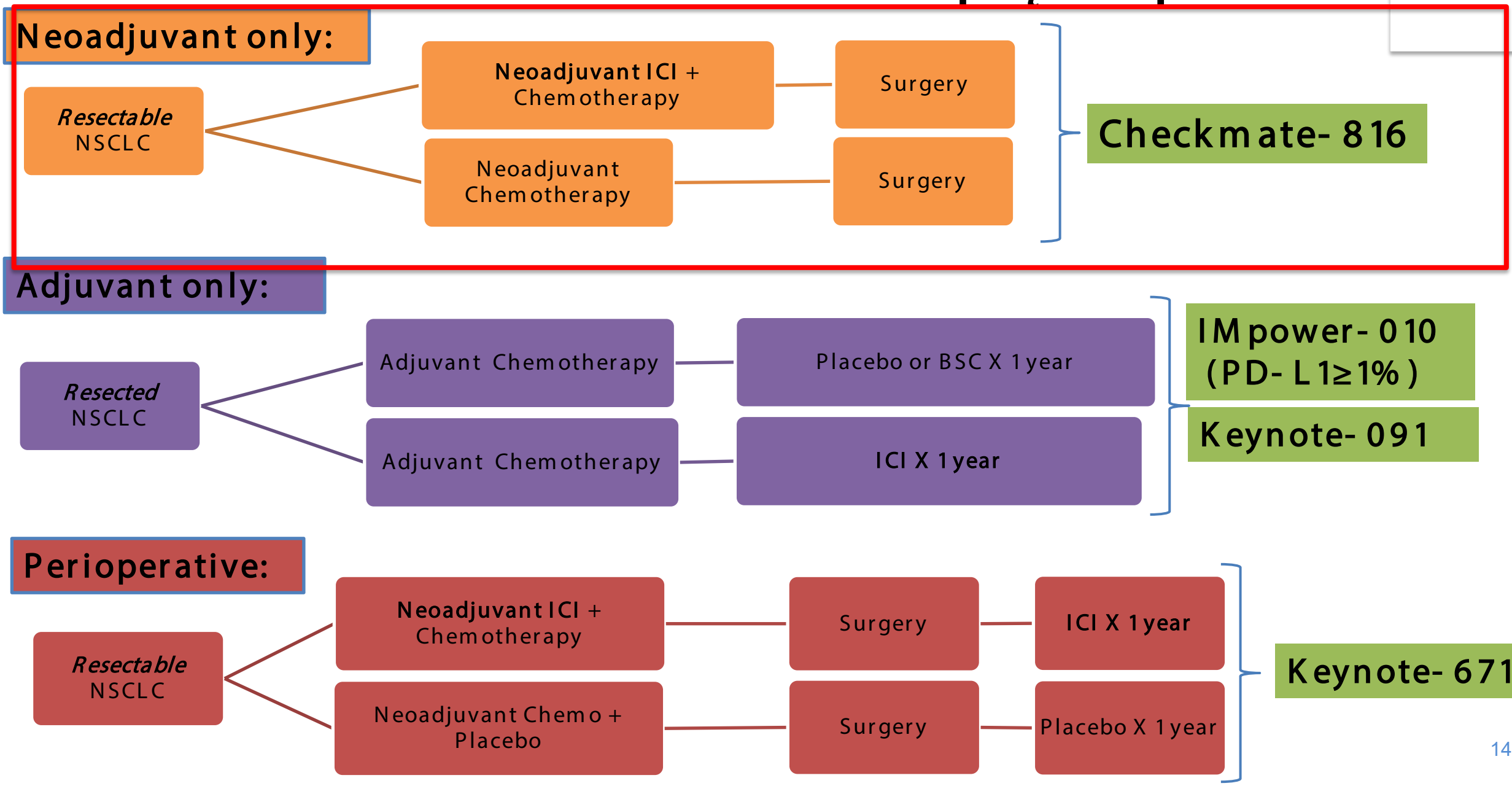


Phase III clinical trials with adjuvant immunotherapy in NSCLC



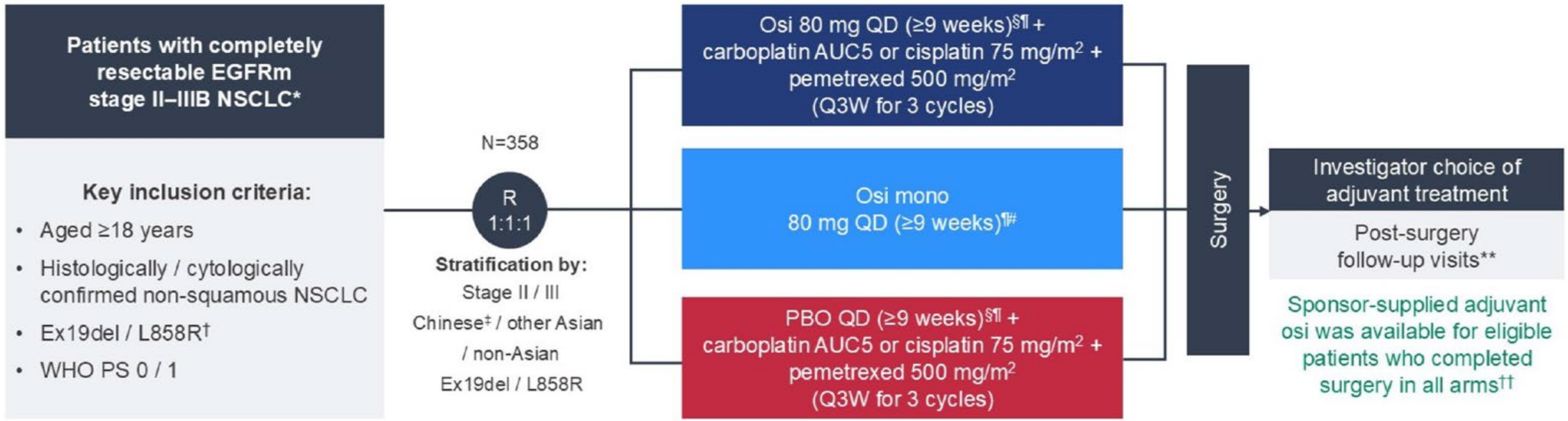
Remon J. et al., JTO 2020

Badania z immunoterapią w op. NDRP



NEOADAURA

OZYMERTYNIB W LECZENIU PRZEDOPERACYJNYM



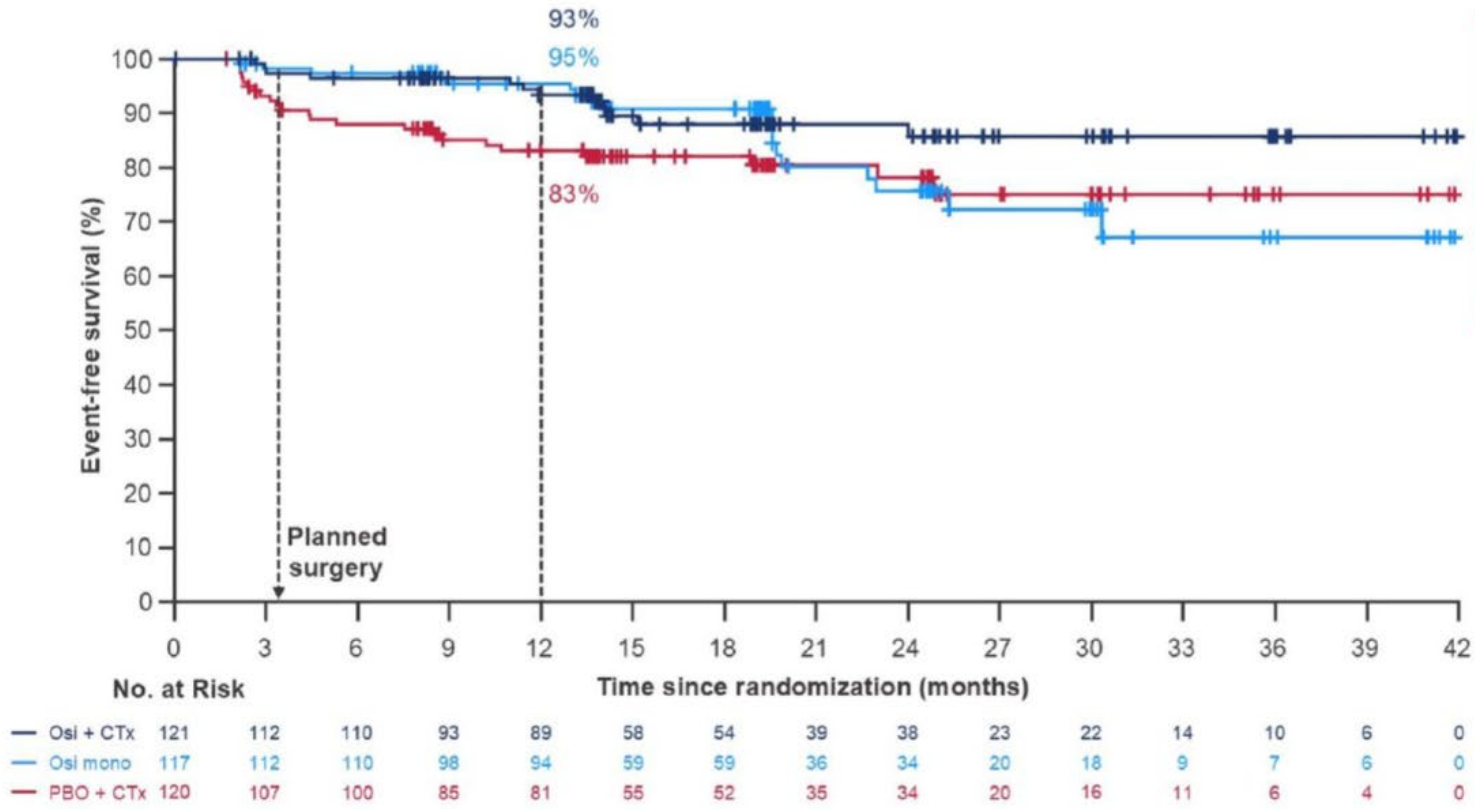
Endpoints:

- **Primary: major pathological response (MPR; by blinded central pathology review)**
- Secondary: event-free survival, pathological complete response, nodal downstaging and safety

NEOADAURA

OZYMERTYNIB W LECZENIU PRZEDOPERACYJNYM

EFS



EFS HR vs PBO + CTx

Osi + CTx: 0.50
(99.8% CI 0.17, 1.41); p=0.0382†

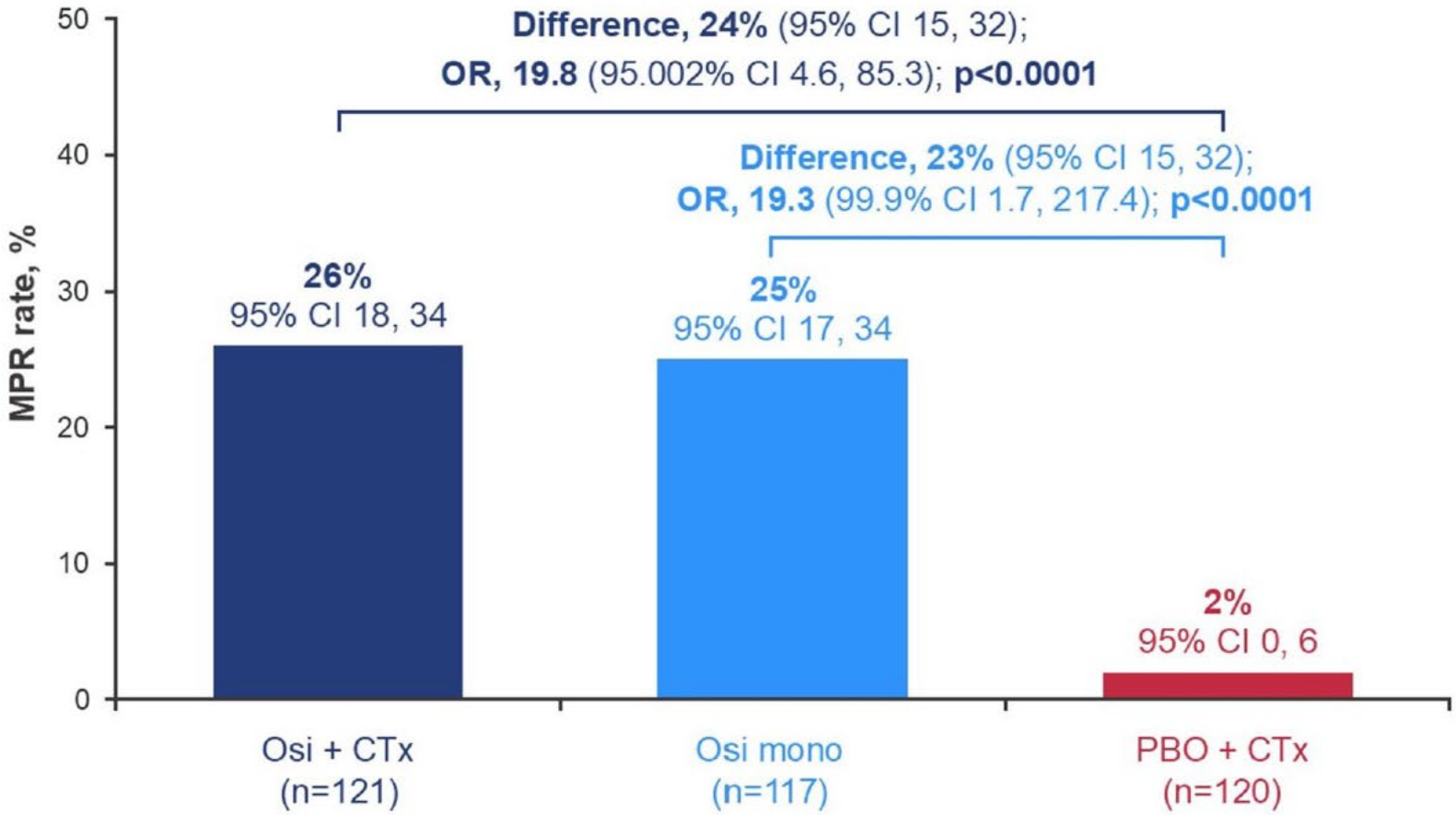
Osi mono: 0.73
(95% CI 0.40, 1.35)†

Median follow-up, months‡
osi + CTx 14.3, osi mono 18.3,
PBO + CTx 14.3

NEOADAURA

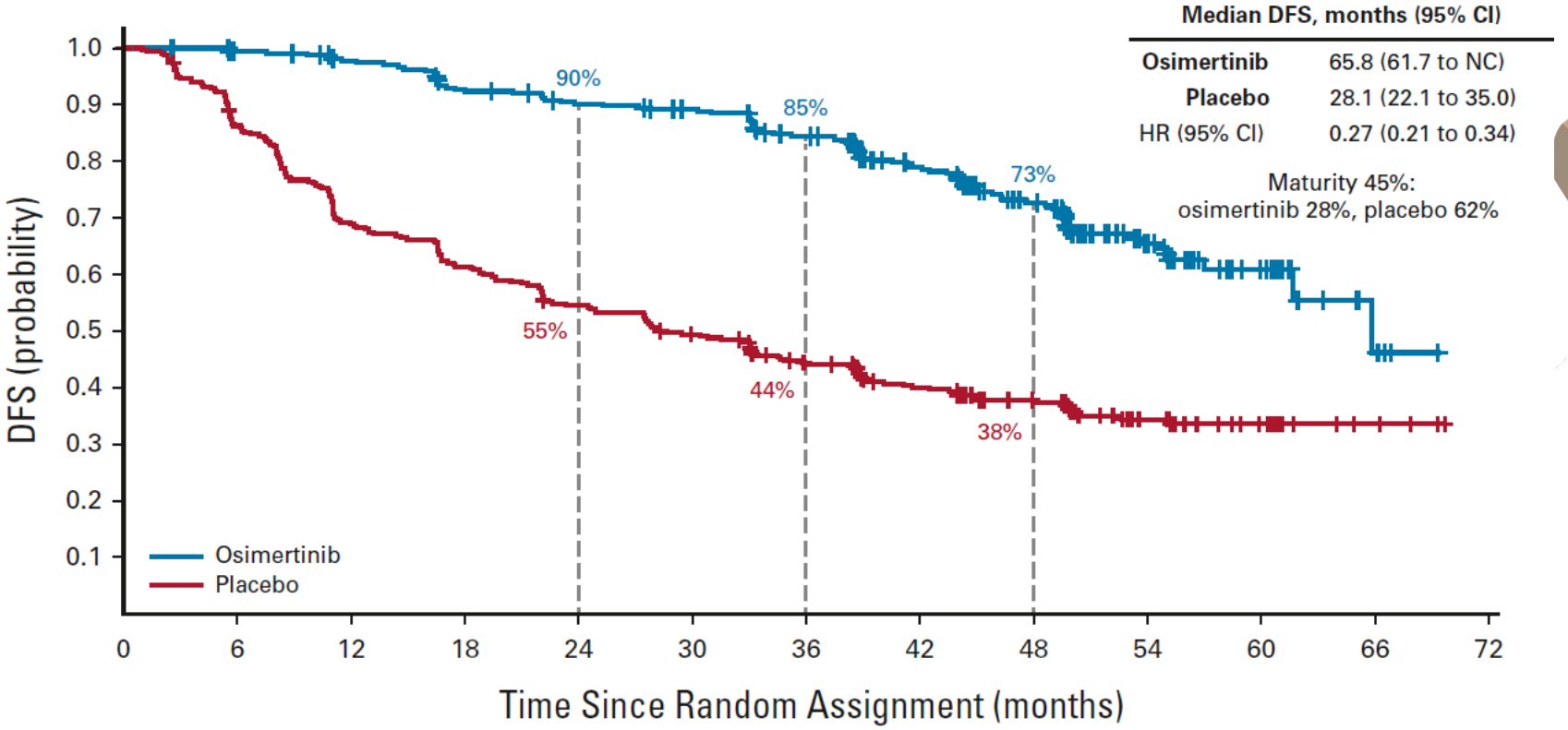
OZYMERTYNIB W LECZENIU PRZEDOPERACYJNYM

MPR



Optimal duration of adjuvant targeted therapy – ADAURA

ADAURA updated results



Median DFS, months (95% CI)	
Osimertinib	65.8 (61.7 to NC)
Placebo	28.1 (22.1 to 35.0)
HR (95% CI)	0.27 (0.21 to 0.34)

Maturity 45%:
osimertinib 28%, placebo 62%

Herbst RS et al., J Clin Oncol 41:1830-1840, 2023.

Rafal Dziadziuszko

A clear distinction between immunotherapies and targeted drugs

Immunotherapy is cytotoxic!

PACMAN GAME

https://www.youtube.com/shorts/prUXht6-d1w

Rafal Dziadziuszko

A clear distinction between immunotherapies and targeted drugs

Targeted therapy is <u>cytostatic!</u>

Pressure on
SPONGE BOB PILLOW

Rafal Dziadziuszko

XXIV SPOTKANIE Po ASCO

Zaawansowany rak płuca

XXIV SPOTKANIE Po ASCO

Zaawansowany rak płuca
- terapie ukierunkowane molekularnie

Rezilient 1: mEGFR ex20+

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**

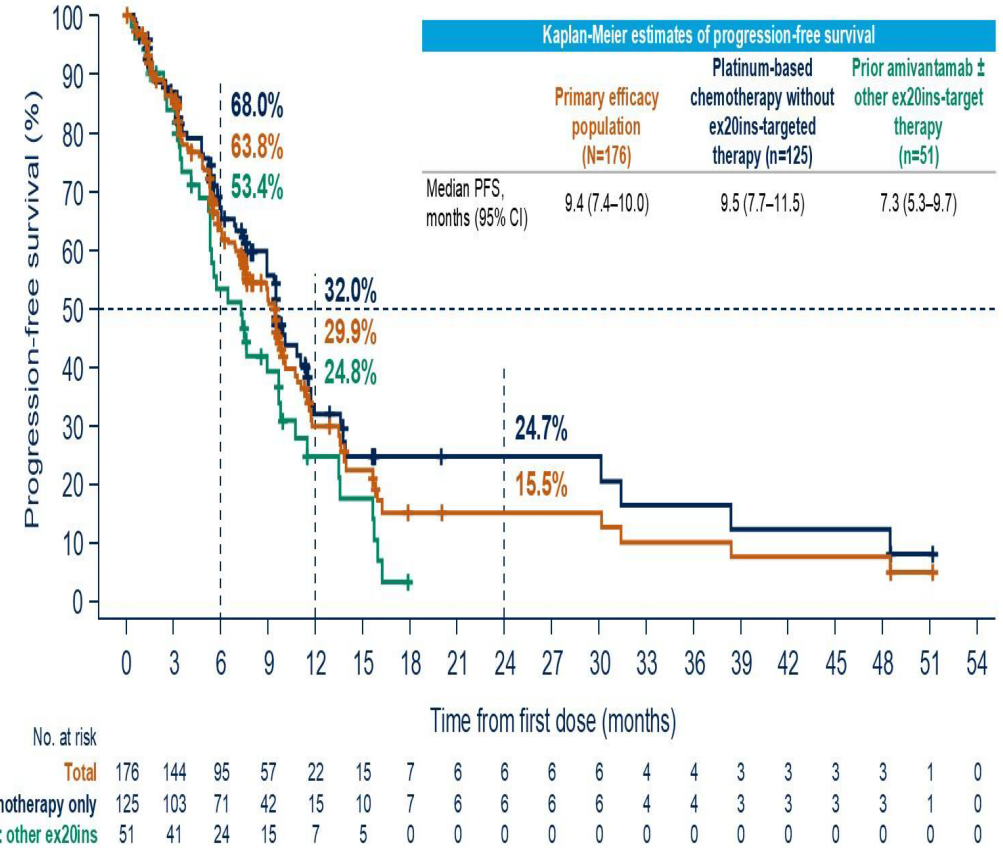
Secondary endpoints:

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

Skuteczność 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)

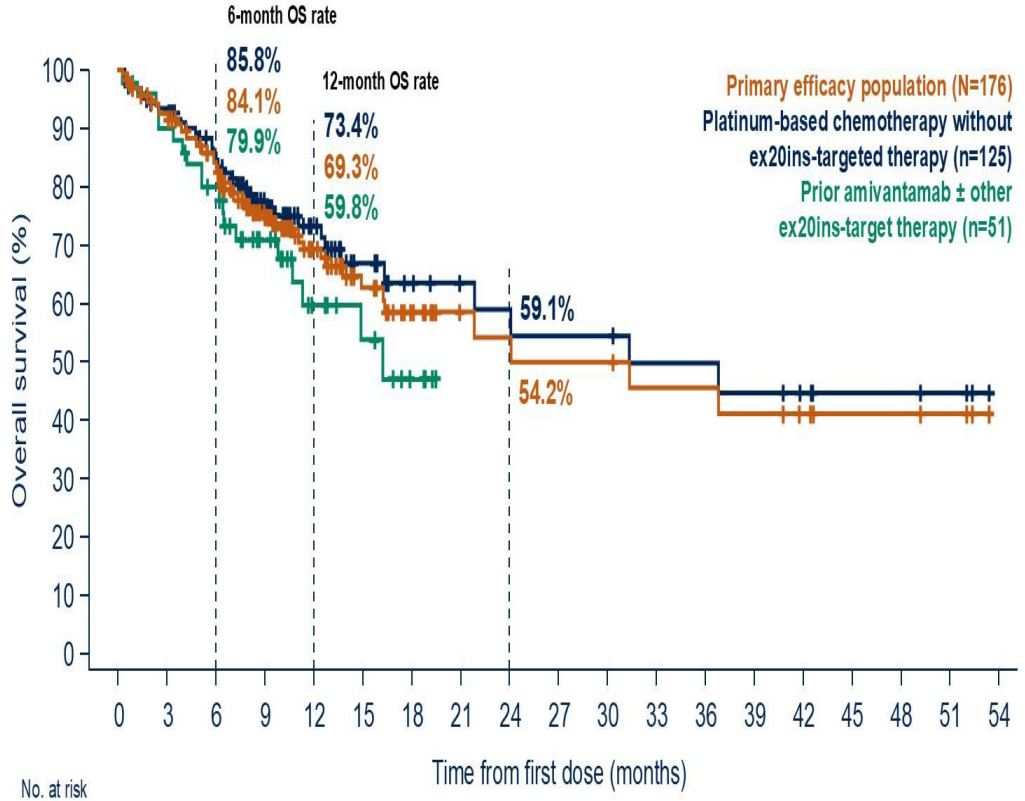
Skuteczność zipalertynibu



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



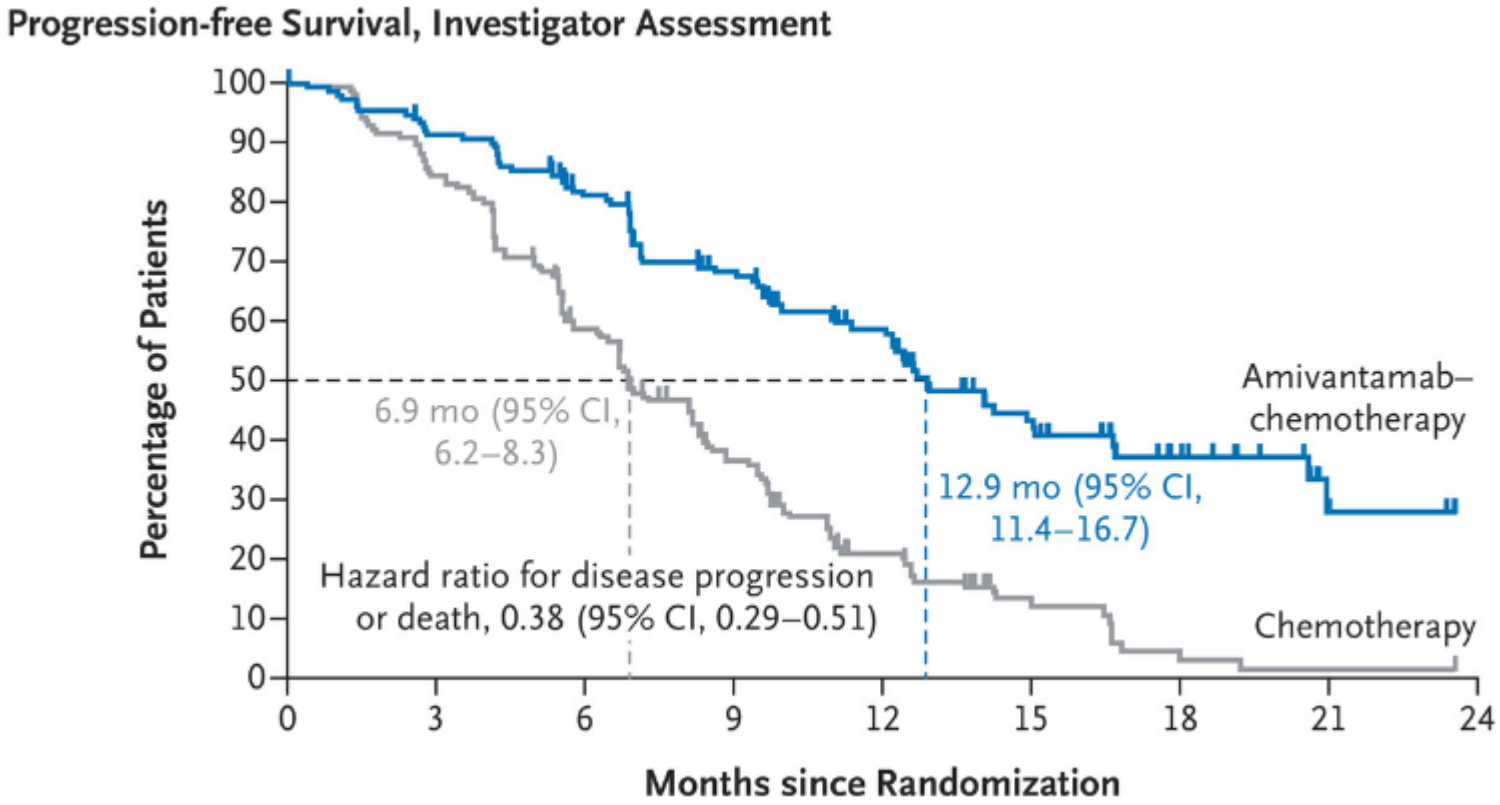
No. at risk																			
Total	176	158	137	88	51	32	21	14	13	12	12	10	10	9	7	5	5	3	0
Platinum-based chemotherapy only	125	113	99	64	38	23	17	14	13	12	12	10	10	9	7	5	5	3	0
Prior amivantamab ± other ex20ins	51	15	38	24	13	9	4	0	0	0	0	0	0	0	0	0	0	0	0

The NEW ENGLAND JOURNAL of MEDICINE

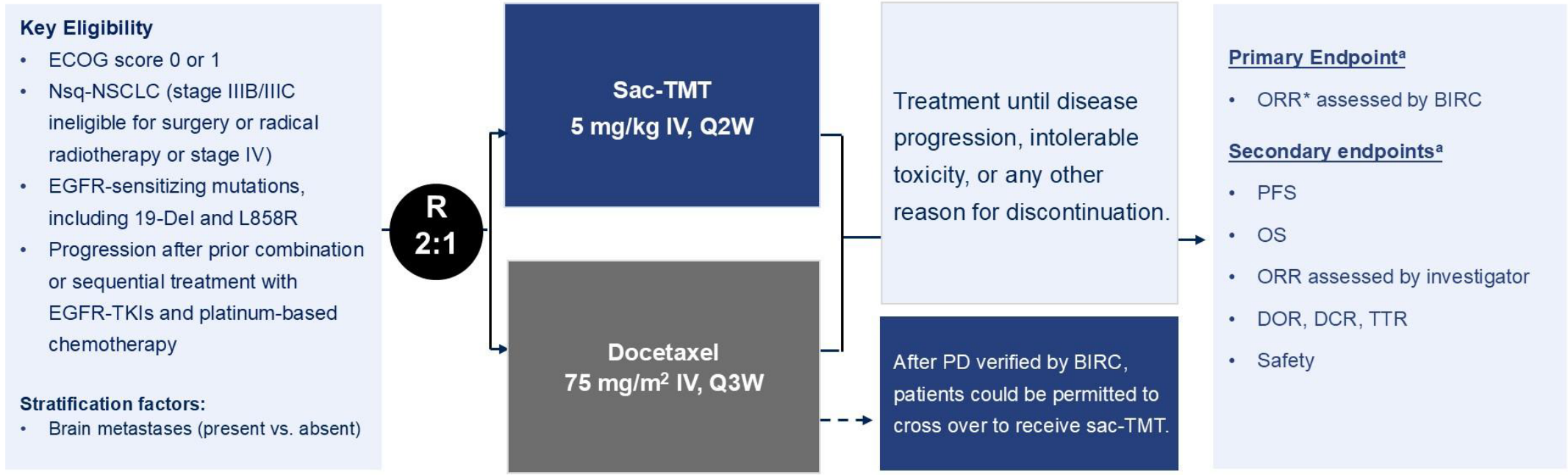
ORIGINAL ARTICLE

Amivantamab plus Chemotherapy in NSCLC with *EGFR* Exon 20 Insertions

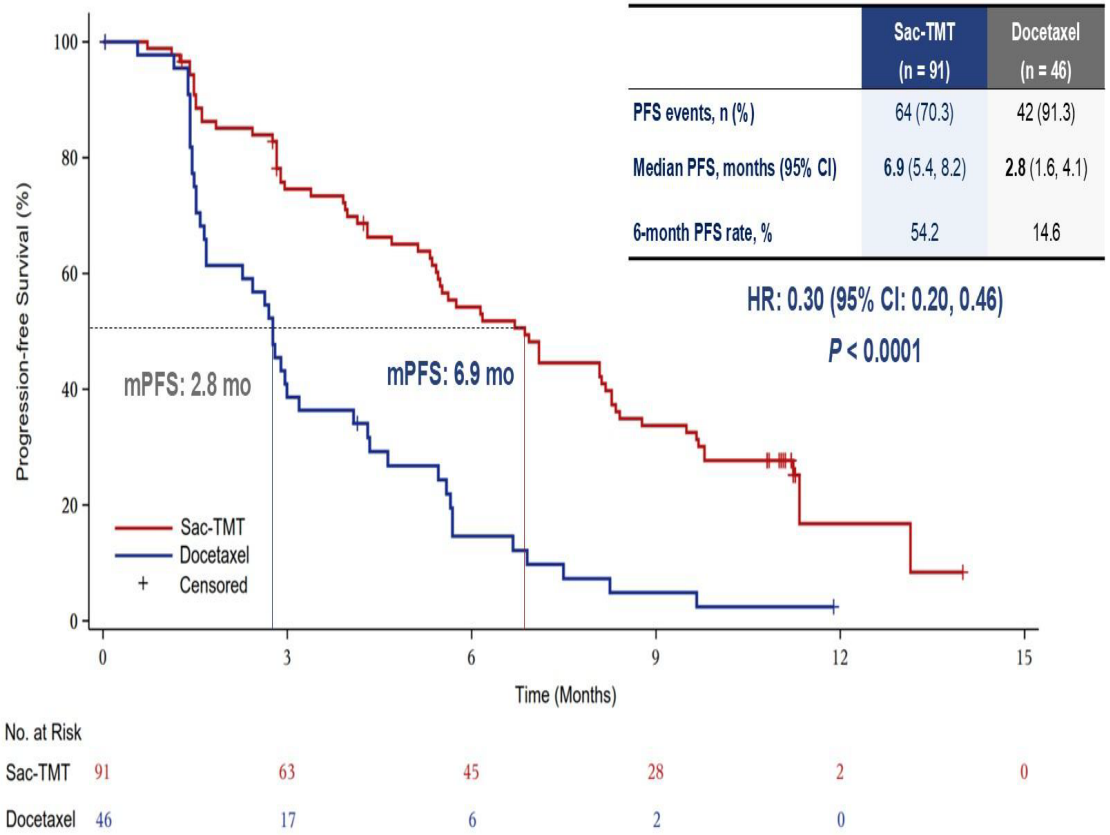
C. Zhou, K.-J. Tang, B.C. Cho, B. Liu, L. Paz-Ares, S. Cheng, S. Kitazono, M. Thiagarajan, J.W. Goldman, J.K. Sabari, R.E. Sanborn, A.S. Mansfield, J.-Y. Hung, M. Boyer, S. Popat, J. Mourão Dias, E. Felip, M. Majem, M. Gumus, S. Kim, A. Ono, J. Xie, A. Bhattacharya, T. Agrawal, S.M. Shreeve, R.E. Knoblauch, K. Park, and N. Girard, for the PAPILLON Investigators*



mEGFR: Schemat badania OptiTROP-Lung03: 3. linia leczenia



Skuteczność

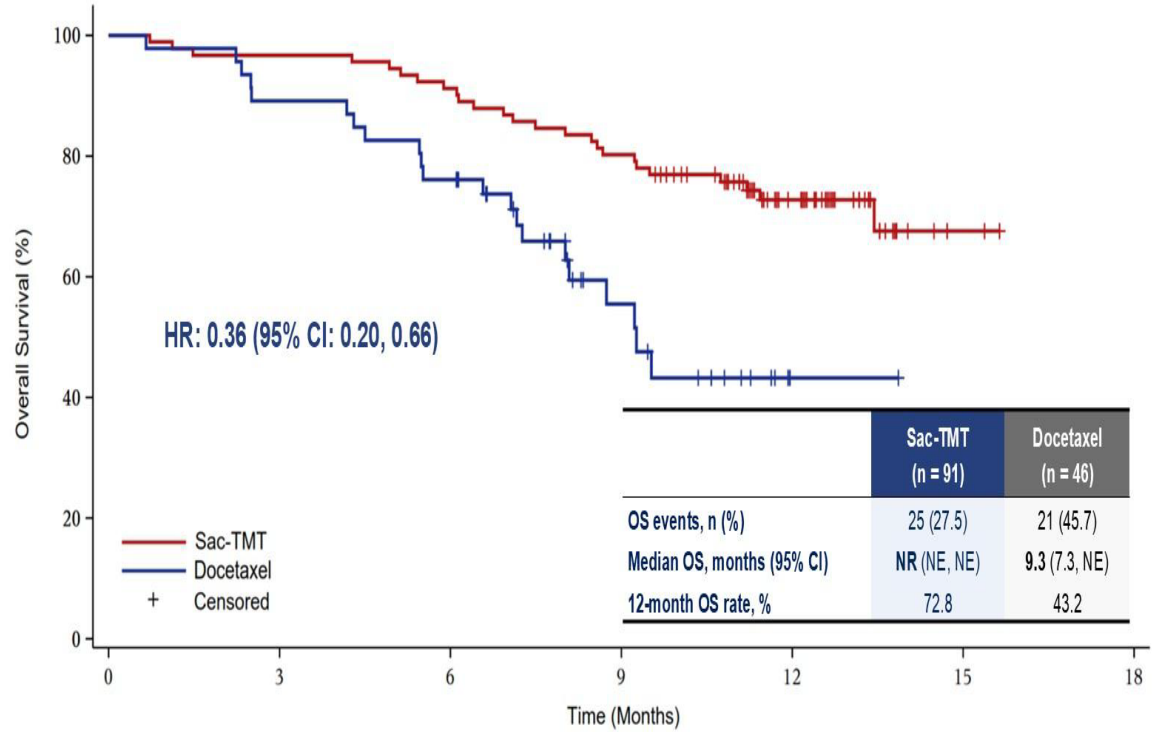


	Sac-TMT (n = 91)	Docetaxel (n = 46)
PFS events, n (%)	64 (70.3)	42 (91.3)
Median PFS, months (95% CI)	6.9 (5.4, 8.2)	2.8 (1.6, 4.1)
6-month PFS rate, %	54.2	14.6

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

P < 0.0001

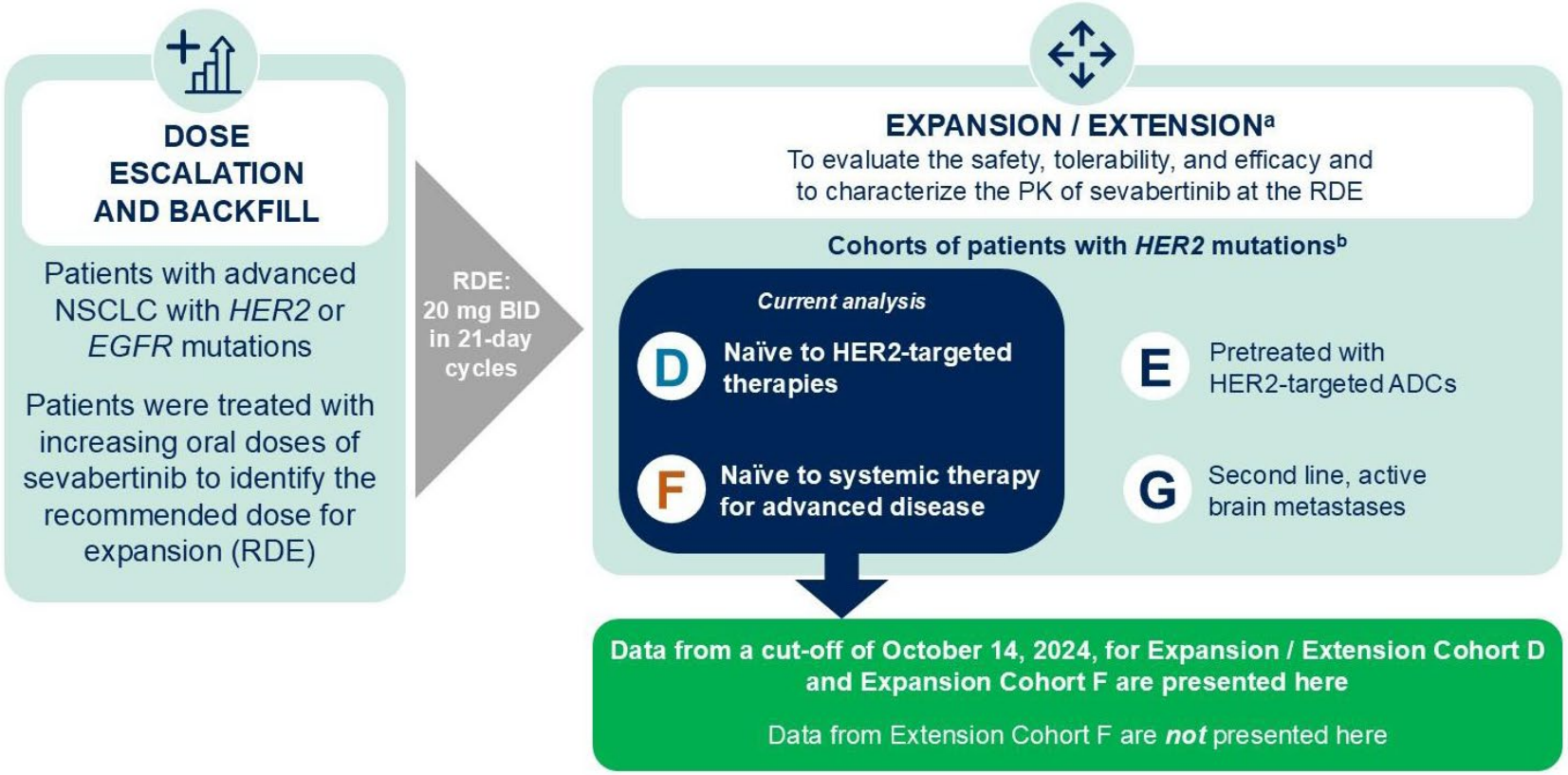
No. at Risk						
Sac-TMT	91	63	45	28	2	0
Docetaxel	46	17	6	2	0	



	Sac-TMT (n = 91)	Docetaxel (n = 46)
OS events, n (%)	25 (27.5)	21 (45.7)
Median OS, months (95% CI)	NR (NE, NE)	9.3 (7.3, NE)
12-month OS rate, %	72.8	43.2

No. at Risk							
Sac-TMT	91	88	83	73	39	2	0
Docetaxel	46	41	35	14	1	0	

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

Skuteczność

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

Median follow-up: 7.3 months[a]

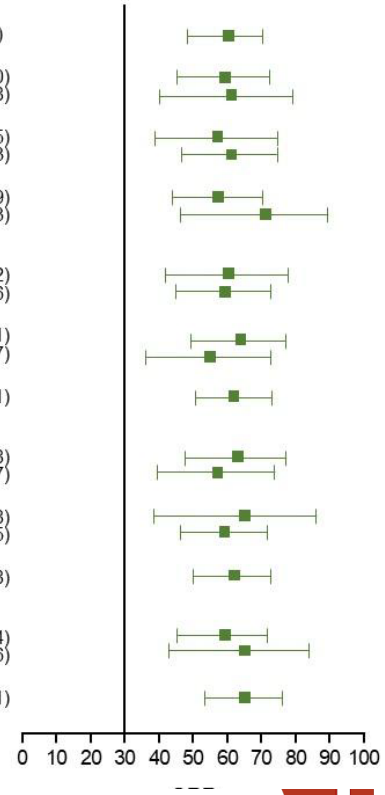
n (%)	INV	BICR
CR	1 (1.2)	1 (1.2)
PR	47 (58.0)	48 (59.3)
SD	22 (27.2)	22 (27.2)
PD	10 (12.3)	7 (8.6)
Not evaluable[b]	1 (1.2)	3 (3.7)
ORR[c] [95% CI]	**48 (59.3)** [47.8, 70.1]	**49 (60.5)** [49.0, 71.2]
DCR[d] [95% CI]	**68 (84.0)** [74.1, 91.2]	**66 (81.5)** [71.3, 89.2]

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]

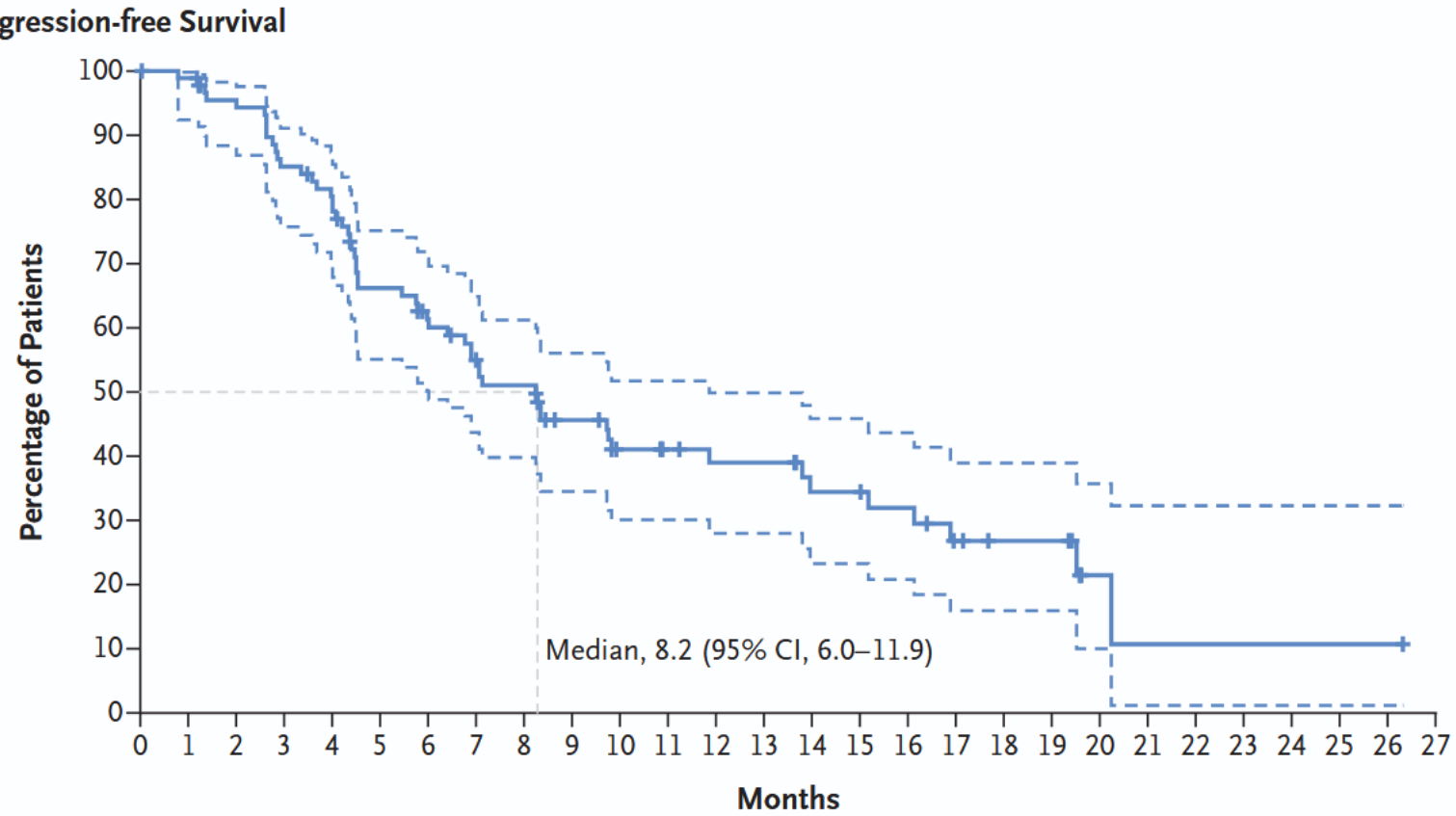
	Participants, *n*	CR / PR, *n*	ORR (95% CI)
All participants			
Overall	81	49	60.5 (49, 71.2)
Age group			
<65	55	33	60.0 (45.9, 73.0)
≥65	26	16	61.5 (40.6, 79.8)
Sex			
Male	31	18	58.1 (39.1, 75.5)
Female	50	31	62.0 (47.2, 75.3)
Race			
Asian	57	33	57.9 (44.1, 70.9)
White	18	13	72.2 (46.5, 90.3)
Other	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



ORIGINAL ARTICLE

Trastuzumab Deruxtecan in *HER2*-Mutant Non–Small-Cell Lung Cancer

Bob T. Li, M.D., Ph.D., M.P.H., Egbert F. Smit, M.D., Ph.D., Yasushi Goto, M.D., Ph.D., Kazuhiko Nakagawa, M.D., Hibiki Udagawa, M.D., Julien Mazières, M.D., Misako Nagasaka, M.D., Ph.D., Lyudmila Bazhenova, M.D., Andreas N. Saltos, M.D., Enriqueta Felip, M.D., Ph.D., Jose M. Pacheco, M.D., Maurice Pérol, M.D., Luis Paz-Ares, M.D., Kapil Saxena, M.D., Ryota Shiga, B.Sc., Yingkai Cheng, M.D., Ph.D., Suddhasatta Acharyya, Ph. Javad Shahidi, M.D., David Planchard, M.D., Ph.D., a for the DESTINY-Lung01 Trial Inv



2025 ASCO ANNUAL MEETING

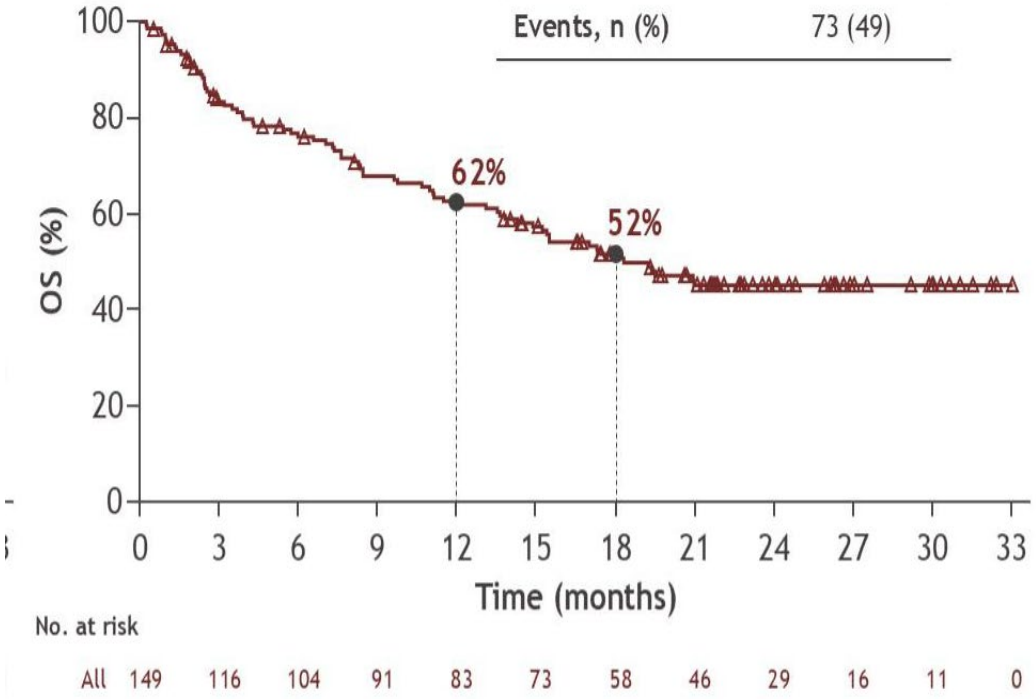
First-line adagrasib (ADA) with pembrolizumab (PEMBRO) in patients with advanced/metastatic *KRAS*^{G12C}-mutated non-small cell lung cancer (NSCLC) from the phase 2 portion of the KRYSTAL-7 study

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]

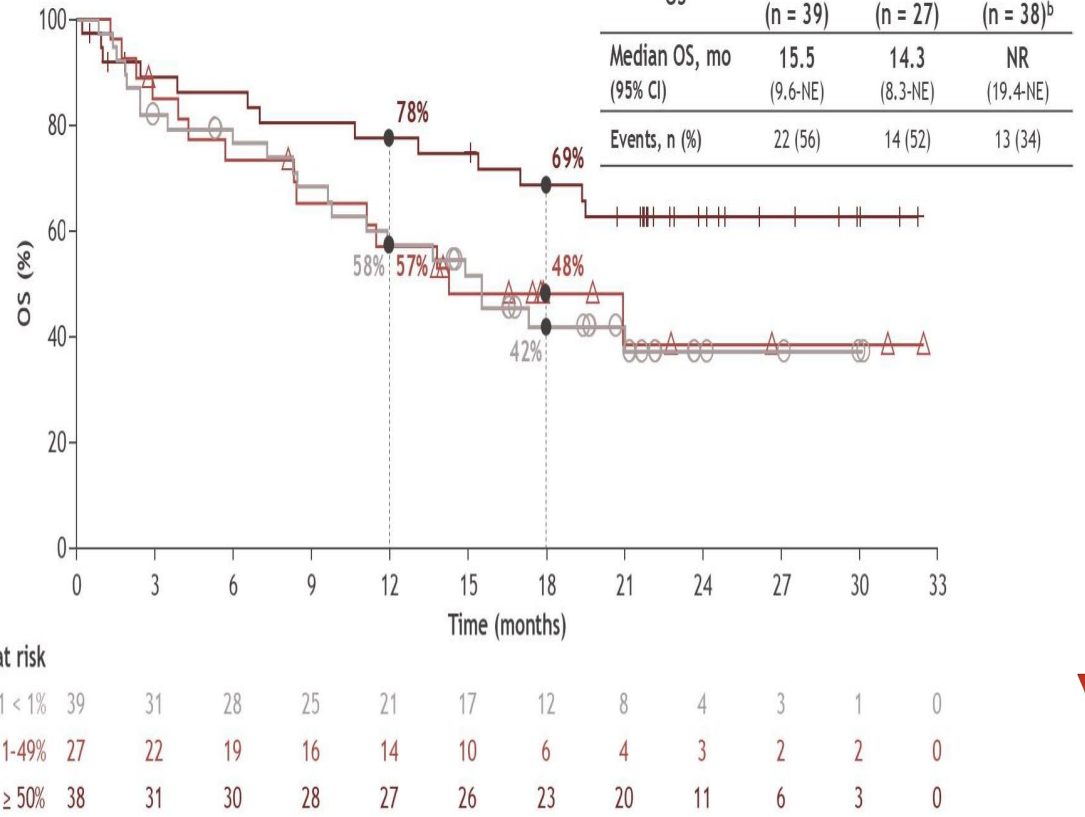
[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]The Netherlands Cancer Institute, Amsterdam, The Netherlands; [3]The University of Chicago, Chicago, IL, USA; [4]Virginia Cancer Specialists, Fairfax, VA, USA; [5]US Oncology Research, The Woodlands, TX, USA; [6]NEXT Oncology, Fairfax, VA, USA; [7]BC 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

Skuteczność

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)



Inhibitory KRAS w raku płuca – faza III:

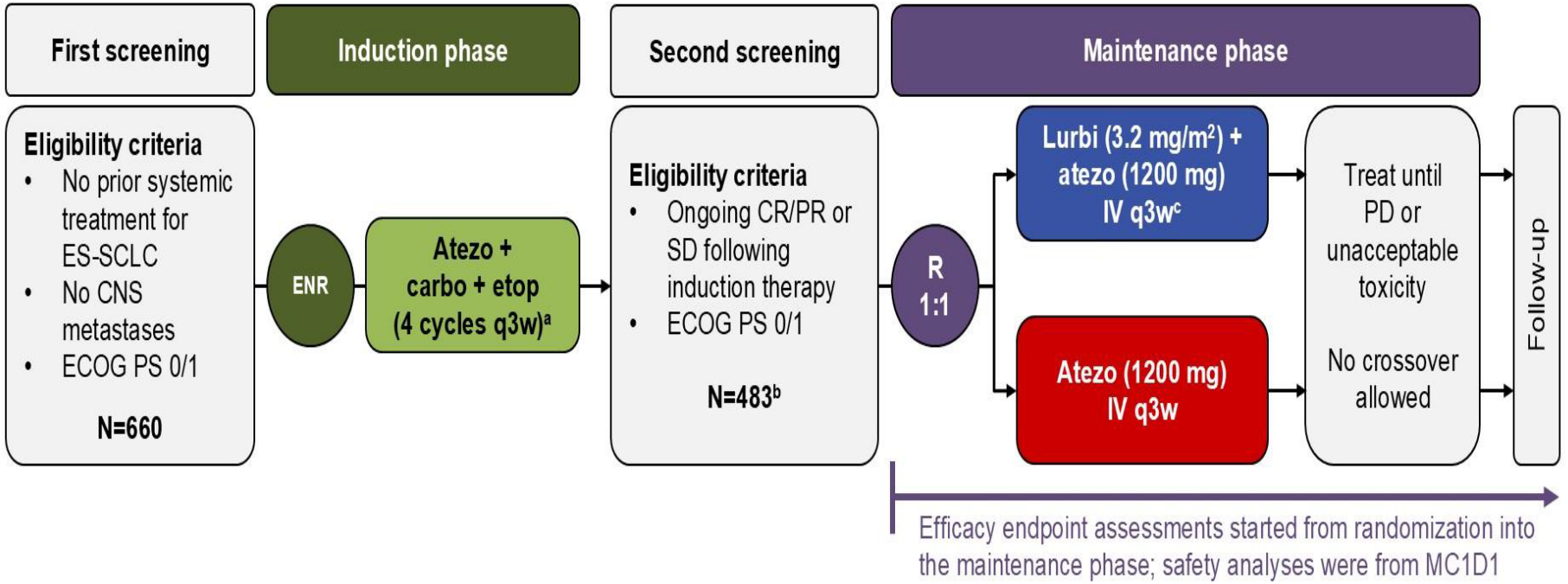
- Divarasib
- Olomorasib
- MK-1034
- Sotorasib
- Adagrasib
- Daraxonrasib (panKRAS)

XXIV SPOTKANIE Po ASCO

Zaawansowany rak płuca - rak drobnokomórkowy

XXIV SPOTKANIE Po ASCO

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

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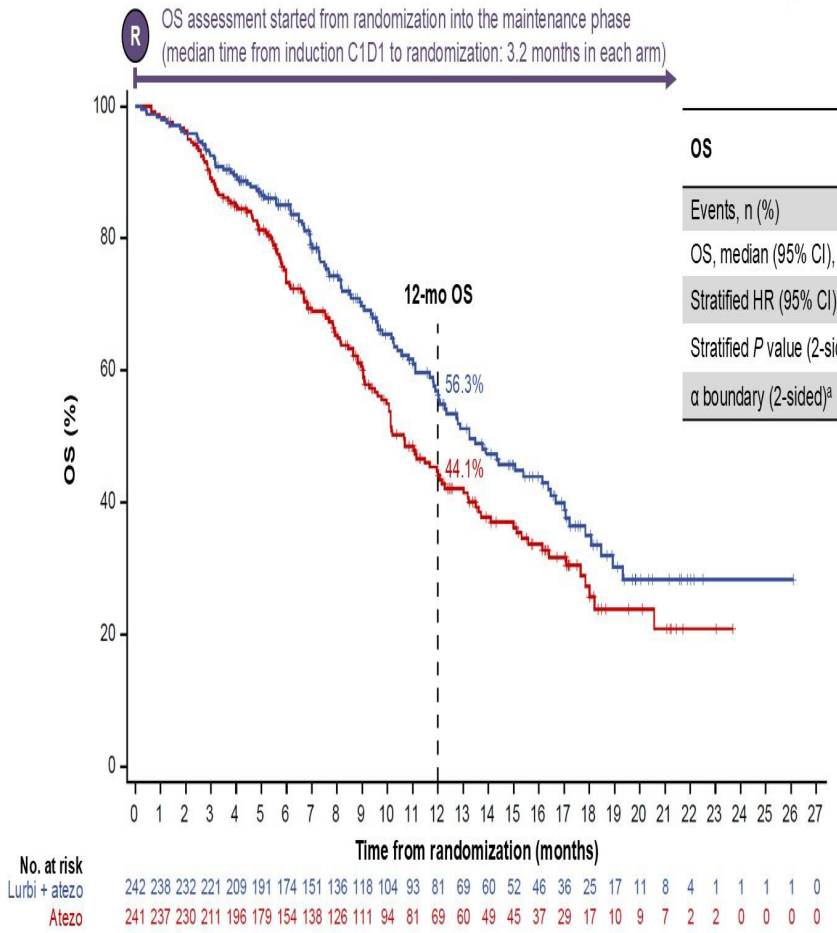
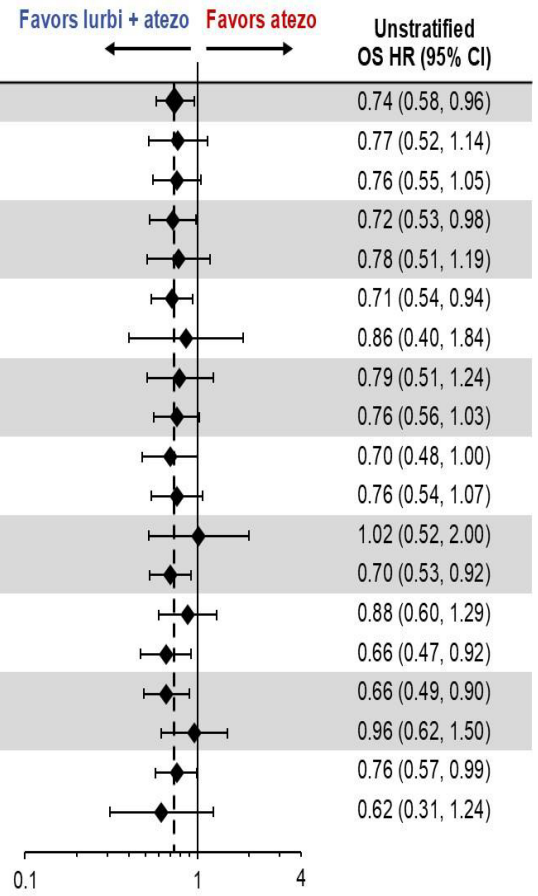
Skuteczność



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	

Baseline risk factors		Events/patients, n/N		Unstratified OS HR (95% CI)
		Lurbi + atezo	Atezo	
All patients		113/242	136/241	0.74 (0.58, 0.96)
Age, years	<65	53/118	49/90	0.77 (0.52, 1.14)
	≥65	60/124	87/151	0.76 (0.55, 1.05)
Sex	Male	75/151	88/151	0.72 (0.53, 0.98)
	Female	38/91	48/90	0.78 (0.51, 1.19)
Race[a]	White	92/195	118/199	0.71 (0.54, 0.94)
	Asian	13/31	14/31	0.86 (0.40, 1.84)
Tobacco use history[a]	Current	38/88	39/73	0.79 (0.51, 1.24)
	Previous	72/147	94/163	0.76 (0.56, 1.03)
Liver metastases at induction BL[b]	Yes	55/100	63/94	0.70 (0.48, 1.00)
	No	58/142	73/147	0.76 (0.54, 1.07)
Prior PCI[b]	Yes	16/34	18/37	1.02 (0.52, 2.00)
	No	97/208	118/204	0.70 (0.53, 0.92)
ECOG PS[b]	0	51/105	53/102	0.88 (0.60, 1.29)
	1	62/137	83/139	0.66 (0.47, 0.92)
LDH[b]	≤ULN	72/176	97/179	0.66 (0.49, 0.90)
	>ULN	41/66	39/62	0.96 (0.62, 1.50)
Response to induction therapy[a,c]	CR/PR	92/206	115/213	0.76 (0.57, 0.99)
	SD	17/28	18/25	0.62 (0.31, 1.24)



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

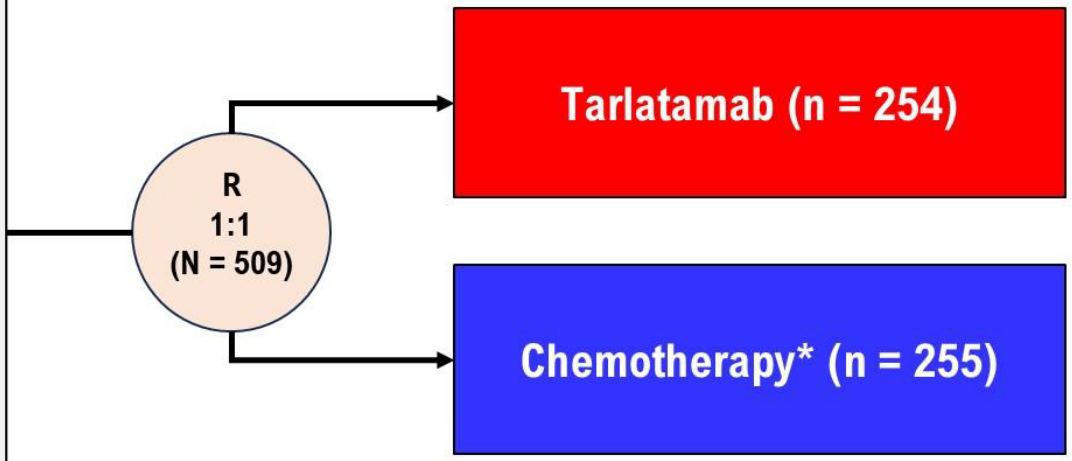
DeLLphi 304

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

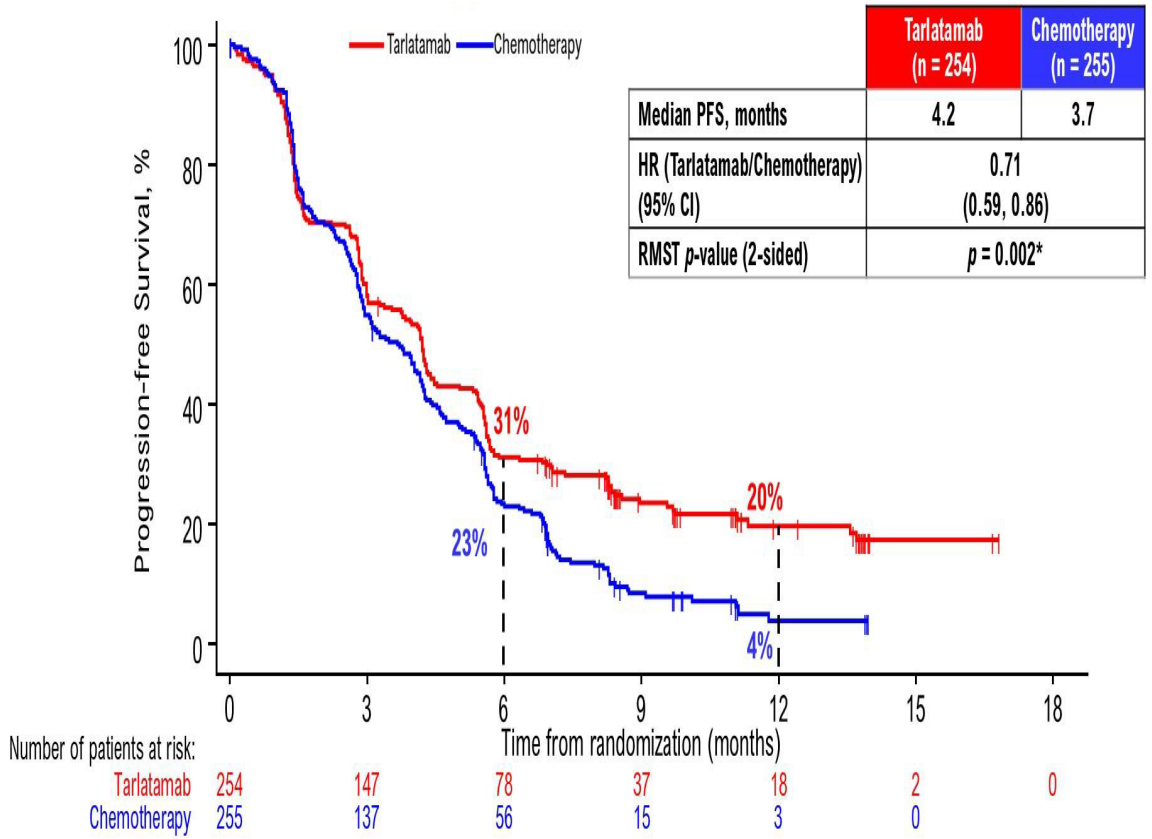
- Prior anti-PD-(L)1 exposure (yes/no)
- Chemotherapy-free interval (< 90 days vs ≥ 90 to < 180 days vs ≥ 180 days)
- Presence of (previous/current) brain metastases (yes/no)
- Intended chemotherapy (topotecan/amrubicin vs lurbinectedin)



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

Skuteczność



	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)

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Rak drobnokomórkowy – podsumowanie:

- Badanie Imforte:
poprawa OS dzięki wczesnej 2 linii chemioterapii?

- Tarlatamab i inne przeciwciała bispecyficzne antyDLL3:
poprawa odległego czasu przeżycia, badania w 1. linii trwają w raku drobnokomórkowym ED i LD