XXIV SPOTKANIE Po ASCO

Nowotwory skóry i mięsaki

Anna M. Czarnecka

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CZERNIAKI

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Badanie **DREAMseq** (ECOG-ACRIN EA6134) Phase III Trial of Treatment Sequences in Patients with BRAFV600-mutant (m) Metastatic Melanoma

2025 ASCO ANNUAL MEETING

DREAMseq (ECOG-ACRIN EA6134): a Phase III Trial of Treatment Sequences in Patients with BRAFV600-mutant (m) Metastatic Melanoma (MM): Final Clinical Results

Michael B. Atkins[1], Sandra J. Lee[2], Bartosz Chmielowski[3], Ahmad A. Tarhini[4], Gary I. Cohen[5], Geoffrey T. Gibney[1], Thach-Giao Truong[6], Diwakar Davar[7], Joe Stephenson[8], Brendan D. Curti[9], Joanna M. Brell[10], Kari L. Kendra[11], Alexandra P. Ikeguchi[12], Zihe Song[2], Samantha Guild[13], Jedd D. Wolchok[14], Antoni Ribas[3], John M. Kirkwood[7]

[1]Georgetown Lombardi Comprehensive Cancer Center, Washington DC; [2]Dana-Farber Cancer Institute, Boston MA; [3]Jonsson Comprehensive Cancer Center University of California Los Angeles, Los Angeles, CA; [4]H. Lee Moffitt Cancer Center and Research Institute, Medical Center, Baltimore MD; [6]Cleveland Clinic, Cleveland, OH; [7]Pittsburgh Cancer Institute, Pittsburgh PA; [8]NCORP of the Carolinas, Greenville SC; [9]Providence Cancer Institute, Portland OR; [10]MetroHealth Medical Center, Cleveland OH; [11]Ohio State University Comprehensive Cancer Center, Columbus OH; [12]University of Oklahoma Medical Center, Oklahoma City OK; [13]AIM at Melanoma Foundation, Sacramento CA; [14]Weill-Cornell Medical Center, New York NY

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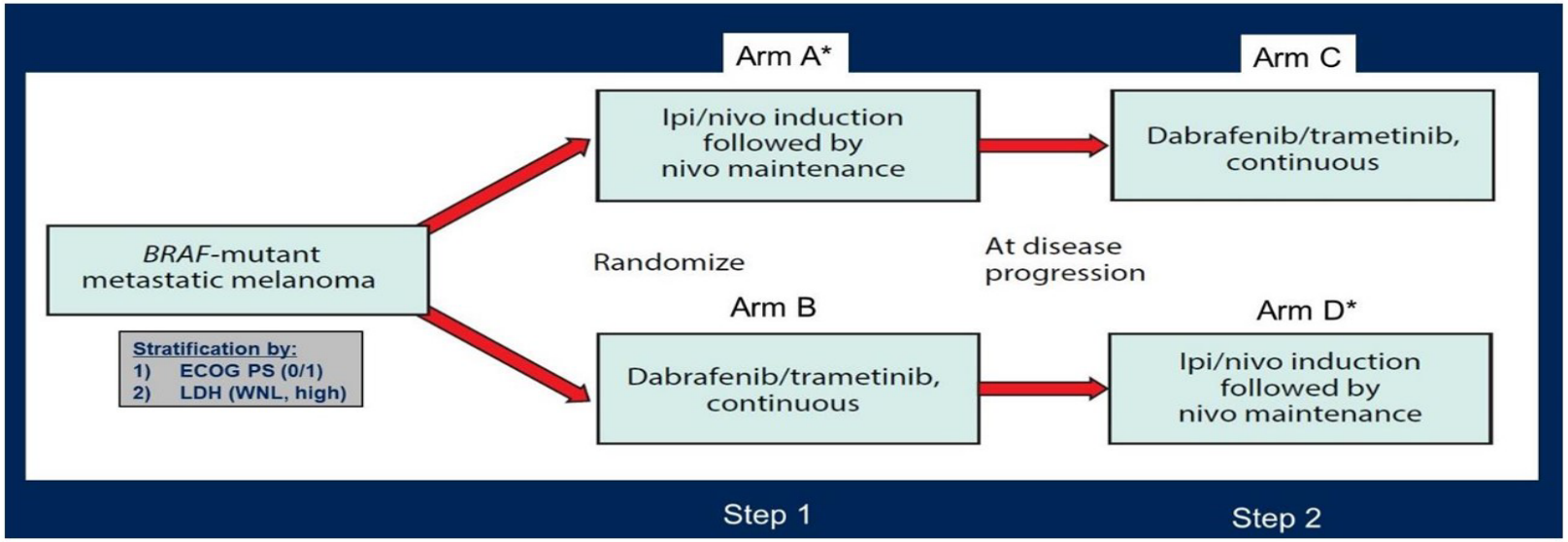
Plan badania DREAMseq

Phase 3 DREAMseq Trial/ECOG-ACRIN EA6134: Study Design

Efficacy and Toxicity of the Sequence of Nivolumab/Ipilimumab Followed by Dabrafenib/Trametinib to the Converse Sequence



At 4th Interim Analysis
59% of Patients at 2 Years from Enrollment
DSMC and NCI CTEP Recommended Halting Accrual and Releasing Data

Primary Endpoint: 2-year OS
Secondary Endpoint: 3-year OS, ORR, DOR, PFS, crossover feasibility and safety

*Nivolumab/Ipilimumab Induction = 12 weeks
Nivolumab Maintenance = 72 weeks.

Atkins MB, et al. *J Clin Oncol*. 2023;41(2):186-197

Wstępne wyniki badania DREAMseq

- Nivo/ipi followed by dab/tram was associated with significantly and clinically meaningful greater 2-year OS (72% vs 52%) (p= 0.01)
  - OS benefit for nivo/ipi first sequence was seen in all clinical subgroups
  - Nivo/ipi resulted in more durable and ongoing responses (88% vs 48% remained in response)
  - Dab/Tram was equally active in 1st and 2nd-line; nivo/ipi had lower ORR and PFS in 2nd-line
- PFS and OS curves were biphasic crossing at 6 and 10 mos, respectively
  - Pts dying early on nivo/ipi had poor prognosis; never received dab/tram (on protocol)
- Grade 3+ TRAE rates were similar between arms; but different AE profiles

Atkins MB, et al. *J Clin Oncol*. 2023;41(2):186-197

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Wyniki badania DREAMseq

Updated Endpoints- Median follow-up 58 mos (range 0-101 mos)

Endpoints (95% CI)	Treatment		P value
1⁰ Endpoint	**Arm A to C (n=135)**	**Arm B to D (n=132)**	
2-yr OS	68.3% (60.8, 76.9)	54.1% (46.1, 63.7)	<0.01
2⁰ Endpoints			
3-yr OS	65.6% (57.3, 73.9)	44.8% (36.7, 54.6)	
5-yr OS	**63.3% (55.4, 72.3)**	**33.9% (25.9, 44.3)**	
2-yr PFS	**Arm A** 50.8% (42.8, 60.3)	**Arm B** 22.9% (16.5, 31.7)	
3-yr PFS	45.0% (37.0, 54.8)	15.9% (10.5, 24.0)	
5-yr PFS	**39.4% (31.3, 49.5)**	**12.8% (7.9, 20.7)**	<0.01
Median PFS (mos)	**Arm A** 26.7 (11.2-47.3)	**Arm B** 8.5 (8.1-12.6)	
	Arm C (n=30) 11.2 (9.5, 22.3)	**Arm D (n=52)** 5.9 (2.9, 22.4)	
ORR	**Arm A (n= 132)** **51.5% (42.7, 60.3)**	**Arm B (n=131)** **51.1% (42.3, 60.0)**	
	Arm C (n=30) 70% (37.4, 74.5)	**Arm D (n= 52)** 46.2% (32.2, 60.5)	
Still in Response-n (%) Median DOR (95% CI) (mos)	**Arm A (n=68);** **52 (76.4%)** Not reached (NR, NR)	**Arm B (n=67);** **16 (23.8%)** 15.5 (11.2, 23.5)	<0.01
	Arm C (n=17); 4 (23.5%) 14.7 (8.2, NR)	**Arm D (n=20);** 12 (60%) 45.2 (19.5, NR)	0.03

Długotrwały OS – badanie DREAMseq

Updated DREAMseq OS: Step 1 +/- Step 2

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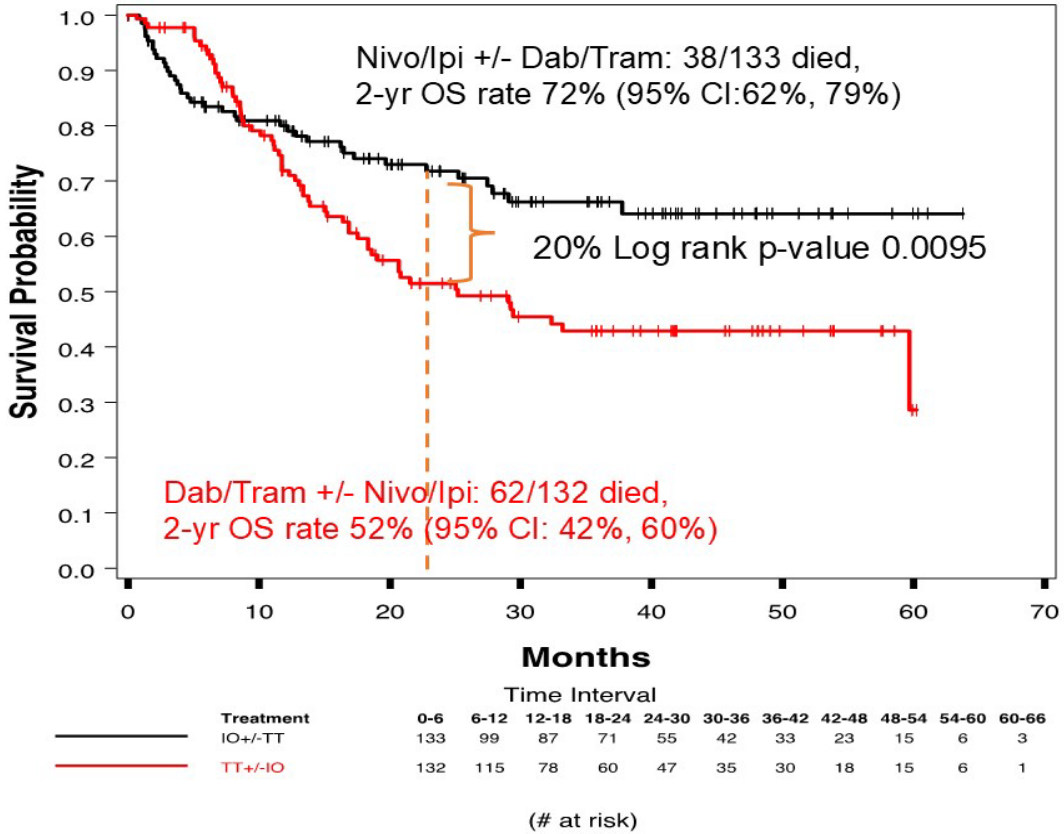
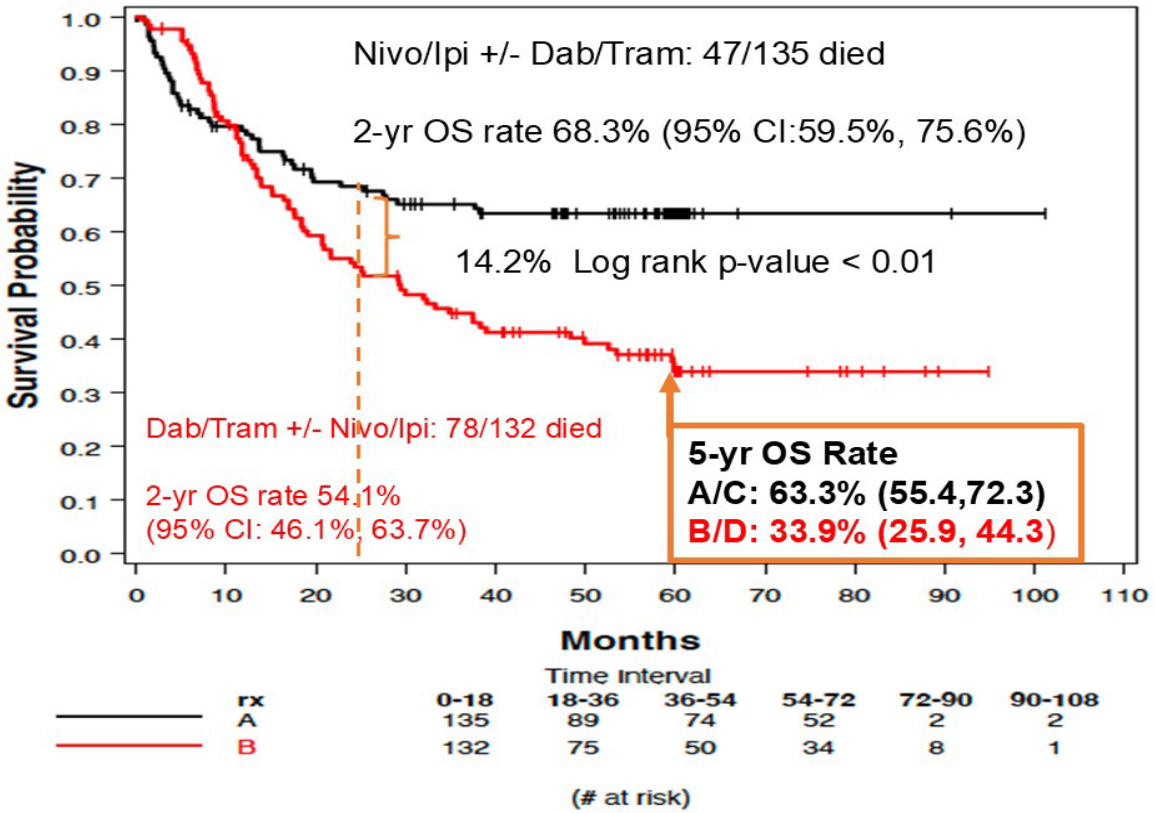


July 2024



PFS – ocena po 66 m – Badanie DREAMseq

Progression Free Survival (PFS): Step1

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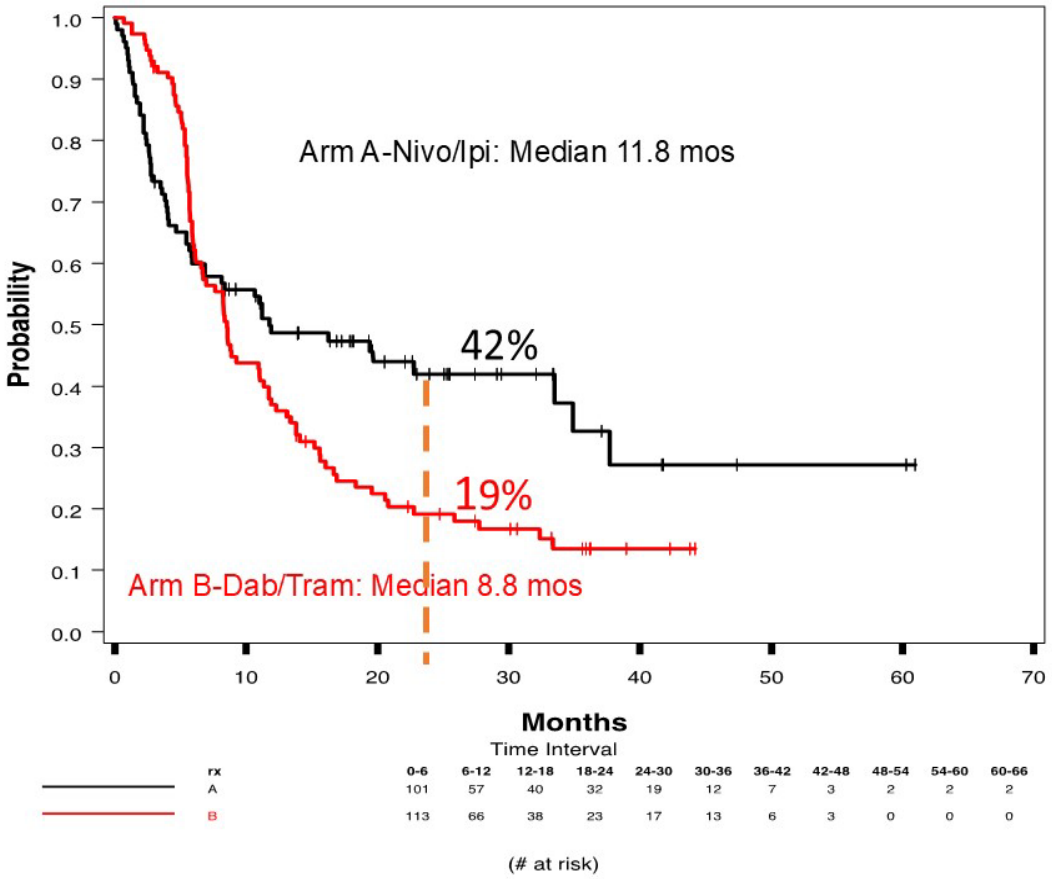

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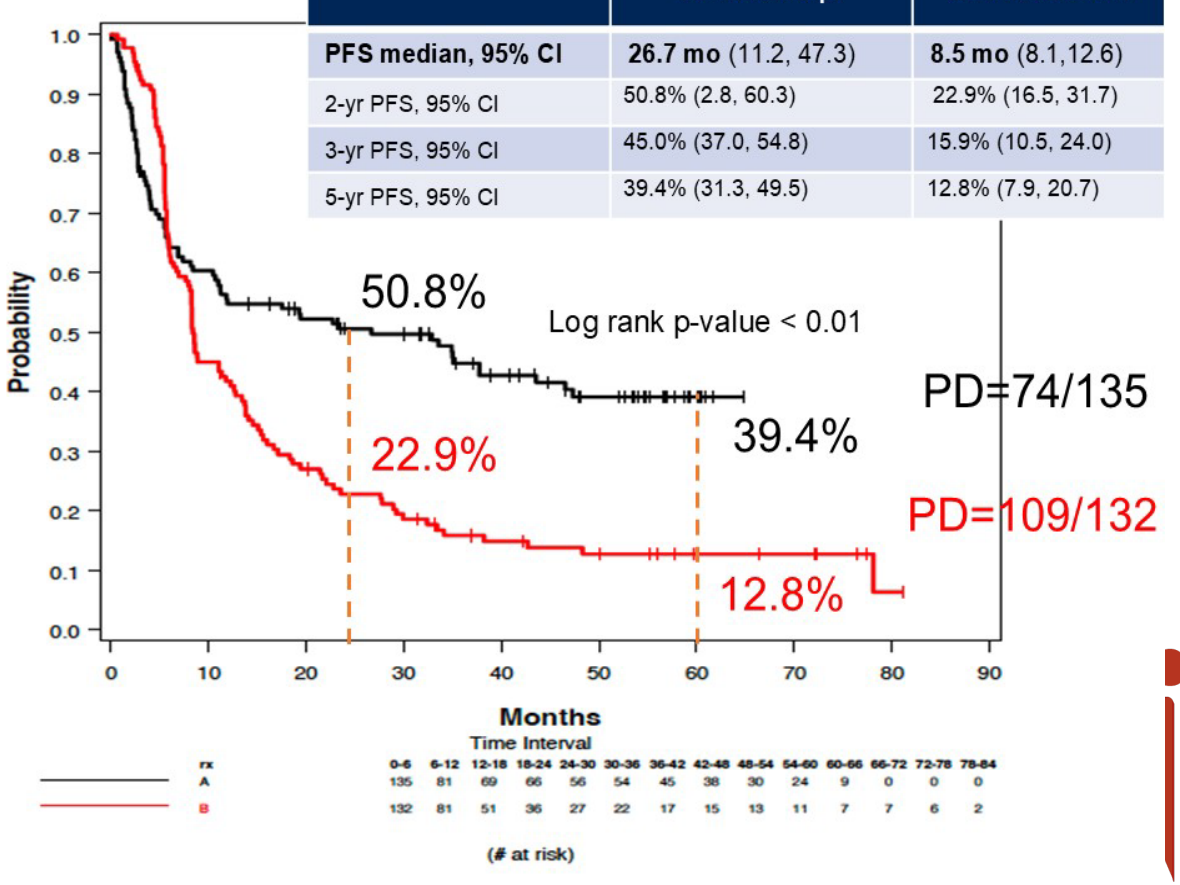
	Arm A-Nivo/ipi	Arm B-Dab/Tram
PFS median, 95% CI	**26.7 mo** (11.2, 47.3)	**8.5 mo** (8.1,12.6)
2-yr PFS, 95% CI	50.8% (2.8, 60.3)	22.9% (16.5, 31.7)
3-yr PFS, 95% CI	45.0% (37.0, 54.8)	15.9% (10.5, 24.0)
5-yr PFS, 95% CI	39.4% (31.3, 49.5)	12.8% (7.9, 20.7)



Analiza podgrup - DREAMseq

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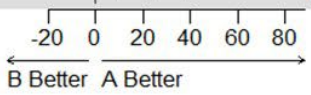
Clinical Subset 4-year PFS by Arm and OS by Sequence

PFS by Arm*

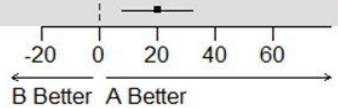
Subgroup	Treatment A	Treatment B	Difference in 4-Yr PFS	95% CI
	4-Yr PFS (%)			
Sex				
Male	39	16		22.42 (8.55 to 36.29)
Female	40	7		32.92 (15.41 to 50.43)
Age (years)				
< 40	60	16		44.29 (7.94 to 80.64)
40-60	43	14		28.53 (11.13 to 45.93)
> 60	33	13		19.73 (4.58 to 34.88)
PS				
0	43	14		29.10 (15.55 to 42.65)
1	31	12		18.36 (-0.59 to 37.31)
Stage				
< M1c	41	17		24.20 (5.37 to 43.03)
M1c	39	12		26.87 (13.63 to 40.11)
LDH				
Low or Normal	46	18		27.76 (12.92 to 42.60)
High	30	8		21.48 (5.78 to 37.18)
Favorable Prognosis				
Yes	50	15		34.34 (11.59 to 57.09)
No	36	13		23.05 (10.45 to 35.65)



*Treatment A = IO, Treatment B=TT

OS by Sequence#

Subgroup	Treatment A	Treatment B	Difference in 4-Yr OS rate	95% CI
	4-Yr OS Rate (%)			
Sex				
Male	61	38		23.00 (4.00 to 41.00)
Female	68	48		20.00 (0.00 to 40.00)
Age (years)				
< 40	81	40		41.00 (10.00 to 72.00)
40-60	67	50		18.00 (-12.00 to 47.00)
> 60	56	35		21.00 (2.00 to 40.00)
PS				
0	70	43		27.00 (12.00 to 41.00)
1	51	38		14.00 (-8.00 to 35.00)
Stage				
< M1c	66	49		17.00 (-3.00 to 36.00)
M1c	61	36		26.00 (10.00 to 41.00)
LDH				
Low or Normal	71	51		21.00 (3.00 to 38.00)
High	51	26		25.00 (8.00 to 42.00)
Favorable Prognosis				
Yes	72	42		30.00 (11.00 to 50.00)
No	61	41		20.00 (8.00 to 32.00)



#Treatment A=IO +/- TT, Treatment B = TT +/- IO

Znaczenie rokownicze LDH – badanie DREAMseq

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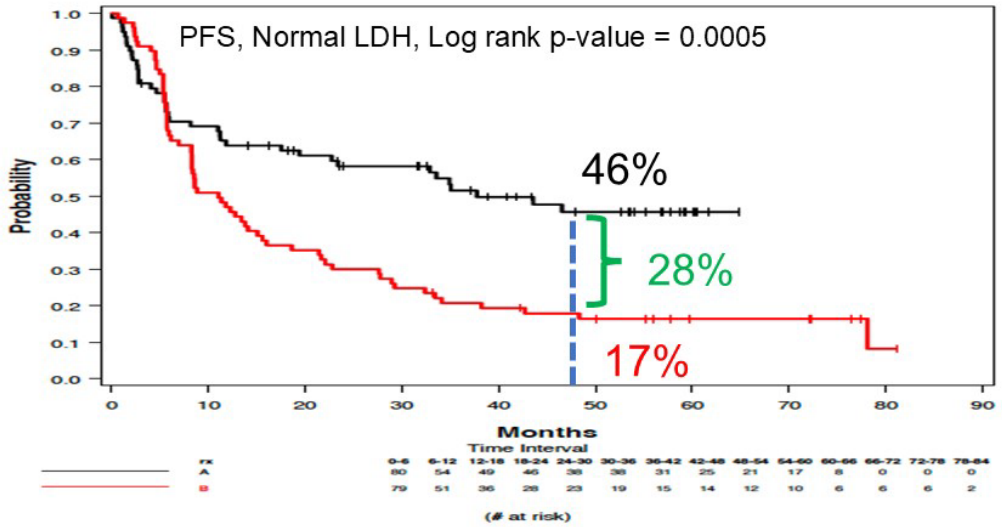
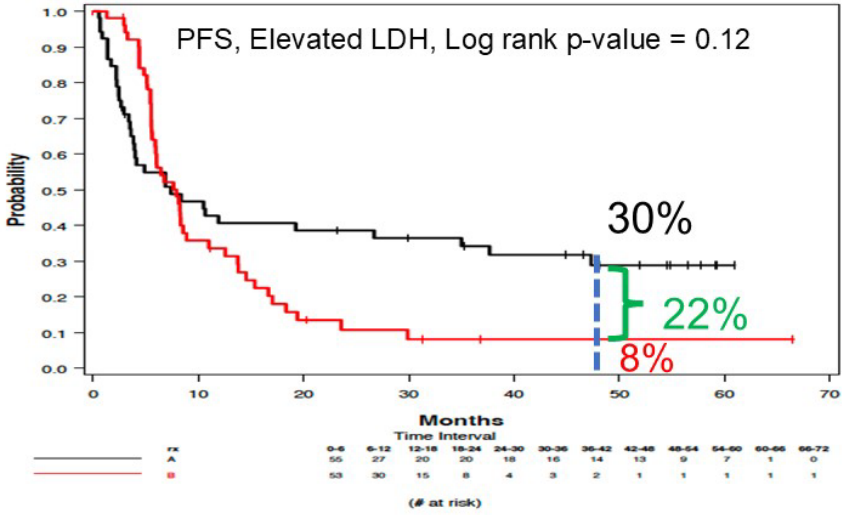
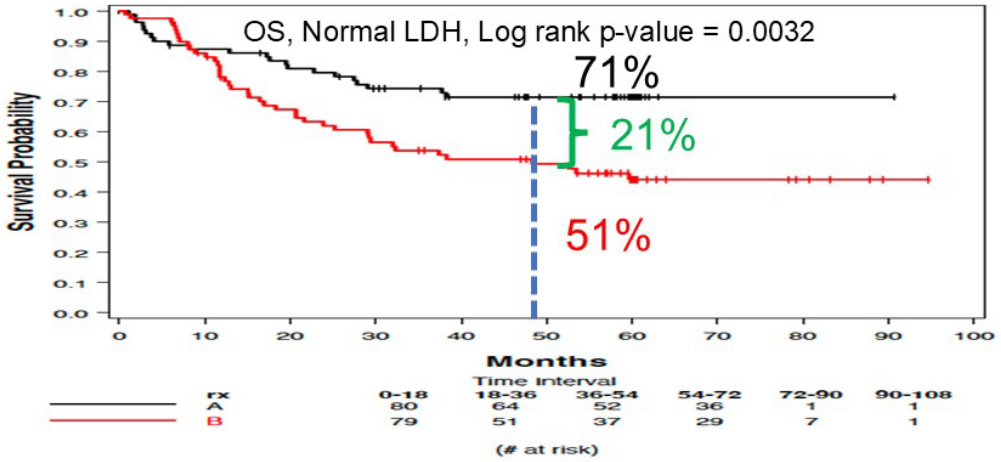
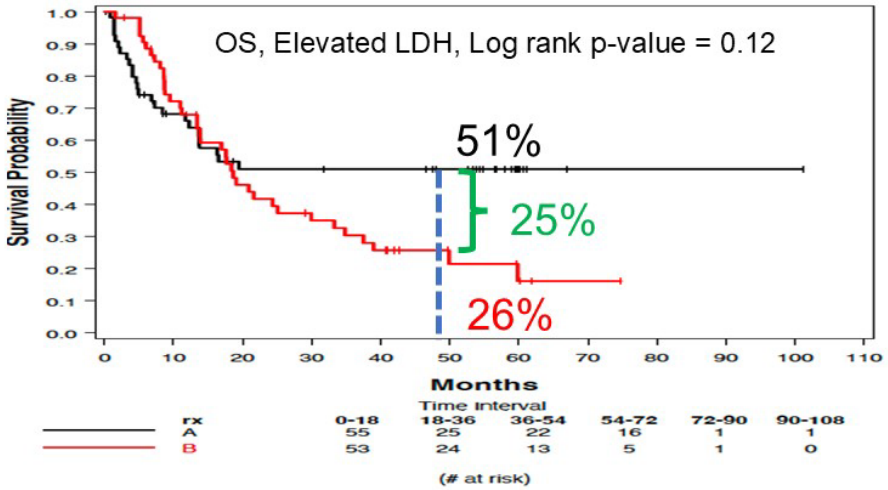
DREAMseq Clinical Factor Subset Analysis: LDH Levels (all subjects)









Czas trwania odpowiedzi – badanie DREAMseq

Duration of Response (DOR)*: Step1

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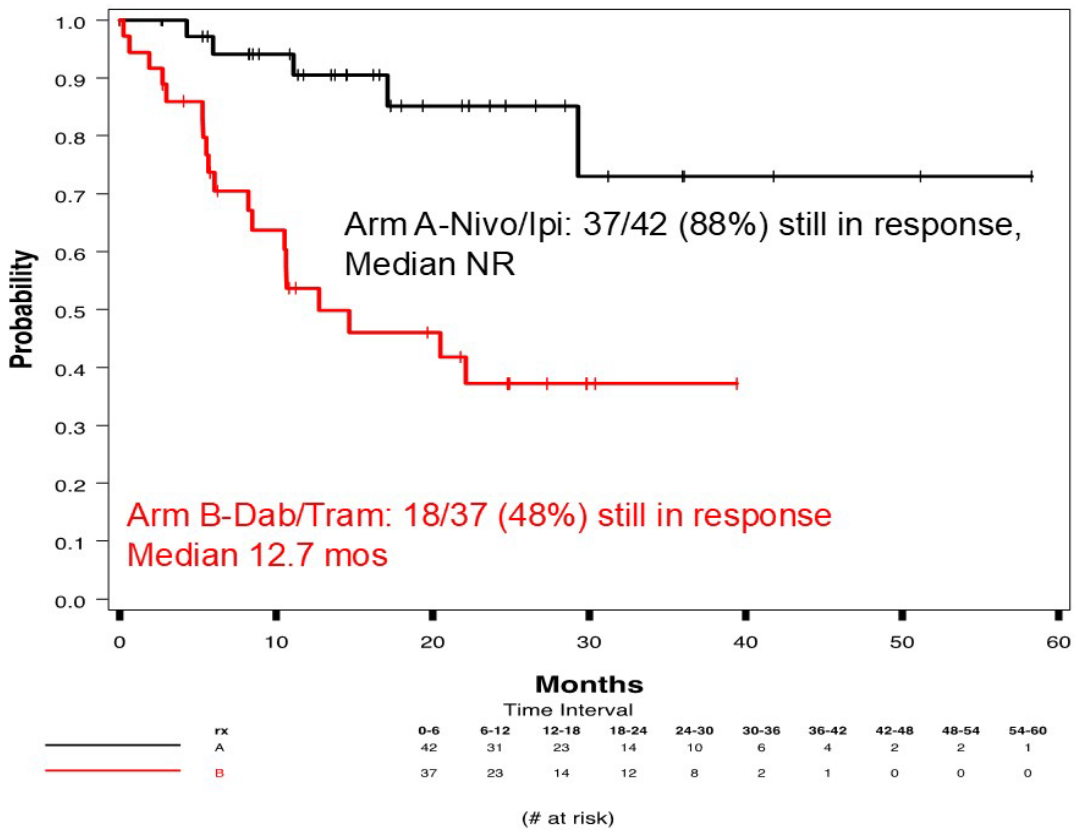
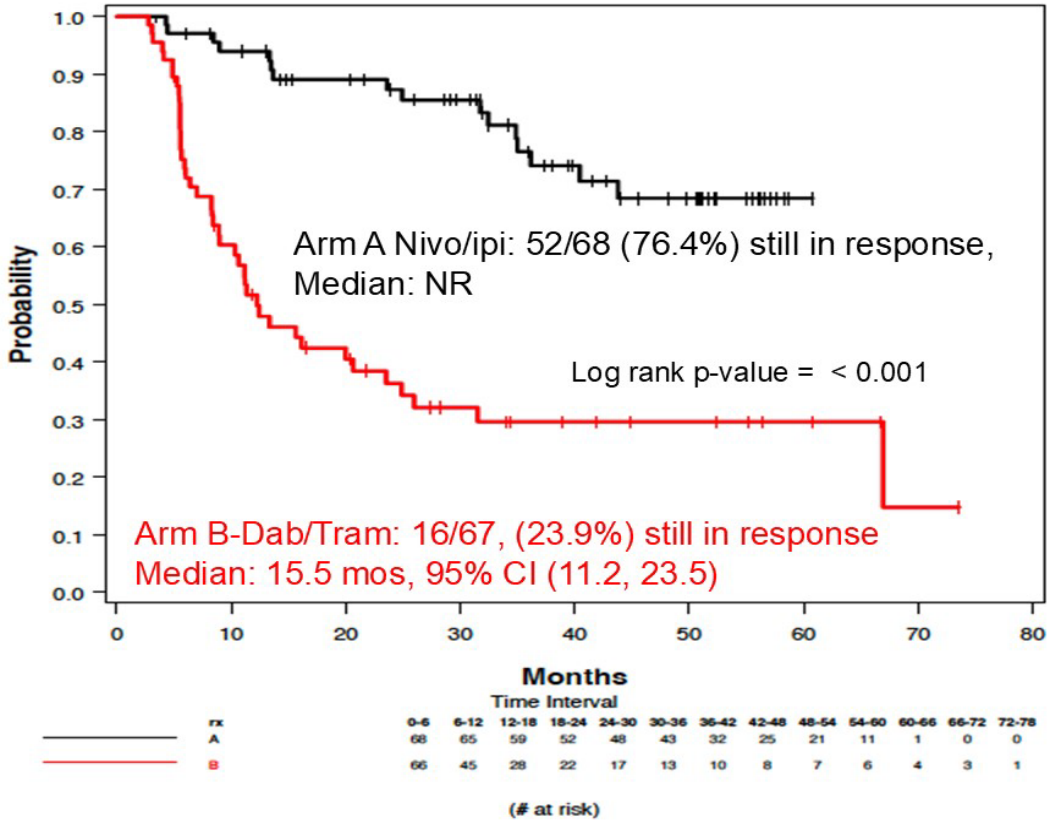


rx	0-6	6-12	12-18	18-24	24-30	30-36	36-42	42-48	48-54	54-60
A	42	31	23	14	10	6	4	2	2	1
B	37	23	14	12	8	2	1	0	0	0

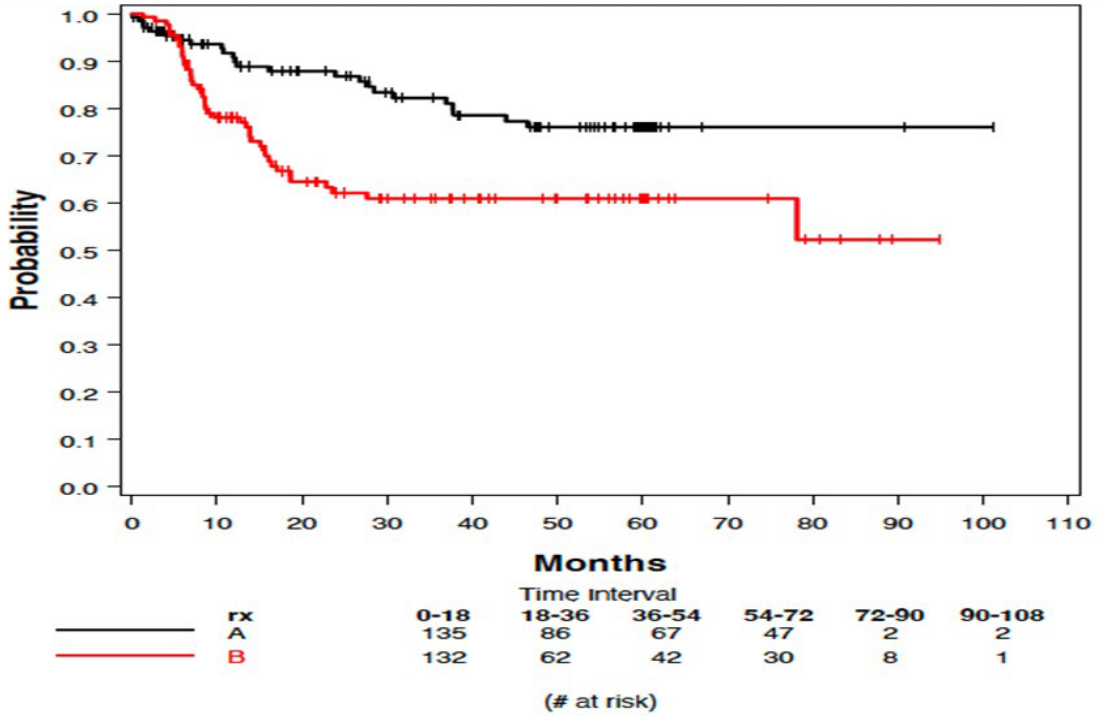
July 2024



rx	0-6	6-12	12-18	18-24	24-30	30-36	36-42	42-48	48-54	54-60	60-66	66-72	72-78
A	68	65	59	52	48	43	32	25	21	11	1	0	0
B	66	45	28	22	17	13	10	8	7	6	4	3	1

Czas wolny od meta OUN – badanie DREAMseq

CNS Metastasis-Free Survival (CMFS)*



- All CNS events were brain
- *CMFS – defined as time from randomization to CNS metastasis, censored at last FU or death

Arm	CNS as First site of Relapse (n)	2-year CMFS	4-year CMFS	P-value by log-rank test
Arm A (IO) (N=135)	24	86.8%, 95% CI (80.4, 93.1)	76.0% 95% CI (67.3, 84.6)	P < 0.01
Arm B (TT) (N=132)	44	62.1% 95% CI (52.8, 71.4)	62.1% 95% CI (52.8, 71.4)	

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Badanie DANTE – 1 vs 2 lata leczenia MM

2025 ASCO ANNUAL MEETING

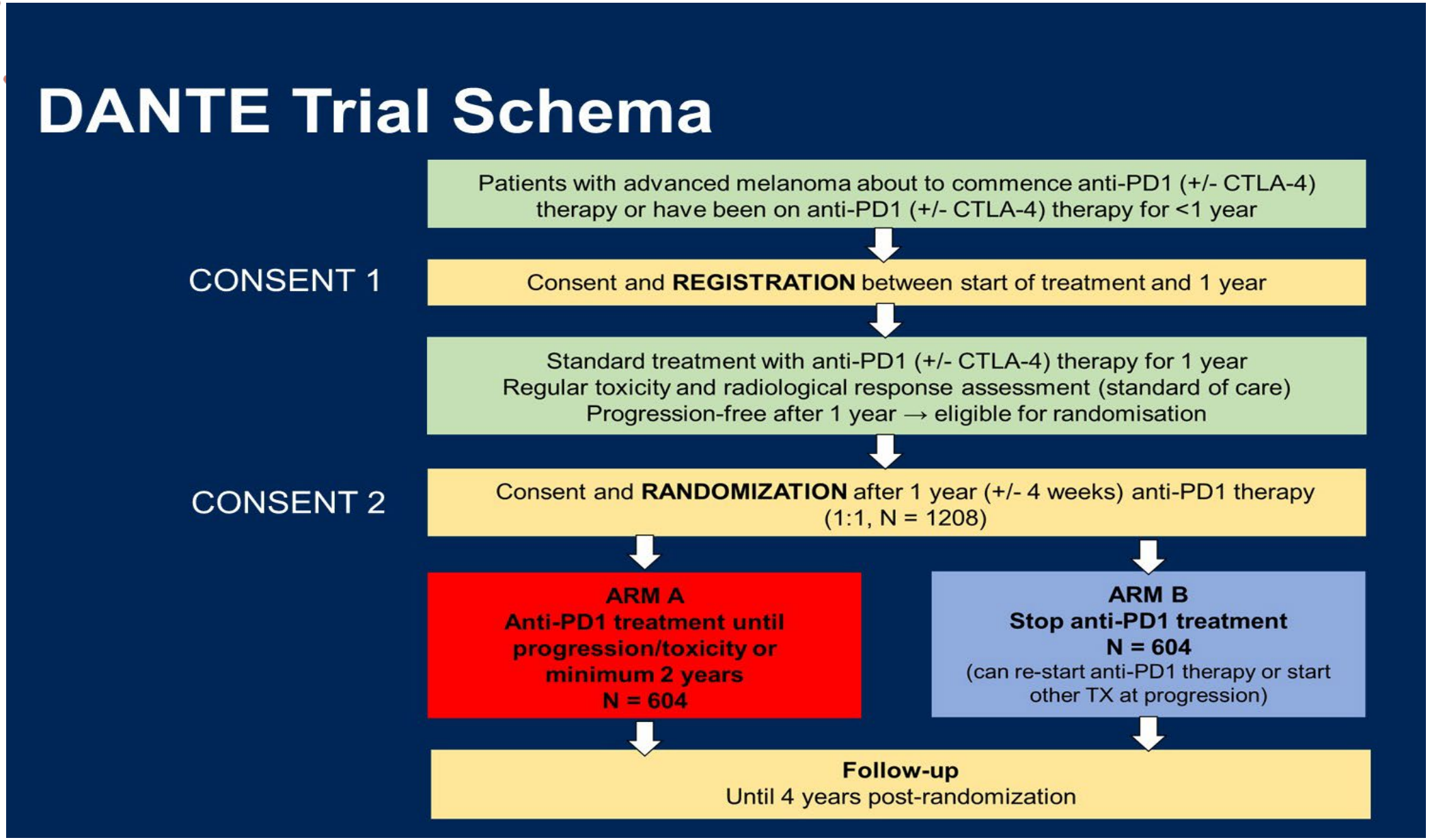
DANTE: **D**uration of **ANT**i-PD1 Therapy for M**E**lanoma

Comparison of 1 year versus minimum 2 years of anti-PD1-based immunotherapy as first line treatment for metastatic melanoma: Results of the DANTE phase III trial

Sarah Danson, Michelle Collinson, Elizabeth Ruth Plummer, Christian H.H Ottensmeier, Shobha Silva, Jane Hook, Brindley Sonal Hapuarachi, Matthew Wheater, Miranda Payne, Olabode Oladipo, Ashita Marie Waterston, Galina Velikova, Ferdia Aidan Gallagher, David M. Meads, Sue E. Bell, Natasha Greatorex, Eszter Katona, Janine Bestall, Susanna Daniels, Philippa Gail Corrie.

Presenter: Sarah Danson, University of Sheffield & Sheffield Teaching Hospitals NHS Foundation Trust, UK

Przebieg leczenia w badaniu DANTE



Pacjenci leczeni w badaniu DANTE

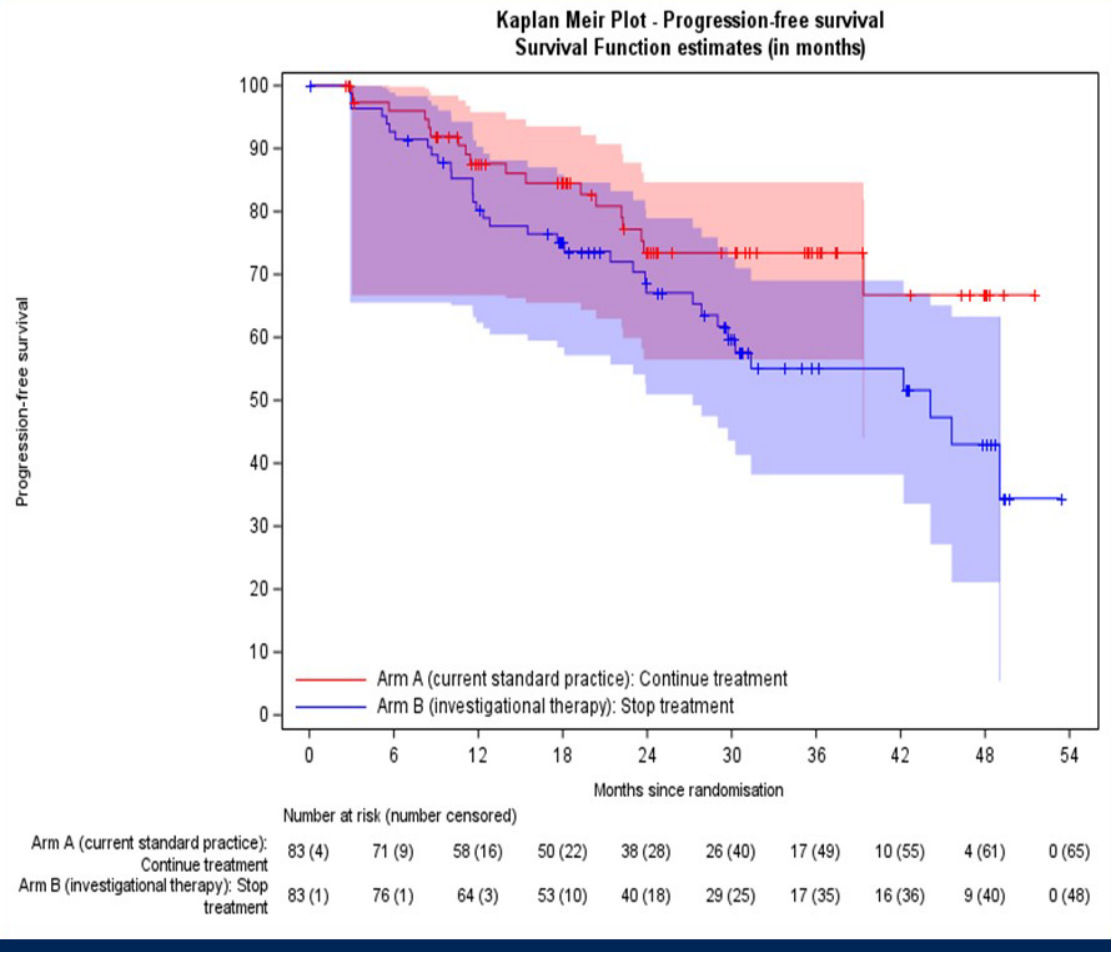
Baseline Characteristics

	Arm A: Continue treatment (n=83)	Arm B: Stop treatment (n=83)	Total (n=166)
Median age in years (IQR)	74 (66-79)	74 (62-80)	74 (66-80)
Male (%)	60 (72%)	48 (58%)	108 (65%)
White ethnicity (%)	80 (96%)	80 (96%)	160 (96%)
BRAF mutant (%)*	24 (29%)	19 (23%)	43 (26%)
Prior *BRAF/MEK* inhibitor therapy (%)*	1 (1%)	5 (6%)	6 (4%)
Prior (neo)adjuvant immunotherapy (%)*	8 (10%)	4 (5%)	12 (7%)
Disease stage IV (%)*	72 (87%)	71 (86%)	143 (86%)
Has brain metastases (%)*	8 (10%)	4 (5%)	12 (7%)
ECOG performance status 0/1 (%)*	82 (99%)	81 (98%)	163 (98%)
Pembrolizumab (%)*	43 (52%)	43 (52%)	86 (52%)
Nivolumab (%)*	23 (28%)	23 (28%)	46 (28%)
Combined ipilimumab and nivolumab (%)*	17 (20%)	17 (20%)	34 (20%)
Complete response after 1 year of therapy (%)*	31 (37%)	28 (34%)	59 (36%)

*Stratification factors

Pierwszorzędowy punkt końcowy – PFS – Badanie DANTE

Results: Primary Outcome (PFS)



	Arm A (n=83)	Arm B (n=83)	Total (n=166)
Follow-up in months (median, IQR)	24 (15-37)	30 (18-43)	29 (18-39)
Alive and progression-free	65 (78%)	48 (58%)	113 (68%)
PFS Events	18 (22%)	35 (42%)	53 (32%)
Progressions	15 (83%)	29 (83%)	44 (83%)
Deaths	3 (17%)	6 (17%)	9 (17%)
PFS at 1 year	**87.6%**	**80.2%**	

- Stopping treatment at 1 year is non-inferior:
- Adjusted HR up to 1 year of 3.0; 90% CI 1.0-8.5
- Absolute difference of -7.4%; 90% CI: -17.1-2.3

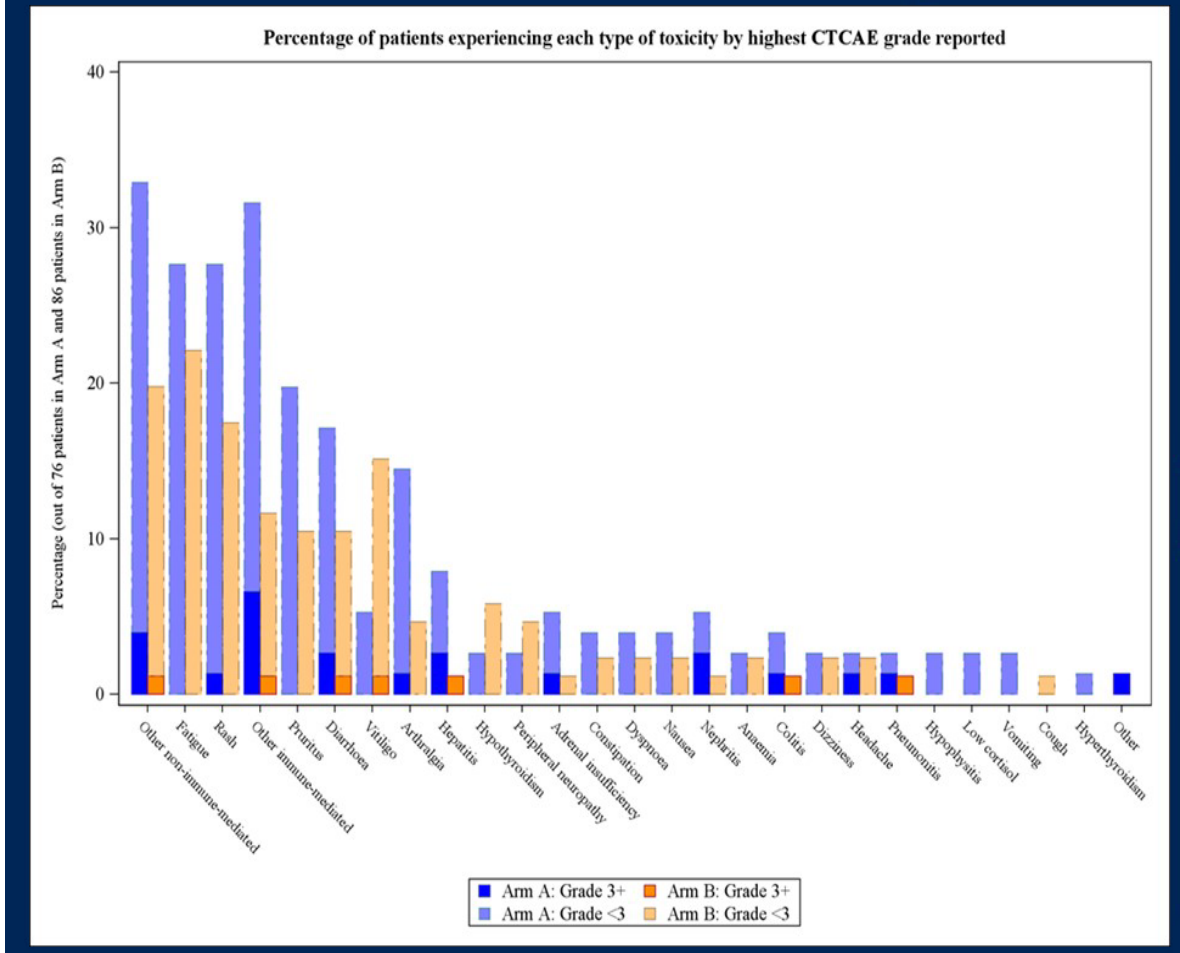
Wyniki leczenia – badanie DANTE

Results: Secondary Outcomes

	Arm A: Continue treatment (n=83)	Arm B: Stop treatment (n=83)	Total (n=166)
Deaths (%)	10 (12%)	14 (17%)	24 (14%)
Mean time to death in months (SD)	19 (9)	28 (11)	24 (11)
Objective response (CR + PR) at end of follow-up	54 (65%)	54 (65%)	108 (65%)
Best response at end of follow-up			
Complete response (%)	44 (53%)	37 (45%)	81 (49%)
Partial response (%)	10 (12%)	17 (20%)	27 (16%)
Stable disease (%)	22 (27%)	25 (30%)	47 (28%)
Progressive disease (%)	3 (4%)	3 (4%)	6 (4%)
Missing / not evaluable (%)	4 (5%)	1 (1%)	5 (3%)

Toksyczność leczenia – badanie DANTE

Results: Secondary Outcomes



	Arm A (n=76)	Arm B (n=86)	Total (n=162)
Any toxicity (%)	61 (80%)	54 (63%)	115 (71%)
Number of toxicities (%)	383	211	594
Median number of toxicities per participant (IQR)	4 (3-7)	2 (1-4)	3 (2-6)
Any Grade 3+ toxicity (%)	19 (25%)	7 (8%)	26 (16%)
Number of Grade 3+ toxicities	28	10	38
Median number of Grade 3+ toxicities per participant (IQR)	1 (1-2)	1 (1-2)	1 (1-2)

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Lifileucel w MM – obserwacja 5 letnie badania C-144-01

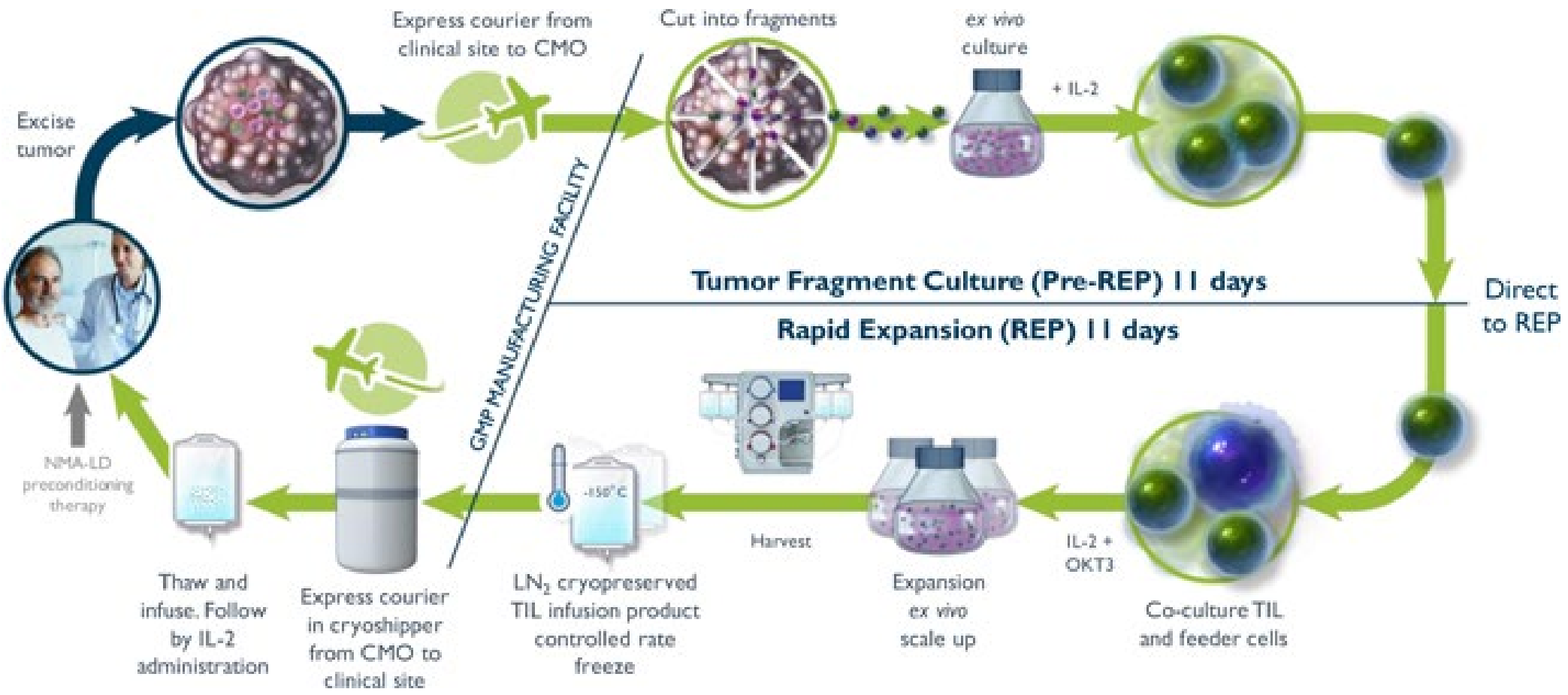
2025 ASCO ANNUAL MEETING

Lifileucel in patients with advanced melanoma: 5-year outcomes of the C-144-01 study

Theresa Medina, MD[1], Jason A Chesney, MD, PhD[2], Harriet M Kluger, MD[3], Omid Hamid, MD[4], Eric D Whitman, MD[5], Mike Cusnir, MD[6], Sajeve A Thomas, MD[7], Martin Wermke, MD[8], Evidio Domingo-Musibay, MD[9], Giao Q Phan, MD[10], John M Kirkwood, MD[11], James Larkin, MD, PhD[12], Jeffrey Weber, MD, PhD[13*], Friedrich Graf Finckenstein, MD[14], Jeffrey Chou, MD, PhD[14], Brian Gastman, MD[14], Xiao Wu, PhD[14], Rana Fiaz, MD[14], Amod A Sarnaik, MD[15]

[1]University of Colorado Cancer Center—Anschutz Medical Campus, Aurora, CO, USA; [2]Brown Cancer Center, Louisville, KY, USA; [3]Yale Cancer Center, New Haven, CT, USA; [4]The Angeles Clinic and Research Institute, a Cedars Sinai Affiliate, Los Angeles, CA, USA; [5]Atlantic Health System, Morristown, NJ, USA; [6]Mount Sinai Medical Center, Miami Beach, FL, USA; [7]AdventHealth Cancer Institute, Orlando, FL, USA; [8]Technical University Dresden—NCT/UCC Early Clinical Trial Unit, Dresden, Germany; [9]Allina Health Cancer Institute, Minneapolis, MN, USA; [10]UConn Health/Neag Cancer Center, Farmington, CT, USA; [11]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [12]The Royal Marsden Hospital NHS Foundation Trust, London, UK; [13]Laura and Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, NY, USA; [14]Iovance Biotherapeutics, Inc., San Carlos, CA, USA; [15]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

Lifileucel


Express courier from clinical site to CMO
Cut into fragments
ex vivo culture
+ IL-2
Excise tumor
GMP MANUFACTURING FACILITY
Tumor Fragment Culture (Pre-REP) 11 days
Rapid Expansion (REP) 11 days
Direct to REP
NMA-LD preconditioning therapy
Thaw and infuse. Follow by IL-2 administration
Express courier in cryoshipper from CMO to clinical site
LN2 cryopreserved TIL infusion product controlled rate freeze
Harvest
Expansion ex vivo scale up
IL-2 + OKT3
Co-culture TIL and feeder cells

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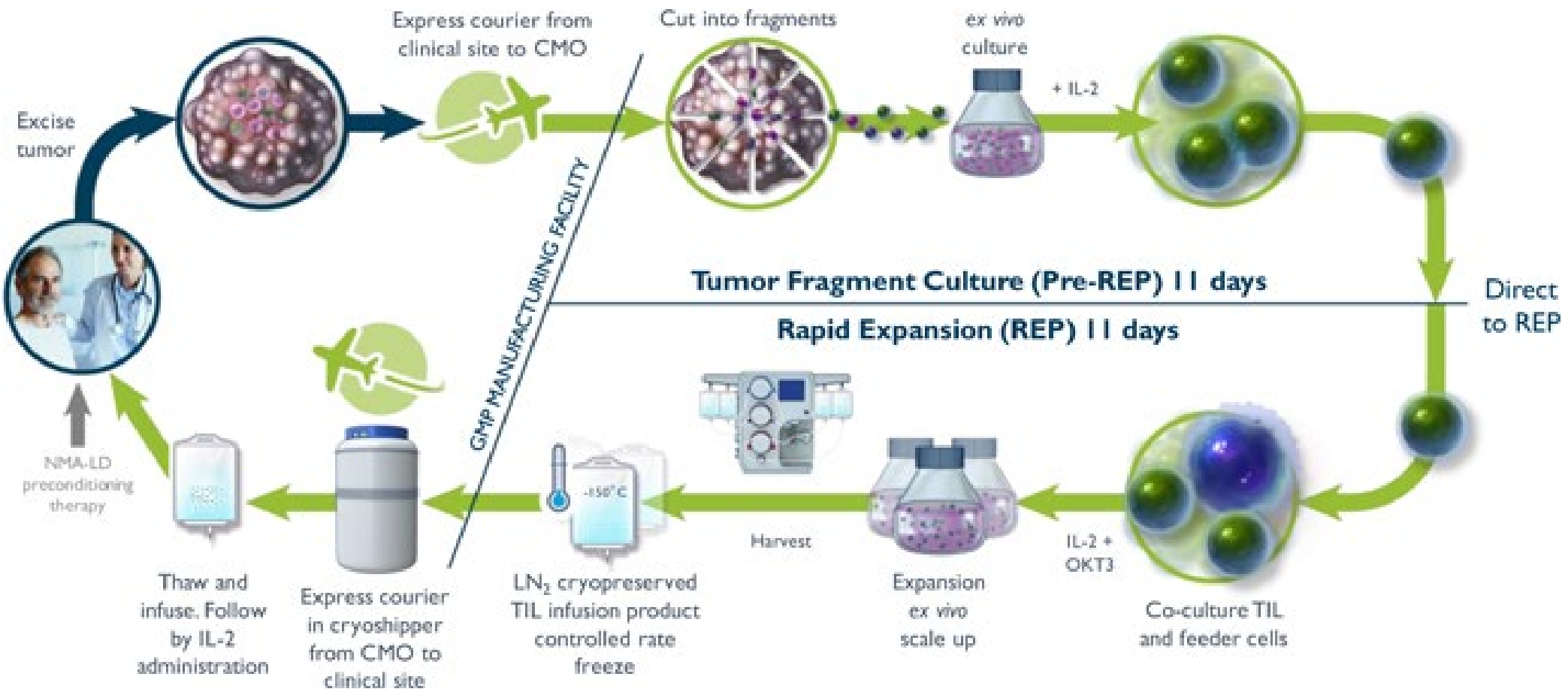
[1]University of Colorado Cancer Center—Anschutz Medical Campus, Aurora, CO, USA; [2]Brown Cancer Center, Louisville, KY, USA; [3]Yale Cancer Center, New Haven, CT, USA; [4]The Angeles Clinic and Research Institute, a Cedars Sinai Affiliate, Los Angeles, CA, USA; [5]Atlantic Health System, Morristown, NJ, USA; [6]Mount Sinai Medical Center, Miami Beach, FL, USA; [7]AdventHealth Cancer Institute, Orlando, FL, USA; [8]Technical University Dresden—NCT/UCC Early Clinical Trial Unit, Dresden, Germany; [9]Allina Health Cancer Institute, Minneapolis, MN, USA; [10]UConn Health/Neag Cancer Center, Farmington, CT, USA; [11]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [12]The Royal Marsden Hospital NHS Foundation Trust, London, UK; [13]Laura and Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, NY, USA; [14]Iovance Biotherapeutics, Inc., San Carlos, CA, USA; [15]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

Lifileucel


Express courier from clinical site to CMO
Cut into fragments
ex vivo culture
+ IL-2
Excise tumor
GMP MANUFACTURING FACILITY
Tumor Fragment Culture (Pre-REP) 11 days
Rapid Expansion (REP) 11 days
Direct to REP
NMA-LD preconditioning therapy
Thaw and infuse. Follow by IL-2 administration
Express courier in cryoshipper from CMO to clinical site
LN2 cryopreserved TIL infusion product controlled rate freeze
Harvest
Expansion ex vivo scale up
IL-2 + OKT3
Co-culture TIL and feeder cells

Pacjenci leczeni Lifileucel-em

Patient disposition and baseline characteristics

Characteristics		Pooled cohorts 2 & 4 (N=153)
Median age, years (range)		56 (20–79)
Male, n (%)		83 (54.2)
ECOG performance status, n (%)	0, 1	104 (68.0), 49 (32.0)
Stage IV melanoma at study entry, n (%)		143 (93.5)
BRAF V600 E/K mutation, n (%)		41 (26.8)
PD-L1 Tumor Proportion Score,[a] n (%)	≥1%, <1%	76 (49.7), 32 (20.9)
LDH level (× ULN), n (%)	<1, 1–2, ≥2	70 (45.8), 54 (35.3), 29 (19.0)
≥3 baseline target and nontarget lesions, n (%)		116 (75.8)
Baseline target lesions in ≥3 anatomic sites, n (%)		109 (71.2)
Liver and/or brain lesions by IRC, n (%)		72 (47.1)
Median target lesion SOD, mm (range)		101.1 (13.5–552.9)
Median number of prior systemic therapies (range)		3 (1–9)
Prior BRAF/MEK inhibitor therapy, n (%)		39 (25.5)
Prior anti–CTLA-4 therapy, n (%)		125 (81.7)
Prior anti–CTLA-4 plus anti–PD-1-combination therapy, n (%)		82 (53.6)
Resistance to anti–PD-1/PD-L1 by SITC criteria, n (%)	primary, secondary	109 (71.2), 41 (26.8)
Median cumulative duration of anti–PD-1/PD-L1 therapy (range), months[1]		7.0 (0.7–75.8)

- At the November 20, 2024, data cutoff, the median follow-up was 57.8 months
- All patients had completed or discontinued the study, with 28 (18.3%) patients completing the 5-year study follow-up

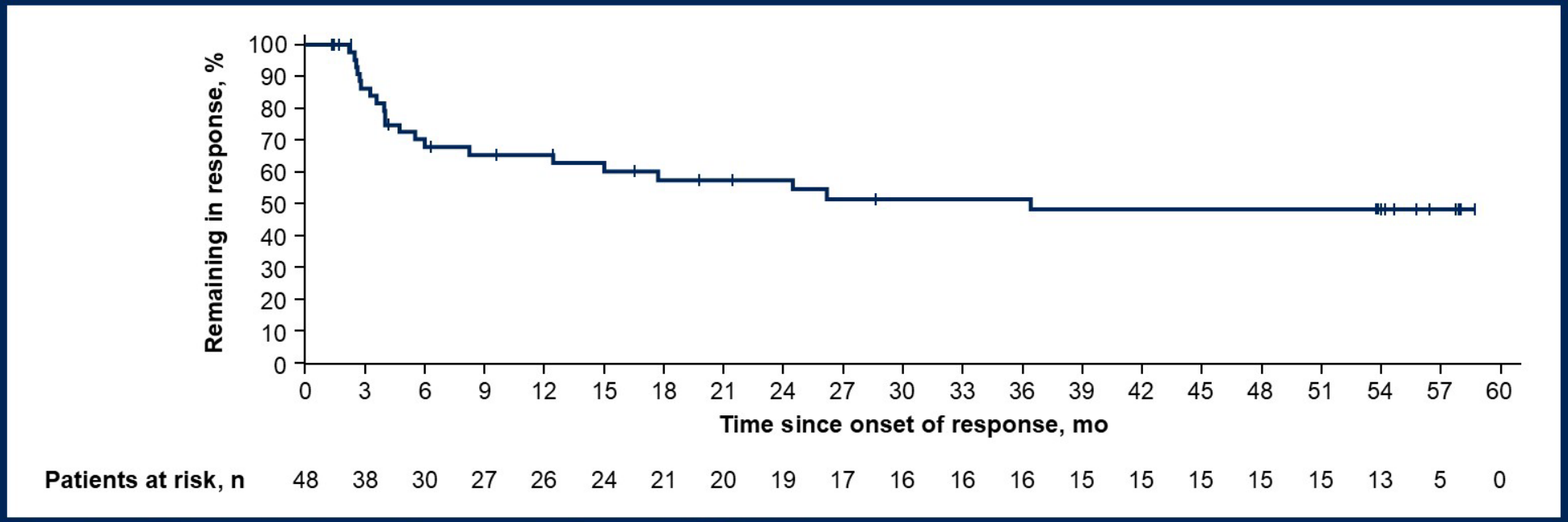
[a]PD-L1 Tumor Proportion Score was missing for 45 patients. 1. Chesney JA, et al. *J Immunother Cancer.* 2022;10:e005755.
CTLA, cytotoxic T-lymphocyte associated protein-4; ECOG, Eastern Cooperative Oncology Group; IRC, independent review committee; LDH, lactate dehydrogenase; PD-1, programmed cell death protein-1; PD-L1, programmed death-ligand 1; SITC, Society for Immunotherapy of Cancer; SOD, sum of diameters; ULN, upper limit of normal

Wyniki leczenia lifileucel-em po 5 latach obserwacji

Durable responses were observed with lifileucel

- The ORR was 31.4% (complete response [CR], 5.9%; partial response [PR], 25.5%), and 79.3% of patients had a reduction in tumor burden
- The median duration of IRC-assessed response was 36.5 months (95% CI: 8.3–NR)
- 31.3% (15/48) of responders completed the 5-year assessment with ongoing responses

Duration of Response

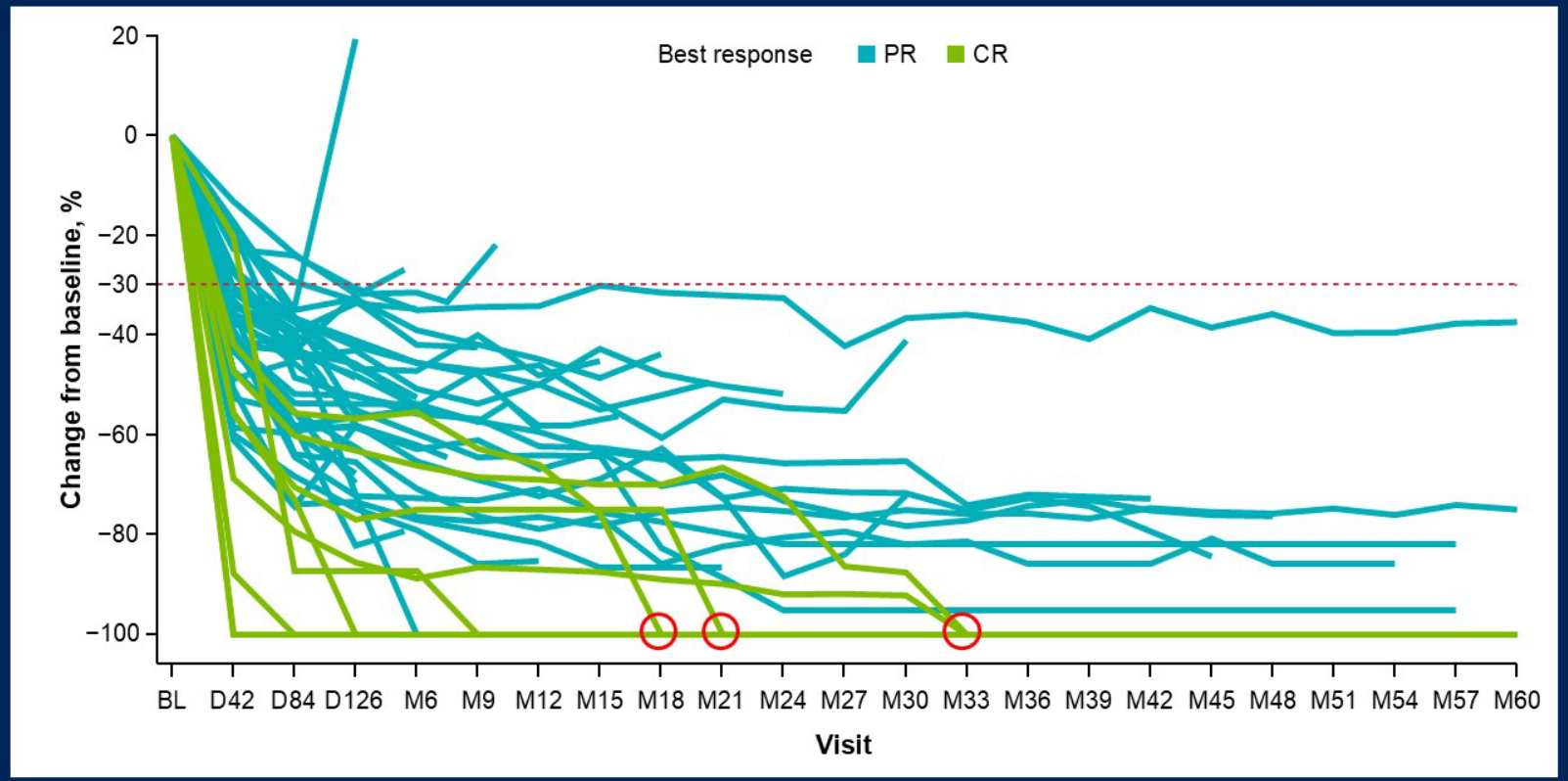


CI, confidence interval; IRC, independent review committee; mo, months; NR, not reached; ORR, objective response rate.

Obiektywne odpowiedzi podczas leczenia lifileucel-em

Ongoing and deepening responses were observed

Percent Change From Baseline in Target Lesion SOD for Confirmed Responders



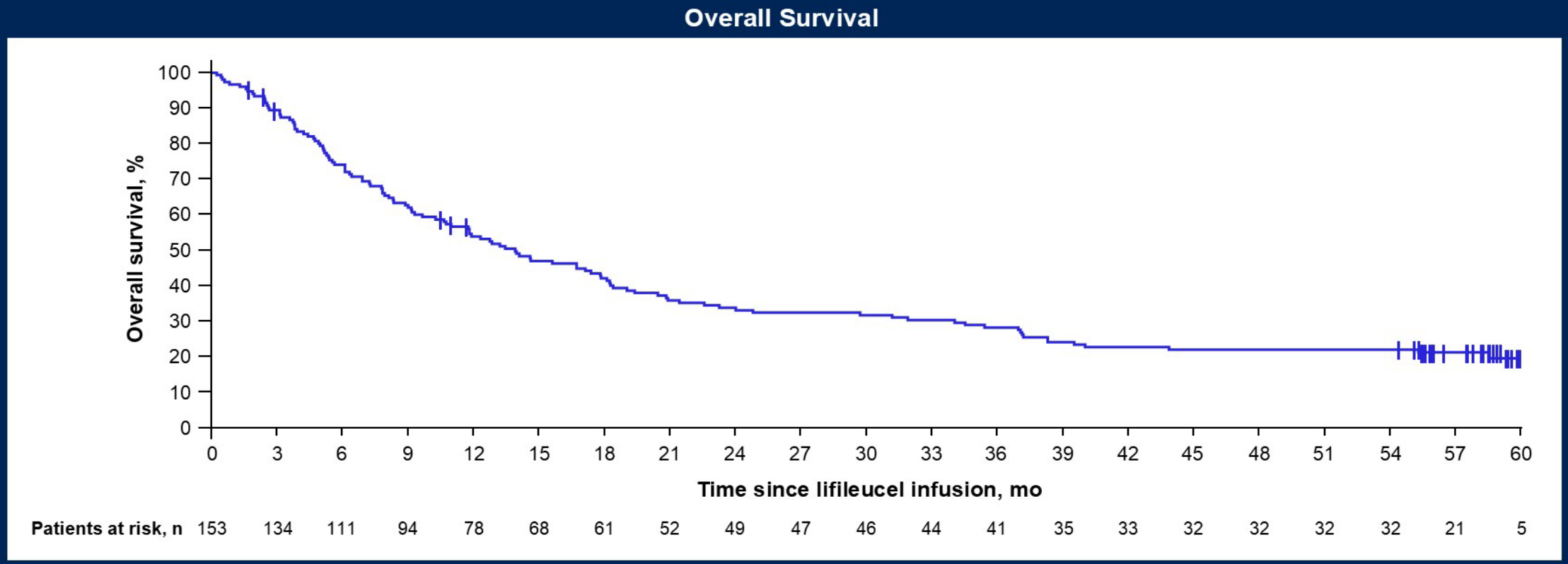
- The longest duration of ongoing response was 58.7 months
- Responses deepened over time
  - 16 patients had stable disease that improved to PR or had achieved PR that improved to CR
  - As depicted by the red circles, 4 patients had a PR 1 year posttreatment that deepened to CR as late as 3 years after lifileucel infusion
- Ongoing responses at year 3 were maintained through year 5

BL, baseline; CR, complete response; D, day; M, month; PR, partial response; SOD, sum of diameters.

Przeżycie całkowite po leczeniu lifileucel-em

Favorable overall survival outcomes were observed

- The median OS for the total population was 13.9 months; the estimated 5-year OS rate was 19.7%



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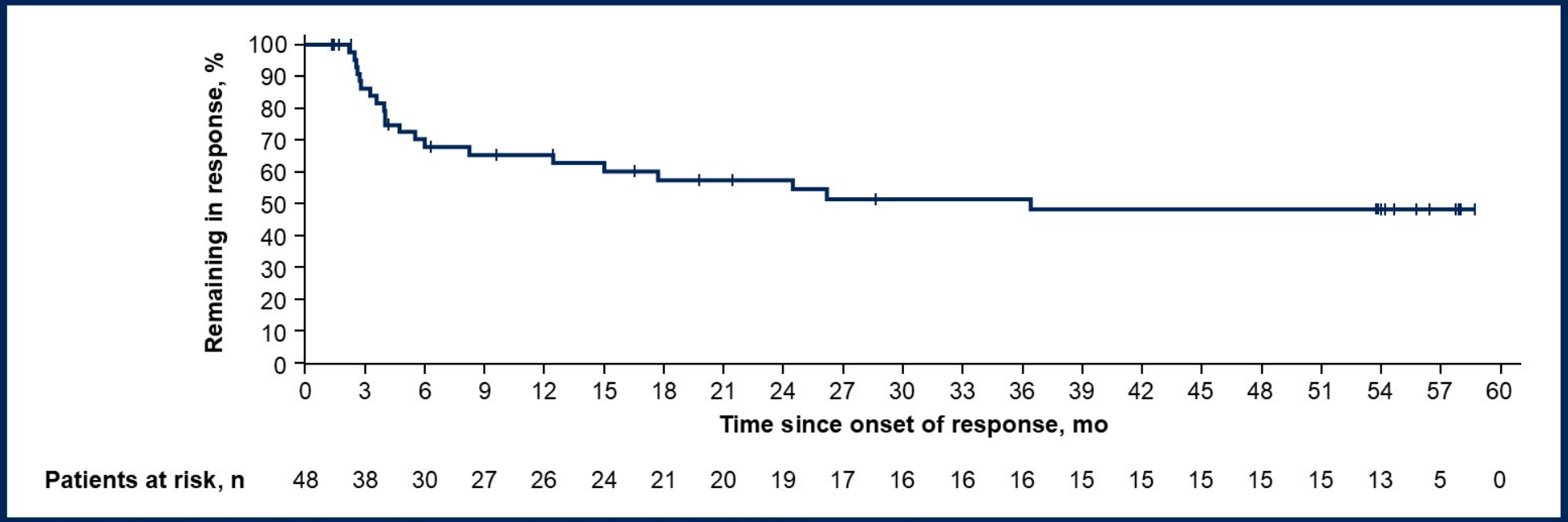

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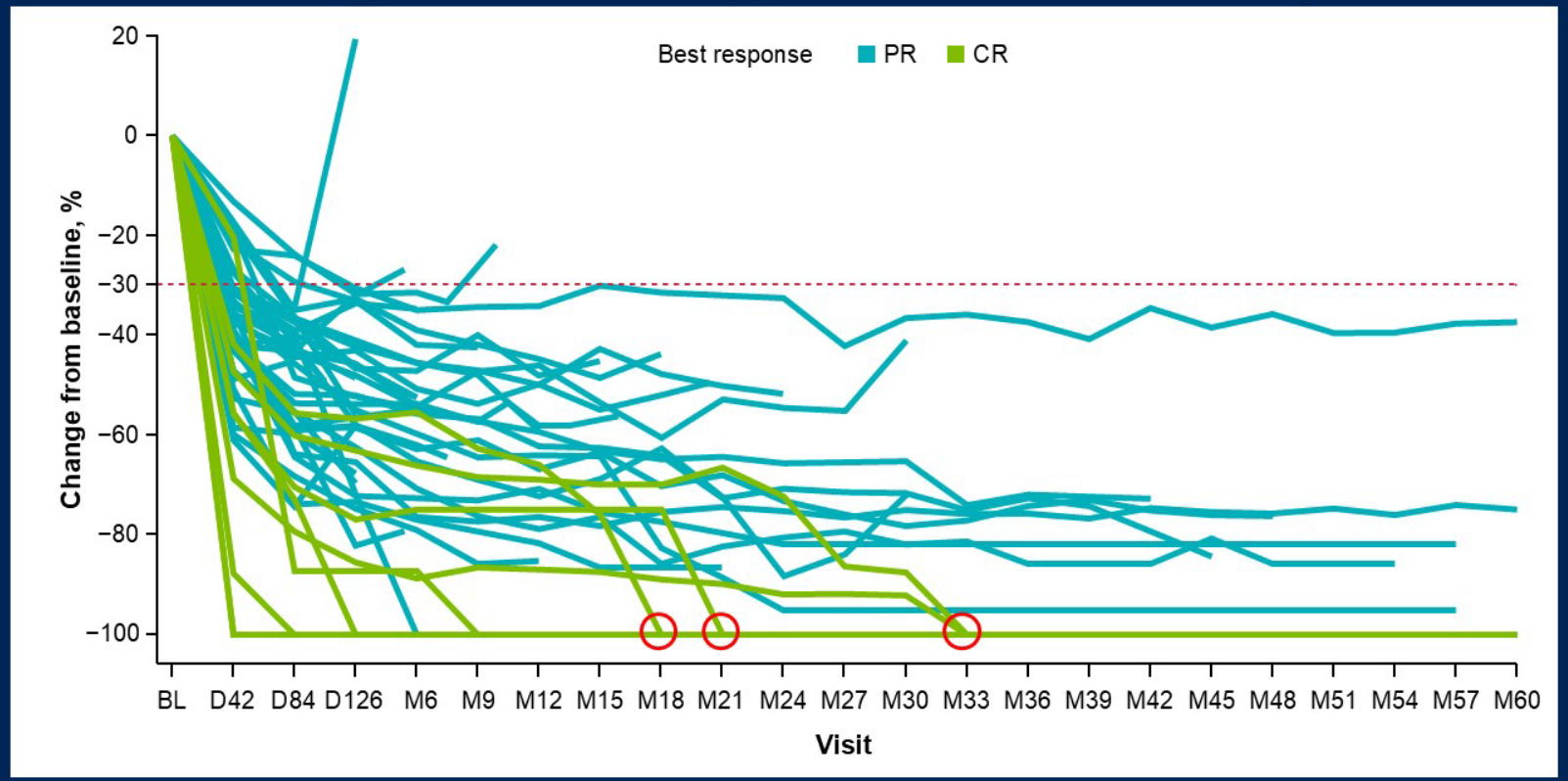

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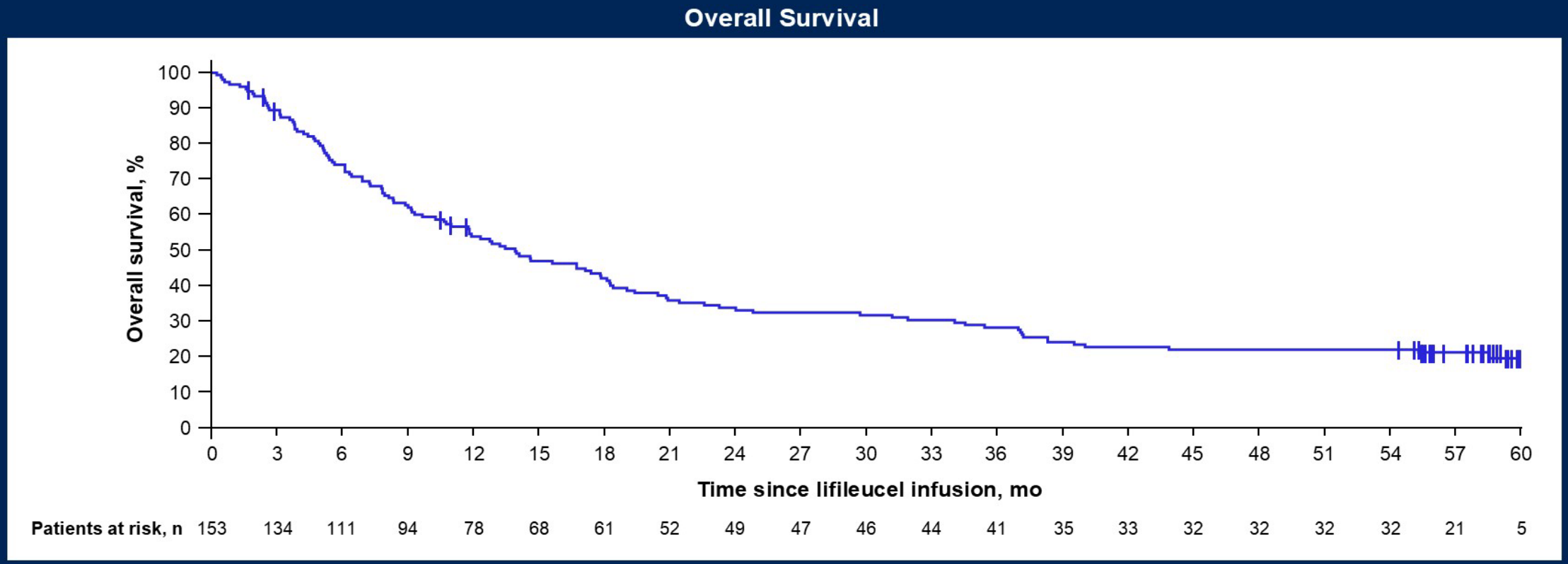


mo, months; OS, overall survival.

XXIV SPOTKANIE Po ASCO

Adjuwantowy niwolumab +/- relatlimab – badanie RELATIVITY-098

2025 ASCO ANNUAL MEETING

Nivolumab plus relatlimab vs nivolumab alone for the adjuvant treatment of completely resected stage III-IV melanoma: primary results from RELATIVITY-098

Georgina V. Long,[1] Paolo A. Ascierto,[2] Jun Guo,[3] Sunandana Chandra,[4] Ahmad A. Tarhini,[5] Eva Munoz Couselo,[6] Michele Del Vecchio,[7] Andreia C. de Melo,[8] Helen Gogas,[9] Reinhard Dummer,[10] Margaret Callahan,[11] Dirk Schadendorf,[12] Peter Kölblinger,[13] Gaelle Quereux,[14] Ioannis Thomas,[15] Bohang Chen,[16] Alicia M. Y. Cheong,[17] Patrick Djidel,[18] Sonia Dolfi,[16] Hussein A. Tawbi[19]

[1]Melanoma Institute Australia, The University of Sydney, Royal North Shore and Mater Hospitals, Sydney, NSW, Australia; [2]Istituto Nazionale dei Tumori IRCCS "Fondazione G. Pascale," Napoli, Italy; [3] Peking University Cancer Hospital & Institute, Beijing, China; [4]Northwestern University, Chicago, IL, USA; [5]H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA; [6]Vall d'Hebron Hospital, Barcelona Spain; [7]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [8]Brazilian National Cancer Institute, Rio de Janeiro, Brazil; [9]National and Kapodistrian University of Athens, Athens, Greece; [10]University of Zurich, Zurich, Switzerland; [11]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [12]University of Essen and the German Cancer Consortium, Essen, Germany; [13]Paracelsus Medical University, Salzburg, Austria; [14]Nantes University Hospital, Skin Cancer Unit, Nantes Cedex, France; [15]University of Tuebingen, Tuebingen, Germany; [16]Bristol Myers Squibb, Princeton, NJ; [17]Bristol Myers Squibb, Uxbridge, United Kingdom; [18]Bristol Myers Squibb, Boudry, Switzerland; [19]The University of Texas MD Anderson Cancer Center, Houston, TX

Abstract number LBA9500

Schemat badania RELATIVITY-098

RELATIVITY-098: study design

Key eligibility criteria
- Aged ≥ 12 years
- Completely resected stage III-IV[a]
- ECOG PS 0-1
- Prior systemic anticancer treatment prohibited[b]

R 1:1

Stratified by
- AJCC v8 stage
  - IIIA-IIIB
  - IIIC
  - IIID-IV[c]
- Geographic region
  - USA/Canada/Australia
  - Europe
  - Rest of world

NIVO 480 mg + RELA 160 mg FDC IV Q4W (N = 547)

NIVO 480 mg IV Q4W (N = 546)

- Treatment to 1 yr, recurrence, unacceptable toxicity, withdrawal, or death
- Patients followed for a min of 8 yrs or until death, lost to follow-up, consent withdrawal, or study end
- **Endpoints included**
  - RFS (primary)
  - OS (key secondary)
  - DMFS, safety, PFS2 (other secondary)
  - Biomarker analysis (exploratory)

- 163 sites across 24 countries
- Clinical cutoff date (LPLV): December 16, 2024
- Minimum follow-up:[d] 23.4 months
- Median follow-up:[e] 26.7 months

RELATIVITY-098 (NCT05002569). [a]Stage IIIA>1 mm tumor in LN)/stage IIIB/C/D or stage IV NED. [b]Exclusions included prior immunotherapy, LAG-3, and BRAFi-MEKi treatment. [c]Including all patients with mucosal melanoma, stage III, stage IVA, stage IVB, and stage IVC. [d]Time from the last subject randomization to the clinical cutoff date. [e]Median time between randomization date and the last known alive date or death.

Pacjenci leczeni w badaniu RELATIVITY-098

Baseline patient characteristics

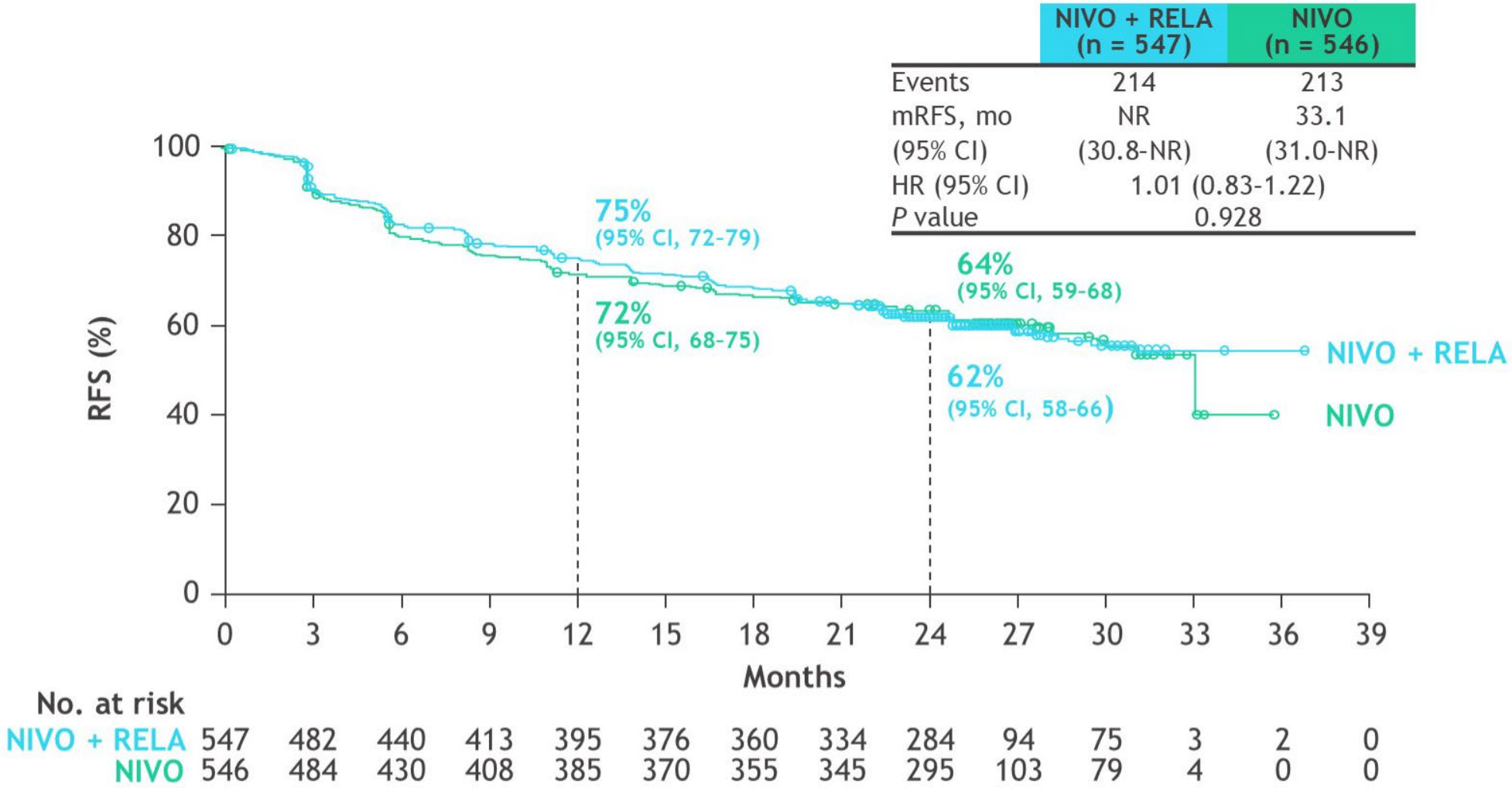
	NIVO + RELA (n = 547)	NIVO (n = 546)
Median age, years (range)	59 (18-89)	59 (19-92)
Male, n (%)	327 (60)	315 (58)
ECOG PS 0, n (%)	494 (90)	498 (91)
LDH level ≤ normal,[a] n (%)	496 (91)	486 (89)
BRAF status, n (%)[b]		
Mutant	220 (40)	217 (40)
Wild type	195 (36)	200 (37)
Tumor PD-L1 status, n (%)[b]		
≥ 1%	136 (25)	123 (23)
< 1%	315 (58)	340 (62)
Indeterminate/unevaluable	93 (17)	81 (15)
LAG-3 status, n (%)[b]		
≥ 1%	352 (64)	352 (64)
< 1%	126 (23)	145 (27)
Indeterminate/unevaluable	66 (12)	48 (9)

	NIVO + RELA (n = 547)	NIVO (n = 546)
Geographic region, n (%)		
USA/Canada	54 (10)	63 (12)
Australia	67 (12)	57 (10)
Europe	318 (58)	319 (58)
Latin America	76 (14)	72 (13)
China	32 (6)	35 (6)
AJCC stage, n (%)		
IIIA-IIIB	209 (38)	199 (36)
IIIC	270 (49)	271 (50)
IIID-IV	68 (12)	76 (14)
Melanoma subtype, n (%)[b]		
Cutaneous nonacral	436 (80)	454 (83)
Cutaneous acral	61 (11)	52 (10)
Mucosal	10 (2)	8 (1)
Unknown primary	38 (7)	32 (6)

In all ***evaluable*** patients, RELATIVITY-098 PD-L1 < 1% = 72% and RELATIVITY-047 PD-L1 < 1% = 59%[1]

Pierwszorzędowy punkt końcowy - RFS

Primary endpoint: RFS by investigator



Patient disposition of treated patients

	NIVO + RELA (n = 543)	NIVO (n = 545)
Completed treatment, n (%)	283 (52.1)	327 (60.0)
Discontinued treatment, n (%)	260 (48)	218 (40)
Study drug toxicity	114 (21)	64 (12)
Disease recurrence	102 (19)	128 (23)

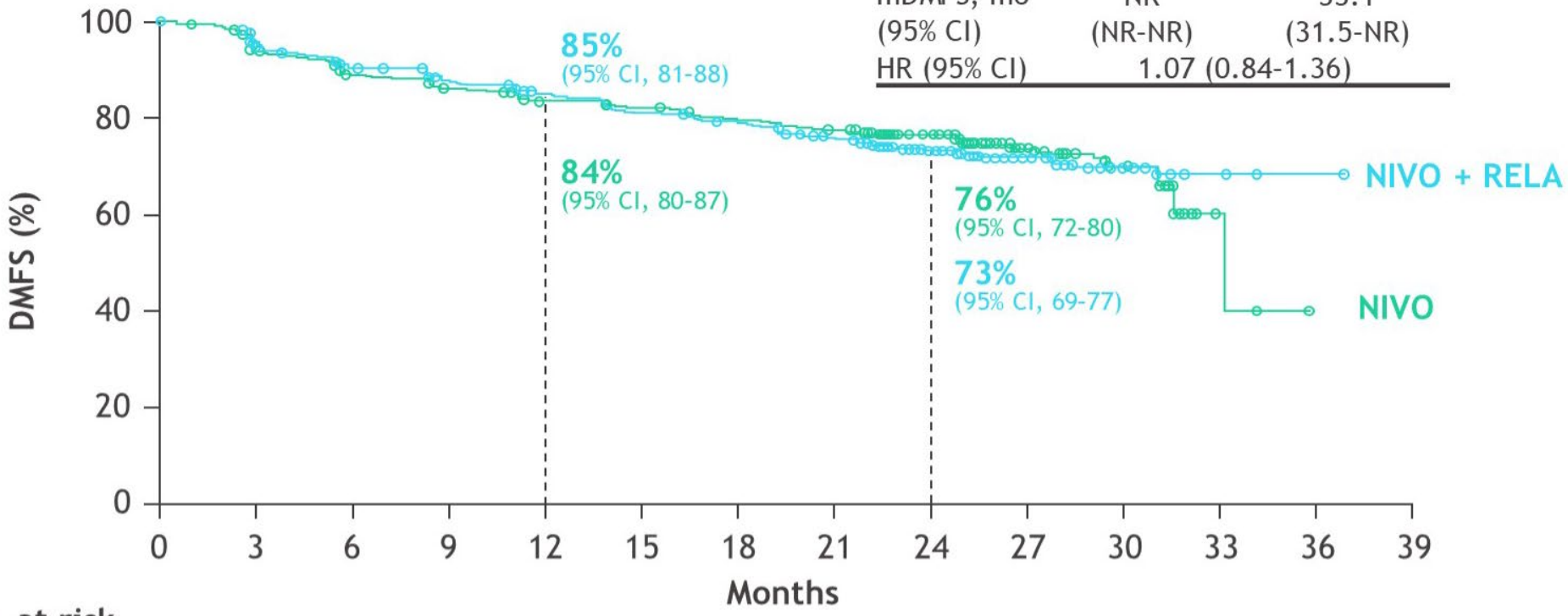
Pattern of RFS events

	NIVO + RELA (n = 547), n (%)	NIVO (n = 546), n (%)
Number of patients with an event	214 (39)	213 (39)
Recurrence[a]	201 (37)	206 (38)
Distant recurrence	104 (19)	109 (20)
Regional node recurrence	53 (10)	51 (9)
Local recurrence	16 (3)	16 (3)
In transit metastasis	21 (4)	22 (4)
New primary invasive melanoma	7 (1)	8 (1)
Death prior to recurrence[b]	13 (2)	7 (1)

Distant metastasis-free survival

Distant metastasis-free survival[a]

	NIVO + RELA (n = 499)	NIVO (n = 494)
Events	133	129
mDMFS, mo	NR	33.1
(95% CI)	(NR-NR)	(31.5-NR)
HR (95% CI)	1.07 (0.84-1.36)	



No. at risk

NIVO + RELA	499	452	430	411	395	377	365	343	287	102	82	4	2	0
NIVO	494	454	426	411	395	387	372	361	309	111	87	3	0	0

RELATIVITY-098 (NCT05002569).[a]ITT subset of patients defined as those with resected stage III-IVA-IVB melanoma (those without presence of baseline metastasis prior to surgical resection, ie stage III cutaneous and stage IVA-IVB mucosal melanoma).

Adverse events

AE	NIVO + RELA (n = 543), n (%)		NIVO (n = 545), n (%)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Any AE	522 (96)	155 (29)	520 (95)	100 (18)
Any AE leading to discontinuation	102 (19)	55 (10)	65 (12)	28 (5)
TRAE	483 (89)	103 (19)	438 (80)	46 (8)
TRAE leading to discontinuation	95 (17)	52 (10)	48 (9)	17 (3)
TRAEs in ≥ 10% patients				
Hypothyroidism	137 (25)	3 (1)	74 (14)	0
Fatigue	132 (24)	1 (< 1)	138 (25)	1 (< 1)
Pruritus	98 (18)	0	102 (19)	1 (< 1)
Hyperthyroidism	95 (17)	3 (1)	53 (10)	0
Rash	83 (15)	0	73 (13)	4 (1)
Arthralgia	72 (13)	2 (< 1)	69 (13)	3 (1)
Diarrhea	61 (11)	6 (1)	54 (10)	2 (< 1)
Treatment-related deaths	2 (< 1)[a]		1 (< 1)[b]	

Immune-mediated AEs by category	NIVO + RELA (n = 543), n (%)		NIVO (n = 545), n (%)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Adrenal insufficiency	33 (6)	6 (1)	9 (2)	1 (< 1)
Hypothyroidism/ thyroiditis	158 (29)	3 (1)	93 (17)	0
Hypothyroidism	152 (28)	3 (1)	82 (15)	0
Thyroiditis	18 (3)	0	14 (3)	0
Diabetes mellitus	11 (2)	7 (1)	8 (1)	6 (1)
Hyperthyroidism	96 (18)	2 (< 1)	56 (10)	0
Hypophysitis	51 (9)	16 (3)	13 (2)	3 (1)
Pneumonitis	8 (1)	3 (1)	10 (2)	2 (< 1)
Diarrhea/colitis	28 (5)	13 (2)	21 (4)	7 (1)
Hepatitis	26 (5)	17 (3)	17 (3)	10 (2)
Nephritis & renal dysfunction	3 (1)	1 (< 1)	3 (1)	2 (< 1)
Rash	49 (9)	4 (1)	40 (7)	4 (1)
Hypersensitivity	12 (2)	1 (< 1)	2 (< 1)	0

Other events of special interest by category	NIVO + RELA (n = 543), n (%)		NIVO (n = 545), n (%)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Myasthenic syndrome	4 (1)	4 (1)	1 (< 1)	1 (< 1)
Myocarditis event[a]	11 (2)	6 (1)	5 (1)	1 (<1)
Myositis/rhabdomyolysis event[b]	13 (2)	7 (1)	5 (1)	0
Demyelination event	2 (< 1)	1 (< 1)	0	0
Guillain-Barre syndrome	0	0	1 (< 1)	1 (< 1)
Pancreatitis event	6 (1)	2 (< 1)	3 (1)	2 (< 1)
Uveitis event	1 (< 1)	0	1 (< 1)	0
Encephalitis event	2 (< 1)	2 (< 1)	0	0
Autoimmune cytopenia	2 (< 1)	2 (< 1)	0	0
Immune-mediated arthritis	1 (< 1)	0	0	0
Meningitis event	1 (< 1)	1 (< 1)	0	0

XXIV SPOTKANIE Po ASCO

Badanie EORTC-2139-MG/Columbus-AD trial: adjuwantowy enkorafenib i binimetynib w II st.

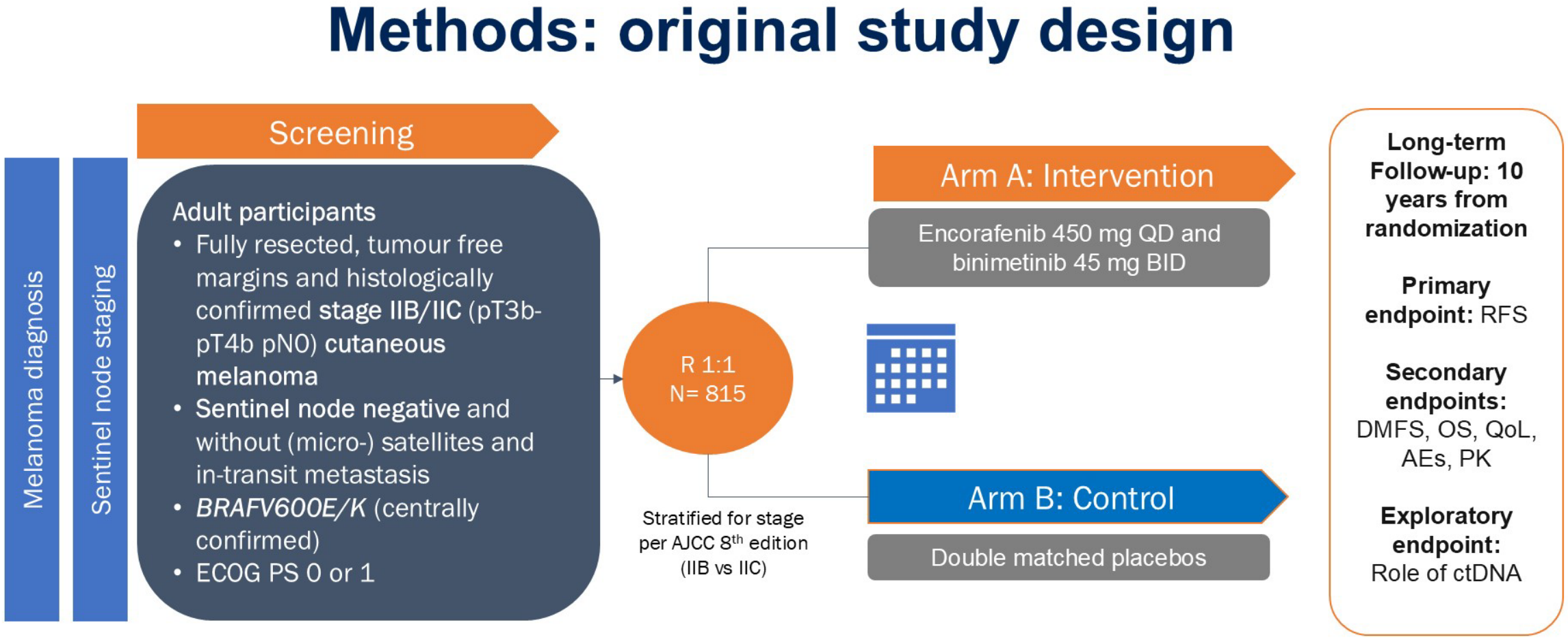
2025 ASCO ANNUAL MEETING

Primary analysis of the EORTC-2139-MG/Columbus-AD trial: A randomized trial of adjuvant encorafenib and binimetinib versus placebo in high-risk stage II melanoma with a *BRAF-V600E/K* mutation

Alexander CJ van Akkooi, Mario Mandala, Michal Kicinski, Anne-Sophie Govaerts, Axel Hauschild, Piotr Rutkowski, Petr Arenberger, Paolo A Ascierto, Piotr Tomczak, Gaëlle Quereux, Federica De Galitiis, Caroline Dutriaux, Christoffer Gebhardt, Ellen Kapiteijn, Laurent Machet, Isabelle Klauck, Benoît Sansas, Paul C Lorigan, Georgina V Long, Alexander MM Eggermont

Alexander C.J. van Akkooi, Melanoma Institute Australia, Faculty of Medicine and Health, University of Sydney, and Department of Melanoma and Surgical Oncology, Institute of Academic Surgery, Royal Prince Alfred Hospital, Sydney, NSW, Australia

Konstrukcja badania Columbus-AD



AEs, adverse events; BID, twice daily; ctDNA, circulating tumor DNA; DMFS, distant metastasis-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; PK, pharmacokinetics; QD, once daily;

QoL, quality of life; R, randomised; RFS, recurrence-free survival.

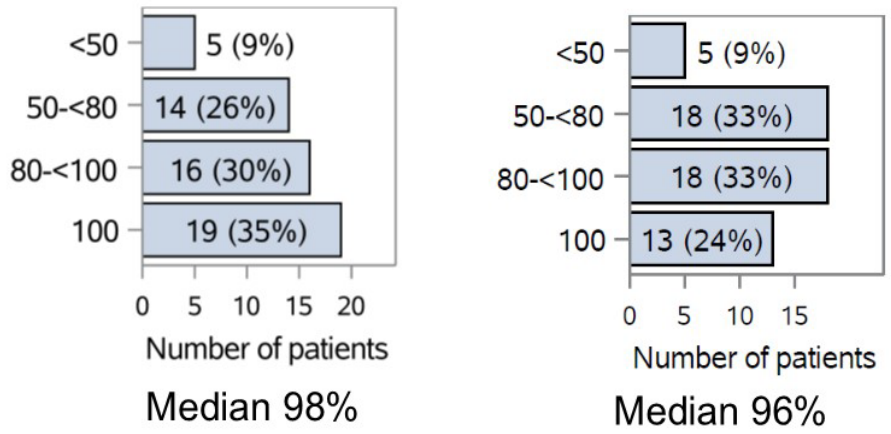
ClinlicalTrials.gov. NCT05270044.

Leczenie w badaniu Columbus-AD

Baseline Characteristics

	Enco-bini (N=55)	Placebo (N=55)
Age: median (range)	58 (27-81)	61 (27-79)
Males, N (%)	25 (46)	34 (62)
BRAF mutation, N (%)		
V600E	44 (80)	43 (78)
V600K	11 (20)	12 (22)
Ulceration, N (%)	46 (84)	41 (75)
Breslow thickness		
Median (IQR), mm	4.3 (3.1-6.0)	4.7 (3.1-6.0)
2-4mm, N (%)	26 (47)	22 (40)
>4mm, N (%)	29 (53)	33 (60)
AJCC8 stage, N (%)		
IIB	35 (64)	36 (65)
IIC	20 (36)	19 (35)

Relative dose intensity (%)*



*Total dose divided by expected dose during the period when the patient was on-treatment

ho started the treatment, N=54)

Toksyczność Leczenia w badaniu Columbus-AD

Safety population (treatment started) (N=54)	All Grade N (%)	Grade 3* N (%)
Adverse Events (AEs)	53 (98)	15 (28)
Suspected to be treatment-related	48 (89)	13 (24)
Serious AEs	6 (11)	4 (7)
Suspected to be treatment-related	1 (2)	0 (0)
TEAEs leading to permanent treatment discontinuation	18 (33)	6 (11)
Suspected to be drug-related	18 (33)	6 (11)

Common adverse events

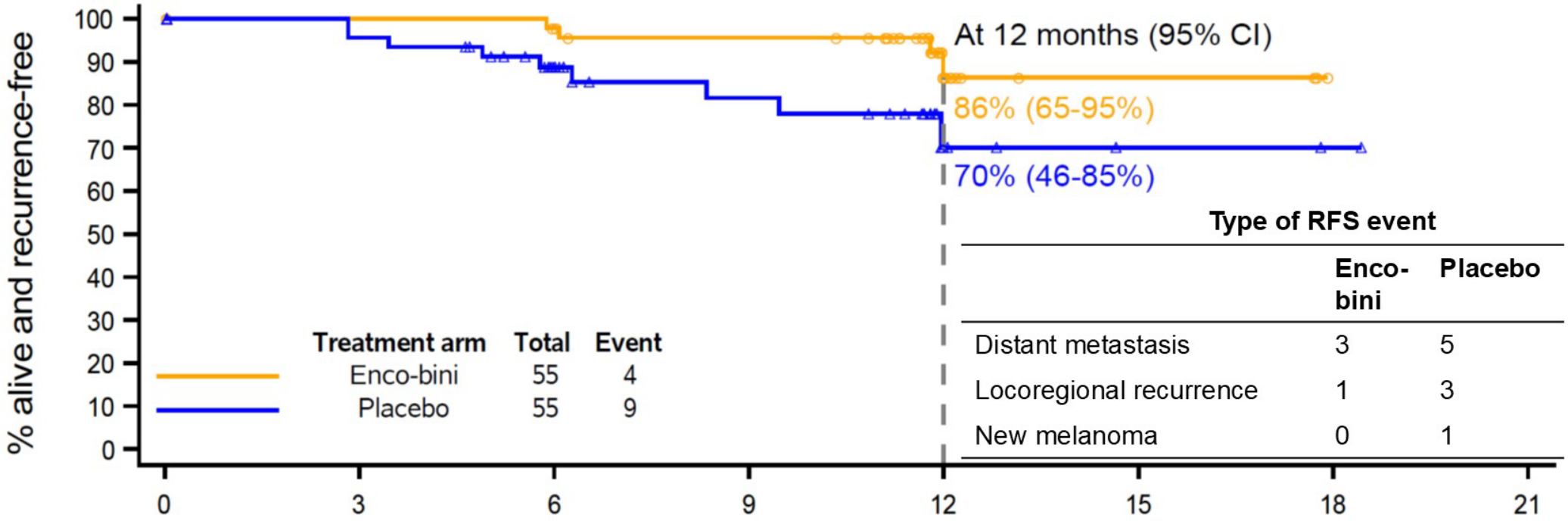
Safety population (treatment started) (N=54)	All Grade N (%)	Grade 3* N (%)
Nausea	20 (37)	0 (0)
Diarrhea	15 (28)	1 (2)
Vomiting	14 (26)	0 (0)
Asthenia	13 (24)	0 (0)
Blood creatine phosphokinase increased	12 (22)	0 (0)
Abdominal Pain	7 (13)	0 (0)
Abdominal Pain Upper	7 (13)	0 (0)
Constipation	7 (13)	0 (0)
Arthralgia	6 (11)	1 (2)
Pyrexia	6 (11)	0 (0)
Visual impairment	6 (11)	0 (0)

* One grade 4 AE; elevated ALT/AST

AEs that began or worsened from baseline between the start of treatment and up to 30 days following the last protocol treatment were considered. Only AEs with an incidence rate of 10% or higher are presented.

RFS w badaniu Columbus-AD

Recurrence-free survival in the ITT population



Type of RFS event

	Enco-bini	Placebo
Distant metastasis	3	5
Locoregional recurrence	1	3
New melanoma	0	1

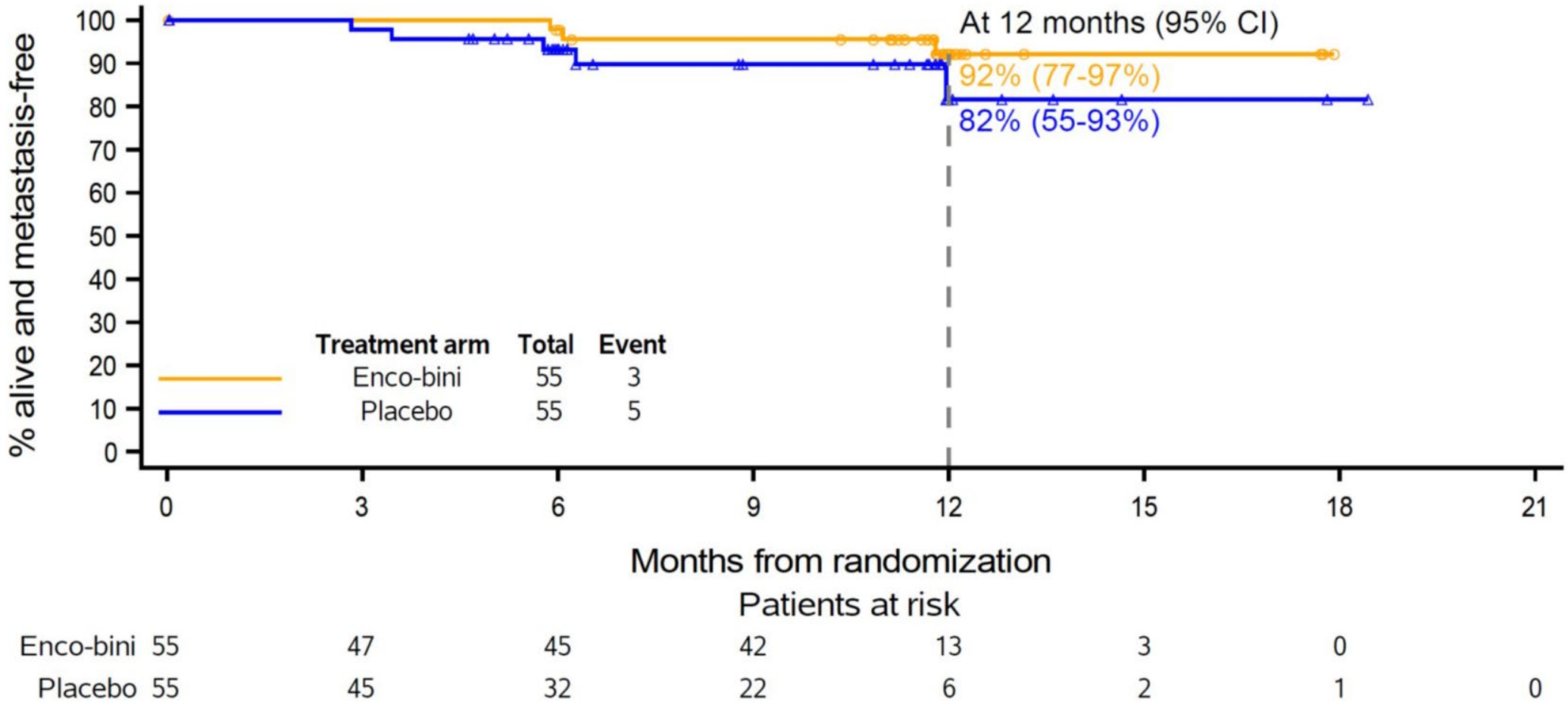
Patients at risk

Enco-bini	55	47	45	42	12	3	0
Placebo	55	44	31	22	5	2	1	0

Median follow-up: 12 (enco-bini) and 7 (placebo) months

DMFS w badaniu Columbus-AD

Distant metastasis-free survival in the ITT population



XXIV SPOTKANIE Po ASCO

Enkorafenib + binimetinib + niwolumab vs ipilimumab + niwolumab – badanie SWOG S2000

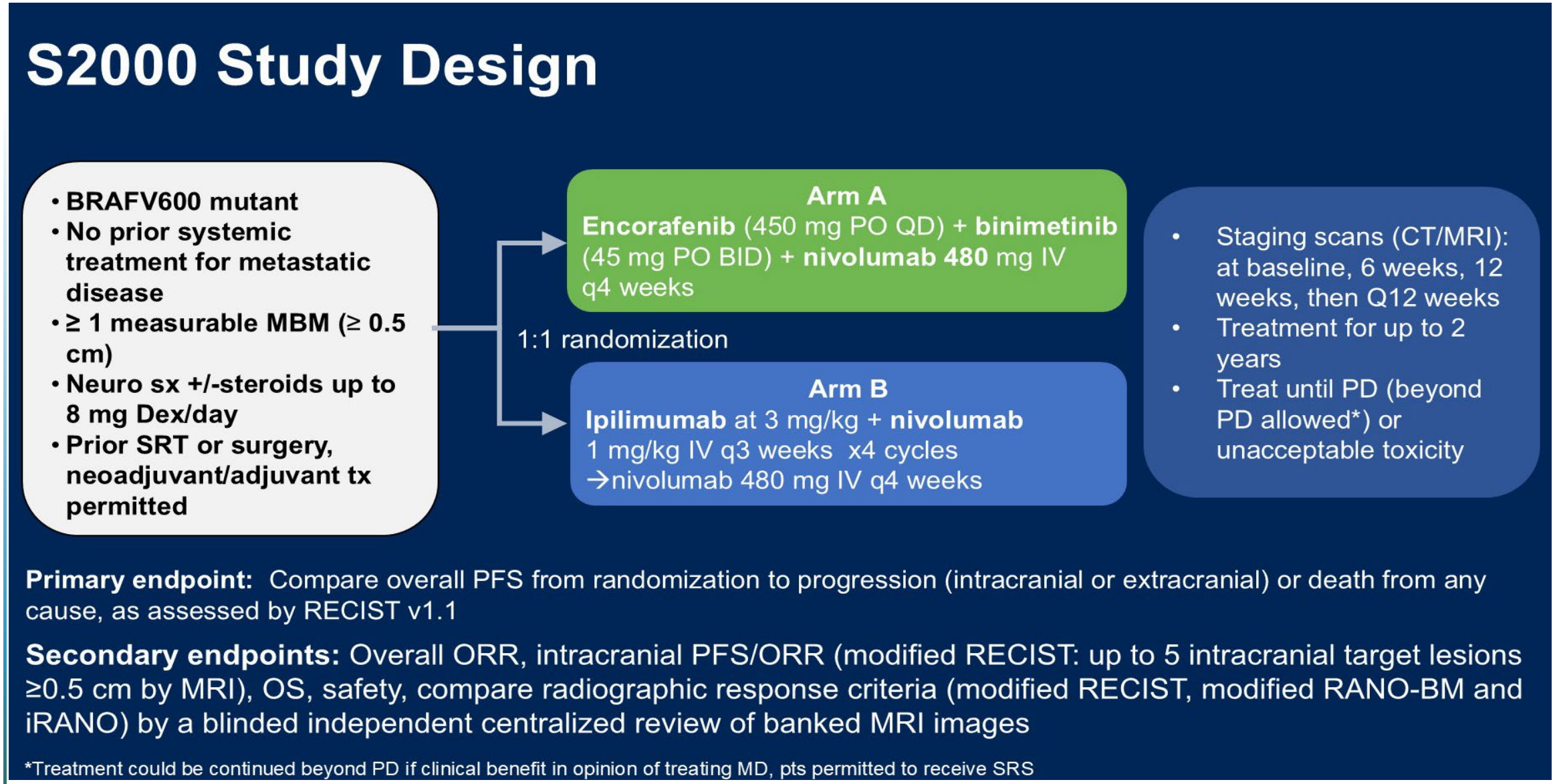
2025 ASCO ANNUAL MEETING

A randomized phase 2 trial of encorafenib + binimetinib + nivolumab vs ipilimumab + nivolumab in BRAFV600-mutant melanoma brain metastases: SWOG S2000

Zeynep Eroglu, James Moon, Yana G. Najjar, Rupesh Kotecha, Michael Wu, Vadim Spektor, Nikhil I. Khushalani, Larissa A. Korde, Elad Sharon, Kenneth F. Grossmann, John M. Kirkwood, Jedd D. Wolchok, Sapna P. Patel, Hussein A. Tawbi

H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; SWOG Statistical Center, Seattle, WA; UPMC Hillman Cancer Center, Pittsburgh, PA; Miami Cancer Institute, Baptist Health South Florida, Miami, FL; Columbia University Irving Medical Center, New York, NY; National Cancer Institute, Bethesda, MD; Providence Cancer Institute, Portland, OR; Weill Cornell Medical College, New York, NY; University of Colorado Cancer Center, Aurora, CO; The University of Texas MD Anderson Cancer Center, Houston, TX

Konstrukcja badania S2000



Pacjenci leczeniu w badaniu S2000

Baseline patient characteristics

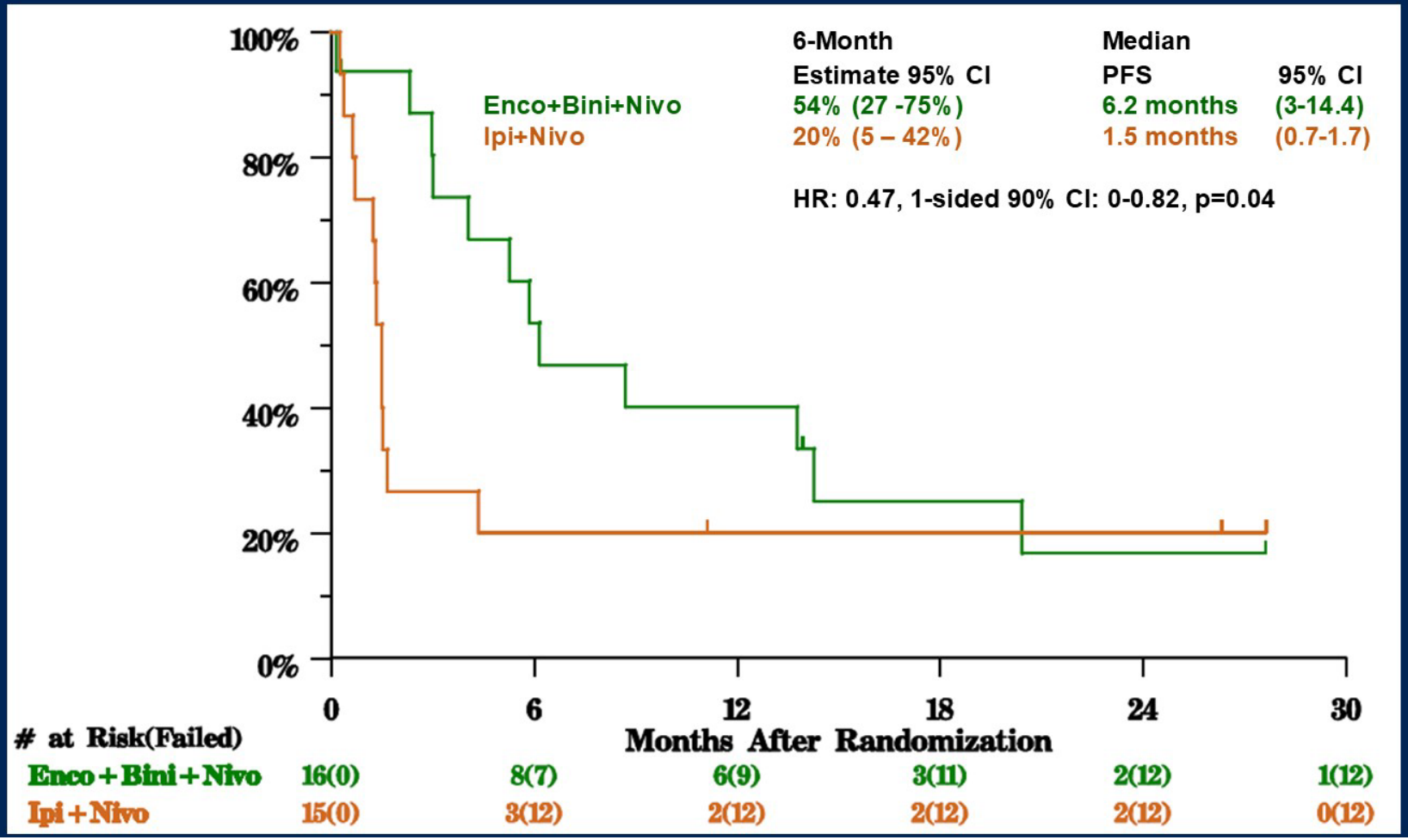
Baseline Characteristics	Encorafenib + Binimetinib + Nivolumab N = 16[1]	Ipilimumab + Nivolumab N = 15[1]
Age	66.9 (35.8-88.9)	60.8 (32.4-75.2)
Male Sex	10 (63%)	12 (80%)
Race		
White	15 (94%)	12 (80%)
Unknown	1 (6.3%)	3 (20%)
Hispanic Ethnicity	1 (6.3%)	0 (0%)
BRAF mutation		
BRAFV600E	9 (56%)	13 (87%)
BRAFV600K/R	7 (44%)	2 (13%)
Elevated LDH	7 (44%)	11 (73%)
Corticosteroid use	6 (38%)	7 (47%)
Prior Surgery to the Brain	5 (31%)	8 (53%)
Prior RT to the Brain	2 (13%)	1 (6.7%)
Prior Systemic Therapy		
Neoadjuvant	0 (0%)	0 (0%)
Adjuvant	1 (6.3%)	2 (13%)
Both	1 (6.3%)	0 (0%)
Number of Target Brain Metastases		
1-2	12 (75%)	8 (53%)
3+	4 (25%)	7 (47%)
Size of Target Brain Metastases(cm)	1.4 (0.5-9.6)	2.3 (0.5-7.9)

[1]Median (Min-Max); n (%)

p = ns between the arms

Całkowity PFS w badaniu S2000

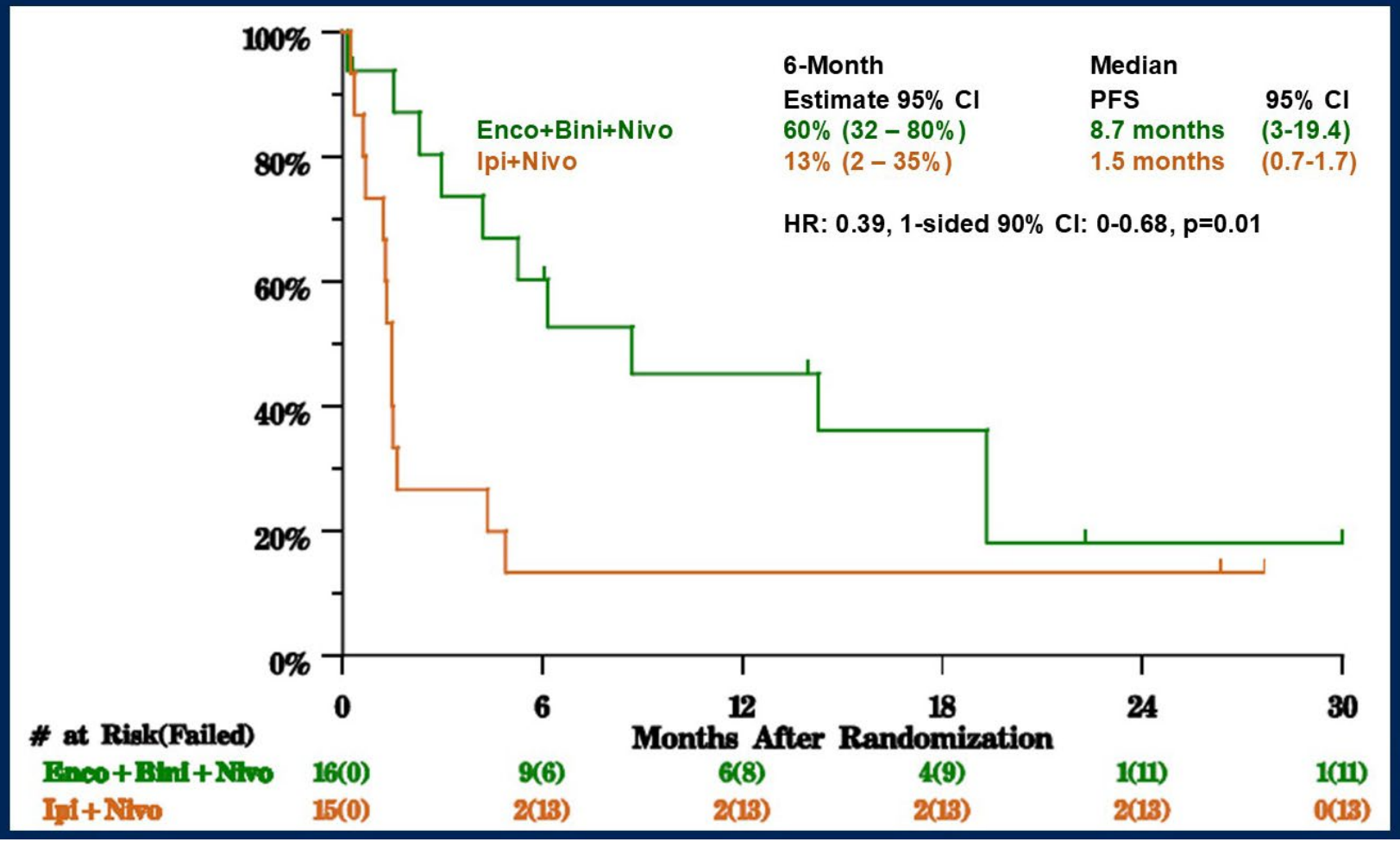
Primary endpoint – Overall PFS



Median follow-up:
18 months

Wewnątrzczaszkowy PFS – badanie S2000

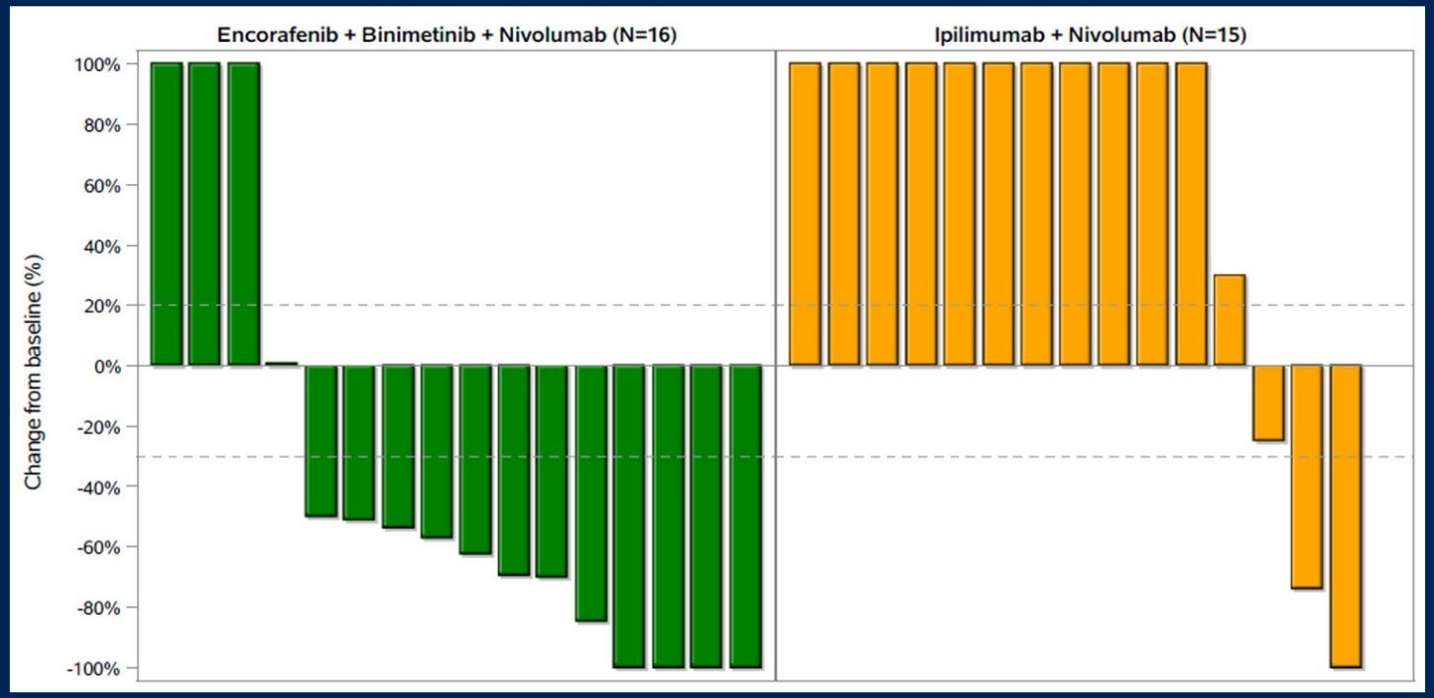
Intracranial Progression Free Survival



Median follow-up: 18 months

Odpowiedź wewnątrzczaszkowa (ICRR per mRECIST)

Intracranial response (per mRECIST)



Intracranial response

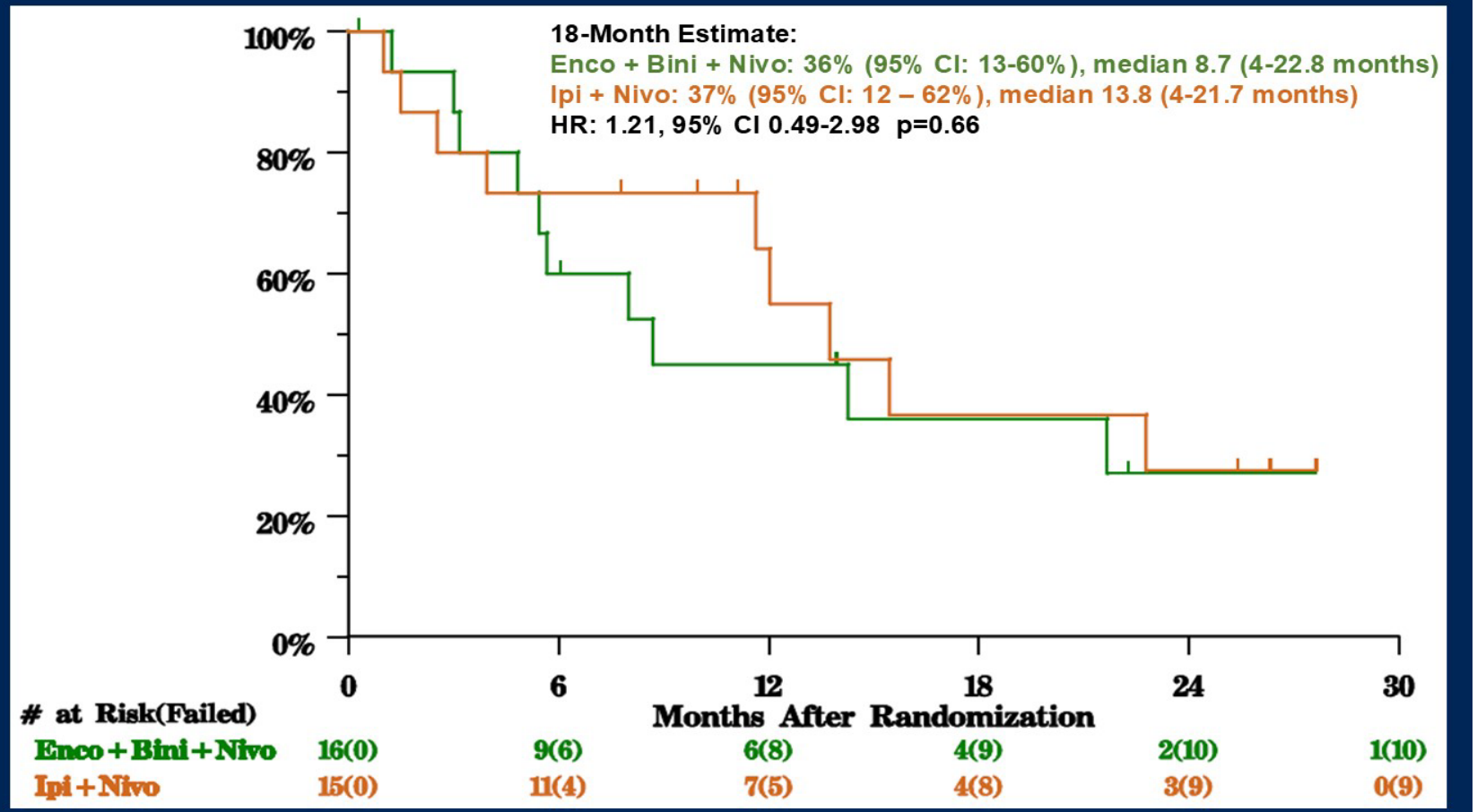
Best Response	Encorafenib + binimetinib + nivolumab (N=16)		Ipilimumab + nivolumab (N=15)	
Complete Response	1	6%	1	7%
Partial Response	11	69%	1	7%
Stable Disease	1	6%	1	7%
Progressive Disease	1	6%	12	80%
Symptomatic Deterioration before tx	2	12%	0	0%
Intracranial response rate	12	**75%**	2	**13%**
P-value/ 95% CI	**0.001**	(54% - 96%)		(0% - 31%)

OS w badaniu S2000

Overall survival

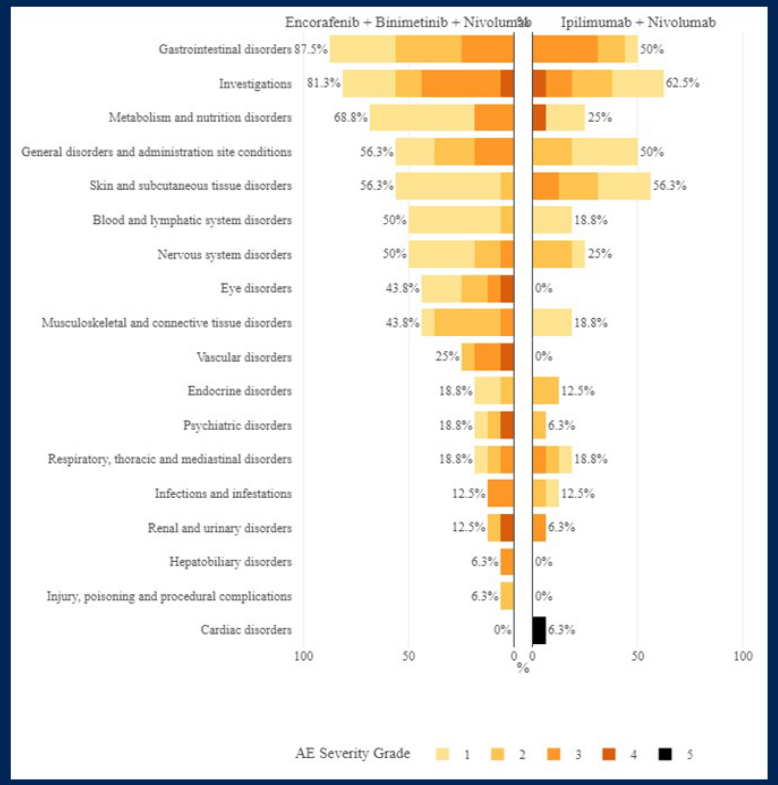
Best Response	Encorafenib + binimetinib + nivolumab (N=15)		Ipilimumab + nivolumab (N=14)	
Partial response	10	67%	2	14%
Stable Disease	1	7%	1	7%
Progressive Disease	2	13%	11	79%
Symptomatic Deterioration before tx	2	14%	0	0%
Overall response rate	10	**67%**	11	**14%**
P-value/ 95% CI	**0.004**	(43% - 91%)		(0% - 33%)

*Symptomatic deterioration included in the denominator as non-responders



Toksyczność leczenia w badaniu S2000

Treatment-related adverse events



	Encorafenib + Binimetinib + Nivolumab (n=16) Grade				Ipilimumab + Nivolumab (n=16) Grade			
ADVERSE EVENTS	**<=2**	**3**	**4**	**5**	**<=2**	**3**	**4**	**5**
Acute kidney injury	15	0	1	0	15	1	0	0
ALT increased	11	5	0	0	15	1	0	0
AST increased	11	5	0	0	16	0	0	0
Blood bilirubin increased	16	0	0	0	15	1	0	0
Cardiac arrest	16	0	0	0	15	0	0	1
Colitis	16	0	0	0	14	2	0	0
Confusion	15	0	1	0	16	0	0	0
Creatinine increased	14	1	1	0	16	0	0	0
Dehydration	14	2	0	0	16	0	0	0
Diarrhea	15	1	0	0	13	3	0	0
Dyspnea	15	1	0	0	16	0	0	0
Enterocolitis	16	0	0	0	14	2	0	0
Extraocular muscle paresis	15	1	0	0	16	0	0	0
Fatigue	13	3	0	0	16	0	0	0
Generalized muscle weakness	15	1	0	0	16	0	0	0
Hypercalcemia	15	1	0	0	16	0	0	0
Hypertension	15	1	0	0	16	0	0	0
MAX. GRADE ANY ADVERSE EVENT	5	7	4	0	6	7	2	1

One pt with grade 5 cardiac arrest related to ipi/nivo

n (%)	Enco + bini + nivo (n=16)	Ipi + Nivo (n=16)
Treatment-related Grade 3-4 AEs	**11 (69%)**	**12 (75%)**
Treatment-related AEs leading to discontinuation	**3(19%)**	**5 (32%)**
Treatment-related AE leading to dose modification or interruption	**12 (75%)**	**5 (32%)**

ations: abnormal lab findings such as ALT, AST, bilirubin, creatinine increase, etc

XXIV SPOTKANIE Po ASCO

2025 ASCO ANNUAL MEETING

Jedna dawka neoadjuwantowego Iipilimumabu z nivolumabem

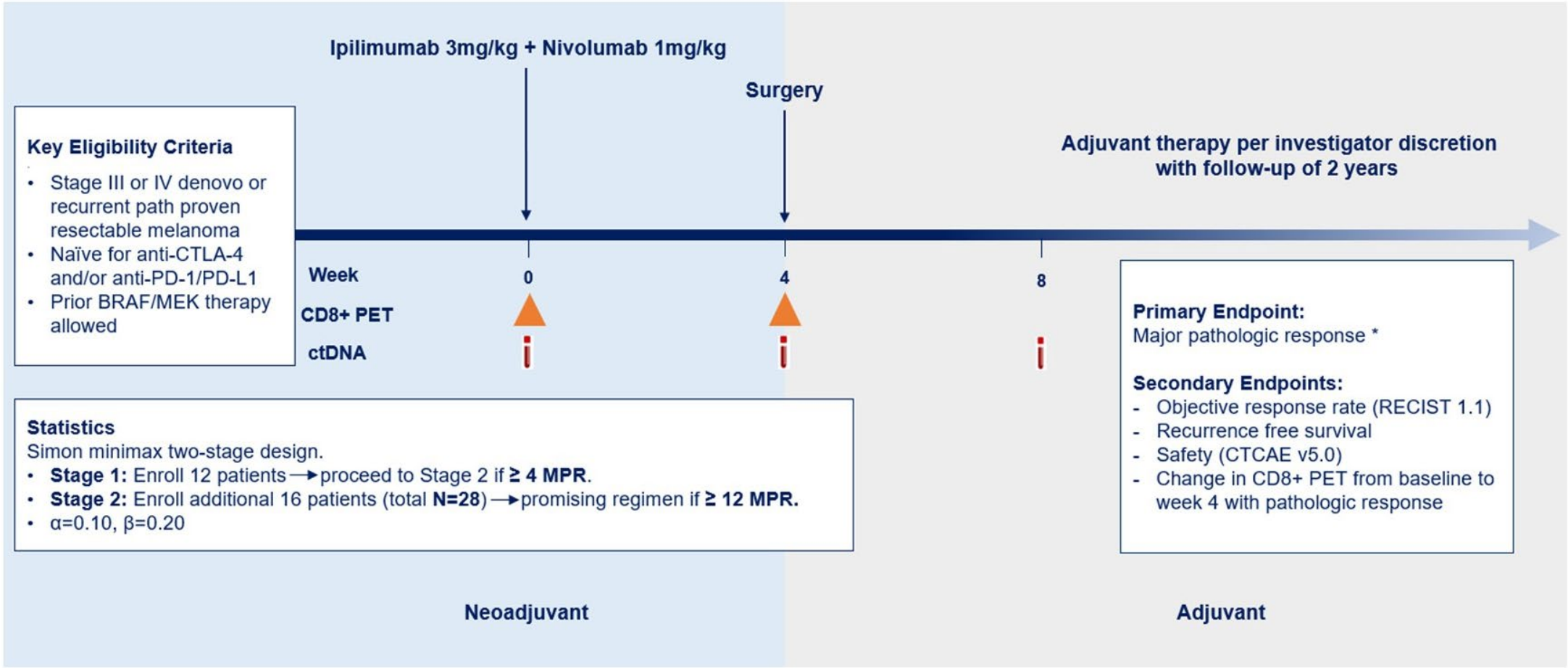
Single dose of Neoadjuvant Ipilimumab and Nivolumab in Resectable Melanoma with CD8+ Cell Imaging: Interim Results of the C-IT Neo Trial.

Sarah E. Lochrin, Cecilia Lezcano, James Russell, Jeeban P. Das, Hannah L. Kalvin, James W. Smithy, Shutian Ruan, Alexander N. Shoushtari, Parisa Momtaz, Monica F. Chen, Claire Thant, Danielle Bello, Edmund Bartlett, Mary Sue Brady, Charlotte E. Ariyan, Katherine S. Panageas, Neeta Pandit-Taskar, and Michael A. Postow.

Memorial Sloan Kettering Cancer Center

Konstrukcja badania C-IT Neo

Study Design



* MPR : major pathologic response rate was defined as (pathologic complete response [0% viable tumor] and pathologic near complete response [≤10% of viable tumor]).

Wyniki leczenia w badaniu C-IT Neo

Primary Endpoint – Major Pathologic Response Rate is 59%

Pathologic Assessment (n=22)	
Major Pathologic Response	**13 (59%)**
Complete response	10 (45%)
Near-complete response	3 (14%)
Partial response	4 (18%)
Nonresponse	5 (23%)

Grade ≥3 TRAEs Occurred in 9% of Patients

Safety	n=22
Any adverse event – no. (%)	21 (96)
Any grade ≥3 adverse event – no. (%)	4 (18)
Serious adverse event – no. (%)	1 (5)
Treatment-related adverse event (TRAE) – no. (%)	18 (82)
TRAE grade ≥3 adverse event – no. (%) *	**2 (9)**
Death due to TRAE – no. (%)	0

*Two patients experienced grade ≥3 TRAE in the neoadjuvant setting; neither required systemic steroids or delay in surgery

ORR w badaniu C-IT Neo

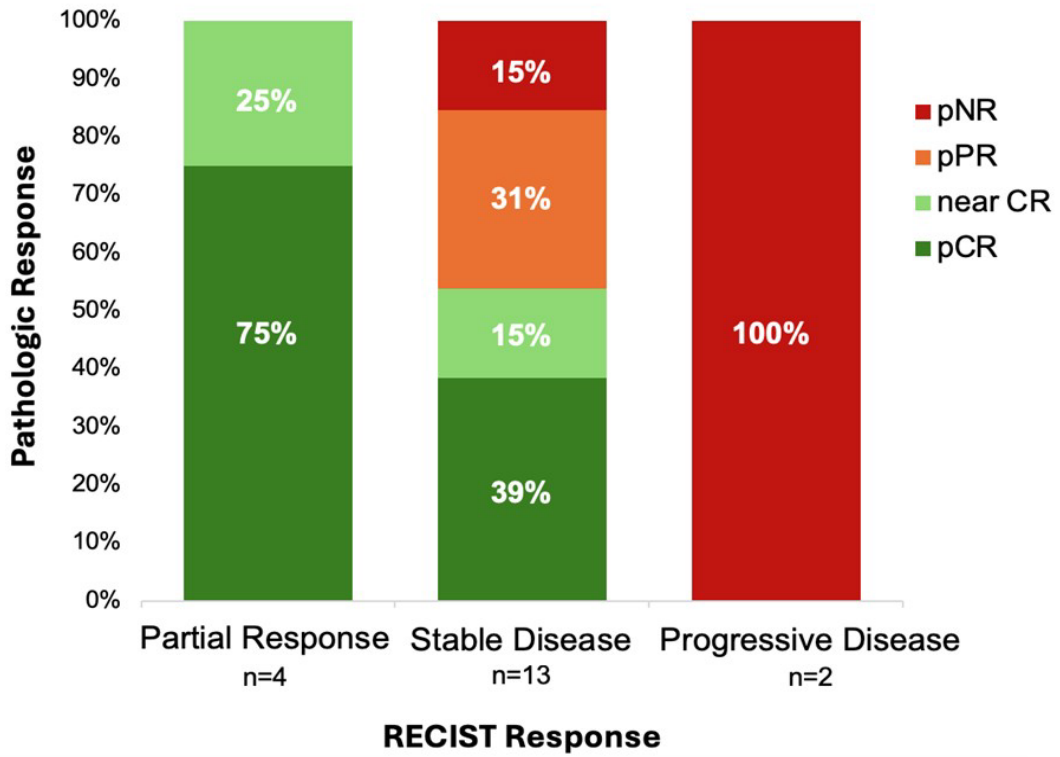
Objective Response Rate at Week 4 was 21%

Radiographic Response

RECIST 1.1	(n=19)
Objective Response Rate	**21%**
Complete Response (CR)	0
Partial response (PR)	4 (21%)
Stable Disease (SD)	13 (68%)
Progressive Disease (PD)	2 (11%)
Non-Evaluable (NE)*	3

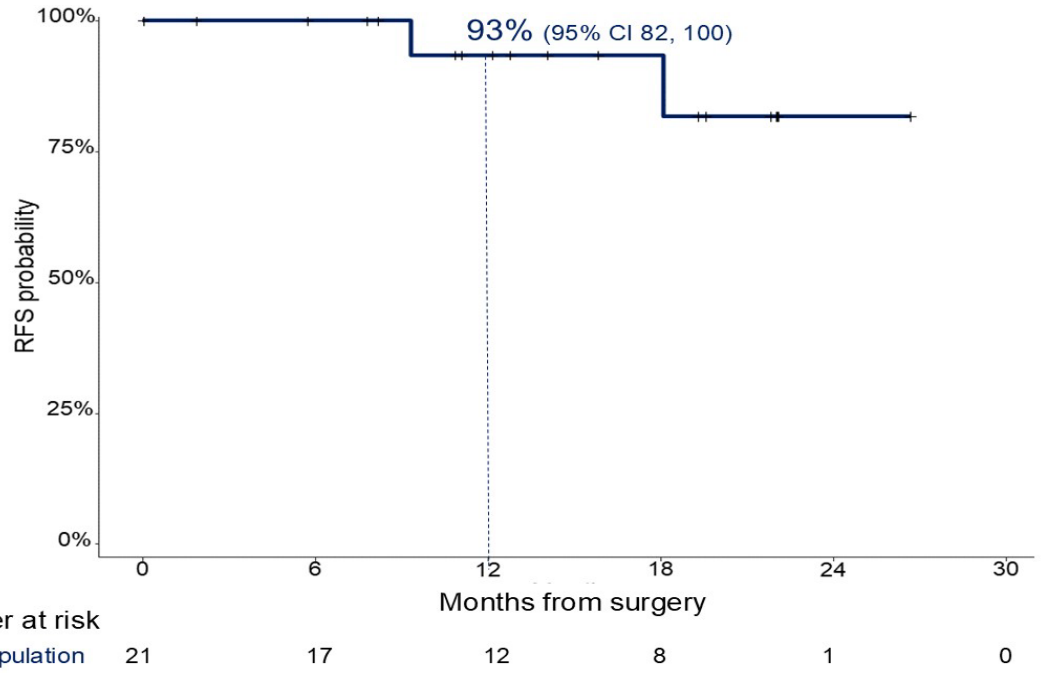
*Non-evaluable: n=1 no pre-surgery imaging; n=2 target lesion LN shortest diameter <15mm.

Radiographic and Pathologic Response Discordance



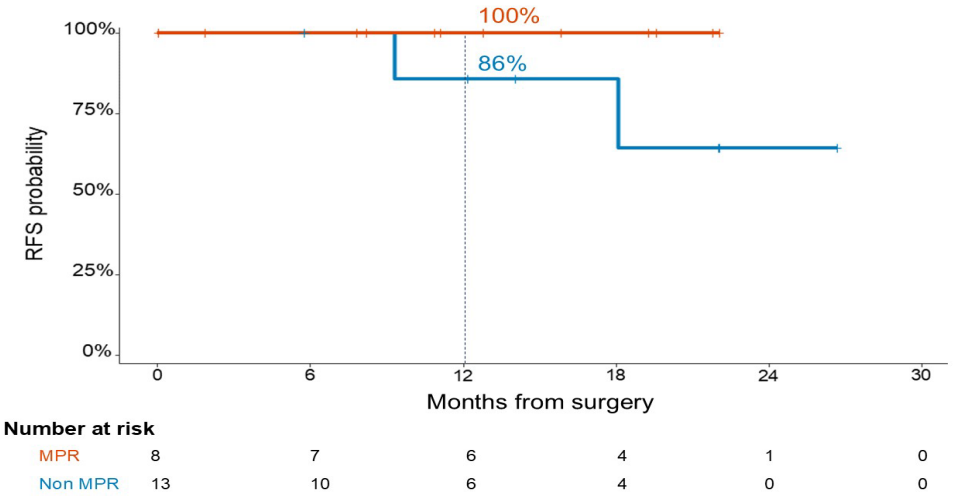
Recurrence Free Survival (RFS) at 12 months is 93%

RFS badaniu C-IT Neo



- Data cut-off (May 15, 2025) with a median follow-up of 15 months (IQR 10, 24)
- One patient excluded due to progression of disease prior to surgery
- 15 (71%) patients rendered NED by surgery proceeded to adjuvant therapy (14 anti-PD-1; 1 BRAF/MEK)

RFS According to Major Pathologic Response



- Of the 15 who received adjuvant therapy, 7 had a MPR and 8 a non-MPR
- All patients who did not received adjuvant therapy had a MPR

XXIV SPOTKANIE Po ASCO

2025 ASCO ANNUAL MEETING

NeoACTIVATE Arm C: neoadjuwantowy atezolizumab i tiragolumab

NeoACTIVATE Arm C: Phase II trial of neoadjuvant atezolizumab and tiragolumab for high-risk operable stage III melanoma

Tina J Hieken, David Zahrieh, Thomas J Flotte, Roxana S Dronca, Evidio Domingo-Musibay, Garth D Nelson, Carrie Strand, Lisa A Kottschade, Heather N Montane, Mara A Piltin, Ruqin Chen, Robert R McWilliams, James W Jakub, Samir Khariwala, Arkadiusz Z Dudek, Jeffrey E Johnson, Svetomir N Markovic, Anastasios Dimou, Kendall Tasche, Matthew S Block

Mayo Clinic, Rochester, MN; Mayo Clinic, Jacksonville, FL; University of Minnesota, Minneapolis, MN USA

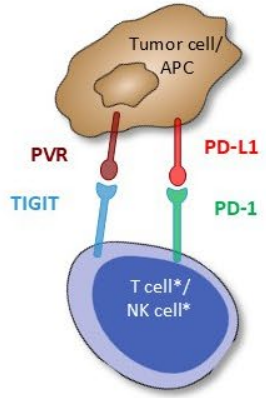
Lay Abstract

Badanie NeoACTIVATE - tiragolumab

NeoACTIVATE Arm C

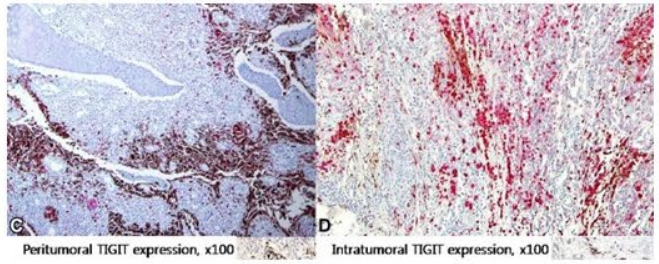
Rationale

- T-cell immunoglobulin and ITIM domain (TIGIT) is a co-inhibitory receptor found on activated T- and NK-cells
  - Often co-expressed with PD-1
  - Competes with costimulatory receptor CD226
  - Leads to immune effector cell exhaustion
- Simultaneous blockade of TIGIT + PD-L1 promotes clonal expansion of non-exhausted T cells
- Trials in other cancers have shown tiragolumab (anti-TIGIT) plus atezolizumab (anti-PD-L1) has efficacy with a more favorable safety profile than other immune checkpoint combinations



Adapted from Manieri et al, *Trends Immunology* 2017

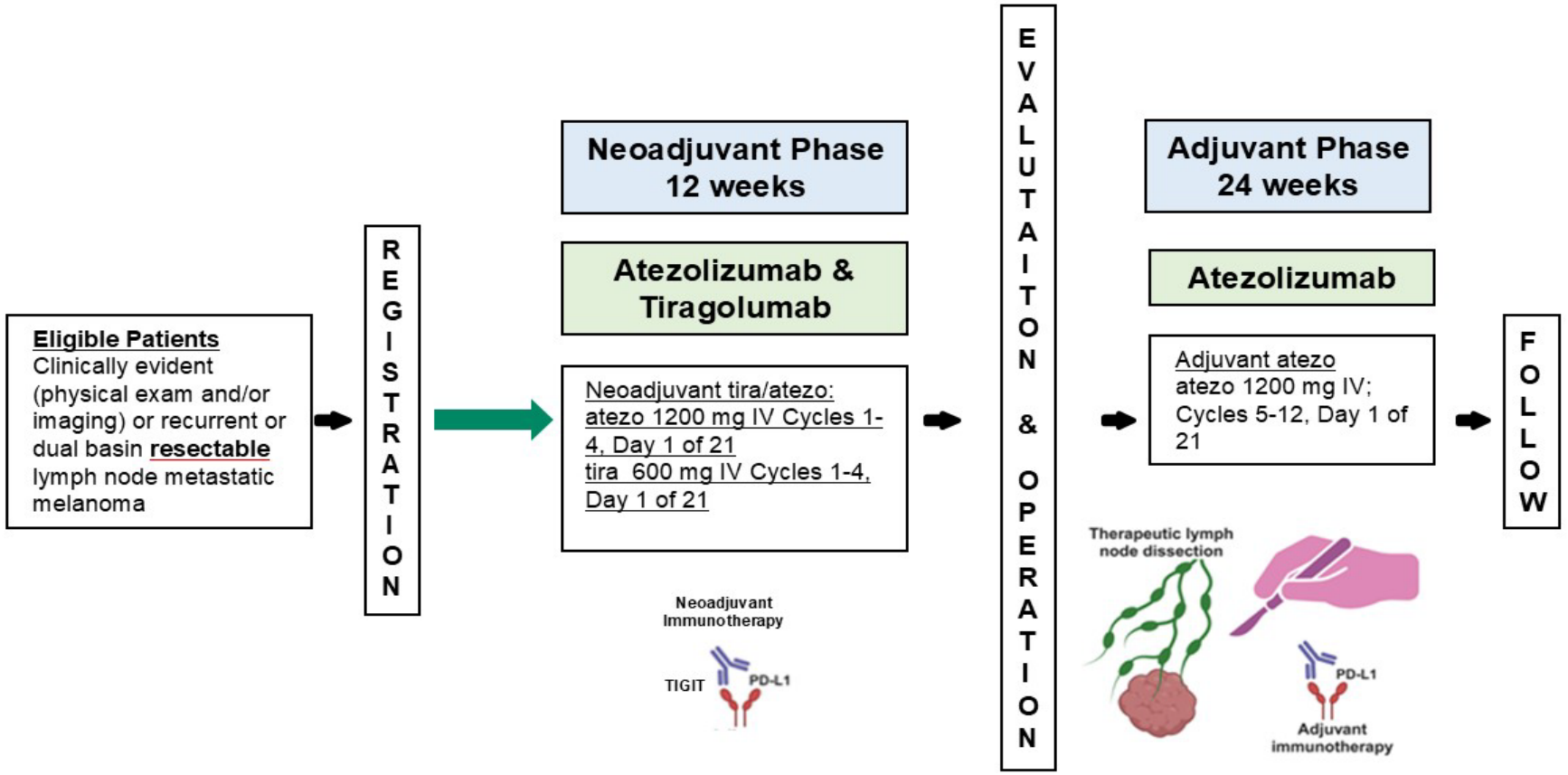
TIGIT expression in melanoma + TILs



Konstrukcja badania NeoActivate

NeoACTIVATE (NCT03554083) Arm C

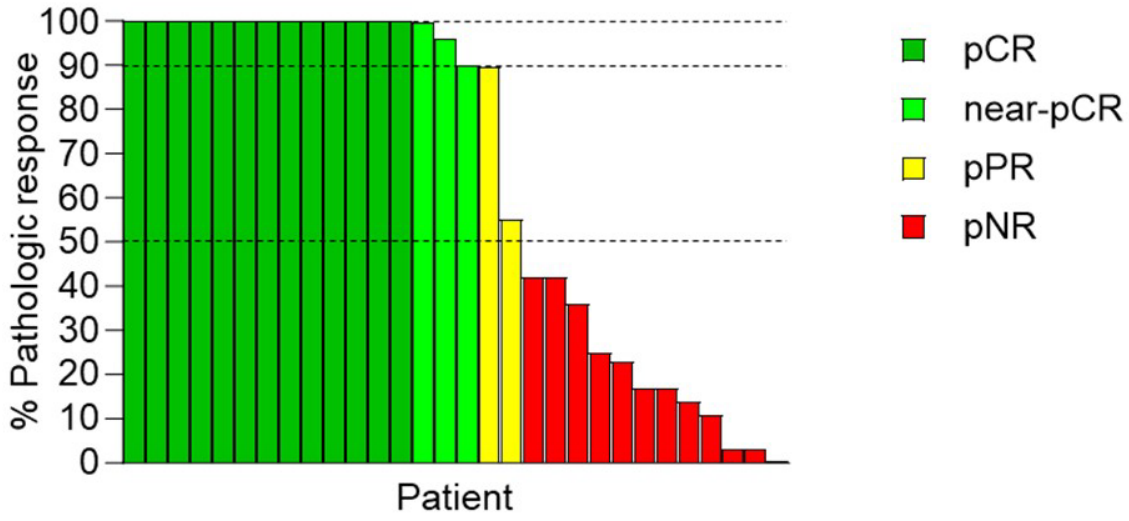
Neoadjuvant therapy for patients with high-risk stage III melanoma



Wyniki leczenia w badaniu NeoActivate

Pathologic Response

- 13/34 pCR + 3/34 near-pCR
- Major pathologic response in 47.7% of patients initiating neoadjuvant treatment



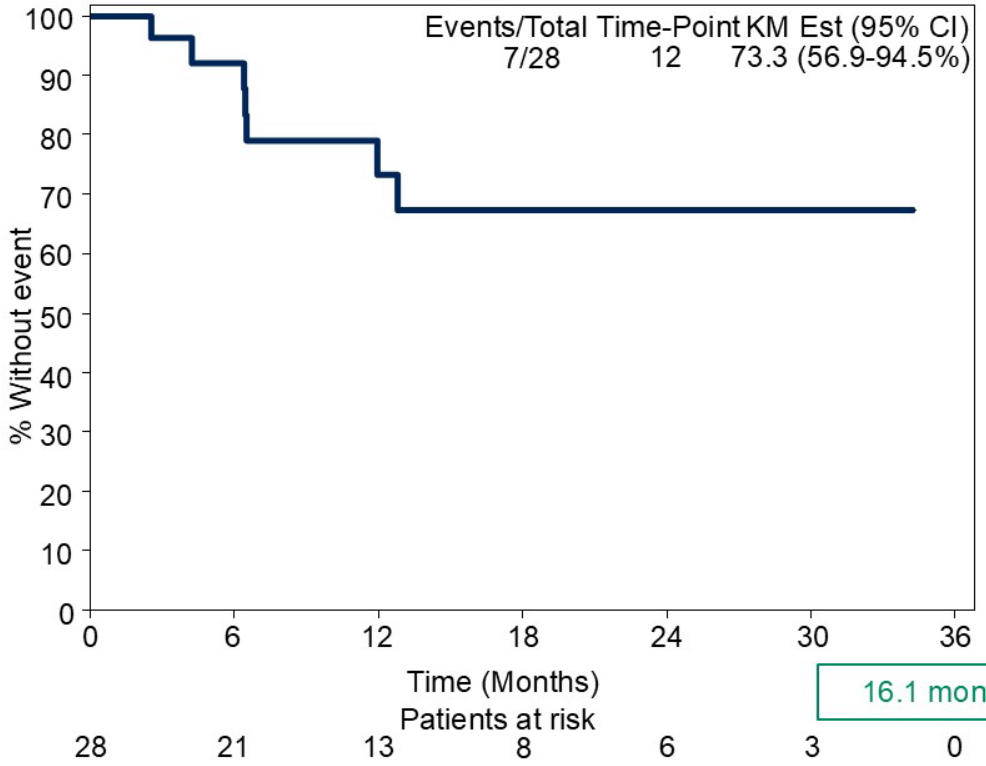
INMC Research Pathology Criteria
- pCR 0% viable tumor
- Near-pCR ≤10% viable tumor
- pPR 10.1-50% viable tumor
- pNR >50% viable tumor

Degree of pathologic response in patients having per protocol operation
n=30

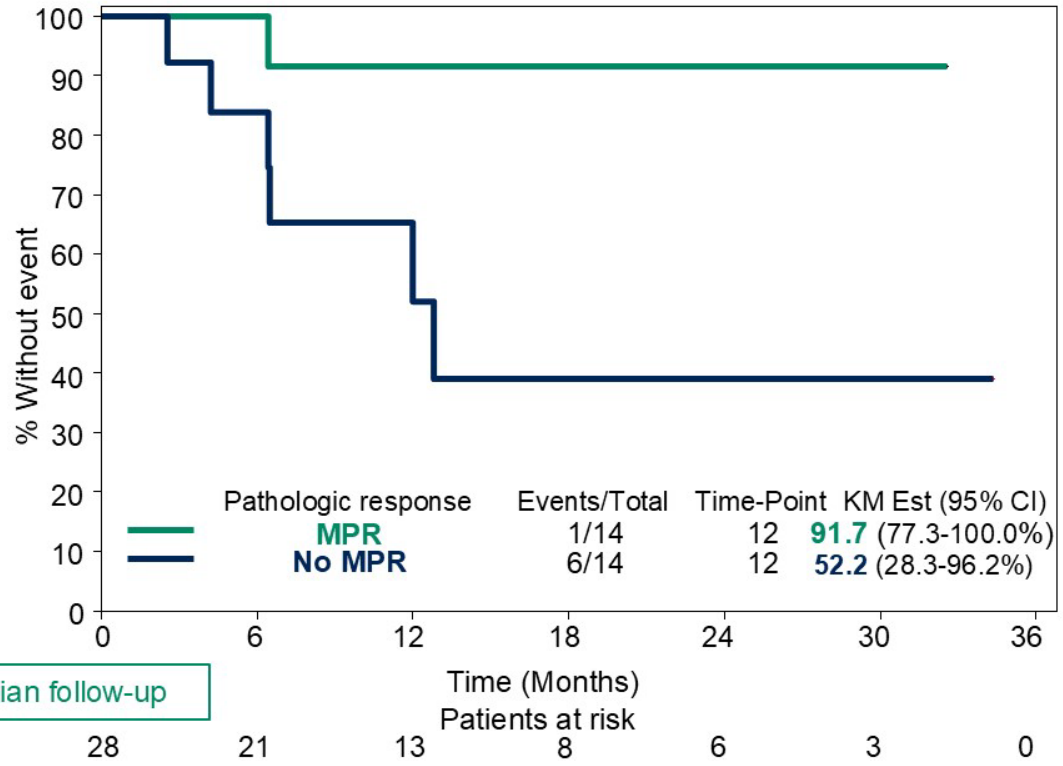
Wyniki leczenia w badaniu NeoActivate

Recurrence Free Survival

28 patients* completing per-protocol operation and initiating adjuvant therapy



16.1 months median follow-up



*2 patients had per protocol TLND, both with an MPR, did not initiate adjuvant therapy, and are without recurrence at 33 and 11 months postoperatively, respectively

XXIV SPOTKANIE Po ASCO

Badanie NEO-MELT – neoadjuwantowy dostarlimab + kobolimab

2025 ASCO ANNUAL MEETING

NEO-MEL-T: A randomized phase II study of neoadjuvant Dostarlimab (PD-1 inhibition) versus Dostarlimab and Cobolimab (TIM-3 inhibition) in high-risk resectable melanoma

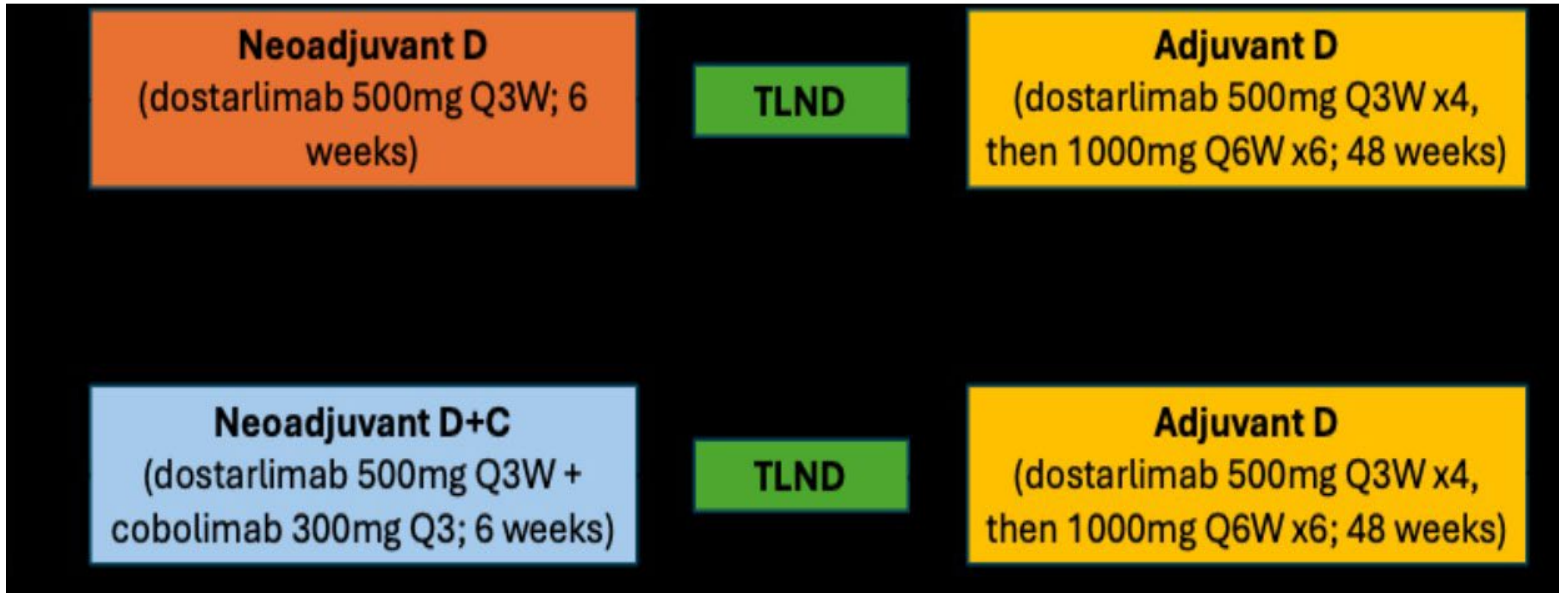
Meghan J. Mooradian, Arivarasan Karunamurthy, Hong Wang, Elizabeth I. Buchbinder, Suthee Rapisuwon, Justine V. Cohen, Geoffrey Thomas Gibney, Ryan J. Sullivan, Jason J. Luke, Yana G. Najjar, John M. Kirkwood, Hassane M Zarour, and **Diwakar Davar**.

Badanie NEO-MEL-T

Results: Demographics

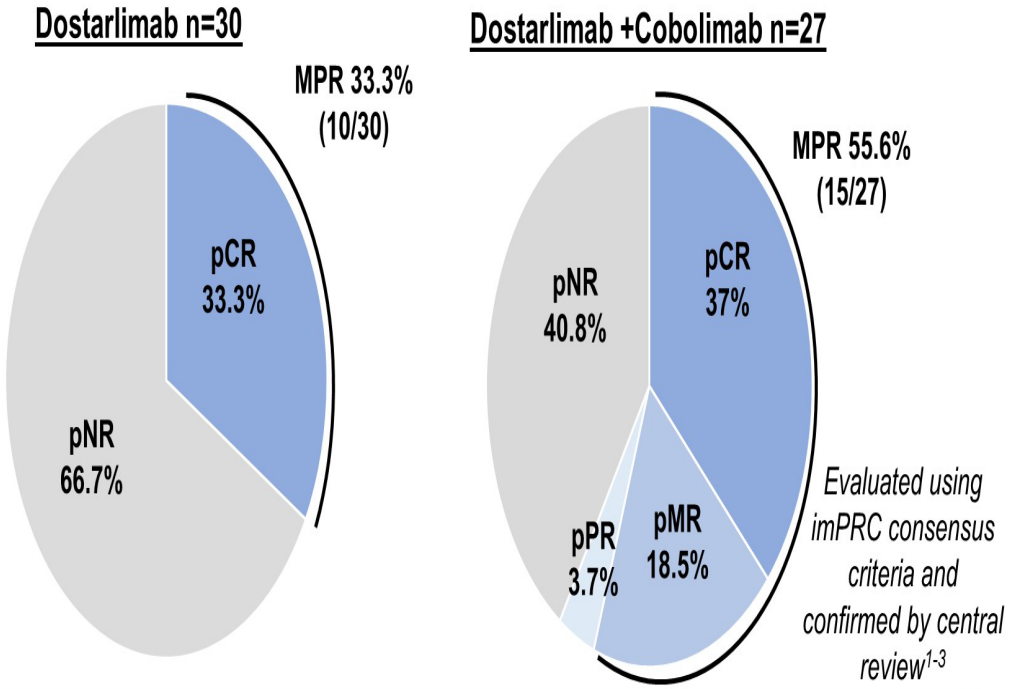
Characteristics	Dostarlimab (n=30)	Dostarlimab + Cobolimab (n=27)
Demographics		
• Median age (yr, range)	65 (37-91)	67 (31-91)
• Male (n,%)	20 (66.7%)	18 (66.7%)
LDH		
• ≥ULN	19 (63.3%)	17 (63.0%)
Molecular alterations		
• BRAF mutant	8 (26.7%)	8 (29.7%)
• NRAS mutant	5 (16.7%)	7 (25.9%)
• Other	5 (16.7%)	5 (18.5%)
• Unknown	12 (40%)	7 (25.9%)
AJCC Stage (8th edition)		
• IIIB	14 (46.7%)	11 (40.8%)
• IIIC	14 (46.7%)	13 (48.1%)
• IIID	2 (6.6%)	0 (0.0%)
• IV-A	0 (0.0%)	3 (11.1%)
Presence of in-transit disease	11 (36.7%)	7 (25.9%)

NEO-MEL-T



Badanie NEO-MEL-T - Wyniki leczenia

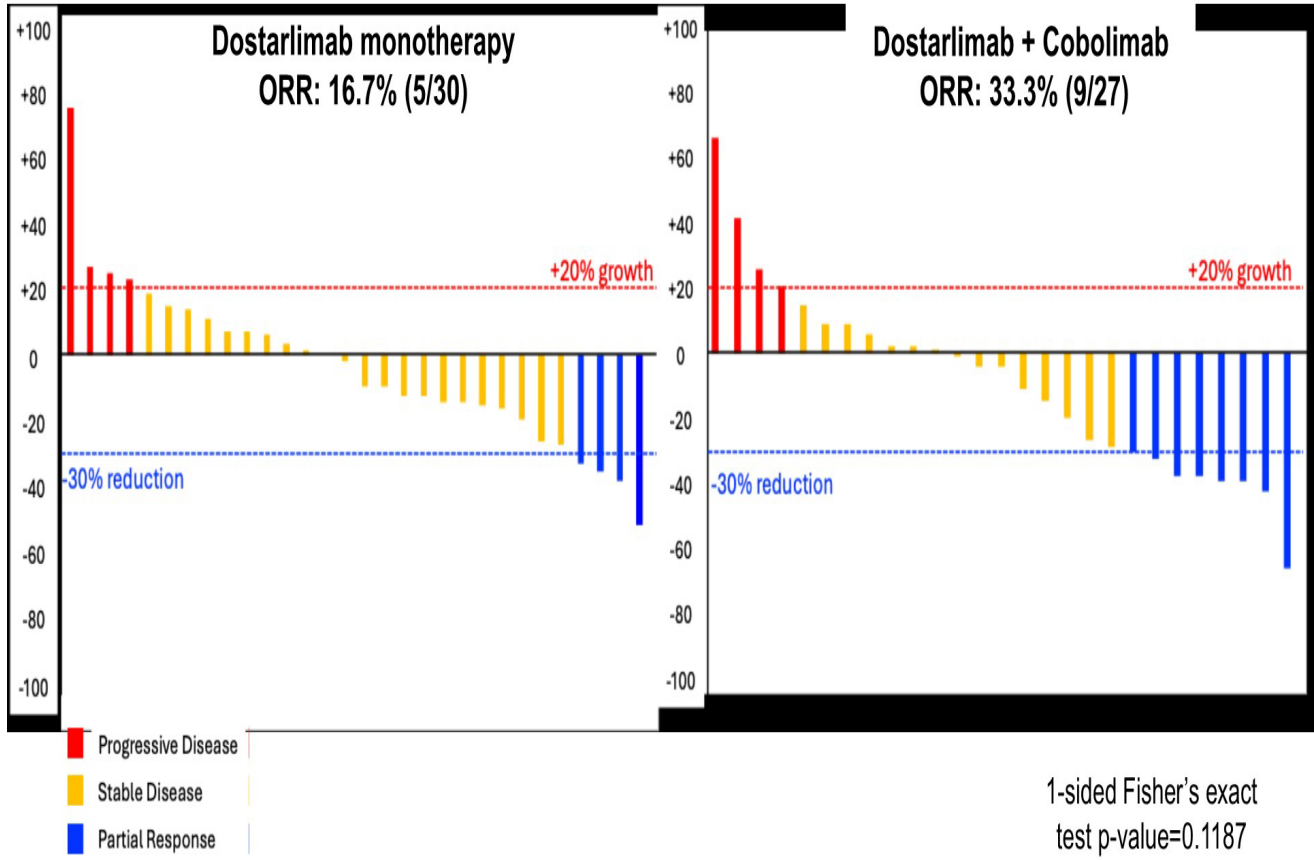
Results: Pathologic response breakdown (by arm, blinded review)



MPR rate with Dostarlimab + Cobolimab significantly exceeded historical control of 30% (p=0.0007, 1-sided z test).

[1]Cottrell TR, et al. *Ann Oncol* 2018; [2]Tetzlaff MT, et al. *Ann Oncol* 2018; [3]Stein JE, et al. *Clin Cancer Res* 2020

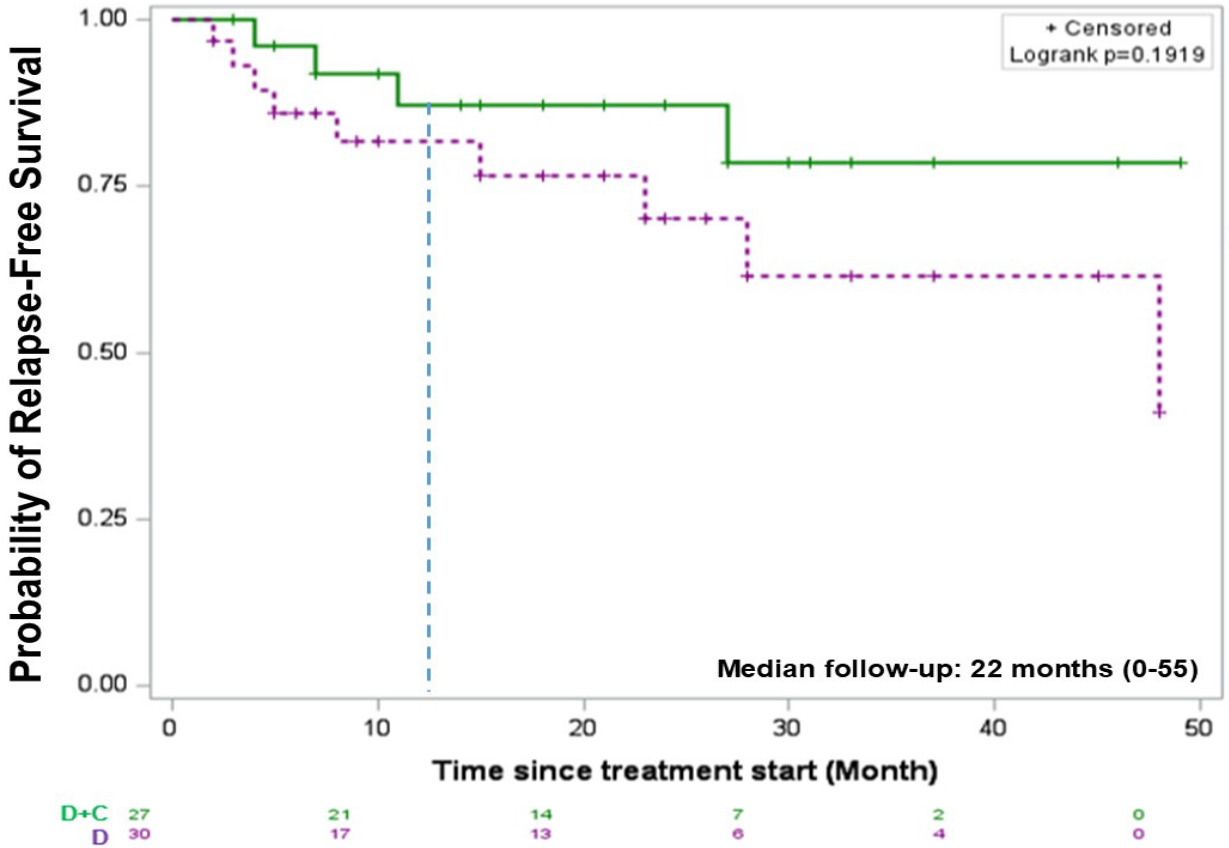
Results: Radiographic response



1-sided Fisher's exact test p-value=0.1187

Badanie NEO-MEL-T - Wyniki leczenia - RFS

Results: RFS (by treatment arm)



Historical control landmark 1-year DFS was 63% with neoadjuvant anti-PD-1 (Huang et al)[1]

Median RFS was non-significantly superior in **D+C combo (unreached)** vs. **D mono** (48 mths) (p = 0.1919, log-rank test).

1-year RFS with **D+C combo (87%)** was not greater than **D mono (82%)**.

1-year RFS with **D+C combo (87%)** was significantly greater than historical neoadjuvant anti-PD-1[1] (p = 0.0155, 1-sided z test).

Median DMFS and **OS** have not been reached in **either arm**

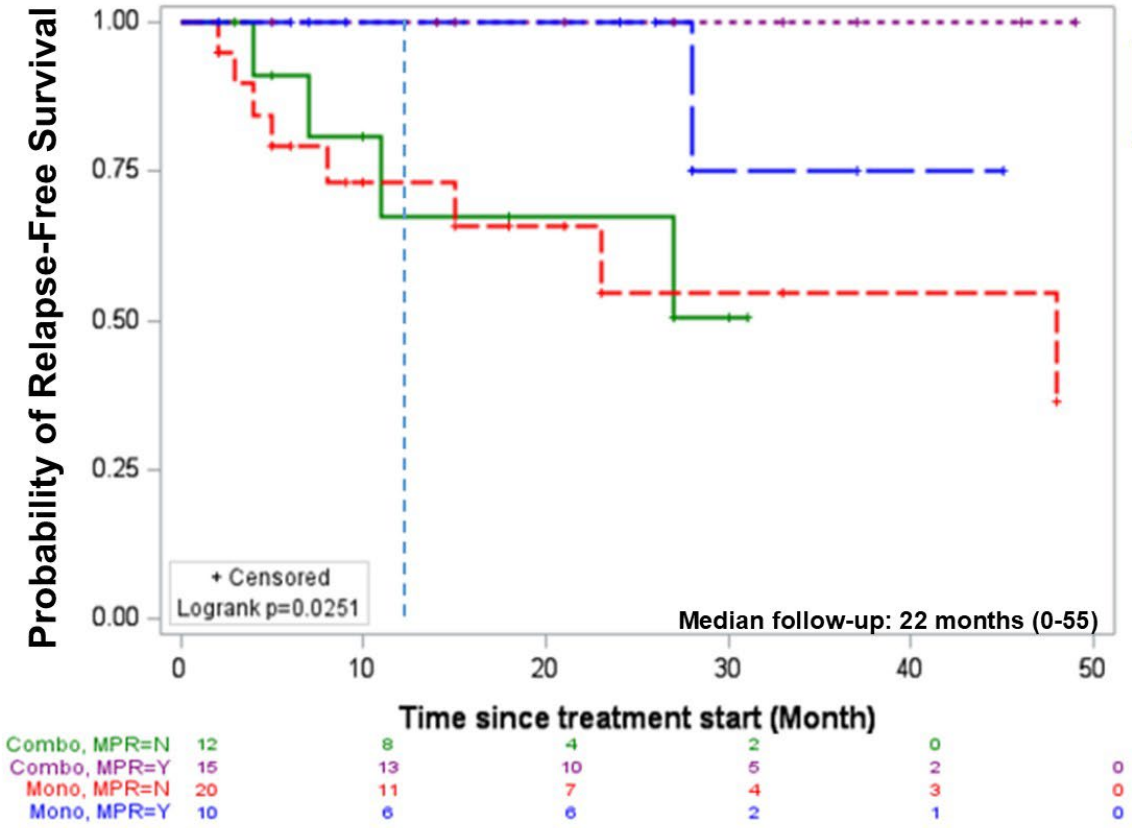
[1]Huang AC, et al. *Nature Medicine 2018*

Badanie NEO-MEL-T - Wyniki leczenia - RFS

Results: Description of events

Events	Dostarlimab (n=30)	Dostarlimab + Cobolimab (n=27)
Unable to complete planned neoadjuvant course	0 (0.0%)	0 (0.0%)
Unable to undergo TLND	0 (0.0%)	0 (0.0%)
Unable to complete adjuvant therapy		
• Toxicity	5 (16.7%)	4 (14.8%)
• Disease progression	6 (20.0%)	3 (11.1%)
• Remains on adjuvant therapy	8 (26.7%)	6 (22.2%)

Results: RFS (by treatment arm, and MPR



Historical control landmark 1-year RFS was 63% with neoadjuvant anti-PD-1 (Huang et al)[1]

1 yr RFS in MPRs (D or D+C): 100%

Median RFS is significantly superior in **all MPR** vs. **all non-MPR** (not reached vs. 48 mths, log rank p = 0.0026).

Median RFS is not reached in **either D+C MPR or D+C non-MPR.**

Median RFS was non-significantly increased in **D MPR** vs. **D non-MPR** (not reached vs. 48 mths, p = 0.1243 log rank test).

[1]Huang AC, et al. *Nature Medicine 2018.*

XXIV SPOTKANIE Po ASCO

Neoadjuwantowy Kamrelizumab + Apatynib + Temozolomid w czerniaku akralnyn – badanie CAP 03-Neo

2025 ASCO ANNUAL MEETING

Neoadjuvant Therapy with Camrelizumab plus Apatinib and Temozolomide in Resectable Stage II/III Acral Melanoma: Results from CAP 03-Neo

Lili Mao [1], Caili Li [1], Jie Dai [1], Xiaoting Wei [1], Junjie Gu [1], Yu Du [1], Yan Kong [1], Xinan Sheng [2], Chuanliang Cui [1], Zhihong Chi [1], Bin Lian [1], Bixia Tang [1], Xieqiao Yan [2], Xuan Wang [1], Siming Li [2], Li Zhou [2], Juan Li [2], Xiaowen Wu [2], Lu Si [1], **Jun Guo** [1]

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Badanie CAP 03-Neo

The CAP 03 [3] trial, which evaluated a combination of camrelizumab(anti-PD-1), apatinib(oral VEGFR-2 TKI), and temozolomide in patients with advanced AM, demonstrated encouraging efficacy, with an **objective response rate (ORR) of 64.0%** and a **median progression-free survival (PFS) of 18.4 months** (2022 ASCO) .

Study Design

Two-stage, single-center, prospective trial. The results of Stage 1 are reported.

Stage 1
Key eligibility criteria

- Age 18–75 years
- Resectable stage II/III acral melanoma with/without lymph node metastasis
- ECOG PS 0-1

Neoadjuvant therapy

Camrelizumab 200 mg Q2W
Apatinib 250 mg QD
Temozolomide 200 mg/m² D1-D5 Q4W

2 cycles

Surgery

Within 4 weeks post treatment

Adjuvant therapy

Camrelizumab 200mg Q3W ×14 doses

Follow up

Stage 2 Based on pNR and risk-benefit assessment, extended enrollment to an additional 30 pts receiving the same treatment.

Endpoints

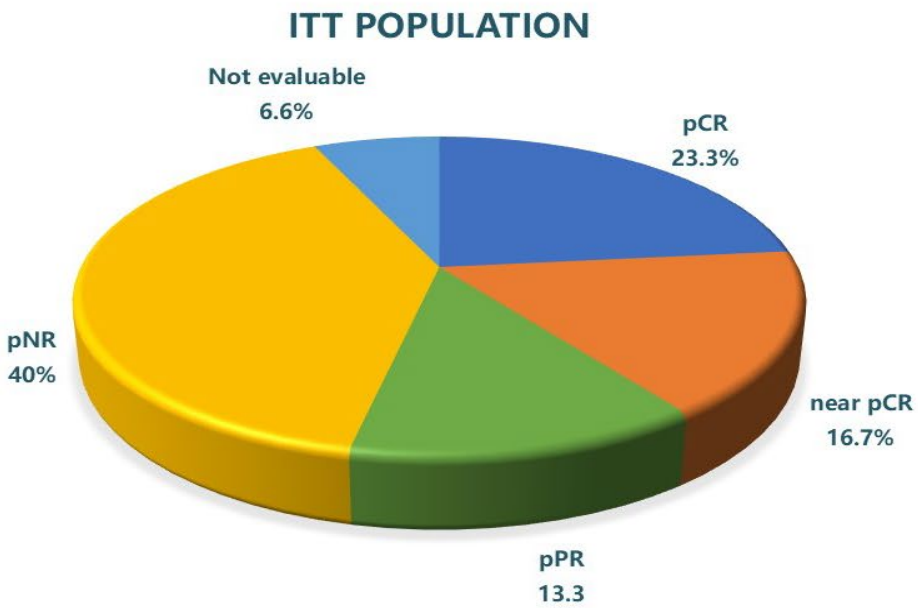
- **Primary endpoint:** Pathologic complete response (pCR)
- **Secondary endpoints:** Event-free survival (EFS); overall survival (OS); safety; biomarkers predictive of response to neoadjuvant therapy

- Clinical trial information: NCT05512481

Badanie CAP 03-NEO - Wyniki leczenia - ORR

Pathologic Response Rate

Pathologic Response	Full Analysis Set (%) (N=30)	Surgery Set (%) N=28	Stage II (%) N=11	Stage III (%) N=17
pCR	7 (23.3)	7 (25.0)	3 (27.3)	4 (23.5)
Near pCR	5 (16.7)	5 (17.9)	0	5 (29.4)
pPR	4 (13.3)	4 (14.3)	1 (9.1)	3 (17.6)
pNR	12 (40.0)	12 (42.9)	7 (63.6)	5 (29.4)
Not evaluable*	2 (6.7)	NA	NA	NA
Pathologic response rate (pCR + Near pCR + pPR)	**16 (53.3)**	**16 (57.1)**	**4 (36.4)**	**12 (70.6)**
CI 95%	34.3 , 71.7	37.2 , 75.5	10.9 , 69.2	44.0 , 89.7



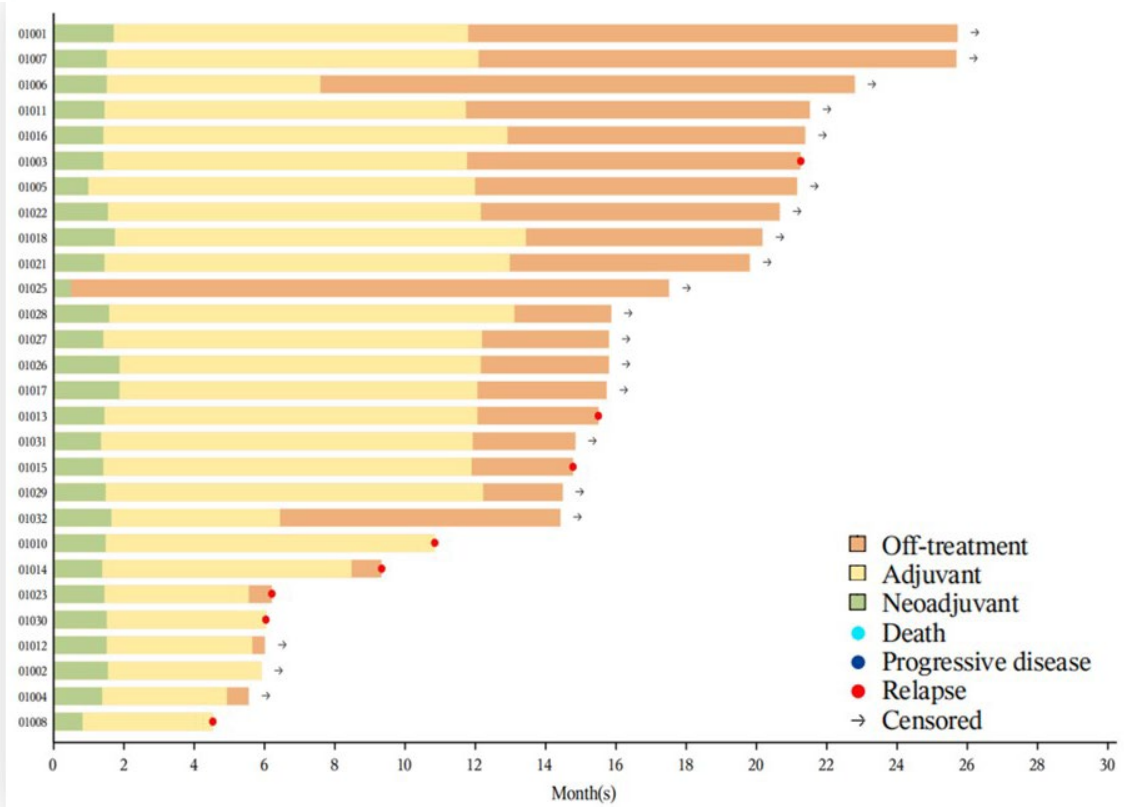
[1] 95% CI is calculated using Clopper-Pearson method.

• Surgical resection was completed in 28 patients; 2 patients did not undergo surgery (1 due to toxicity, 1 due to disease progression).

Neoadjuvant endpoints consider:

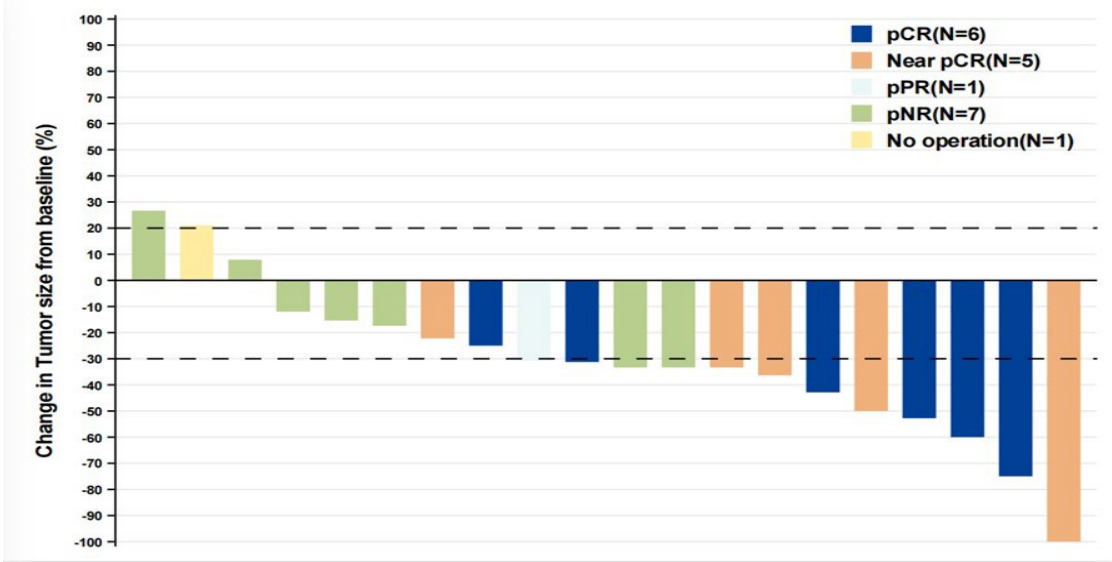
pCR :no viable tumor
pPR:11-49% viable tumor
near pCR: ≤ 10% viable tumor
pNR: >50% viable tumor

Badanie CAP 03-NEO – Wyniki leczenia



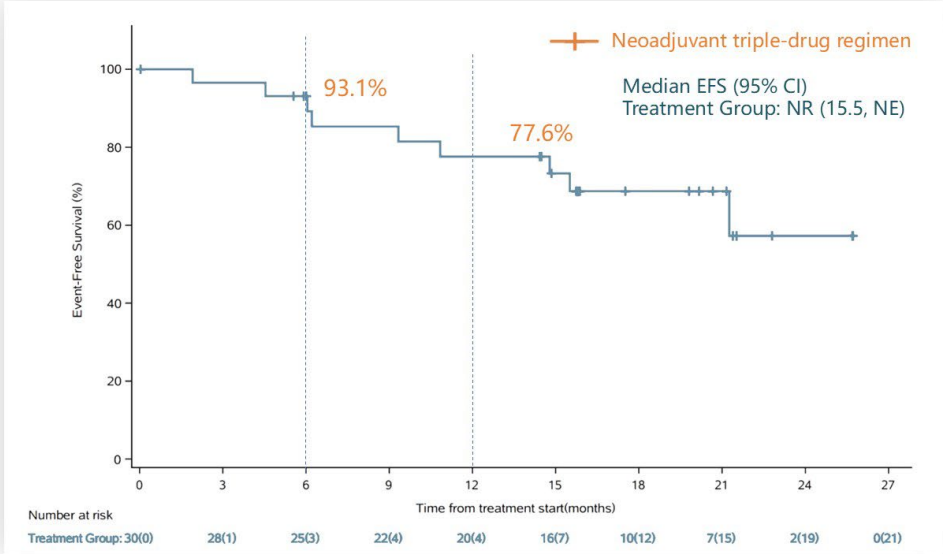
Swimmer Plot (Surgery Set)

- As of April 2025, the median follow-up time was 18.1 months (range, 1.9–25.7 months).



Waterfall Plot of Best Percent Change from Baseline in the Sum of Target Lesions at Week 8

EFS per INV : secondary endpoint

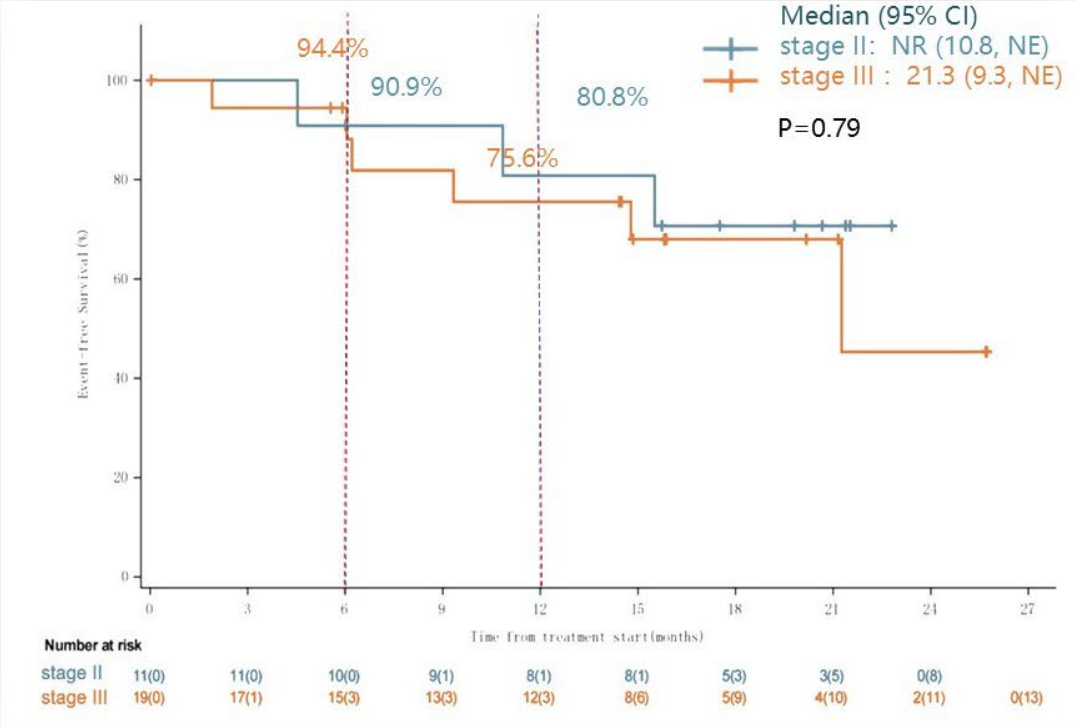


The median EFS has not been reached, with a 12-month EFS rate of 77.6% (95% CI: 56.7 - 89.3).

Badanie CAP 03-NEO - Wyniki leczenia - EFS

EFS by Stage and RFS Stratified by Pathologic Response

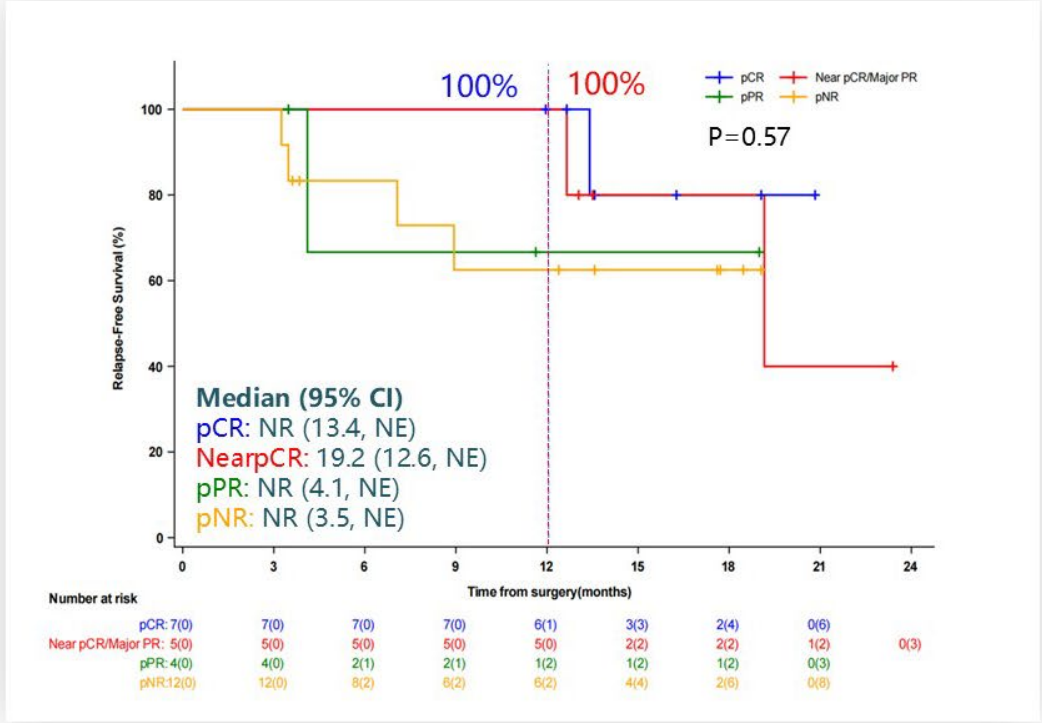
EFS by Stage per INV



The EFS for Stage II patients has not yet been reached.

The median EFS for Stage III patients is 21.3 months (95% CI: 9.3, NE).

RFS Stratified by Pathologic Response



The 12-month RFS rate was 100% in patients who achieved pCR or MPR after neoadjuvant therapy.

XXIV SPOTKANIE Po ASCO

RAKI SKÓRY

XXIV SPOTKANIE Po ASCO

Leczenie neoadjuwantowe raka Merkla - Lenwatynib + Pembrolizumab

2025 ASCO ANNUAL MEETING

A Phase II Study of Neoadjuvant Lenvatinib plus Pembrolizumab in Merkel Cell Carcinoma

Andrew S Brohl[1], Vernon K Sondak[1], Evan Wuthrick[2], Youngchul Kim[3], Zeynep Eroglu[1], Joseph Markowitz[1], Ahmad A Tarhini[1], Wenyi Fan[3], Justin Martin[1], Lymon Sneed[1], Matthew Perez[1], Amod Sarnaik[1], Michael Harrington[1], Rogerio Neves[1], Ricardo J Gonzalez[1], C. Wayne Cruse[1], Jonathan S. Zager[1], Kenneth Y Tsai[4], Nikhil I Khushalani[1]

[1]Cutaneous Department, [2]Department of Radiation Oncology, [3]Department of Biostatistics and Bioinformatics, [4]Department of Anatomic Pathology. H. Lee Moffitt Cancer Center and Research Institute. Tampa, FL. USA.

Konstrukcja badania neoadjuwantowego w MCC

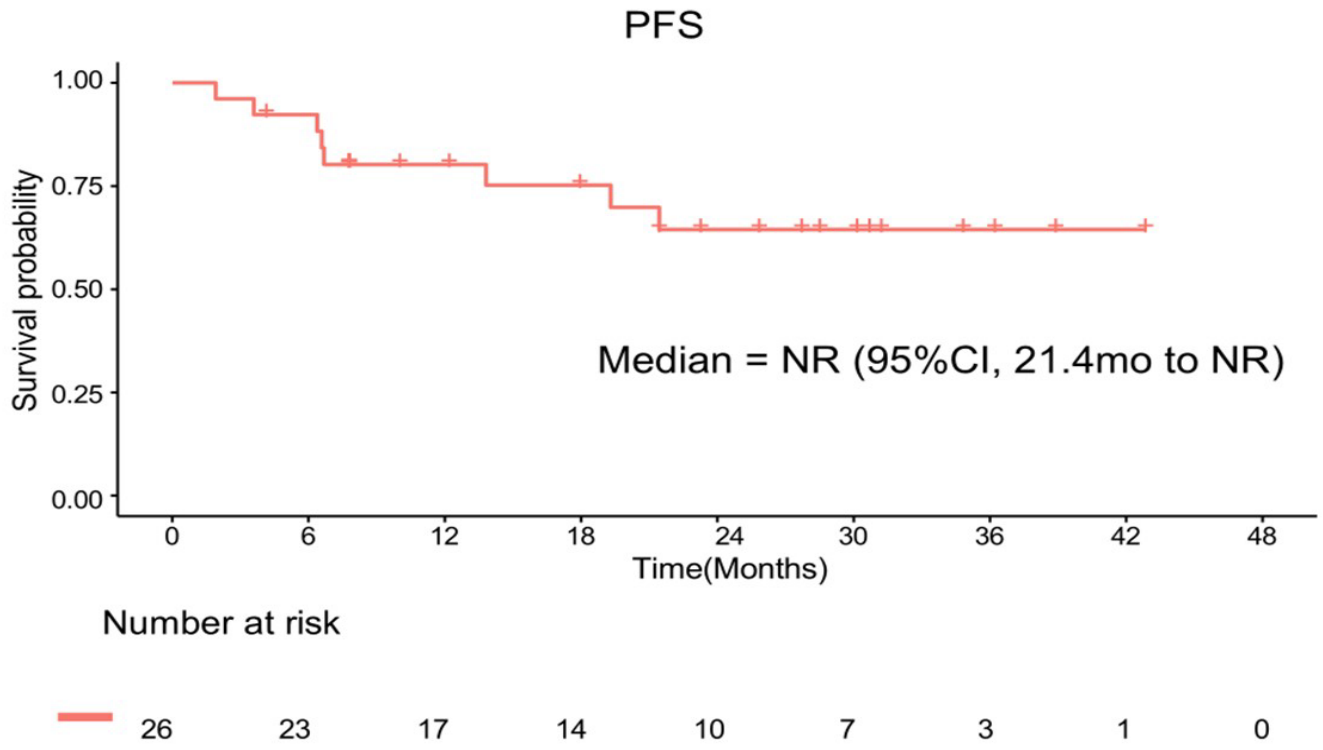
- Single arm, single center, open label design
  - Neoadjuvant Pembrolizumab 200mg IV q3wk, Lenvatinib 20mg PO daily x 6 weeks
  - Adjuvant pembrolizumab monotherapy to complete 1-year total systemic therapy
  - Resectable Stage II-IV MCC

Wyniki neoadjuwantowego leczenia MCC

Results

Pathologic Response[1]	
CR	**15 (58%)**
MPR	1 (4%)
PR	2 (8%)
NR	6 (23%)
Not surgical candidate[2]	2 (8%)
Disease Progression	
Neoadjuvant	1 (4%)
Post-operative	1 (4%)
Adjuvant	2 (8%)
Post-adjuvant	2 (8%)
Total	**6 (23%)**

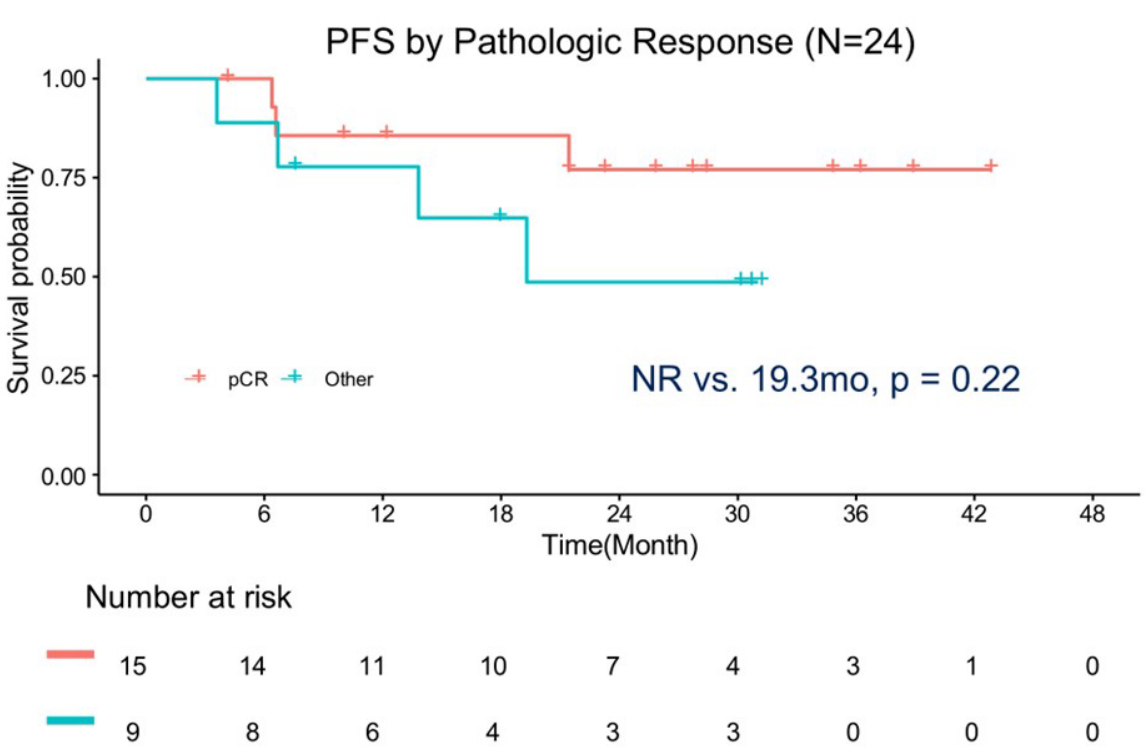
[1]Two patients with biopsy-only for pathologic response assessment
[2]Disease progression (1), TRAE (1)

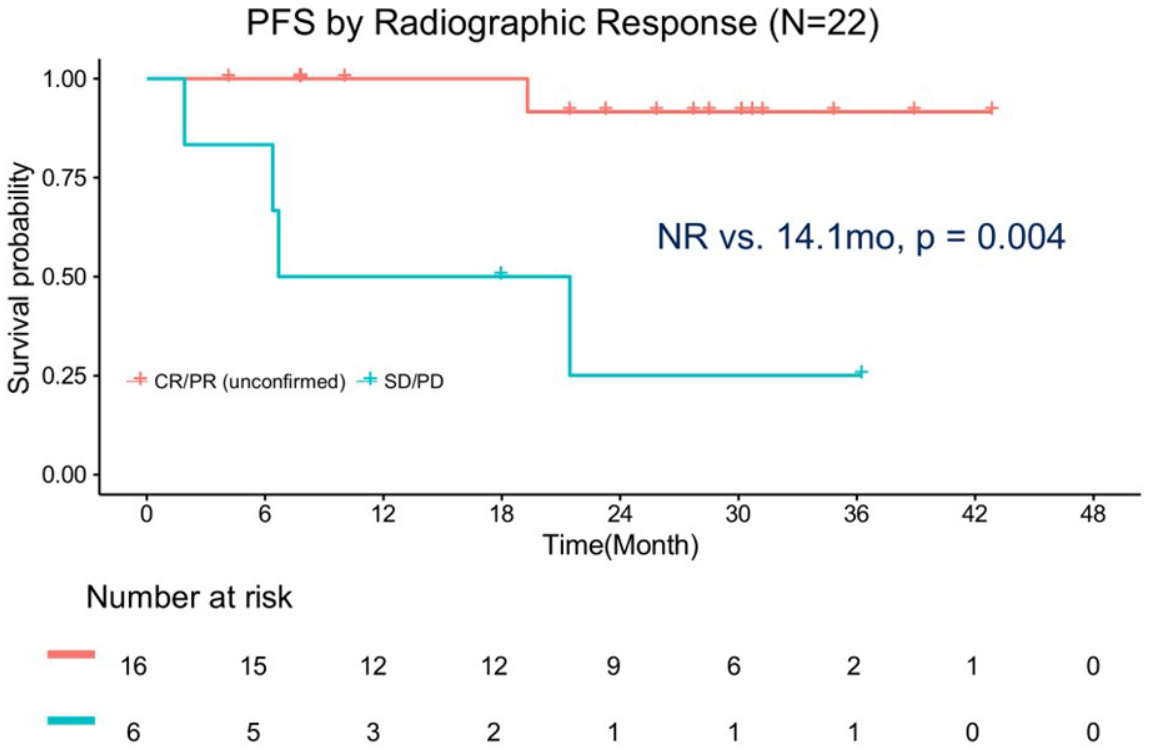


- Unconfirmed radiographic progression following neoadjuvant treatment NOT considered progression event if patient still underwent surgery
- 2 patient deaths without progression of disease/unrelated to MCC

Wyniki neoadjuwantowego leczenia MCC

Results





No “in field” recurrences in 13 pCR patients treated *without* adjuvant RT

Bezpieczeństwo leczenia neoadjuwantowego MCC

Treatment Related Adverse Events

- 14 patients (54%) experienced a G3 TRAE
  - 42% G3 HTN
- 3 patients (12%) experienced a G3 irAE
  - arthritis (1), dyspnea (1), neuropathy (1)
- No G4-5 TRAEs

	N = 26		
Adverse Event	Grade 1-2	Grade 3	Any Grade
Any AE	26 (100)	14 (54)	26 (100)
Fatigue	21 (81)	1 (3.8)	22 (85)
Hypertension	10 (38)	11 (42)	21 (81)
Diarrhea	14 (54)	1 (3.8)	15 (58)
Headache	13 (50)	—	13 (50)
Arthralgia	10 (38)	—	10 (38)
Hoarseness	9 (35)	—	9 (35)
Nausea	9 (35)	—	9 (35)
Rash maculo-papular	8 (31)	—	8 (31)
Constipation	7 (27)	—	7 (27)
Anorexia	6 (23)	—	6 (23)
Aspartate aminotransferase increased	6 (23)	—	6 (23)
Myalgia	6 (23)	—	6 (23)
Blood lactate dehydrogenase increased	5 (19)	—	5 (19)
Dizziness	5 (19)	—	5 (19)
Hematuria	5 (19)	—	5 (19)
Hypoalbuminemia	5 (19)	—	5 (19)
Hyponatremia	4 (15)	1 (3.8)	5 (19)
Hypothyroidism	5 (19)	—	5 (19)
Insomnia	5 (19)	—	5 (19)
Platelet count decreased	5 (19)	—	5 (19)
Proteinuria	5 (19)	—	5 (19)
Pruritus	5 (19)	—	5 (19)
Abdominal pain	4 (15)	—	4 (15)
Alanine aminotransferase increased	4 (15)	—	4 (15)
Generalized muscle weakness	4 (15)	—	4 (15)
Hyperkalemia	4 (15)	—	4 (15)
Weight loss	4 (15)	—	4 (15)
Amnesia	3 (12)	—	3 (12)
Arthritis	2 (7.7)	1 (3.8)	3 (12)
Cough	3 (12)	—	3 (12)
Dry mouth	3 (12)	—	3 (12)
Dysgeusia	3 (12)	—	3 (12)
Pain	2 (7.7)	1 (3.8)	3 (12)
Urinary frequency	3 (12)	—	3 (12)
Vomiting	3 (12)	—	3 (12)
Dyspnea	1 (3.8)	1 (3.8)	2 (7.7)
Atrial fibrillation	—	1 (3.8)	1 (3.8)
Neuropathy	—	1 (3.8)	1 (3.8)

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MIĘSAKI

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Pimicotinib w leczeniu TGCT- badanie fazy III MANEUVER

2025 ASCO ANNUAL MEETING

Pimicotinib in tenosynovial giant cell tumor (TGCT): Efficacy, safety and patient-reported outcomes of Phase 3 MANEUVER study

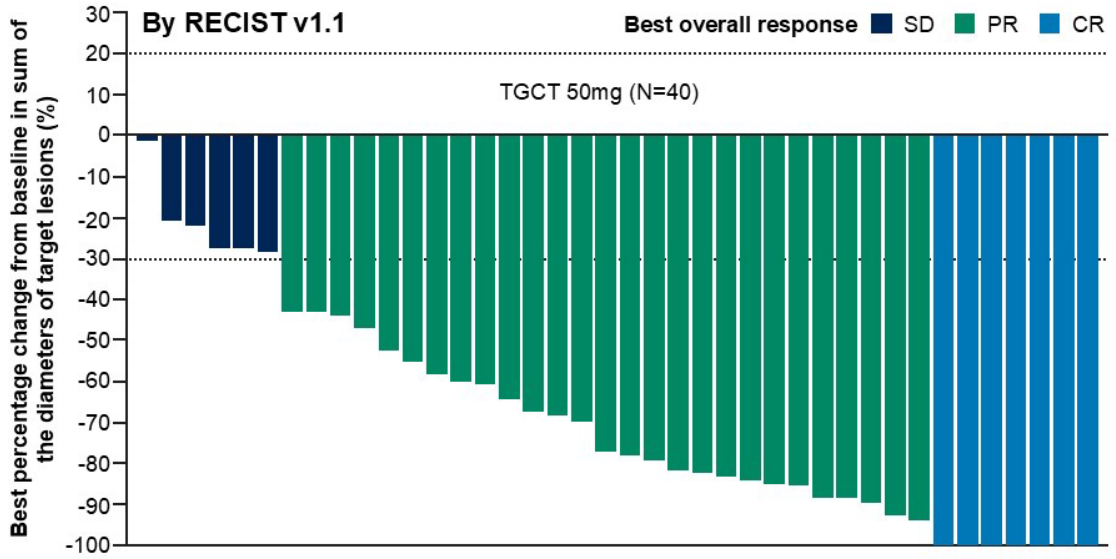
June 1, 2025

Xiaohui Niu, Vinod Ravi, Javier Martín-Broto, Yong Zhou, Albiruni Ryan Abdul Razak, Ramy Saleh, Jingnan Shen, Tang Liu, Silvia Stacchiotti, Kamalesh K Sankhala, César Serrano, Jing Wang, Yingqi Hua, Piotr Rutkowski, Xiaojing Zhang, Yi Feng, Tao Li, Giacomo Giulio Baldi, Hairong Xu, Hans Gelderblom on behalf of the MANEUVER investigators

Pimicotinib is a once-daily, oral, CSF-1R inhibitor under investigation for the treatment of patients with TGCT[1,2]

- Pimicotinib is thought to block CSF-1R signaling and disrupt inflammatory cell recruitment[1]
- Pimicotinib is highly specific for CSF-1R, potentially reducing off-target effects[1]
- In the Phase 1b study, at an RP2D of 50 mg once-daily, pimicotinib showed strong clinical activity in patients with TGCT (n=42)[3]
  - ORR by RECIST v1.1 at Week 25 was 67.5%[a]
  - ORR by RECIST v1.1 at 2-year follow-up was 85.0%[a]
  - Safety profile was tolerable, with mostly grade 1/2 TEAEs and no serious liver injuries or hair color changes

Best percentage change from baseline at 2 years in target lesions by IRC based on RECIST v1.1 from the Phase 1b study[3]

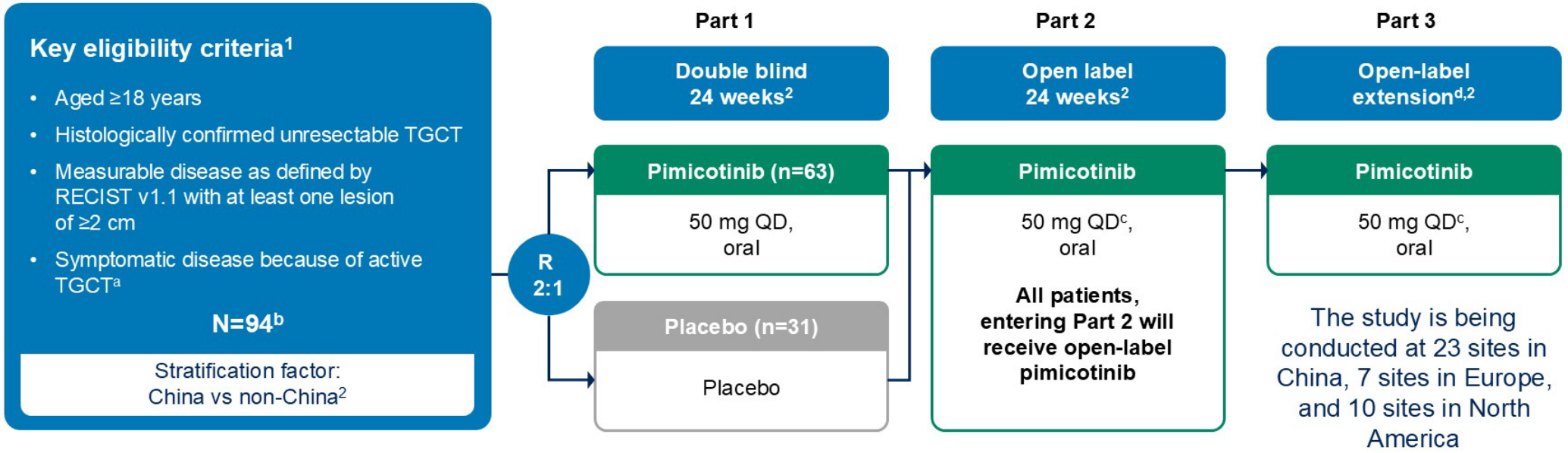


[a]As of June 30, 2024, 40 patients in the 50 mg QD pimicotinib group had completed at least one post-treatment tumor assessment by IRC based on RECIST v1.1
CR, complete response; IRC, independent review committee; PR, partial response; QD, once daily; RP2D, recommended Phase 2 dose; SD, stable disease; TEAE, treatment-emergent adverse event
1. Yang S et al. Cancer Res 2018;78(13_Suppl):LB-288; 2. Niu X et al. Future Oncol 2024;1–8; 3. Xu H et al. CTOS 2024 [P407]

Plan badania MANEUVER

MANEUVER: A Phase 3, randomized, double-blind, placebo-controlled global study of pimicotinib in TGCT

Study design



[a]Defined as one or more of the following: (i) a worst pain of ≥4 within 2 weeks prior to randomization (based on scale of 0 to 10, with 10 representing "pain as bad as you can imagine"), (ii) a worst stiffness of ≥4 within 2 weeks prior to randomization (based on a scale of 0 to 10, with 10 representing "stiffness as bad as you can imagine); [b]Between April 27, 2023 and March 29, 2024, 94 adults with TGCT underwent randomization: 63 were assigned to pimicotinib 50 mg QD and 31 to matching placebo; [c]If a patient has dose modification in Part 1/Part 2, the patient will continue to be administered at the modified dose in Part 2/Part 3; [d]All patients who complete 24 weeks of dosing in Part 2 will be eligible to enter the open-label extension treatment phase (ie, Part 3) for a longer treatment period and safety follow-up; R, randomization

Chorzy leczeni w ramach badania MANEUVER

Baseline characteristics were balanced between treatment groups

A total of 59 patients in the pimicotinib arm (93.7%) and 29 (93.5%) patients in the placebo arm completed the double-blind period[a]

Baseline characteristic	Pimicotinib (n=63)	Placebo (n=31)	Total (N=94)
Median age (range), years	41.0 (18–69)	36.0 (18–66)	40.0 (18–69)
Sex, n (%)			
Female	45 (71)	19 (61)	64 (68)
Geographic region, n (%)			
China	31 (49)	14 (45)	45 (48)
Europe	18 (29)	10 (32)	28 (30)
North America	14 (22)	7 (23)	21 (22)
Tumor location, n (%)			
Knee	33 (52)	14 (45)	47 (50)
Ankle	9 (14)	5 (16)	14 (15)
Hip	7 (11)	6 (19)	13 (14)
Other[b]	14 (22)	6 (19)	20 (21)
Prior surgery for TGCT, n (%)	37 (59)	19 (61)	56 (60)
Prior systemic therapy for TGCT (imatinib), n (%)	2 (3)	4 (13)	6 (6)

Data cutoff date Sep 23, 2024

[a]Between April 27, 2023 and March 29, 2024, 94 adults with TGCT were randomized; [b]Including 8 patients reported as foot, 7 patients reported as wrist, 2 patients reported as elbow, and one patient each reported as shoulder, right foot (big thumb) and left jaw

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Odpowiedź RECIST na leczenie pimikotynibem

Pimicotinib showed marked and significant antitumor efficacy per RECIST v1.1

At Week 25	Pimicotinib (n=63)	Placebo (n=31)
ORR using RECIST v1.1, n (%)		
CR	1 (1.6)	0
PR	33 (52.4)	1 (3.2)
SD	20 (31.7)	28 (90.3)
PD	2 (3.2)[a]	0
NE	7 (11.1)	2 (6.5)
ORR using RECIST v1.1, n (%)	**34 (54.0)**	**1 (3.2)[b]**
95% CI[c]	(40.9–66.6)	(0.1–16.7)
Groups' difference (95% CI)[d]	50.7 (37.0–64.5)	
p-value[e]	<0.0001	
Median duration of response (range)	Not reached (0.03+, 11.76+)	Not reached NA

- The primary endpoint was met:
  - ORR by BIRC (RECIST v1.1) was 54.0% vs 3.2% at Week 25 ($p<0.0001$)
- Early onset of response was observed at Week 13, with 26 of 63 (41.3%) pimicotinib-treated patients achieving an objective tumor response
- The effect of pimicotinib on ORR was consistent across all prespecified subgroups[f]

Data cutoff date Sep 23, 2024; [a]One patient initially experienced a decrease in tumor size of 52% (PR) by Week 13 and then a subsequent increase of 38% (PD) at Week 25; however, by Week 37 the tumor size had reduced by 62% (PR), and the patient was still on treatment; [b]The single placebo responder, who had been receiving imatinib from May 2022 until discontinuation in February 2024 (4 weeks prior to study treatment initiation), with stable disease as the best overall response, showed a partial response under placebo; the possibility of a spontaneous regression or a delayed effect from imatinib cannot be ruled out; [c]95% CIs for rates were calculated using the exact Clopper-Pearson method; [d]95% CI for ratio difference was derived using the Wilson method; [e]p-values were obtained using Fisher's exact test; [f]Prespecified subgroups were based on age, sex, region, race, ethnicity, tumor location, TGCT type, ECOG PS, number of prior surgeries and prior systemic therapy
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; NA, not applicable; NE, not evaluable; PD, progressive disease

Odpowiedź na leczenie pimikotynibem w MRI

Pimicotinib showed marked and significant antitumor efficacy by TVS

At Week 25	Pimicotinib (n=63)	Placebo (n=31)
ORR using TVS, n (%)		
CR	1 (1.6)	0
PR	38 (60.3)	1 (3.2)
SD	16 (25.4)	28 (90.3)
PD	1 (1.6)	0
NE	7 (11.1)	2 (6.5)
ORR using TVS, n (%)	**39 (61.9)**	**1 (3.2)**
95% CI[a]	(48.8–73.9)	(0.1–16.7)
Groups' difference, % (95% CI)[b]	58.7 (45.2–72.2)	
p-value[c]	<0.0001	
Median duration of response (range)	Not reached (0.03+, 14.13+)	Not reached (3.22+, 3.22+)

- ORR by BIRC (using TVS) at Week 25 was 61.9% vs 3.2% (p<0.0001)

The TVS is designed specifically for TGCT to estimate tumor volume;
a response by TVS is defined as at least a 50% decrease in tumor volume[1]

Data cutoff date Sep 23, 2024

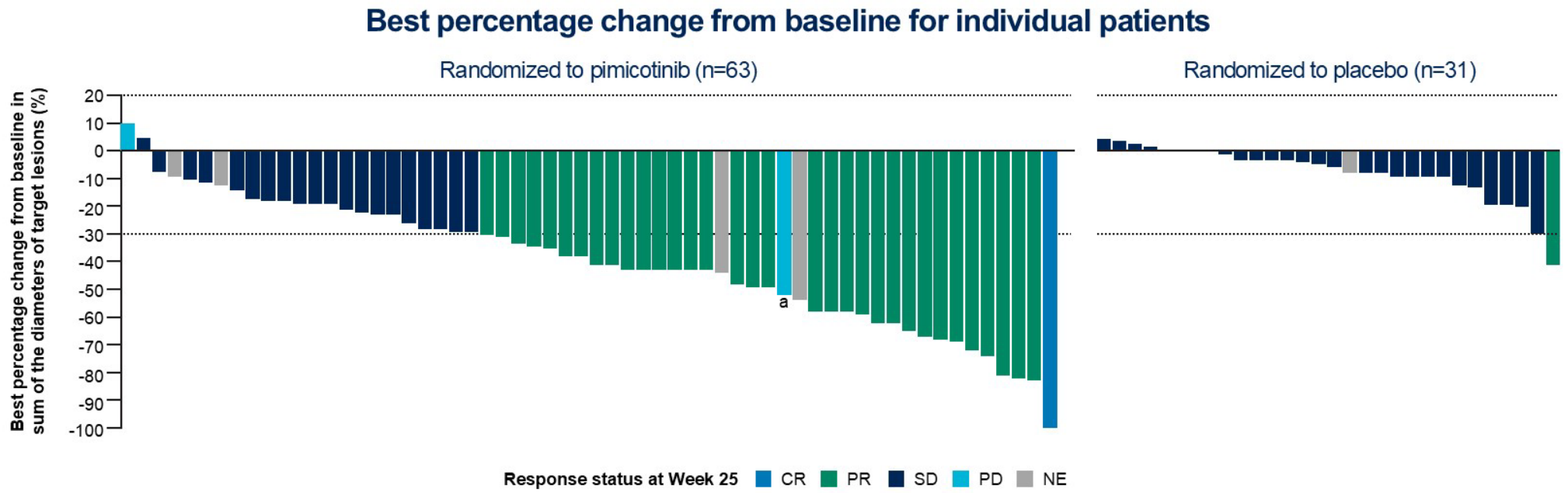
[a]95% CIs for rates were calculated from the exact Clopper-Pearson method; [b]95% CI for ratio difference was derived from the Wilson method; [c]p-value was obtained from Fisher's exact test

1. Peterfy C et al. Future Oncol 2022;18:1449–59

Odpowiedź radiologiczna na leczenie pimikotynibem

Pimicotinib resulted in substantial reductions in tumor size

By the data cutoff, 58 of 63 patients (92.1%) in the pimicotinib group had a decrease in tumor size per BIRC based on RECIST v1.1



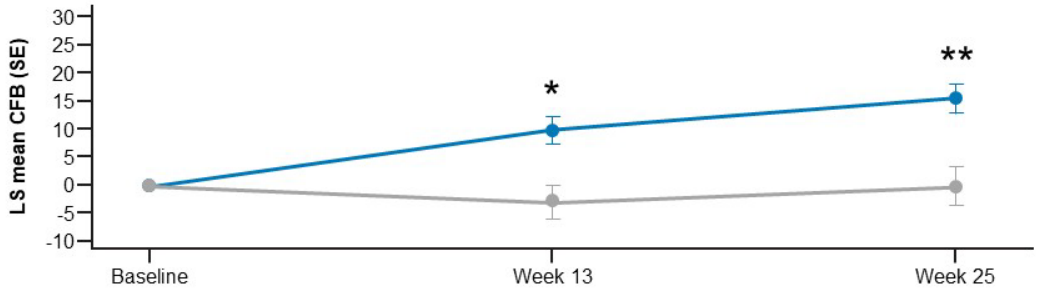
Data cutoff date Sep 23, 2024

[a]This patient initially experienced a decrease in tumor size of 52% (PR) by Week 13 and then a subsequent increase of 38% (PD) at Week 25; however, by Week 37 the tumor size had reduced by 62% (PR), and patient was still on treatment

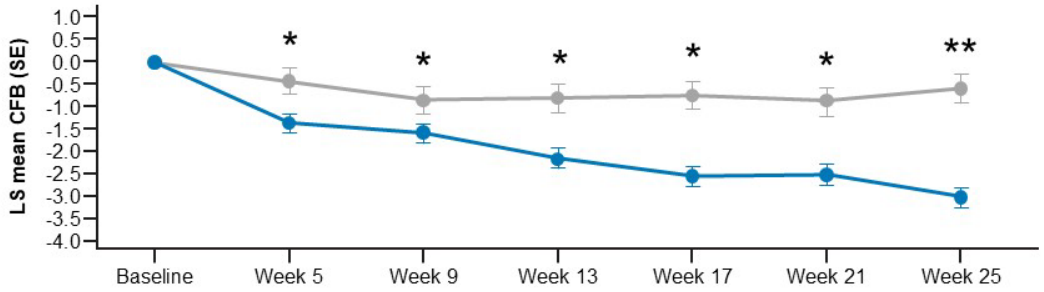
Odpowiedź kliniczna na leczenie pimikotynibem

Pimicotinib demonstrated early improvements in relative ROM, worst pain, worst stiffness, and PROMIS-PF T-score

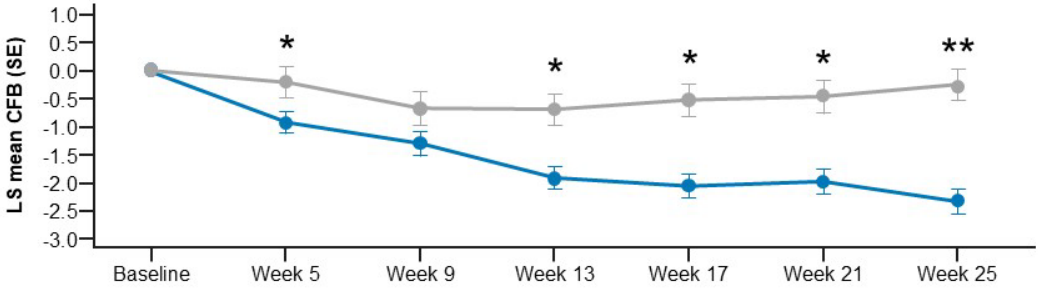
Relative ROM LS mean CFB by visit



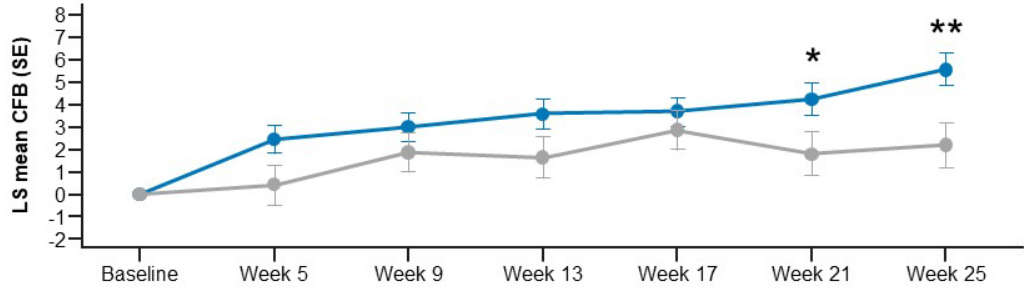
Worst stiffness NRS LS mean CFB by visit



BPI worst pain NRS LS mean CFB by visit



PROMIS-PF T-score LS mean CFB by visit



Treatment: Placebo Pimicotinib

Data cutoff date Sep 23, 2024
*p<0.05 for LS mean group difference at this timepoint; p-values are nominal; **p<0.05 for LS mean group difference at Week 25; p-values are significant (tested in hierarchical order)
CFB, change from baseline; SE, standard error

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

Tolerancja leczenia pimikotynibem

Pimicotinib was well tolerated, with a low rate of dose reductions and treatment discontinuations

TEAEs by week 25, n (%)	Pimicotinib n=63	Placebo n=31
Any TEAE	63 (100)	29 (93.5)
Any treatment-related TEAE	62 (98.4)	18 (58.1)
Any ≥Grade 3 TEAE	22 (34.9)	1 (3.2)
Any serious TEAE[a]	3 (4.8)	1 (3.2)
Any TEAE leading to dose reduction	5 (7.9)[b]	0
Any TEAE leading to dose interruption	34 (54.0)[c]	2 (6.5)
Any TEAE leading to treatment discontinuation	1 (1.6)[d]	0

Dose intensity[e] remained high (median 94.6%) despite treatment interruptions in the pimicotinib arm

Data cutoff date Sep 23, 2024

[a]Serious TEAEs in the pimicotinib arm included infectious enterocolitis, increased blood pressure, and erythema nodosum, and in the placebo arm included prostate cancer. Only increased blood pressure was considered related to pimicotinib by the investigator; [b]Dermatitis, rash, fatigue, headache, hypersomnia, and blood CPK increase each occurring in 1 patient, all Grade 1 or 2 TEAEs; [c]Including 14 Grade ≥3 TEAEs; [d]Grade 2 fatigue; [e]Percentage intended dose

Bezpieczeństwo leczenia pimikotynibem

Most frequent (≥20%) and class-specific TEAEs with pimicotinib

Most common TEAEs (≥20%) by Week 25, n (%)	Pimicotinib n=63		Placebo n=31	
Preferred term	**All grades**	**Grade 3/4**	**All grades**	**Grade 3/4**
Clinical AEs				
Pruritus	33 (52.4)	2 (3.2)	1 (3.2)	0
Face edema	30 (47.6)	0	0	0
Rash	22 (34.9)	2 (3.2)	0	0
Periorbital edema	20 (31.7)	0	3 (9.7)	0
Fatigue	18 (28.6)	0	7 (22.6)	0
Nausea	17 (27.0)	0	2 (6.5)	0
Headache	13 (20.6)	0	2 (6.5)	0

- There was no evidence of hair/skin hypopigmentation
- TEAEs of hypertension occurred in 14.3% of patients treated with pimicotinib (Grade 3, 3.2%)

Most common TEAEs (≥20%) by Week 25, n (%)	Pimicotinib n=63		Placebo n=31	
Preferred term	**All grades**	**Grade 3/4**	**All grades**	**Grade 3/4**
Laboratory AEs[a]				
Blood CPK increased	45 (71.4)	8 (12.7)	5 (16.1)	0
Blood LDH increased	36 (57.1)	0	0	0
AST increased	34 (54.0)	0	3 (9.7)	0
Amylase increased	22 (34.9)	0	0	0
α-HBDH increased	16 (25.4)	0	0	0
Lipase increased	15 (23.8)	2 (3.2)	1 (3.2)	0

- In the pimicotinib arm, AST/ALT elevations were mainly Grade 1 (50.8%/15.9%; Grade 2 3.2%/1.6%), and there was no evidence of cholestatic hepatotoxicity or drug-induced liver injury

Data cutoff date Sep 23, 2024; [a]Laboratory abnormalities were all asymptomatic and responded well to brief dose interruptions. Asymptomatic serum enzyme elevations were consistent with the known mechanism of action of CSF-1R inhibitors;
α-HBDH, alpha hydroxybutyrate dehydrogenase; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; LDH, lactate dehydrogenase

PRESENTED BY: Hans Gelderblom, M.D. Department of Medical Oncology, Leiden University Medical Center, Leiden, The Netherlands

2025 ASCO ANNUAL MEETING

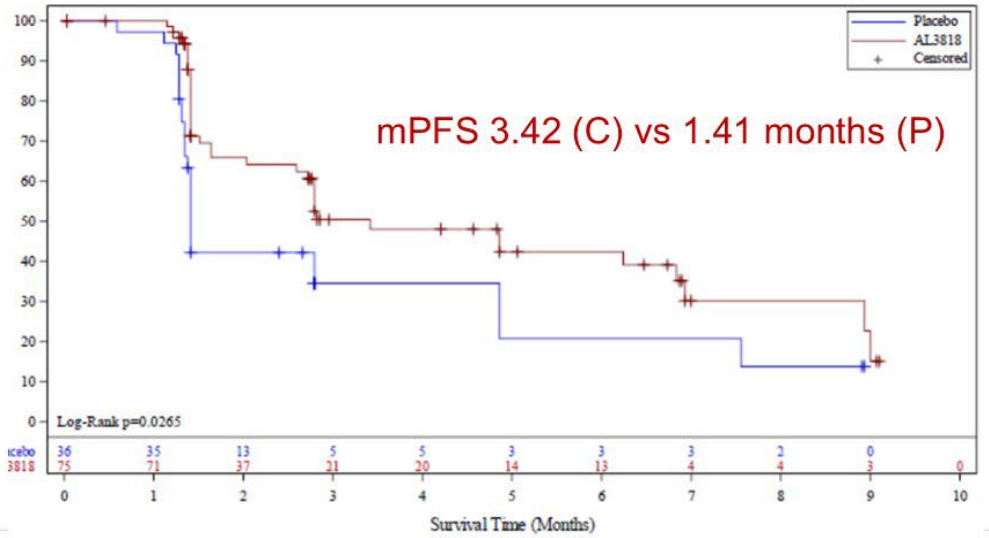
Randomized Phase III Trial of Catequentinib Hydrochloride (AL3818) versus Placebo in Metastatic or Advanced Leiomyosarcoma

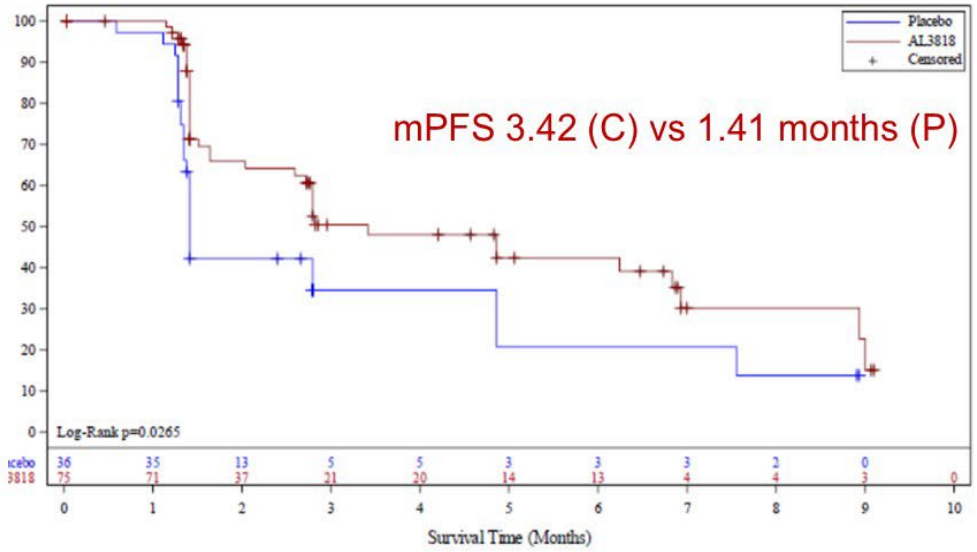
Robin L Jones, Neal Shiv Chawla, Steven Attia, Seth Pollack, Lee D. Cranmer, Antonio Lopez-Pousa, Mahesh Seetharam, Melissa Amber Burgess, Bartosz Chmielowski, Brittany L Siontis, Jonathan C. Trent, Breelyn A. Wilky, Nam Bui, Rashmi Chugh, Neeta Somaiah, Brian Andrew Van Tine, Sant P. Chawla

- Catequentinib is a novel kinase inhibitor: VEGFR, PDGFR, FRGR, c-KIT, RET.
- 110 patients with advanced LMS (uLMS 49)
- 2:1
- 31 crossed over to active treatment upon progression
- PFS primary endpoint

Catequentinib is a new active agent for patients with leiomyosarcoma.

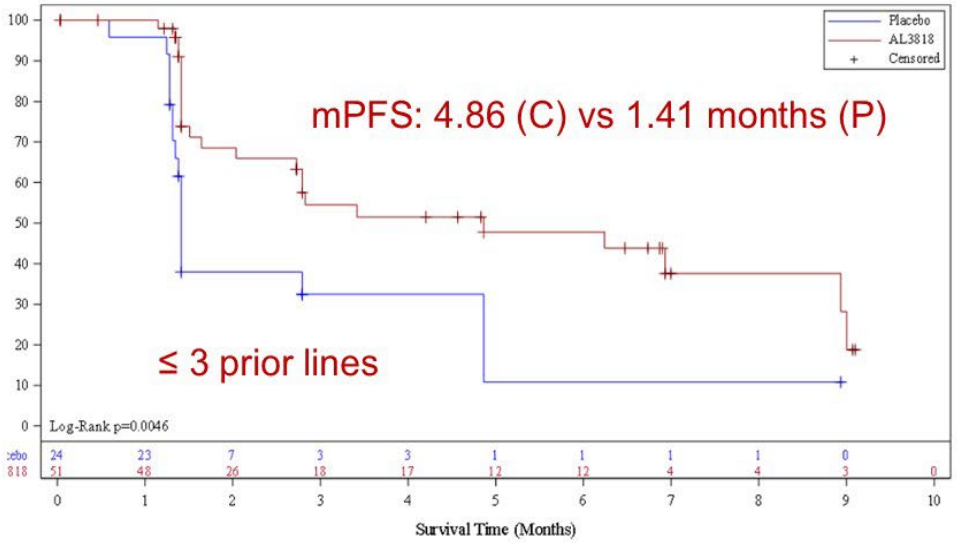
Catequentinib (INN; formerly **anlotinib**)

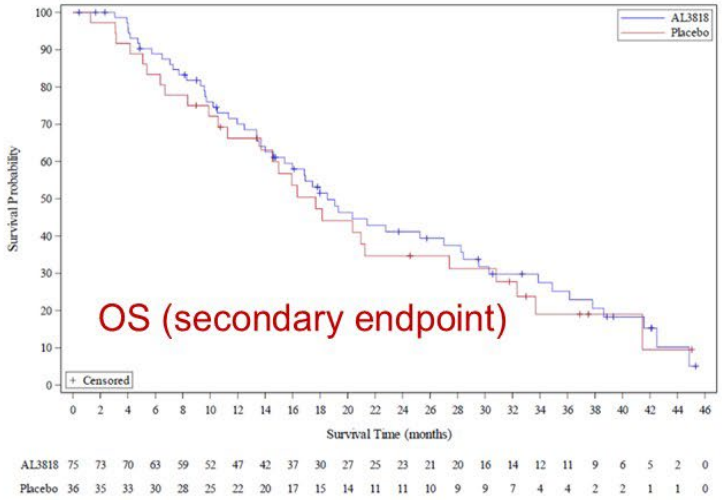




Phase III Catequentinib - Results[5]

- PFS: 3.4 vs 1.4 months
- Benefit is higher is patient that received 3 or fewer lines of treatment with PSF 4.8 months
- No survival advantage
- No unexpected toxicity





Jones ASCO 2025

Later Lines Therapies for LMS- selected trials

	LMS (uLMS)	PFS (months)	ORR (%)	OS	Author
Trabectedin FDA APPROVED	252 LMS (134)	4.3 4.0 (uLMS)	9.9	12.4	Demetri, 2015 Hensley, 2017
Eribulin	152 (68)	2.2	5	12.7	Schoffski, 2016
Dacarbazine	126 (78) 145 (73)	1.6 – 2.6	6.9 - 7	12.9 - 13	Demetri, 2015 Schoffski, 2016
Pazopanib FDA APPROVED	142	4.6	6	12.5	van der Graaf, 2012
Catequentinib	110	3.4 vs 1.4 >3 L 4.8 vs 1.4 ≤ 3 L	2.27	17.4 vs 16.3	Jones, ASCO 2025

- Limited options for later-lines treatment
- Trabectedin now is often used in the as first line in combination and maintenance
- PFS of Catequentinib in line with other agents
- ORR is low across studies

- Palliative treatment: disease control while preserving QoL
- Personalized treatment decisions: patient preference, prior toxicities, route of administration
- A new oral agent is a welcome addition to the treatment landscape

XXIV SPOTKANIE Po ASCO

2025 ASCO ANNUAL MEETING

Subgroup Analysis of the Phase 2 Part of the RINGSIDE Phase 2/3 Trial of Varegacestat for Treatment of Desmoid Tumors

Rashmi Chugh, MD

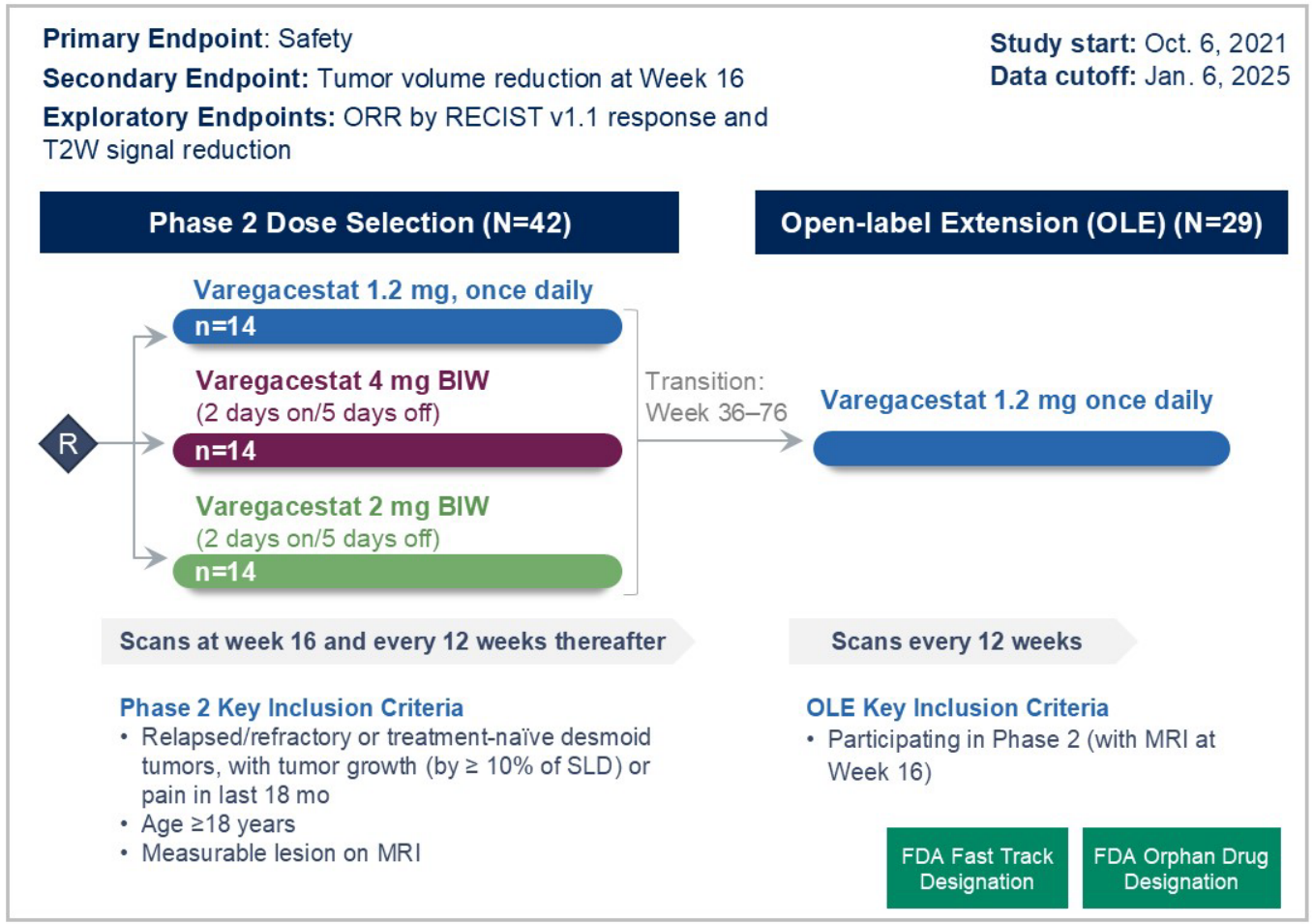
University of Michigan, Ann Arbor, MI, USA

Co-authors: Mrinal Gounder, MD, Arun Singh, MD, Brian A. Van Tine, MD, PhD, Vladimir Andelkovic, MD, Janet Yoon, MD, Edwin Choy, MD, PhD, Jeremy Lewin, MBBS, Javier Martin-Broto, MD, PhD, Ravin Ratan, MD, Nam Bui, MD, Winette van der Graaf, MD, PhD, Lara Davis, MD, Atrayee Basu Mallick, MD, HyoSong Kim, Robin L. Jones, MD, Eric Song, PhD, Kathryn Newhall, PhD, Jonathan Yovell, MD, Bernd Kasper, MD, PhD

Badanie RINGSIDE- desmoid tumor

Background & Methods: Phase 2 of the RINGSIDE Study

- Desmoid tumors (DTs) are rare locally aggressive connective tissue tumors with variable clinical presentations and behavior and different underlying pathogenic mutations
- Gamma secretase inhibitors (GSIs) have biological rationale and have shown anti-tumor activity in DTs
- RINGSIDE Phase 2 demonstrated safety and responses in patients with DTs when treated with the GSI varegacestat (AL102)[1]
- We evaluated treatment responses in key patient subgroups to determine if signals of activity were broad or limited



1. Kasper B, et al. European Society for Medical Oncology Annual Meeting, Sep.13-17, 2024, Barcelona, Spain.

Badanie RINGSIDE- varegacestat

Baseline Characteristics & Safety Summary

- 42 participants (pts) enrolled, 29 (69%) entered the OLE
- 12 pts (29%) still on treatment
- Median time on treatment: 23.3 months (0.7 – 38.8)

Characteristics		All patients all doses (N=42)
Age (years), median (min, max)		38.5 (19-72)
Sex, n (%)	Female	31 (73.8)
	Male	11 (26.2)
ECOG Performance Status, n (%)	0	35 (83.3)
	1	7 (16.7)
Tumor Location at Screening, n (%)		
Intra Abdominal		12 (28.6)
Extra Abdominal		30 (71.4)
Tumor size at baseline by BICR, (mm) median (min, max)		69.40 (17.0, 156.2)
Prior DT Therapy, n (%)	Systemic	29 (69.0)
	Surgery	19 (45.2)
	Radiation	4 (9.5)

- 8 pts (19%) had a serious adverse event (AE)
- 9 pts (21%) discontinued due to an AE
- 14 (33%) pts had treatment-related Grade 3 AEs | No Grade 4-5 AEs

Most Common Adverse Events, n (%)	All patients all doses (N=42)	
	All Grades	Grade ≥3*
Diarrhoea	35 (83.3)	5 (11.9)
Nausea	23 (54.8)	0
Fatigue	22 (52.4)	2 (4.8)
Hypophosphatemia	15 (35.7)	0
Stomatitis	15 (35.7)	1 (2.4)
Cough	14 (33.3)	1 (2.4)
Headache	14 (33.3)	0
Rash	14 (33.3)	0
Alopecia	13 (31.0)	0
Dry mouth	13 (31.0)	0
Dry skin	13 (31.0)	0

*No Grade 4 or Grade 5 events were reported

2025 ASCO ANNUAL MEETING

Alliance A092104: A randomized phase 2/3 study of olaparib plus temozolomide versus investigator's choice for the treatment of patients with advanced uterine leiomyosarcoma after progression on prior chemotherapy

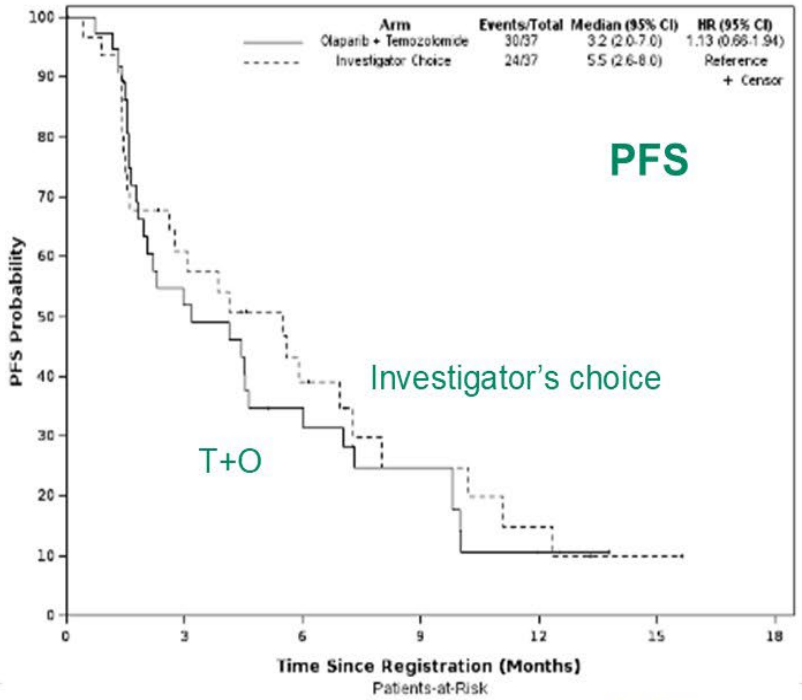
Brian A. Van Tine, M.D., Ph.D.

Washington University School of Medicine, Saint Louis, MO, USA

Co-authors: Jacob B. Allred, Martee Leigh Hensley, Rebecca Christian Arend, John A. Charlson, Gina Z. D'Amato, Teresa Lee, Elizabeth Trice Loggers, Stephanie A. Berg, Matthew Ingham, Sumithra J. Mandrekar, Pamela N. Munster, Gary K. Schwartz

- Phase II/III
- 74 patients with advanced uLMS
- Temozolomide (T) + Olaparib (O) vs Investigator Choice treatment (Pazopanib or Trabectedin)
- PFS/OS endpoints
- Accrual met (exceeded expectations)
- Trial closed for futility during phase II

The combination of Olaparib and Temozolomide provides only limited benefit in an unselected population of patients with uterine LMS (uLMS).



Sunitynib + niwolumab w extraskeletal myksoid chondrosarcoma

2025 ASCO ANNUAL MEETING

GEIS GRUPO ESPAÑOL DE INVESTIGACIÓN EN SARCOMAS

Italian Sarcoma Group

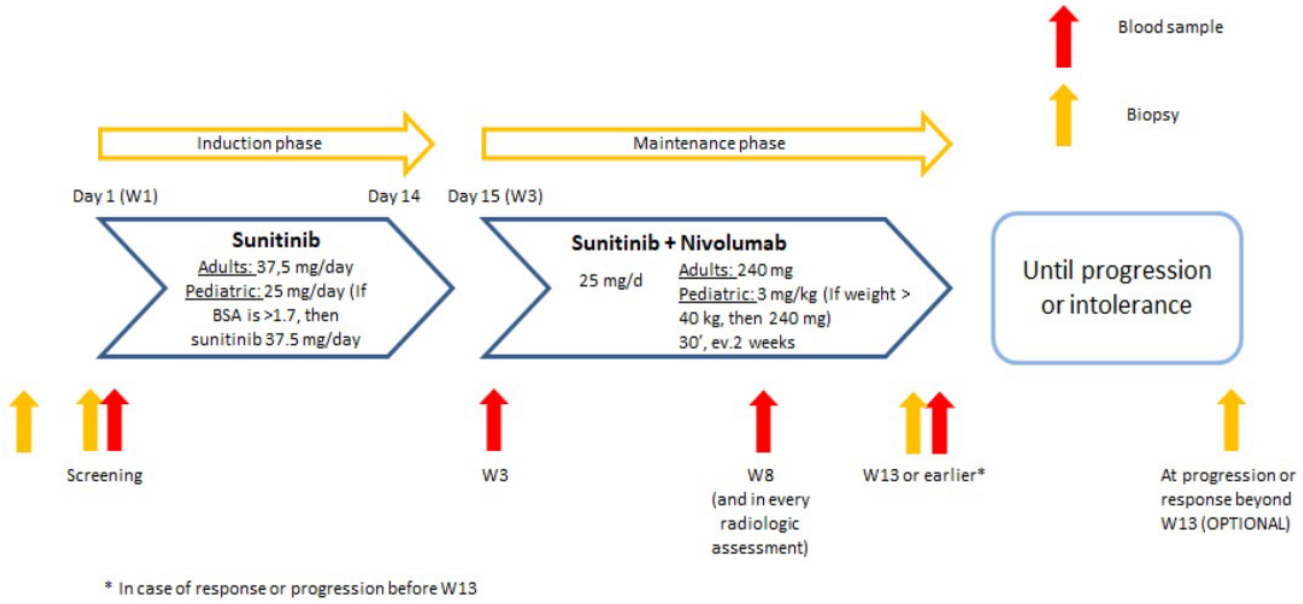
UCL

Phase II of sunitinib plus nivolumab in extraskeletal myxoid chondrosarcoma: Results from the GEIS, ISG, and UCL IMMUNOSARC II Study

Nadia Hindi[1,2], Emanuela Palmerini[3], Irene Carrasco-Garcia[4], Enrique González Billalabeitia[5], Claudia Valverde[6], Sandra J. Strauss[7], Toni Ibrahim[3], Ana Sebio[8], Robert Díaz-Beveridge[9], Javier Martínez-Trufero[10], Silvia Stacchiotti[11], Paola Collini[11], Roberto Tirabosco[12], Rafael Ramos[13], Antonio Gutierrez[13], David Silva Moura[2], Javier Martin Broto[1,2]

1. Fundación Jimenez Diaz University Hospital, Madrid, Spain; University Hospital General de Villalba, Madrid, Spain; 2. Instituto de Investigacion Sanitaria Fundacion Jimenez Diaz (IIS/FJD; UAM), Madrid, Spain; 3. Osteoncologia, Sarcomi dell'Osso e dei Tessuti Molli, e Terapie Innovative - IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy; 4. Hospital Universitario Virgen del Rocio, Seville, Spain; 5. Hospital Universitario 12 de Octubre, Madrid, Spain; 6. Vall d'Hebron University Hospital, Barcelona, Spain; 7. University College of London, London, United Kingdom; 8. Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; 9. Hospital Universitario y Politécnico La Fe, Valencia, Spain; 10. Instituto Aragonés de Investigación Sanitaria, Hospital Universitario Miguel Servet, Zaragoza, Spain; 11. Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 12. Royal National Orthopaedic Hospital, Stanmore, United Kingdom; 13. University Hospital Son Espases, Mallorca, Spain.

Leczenie EMC sunitynib + niwolumab



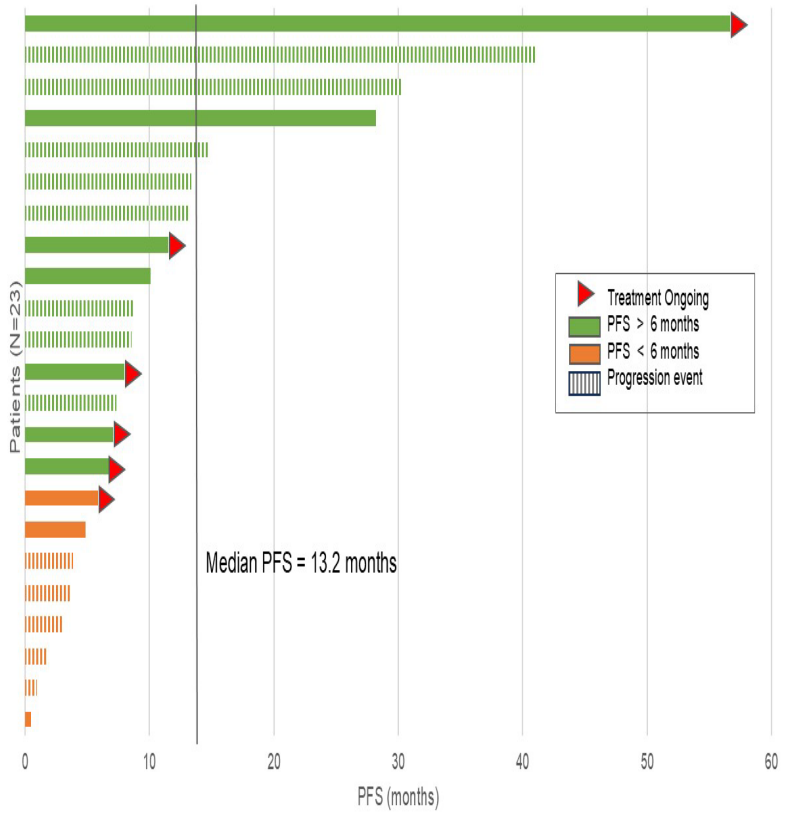
- INCLUSION CRITERIA:
  - > 18 years
  - Advanced irresectable/metastatic disease
  - Progressive disease, measurable (RECIST 1.1)
  - Centrally confirmed diagnosis
- CT/MRI every 8 weeks.
- **Primary endpoint**: 6-month-PFS rate
- <u>Statistical assumptions:</u>

6m-PFSR in at least 15 out of 22 patients, with H_0= 50% and H_1= 80%, (α 0.05; β 0.10).

Wyniki leczenia sunitynib + niwolumab w EMC

Reasons for treatment discontinuation:

- Progression: 12 (50%)
- Lost to follow-up: 3 (12%)
- Patient consent withdrawal: 1 (4%)
- Advanced dementia: 1 (4%)
- Early non-related death: 1 (4%)
- Ongoing: 6 (25%)



Overall Response Rate: 9%

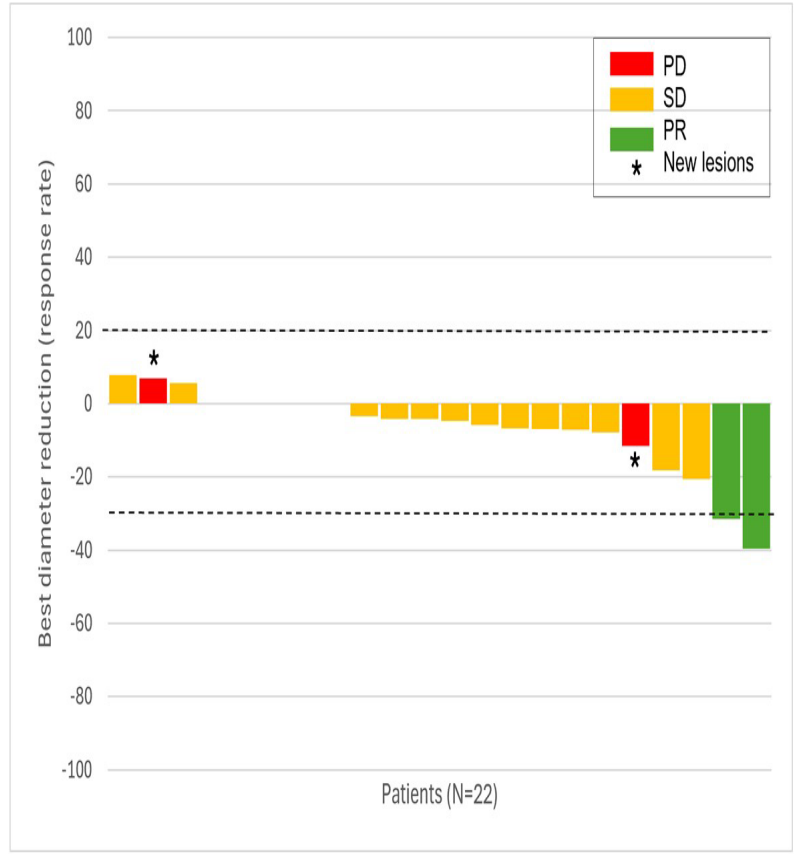
Clinical Benefit Rate: 91%

63% patients experienced any tumor shrinkage

2(9%) PR

18 (82%) SD

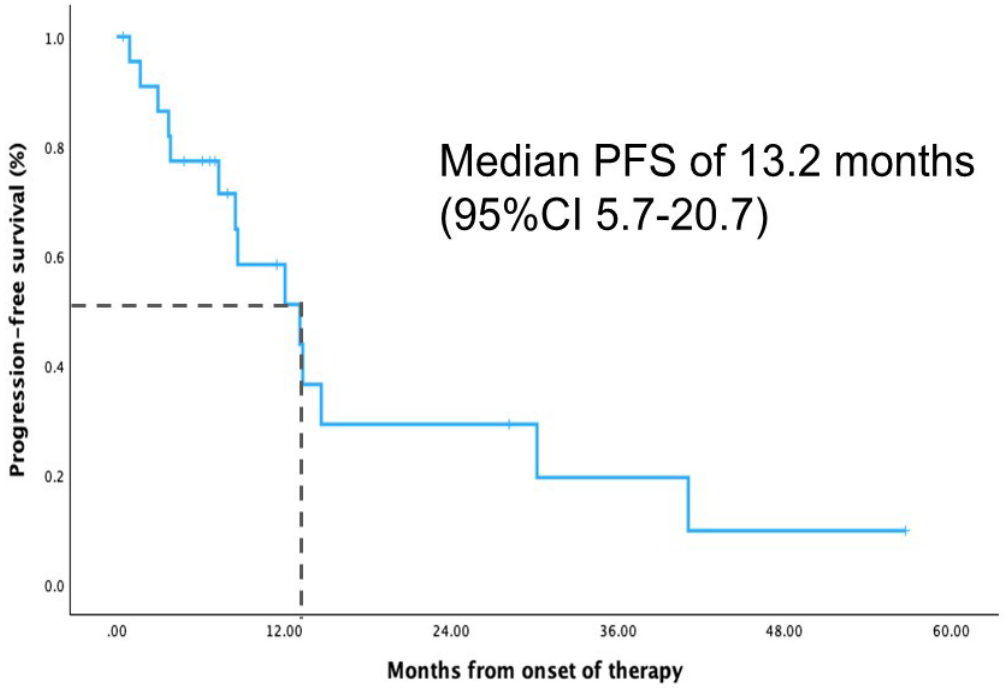
2 (9%) PD



2025 ASCO #ASCO25 PRESENTED BY: Nadia Hindi, MD, MSc
ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Wyniki leczenia sunitynib + niwolumab w EMC

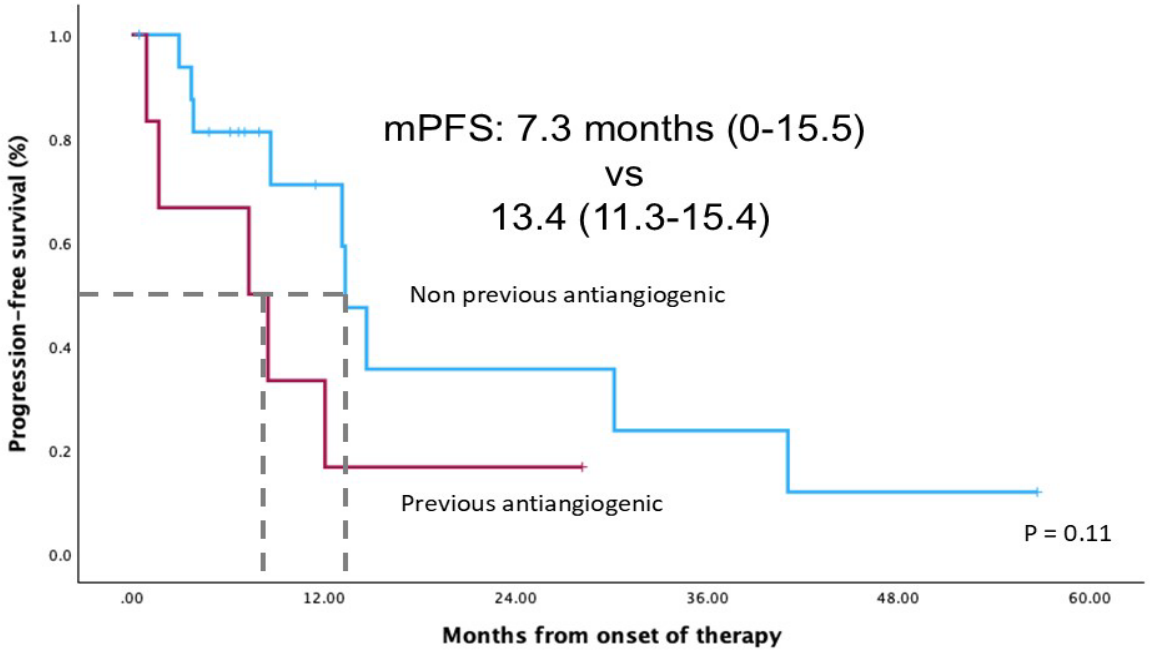
- Median Follow-up: 18 months (95% CI 8-29)
- **6m-PFSR was 77%** with 16/23 patients free of progression at 6 months
- Median OS has not been reached and **12m-OS was 90%** (95%CI 77-100).

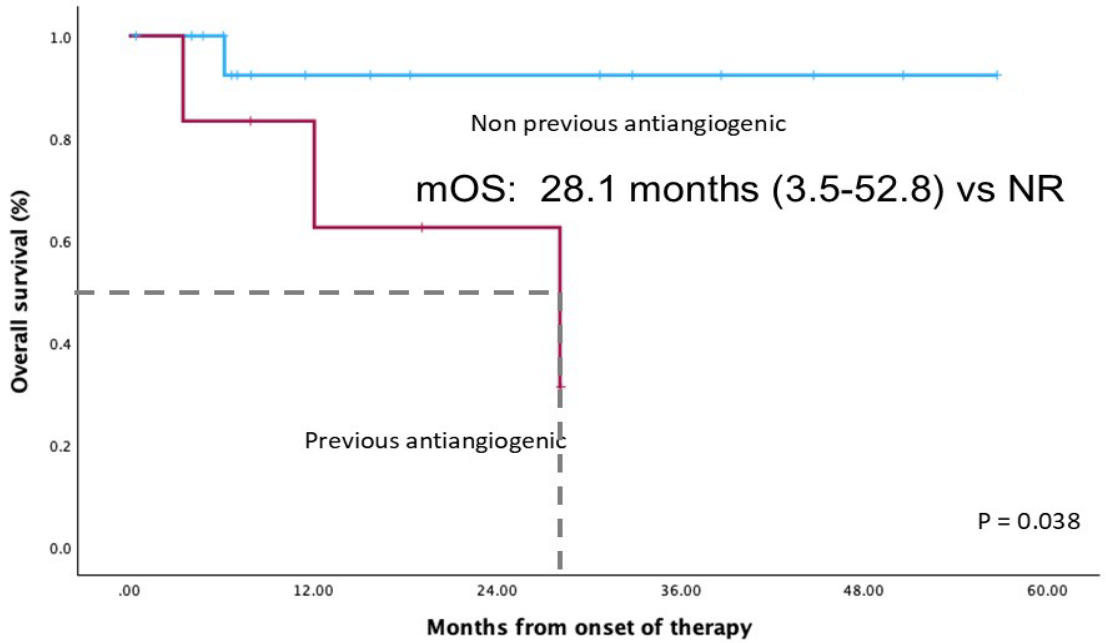


Median PFS of 13.2 months (95%CI 5.7-20.7)

Wyniki leczenia sunitynib + niwolumab w EMC

Results: Outcomes (IV)





Patients (6/23) previously treated with antiangiogenic had a trend towards a shorter mPFS and a significantly shorter OS (28 months vs NR, p = 0.038).

Bezpieczeństwo leczenia sunitynib + niwolumab w EMC

Results: adverse events

EVENT	ANY GRADE	GRADE 1-2	GRADE 3	GRADE 4
Thrombocytopenia	13 (54.2%)	12 (50.0%)	1 (4.2%)	0
Neutropenia	12 (50.0%)	10 (41.7%)	2 (8.3%)	0
Leukopenia	10 (41.7%)	7 (29.2%)	2 (8.3%)	1 (4.2%)
Lymphocytopenia	7 (29.2%)	4 (16.7%)	3 (12.5%)	0
Anemia	4 (16.7%)	3 (12.5%)	1 (4.2%)	0
Lymphocytosis	4 (16.7%)	2 (8.3%)	2 (8.3%)	0
Leukocytosis	1 (4.2%)	1 (4.2%)	0	0

Most common Grade 3-4 Adverse Events (AE) were: ALT and AST increase (16.7 and 12.5% respectively), bilirubin increase (12.5%), Lymphocytopenia (12.5%).

No toxic deaths were registered

EVENT	ANY GRADE	GRADE 1-2	GRADE 3	GRADE 4
Diarrhea	12 (50.0%)	11 (45.8%)	1 (4.2%)	0
Fatigue	10 (41.7%)	9 (37.5%)	1 (4.2%)	0
ALT increased	9 (37.5%)	5 (20.8%)	3 (12.5%)	1 (4.2%)
Hypertension	8 (33.3%)	7 (29.2%)	1 (4.2%)	0
Mucositis oral	8 (33.3%)	7 (29.2%)	1 (4.2%)	0
Pain	8 (33.3%)	6 (25.0%)	2 (8.3%)	0
Dysgeusia	6 (25.0%)	6 (25.0%)	0	0
AST increased	6 (25.0%)	3 (12.5%)	3 (12.5%)	0
Anorexia	5 (20.8%)	5 (20.8%)	0	0
Blood bilirubin increased	5 (20.8%)	2 (8.3%)	2 (8.3%)	1 (4.2%)
Skin and hair efects	5 (20.8%)	5 (20.8%)	0	0
ALP increased	4 (16.7%)	4 (16.7%)	0	0
GGT increased	4 (16.7%)	4 (16.7%)	0	0
Vomiting	3 (12.5%)	3 (12.5%)	0	0
Dry mouth	2 (8.3%)	2 (8.3%)	0	0
Constipation	2 (8.3%)	2 (8.3%)	0	0
Creatinine increased	2 (8.3%)	2 (8.3%)	0	0
Gastroesophageal reflux disease	2 (8.3%)	2 (8.3%)	0	0
Headache	2 (8.3%)	2 (8.3%)	0	0
Hyperkalemia	2 (8.3%)	1 (4.2%)	0	1 (4.2%)
Hyperthyroidism	2 (8.3%)	2 (8.3%)	0	0
Hypokalemia	2 (8.3%)	1 (4.2%)	1 (4.2%)	0
Pneumonitis	2 (8.3%)	2 (8.3%)	0	0

2025 ASCO ANNUAL MEETING

GEIS
GRUPO ESPAÑOL DE INVESTIGACION EN SARCOMA

ImmunoSarc II (Cohort 7a): A Spanish Sarcoma Group (GEIS) phase Ib trial of epirubicin and ifosfamide plus nivolumab in first line of advanced Undifferentiated Pleomorphic Sarcoma (UPS)

Javier Martin-Broto[1], Javier Martinez-Trufero[2], Roberto Diaz-Beveridge[3], Irene Carrasco[4], David Moura[1], Ana Sebio[5], Enrique González.Billalabeitia[6], Rafael Ramos[7], Antonio Gutierrez[7], Josefina Cruz-Jurado[8], Claudia Valverde[9], Patricio Ledesma[10], Nadia Hindi[1]

(1) Hospital Universitario Fundación Jiménez Díaz; (2) Hospital Universitario Miguel Servet ; (3) Hospital Universitari i Politècnic la Fe; (4) Hospital Universitario Virgen del Rocío; (5) Hospital de la Santa Creu i Sant Pau; (6) Hospital Universitario 12 de Octubre; (7) Hospital Universitari Son Espases; (8) Hospital Universitario de Canarias; (9) Hospital Universitari Vall d'Hebron; (10) Sofpromed Clnical Research

Badanie IMMUNOSARC 7a - konstrukcja

HODS

IMMUNOSARC TRIAL cohort 7A

.- Phase Ib trial with 2 dose-levels: (3+3 design with a range 10-20 evaluable patients)

- **Level 0**: Epirubicin 60 mg/m^2/d d1-2+ Ifosfamide 3 g/m^2/d d1-3 + Nivolumab 360 mg on day 3/ 21d + GCSF
- **Level -1**: Epirubicin 60 mg/m^2/d d1-2+ Ifosfamide 3 g/m^2/d d1-3 + Nivolumab 240 mg on day 3/ 21d + GCSF

.- After 6 cycles, Nivolumab/21d during 1 year as maintenance phase

.- Main Inclusion/Exclusion criteria:

- Anthracycline naïve; Advanced centrally confirmed UPS; ECOG 0-1; Measurable disease

.- Main Endpoint: To determine the MTD/RP2D based on DLTs observed during the first 21-day cycle

.- Secondary Objectives: Safety profile (CTCAE 5.0); ORR (RECIST 1.1); mPFS; mOS; Translational Research

Badanie IMMUNOSARC 7a – wyniki leczenia

.- Median follow-up: 16.3 months (95% CI, 7.2-25.4)

.- #Cycles (combo): 71. Median: 5 (1-6)

.- #Cycles Nivo Maintenance: 98. Median 5 (0-15)

.- **ORR from 16 evaluable patients: 68.8%**

1 CR (6.3%); 10 PR (62.5%); 4 SD (25 %); 1 PD (6.3%)

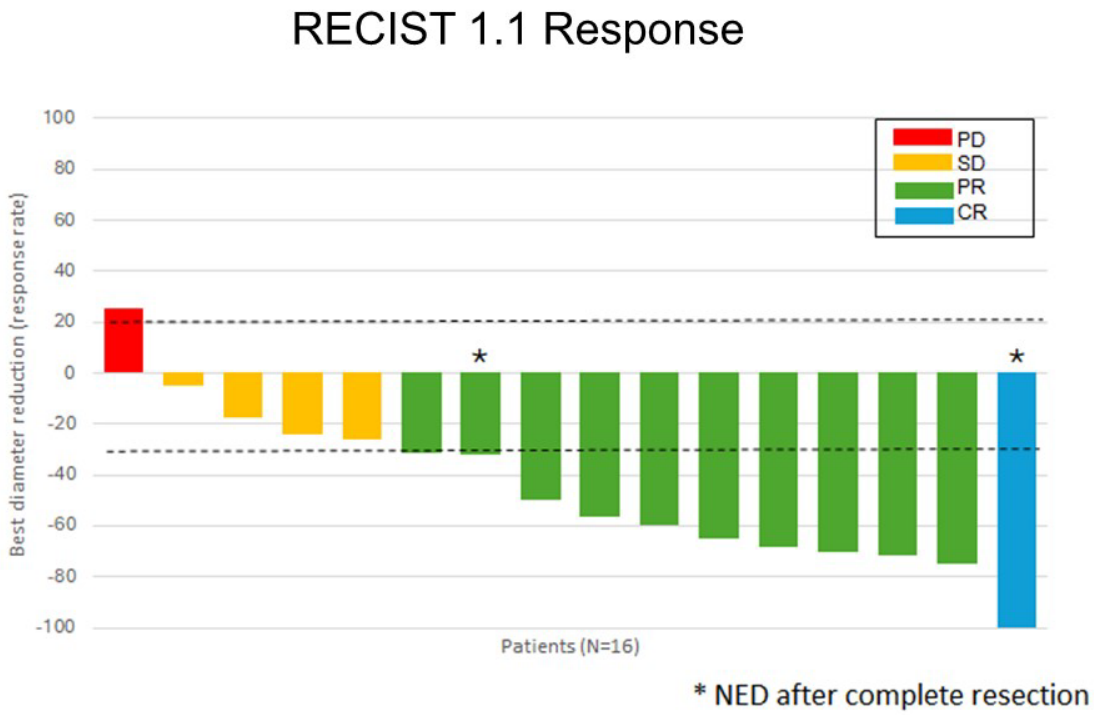
Some Shrinkage in 15 of 16 (94%)

.- mOS not reached

.- 1-Year OS: 81% (95% CI, 62-100)

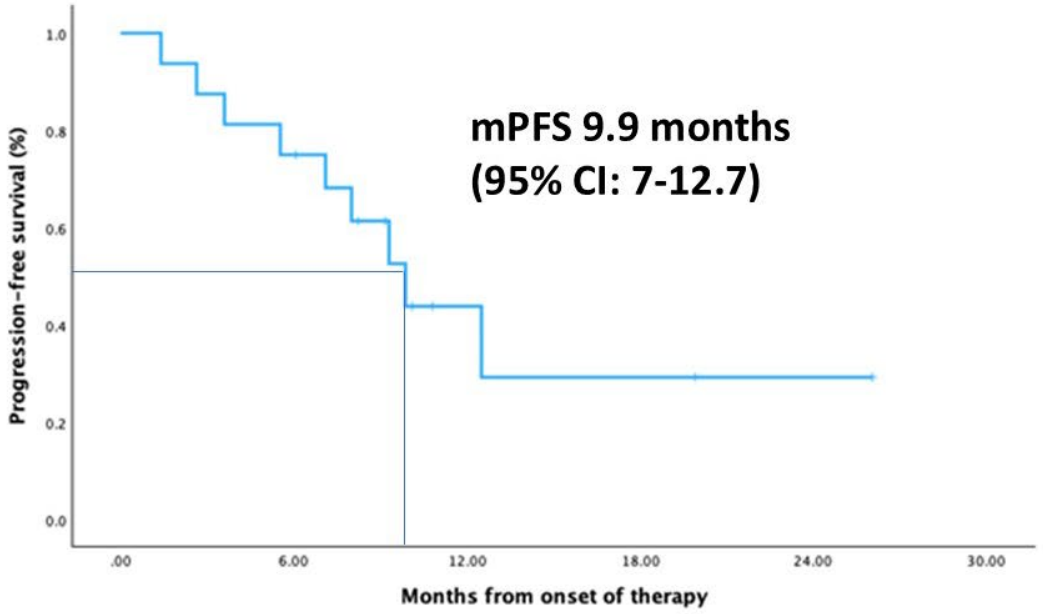
.- **mDOR: not reached**;

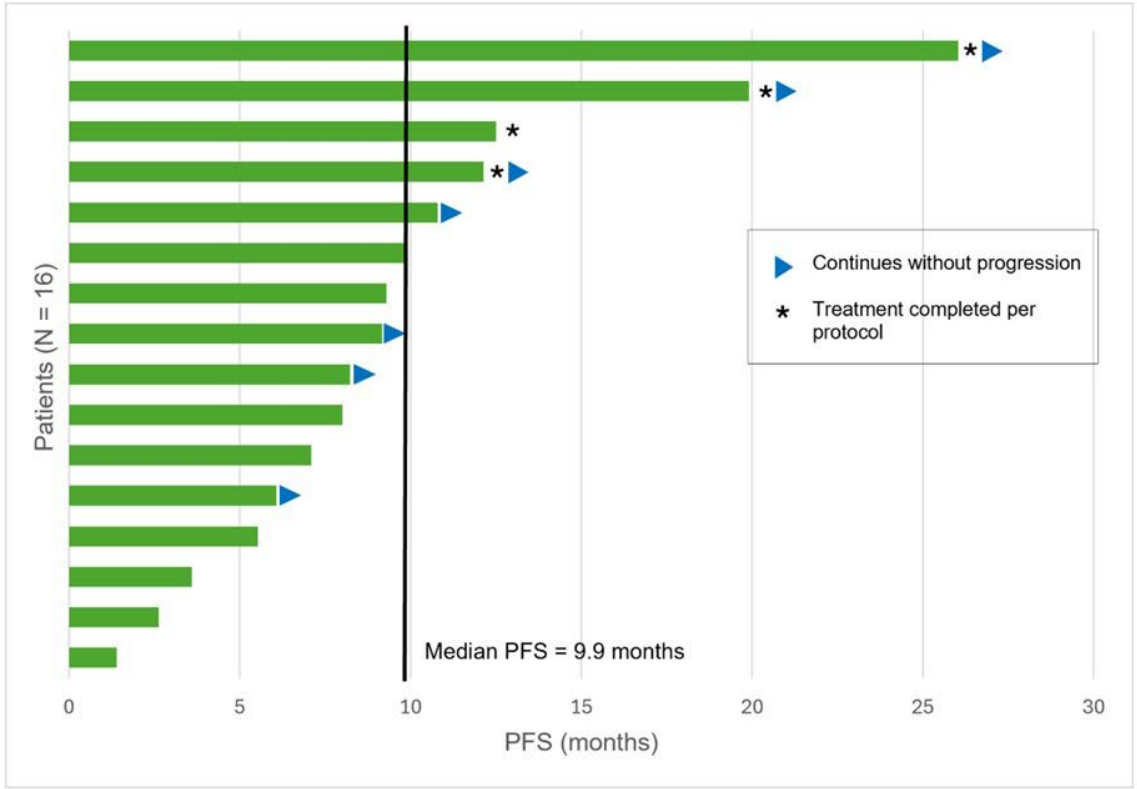
-**18 months 67% without PD (95% CI, 35-98)**



Badanie IMMUNOSARC Wyniki leczenia

- The combination of Epirubicin 60 mg/m^2/d d1-2 + Ifosfamide 3 g/m^2/d d1-3 + Nivolumab 360 mg on day 3 + GCSF every 21 days is <u>feasible and manageable.</u>
- The preliminary <u>activity is highly encouraging</u> (improving historical efficacy/outcomes) as a systemic upfront line in patients with advanced UPS.
- At the time of cutoff, <u>50% of patients had not progression.</u>
- This combination induces <u>prolonged responses.</u>
- <u>This scheme deserve further development in UPS.</u>





Badanie IMMUNOSARC – toksyczność leczenia

ITEM Toxicity CTCAE v6.0	ANY_GRADE	GRADE_1_2	GRADE_3	GRADE_4
Neutropenia	10 (62.5%)	0	3 (18.8%)	7 (43.8%)
Anemia	9 (56.3%)	4 (25.0%)	5 (31.3%)	0
Leukopenia	9 (56.3%)	3 (18.8%)	1 (6.3%)	5 (31.3%)
Thrombocytopenia	9 (56.3%)	5 (31.3%)	2 (12.5%)	2 (12.5%)
Febrile neutropenia	3 (18.8%)	0	0	3 (18.8%)
Pancytopenia	1 (6.3%)	0	0	1 (6.3%)
Asthenia	12 (75.0%)	9 (56.3%)	2 (12.5%)	1 (6.3%)
Nausea	12 (75.0%)	12 (75.0%)	0	0
Mucositis oral	10 (62.5%)	9 (56.3%)	1 (6.3%)	0
Alopecia	6 (37.5%)	6 (37.5%)	0	0
Vomiting	6 (37.5%)	6 (37.5%)	0	0
Dysgeusia	4 (25.0%)	4 (25.0%)	0	0
Anorexia	3 (18.8%)	3 (18.8%)	0	0
Hypocalcemia	3 (18.8%)	3 (18.8%)	0	0
Blood bilirubin increased	2 (12.5%)	2 (12.5%)	0	0
Creatinine increased	2 (12.5%)	2 (12.5%)	0	0
Eye disorders	2 (12.5%)	2 (12.5%)	0	0
Hyperkalemia	2 (12.5%)	2 (12.5%)	0	0
Hypoalbuminemia	2 (12.5%)	2 (12.5%)	0	0
Neurotoxicity	1 (6.3%)	0	0	1 (6.3%)
Pain	2 (12.5%)	2 (12.5%)	0	0

All patients were treated at L0. No DLTs were reported. SARS: Febrile neutropenia 2; G4 Thrombopenia 2; G3 Anemia 1; G3 Tooth infection 1; G3 Dyspnea; G5 CNS hemorrhage after a brain traumatism (thrombopenia G4)

XXIV SPOTKANIE Po ASCO

2025 ASCO ANNUAL MEETING

Badanie fazy 2 gemcytabina + doxorubicyna + docetaxel + niwolumab w leiomyosarcoma i liposarcoma

A phase 2 study using metronomic gemcitabine, doxorubicin and docetaxel plus nivolumab in advanced leiomyosarcoma and liposarcoma

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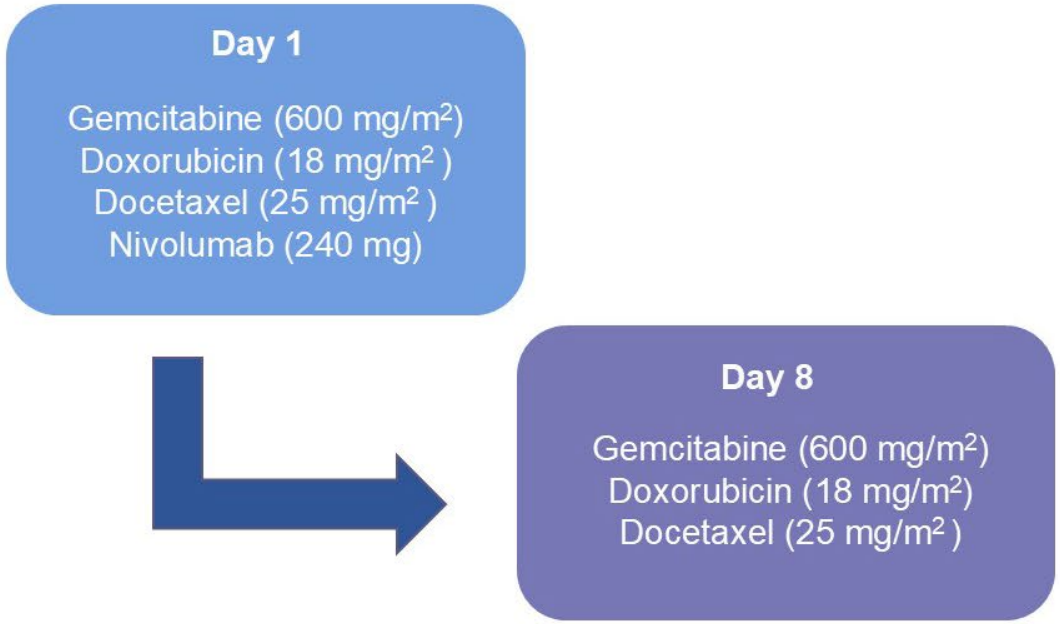

- **Gemcitabine** (600 mg/m^2; max: 1000 mg) on Day 1 and Day 8
- **Doxorubicin** (18 mg/ m^2; max: 32 mg) on Day 1 and Day 8
- **Docetaxel** (25 mg/ m^2; max: 42 mg) on Day 1 and Day 8
- **Nivolumab** (240 mg) on Day 1 only
- Repeat treatment cycles may be given every three weeks if the toxicity grade is $\leq$ 1.

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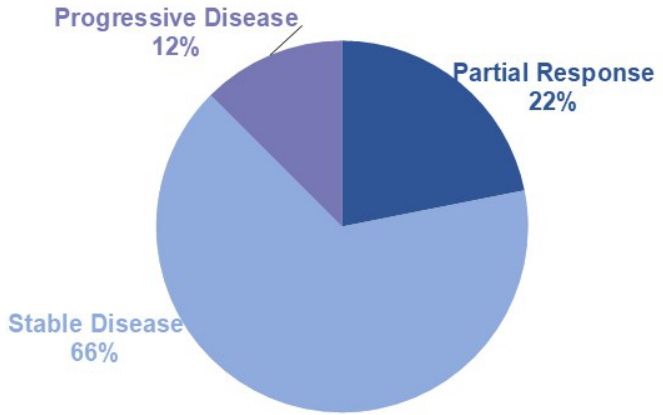
- The intention-to-treat (ITT) population (n = 41) includes patients who received at least one dose of gemcitabine, doxorubicin, and docetaxel.
  - ITT was used to determine median OS and incidence of adverse events.
- The modified-intention-to-treat (MITT) population (n = 31) includes patients who completed at least the first 2 treatment cycles and follow-up CT/MRI.
  - MITT was used to determine median PFS, Overall Response Rate (ORR), Disease Control Rate (DCR), 6-month PFS, 6-month OS, 12-month PFS, and 12-month OS.

Overall Response Rate	Disease Control Rate
22.6%	87.5%



- Best Overall Response = 7 Partial Response, 21 Stable Disease, 4 Progressive Disease

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Results – Progression-Free Survival

Median PFS	6-month PFS	12-month PFS
8.6 months (95% CI: 3.3 – 12.0)	58%	35.5%

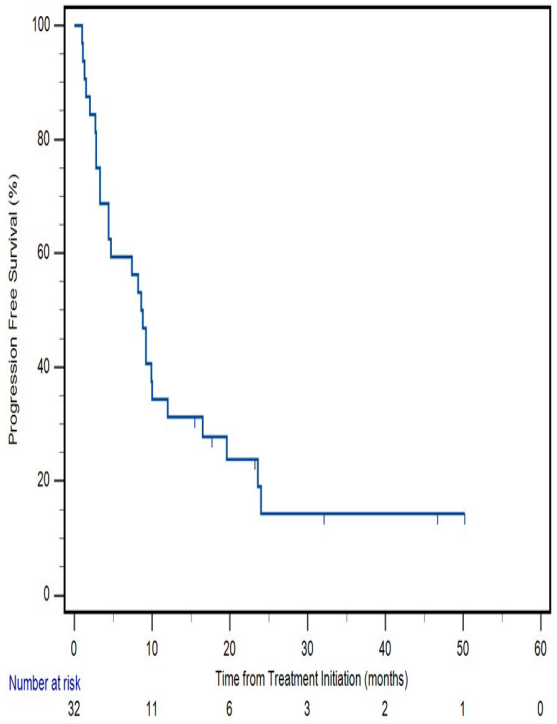

Figure 1: Kaplan-Meier Curve for Progression-Free Survival

Results – Overall Survival

Median OS	6-month OS	12-month OS
16.1 months (95% CI: 7.4 – 20.1)	70.7%	59.1%

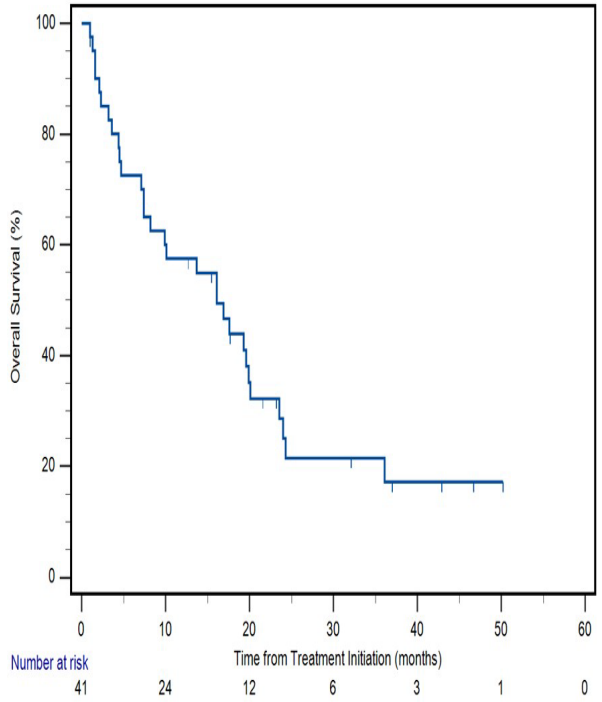

Figure 2: Kaplan-Meier Curve for Overall Survival

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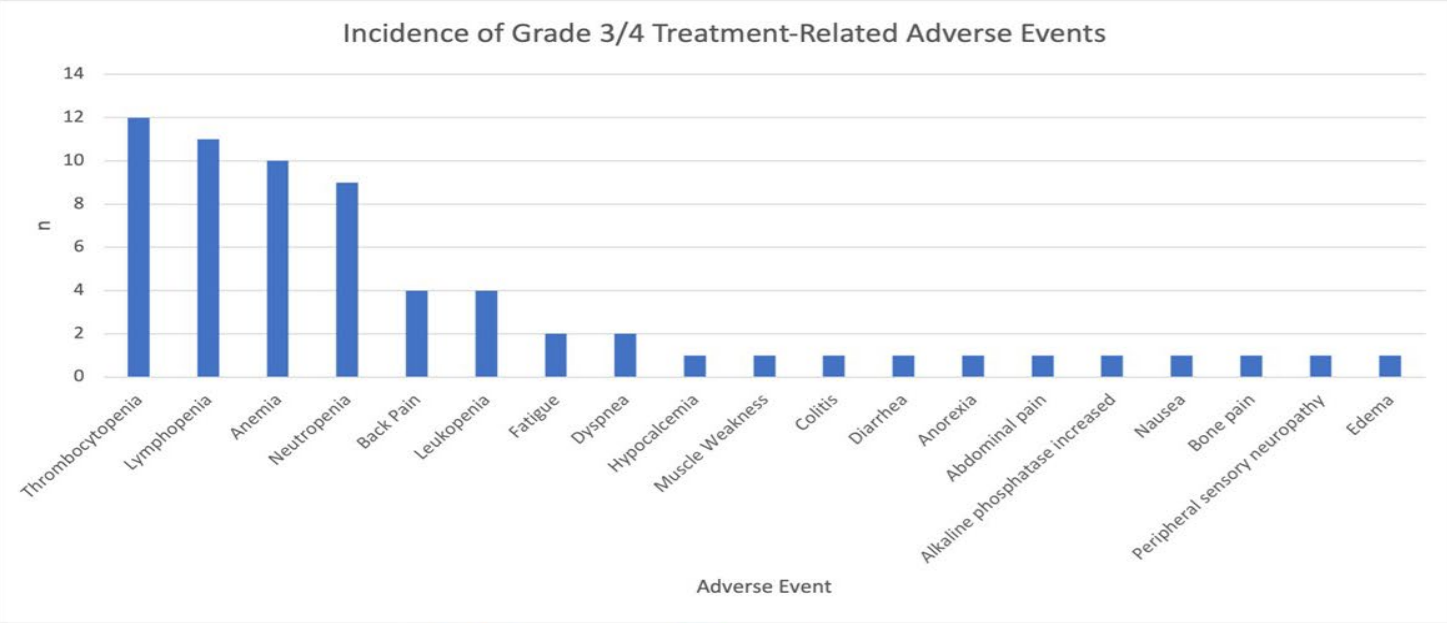
Safety (n = 41)

- 28 of 41 patients (68%) experienced Grade 3/4 Treatment-Related Adverse Events (TRAEs):



- There were no unexpected Adverse Events

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