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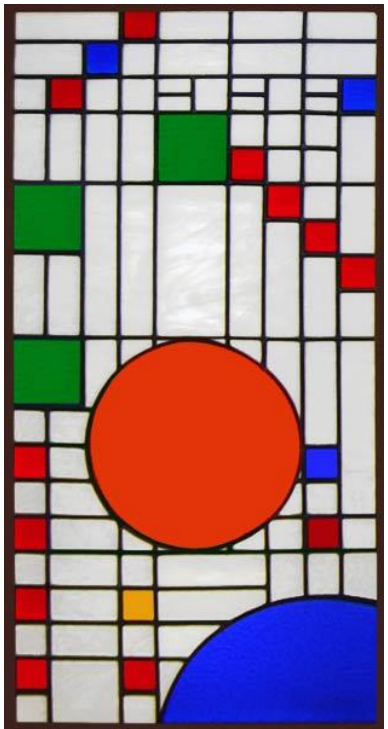
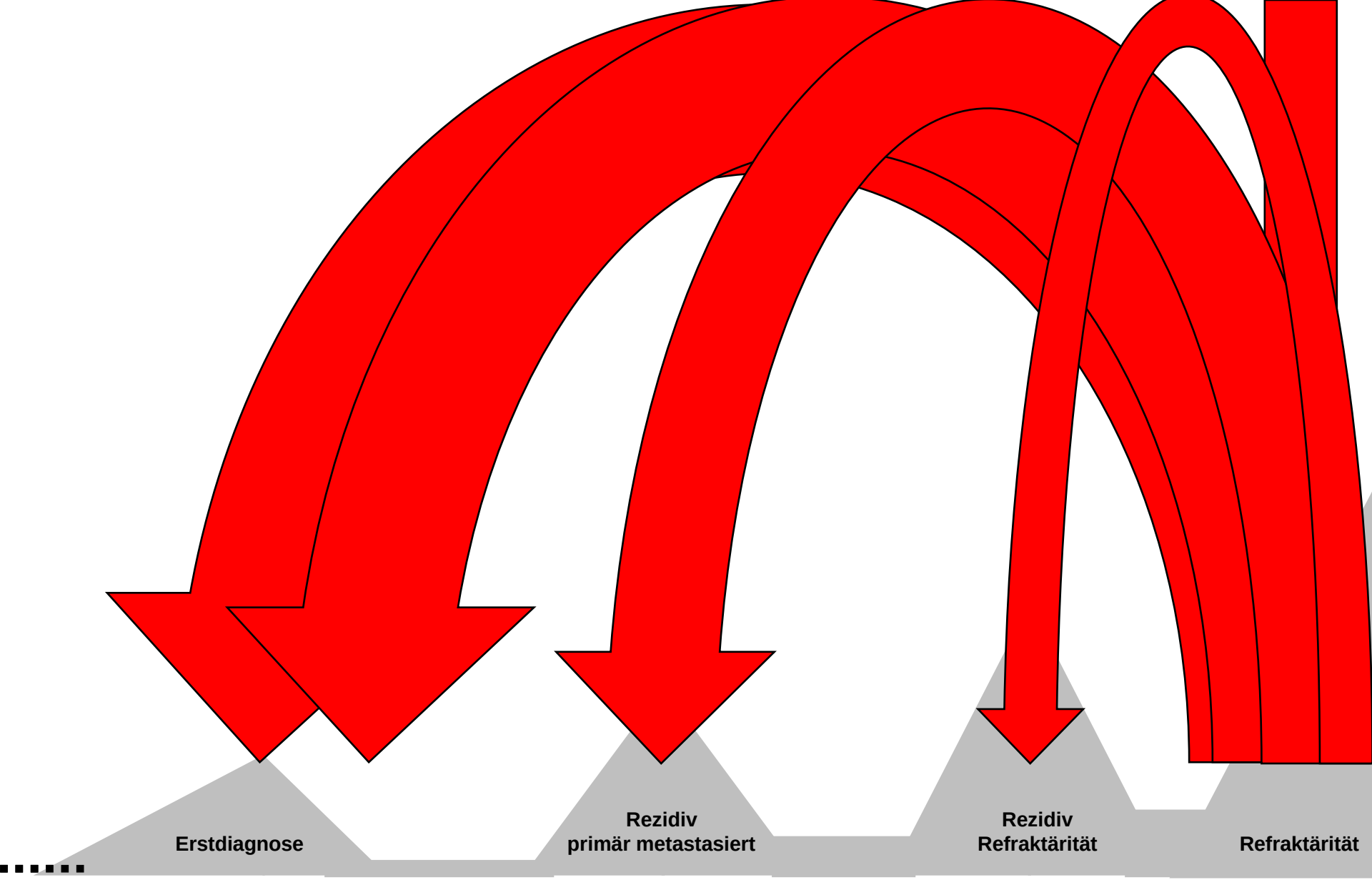
2. – 6. Juni 2023



8. – 11. Juni 2023

- Gliom
- Kolonkarzinom
- Lungenkarzinom
- Mammakarzinom
- Ovarialkarzinom
- Pankreaskarzinom
- Prostatakarzinom
- Rektumkarzinom
- Urothelkarzinom
- Weichgewebssarkom
- Zervixkarzinom

- Akute Myeloische Leukämie
- Hodgkin Lymphom
- Hämochromatose
- Multiples Myelom
- Myelodysplastische Neoplasien
- PMBCL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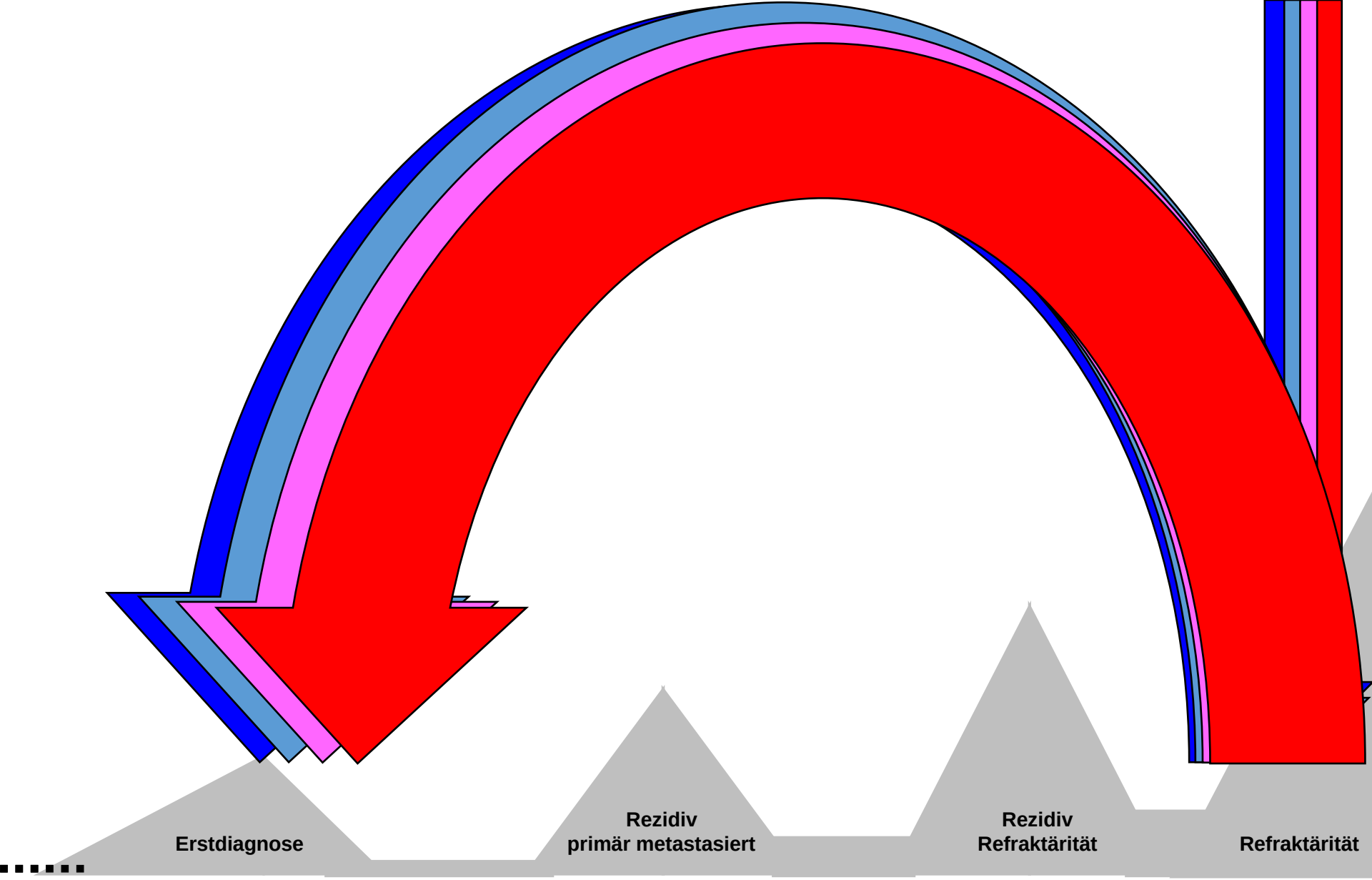
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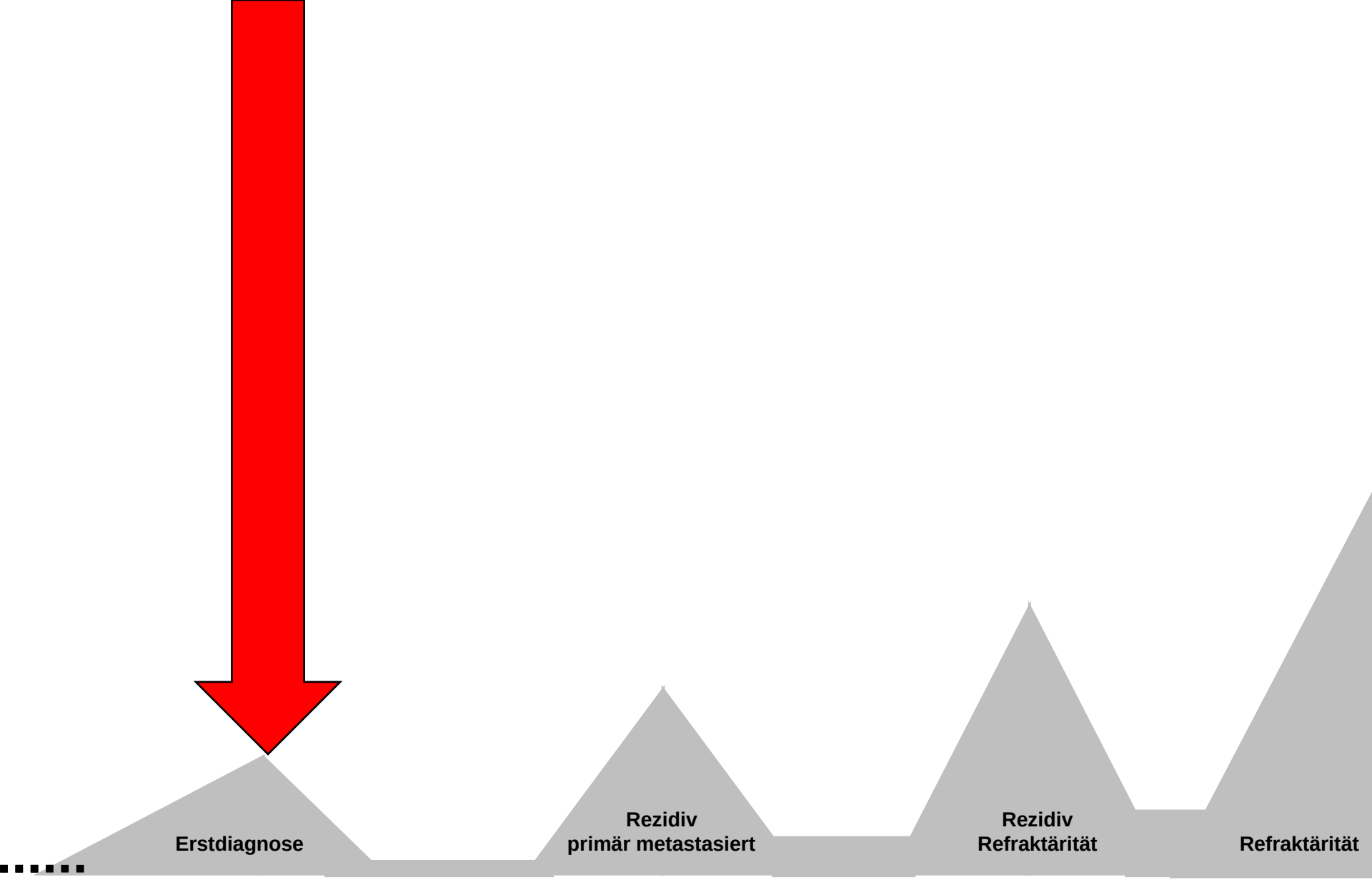
Erstdiagnose
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Refraktärität
Refraktärität

The NEW ENGLAND JOURNAL of MEDICINE

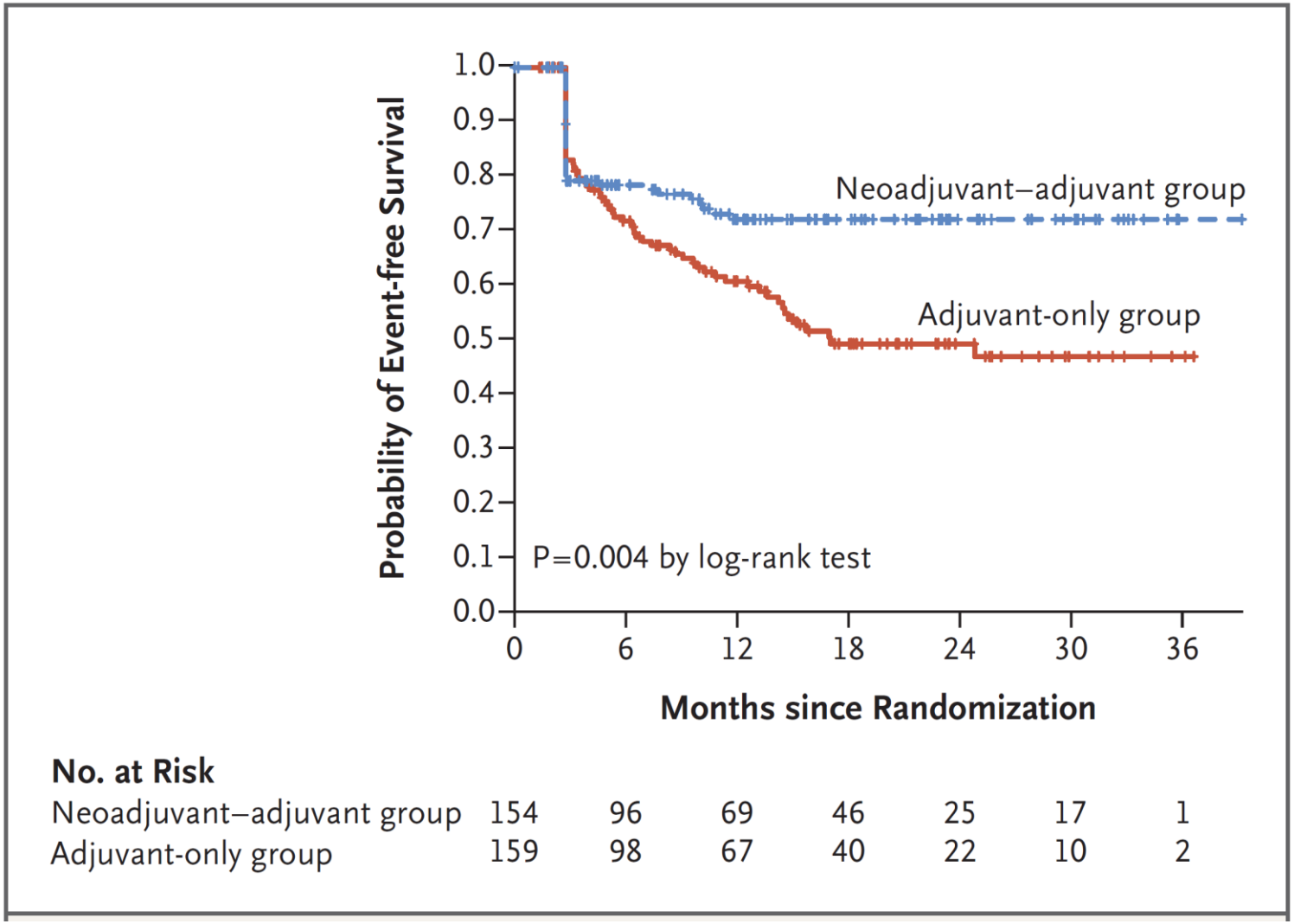
ORIGINAL ARTICLE

Neoadjuvant–Adjuvant or Adjuvant-Only Pembrolizumab in Advanced Melanoma

S.P. Patel, M. Othus, Y. Chen, G.P. Wright, Jr., K.J. Yost, J.R. Hyngstrom, S. Hu-Lieskovan, C.D. Lao, L.A. Fecher, T.-G. Truong, J.L. Eisenstein, S. Chandra, J.A. Sosman, K.L. Kendra, R.C. Wu, C.E. Devoe, G.B. Deutsch, A. Hegde, M. Khalil, A. Mangla, A.M. Reese, M.I. Ross, A.S. Poklepovic, G.Q. Phan, A.A. Onitilo, D.G. Yasar, B.C. Powers, G.C. Doolittle, G.K. In, N. Kokot, G.T. Gibney, M.B. Atkins, M. Shaheen, J.A. Warneke, A. Ikeguchi, J.E. Najera, B. Chmielowski, J.G. Crompton, J.D. Floyd, E. Hsueh, K.A. Margolin, W.A. Chow, K.F. Grossmann, E. Dietrich, V.G. Prieto, M.C. Lowe, E.I. Buchbinder, J.M. Kirkwood, L. Korde, J. Moon, E. Sharon, V.K. Sondak, and A. Ribas

Melanom

Stadium IIIB-IVC, resektabel



No. at Risk

Neoadjuvant–adjuvant group	154	96	69	46	25	17	1
Adjuvant-only group	159	98	67	40	22	10	2

Patel et al., NEJM 3/2023

NSCLC

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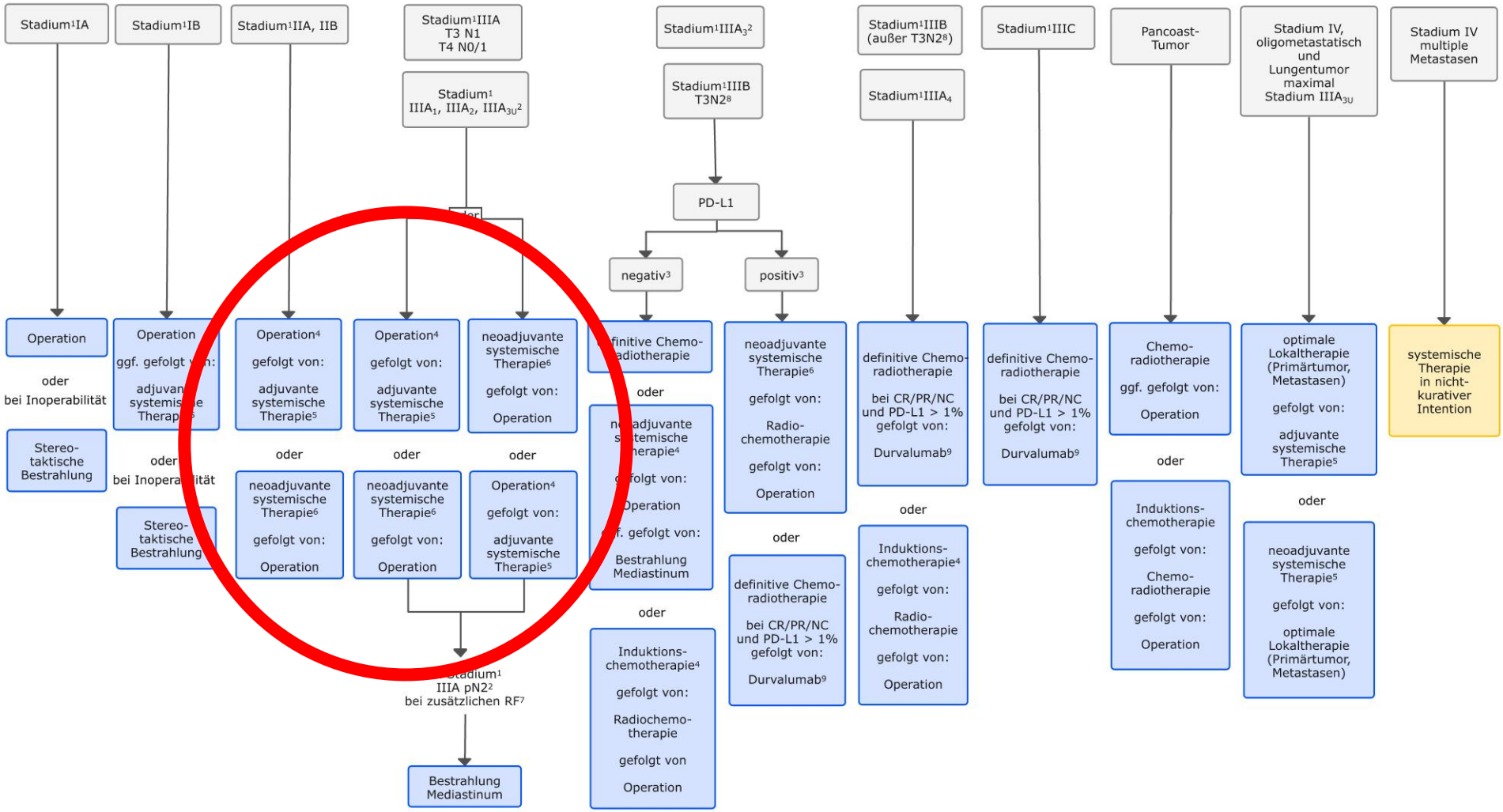
kurative Therapie



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 26, 2022 VOL. 386 NO. 21

Neoadjuvant Nivolumab plus Chemotherapy in Resectable Lung Cancer

P.M. Forde, J. Spicer, S. Lu, M. Provencio, T. Mitsudomi, M.M. Awad, E. Felip, S.R. Broderick, J.R. Brahmer, S.J. Swanson, K. Kerr, C. Wang, T.-E. Ciuleanu, G.B. Saylors, F. Tanaka, H. Ito, K.-N. Chen, M. Liberman, E.E. Vokes, J.M. Taube, C. Dorange, J. Cai, J. Fiore, A. Jarkowski, D. Balli, M. Sausen, D. Pandya, C.Y. Calvet, and N. Girard, for the CheckMate 816 Investigators*

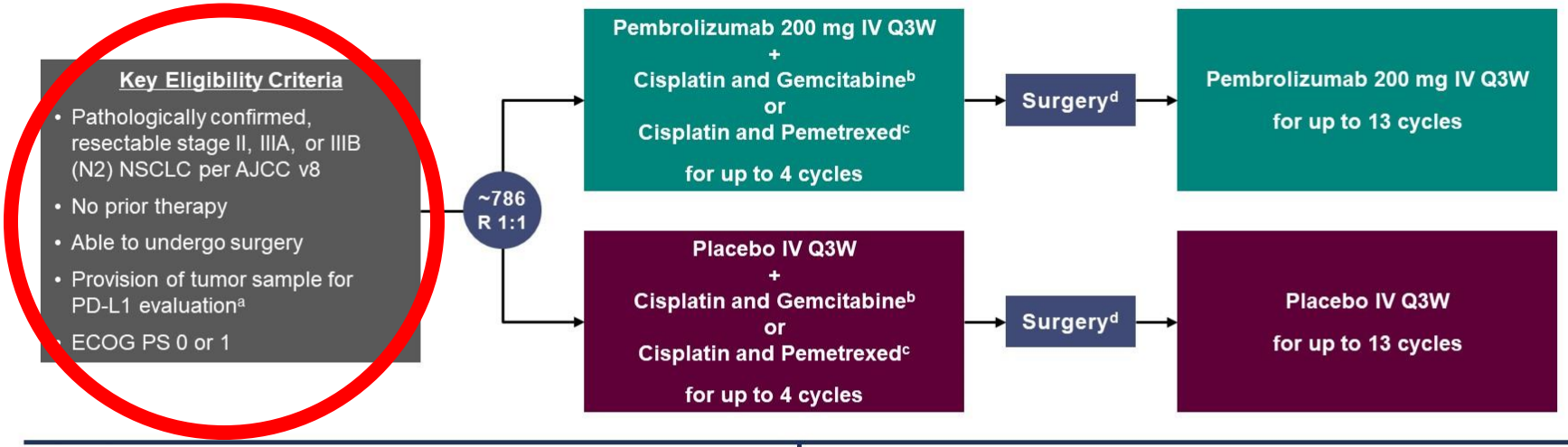
2023 ASCO ANNUAL MEETING

KEYNOTE-671: Randomized, Double-Blind, Phase 3 Study of Pembrolizumab or Placebo plus Platinum-Based Chemotherapy Followed by Resection and Pembrolizumab or Placebo for Early-Stage NSCLC

Heather Wakelee,[1] Moishe Liberman,[2] Terufumi Kato,[3] Masahiro Tsuboi,[4] Se-Hoon Lee,[5] Jie He,[6] Shugeng Gao,[6] Ke-Neng Chen,[7] Christophe Dooms,[8] Margarita Majem,[9] Ekkehard Eigendorff,[10] Gastón L Martinengo,[11] Olivier Bylicki,[12] Delvys Rodríguez-Abreu,[13] Jamie Chaft,[14] Silvia Novello,[15] Jing Yang,[16] Steven M Keller,[16] Ayman Samkari,[16] Jonathan D Spicer,[17] on behalf the KEYNOTE-671 Investigators

[1]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; [2]Centre Hospitalier de Universite to Montréal (CHUM), Montréal, QC, Canada; [3]Kanagawa Cancer Center, Yokohama, Japan; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [6]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [7]Beijing Cancer Hospital, Peking University, Beijing, China; [8]University Hospitals Leuven, Leuven, Belgium; [9]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [10]Zentralklinik Bad Berka, Bad Berka, Germany; [11]Sanatorio Parque, Córdoba, Argentina; [12]HIA Sainte-Anne, Toulon, France; [13]Hospital Universitario Insular de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain; [14]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA; [15]Department of Oncology, University of Turin, A.O.U. San Luigi Gonzaga di Orbassano, Turin, Italy; [16]Merck & Co. Inc., Rahway, NJ, USA; [17]McGill University Health Centre, Montréal, QC, Canada

KEYNOTE-671 Study Design
Randomized, Double-Blind, Phase 3 Trial



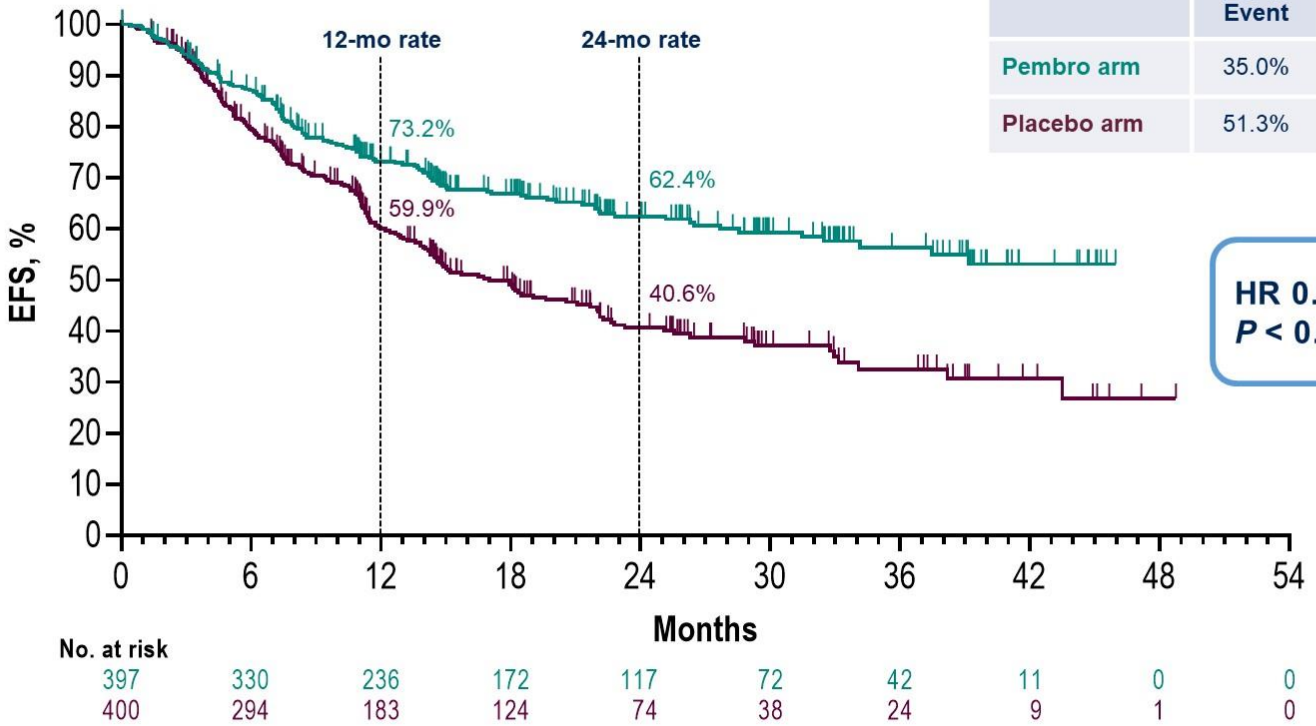
Stratification Factors
- Disease stage (II vs III)
- PD-L1 TPS[a] (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (east Asia vs not east Asia)

Dual primary end points: EFS per investigator review and OS

Key secondary end points: mPR and pCR per blinded, independent pathology review, and safety

[a] Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. [b] Cisplatin 75 mg/m^2 IV Q3W + gemcitabine 1000 mg/m^2 IV on days 1 and 8 Q3W was permitted for squamous histology only. [c] Cisplatin 75 mg/m^2 IV Q3W + pemetrexed 500 mg/m^2 IV Q3W was permitted for nonsquamous histology only. [d] Radiotherapy was to be administered to participants with microscopic positive margins, gross residual disease, or extracapsular nodal extension following surgery and to participants who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.

Event-Free Survival



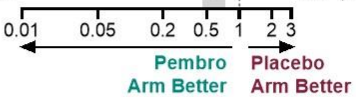
	Pts w/ Event	Median (95% CI), mo
Pembro arm	35.0%	NR (34.1-NR)
Placebo arm	51.3%	17.0 (14.3-22.0)

HR 0.58 (95% CI, 0.46-0.72)
***P* < 0.00001**

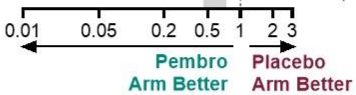
EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause.
Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

Event-Free Survival in Subgroups

Subgroup	Events/participants: Pembro Arm	Events/participants: Placebo Arm	Hazard ratio (95% CI)
Overall	139/397	205/400	0.58 (0.46-0.72)
Age			
<65 y	74/221	113/214	0.53 (0.39-0.71)
≥65 y	65/176	92/186	0.64 (0.46-0.88)
Sex			
Female	31/118	55/116	0.44 (0.28-0.68)
Male	108/279	150/284	0.63 (0.49-0.80)
Race			
White	85/250	123/239	0.54 (0.41-0.72)
All others	46/134	70/145	0.62 (0.42-0.89)
Geographic region			
East Asia	43/123	57/121	0.66 (0.45-0.99)
Not east Asia	96/274	148/279	0.54 (0.41-0.69)
Smoking status			
Current	37/96	57/103	0.52 (0.34-0.78)
Former	84/247	128/250	0.57 (0.43-0.75)
Never	18/54	20/47	0.68 (0.36-1.30)
Histology			
Nonsquamous	73/226	107/227	0.58 (0.43-0.78)
Squamous	66/171	98/173	0.57 (0.41-0.77)



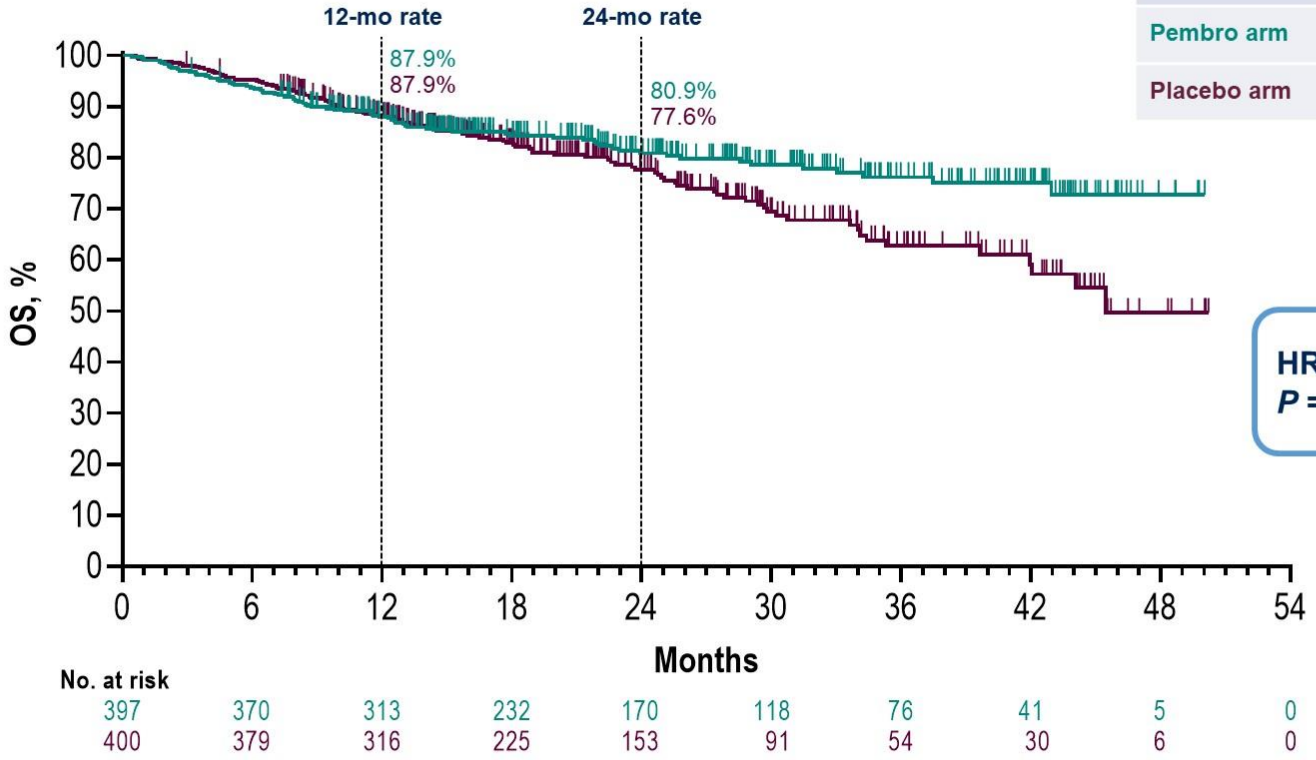
Subgroup	Events/participants: Pembro Arm	Events/participants: Placebo Arm	Hazard ratio (95% CI)
Overall	139/397	205/400	0.58 (0.46-0.72)
Pathologic stage			
II	34/118	48/121	0.65 (0.42-1.01)
IIIA	80/217	124/225	0.54 (0.41-0.72)
IIIB	25/62	33/54	0.52 (0.31-0.88)
pN status			
pN0	51/148	70/142	0.57 (0.40-0.82)
pN1	25/81	33/71	0.60 (0.36-1.01)
pN2	63/168	102/187	0.57 (0.42-0.78)
PD-L1 TPS			
<1%	63/138	80/151	0.77 (0.55-1.07)
1-49%	44/127	62/115	0.51 (0.34-0.75)
≥50%	32/132	63/134	0.42 (0.28-0.65)
[illegible]			
No	31/111	64/127	0.48 (0.31-0.74)
Yes	1/14	10/19	0.09 (0.01-0.74)
Unknown	107/272	131/254	0.64 (0.49-0.83)
***ALK* translocation**			
No	29/104	76/133	0.41 (0.26-0.62)
Unknown	106/281	128/258	0.63 (0.49-0.82)



EFS defined as time from randomization to first occurrence of local progression precluding planned surgery, unresectable tumor, progression or recurrence per RECIST v1.1 by investigator assessment, or death from any cause. Per the prespecified analysis plan, subgroups with <30 participants are excluded from the forest plot. Subgroups for stage IIIA and IIIB and pN status were post hoc; all other subgroups were prespecified. Data cutoff date for IA1: July 29, 2022.

Overall Survival

	Pts w/ Event	Median (95% CI), mo
Pembro arm	19.1%	NR (NR-NR)
Placebo arm	25.3%	45.5 (42.0-NR)



HR 0.73 (95% CI, 0.54-0.99)
***P* = 0.02124[a]**

OS defined as time from randomization to death from any cause. [a] Significance boundary not met at IA1; OS will continue to be tested according to the analysis plan. Data cutoff date for IA1: July 29, 2022 (median follow-up, 25.2 mo [range, 7.5-50.6]).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

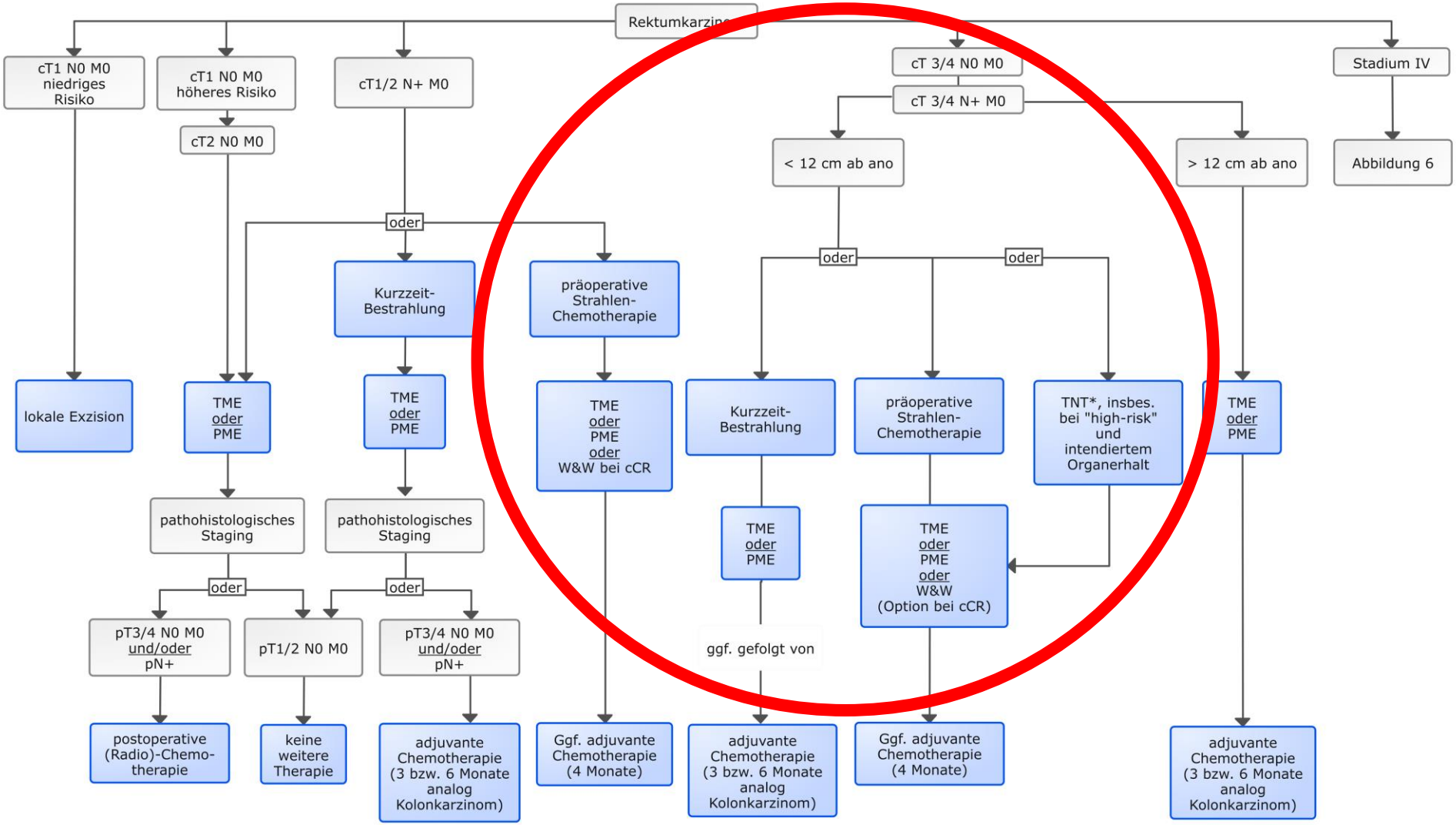
Perioperative Pembrolizumab for Early-Stage Non–Small-Cell Lung Cancer

H. Wakelee, M. Liberman, T. Kato, M. Tsuboi, S.-H. Lee, S. Gao, K.-N. Chen, C. Dooms, M. Majem, E. Eigendorff, G.L. Martinengo, O. Bylicki, D. Rodríguez-Abreu, J.E. Chaft, S. Novello, J. Yang, S.M. Keller, A. Samkari, and J.D. Spicer, for the KEYNOTE-671 Investigators*

Rektumkarzinom

onkopedia

kurative Therapie



Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: 7-year results of PRODIGE 23 phase III trial, a UNICANCER GI trial.

T. Conroy, P-L. Etienne, E. Rio, L. Evesque, N. Mesgouez-Nebout, V. Vendrely, X. Artignan, O. Bouché, A. Boilève, M. Delaye, D. Gargot, V. Boige, N. Bonichon-Lamichhane, C. Louvet, C. de la Fouchardière, C. Morand, V. Pezzella, E. Rullier, F. Castan, and C. Borg

2023 ASCO ANNUAL MEETING #ASCO23

PRESENTED BY: T Conroy, MD

PRODIGE 23 trial: trial design

MRI staging
Randomisation: 1/1
Stratification:
- center
- cT3 vs cT4
- cN0 vs cN+
- T extramural extension (≥5 vs. <5 mm)
- tumor location (cm from anal verge)

461 patients included

RANDOMIZE

SoC arm

Radiotherapy 50.4 Gy /5wks + capecitabine 1600 mg/m²/d 5 days/7 → 7 weeks → TME → mFOLFOX6, 12 cycles or capecitabine, 8 cycles*(6 months)

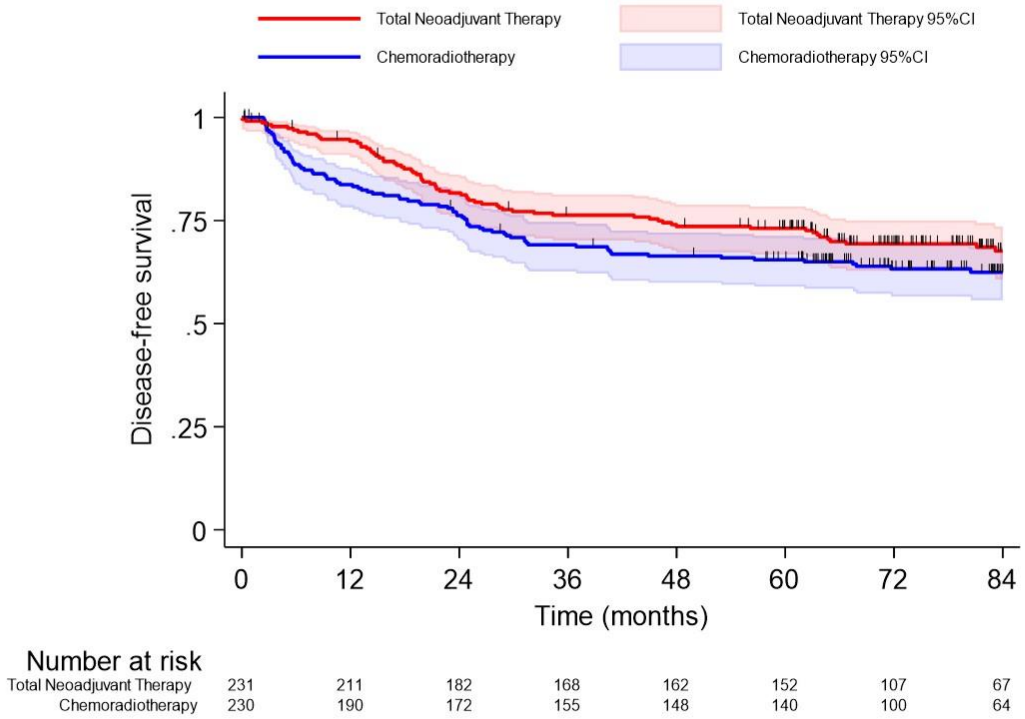
TNT arm

mFOLFIRINOX** 6 cycles, 3 months → Radiotherapy 50.4 Gy /5 wks + capecitabine 1600 mg/m²/d 5 days/7 → 7 weeks → TME → mFOLFOX6, 6 cycles or capecitabine, 4 cycles* (3 months)

**mFOLFIRINOX: At d1, Oxaliplatin 85 mg/m², Leucovorin 400 mg/m², Irinotecan 180 mg/m²; Fluorouracil continuous IV infusion 2.4 g/m² over 46 hours (no bolus Fluorouracil)

***according to center choice throughout the study; adjuvant chemotherapy was mandatory in both arms regardless of ypTNM stage.**

Disease-Free Survival



155 events

7-yr DFS rate:

- 67.6% [95%CI: 60.7-73.6] TNT arm
- 62.5% [95%CI: 55.6-68.6] SoC arm

5-yr DFS rate:

- 73.1% [95%CI: 66.8-78.4] TNT arm
- 65.5% [95%CI: 58.9-71.3] SoC arm

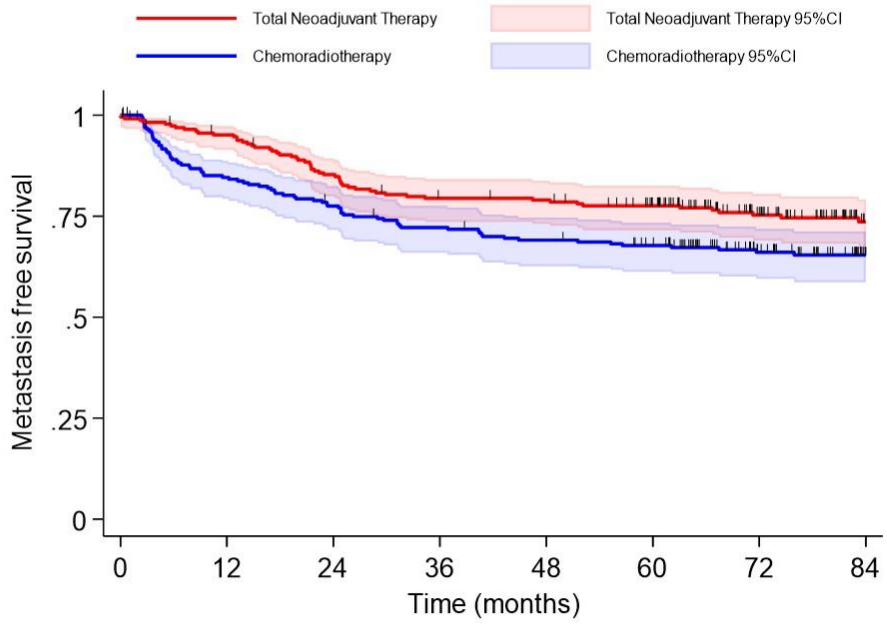
RMST (7-yr), months:

5.73 [0.05-11.41] DFS benefit for TNT arm

p=0.048

Metastasis-free Survival

At 5 years, the cumulative incidence of developing metastatic recurrences was 18.4% in the TNT arm vs 26.6% in the SoC arm.



Number at risk

Total Neoadjuvant Therapy	231	213	190	175	173	159	115	72
Chemoradiotherapy	230	192	175	162	154	145	105	69

138 events

7-yr MFS:

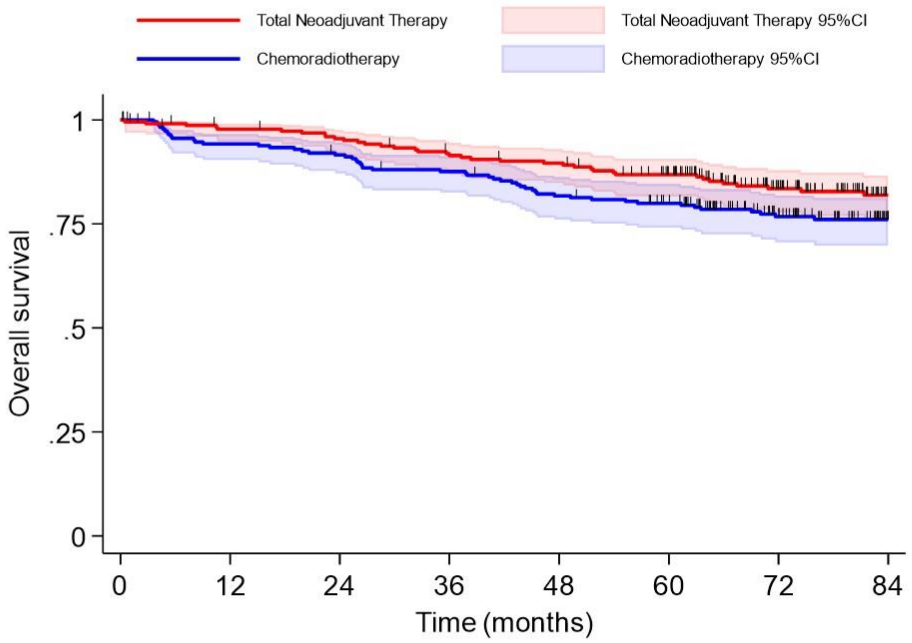
- 73.6% [95%CI: 67.0-79.2] TNT arm
- 65.4% [95%CI: 58.7-71.3] SoC arm

5-yr MFS:

- 77.6% [95%CI: 71.5-82.5] TNT arm
- 67.7% [95%CI: 61.2-73.4] SoC arm

RMST (7-yr), months:
7.1 [1.65-12.63] MFS benefit for TNT arm
p=0.011

Overall Survival



Number at risk

Total Neoadjuvant Therapy	231	218	212	201	196	179	127	79
Chemoradiotherapy	230	213	206	196	182	171	125	79

98 events.

7-yr OS:

- 81.9% [95%CI: 75.8-86.7] TNT arm
- 76.1% [95%CI: 69.8-81.3] SoC arm

5-yr OS:

- 86.9% [95%CI: 81.6-90.7] TNT arm
- 80.0% [95%CI: 74.1-84.6] SoC arm

RMST (7-yr), months:
4.37 [0.35-8.38] benefit for TNT arm
p=0.033

2023 ASCO ANNUAL MEETING

Preoperative Chemotherapy with Selective Chemoradiation versus Chemoradiation for Locally Advanced Rectal Cancer:

The PROSPECT Trial (Alliance N1048)

D Schrag MD MPH Q Shi PhD MR Weiser MD MJ Gollub MD LB. Saltz MD BL Musher MD J. Goldberg MD T. Al Baghdadi MD KA Goodman MD RR McWilliams MD MSc JM Farma MD TJ George MD HF Kennecke MD A Shergill MD M Montemurro MD GD Nelson MS B Colgrove BS V Gordon MD AP Venook MD EM O'Reilly MD JA Meyerhardt MD MPH AC Dueck PhD E. Basch MD MSc GJ Chang MD HJ Mamon MD PhD

ClinicalTrials.gov Identifier: NCT01515787

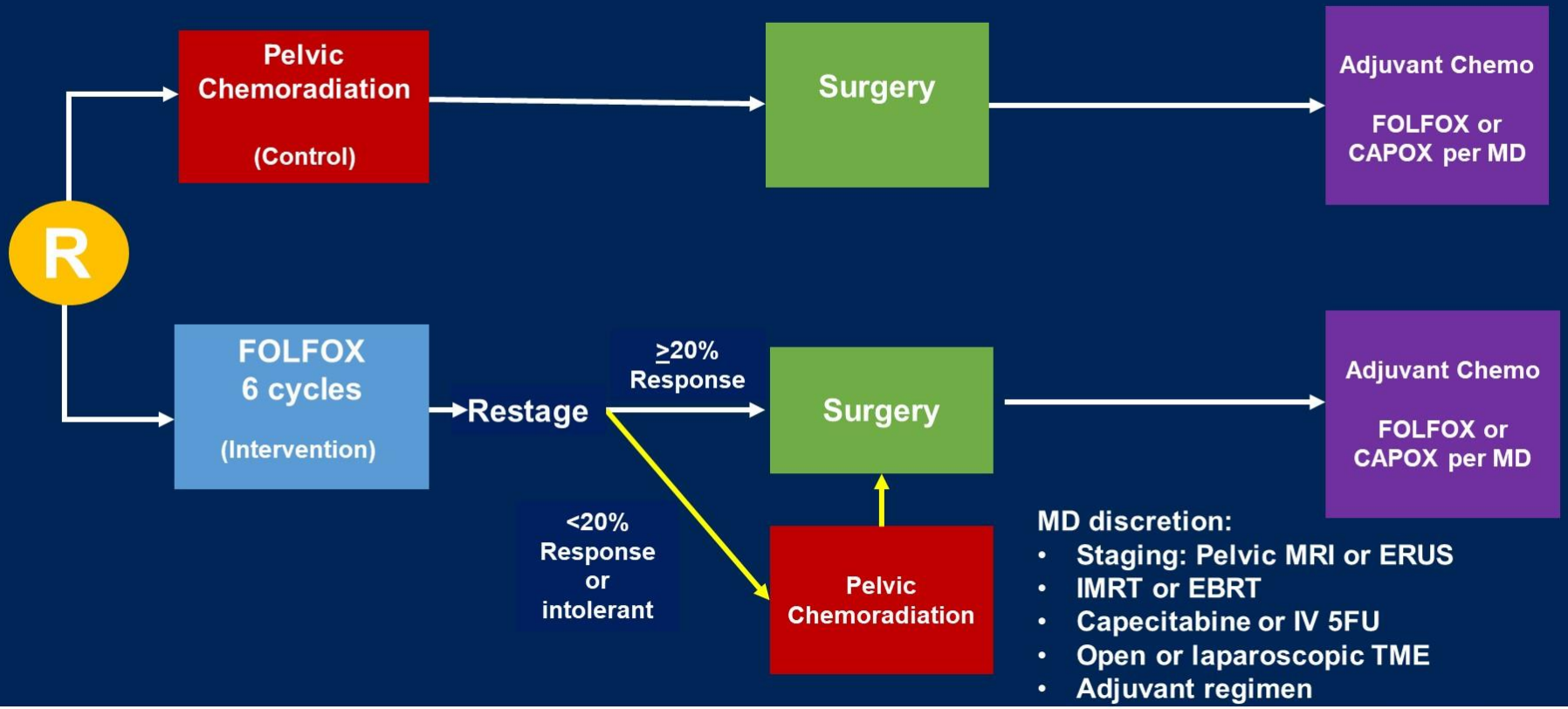
ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network

PRESENTED BY: Deb Schrag MD MPH FASCO, Attending, Gastrointestinal Oncology Service, Memorial Sloan Kettering NY, NY USA

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

PROSPECT Study Full Schema



PROSPECT Main Eligibility Criteria

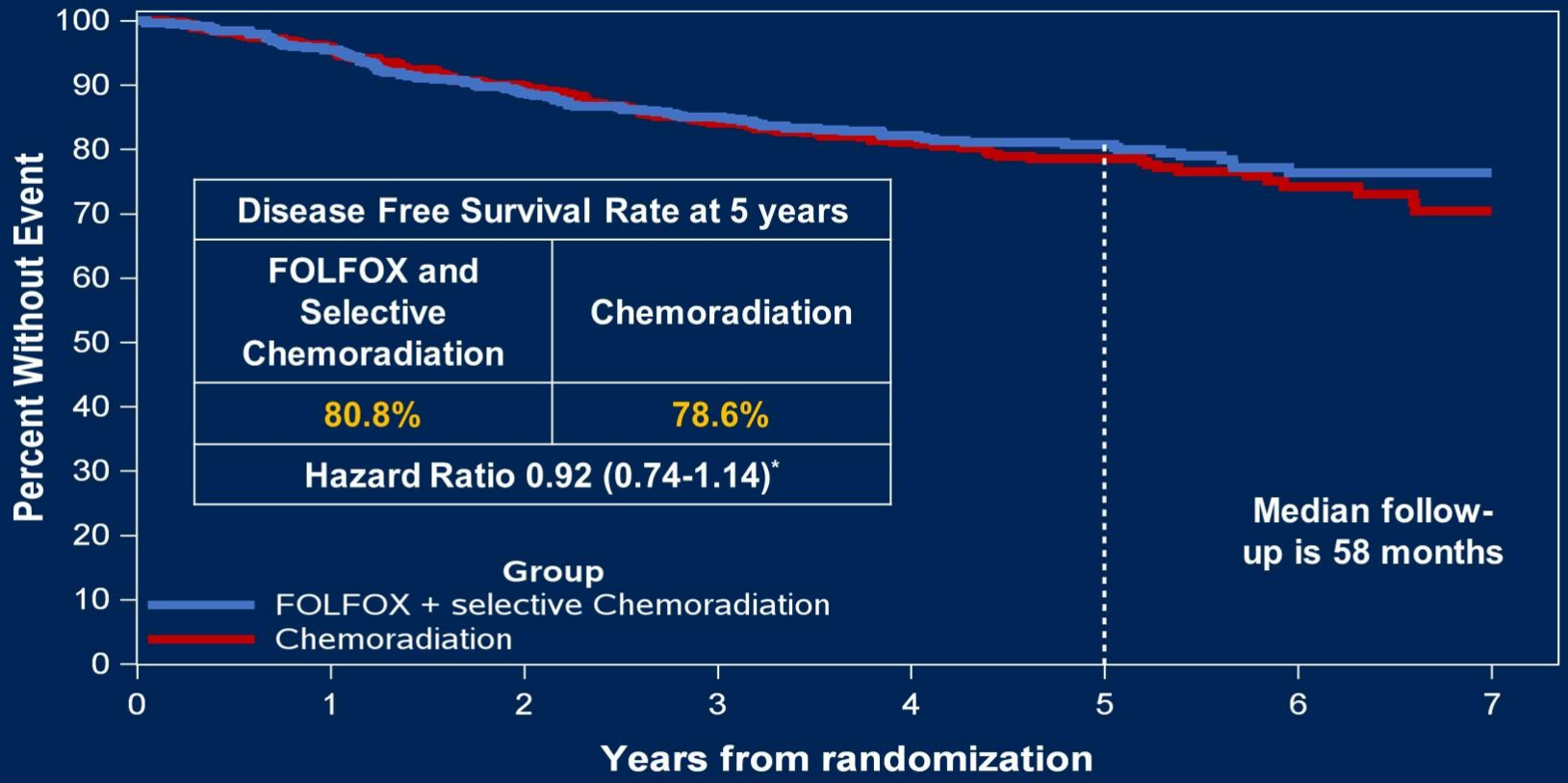
Inclusion:

- Clinical Stage T2N+, T3N-, T3N+
- Chemoradiation is indicated
- Candidate for sphincter-sparing surgery

Exclusion:

- Tumor requiring an APR
- cT4 tumor
- ≥ 4 pelvic lymph nodes ≥ 1cm in short axis

PROSPECT: Disease Free Survival

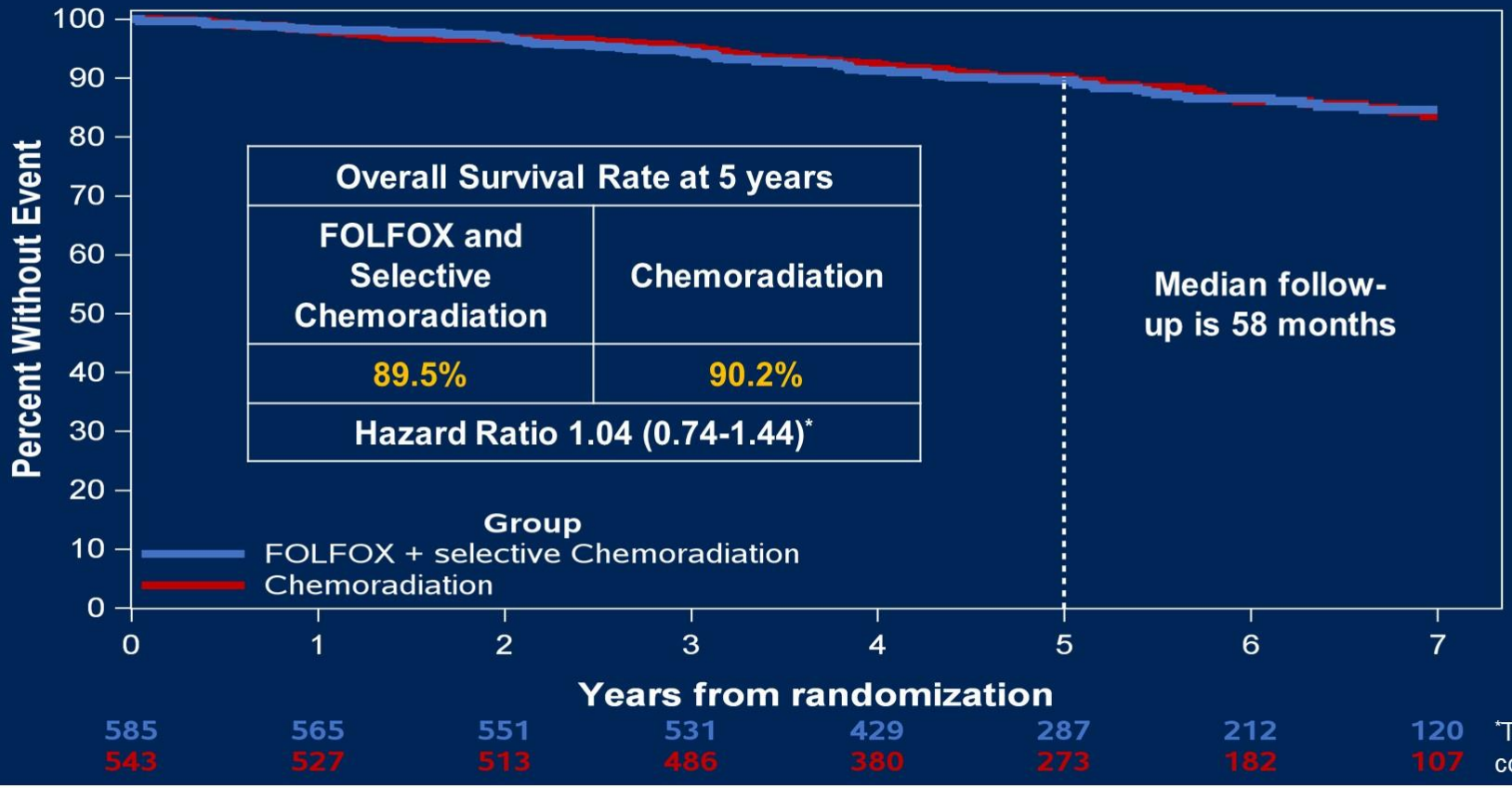


Disease Free Survival Rate at 5 years	
FOLFOX and Selective Chemoradiation	Chemoradiation
80.8%	78.6%
Hazard Ratio 0.92 (0.74-1.14)*	

*Two-sided 90.2% confidence interval

PRESENTED BY: Deb Schrag MD MPH FASCO

PROSPECT: Overall Survival



*Two-sided 95% confidence interval

PROSPECT: Clinician-Reported Toxicity

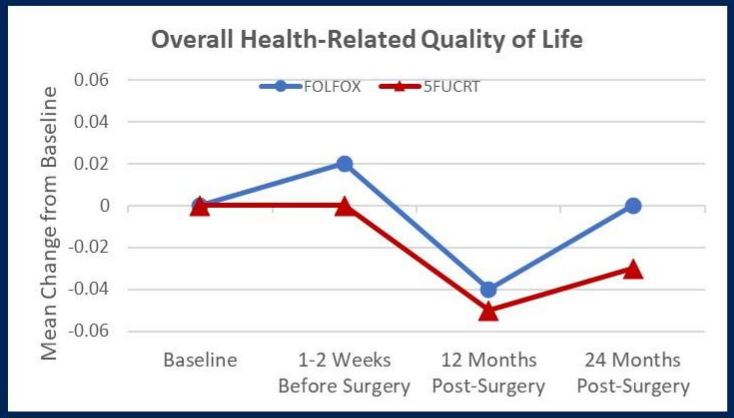
Most severe toxicity during observation period based on CTCAE v. 4.0	FOLFOX and Selective Chemoradiation 12 weeks* 535 patients	Chemoradiation 6 weeks 510 patients
Neoadjuvant grade ≥3 adverse events	41%	23%
Adjuvant grade ≥3 adverse events	25%	39%

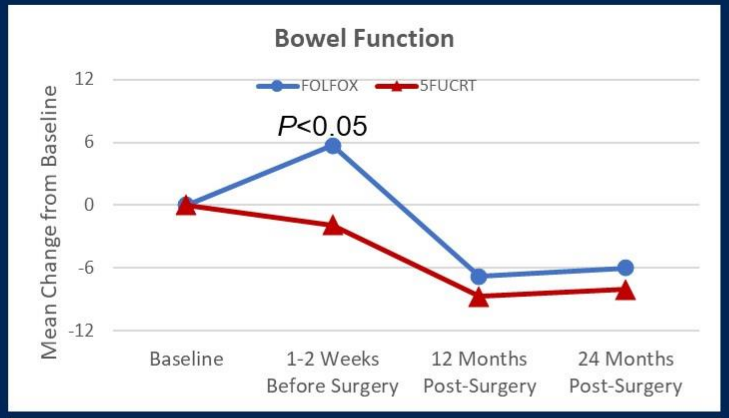
*22 weeks if also treated with chemoradiation

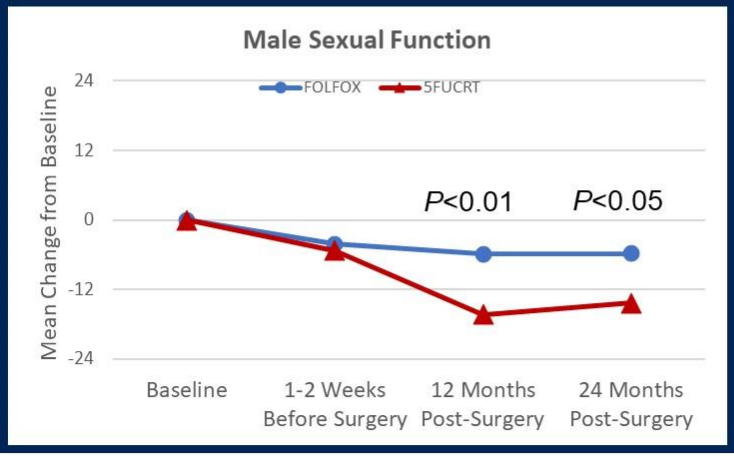
During Neoadjuvant treatment:
- More diarrhea in the RT group
- More neuropathy in the FOLFOX group

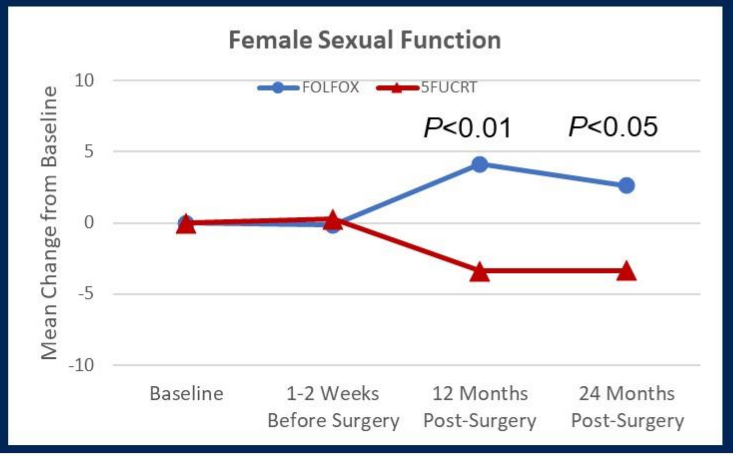
During Adjuvant treatment:
- More diarrhea in the RT group
- More neuropathy in the RT group

PROSPECT: Quality of Life Evaluation









Quality of Life: Trend, but no significant difference between groups

Bowel function and sexual function favor FOLFOX group

N-373

Positive values represent improvement compared to baseline

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preoperative Treatment of Locally Advanced Rectal Cancer

Deborah Schrag, M.D., M.P.H., Qian Shi, Ph.D., Martin R. Weiser, M.D., Marc J. Gollub, M.D., Leonard B. Saltz, M.D., Benjamin L. Musher, M.D., Joel Goldberg, M.D., Tareq Al Baghdadi, M.D., Karyn A. Goodman, M.D., Robert R. McWilliams, M.D., Jeffrey M. Farma, M.D., Thomas J. George, M.D., Hagen F. Kennecke, M.D., Ardaman Shergill, M.D., Michael Montemurro, M.D., Garth D. Nelson, M.S., Brian Colgrove, B.S., Vallerie Gordon, M.D., Alan P. Venook, M.D., Eileen M. O'Reilly, M.D., Jeffrey A. Meyerhardt, M.D., M.P.H., Amylou C. Dueck, Ph.D., Ethan Basch, M.D., George J. Chang, M.D., and Harvey J. Mamon, M.D., Ph.D.

2023 ASCO ANNUAL MEETING

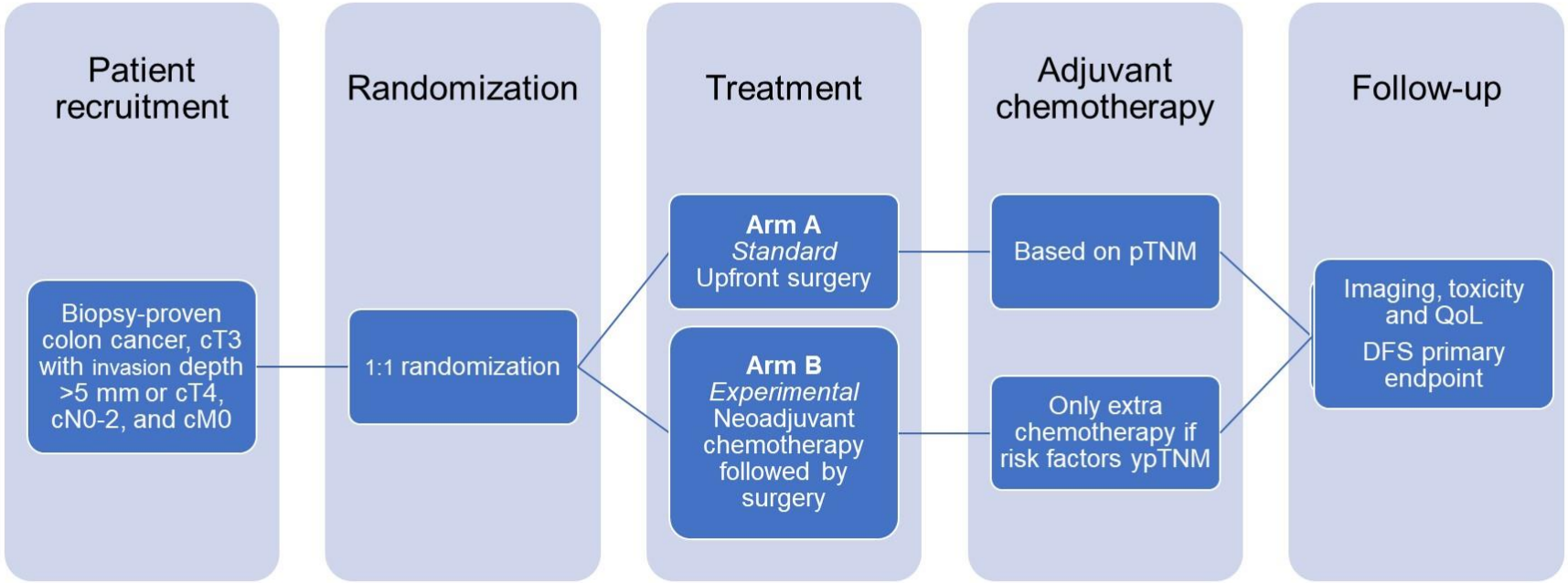
Phase III randomized clinical trial comparing the efficacy of neoadjuvant chemotherapy and standard treatment in patients with locally advanced colon cancer

The Scandinavian **NeoCoI** trial

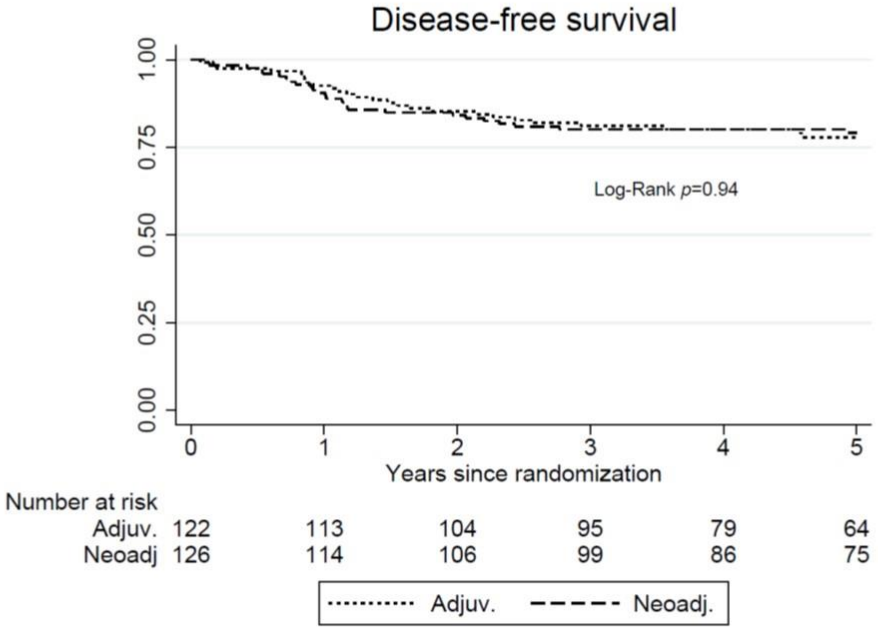
Lars Henrik Jensen MD PhD

PRESENTED BY:

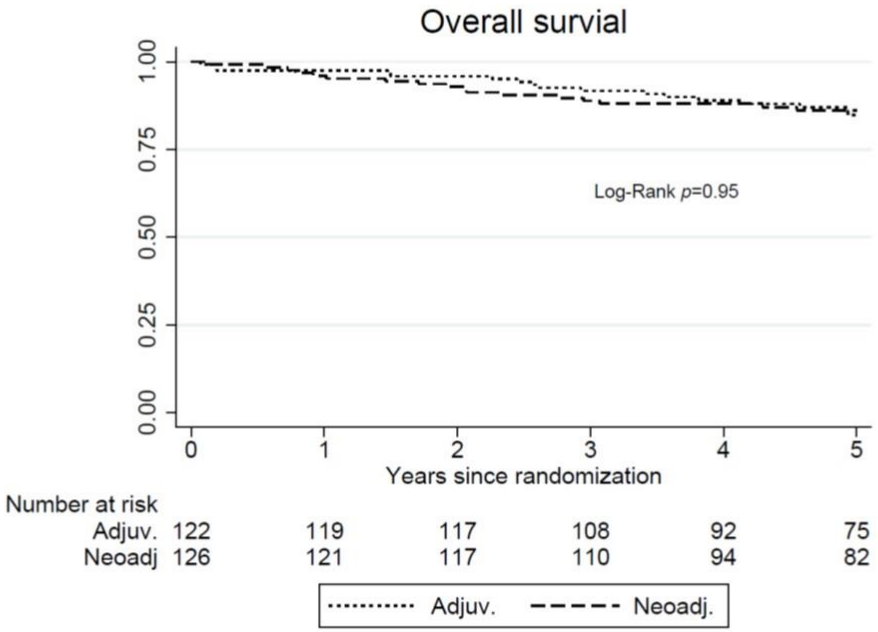
Study design



Efficacy outcomes - Disease-free survival (DFS)



Efficacy outcomes - Overall survival (OS)



DGHO
DEUTSCHE GESELLSCHAFT FÜR
HÄMATOLOGIE UND MEDIZINISCHE ONKOLOGIE

22. 5. 2023

Rektumkarzinom, dMMR/MSI-H positiv

Neoadjuvante Therapie mit Dostarlimab

Aktuelle Empfehlungen zu Durchführung und Kostenübernahme

2023 ASCO ANNUAL MEETING

Short-course neoadjuvant FOLFIRINOX versus upfront surgery for resectable pancreatic head cancer - A multicenter randomized phase-2 trial (NORPACT-1)

KJ Labori, SO Bratlie, C Biörserud, B Björnsson, EA Bringeland, N Elander, JE Grønbech, J Haux, O Hemmingsson, LS Nymo, P Pfeiffer, V Sallinen, E Sparrelid, K Søreide, B Tingstedt, C Verbeke, L Klint, S Dueland, and K Lassen for the **NORPACT-1 study group**

PRESENTED BY: Knut Jørgen Labori, Dept. of HPB Surgery, Oslo University Hospital and University of Oslo, Norway

Cancer Medicine

Cancer Medicine 2015, 4(6):853–863

Open Access

REVIEW

Pancreatic cancer and FOLFIRINOX: a new era and new questions

Robert De W. Marsh[1], Mark S. Talamonti[2], Matthew Harold Katz[3] & Joseph M. Herman[4]

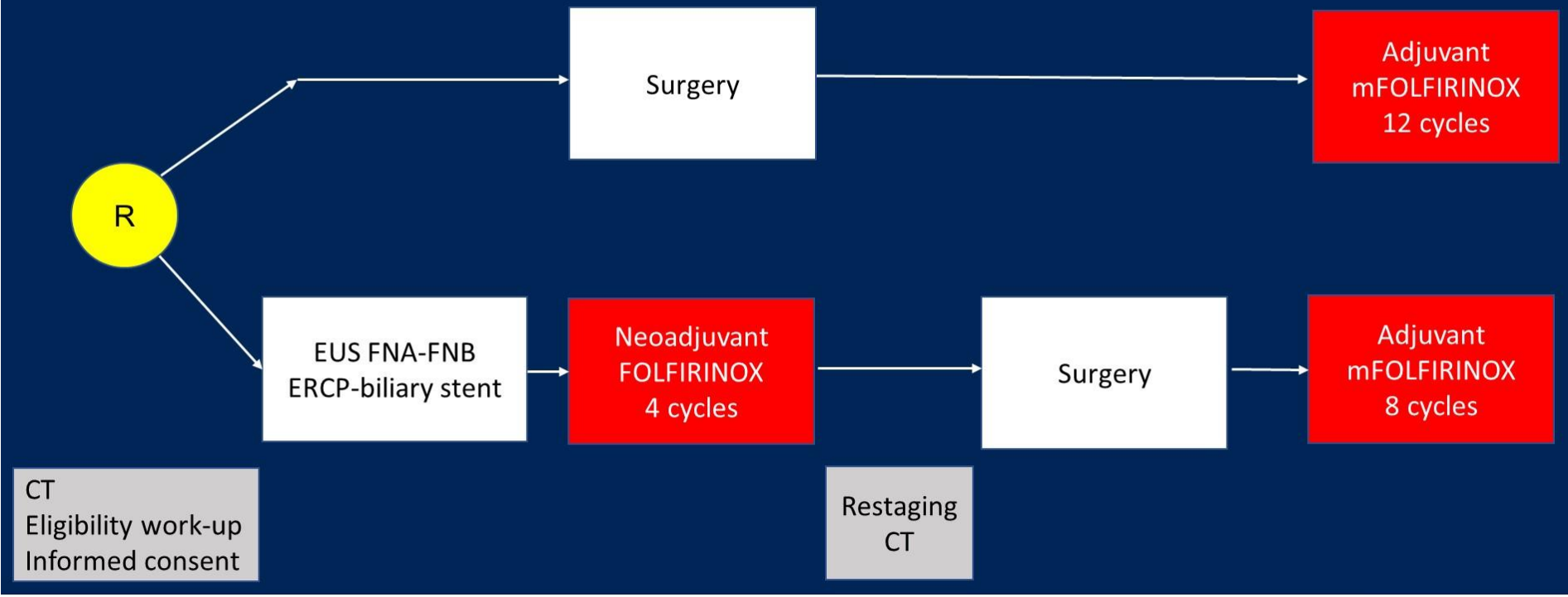
Conroy T, Desseigne F, Ychou M, et al. N Engl J Med 2011

FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer

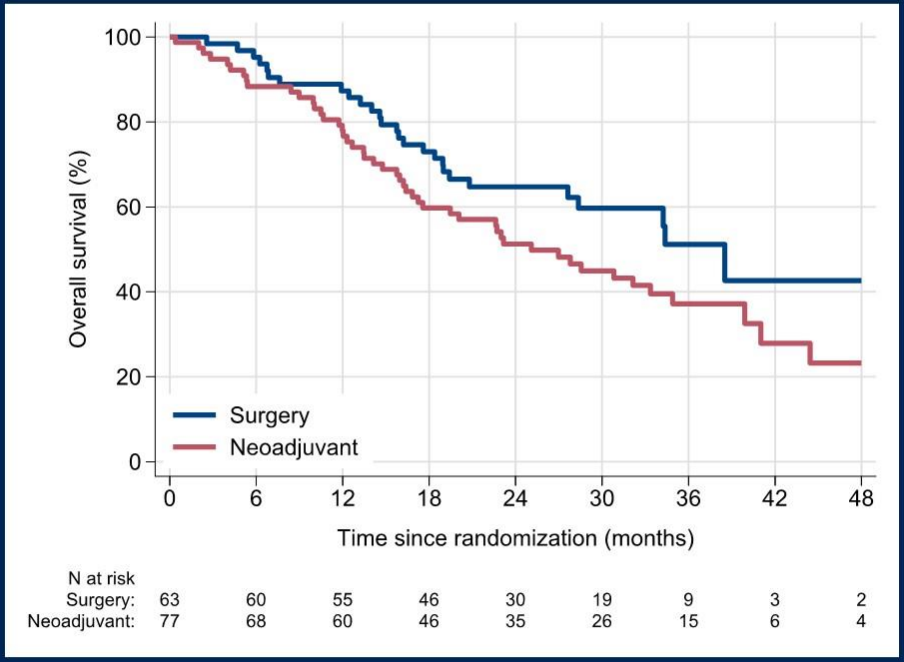
Suker M, Beumer BR, Sadot E, et al. Lancet Oncol 2016

FOLFIRINOX for locally advanced pancreatic cancer: a systematic review and patient-level meta-analysis

Trial design

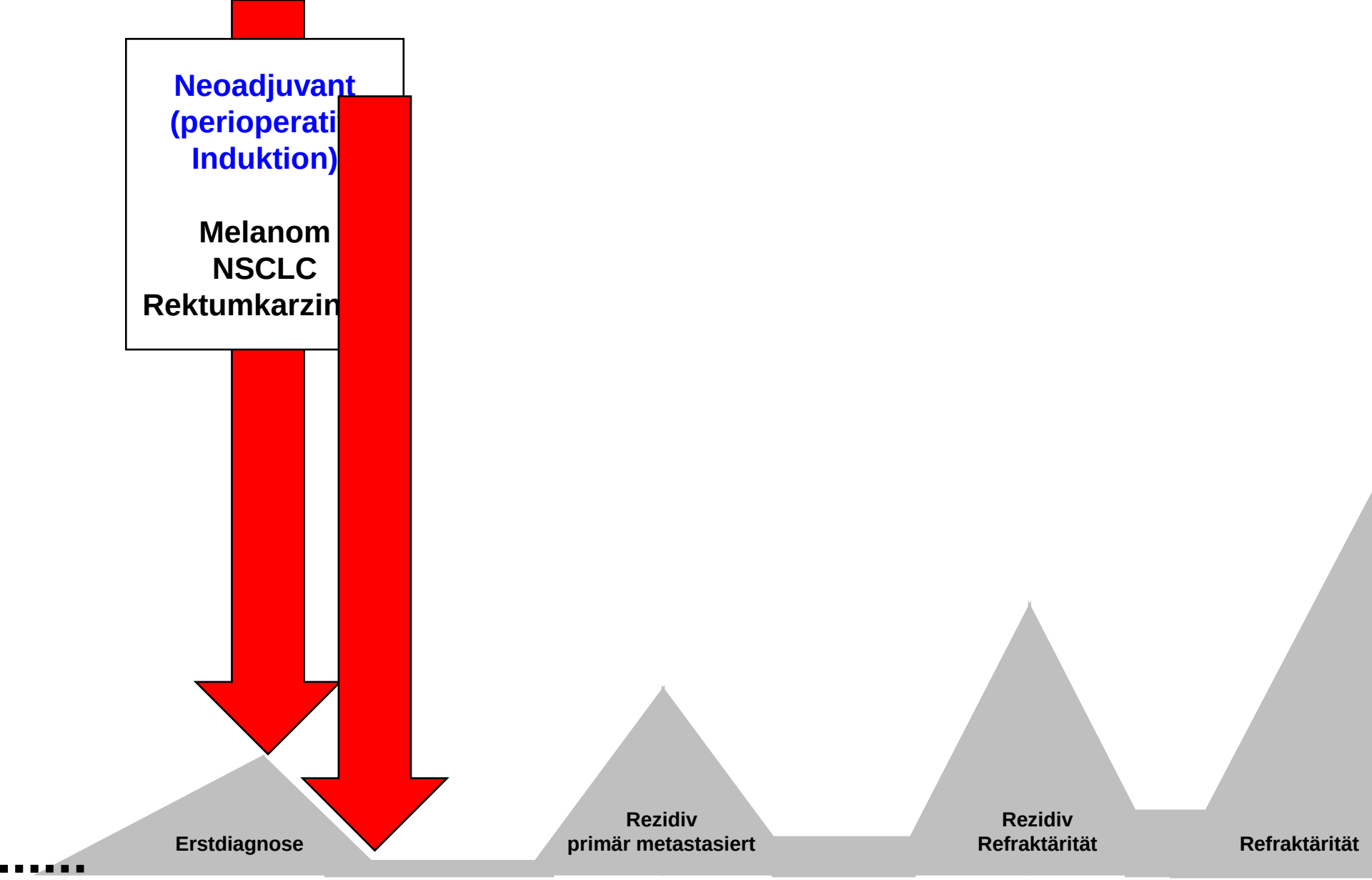


Overall survival - Intention-to-treat



Median overall survival
25.1 months (neoadjuvant)
38.5 months (upfront surgery)
HR 1.52 (95% CI, 0.94-2.46), p=0.096

Proportion alive at 18 months
60% vs 73%, p=0.1


Neoadjuvant
(perioperati
Induktion)
Melanom
NSCLC
Rektumkarzin
Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität

2023 ASCO ANNUAL MEETING

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

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

[1]Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA; [2]Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [3]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia; [4]Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; [5]Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6]Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; [7]Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China; [8]David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA; [9]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [10]Department of Oncology, National Cheng Kung University, Tainan, Taiwan; [11]Thoracic Oncology Division, European Institute of Oncology (IEO), IRCCS, Milan, Italy; [12]Department of Medical Oncology and Hematology, University Health Network, Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [13]Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, Republic of Korea; [14]Ho Chi Minh City Oncology Hospital, Binh Thanh District, Ho Chi Minh City, Vietnam; [15]Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; [16]Department of Lung Cancer and Thoracic Tumours, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [17]Oncology Biometrics, AstraZeneca, Cambridge, UK; [18]Late Oncology Research & Development, AstraZeneca, Warsaw, Poland; [19]Oncology Research & Development, AstraZeneca, Cambridge, UK; [20]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China

PRESENTED BY: Roy S. Herbst

ADAURA Phase III study design

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

Key inclusion criteria:
- ≥18 years (Japan / Taiwan: ≥20)
- WHO performance status 0 / 1
- Confirmed primary non-squamous NSCLC Ex19del / L858R‡
- Brain imaging, if not completed pre-operatively
- Complete resection with negative margins§
- Maximum interval between surgery and randomization:
  - 10 weeks without adjuvant chemotherapy
  - 26 weeks with adjuvant chemotherapy

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

Randomization 1:1 (N=682)

- **Osimertinib 80 mg, once daily**
- **Placebo, once daily**

Planned treatment duration: 3 years

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

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

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

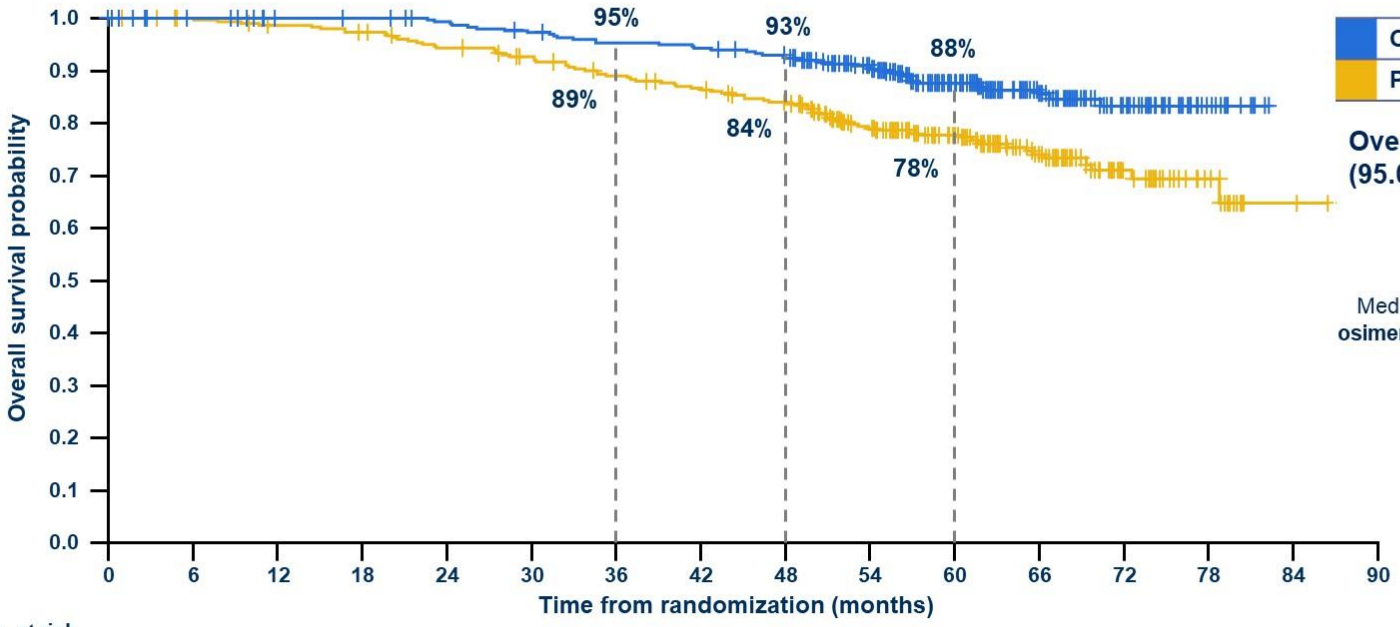
*At the time of recruitment, staging was determined by the AJCC / UICC Staging Manual 7th edition. Patients with stage IB disease were not eligible in Japan. †Pre-operative, post-operative, or planned radiotherapy was not allowed. ‡Centrally confirmed in tissue. §Patients received a CT scan after resection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

PRESENTED BY: Roy S. Herbst

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

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

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



No. at risk																
Osimertinib	339	332	325	324	319	311	304	301	294	252	176	108	50	15	0	-
Placebo	343	338	332	326	314	304	290	281	267	223	164	97	44	17	3	0

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

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

Maturity: 18%
osimertinib 12%, placebo 24%

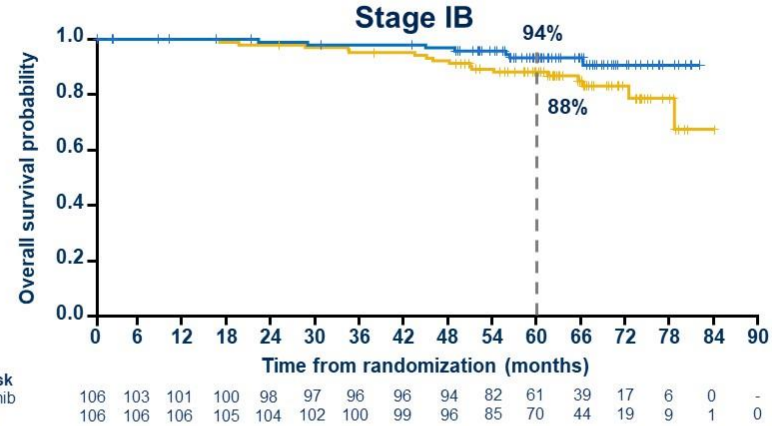
Median follow-up for OS* (censored patients):
osimertinib 61.5 months, placebo 61.5 months

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

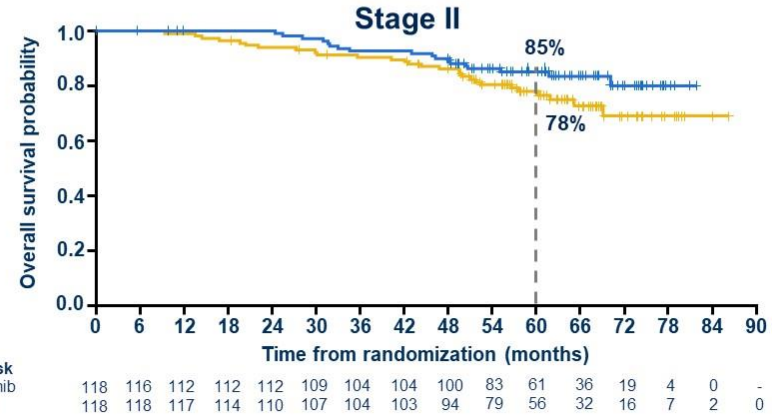
CI, confidence interval; HR, hazard ratio; OS, overall survival

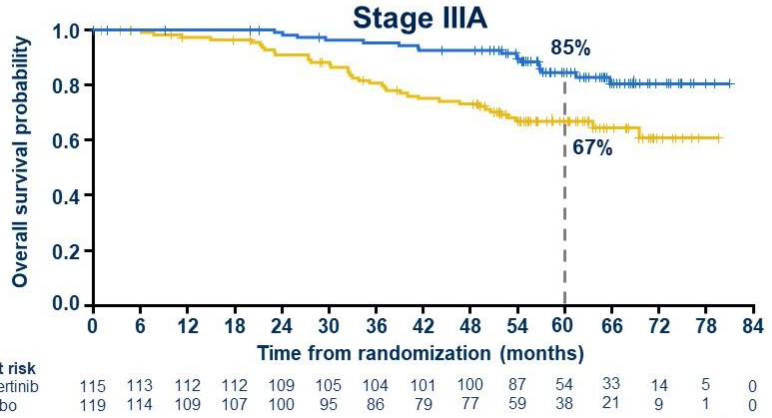
PRESENTED BY: Roy S. Herbst

Overall survival by disease stage



	Stage IB	Stage II	Stage IIIA
5 year OS rate, % (95% CI)			
Osimertinib	94 (86, 97)	85 (77, 91)	85 (76, 91)
Placebo	88 (80, 93)	78 (69, 85)	67 (57, 75)
Overall HR (95% CI)	0.44 (0.17, 1.02)	0.63 (0.34, 1.12)	0.37 (0.20, 0.64)





PRESENTED BY: Roy S. Herbst

Data cut-off: January 27, 2023. Tick marks indicate censored data.
CI, confidence interval; HR, hazard ratio; OS, overall survival

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Overall Survival with Osimertinib in Resected *EGFR*-Mutated NSCLC

Masahiro Tsuboi, M.D., Roy S. Herbst, M.D., Ph.D., Thomas John, M.B., B.S., Ph.D., Terufumi Kato, M.D., Margarita Majem, M.D., Ph.D., Christian Grohé, M.D., Jie Wang, M.D., Ph.D., Jonathan W. Goldman, M.D., Shun Lu, M.D., Wu-Chou Su, M.D., Filippo de Marinis, M.D., Frances A. Shepherd, M.D., Ki Hyeong Lee, M.D., Ph.D., Nhieu Thi Le, M.D., Arunee Dechaphunkul, M.D., Dariusz Kowalski, M.D., Ph.D., Lynne Poole, M.Sc., Ana Bolanos, M.D., Yuri Rukazenkov, M.D., Ph.D., and Yi-Long Wu, M.D., for the ADAURA Investigators*

EGFRm, epidermal growth factor receptor-mutated; NSCLC, non-small cell lung cancer

2023 ASCO ANNUAL MEETING

Ribociclib and endocrine therapy as adjuvant treatment in patients with HR+/HER2− early breast cancer: primary results from the Phase III NATALEE trial

Dennis Slamon,[1] Daniil Stroyakovskiy,[2] Denise A. Yardley,[3] Chiun-Sheng Huang,[4] Peter A. Fasching,[5] John Crown,[6] Aditya Bardia,[7] Stephen Chia,[8] Seock-Ah Im,[9] Miguel Martin,[10] Sherene Loi,[11] Binghe Xu,[12] Sara Hurvitz,[13] Carlos Barrios,[14] Michael Untch,[15] Rebecca Moroose,[16] Frances Visco,[17] Rodrigo Fresco,[18] Tetiana Taran,[19] Gabriel N. Hortobagyi[20]

[1]David Geffen School of Medicine at UCLA, Los Angeles, CA; [2]Moscow City Oncology Hospital No. 62 of Moscow Healthcare Department, Moscow Oblast, Russia; [3]Sarah Cannon Research Institute, Tennessee Oncology, Nashville, TN; [4]National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei City, Taiwan; [5]University Hospital Erlangen Comprehensive Cancer Center Erlangen-EMN, Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany; [6]St. Vincent's University Hospital, Dublin, Ireland; [7]Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA; [8]British Columbia Cancer Agency, Vancouver, BC, Canada; [9]Cancer Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea; [10]Instituto de Investigación Sanitaria Gregorio Marañon, Centro de Investigación Biomédica en Red de Cáncer, Grupo Español de Investigación en Cáncer de Mama, Universidad Complutense, Madrid, Spain; [11]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [12]Department of Medical Oncology Cancer Hospital, Chinese Academy of Medical Sciences (CAMS), and Peking Union Medical College (PUMC), Beijing, China; [13]University of California, Los Angeles, Jonsson Comprehensive Cancer Center, Los Angeles, CA; [14]Latin American Cooperative Oncology Group (LACOG), Porto Alegre, Brazil; [15]Interdisciplinary Breast Cancer Center, Helios Klinikum Berlin-Buch, Berlin, Germany; [16]Orlando Health Cancer Institute, Orlando, FL; [17]National Breast Cancer Coalition, Washington DC; [18]TRIO - Translational Research in Oncology, Montevideo, Uruguay; [19]Novartis Pharma AG, Basel, Switzerland; [20]Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

PRESENTED BY: Dennis Slamon MD, PhD

NATALEE study design[1,2]

- Adult patients with HR+/HER2− EBC
- Prior ET allowed up to 12 mo
- **Anatomical stage IIA**[a]
  - **N0** with:
    - Grade 2 and evidence of high risk:
      - Ki-67 ≥ 20%
      - Oncotype DX Breast Recurrence Score ≥ 26 *or*
      - High risk via genomic risk profiling
    - Grade 3
  - **N1**
- **Anatomical stage IIB**[a]
  - N0 or N1
- **Anatomical stage III**
  - N0, N1, N2, or N3

N = 5101[b]

R 1:1[c]

Ribociclib
400 mg/day
3 weeks on/1 week off
for 3 y

NSAI
Letrozole or anastrozole[d] for ≥ 5 y
+ goserelin in men and premenopausal women

NSAI
Letrozole or anastrozole[d] for ≥ 5 y
+ goserelin in men and premenopausal women

Randomization stratification
Anatomical stage: II vs III
Menopausal status: men and premenopausal women vs postmenopausal women
Receipt of prior (neo)adjuvant chemotherapy: yes vs no
Geographic location: North America/Western Europe/Oceania vs rest of world

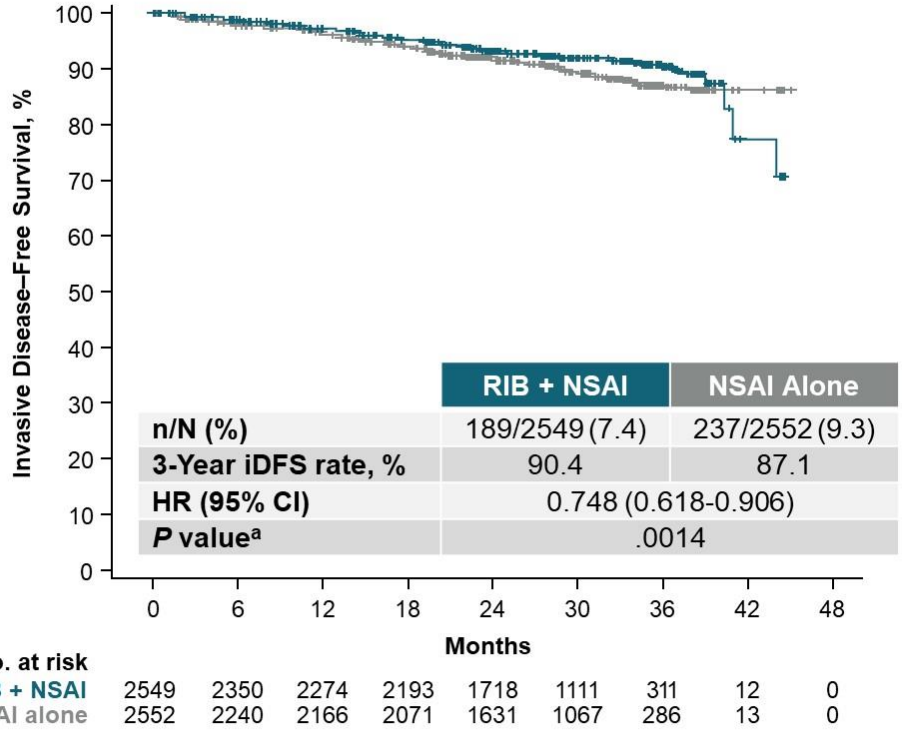
Primary End Point
- iDFS using STEEP criteria

Secondary End Points
- Recurrence-free survival
- Distant disease–free survival
- OS
- PROs
- Safety and tolerability
- PK

Exploratory End Points
- Locoregional recurrence–free survival
- Gene expression and alterations in tumor ctDNA/ctRNA samples

[a] Enrollment of patients with stage II disease was capped at 40%. [b] 5101 patients were randomized from 10 Jan 2019 to 20 April 2021. [c] Open-label design. [d] Per investigator choice.
CT, chemotherapy; ctDNA/RNA, circulating tumor DNA/RNA; EBC, early breast cancer; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IDFS, invasive disease-free survival; N, node; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PAM50, prediction analysis of microarray 50; PK, pharmacokinetics; PRO, patient reported outcome; R, randomized; STEEP, Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials.
1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03701334. Accessed April 6 2023. 2. Slamon DJ, et al. *J Clin Oncol*. 2019;37(15 suppl) [abstract TPS597].

Ribociclib achieved highly significant iDFS benefit



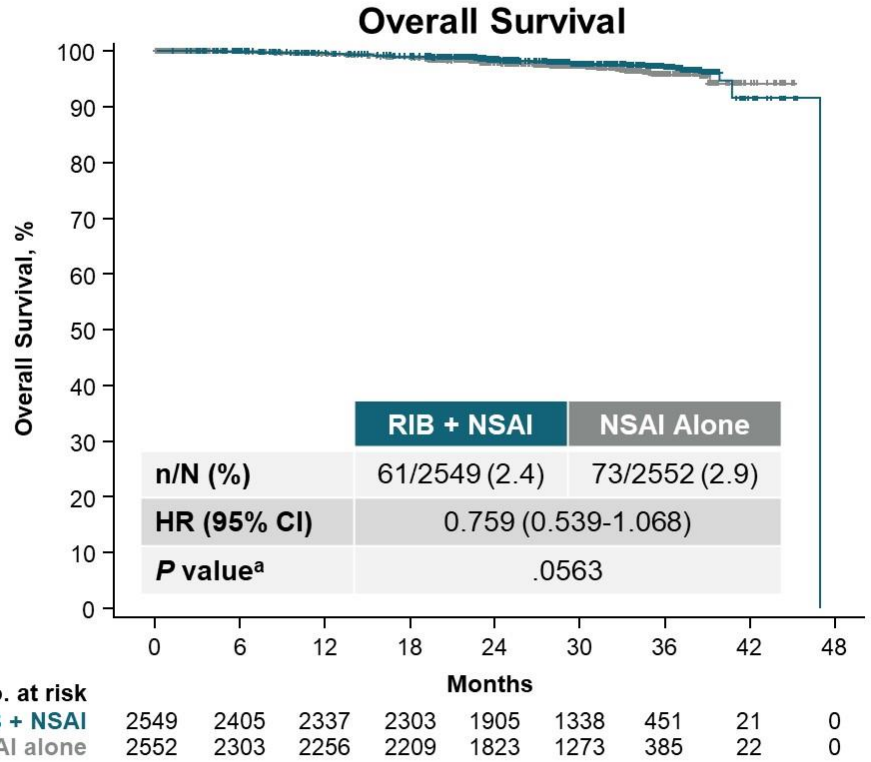
	RIB + NSAI	NSAI Alone
n/N (%)	189/2549 (7.4)	237/2552 (9.3)
3-Year iDFS rate, %	90.4	87.1
HR (95% CI)	0.748 (0.618-0.906)	
P value[a]	.0014	

No. at risk									
RIB + NSAI	2549	2350	2274	2193	1718	1111	311	12	0
NSAI alone	2552	2240	2166	2071	1631	1067	286	13	0

- Median follow-up for iDFS was 27.7 months
- Based on the *P* value of 0.0014, the IDMC concluded that the results met the criteria to demonstrate statistically significant and clinically superior efficacy
- Absolute iDFS benefit with RIB + NSAI at 3 years was 3.3%
- Risk of invasive disease was reduced by 25.2% with RIB + NSAI vs NSAI alone
- Ongoing patients will remain on treatment and follow-up will continue as prespecified

iDFS, invasive disease–free survival; IDMC, Independent Data Monitoring Committee; HR, hazard ratio; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.
[a] One-sided *P* value.

Ribociclib showed a trend for improved OS

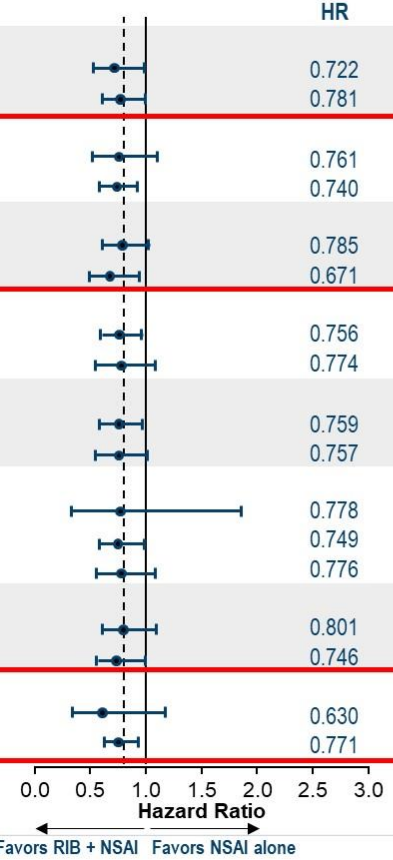


HR, hazard ratio; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; RIB, ribociclib.
[a] One-sided nominal *P* value.

- Median follow-up for OS was 30.4 months
- Additional follow-up for OS is planned

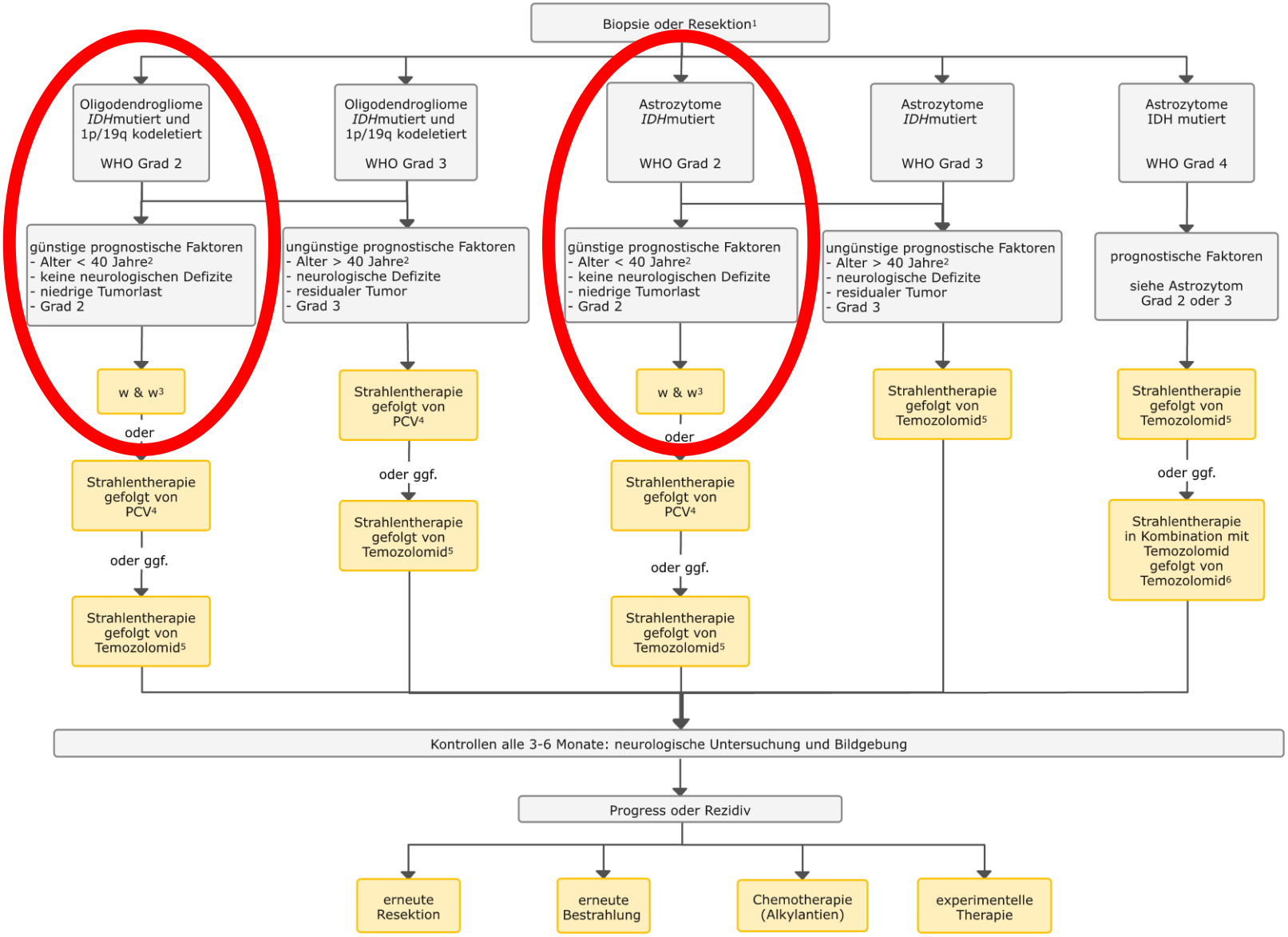
iDFS benefit was consistent across prespecified key subgroups

Subgroup	RIB + NSAI n = 2549	NSAI Alone n = 2552	HR	(95% CI)
Menopausal status				
Men and premenopausal women	71/1126	93/1132	0.722	(0.530-0.983)
Postmenopausal women	118/1423	144/1420	0.781	(0.613-0.997)
AJCC stage				
Stage II	49/1011	65/1034	0.761	(0.525-1.103)
Stage III	140/1528	172/1512	0.740	(0.592-0.925)
Prior CT				
Neoadjuvant	111/1085	132/1095	0.785	(0.610-1.011)
Adjuvant	63/1223	89/1220	0.671	(0.486-0.927)
Prior ET				
Yes	127/1824	157/1801	0.756	(0.598-0.955)
No	62/725	80/751	0.774	(0.556-1.079)
Region				
North America/Western Europe/Oceania	111/1563	139/1565	0.759	(0.591-0.974)
Rest of world	78/986	98/987	0.757	(0.562-1.019)
Histological grade at time of surgery				
Grade 1	9/213	12/217	0.778	(0.328-1.846)
Grade 2	102/1460	125/1432	0.749	(0.577-0.973)
Grade 3	61/684	78/702	0.776	(0.555-1.085)
Ki-67 status[a]				
Ki-67 ≤ 20%	76/1199	95/1236	0.801	(0.593-1.083)
Ki-67 > 20%	82/920	105/938	0.746	(0.559-0.996)
Nodal status[b,c]				
N0	16/285	28/328	0.630	(0.341-1.165)
N1-N3	173/2261	208/2219	0.771	(0.630-0.944)



AJCC, American Joint Committee on Cancer; CT, chemotherapy; ET, endocrine therapy; iDFS, invasive disease–free survival; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.
[a] From archival tumor tissue. [b] Nodal status classification according to AJCC staging. [c] Nodal status is from the worse stage derived per surgical specimen or at diagnosis.

Gliom


Biopsie oder Resektion[1]
Oligodendrogliome IDHmutiert und 1p/19q kodeletiert WHO Grad 2
Oligodendrogliome IDHmutiert und 1p/19q kodeletiert WHO Grad 3
Astrozytome IDHmutiert WHO Grad 2
Astrozytome IDHmutiert WHO Grad 3
Astrozytome IDH mutiert WHO Grad 4
günstige prognostische Faktoren - Alter < 40 Jahre[2] - keine neurologischen Defizite - niedrige Tumorlast - Grad 2
ungünstige prognostische Faktoren - Alter > 40 Jahre[2] - neurologische Defizite - residualer Tumor - Grad 3
günstige prognostische Faktoren - Alter < 40 Jahre[2] - keine neurologischen Defizite - niedrige Tumorlast - Grad 2
ungünstige prognostische Faktoren - Alter > 40 Jahre[2] - neurologische Defizite - residualer Tumor - Grad 3
prognostische Faktoren siehe Astrozytom Grad 2 oder 3
w & w[3]
oder
Strahlentherapie gefolgt von PCV[4]
oder ggf.
Strahlentherapie gefolgt von Temozolomid[5]
Strahlentherapie gefolgt von PCV[4]
oder ggf.
Strahlentherapie gefolgt von Temozolomid[5]
w & w[3]
oder
Strahlentherapie gefolgt von PCV[4]
oder ggf.
Strahlentherapie gefolgt von Temozolomid[5]
Strahlentherapie gefolgt von Temozolomid[5]
Strahlentherapie gefolgt von Temozolomid[5]
oder ggf.
Strahlentherapie in Kombination mit Temozolomid gefolgt von Temozolomid[6]
Kontrollen alle 3-6 Monate: neurologische Untersuchung und Bildgebung
Progress oder Rezidiv
erneute Resektion
erneute Bestrahlung
Chemotherapie (Alkylantien)
experimentelle Therapie

2023 ASCO ANNUAL MEETING

INDIGO: a Phase 3 global, randomized, double-blinded study of vorasidenib versus placebo in patients with residual or recurrent grade 2 glioma with an IDH1/2 mutation

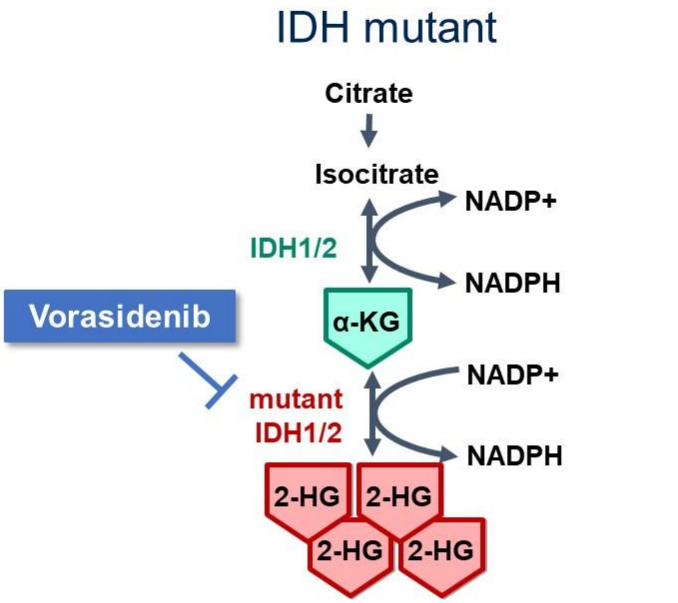
Ingo K. Mellinghoff,[1] Martin J. van den Bent,[2] Deborah T. Blumenthal,[3] Mehdi Touat,[4] Katherine B. Peters,[5] Jennifer Clarke,[6] Joe Mendez,[7] Liam Welsh,[8] Warren P. Mason,[9] Andreas F. Hottinger,[10] Juan M. Sepulveda,[11] Wolfgang Wick,[12] Riccardo Soffietti,[13] Steven Schoenfeld,[14] Dan Zhao,[14] Susan Pandya,[14] Lori Steelman,[14] Islam Hassan,[14] Patrick Y. Wen,[15]* Timothy F. Cloughesy[16]*

*[1]Memorial Sloan-Kettering Cancer Center, New York City, NY, USA; [2]Erasmus Medical Center, Rotterdam, Netherlands; [3]Tel Aviv Sourasky Medical Center, Tel Aviv University, Tel Aviv, Israel; [4]Pitié Salpêtrière Hospital, Assistance Publique-Hôpitaux de Paris (AP-HP) Sorbonne Université, Paris, France, [5]Duke University Medical Center, Durham, NC, USA; [6]University of California, San Francisco; [7]Huntsman Cancer Institute at the University of Utah, Salt Lake City, UT, USA; [8]The Royal Marsden Hospital, London, UK; [9]Toronto General Hospital, Toronto, M5G2C4, Canada; [10]University Hospital of Lausanne, Lausanne, Switzerland; [11]Hospital Universitario 12 de Octubre, Madrid, Spain; [12]Universitatsklinikum Heidelberg, Heidelberg, Germany; [13]University of Turin, Torino, Italy; [14]Servier Pharmaceuticals, Boston, MA, USA; [15]Dana-Farber Cancer Institute, Boston, MA, USA; [16]University of California, Los Angeles, CA, USA. *These authors contributed equally*

ClinicalTrials.gov identifier: NCT04164901. This study was sponsored by Servier

Vorasidenib

- Oral inhibitor of mutant IDH1 and IDH2[1]
- Specifically designed for brain penetrance[1]
- Reduced tumor 2-HG by >90% in resected grade 2/3 non-enhancing diffuse glioma[1]
- 2-HG reduction associated with:[2]
  - Lower tumor cell proliferation
  - Reversal of IDH1/2 mutation-associated gene expression programs
  - Increased DNA 5-hydroxy-methylcytosine
  - Increased tumor infiltrating lymphocytes



Competitive inhibition of α-KG-dependent enzymes

1. Mellinghoff I *et al. Nat Med* 2023;29:615–22; 2. Lu M et al. Presented at the American Association for Cancer Research Virtual Annual Meeting II June 22–24, 2020: abstract 2046.

INvestigating vorasiDenIb in GliOma (NCT04164901)

Key eligibility criteria

- ≥12 years of age
- IDH1/2-mutated* grade 2 oligodendroglioma or astrocytoma per WHO 2016 guidelines
- Prior surgery only
- Measurable non-enhancing disease (≥1 target lesion measuring ≥1 cm × ≥1 cm), confirmed by blinded review
- Not in need of immediate chemotherapy or radiotherapy per investigator assessment

1:1 double-blind randomization (N=331)

Stratified by 1p19q status and baseline tumor size

Vorasidenib 40 mg (N=168)

Orally, once daily, 28-day cycles

Centrally confirmed progressive disease permitted unblinding and crossover†

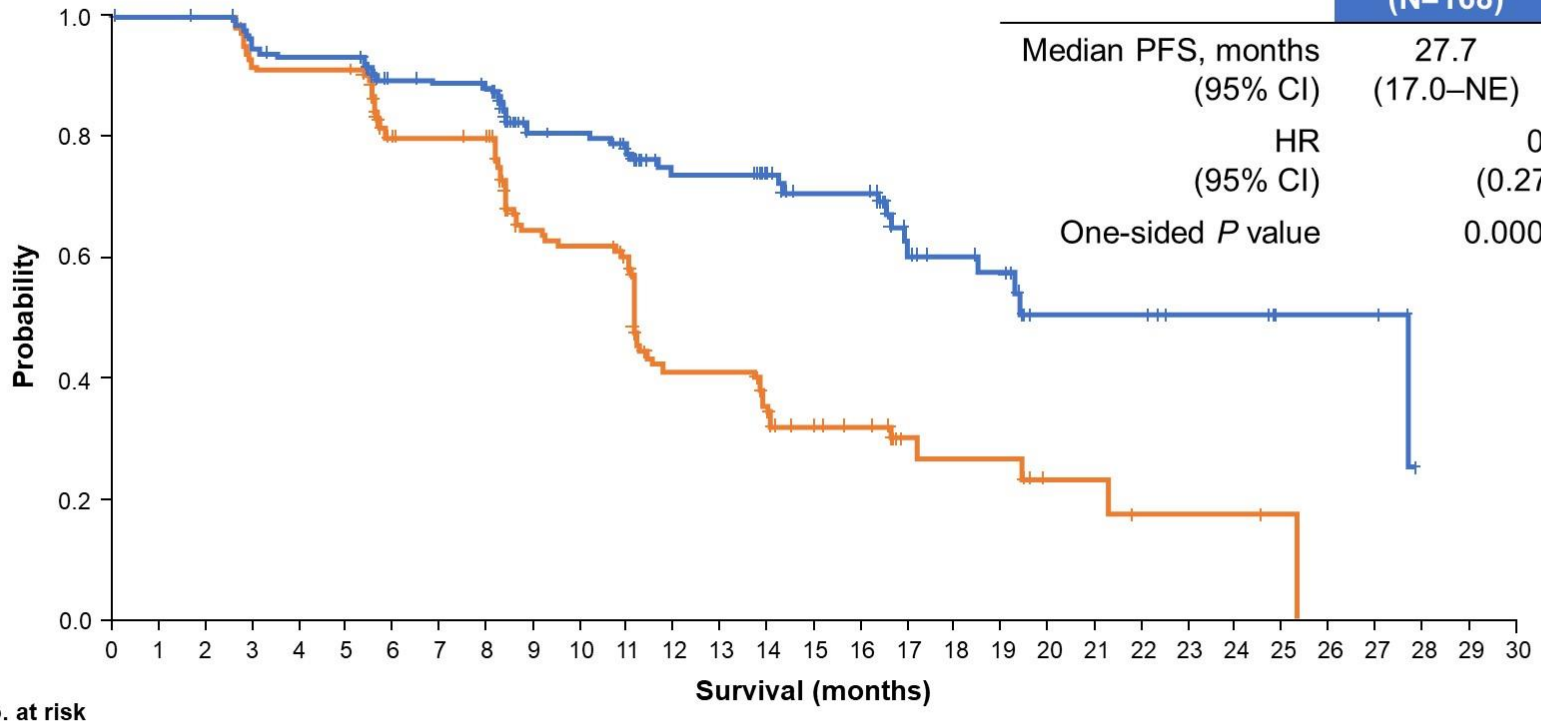
Placebo (N=163)

IDMC regularly reviewed safety and other clinical data, as well as the efficacy data following prespecified interim analyses

*Centrally confirmed using an investigational clinical trial assay, based on the Oncomine Dx Target Test and developed in partnership with Thermo Fisher Scientific Inc.;
†Real-time single BIRC reader.
IDMC, independent data monitoring committee.

PRESENTED BY: Ingo K. Mellinghoff, MD; Memorial Sloan Kettering Cancer Center

Primary endpoint: PFS per BIRC



	Vorasidenib (N=168)	Placebo (N=163)
Median PFS, months (95% CI)	27.7 (17.0–NE)	11.1 (11.0–13.7)
HR (95% CI)	0.39 (0.27–0.56)	
One-sided *P* value	0.000000067	

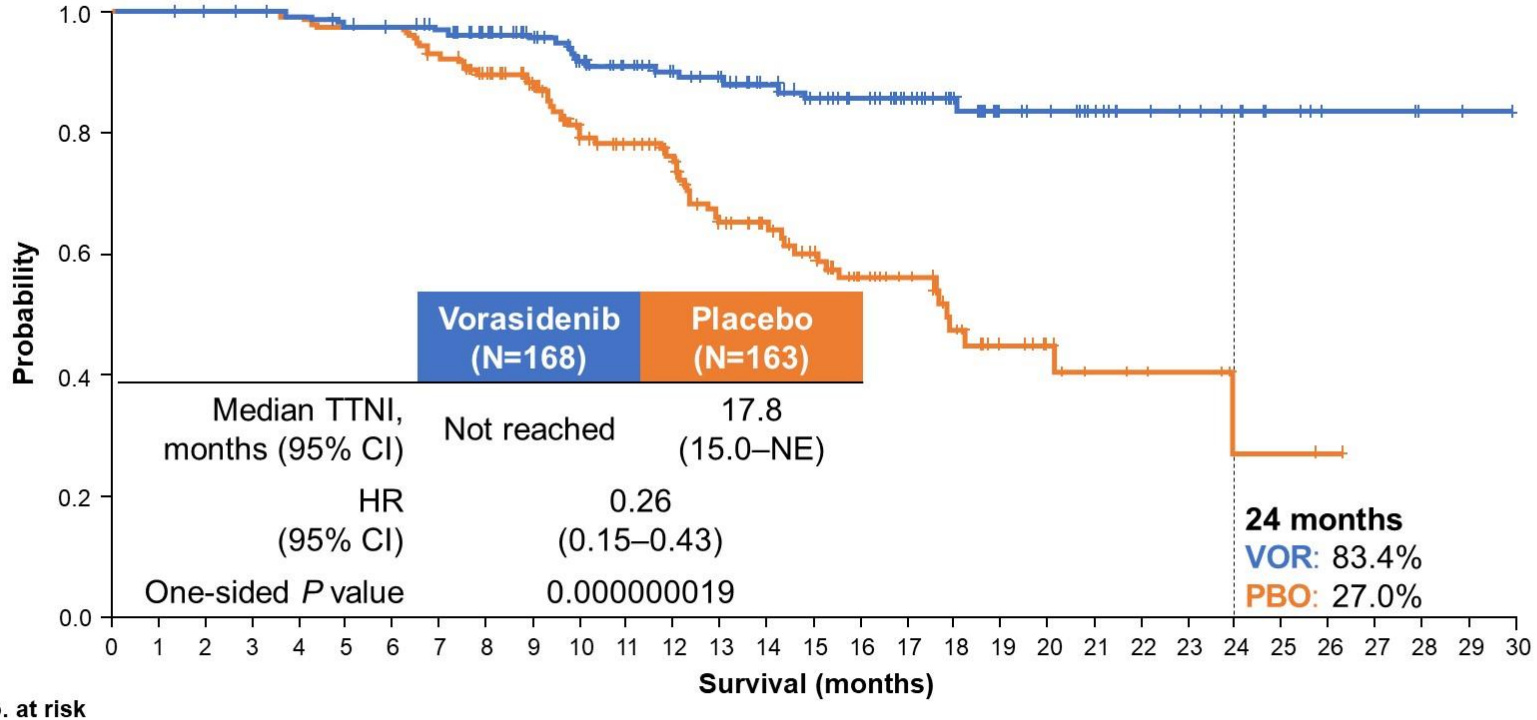
No. at risk

VOR	168	166	166	157	154	154	133	131	129	93	91	81	63	63	52	45	45	25	22	20	11	11	11	7	7	4	4	4	0
PBO	163	162	161	146	145	145	117	116	114	73	70	65	38	38	29	21	19	9	8	8	4	4	2	2	2	1	0		

+ Censored.
P value is from one-sided stratified log-rank test.
NE, not estimable; PBO, placebo; VOR, vorasidenib.

PRESENTED BY: Ingo K. Mellinghoff, MD; Memorial Sloan Kettering Cancer Center

Key secondary endpoint: TTNI



No. at risk

VOR	168	168	167	167	165	161	160	156	146	130	117	105	95	86	75	65	57	48	38	27	25	18	15	13	11	7	4	4	2	1	0
PBO	163	163	162	161	159	156	155	146	134	119	97	88	77	60	54	45	35	30	21	14	11	7	6	5	2	2	1	0			

+ Censored.
P value is from one-sided stratified log-rank test.

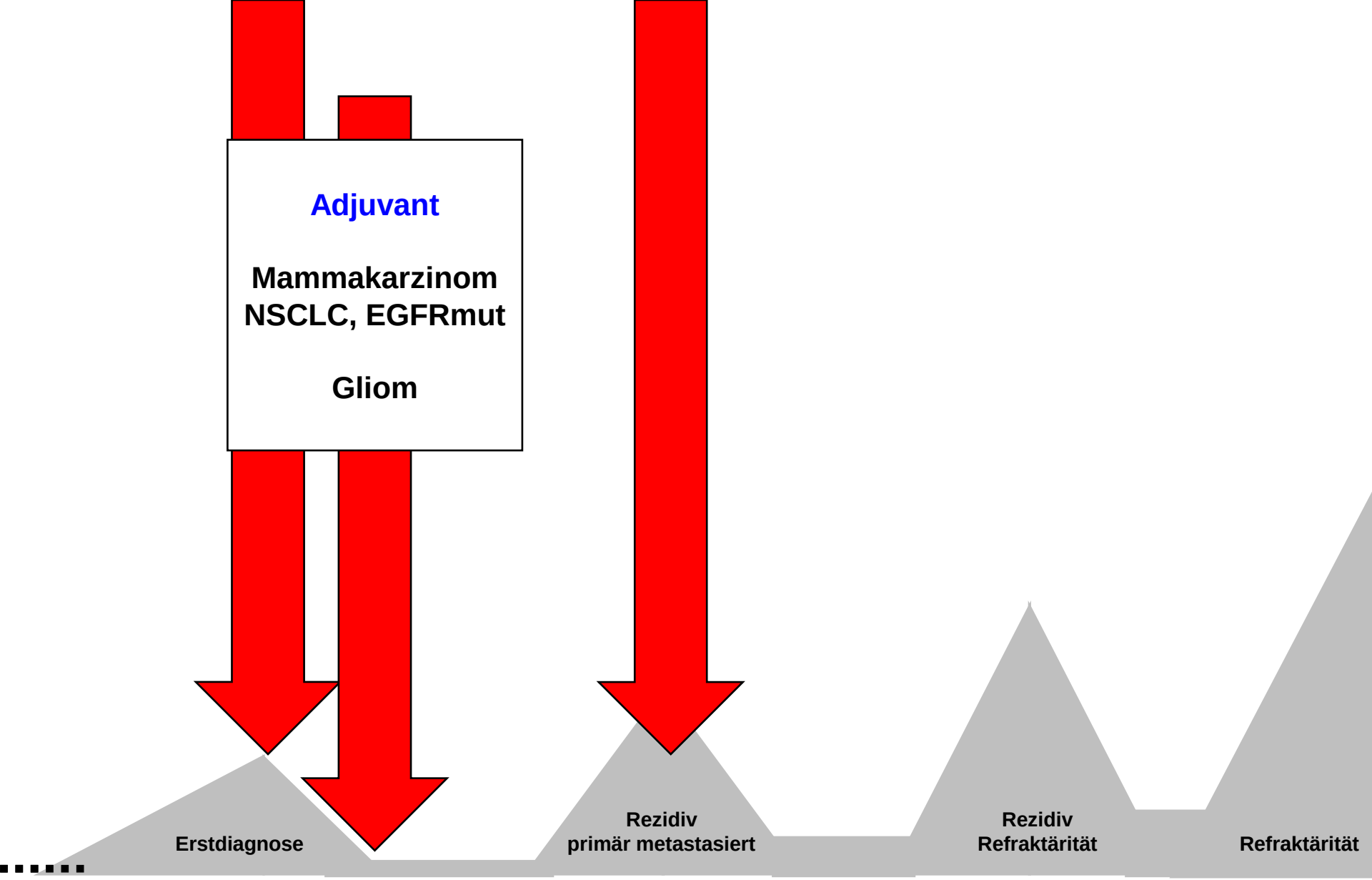
PRESENTED BY: Ingo K. Mellinghoff, MD; Memorial Sloan Kettering Cancer Center

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vorasidenib in IDH1- or IDH2-Mutant Low-Grade Glioma

I.K. Mellinghoff, M.J. van den Bent, D.T. Blumenthal, M. Touat, K.B. Peters, J. Clarke, J. Mendez, S. Yust-Katz, L. Welsh, W.P. Mason, F. Ducray, Y. Umemura, B. Nabors, M. Holdhoff, A.F. Hottinger, Y. Arakawa, J.M. Sepulveda, W. Wick, R. Soffietti, J.R. Perry, P. Giglio, M. de la Fuente, E.A. Maher, S. Schoenfeld, D. Zhao, S.S. Pandya, L. Steelman, I. Hassan, P.Y. Wen, and T.F. Cloughesy*


Adjuvant
Mammakarzinom
NSCLC, EGFRmut
Gliom
Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität

2023 ASCO ANNUAL MEETING

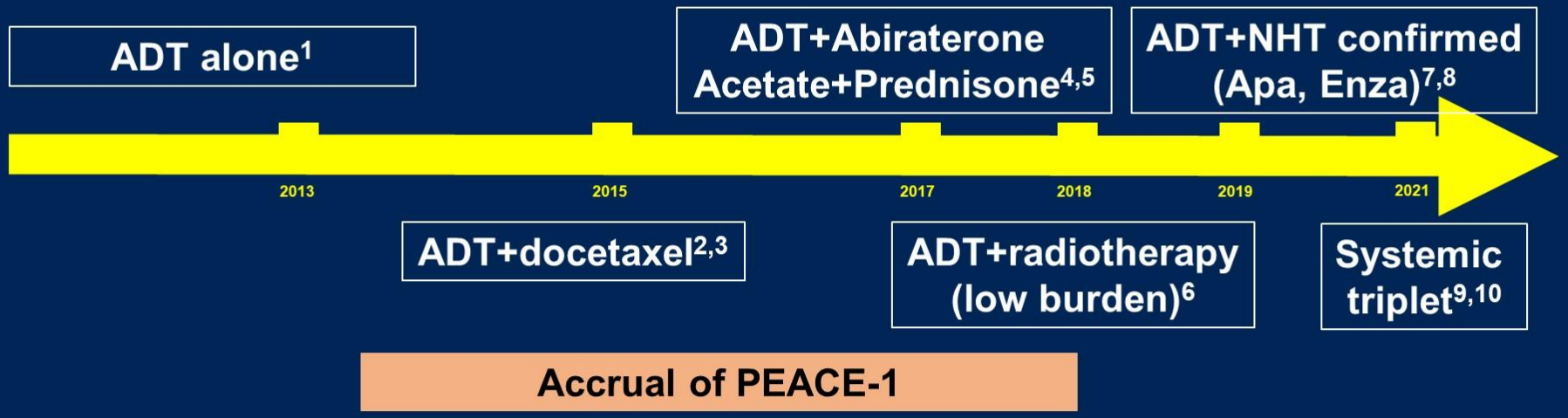
Prostate irradiation in men with *de novo*, low-volume, metastatic castration-sensitive prostate cancer (mCSPC): Results of PEACE-1, a phase 3 randomized trial with a 2x2 design

Alberto BOSSI,
Institut Gustave Roussy, Amethyst RT Group, France

Stéphanie Foulon, Xavier Maldonado, Paul Sargos, Ray McDermott, Paul Kelly, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacso, Naji Salem, Fabio Calabro', Jean-François Berdah, Ali Hasbini, Marlon Silva, Jihane Boustani, Hélène Ribault, Karim Fizazi

Background

Very rapidly evolving Standard of Care (SOC) for men with metastatic castration-sensitive prostate cancer (mCSPC)



[1]Gravis G, Lancet Oncol 2013, [2]Sweeney C, NEJM 2015, [3]James N, Lancet 2016, [4]Fizazi K, NEJM 2017, [5]James N, NEJM 2017, [6]Parker C, Lancet 2018,[7]Davis I, NEJM 2019, [8]Chi K, NEJM 2019, [9] Fizazi K, Lancet 2022, [10]Smith M, NEJM 2022

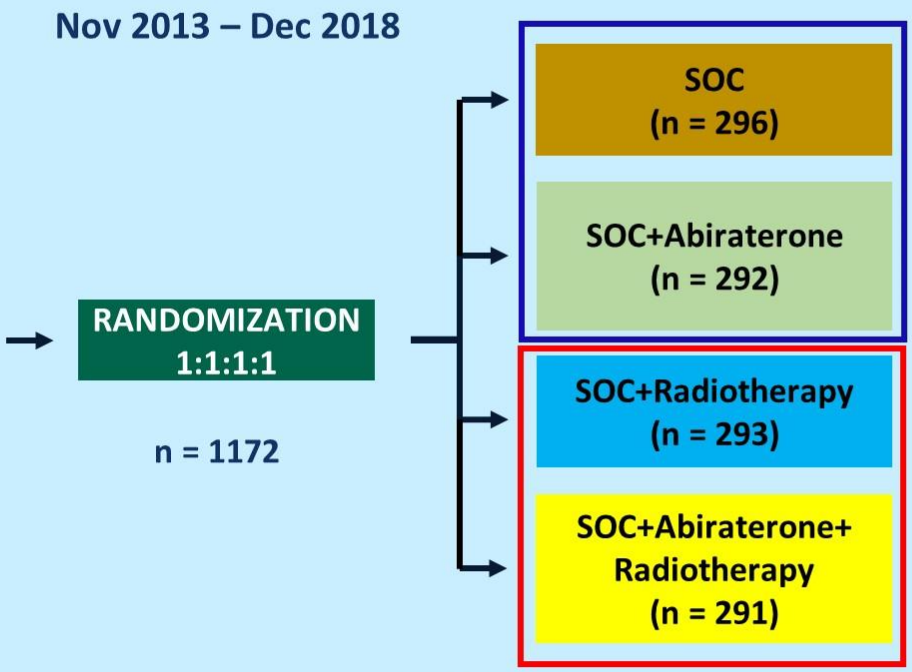
Design of PEACE-1

Key Eligibility Criteria
De novo mCSPC
Distant metastatic disease: ≥ 1 lesion on bone scan and/or CT scan
ECOG PS 0 -2

On-Study Requirement
Continuous ADT

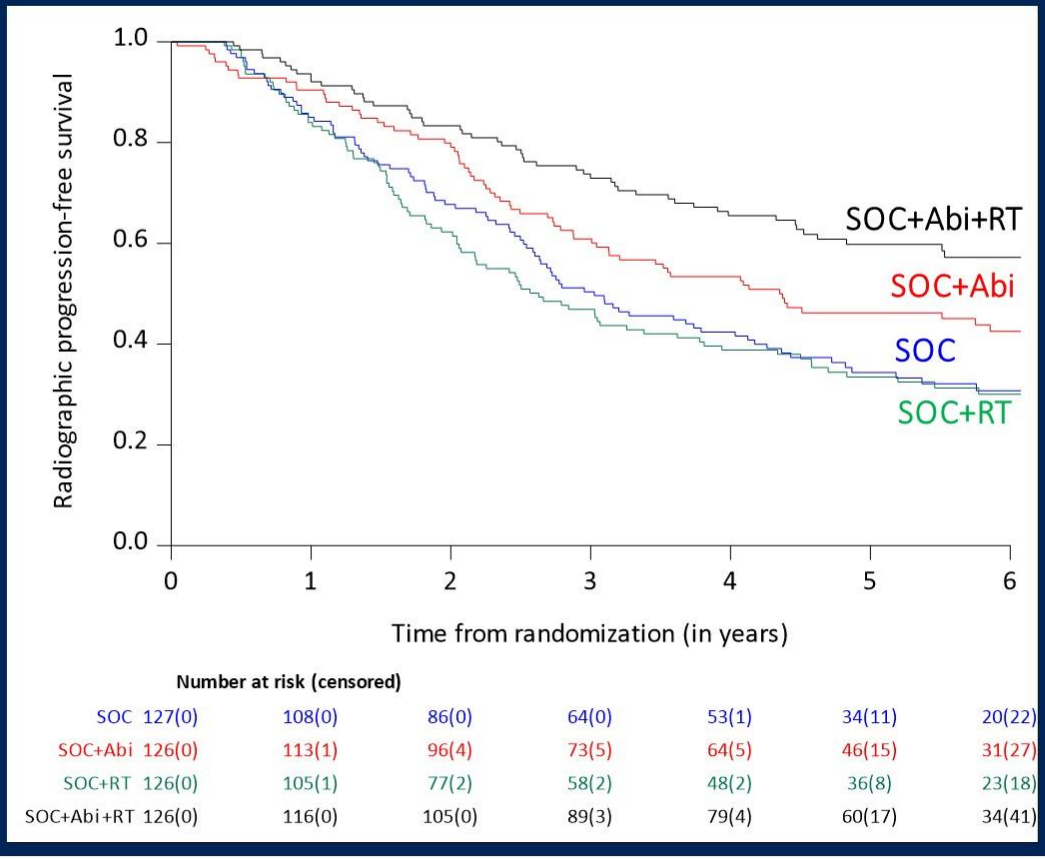
Permitted
ADT ≤ 3 months

Stratification
ECOG PS (0 vs 1-2)
Metastatic sites (LN vs bone vs visceral)
Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)
Docetaxel (yes vs no)



ECOG PS, Eastern Cooperative Oncology Group performance status

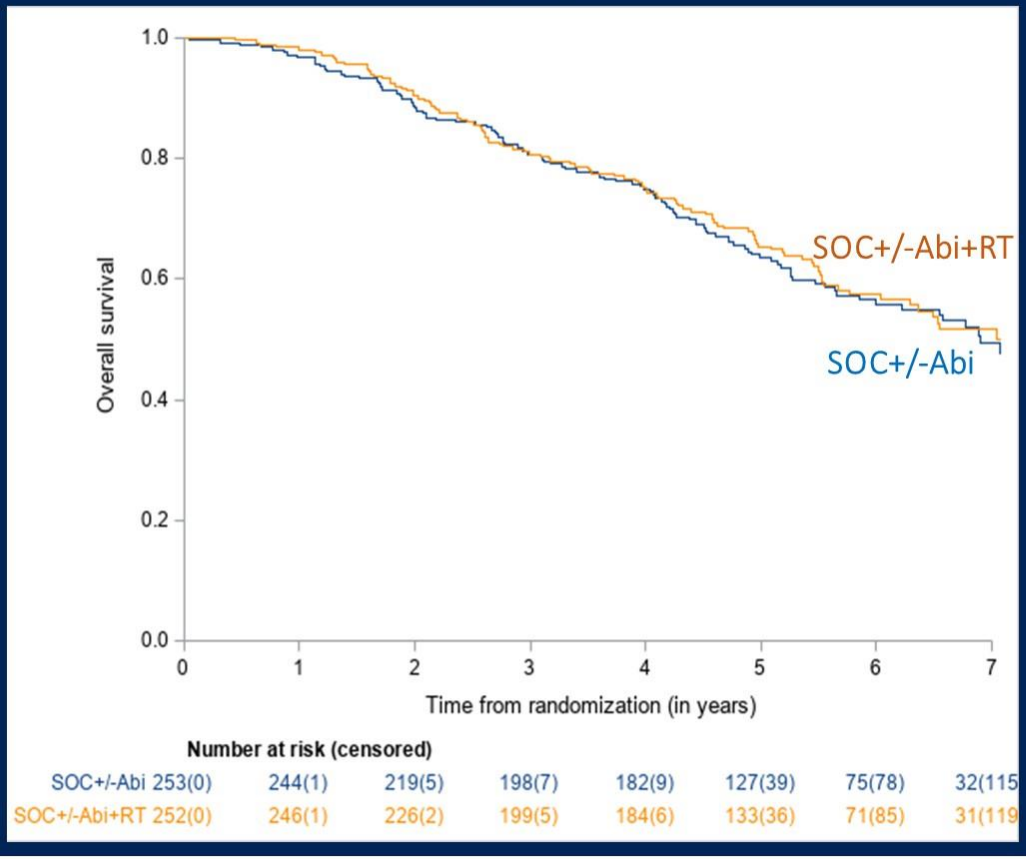
rPFS (low volume population)



	SOC (n=127)	SOC+RT (n=126)	SOC+Abi (n=126)	SOC+Abi+RT (n=126)
Median, ys. (99.9% CI)	3.0 (2.3-4.8)	2.6 (1.7-4.6)	4.4 (2.5-7.3)	7.5 (4,0-NE)
Events, n.	87	89	74	55
HR (99.9%CI)*	Ref	1.11 (0.67-1.84)	0.76 (0.45-1,28)	0.50 (0.28-0.88)
Global p-value	<0.0001			
HR (99.9% CI)*	Ref	1.08 (0.65-1.80)	Ref	0.65 (0.36-1.19)
P-values arms w/wo Abi	0.61		0.02	

*Adjusted on stratification factors (PS, type of castration, docetaxel)

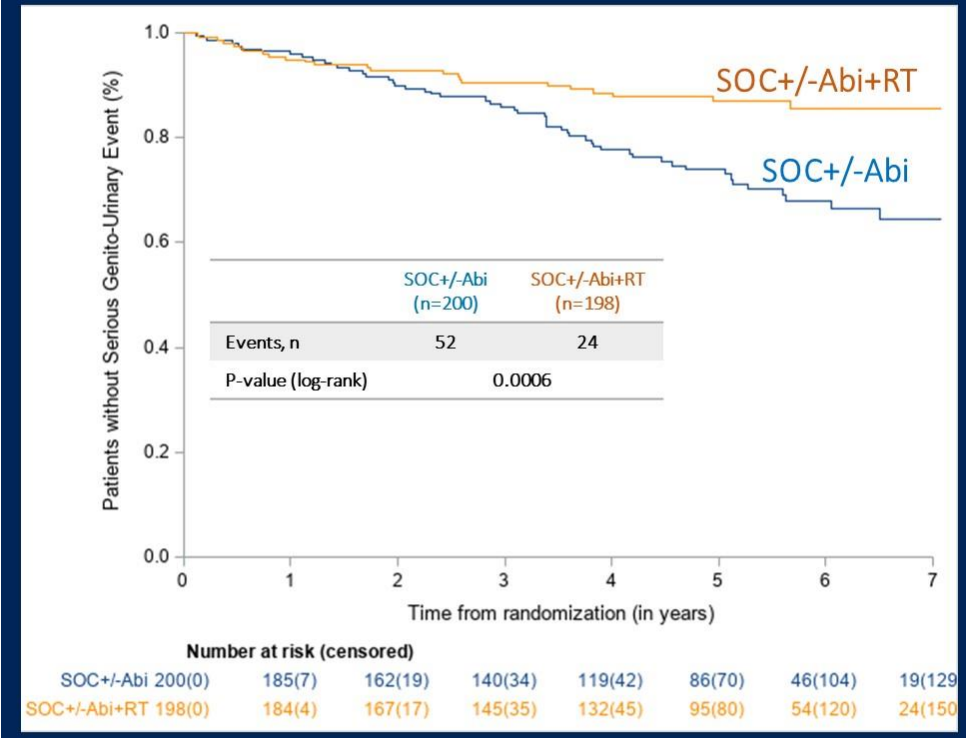
OS (low volume population)

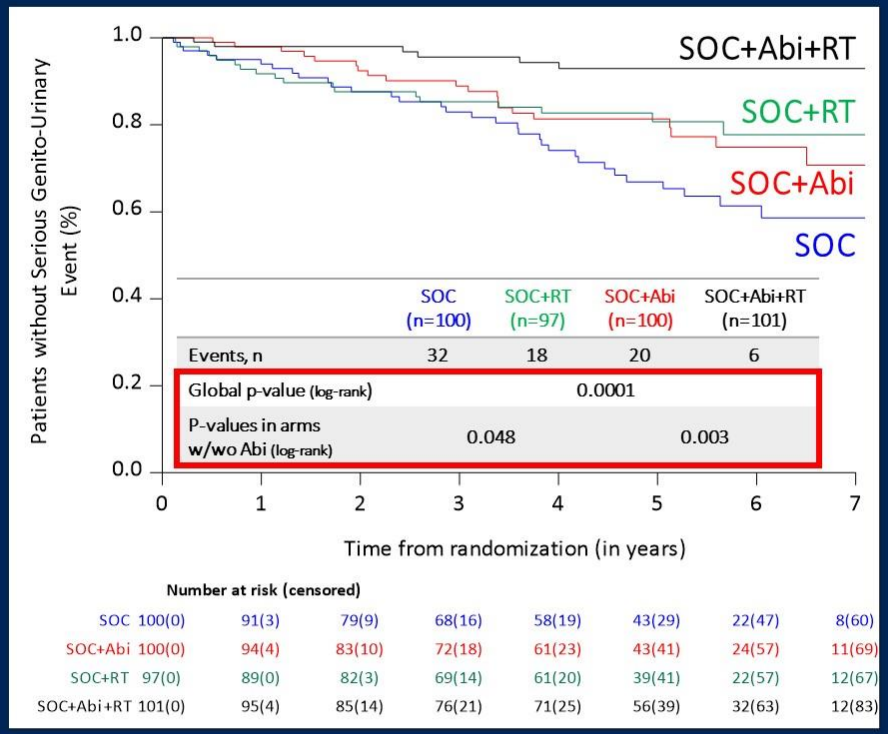


	SOC+/Abi (n=253)	SOC+/-Abi++RT (n=252)
Median, ys. (95.1% CI)	6.9 (5,9-7,5)	7.5 (6-NE)
Events, n	111	104
HR*	Ref	0.98 (0.74-1.28)
p-value	0.86	

*Adjusted on Abitraterone and stratification factors (PS, type of castration, docetaxel)

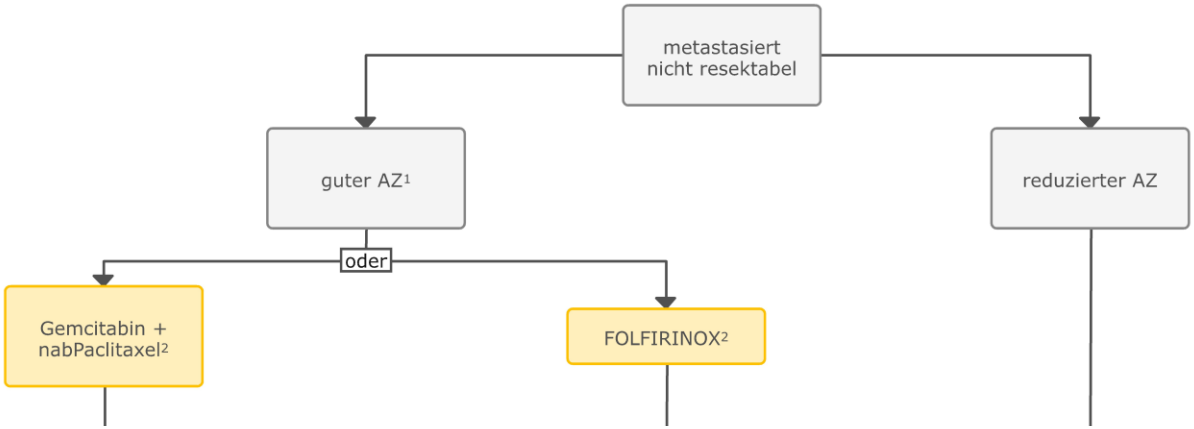
Time to Serious Genito-Urinary events (low volume pop.)





Pankreaskarzinom

palliative Therapie



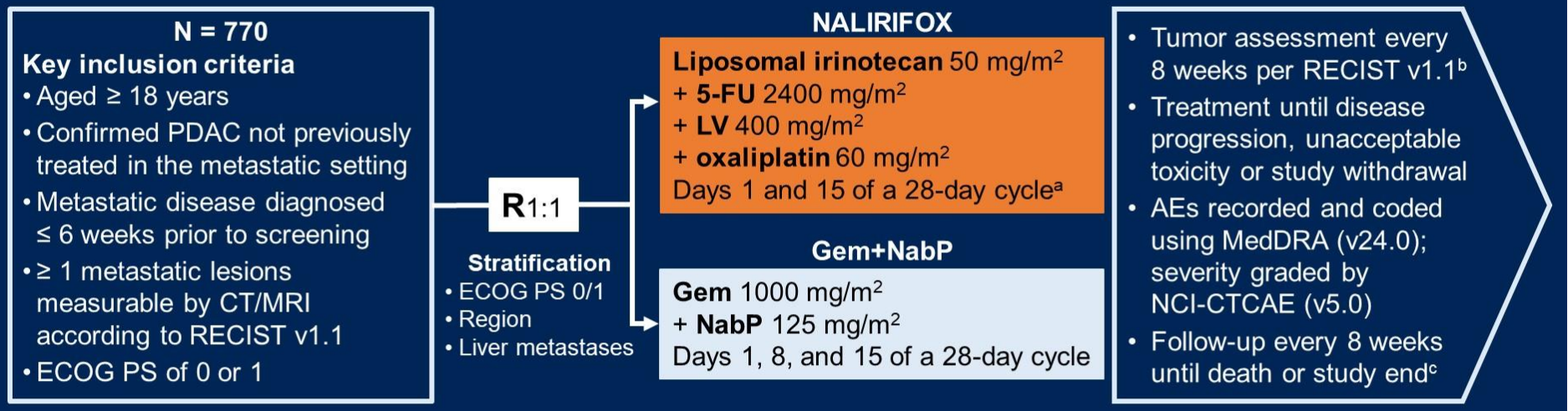
2023 ASCO ANNUAL MEETING

NALIRIFOX versus nab-paclitaxel + gemcitabine in treatment-naive patients with mPDAC: additional results from the phase 3 NAPOLI 3 trial

Eileen M O'Reilly,[1] Davide Melisi,[2] Teresa Macarulla,[3] Roberto A Pazo Cid,[4] Sreenivasa R Chandana,[5] Christelle De La Fouchardière,[6] Andrew Dean,[7] Igor Kiss,[8] Woo Jin Lee,[9] Thorsten O Goetze,[10] Eric Van Cutsem,[11] Scott Paulson,[12] Tanios Bekaii-Saab,[13] Shubham Pant,[14] Richard Hubner,[15] Zhimin Xiao,[16] Huanyu Chen,[16] Fawzi Benzaghou,[16] Zev A Wainberg[17]

[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Investigational Cancer Therapeutics Clinical Unit, Azienda Ospedaliera Universitaria Integrata, Verona, Italy; [3]Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; [4]Hospital Universitario Miguel Servet, Zaragoza, Spain; [5]Cancer and Hematology Centers of Western Michigan, Grand Rapids, MI, USA; [6]Centre Léon Bérard, Lyon, France; [7]St John of God Subiaco Hospital, Subiaco, WA, Australia; [8]Masaryk Memorial Cancer Institute and Faculty of Medicine, Masaryk University, Brno, Czechia; [9]National Cancer Center, Goyang, Republic of Korea; [10]Krankenhaus Nordwest, Frankfurt, Germany; [11]University Hospitals Gasthuisberg and KULeuven, Leuven, Belgium; [12]Texas Oncology-Baylor Charles A. Sammons Cancer Center, Dallas, TX, USA; [13]Mayo Clinic, Scottsdale, AZ, USA; [14]MD Anderson Cancer Center, Houston, TX, USA; [15]The Christie NHS Foundation Trust, Manchester, UK; [16]Ipsen, Cambridge, MA, USA; [17]University of California, Los Angeles, CA, USA

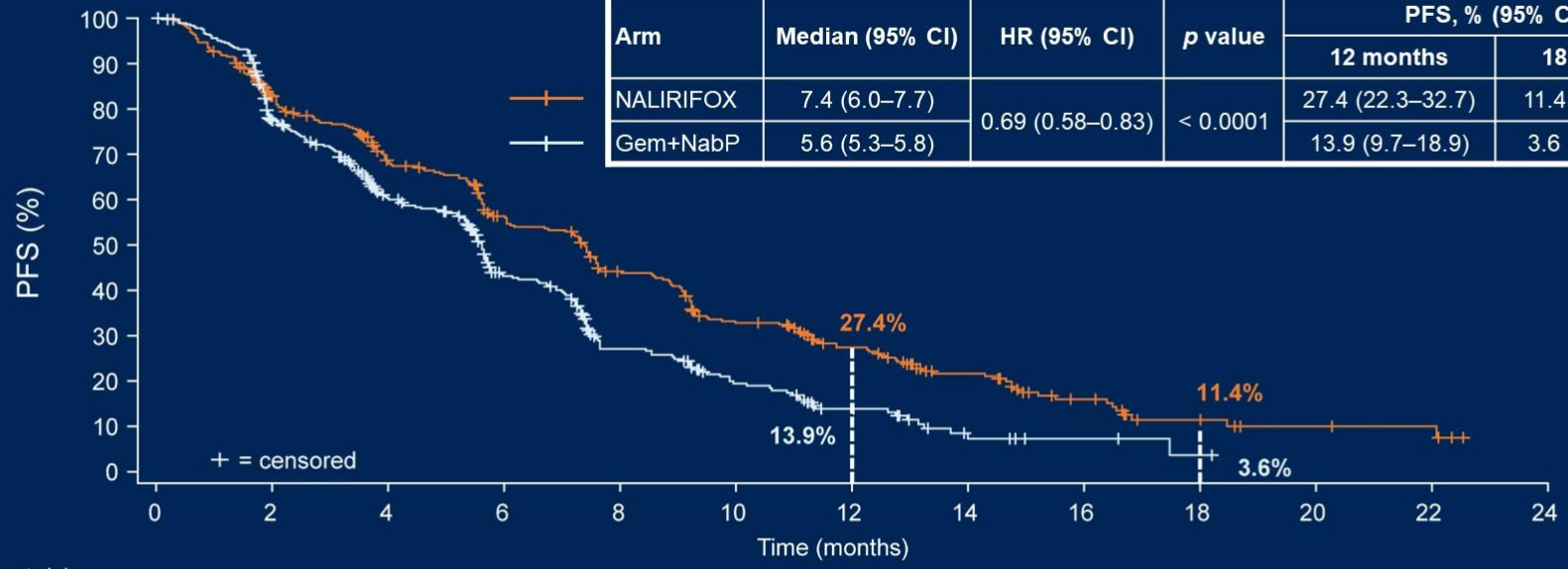
NAPOLI 3: Study design



[a]Administered sequentially as a continuous infusion over 46 hours on days 1 and 15 of a 28-day cycle (dose delays and oxaliplatin discontinuation were permitted). [b]Until progressive disease. [c]The study was completed once all patients had discontinued the study treatment and at least 543 OS events had occurred in randomized patients.
5-FU, 5-fluorouracil; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; Gem, gemcitabine; LV, leucovorin; MedDRA, Medical Dictionary for Regulatory Activities; MRI, magnetic resonance imaging; NabP, nab-paclitaxel; NALIRIFOX, liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; PDAC, pancreatic ductal adenocarcinoma; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors.

NAPOLI 3: PFS per investigator (ITT population)

Arm	Median (95% CI)	HR (95% CI)	*p* value	PFS, % (95% CI)	
				12 months	18 months
NALIRIFOX	7.4 (6.0–7.7)	0.69 (0.58–0.83)	< 0.0001	27.4 (22.3–32.7)	11.4 (7.1–16.9)
Gem+NabP	5.6 (5.3–5.8)			13.9 (9.7–18.9)	3.6 (0.5–12.3)



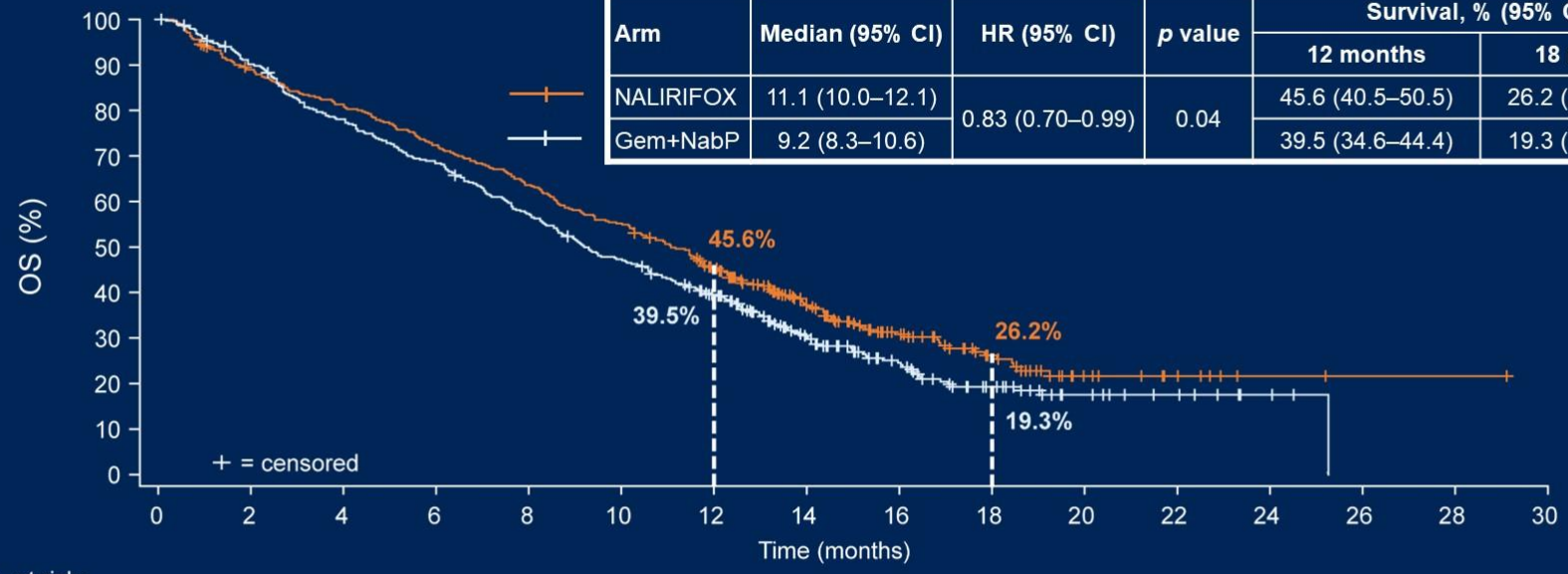
No. at risk:

NALIRIFOX	383	271	210	164	122	87	61	39	20	9	5	4	0
Gem+NabP	387	267	182	112	60	38	19	6	3	1	0	0	0

Hazard ratio and 95% CI based on a Cox proportional hazards regression model, stratified by ECOG PS (0 vs 1), region (North America vs ROW), liver metastases (yes vs no) per IRT. P boundary for efficacy claim *p* value < 0.048.
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; Gem, gemcitabine; HR, hazard ratio; IRT, interactive response technology; ITT, intention-to-treat; NabP, nab-paclitaxel; NALIRIFOX, liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin; PFS, progression-free survival; ROW, rest of world.

NAPOLI 3: OS (ITT population)

Arm	Median (95% CI)	HR (95% CI)	*p* value	Survival, % (95% CI)	
				12 months	18 months
NALIRIFOX	11.1 (10.0–12.1)	0.83 (0.70–0.99)	0.04	45.6 (40.5–50.5)	26.2 (20.9–31.7)
Gem+NabP	9.2 (8.3–10.6)			39.5 (34.6–44.4)	19.3 (14.8–24.2)

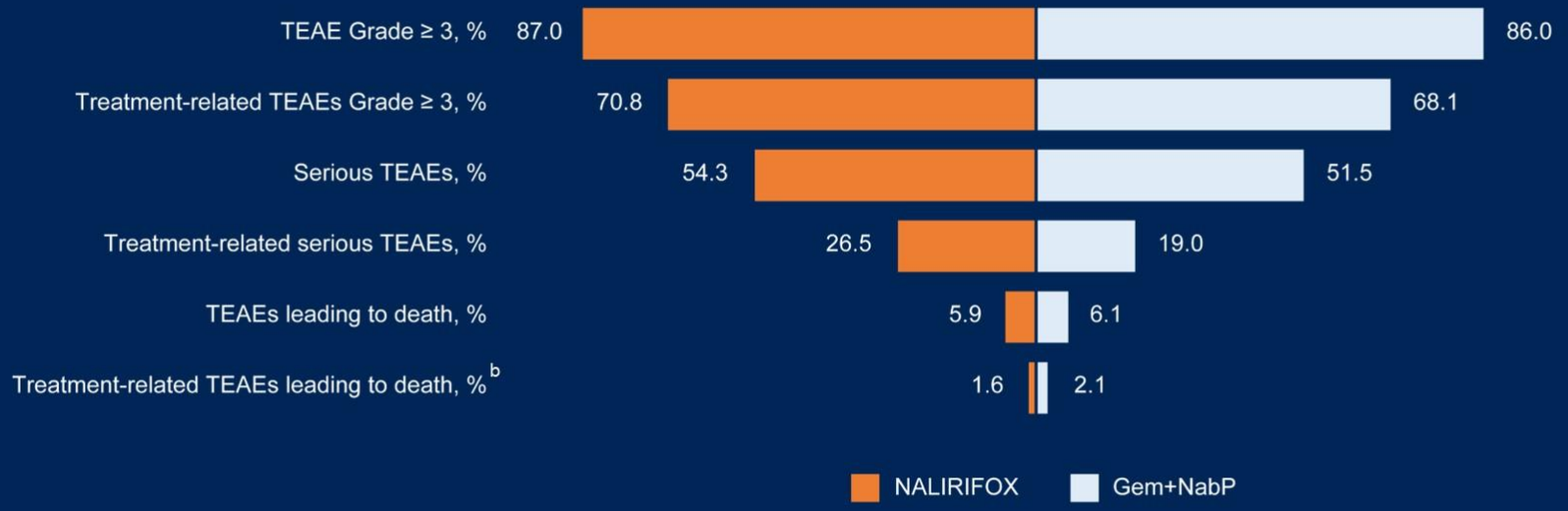


No. at risk:

NALIRIFOX	383	337	308	274	241	209	162	98	59	32	13	7	2	1	1	0
Gem+NabP	387	345	298	261	218	179	140	80	50	28	15	10	3	0	0	0

Hazard ratio and 95% CI based on a Cox proportional hazards regression model, stratified by ECOG PS (0 vs 1), region (North America vs ROW), liver metastases (yes vs no) per IRT. P boundary for efficacy claim *p* value < 0.048.
CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; Gem, gemcitabine; HR, hazard ratio; IRT, interactive response technology; ITT, intention-to-treat; NabP, nab-paclitaxel; NALIRIFOX, liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin; OS, overall survival; ROW, rest of world.

NAPOLI 3: Overall summary of adverse events[a]



Median (range) duration of treatment was 24.3 (0.4–100.9) weeks with NALIRIFOX and 17.6 (0.7–81.7) weeks with Gem+NabP

[a]Safety population. [b]Treatment-related TEAEs leading to death occurred in 6 patients receiving NALIRIFOX and 8 patients receiving Gem+NabP.
Gem, gemcitabine; NabP, nab-paclitaxel; NALIRIFOX, liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin; TEAE, treatment-emergent adverse event.

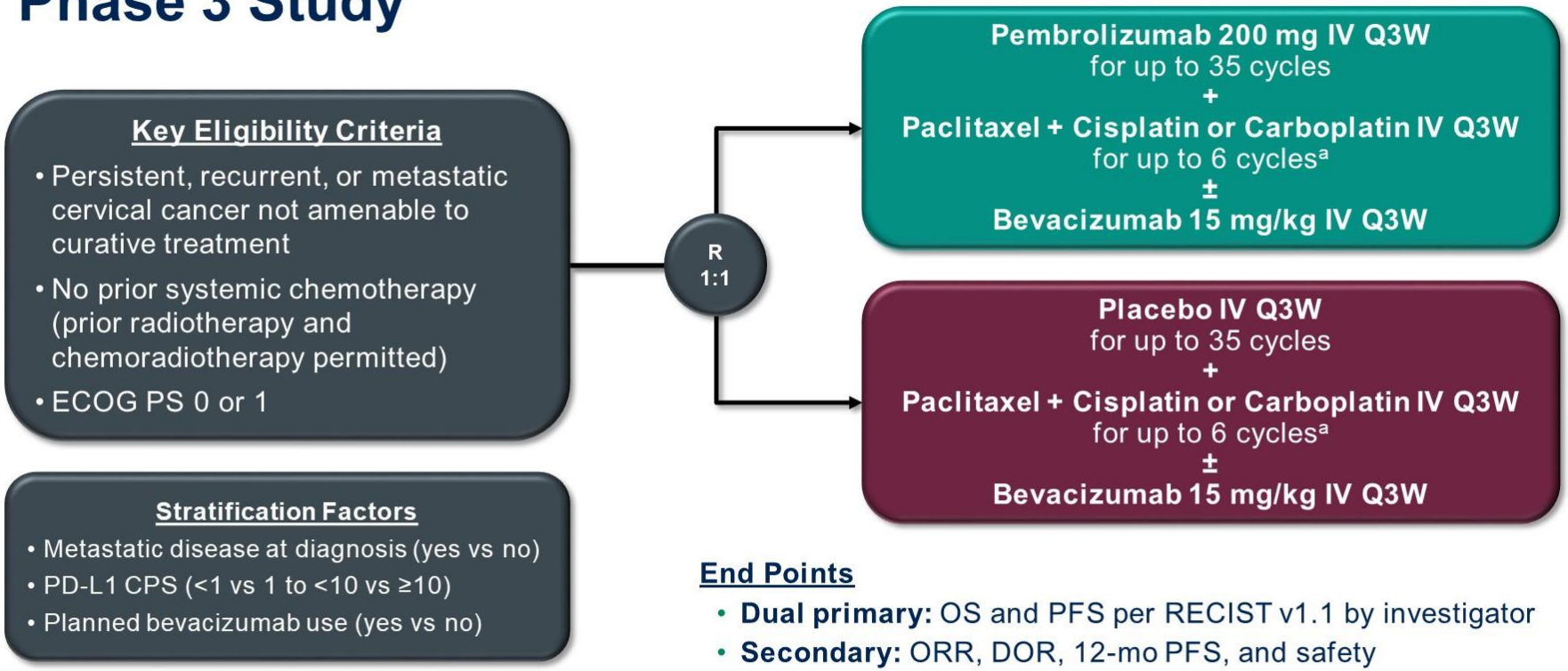
2023 ASCO ANNUAL MEETING

Pembrolizumab + Chemotherapy versus Placebo + Chemotherapy for Persistent, Recurrent, or Metastatic Cervical Cancer: Final Overall Survival Results of KEYNOTE-826

Bradley J. Monk,[1] Nicoletta Colombo,[2,3] Krishnansu S. Tewari,[4] Coraline Dubot,[5] M. Valeria Caceres,[6] Kosei Hasegawa,[7] Ronnie Shapira-Frommer,[8] Pamela Salman,[9] Eduardo Yañez,[10] Mahmut Gümüş,[11] Mivael Olivera Hurtado de Mendoza,[12] Vanessa Samouëlian,[13] Vincent Castonguay,[14] Alexander Arkhipov,[15] Cumhur Tekin,[16] Kan Li,[16] Stephen M. Keefe,[16] Domenica Lorusso,[17] on behalf of the KEYNOTE-826 Investigators

[1]HonorHealth Research Institute, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ, USA; [2]Gynecologic Oncology, European Institute of Oncology IRCCS and [3]Università degli Studi di Milano Bicocca, Milan, Italy; [4]Obstetrics & Gynecology, University of California, Irvine, Orange, CA, USA; [5]Oncologie Médicale, Institut Curie Saint Cloud, and GINECO, Paris, France; [6]Medical Oncology, Instituto de Oncologia Angel H. Roffo, Buenos Aires, Argentina; [7]Gynecologic Oncology, Saitama Medical University International Medical Center, Hidaka, Japan; [8]Ella Lemelbaum Institute for Immuno-Oncology, Sheba Medical Center, Ramat Gan, Israel; [9]Medical Oncology, Oncovida Cancer Center, Providencia, Santiago, Chile; [10]Medical Oncology, Universidad de la Frontera, Temuco, Chile; [11]Medical Oncology, Istanbul Medeniyet University Hospital, Istanbul, Turkey; [12]Medical Oncology, Instituto Nacional de Enfermedades Neoplásicas, Lima, Peru; [13]Gynecologic Oncology, Centre Hospitalier de l'Université de Montréal (CHUM), Centre de Recherche de l'Université de Montréal (CRCHUM), Université de Montréal, Montreal, QC, Canada; [14]Medical Oncology, Centre Hospitalier Universitaire de Québec, Université Laval, Quebec City, QC, Canada; [15]Oncology and Chemical Therapy, Medical Rehabilitation Center under the Ministry of Health of Russian Federation, Moscow, Russian Federation; [16]Oncology, Merck & Co., Inc., Rahway, NJ, USA; [17]Gynaecology Oncology Unit, Fondazione Policlinico Universitario A Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy

KEYNOTE-826: Randomized, Double-Blind, Phase 3 Study



End Points

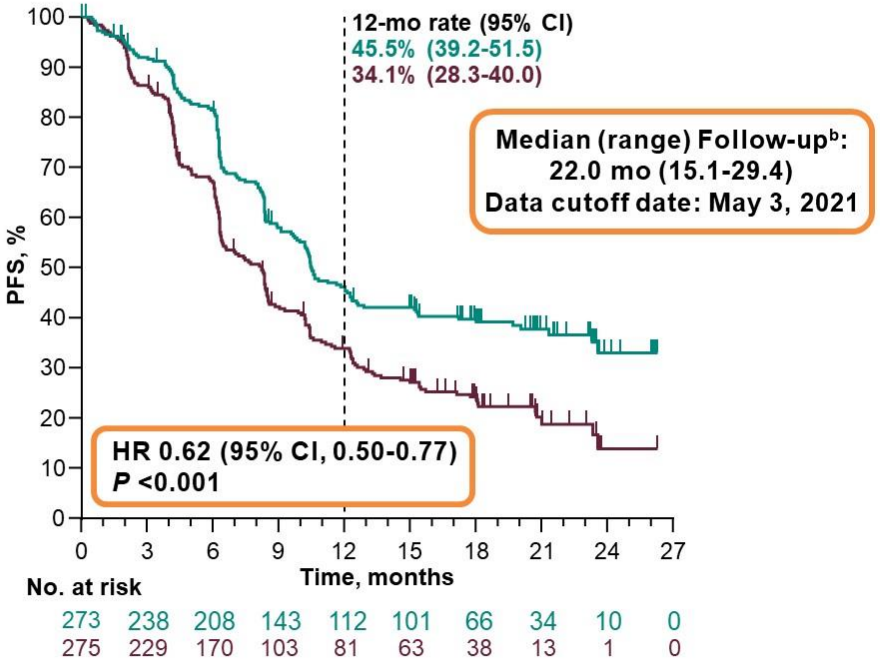
- **Dual primary:** OS and PFS per RECIST v1.1 by investigator
- **Secondary:** ORR, DOR, 12-mo PFS, and safety

[a]Paclitaxel: 175 mg/m^2. Cisplatin: cisplatin 50 mg/m^2. Carboplatin: AUC 5 mg/mL/min. The 6-cycle limit was introduced with protocol amendment 2, although participants with ongoing clinical benefit who were tolerating chemotherapy could continue beyond 6 cycles after sponsor consultation. CPS, combined positive score (number of PD-L1–staining cells [tumor cells, lymphocytes, macrophages] divided by the total number of viable tumor cells, multiplied by 100). KEYNOTE-826 ClinicalTrials.gov identifier, NCT03635567.

Dual Primary Endpoints at IA1: PD-L1 CPS ≥1 Population

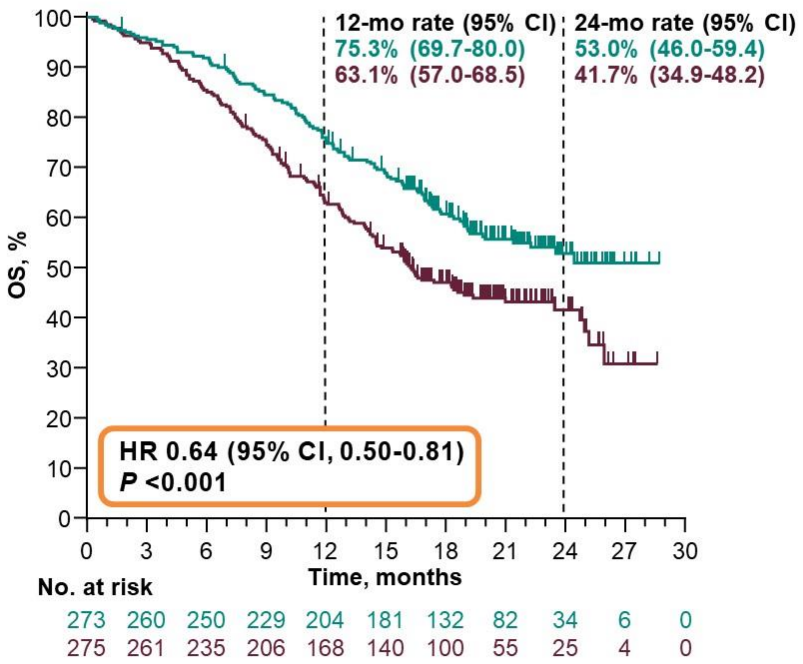
PFS[a]

	Pts w/Event	Median, mo (95% CI)
Pembro + Chemo ± Bev	57.5%	10.4 (9.7-12.3)
Pbo + Chemo ± Bev	72.0%	8.2 (6.3-8.5)



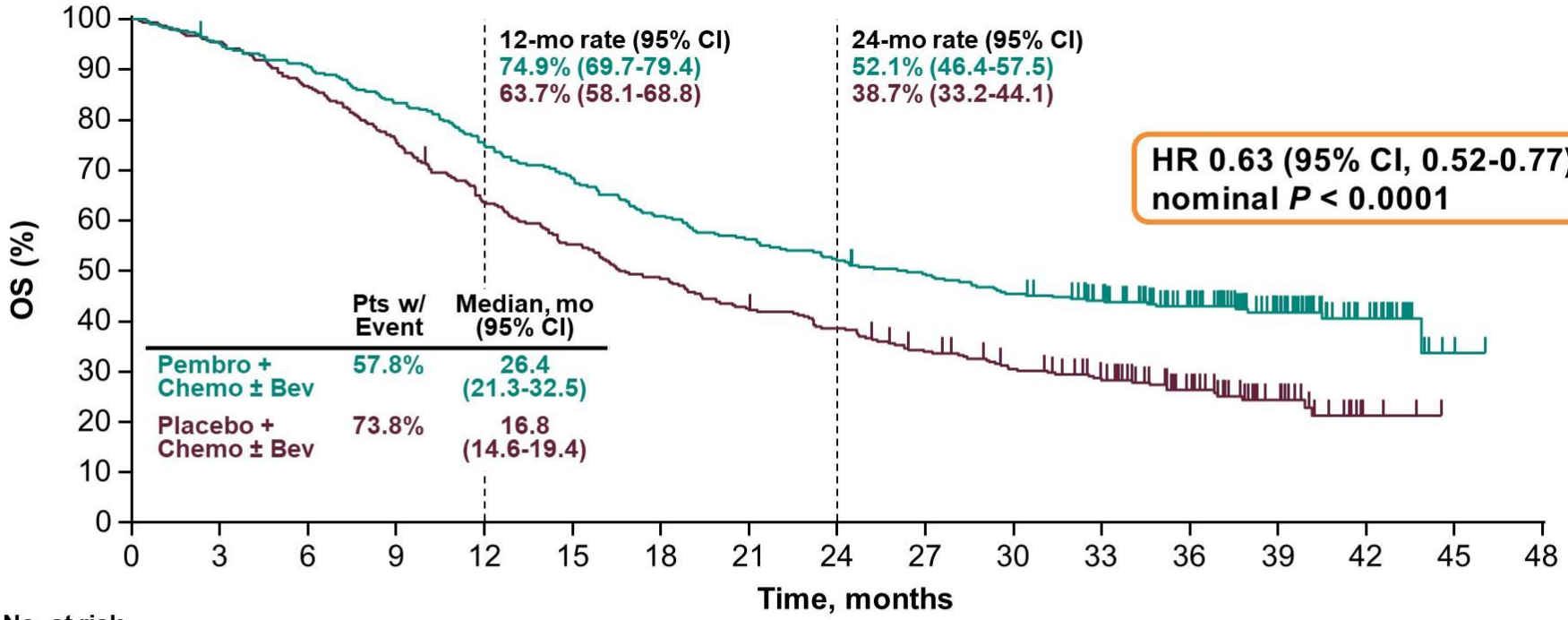
Interim OS

	Pts w/Event	Median, mo (95% CI)
Pembro + Chemo ± Bev	43.2%	NR (19.8-NR)
Pbo + Chemo ± Bev	56.0%	16.3 (14.5-19.4)



Colombo N et al. *N Engl J Med* 2021;385:1856-67. [a]Response assessed per RECIST v1.1 by investigator review. [b]Defined as the time from randomization to the data cutoff date of May 3, 2021.

Protocol-Specified Final OS: All-Comer Population

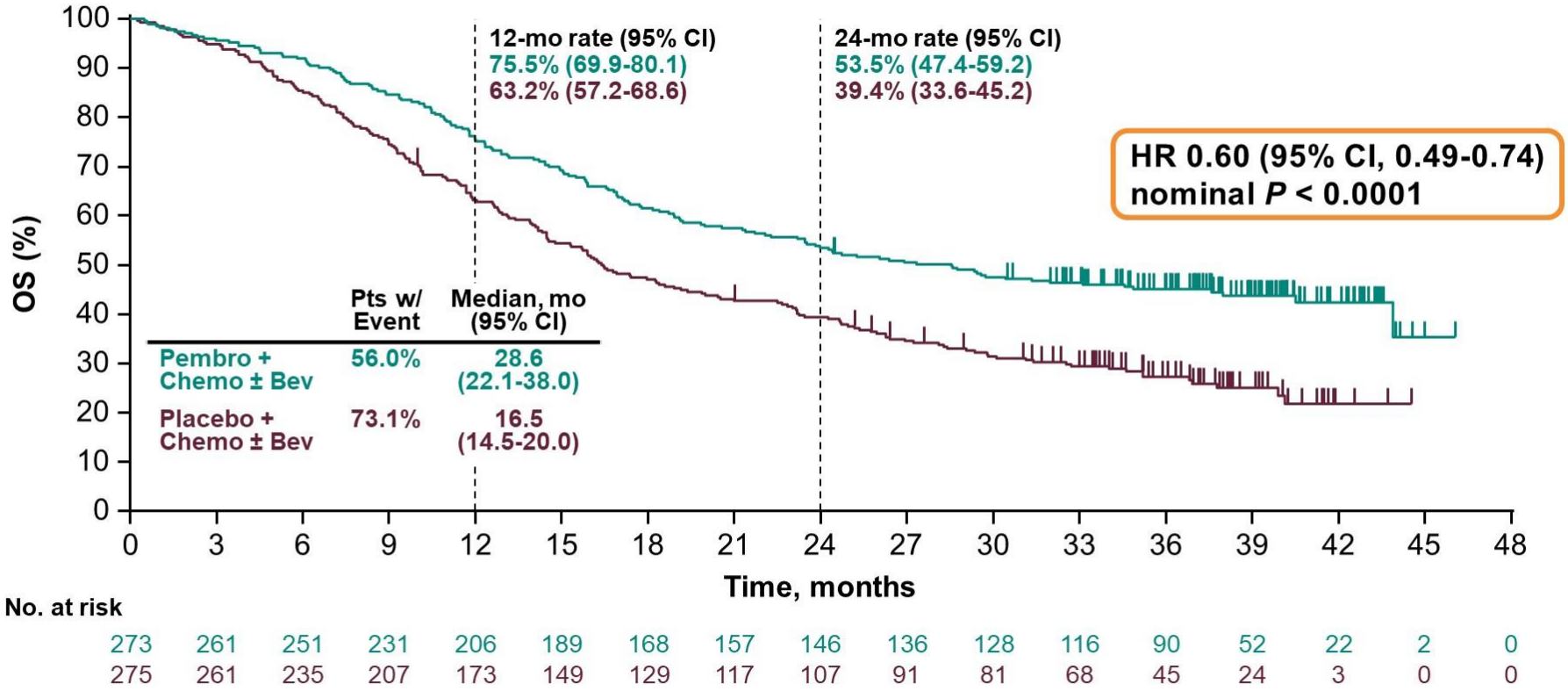


No. at risk

308	292	278	256	230	210	187	173	160	150	138	125	95	55	22	2	0
309	295	268	235	196	170	149	130	118	101	87	72	48	26	3	0	0

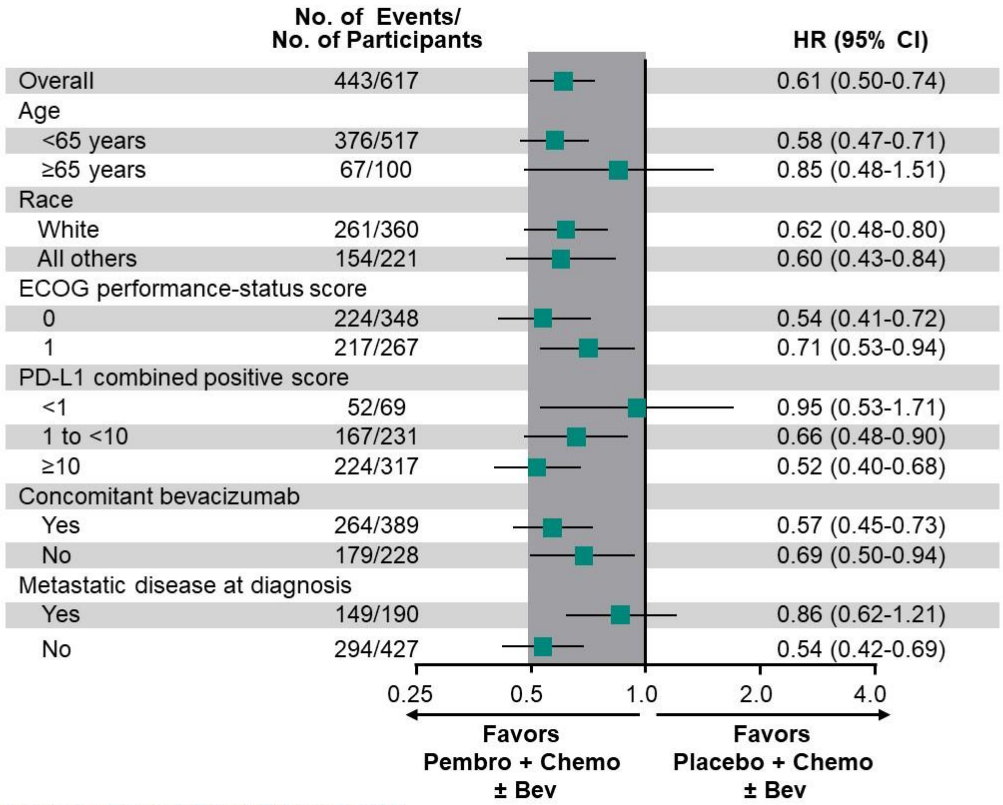
Data cutoff date: October 3, 2022.

Protocol-Specified Final OS: PD-L1 CPS ≥1 Population

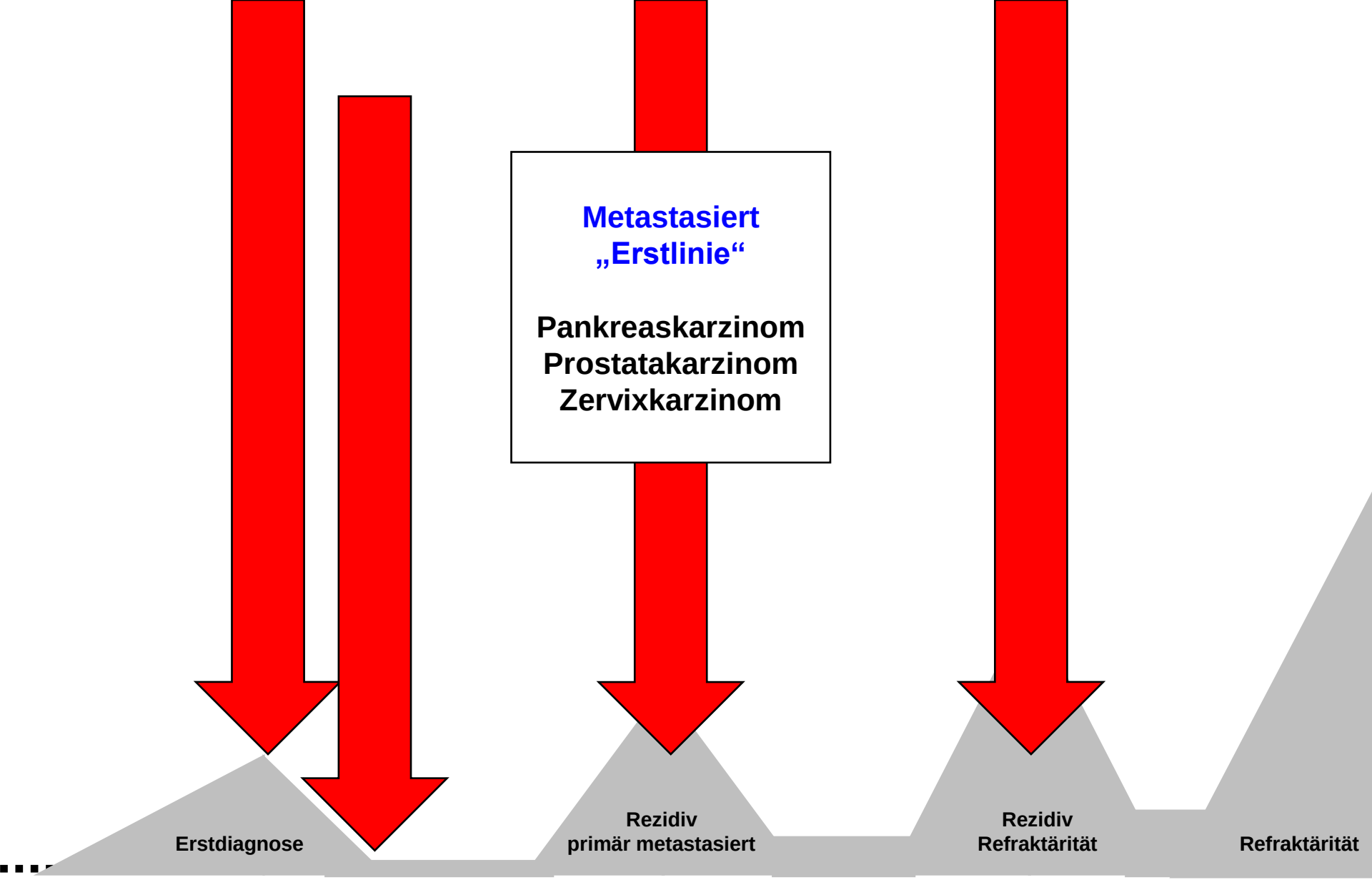


Data cutoff date: October 3, 2022.

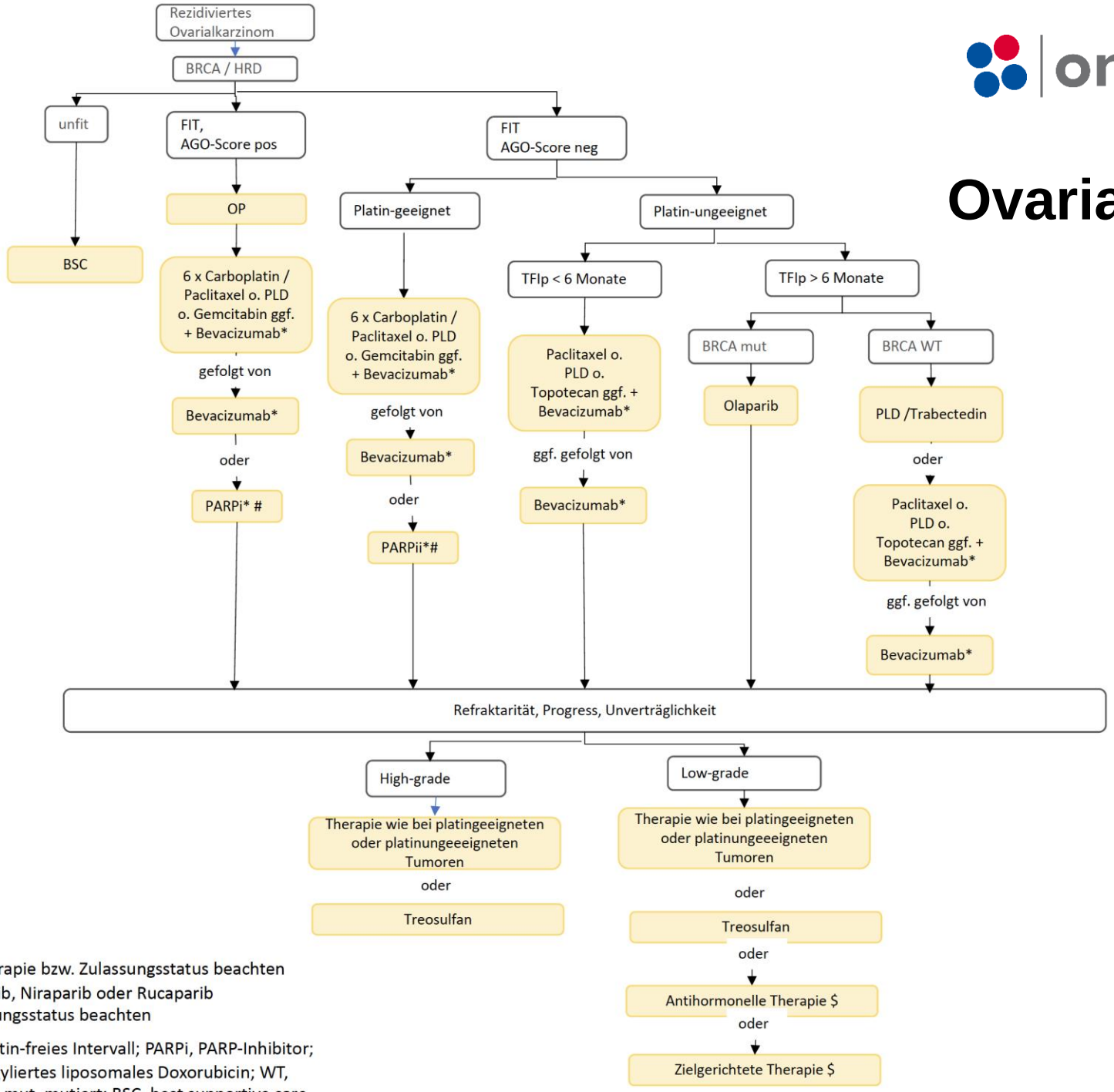
Protocol-Specified Final PFS in Subgroups, All-Comer Population



Response assessed per RECIST v1.1 by investigator review. Data cutoff date: October 3, 2022.


Metastasiert
„Erstlinie“
Pankreaskarzinom
Prostatakarzinom
Zervixkarzinom
Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität

Ovarialkarzinom



* Vortherapie bzw. Zulassungsstatus beachten
# Olaparib, Niraparib oder Rucaparib
$ Zulassungsstatus beachten

TFIp, Platin-freies Intervall; PARPi, PARP-Inhibitor; PLD, pegyliertes liposomales Doxorubicin; WT, Wildtyp; mut, mutiert; BSC, best supportive care

2023 ASCO ANNUAL MEETING

Phase III MIRASOL (GOG 3045/ENGOT-ov55) Study: Mirvetuximab Soravtansine vs. Investigator's Choice of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancers with High Folate Receptor-Alpha (FRα) Expression

Kathleen N. Moore[1], Antoine Angelergues[2], Gottfried E. Konecny[3], Susana Banerjee[4], Sandro Pignata[5], Nicoletta Colombo[6], John Moroney[7], Casey Cosgrove[8], Jung-Yun Lee[9], Andrzej Roszak[10], Shani Breuer[11], Jacqueline Tromp[12], Diana Bello Roufai[13], Lucy Gilbert[14], Rowan Miller[15], Tashanna Myers[16], Yuemei Wang[17], Anna Berkenblit[17], Domenica Lorusso[18], Toon Van Gorp[19]

[1]Stephenson Cancer Center University of Oklahoma College of Medicine, Oklahoma City, OK, USA; [2]Groupe Hospitalier Diaconesses Croix Saint Simon, Paris, France; [3]UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA, USA; [4]The Royal Marsden NHS Foundation Trust - Royal Marsden Hospital, London, UK; [5]Istituto Nazionale Tumori- G. Pascale, Naples, Italy; [6]European Institute of Oncology IRCCS, Milan, Italy and University of Milan-Bicocca, Milan, Italy; [7]The University of Chicago, Chicago, IL, USA; [8]The Ohio State University, Columbus, OH, USA; [9]Severance Hospital, Seoul, South Korea; [10]Wielkopolskie Centrum Onkologii, Poznan, Poland; [11]Hadassah Ein Kerem – Sharett, Jerusalem, Israel; [12]Amsterdam UMC, Amsterdam, The Netherlands; [13]Hopital Rene Huguenin, Institut Curie, Saint-Cloud, France; [14]McGill University Health Centre, Montreal, Canada; [15]University College London Hospital, London, UK; [16]Baystate Medical Center, Springfield, MA, USA; [17] ImmunoGen, Inc., Waltham, MA, USA; [18]Fondazione Policlinico Universitario A. Gemelli, IRCCS and Catholic University of Sacred Heart, Rome, Italy; [19]University Hospital Leuven Leuven Cancer Institute, Leuven, Belgium

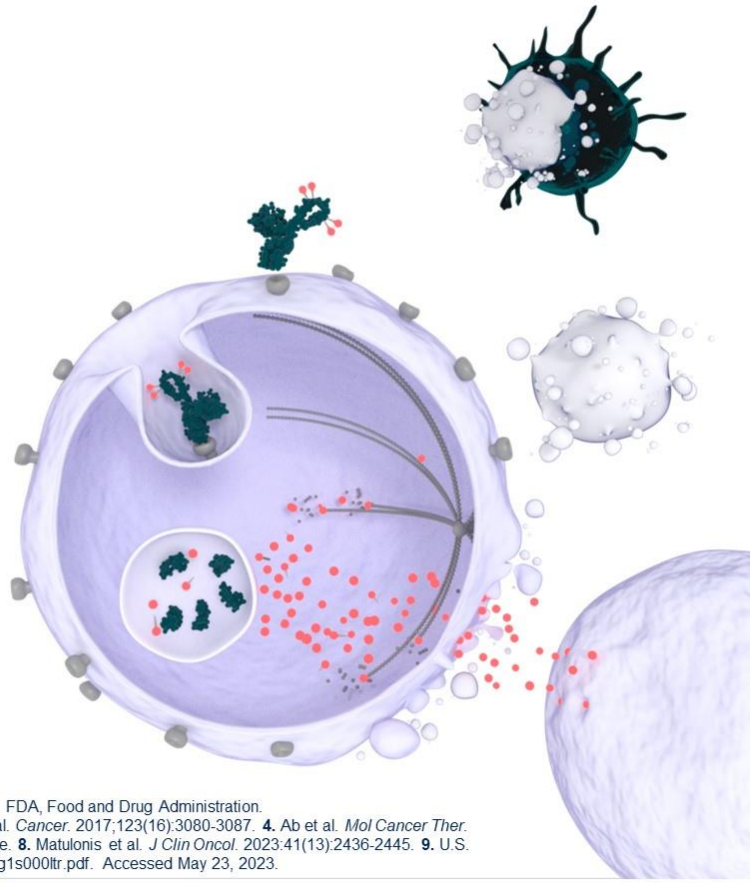
ENGOT European Network of Gynaecological Oncological Trial groups

GOG FOUNDATION® Transforming the standard of care™

PRESENTED BY: Kathleen Moore, Associate Director of Clinical Research, Stephenson Cancer Center University of Oklahoma College of Medicine

Background

- No trial has shown an overall survival (OS) benefit in platinum-resistant ovarian cancer (PROC)[1, 2]
- Mirvetuximab soravtansine (MIRV) is an ADC comprising a FRα-binding antibody, cleavable linker, and maytansinoid DM4, a potent tubulin-targeting agent[3,4]
- FRα is expressed in ~90% of ovarian carcinomas,[5,6] with 35-40%[7] of PROC tumors exhibiting high FRα expression (≥75% of tumor cells positive with ≥2+ intensity)[8]
- MIRV demonstrated an ORR of 32% and mDOR 6.9 months in the single-arm study, SORAYA[8], of BEV pre-treated PROC to support accelerated approval by the FDA[9]
- MIRASOL is the confirmatory, randomized, global phase 3 trial designed to support full approval in the US and EU

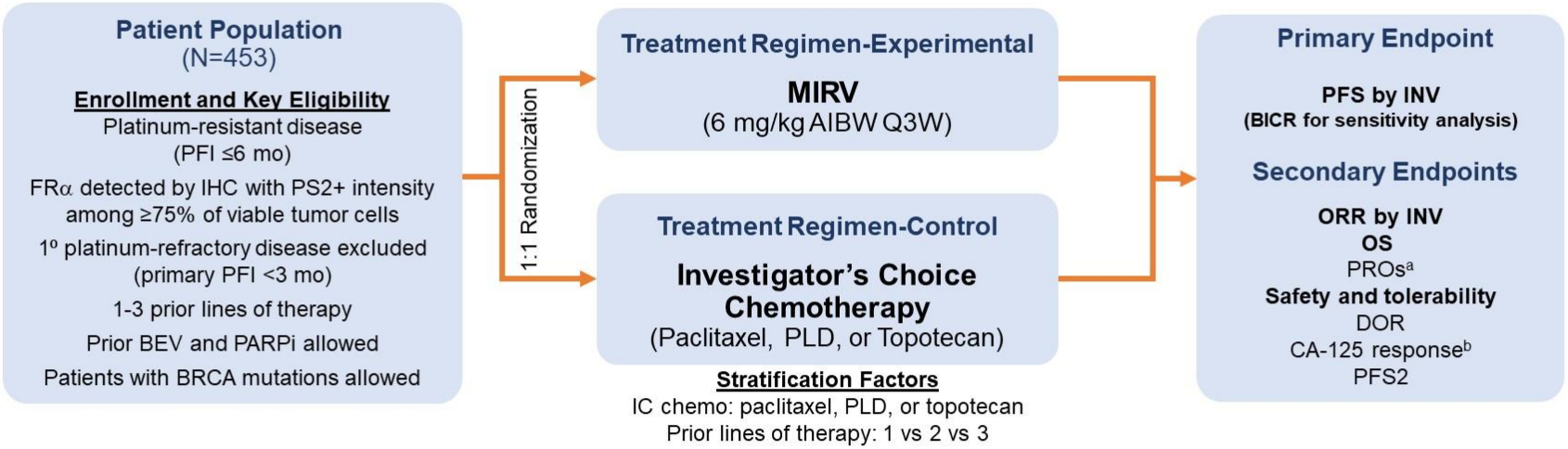


PFS, progression-free survival; OS, overall survival; FRα, folate receptor alpha; ORR, objective response rate; mDOR, median duration of response; FDA, Food and Drug Administration.

1. Pujade-Lauraine et al. *J Clin Oncol.* 2014;32(13):1302-1308. **2.** Richardson et al. *JAMA Oncol.* 2023;10.1001/jamaoncol.2023.0197. **3.** Moore et al. *Cancer.* 2017;123(16):3080-3087. **4.** Ab et al. *Mol Cancer Ther.* 2015;14(7):1605-1613. **5.** Markert et al. *Anticancer Res.* 2008;28(6A):3567-3572. **6.** Martin et al. *Gynecol Oncol.* 2017;147(2):402-407. 7. Data on file. **8.** Matulonis et al. *J Clin Oncol.* 2023:41(13):2436-2445. **9.** U.S. FOOD & DRUG ADMINISTRATION. BLA ACCELERATED APPROVAL. https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/761310Orig1s000ltr.pdf. Accessed May 23, 2023.

MIRASOL (NCT04209855) – Study Design[1,2]

An open-label, phase 3 randomized trial of MIRV vs investigator's choice chemotherapy in patients with FRα-high platinum-resistant ovarian cancer



AIBW, adjusted ideal body weight; BEV; bevacizumab; BICR, blinded independent central review; BRCA, BReast CAncer gene; CA-125, cancer antigen 125; chemo, chemotherapy; DOR, duration of response; FRα, folate receptor alpha; IC, investigator's choice; IHC, immunohistochemistry; INV, investigator; MIRV, mirvetuximab soravtansine; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitors; PFI, platinum-free interval; PFS, progression-free survival; PFS2, time from randomization until second disease progression; PLD, pegylated liposomal doxorubicin; PROs, patient-reported outcomes; PS2+, positive staining intensity ≥2; Q3W, every 3 weeks.

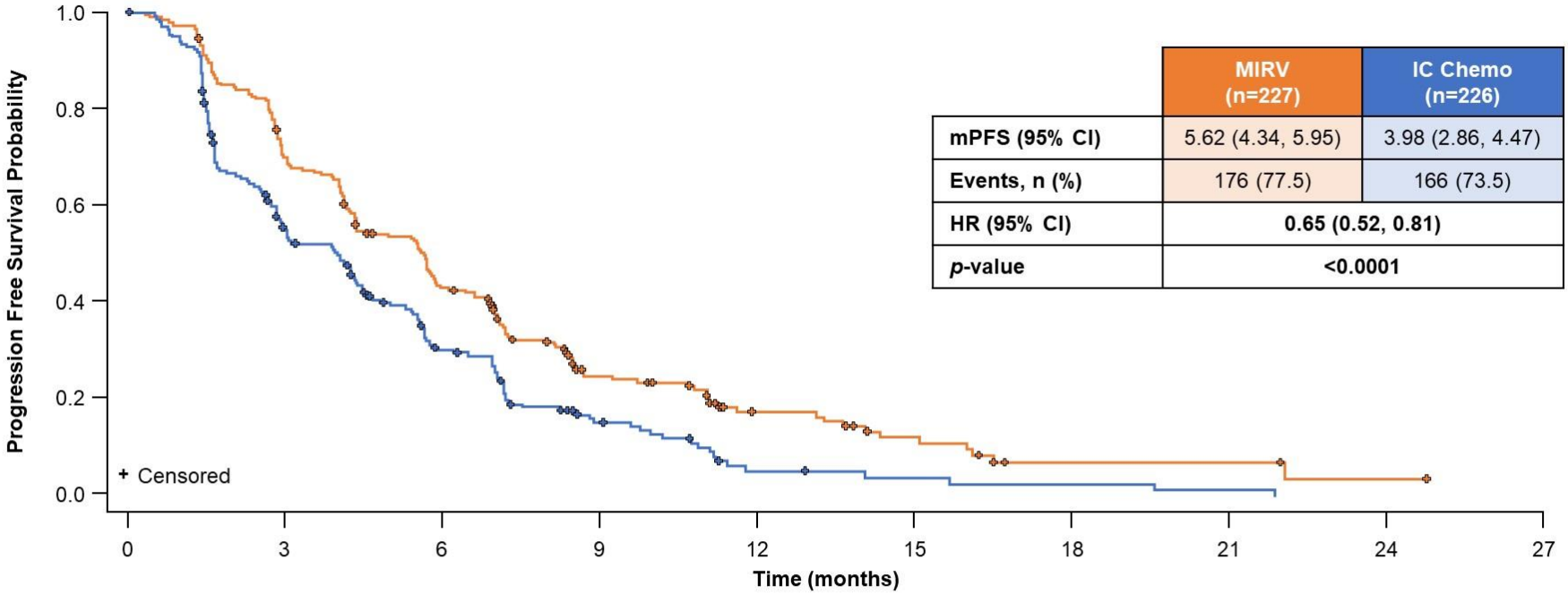
[a]PROs will be measured using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire, 28-item Ovarian Cancer Module (OV28) study instrument.

[b]Gynecological Cancer InterGroup (GCIG) criteria.

1. ClinicalTrials.gov identifier: NCT04209855. Updated June 16, 2022. Accessed October 5, 2022. https://clinicaltrials.gov/ct2/show/NCT04209855

2. Moore K, et al. Presented at: 2020 American Society of Clinical Oncology Annual Meeting; May 29-31, 2020; Virtual. Abstract TPS6103.

Primary Endpoint: Progression-Free Survival by Investigator



	MIRV (n=227)	IC Chemo (n=226)
mPFS (95% CI)	5.62 (4.34, 5.95)	3.98 (2.86, 4.47)
Events, n (%)	176 (77.5)	166 (73.5)
HR (95% CI)	**0.65 (0.52, 0.81)**	
***p*-value**	**<0.0001**	

No. Participants at Risk

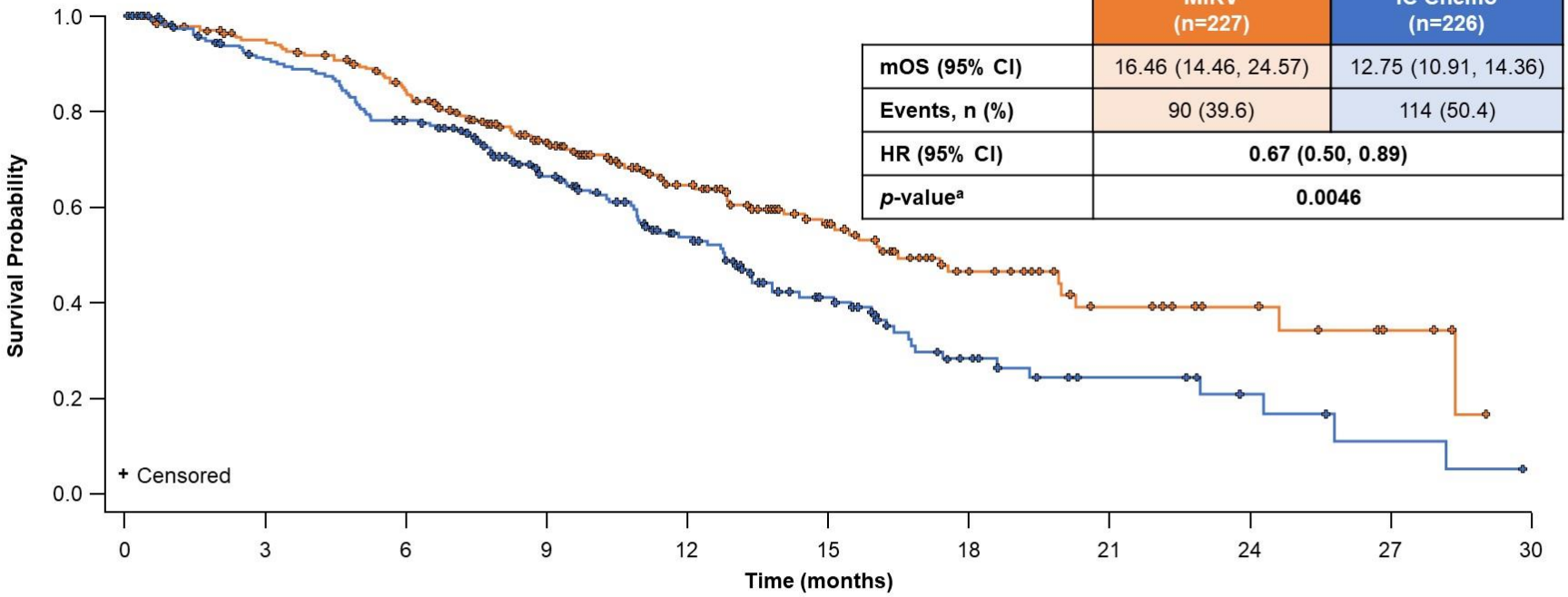
MIRV	227	151	89	38	18	10	3	3	1	0
IC Chemo	226	98	48	19	5	3	2	1	0	

Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo, investigator's choice chemotherapy; mPFS, median progression-free survival; CI, confidence interval; HR, hazard ratio.

PRESENTED BY: Kathleen Moore, Associate Director of Clinical Research, Stephenson Cancer Center University of Oklahoma College of Medicine

Overall Survival



	MIRV (n=227)	IC Chemo (n=226)
mOS (95% CI)	16.46 (14.46, 24.57)	12.75 (10.91, 14.36)
Events, n (%)	90 (39.6)	114 (50.4)
HR (95% CI)	0.67 (0.50, 0.89)	
p-value[a]	0.0046	

No. Participants at Risk

MIRV	227	204	175	128	82	53	28	15	9	4	0
IC Chemo	226	185	157	107	68	39	18	9	5	2	0

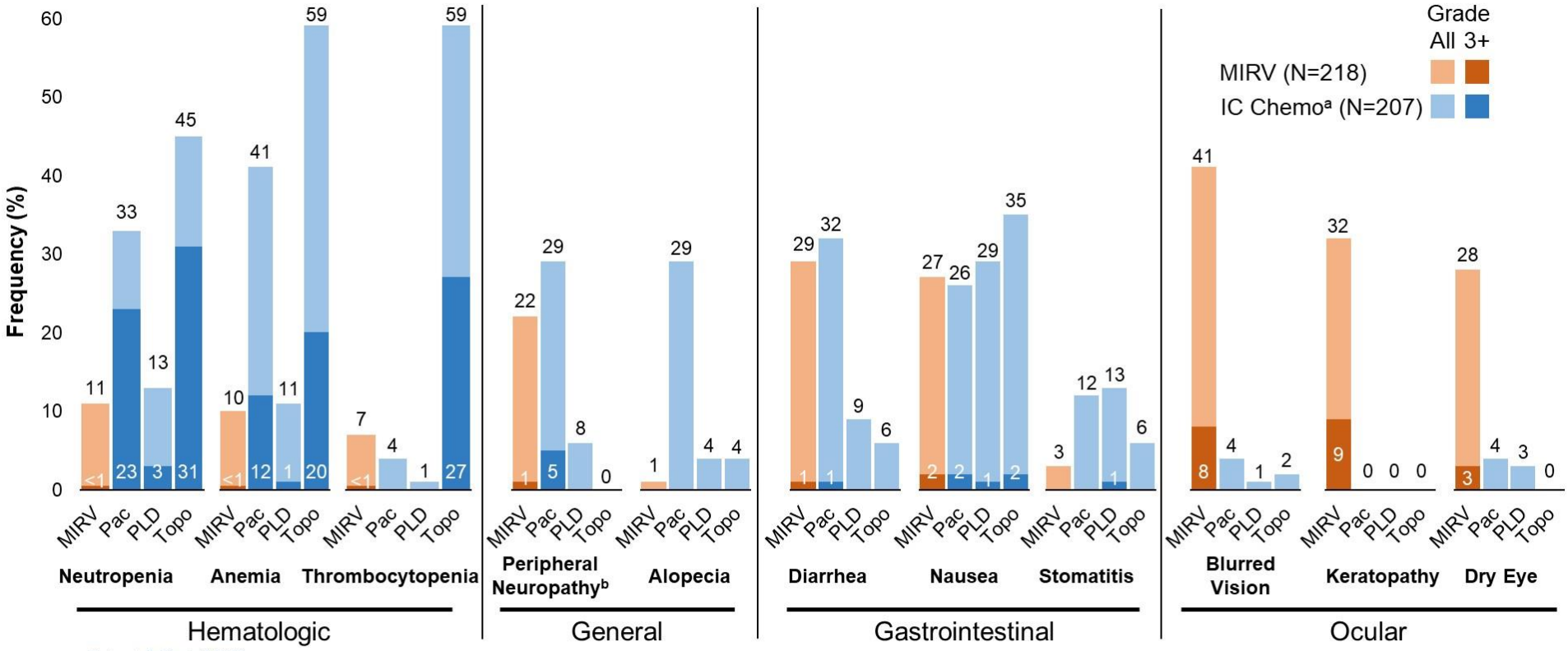
Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo, investigator choice chemotherapy; mOS, median overall survival; CI, confidence interval; HR, hazard ratio.

[a]Overall survival is statistically significant based on pre-specified boundary p-value at interim analysis = 0.01313

PRESENTED BY: Kathleen Moore, Associate Director of Clinical Research, Stephenson Cancer Center University of Oklahoma College of Medicine

Differentiated Safety Profile: Treatment-Emergent Adverse Events



Data cutoff: March 6, 2023

MIRV, mirvetuximab soravtansine; IC Chemo: investigator's choice of chemotherapy; Pac, paclitaxel; PLD, pegylated liposomal doxorubicin; Topo, topotecan.

[a]Pac n=82, PLD n=76, Topo n=49. [b]Grade 2+ peripheral neuropathy events were observed in 12% and 16% of patients that received MIRV or paclitaxel, respectively.

Phase 3 THOR Study: Results of Erdafitinib Versus Chemotherapy in Patients With Advanced or Metastatic Urothelial Cancer With Select Fibroblast Growth Factor Receptor Alterations

Yohann Loriot[1], Nobuaki Matsubara[2], Se Hoon Park[3] , Robert A. Huddart[4], Earle F. Burgess[5], Nadine Houede[6], Severine Banek[7], Brigitte Laguerre[8], Valentina Guadalupi[9], Ja Hyeon Ku[10], Spyros Triantos[11], Sydney Akapame[11], Kris Deprince[12], Sutapa Mukhopadhyay[13], Arlene O Siefker-Radtke[14]

[1]Department of Cancer Medicine, INSERM U981, Gustave Roussy, Université Paris-Saclay, Villejuif, France; [2]Department of Medical Oncology, National Cancer Center Hospital East, Chiba, Japan; [3]Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [4]Section of Radiotherapy and Imaging, Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Sutton, UK; [5]Medical Oncology Department, Levine Cancer Institute, Charlotte, NC; [6]Medical Oncology Department, Institut de Cancérologie du Gard - CHU Caremeau, Nîmes, France and Montpellier University, Montpellier, France; [7]Department of Urology, University Hospital Frankfurt, Goethe Universtity Frankfurt, Frankfurt am Main, Germany; [8]Department of Medical Oncology, Centre Eugene Marquis, Rennes, France; [9]Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy; [10]Seoul National University Hospital, Seoul, South Korea; [11]Janssen Research & Development, Spring House, PA; [12]Janssen Research & Development, Beerse, Belgium; [13]Janssen Research & Development, Lexington, MA; [14]Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX

Presented at the 2023 ASCO Annual Meeting; June 2-6, 2023; Chicago, IL, USA.

Erdafitinib is a Pan-FGFR Inhibitor With Activity in Metastatic Urothelial Carcinoma

- ***FGFRalt*** are observed in **~20% of advanced or mUC** and may function as oncogenic drivers[1,2]

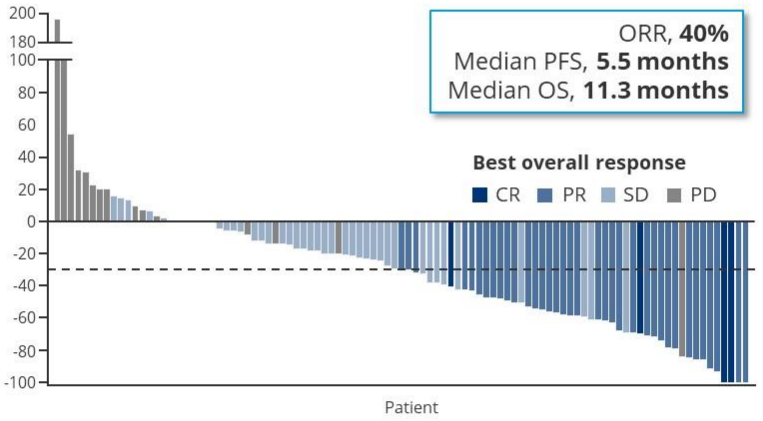
Erdafitinib is an oral selective pan-FGFR tyrosine kinase inhibitor[3]

  - Erdafitinib was granted accelerated approval in the United States and is approved in 17 other countries to treat locally advanced or mUC in adults with susceptible *FGFR3/2alt* who have progressed after platinum-containing chemotherapy[4-6]

- **THOR** is a confirmatory, randomized phase 3 study:

  - Cohort 1 assessed whether erdafitinib improved survival over chemotherapy in patients with *FGFRalt* mUC who progressed on or after ≥1 prior treatment that included anti–PD-(L)1

In the single-arm phase 2 BLC2001 trial, erdafitinib showed a benefit in patients with *FGFR-altered* advanced urothelial cancer[4]



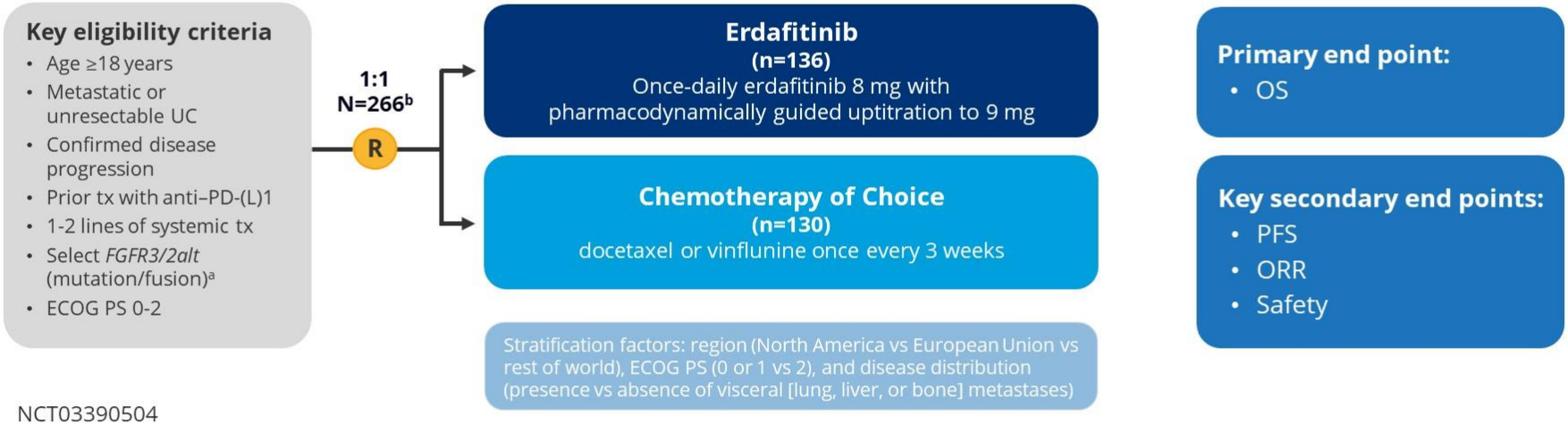
Patients received erdafitinib 8 mg/d with pharmacodynamically guided uptitration to 9 mg/d.

FGFR, fibroblast growth factor receptor; *FGFRalt*, *FGFR* alterations; mUC, metastatic urothelial carcinoma; ORR, overall response rate; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PFS, progression-free survival.
[a]Patients received erdafitinib 8 mg/d with pharmacodynamically guided uptitration to 9 mg/d.

1. Necchi A, et al. *Eur Urol Focus*. 2019;5:853-586; 2. di Martino E, et al. *Future Oncol.* 2016;12:2243-2263; 3. Perera TPS, et al. *Mol Cancer Ther.* 2017;16:1010-1020; 4. Loriot Y, et al. *N Engl J Med.* 2019;381:338-348; 5. BALVERSA® (erdafitinib) [package insert]. Horsham, PA: Janssen Products, LP; 2023; 6. Siefker-Radtke AO, et al. *Lancet Oncol.* 2022;23:248-258.

Phase 3 THOR Study: Erdafitinib Versus Chemotherapy of Choice in Patients With Advanced Urothelial Cancer and Selected FGFR Aberrations

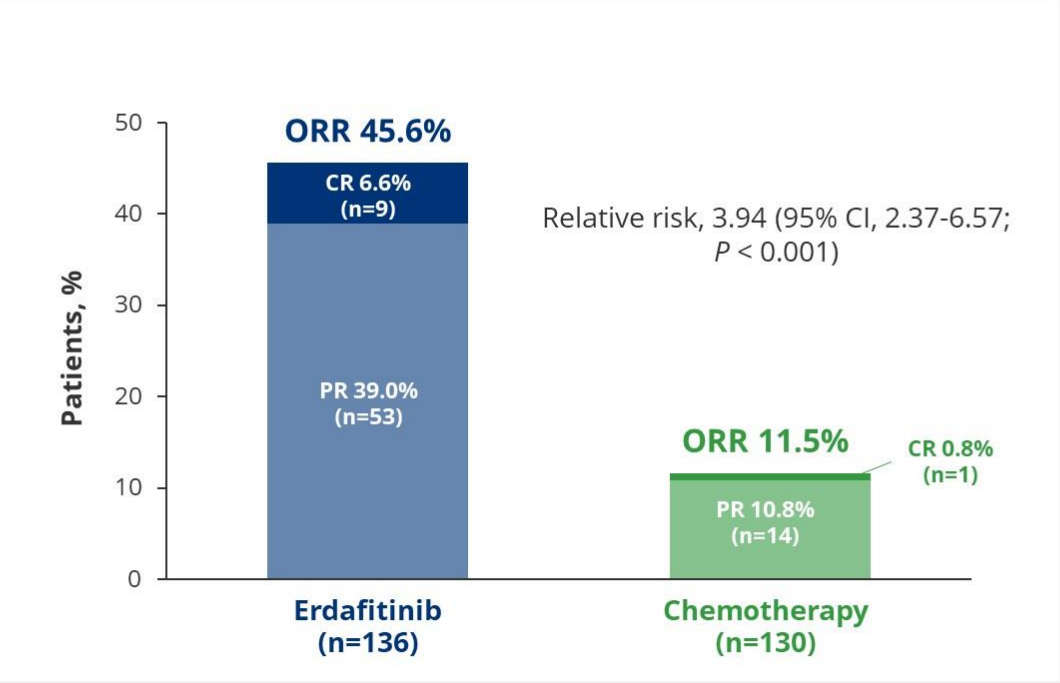
Cohort 1



NCT03390504

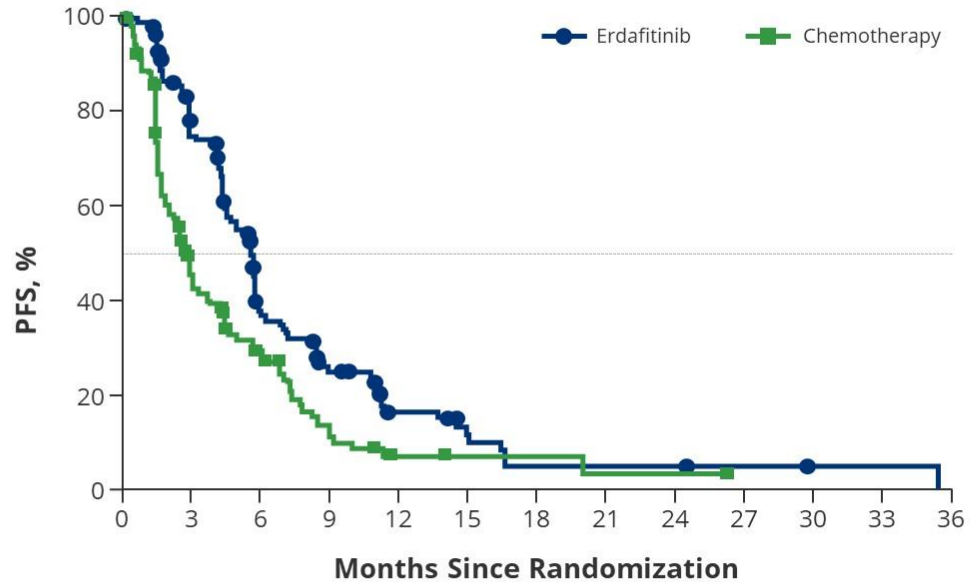
[a]Molecular eligibility can be confirmed using either central or local historical *FGFR* test results (Qiagen assay). If a patient was enrolled based on local historical testing, a tissue sample must still be submitted at the time of enrollment for retrospective confirmation (by central lab) of *FGFR* status. Tumors must have ≥1 of the following translocations: *FGFR2-BICC1*, *FGFR2-CASP7*, *FGFR3-TACC3_V1*, *FGFR3-TACC3_V3*, *FGFR3-BAIAP2L1*; or 1 of the following *FGFR3* gene mutations: R248C, S249C, G370C, Y373C.
[b]Number of patients randomized at the time of the interim analysis (data cutoff January 15, 2023).
ECOG PS, Eastern Cooperative Oncology Group performance status; FGFR, fibroblast growth factor receptor; *FGFR3/2alt*, *FGFR3/2* alterations; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; Q3W, every 3 weeks; tx, treatment; UC, urothelial cancer.

Objective Response Rate Was Significantly Higher for Erdafitinib Versus Chemotherapy[a]



CI, confidence interval; CR, complete response; ORR, objective response rate; PR, partial response.
[a]Responses were best overall response per investigator assessment.

Erdafitinib Significantly Improved Progression-Free Survival Versus Chemotherapy

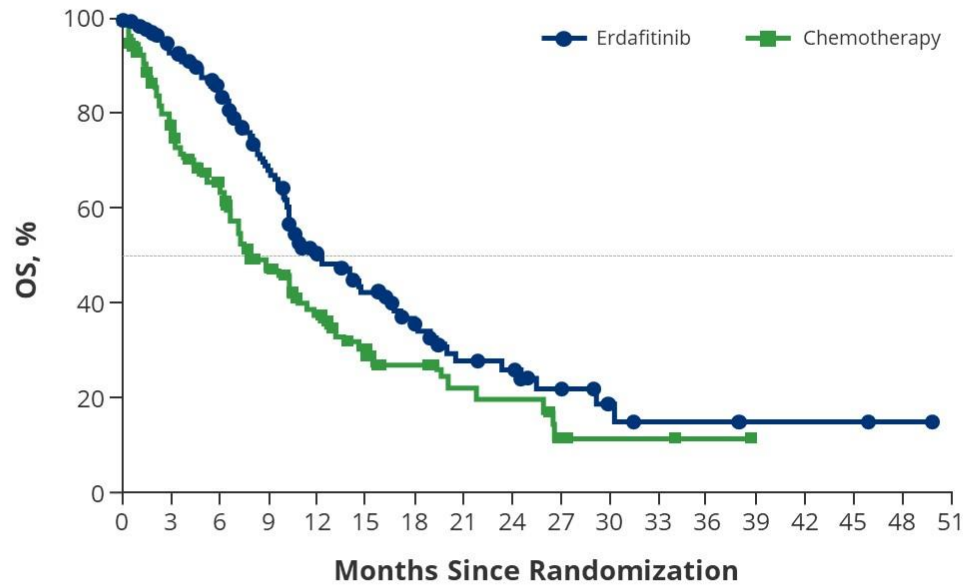


No. at risk												
Erdafitinib	136	90	39	24	12	7	3	3	3	2	1	1	0
Chemotherapy	130	43	23	9	4	2	2	1	1	0	0	0	0

- Median PFS was 5.6 versus 2.7 months for erdafitinib versus chemotherapy
- Erdafitinib reduced the risk of progression or death by 42% versus chemotherapy
  - HR, 0.58 (95% CI, 0.44-0.78; *P* = 0.0002)

CI, confidence interval; HR, hazard ratio; PFS, progression-free survival.

Overall Survival for Erdafitinib Was Superior to Investigator's Choice of Chemotherapy



No. at risk																	
Erdafitinib	136	117	97	74	46	35	25	17	15	9	5	3	3	2	2	2	1	0
Chemotherapy	130	87	66	43	30	18	13	9	8	3	2	2	1	0	0	0	0	0

- Median follow-up was 15.9 months
- Median OS was 12.1 months for erdafitinib versus 7.8 months for chemotherapy
- Erdafitinib reduced the risk of death by 36% versus chemotherapy
  - HR, 0.64 (95% CI, 0.47-0.88; *P* = 0.005)[a]
- Based on these interim analysis results, the IDMC recommended to stop the study, unblind data, and cross over patients from chemotherapy to erdafitinib

CI, confidence interval; HR, hazard ratio; IDMC, independent data monitoring committee; OS, overall survival.
[a]The significance level for stopping for efficacy was p=0.019, corresponding to a HR of 0.69.

The Safety Profiles Were Consistent With the Known Profiles of Erdafitinib and Chemotherapy (2/2)

Patients with AEs of interest, n (%)	Erdafitinib (n=135)		Chemotherapy (n=112)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
Nail disorders[a]	90 (66.7)	15 (11.1)	6 (5.4)	0
Skin disorders[b]	74 (54.8)	16 (11.9)	14 (12.5)	0
Eye disorders (excluding central serous retinopathy)[c]	57 (42.2)	3 (2.2)	6 (5.4)	0
Central serous retinopathy[d]	23 (17.0)	3 (2.2)	0	0

[a]Nail disorders: nail bed bleeding, nail discoloration, nail disorder, nail dystrophy, nail ridging, nail toxicity, onychalgia, onychoclasis, onycholysis, paronychia, onychomadesis.
[b]Skin disorders: blister, dry skin, erythema, hyperkeratosis, palmar erythema, palmar-plantar erythrodysesthesia syndrome, plantar erythema, rash, rash erythematous, rash generalized, rash macular, rash maculo-papular, skin atrophy, skin exfoliation, skin fissures, skin lesion, skin ulcer, toxic skin eruption, xeroderma.
[c]Eye disorders (excluding central serous retinopathy): blepharitis, cataract, cataract subcapsular, conjunctival hemorrhage, conjunctival hyperemia, conjunctival irritation, corneal erosion, corneal infiltrates, dry eye, eye inflammation, eye irritation, eye pain, foreign body sensation in eyes, keratitis, lacrimation increased, night blindness, ocular hyperemia, photophobia, vision blurred, visual acuity reduced, visual impairment, xanthopsia, xerophthalmia, chorioretinitis, conjunctivitis, ulcerative keratitis.
[d]Central serous retinopathy: retinal detachment, vitreous detachment, retinal edema, retinopathy, chorioretinopathy, detachment of retinal pigment epithelium, detachment of macular retinal pigment epithelium, macular detachment, serous retinal detachment, subretinal fluid, retinal thickening, chorioretinitis, serous retinopathy, maculopathy, choroidal effusion.
AE, adverse event.

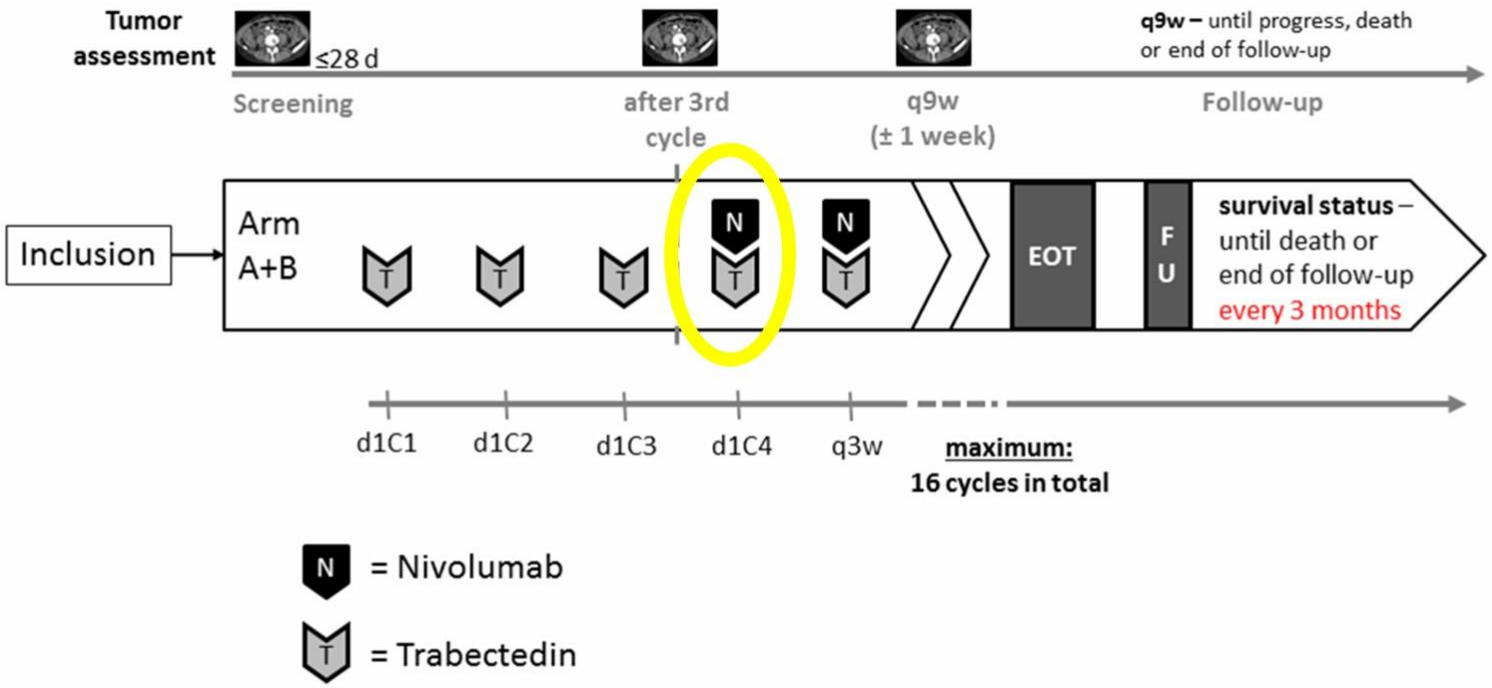
2023 ASCO ANNUAL MEETING

Efficacy and safety of nivolumab and trabectedin in pretreated patients with advanced soft tissue sarcomas (STS) - results of a phase II trial of the German Interdisciplinary Sarcoma Group (GISG-15, NitraSarc)

Peter Reichardt[1], Dimosthenis Andreou[2], Anne Flörcken[3], Thorben Groß[4], Stephan Richter[5], Torsten Kessler[6], Martin Kortüm[7], Christian A Schmidt[8], Bernd Kasper[9], Eva Wardelmann[6], Benedict Atzler[10], Disorn Sookthai[10], Daniel W Mueller[10], Daniel Pink[8, 11]

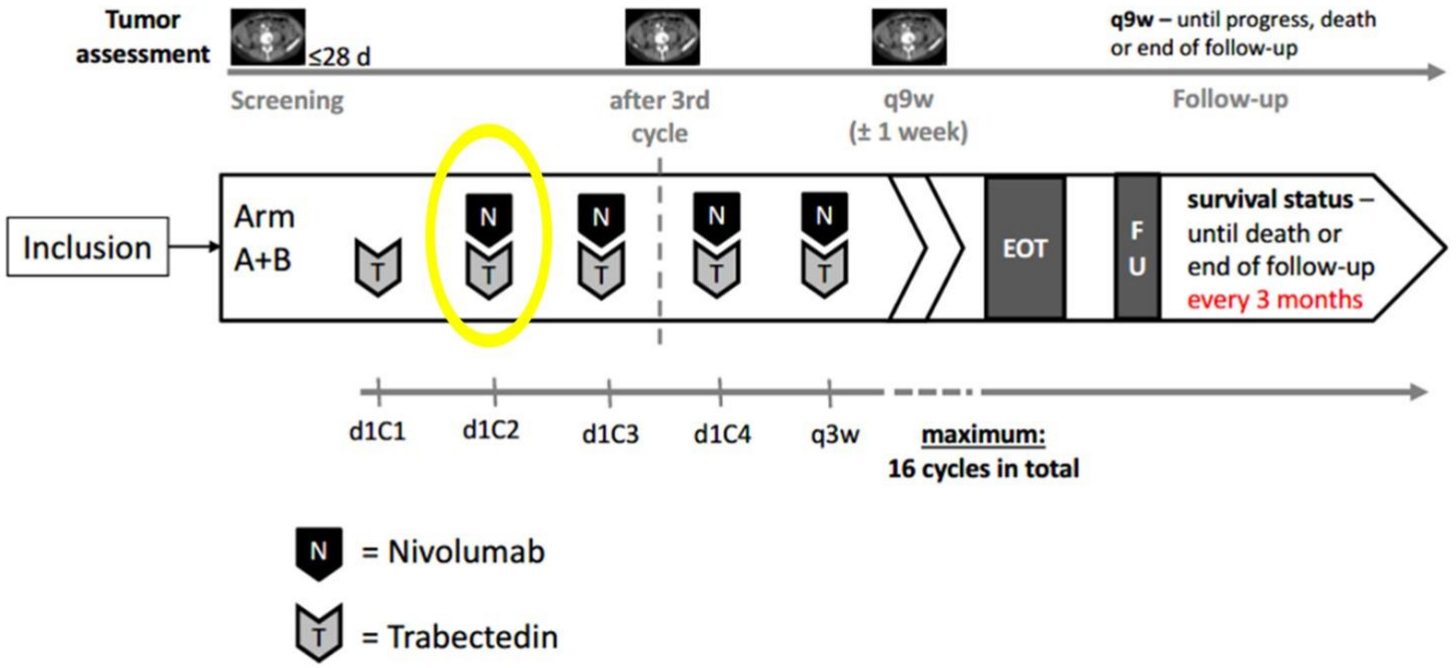
[1] Helios Klinikum Berlin-Buch, Medical School Berlin, Berlin, Germany. [2] Medizinische Universität Graz, Austria. [3] Charité–Universitätsmedizin Berlin, Berlin, Germany. [4] Universitätsklinikum Tübingen, Tübingen, Germany. [5] Universitätsklinikum Carl „Gustav Carus“, Dresden, Germany. [6] Universitätsklinikum Münster, Münster, Germany. [7] Universitätsklinikum Würzburg, Germany. [8] Universitätsmedizin Greifswald, Greifswald, Germany. [9] Universität Heidelberg, Mannheim Cancer Center (MCC), Mannheim, Germany. [10] Institut für Klinische Krebsforschung IKF GmbH am Krankenhaus Nordwest, Frankfurt Am Main, Germany. [11] Helios Klinikum Bad Saarow, Bad Saarow, Germany

Study Design (late combination cohort; LCC)



Study Design (early combination cohort; ECC)

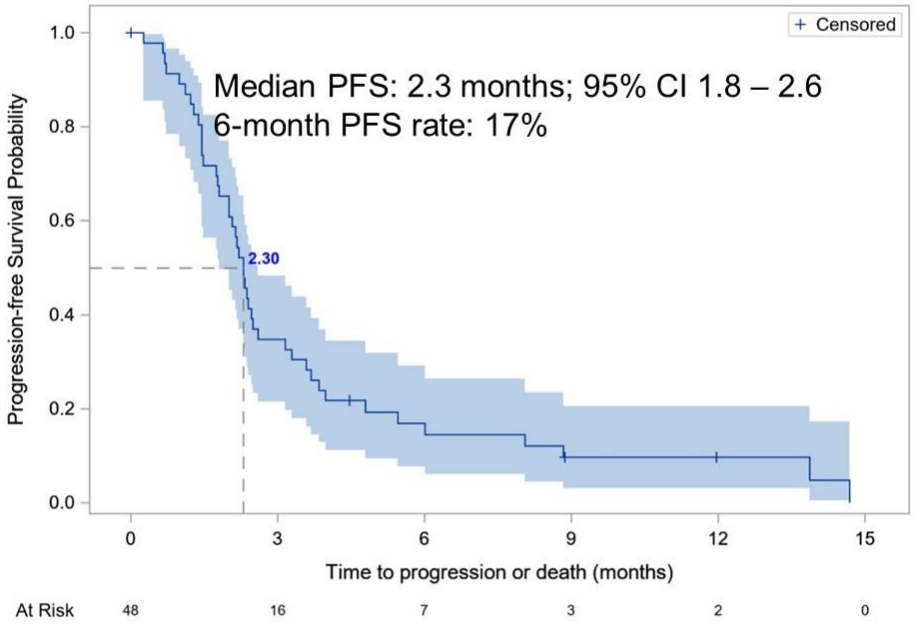
Amendment after preplanned interim safety analysis and with new published data*



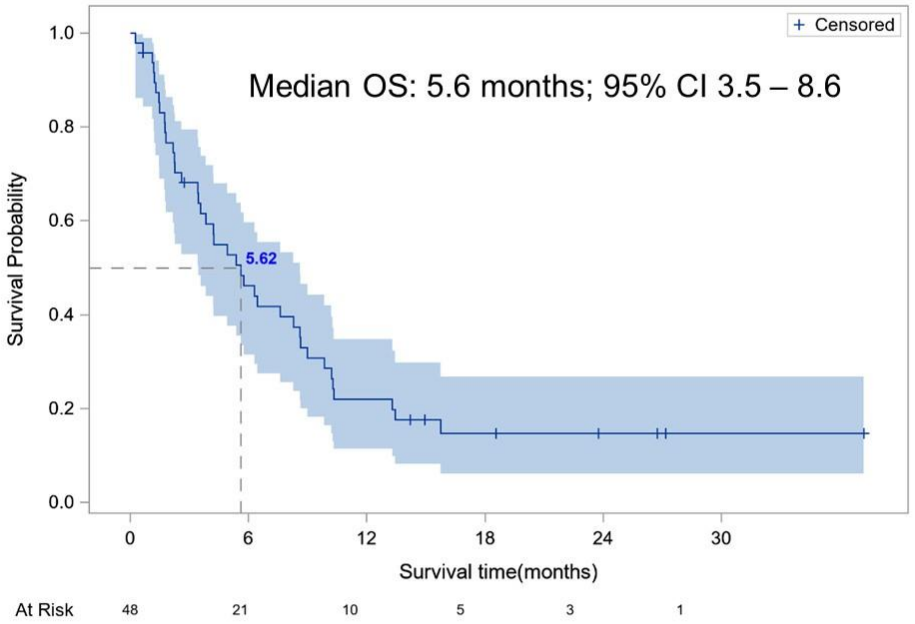
*Chawla SP, Sankhala KK, Ravicz JR, Kang GE, Liu S, Assudani N, et al. Clinical Experience with Combination Chemo-/Immunotherapy using Trabectedin and Nivolumab for Advanced Soft Tissue Sarcoma. J Sarcoma Res. 2018; 2(1): 1009.

Non-L-Sarcoma (Group B): Survival

progression-free survival

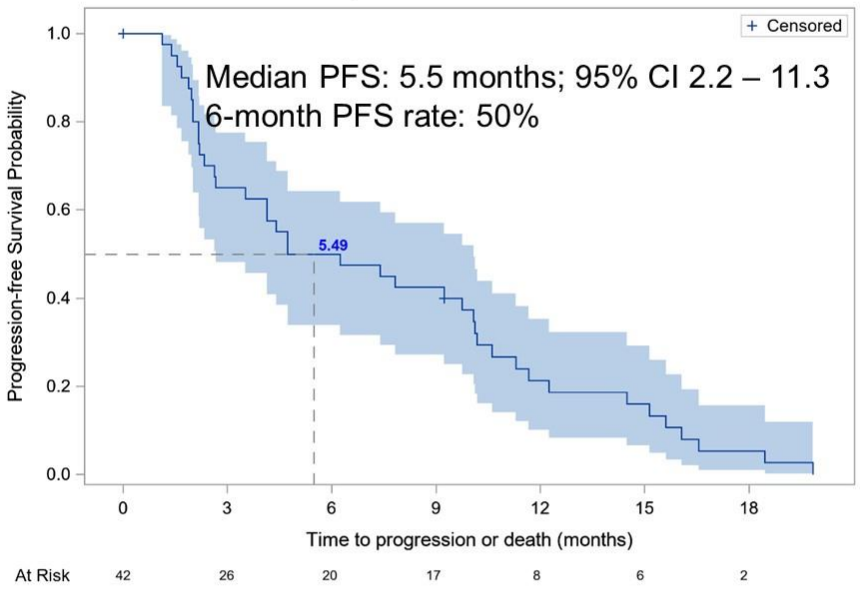


overall survival

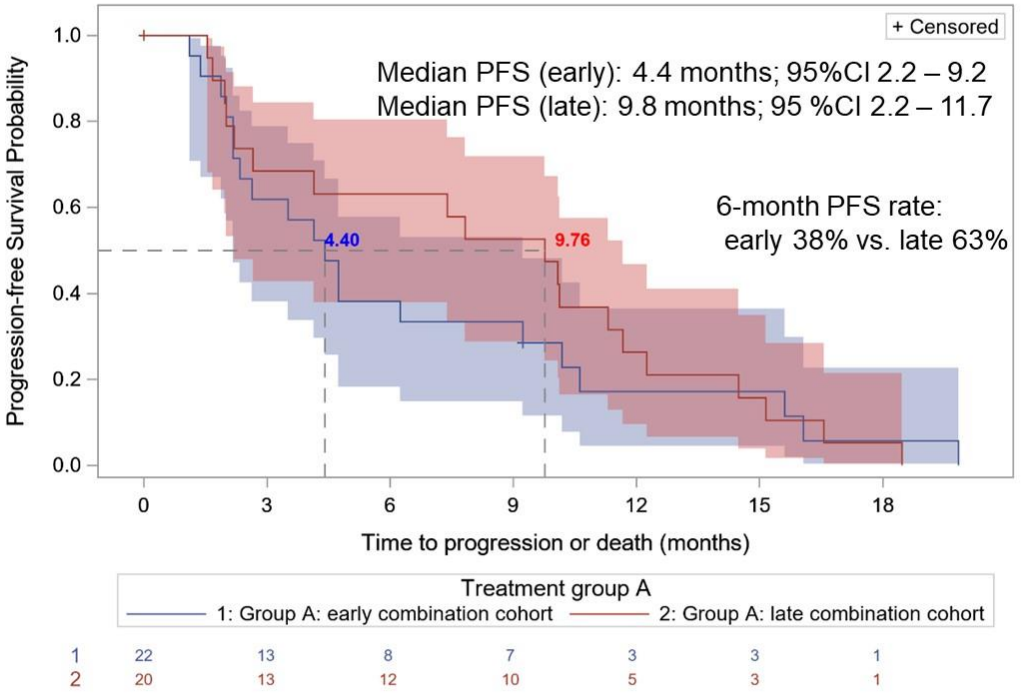


L-Sarcoma (Group A): progression-free survival

Group A: overall

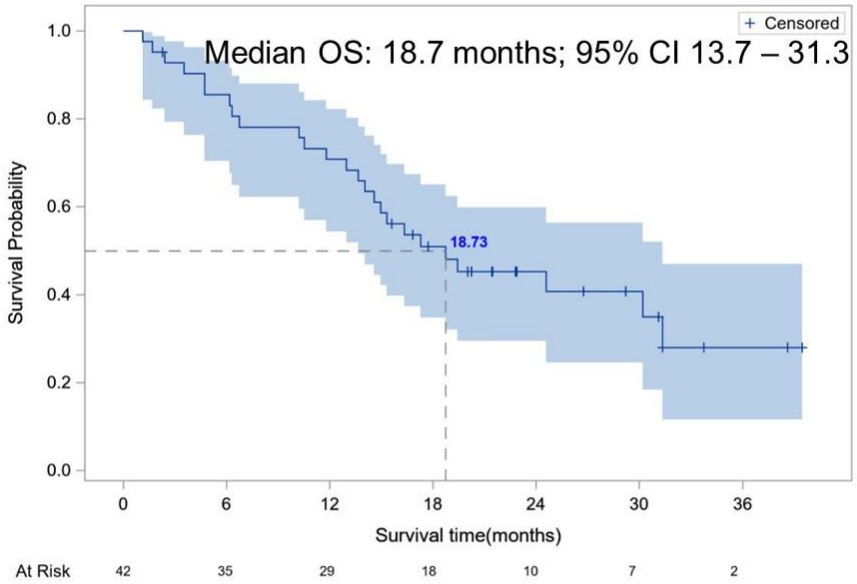


early combination vs. late combination

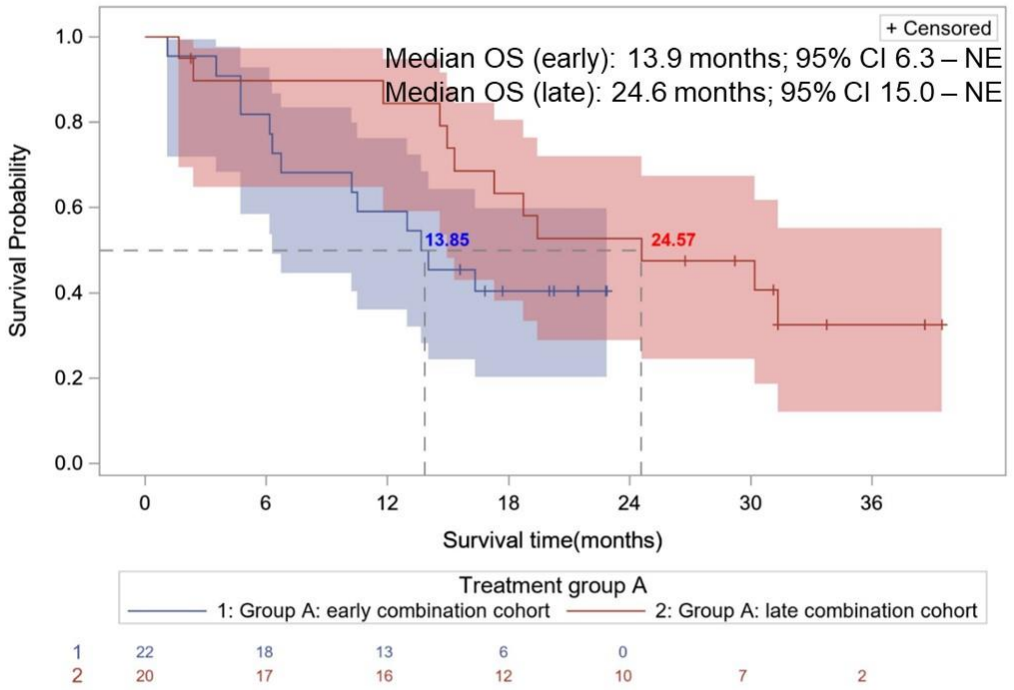


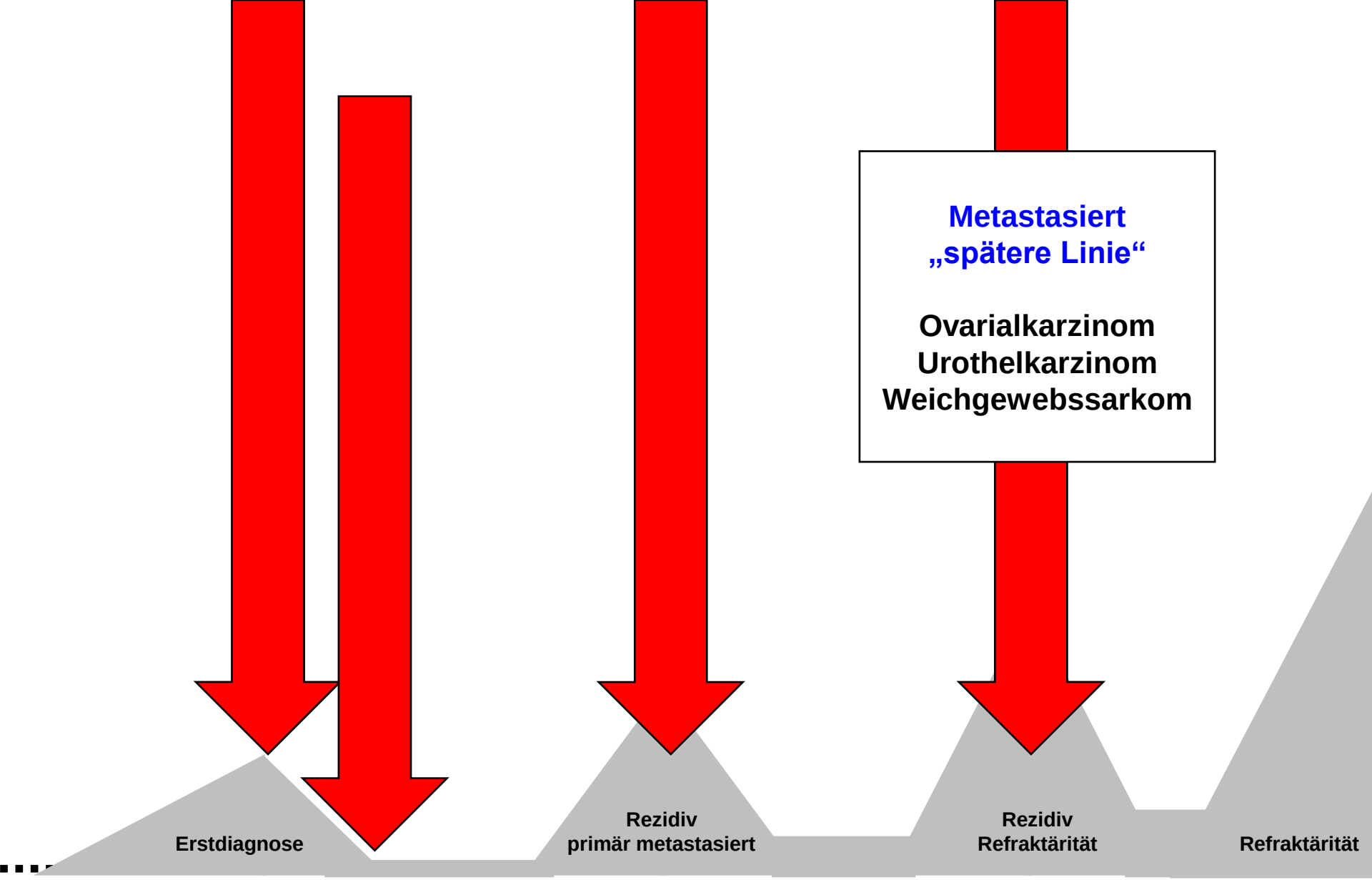
L-Sarcoma (Group A): overall survival

Group A: overall



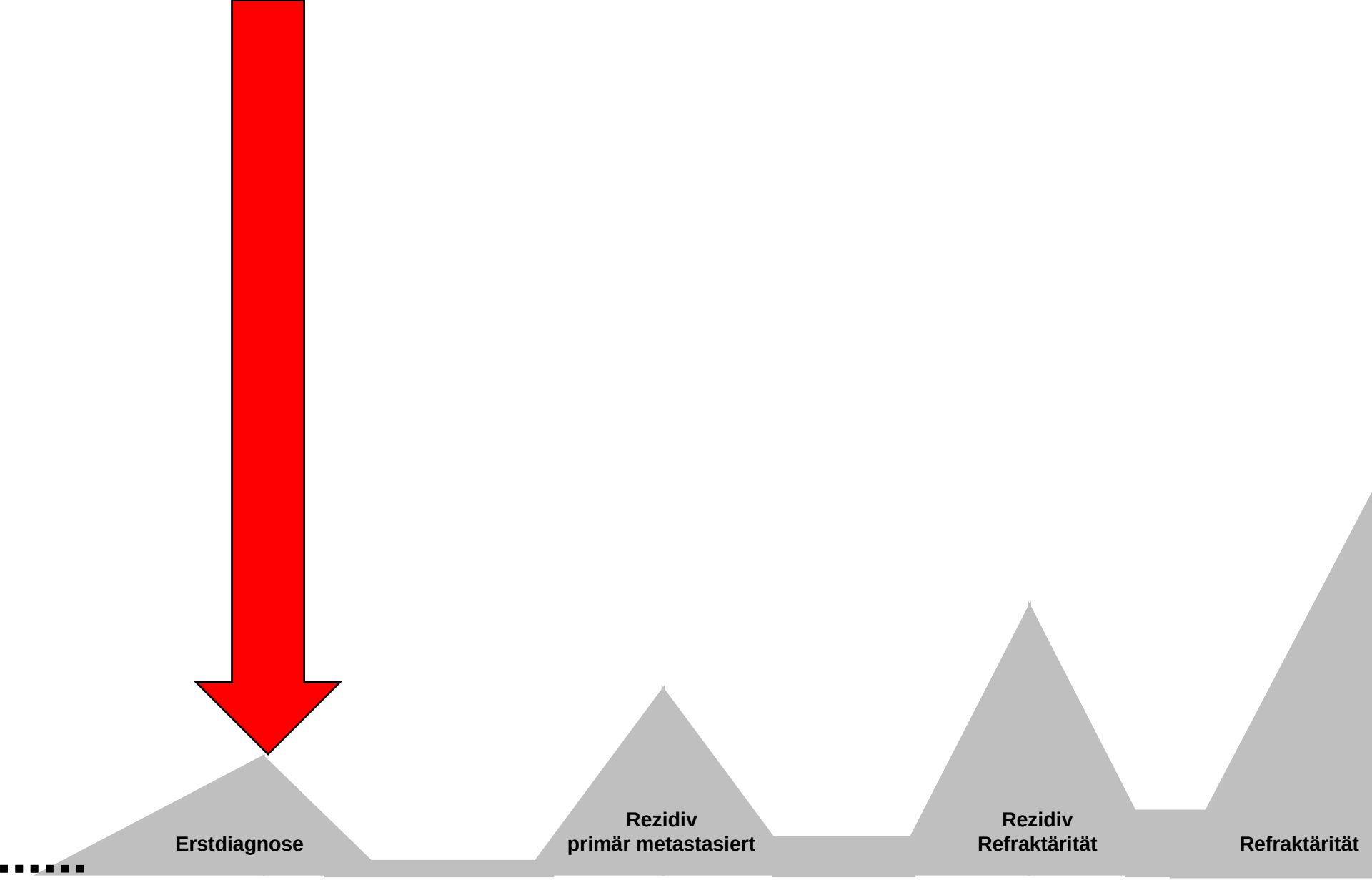
early combination vs. late combination



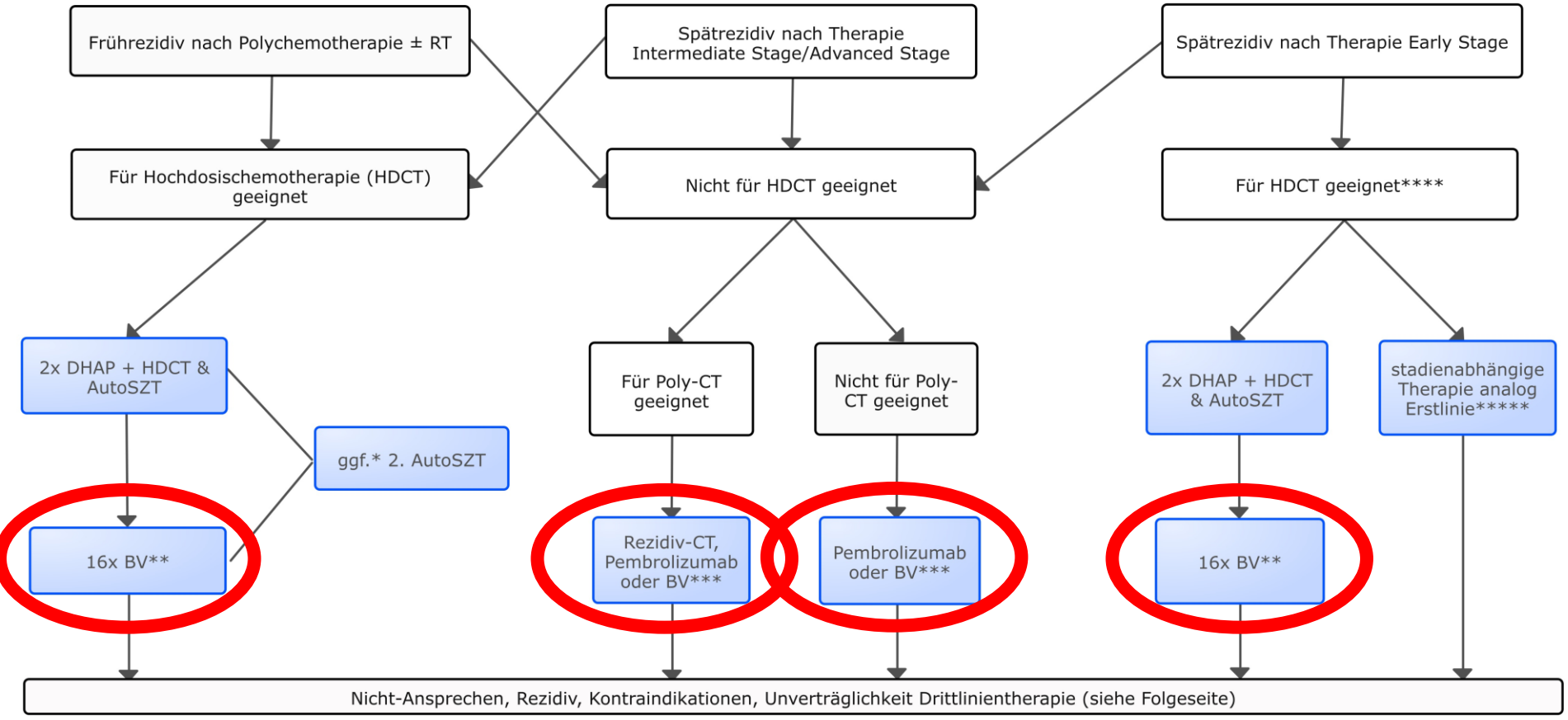

Metastasiert
„spätere Linie“
Ovarialkarzinom
Urothelkarzinom
Weichgewebssarkom
Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität

- Gliom
- Kolonkarzinom
- Lungenkarzinom
- Mammakarzinom
- Ovarialkarzinom
- Pankreaskarzinom
- Prostatakarzinom
- Rektumkarzinom
- Urothelkarzinom
- Weichgewebssarkom
- Zervixkarzinom

- Akute Myeloische Leukämie
- Hodgkin Lymphom
- Hämochromatose
- Multiples Myelom
- Myelodysplastische Neoplasien
- PMBCL


Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität

Hodgkin Lymphom



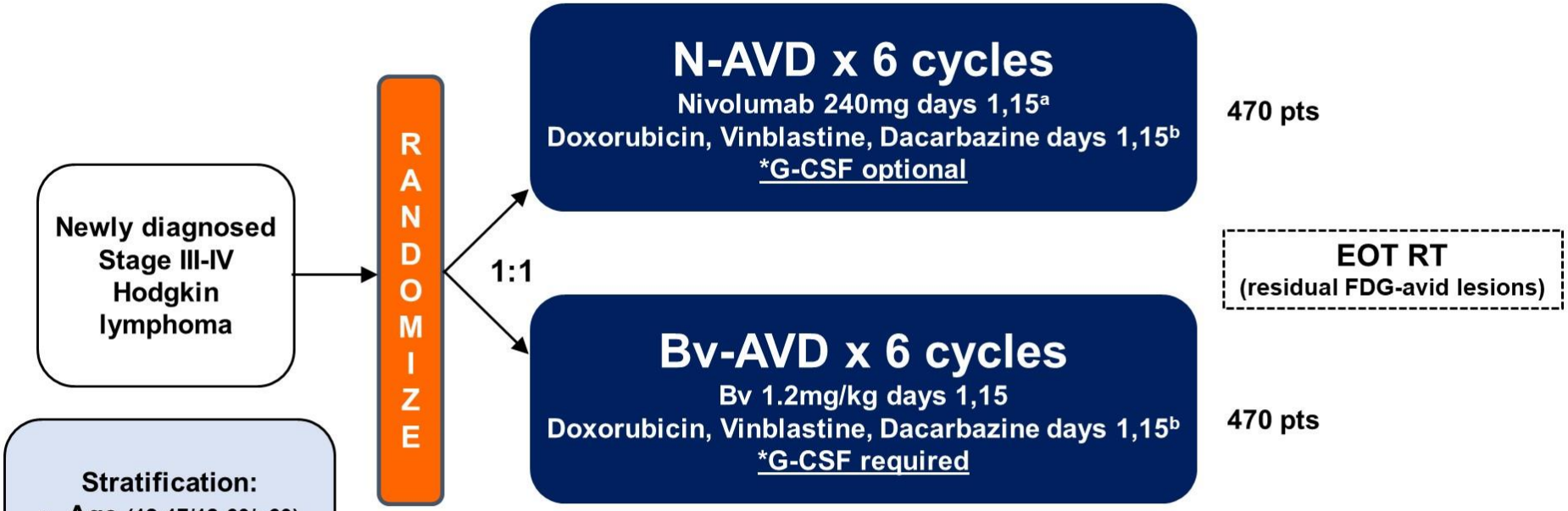
2023 ASCO ANNUAL MEETING

SWOG S1826, a Randomized Study of Nivolumab(N)-AVD Versus Brentuximab Vedotin(Bv)-AVD in Advanced Stage Classic Hodgkin Lymphoma (cHL)

Alex F. Herrera, MD[1], *Michael L. LeBlanc, PhD*[2], *Sharon M. Castellino, MD, MSc*[3], *Hongli Li, MS*[2], *Sarah C. Rutherford, MD*[4], *Andrew M Evens, DO, MSc*[5], *Kelly Davison, MD*[6], *Angela Punnett, MD*[7], *David C. Hodgson, MD, MPH, FRCPC*[8], *Susan K Parsons, MD, MRP*[9], *Sairah Ahmed, MD*[10], *Carla Casulo, MD*[11], *Nancy L. Bartlett, MD*[12], *Joo Y. Song, MD*[13], *Richard F. Little*[14], *Brad S. Kahl, MD*[12], *John P. Leonard, MD*[4], *Sonali M. Smith, MD*[15], *Kara M. Kelly, MD*[16], *and Jonathan W. Friedberg, MD, MSSc*[11]

[1]City of Hope, Duarte, CA, [2]SWOG Statistical Center, Fred Hutchinson Cancer Center, Seattle, WA, [3]Emory University, Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta, Atlanta, GA, [4]Weill Cornell Medicine-New York Presbyterian Hospital, New York, NY, [5]Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, [6]McGill University, Montreal, QC, Canada, [7]Hospital for Sick Children, Toronto, ON, Canada, [8]Department of Radiation Oncology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada, [9]Tufts Medical Center, Tufts University School of Medicine, Boston, MA, [10] University of Texas M.D. Anderson Cancer Center, Houston, TX, [11]Division of Hematology/Oncology, University of Rochester, Rochester, NY [11]Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada, [12]Washington University School of Medicine in St. Louis, St. Louis, MO, [13]Department of Pathology, City of Hope, CA [14]Cancer Therapy Evaluation Program, National Cancer Institute, Bethesda, MD [15] Department of Oncology, University of Chicago, Chicago, IL, [16]Department of Pediatric Oncology, Roswell Park Comprehensive Cancer Center, Buffalo, NY

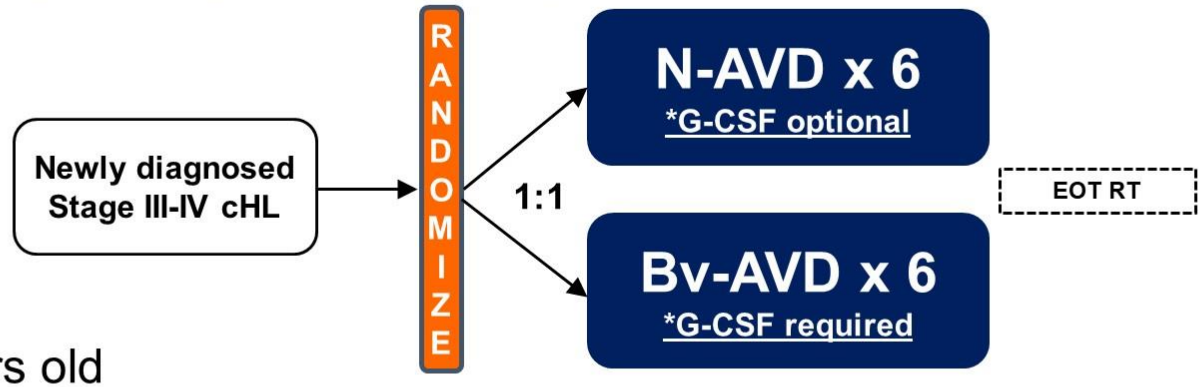
S1826 Study Design



- Primary endpoint: PFS
- Assume 84% 2-year PFS for BV-AVD, 90% 2-year PFS in N-AVD, final analysis @ 179 events

[a] Nivolumab 3mg/kg for ages ≤ 17, max 240mg
[b] Conventional doses of AVD: Stephens DM et al Blood 2019, Ansell SM et al NEJM 2022

S1826 Eligibility Criteria (abbreviated)



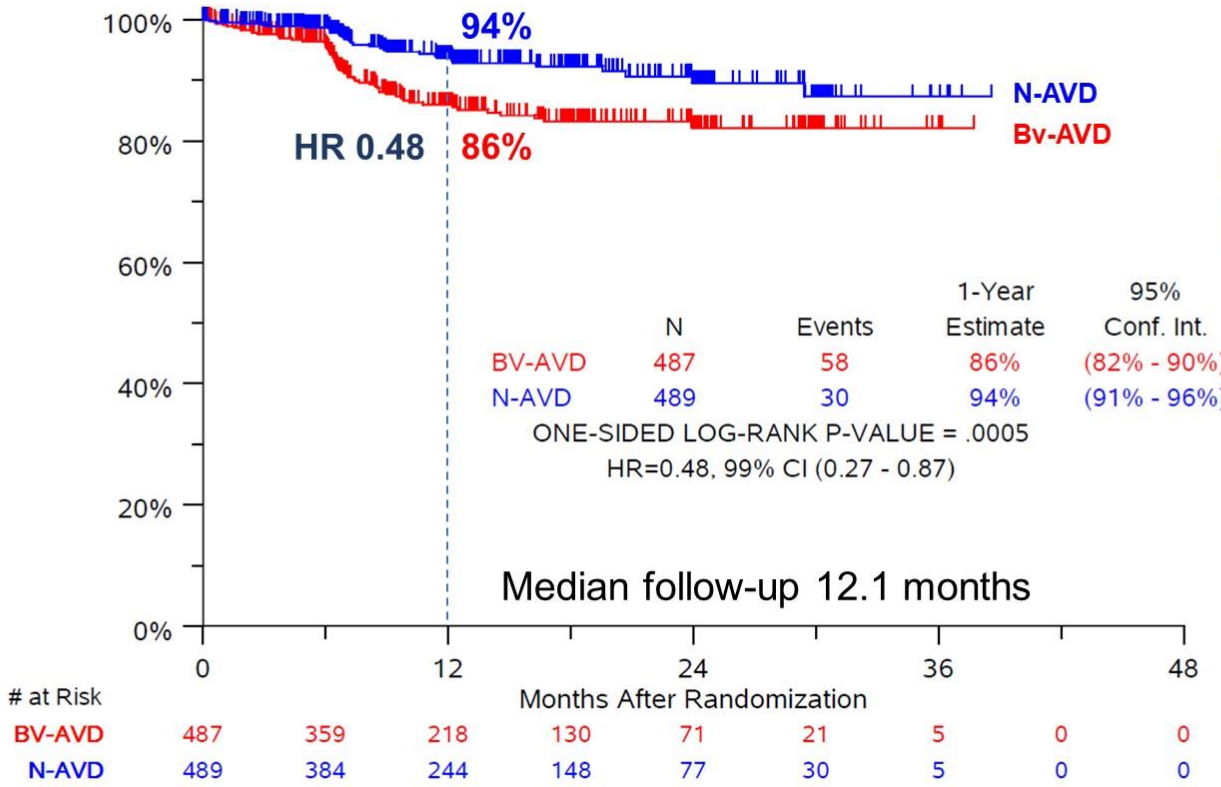
Key Inclusion

- Age ≥ 12 years old
- HIV+ eligible, if controlled
- Zubrod PS 0-2 (Peds: Lansky)
- LVEF ≥ 50% (or SF ≥ 27%)
- CrCl ≥ 30 mL/min (Peds: CrCl/GFR ≥ 70, SCr ≤ 1.5 ULN)
- Tbili ≤ 2 x ULN and AST/ ALT ≤ 3 x ULN

Key Exclusion

- Interstitial lung disease or pneumonitis
- Peripheral neuropathy ≥ Gr2
- Active autoimmune disease

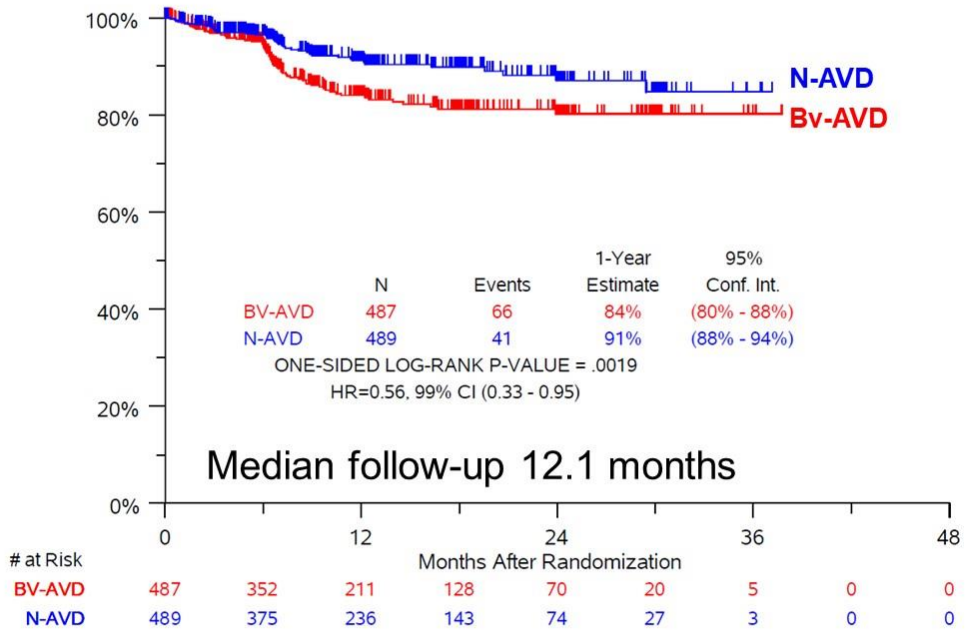
N-AVD improves PFS compared to Bv-AVD



1-year PFS
N-AVD 94%
Bv-AVD 86%

PRESENTED BY: Alex F. Herrera, MD

Event-Free Survival



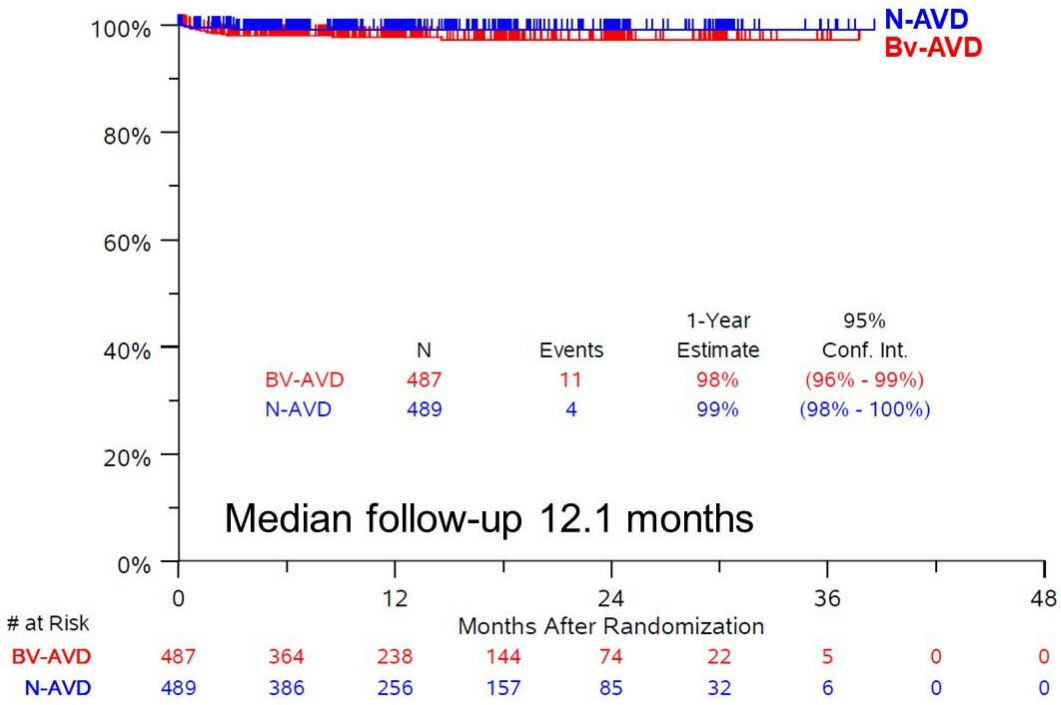
1-year EFS
N-AVD 91%
Bv-AVD 84%

EFS events: death, progression, non-protocol treatment before progression

EFS event	N-AVD	Bv-AVD
Non-protocol chemo before PD	9	6
Non-protocol immunotx before PD	1	0
Non-protocol RT prior to PD	1*	3**
Progression/Relapse	**26**	**47**
Death without progression	**4**	**10**
Total EFS Event	**41**	**66**

* Intended for RT, EOT DS=3, received RT anyways
**1/3 intended for RT, 1 with EOT DS=2 and off tx due to AE then received RT, 2 with EOT DS=3 and received RT anyways

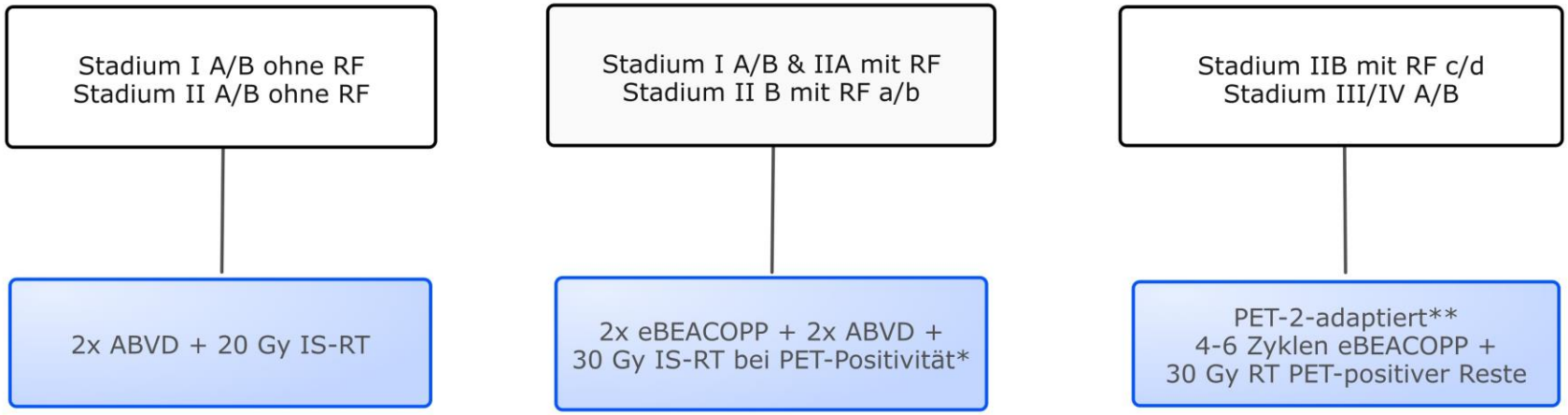
Overall Survival



Cause of death	N-AVD	Bv-AVD
Infection	2	4
Sepsis	1	2*
Cardiac arrest	0	1
Pneumonitis	0	1
Dehydration, vomiting, cHL	0	1
cHL	1**	0
Unknown	1	2
Total OS events	**4**	**11**

* 1 death from COVID-19/sepsis
** never received treatment, ineligible on C1D1

Hodgkin Lymphom



Hodgkin Lymphom

Ergebnisse

Studie	Risikogruppe	Kontrolle	Neue Therapie	N[1]	PFÜ[2] (HR)[3]	ÜL[4] (HR)[3]
HD21	Hodgkin Lymphom, fortgeschritten Alter ≥18 Jahre	eBEACOPP	BrECADD	1482	92,3 vs 94,4[5] 0,63[6] KI 0,37-1,07[7]	98,5 vs 98,5 n. s.[8]

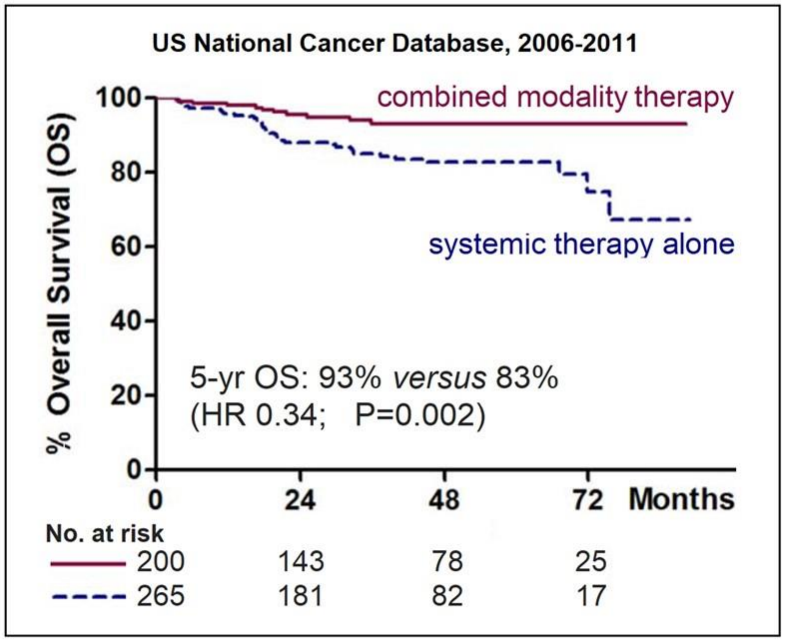
[1] N – Anzahl Pat.; [2] PFÜ – progressionsfreies Überleben nach 3 Jahren, Rate in %; [3] HR – Hazard Ratio; [4] %; [5] ÜL – Gesamtüberleben nach 3 Jahren, Rate in %; [5] **Ergebnis für Kontrolle**, **Ergebnis für Neue Therapie**; [6] **Hazard Ratio für Neue Therapie**; [8] n.s. – nicht signifikant;

2023 ASCO ANNUAL MEETING

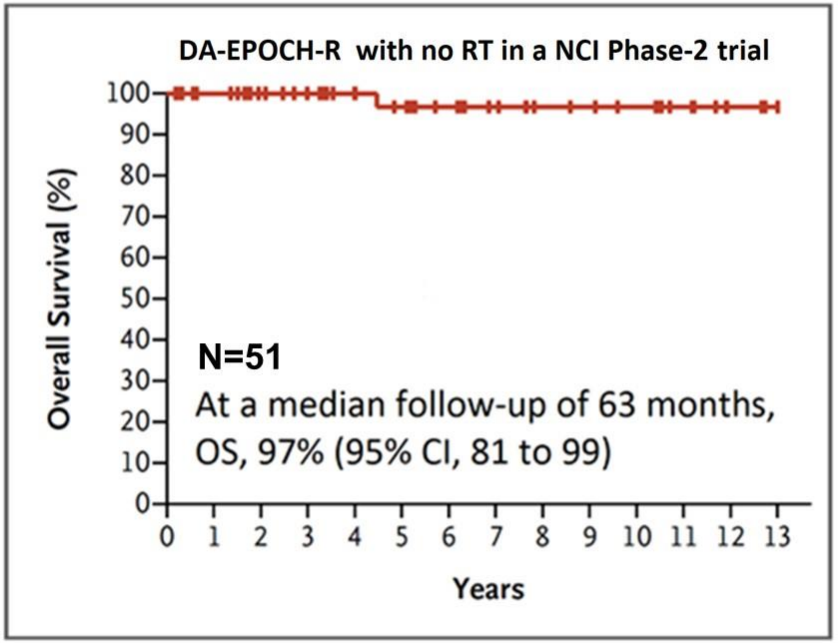
Observation vs. radiotherapy in PMBCL patients with complete response to standard immunochemotherapy: The IELSG37 randomized trial (NCT01599559)

Prof. Emanuele Zucca, M.D.
Oncology Institute of Southern Switzerland, Ente Ospedaliero Cantonale, Bellinzona, Switzerland
International Extranodal Lymphoma Study Group, Institute of Oncology Research, Bellinzona, Switzerland
Faculty of Biomedical Sciences, Università della Svizzera italiana, Lugano, Switzerland

Radiotherapy in PMBCL: a therapeutic dilemma

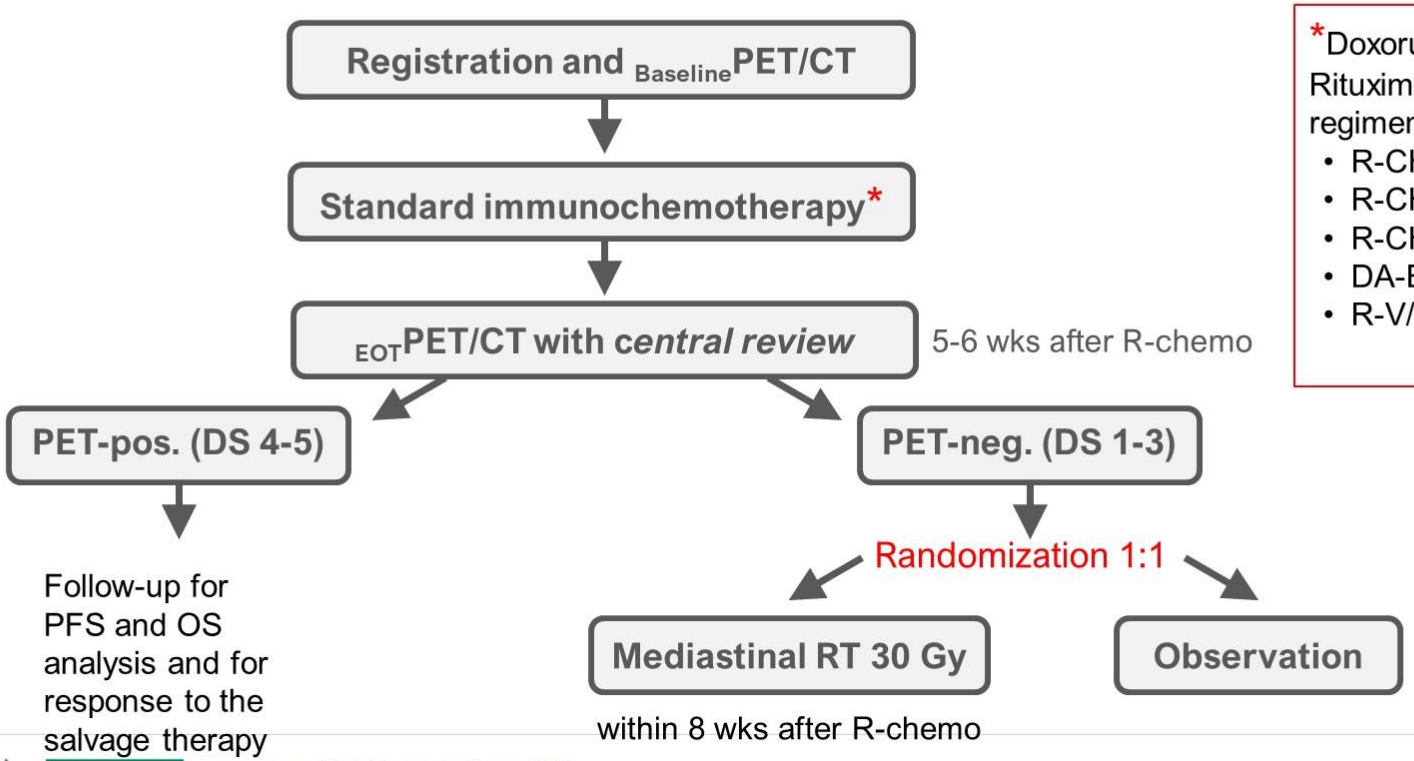


MW Jackson et al. Am J Hematol. 2016; 91:476-80



K Dunleavy et al. NEJM. 2013; 368:1408-16

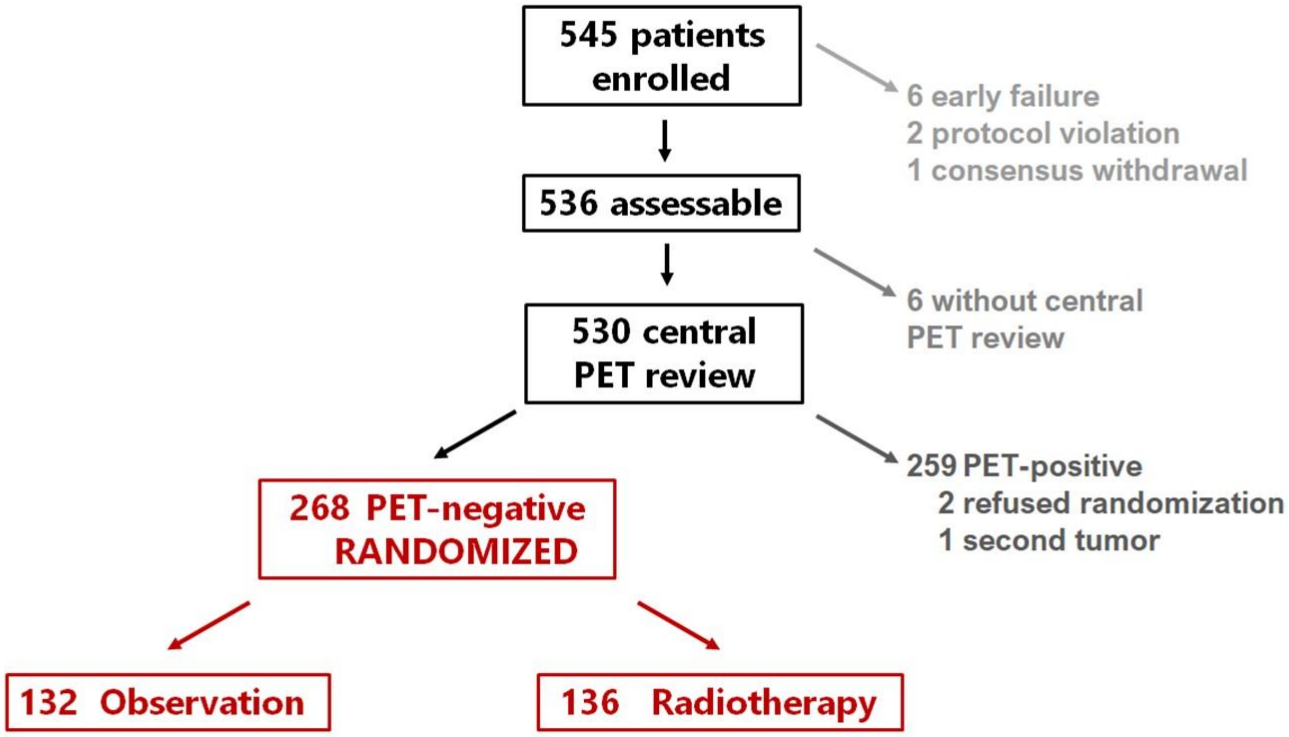
Randomized non-inferiority trial design



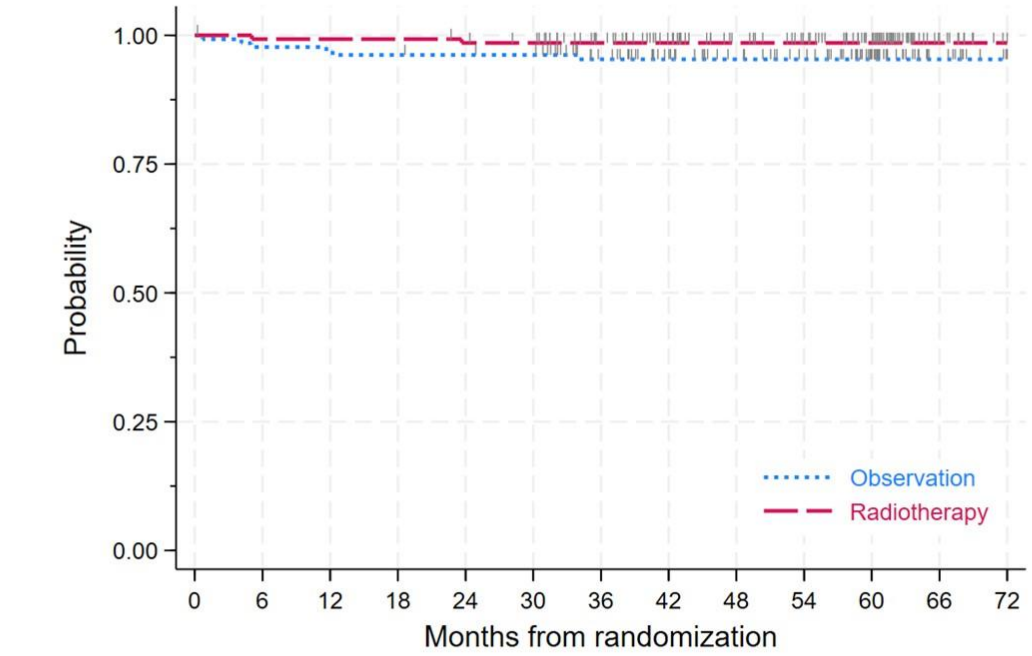
*Doxorubicin- and Rituximab-containing regimen, such as

- R-CHOP21 (like)
- R-CHOP14
- R-CHOEP
- DA-EPOCH-R
- R-V/MACOP-B

Patient flow



Progression-free survival



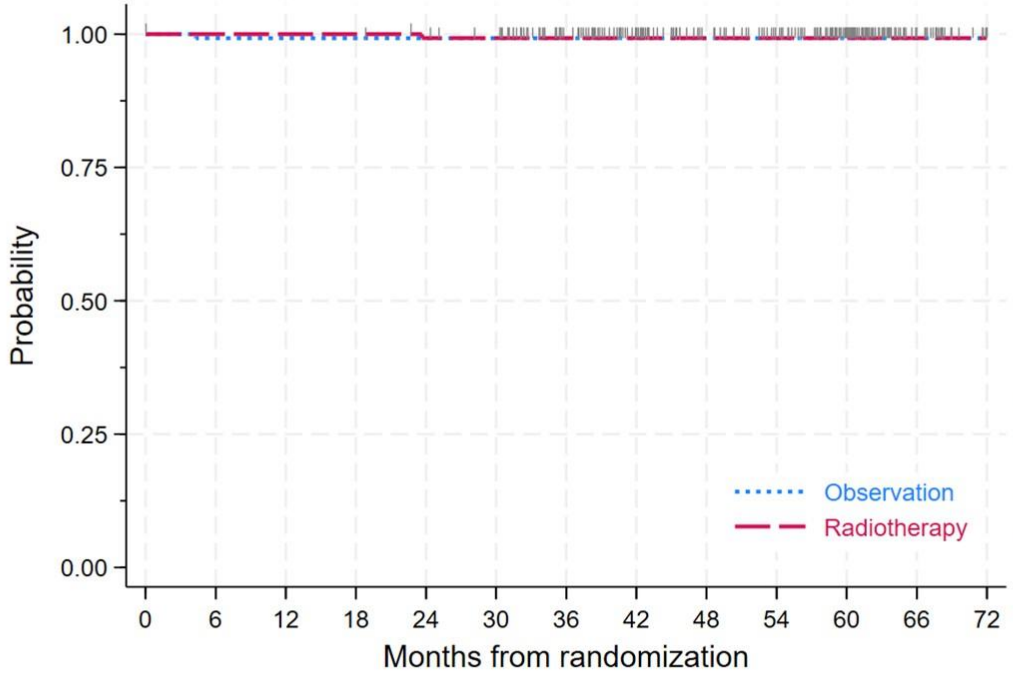
30-months PFS
96.2% (95%CI, 91.1-98.4)
98.5% (95%CI, 94.2-99.6)

HR= 0.47 (95%CI, 0.12-1.88)
Logrank test, P= 0.274

Number at risk

Observation	132	128	127	126	125	124	109	94	84	76	50	23	13
Radiotherapy	136	135	135	135	133	131	116	102	88	79	62	27	16

Overall survival



30-months OS
99.2% (95%CI, 94.7-99.9)
99.3% (95%CI, 94.9-99.9)

HR= 1.87 (95%CI, 0.17-20.7)
Logrank test, P=0.601

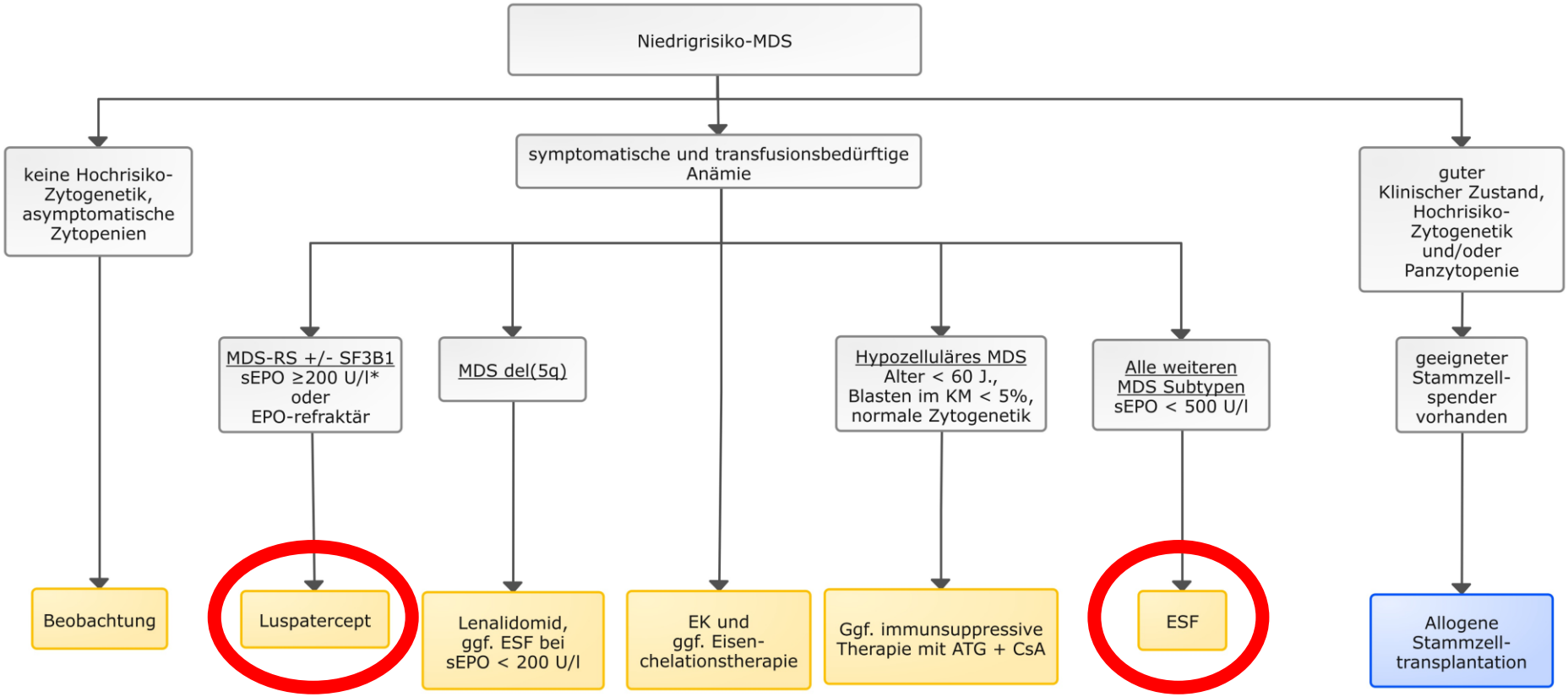
Number at risk

Observation	132	130	130	130	129	128	114	98	88	80	54	24	13
Radiotherapy	136	136	136	136	134	132	117	103	89	80	62	27	16

Take home message

- IELSG37 is the largest randomized trial of PMBCL ever conducted.
- Mediastinal RT in patients with CMR after front-line immunochemotherapy can be safely omitted.
- Longer follow-up is needed to examine late toxicity.
- To date 3 severe cardiac events and 3 second cancers recorded, all in patients randomized to RT.

Myelodysplastische Neoplasien



2023 ASCO ANNUAL MEETING

Efficacy and safety results from the COMMANDS trial: a phase 3 study evaluating luspatercept vs epoetin alfa in erythropoiesis-stimulating agent-naive transfusion-dependent patients with lower-risk myelodysplastic syndromes

Guillermo Garcia-Manero,[1] Uwe Platzbecker,[2] Valeria Santini,[3] Amer M. Zeidan,[4] Pierre Fenaux,[5] Rami S. Komrokji,[6] Jake Shortt,[7] David Valcarcel,[8] Anna Jonasova,[9] Sophie Dimicoli-Salazar,[10] Ing Soo Tiong,[11] Chien-Chin Lin,[12] Jiahui Li,[13] Sandra Kreitz,[14] Veronika Pozharskaya,[13] Jeevan K. Shetty,[14*] Andrius Degulys,[15] Carlo Finelli,[16] Thomas Cluzeau,[17] Matteo Giovanni Della Porta[18,19]

[1]Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Medical Clinic and Policlinic 1, Hematology and Cellular Therapy, University Hospital Leipzig, Leipzig, Germany; [3]MDS Unit, Hematology, University of Florence, AOUC, Florence, Italy; [4]Department of Internal Medicine, Yale School of Medicine and Yale Cancer Center, Yale University, New Haven, CT, USA; [5]Service d'Hématologie Séniors, Hôpital Saint-Louis, Université Paris 7, Paris, France; [6]Moffitt Cancer Center, Tampa, FL, USA; [7]Monash University and Monash Health, Melbourne, VIC, Australia; [8]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [9]Medical Department Hematology, Charles University General University Hospital, Prague, Czech Republic; [10]Hôpital Haut-Lévêque, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France; [11]Malignant Haematology & Stem Cell Transplantation, The Alfred, Melbourne, VIC, Australia; [12]Department of Laboratory Medicine, National Taiwan University Hospital, Taipei, Taiwan; [13]Bristol Myers Squibb, Princeton, NJ, USA; [14]Celgene International Sàrl, a Bristol-Myers Squibb Company, Boudry, Switzerland; [15]Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania; Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius, Lithuania; [16]IRCCS Azienda Ospedaliero-Universitaria di Bologna - Istituto di Ematologia "Seràgnoli", Bologna, Italy; [17]Département d'Hématologie Clinique, Université Cote d'Azur, CHU Nice, Nice, France; [18]Cancer Center IRCCS Humanitas Research Hospital, Milan, Italy; [19]Department of Biomedical Sciences, Humanitas University, Milan, Italy. *At the time the study was conducted.

Abstract number 7003

The COMMANDS study

The COMMANDS study (NCT03682536) is a global, phase 3, open-label, randomized trial comparing the efficacy and safety of luspatercept versus epoetin alfa for the treatment of anemia due to IPSS-R LR-MDS in ESA-naive patients who require RBC transfusions

Key eligibility criteria

- ≥ 18 years of age
- IPSS-R Very low-, Low-, or Intermediate-risk MDS (with or without RS) by WHO 2016, with < 5% blasts in bone marrow[a]
- Required RBC transfusions (2-6 pRBC units/8 weeks for a minimum of 8 weeks immediately prior to randomization)
- Endogenous sEPO < 500 U/L
- ESA-naive

Patients stratified by:

- Baseline sEPO level
- Baseline RBC transfusion burden
- RS status

Randomized 1:1

Luspatercept (N = 178)
1.0 mg/kg s.c. Q3W
titration up to 1.75 mg/kg

Epoetin alfa (N = 178)
450 IU/kg s.c. QW
titration up to 1050 IU/kg

Response assessment at day 169 and every 24 weeks thereafter

End treatment
Due to lack of clinical benefit[b] or disease progression per IWG criteria

Post-treatment safety follow-up

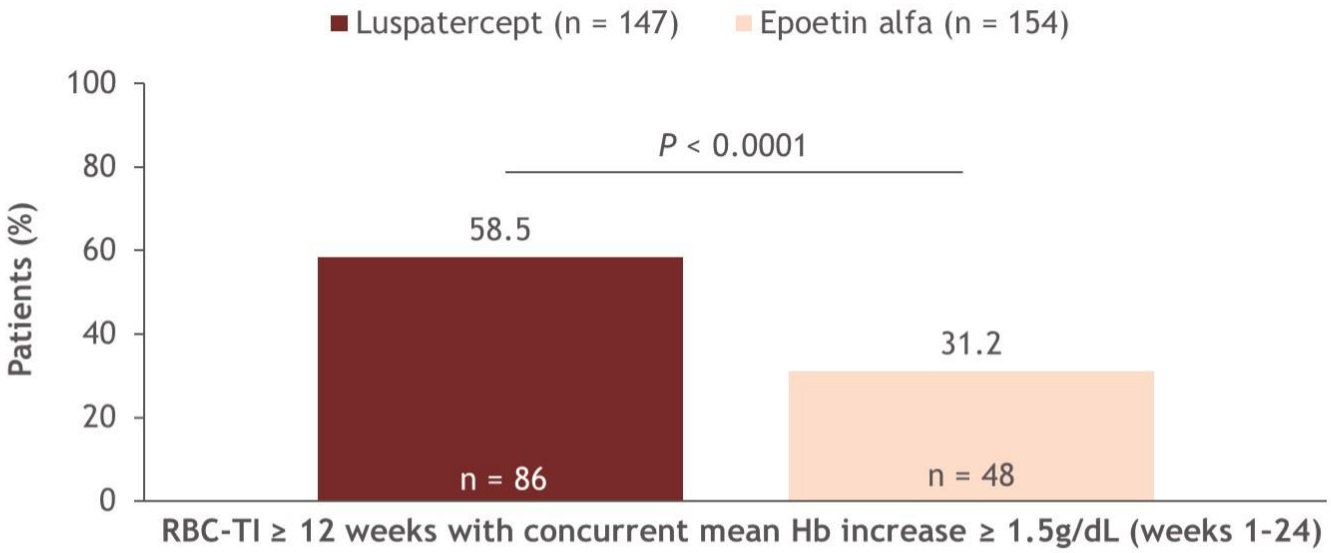
- Monitoring for other malignancies, HR-MDS or AML progression, subsequent therapies, survival
- For 5 years from first dose or 3 years from last dose, whichever is later

[a]MDS with del(5q) were excluded; [b]Clinical benefit defined as transfusion reduction of ≥ 2 pRBC units/8 weeks versus baseline.
AML, acute myeloid leukemia; HR-MDS, higher risk-myelodysplastic syndromes; IPSS-R, Revised International Prognostic Scoring System; IWG, International Working Group; pRBC, packed RBC; QW, once weekly; Q3W, every 3 weeks; s.c., subcutaneously; sEPO, serum erythropoietin; WHO, World Health Organization.

Garcia-Manero G, et al. ASCO 2023 [Abstract #7003]

COMMANDS primary endpoint: luspatercept superior to epoetin alfa

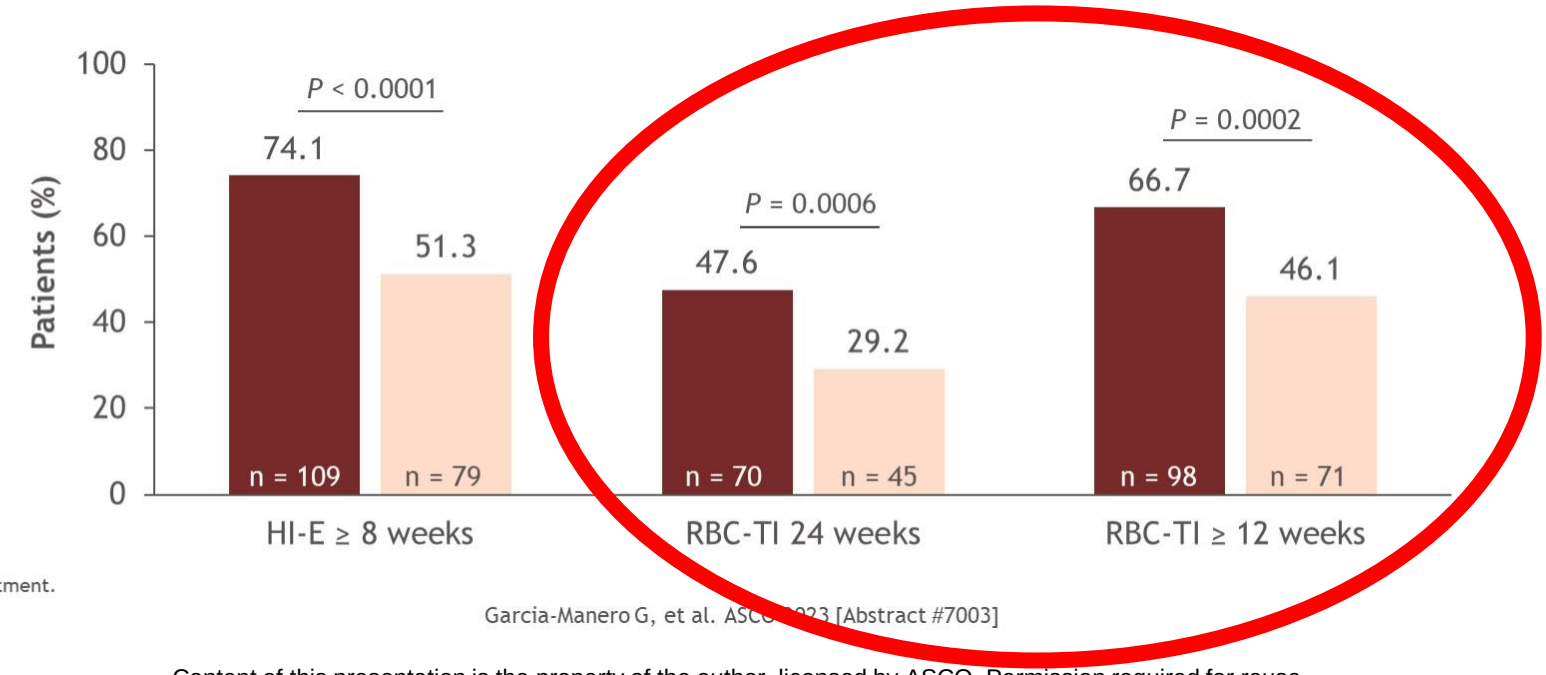
- Of 301 patients included in the efficacy analysis, 86 (58.5%) patients receiving luspatercept and 48 (31.2%) epoetin alfa achieved the primary endpoint



Garcia-Manero G, et al. ASCO 2023 [Abstract #7003]

COMMANDS secondary endpoints: luspatercept superior to epoetin alfa

Time to response, median (range), days	Luspatercept (n = 147)	Epoetin alfa (n = 154)
Time to first RBC transfusion (week 1-EOT)	n = 93 168.0 (64.0-323.0)	n = 116 42.0 (22.0-55.0)



EOT, end of treatment.

Garcia-Manero G, et al. ASCO 2023 [Abstract #7003]

2023 ASCO ANNUAL MEETING

IMerge: Results From a Phase 3, Randomized, Double-blind, Placebo-Controlled Study of Imetelstat in Patients With Heavily Transfusion Dependent Non-Del(5q) Lower-Risk Myelodysplastic Syndromes Relapsed/Refractory to Erythropoiesis Stimulating Agents

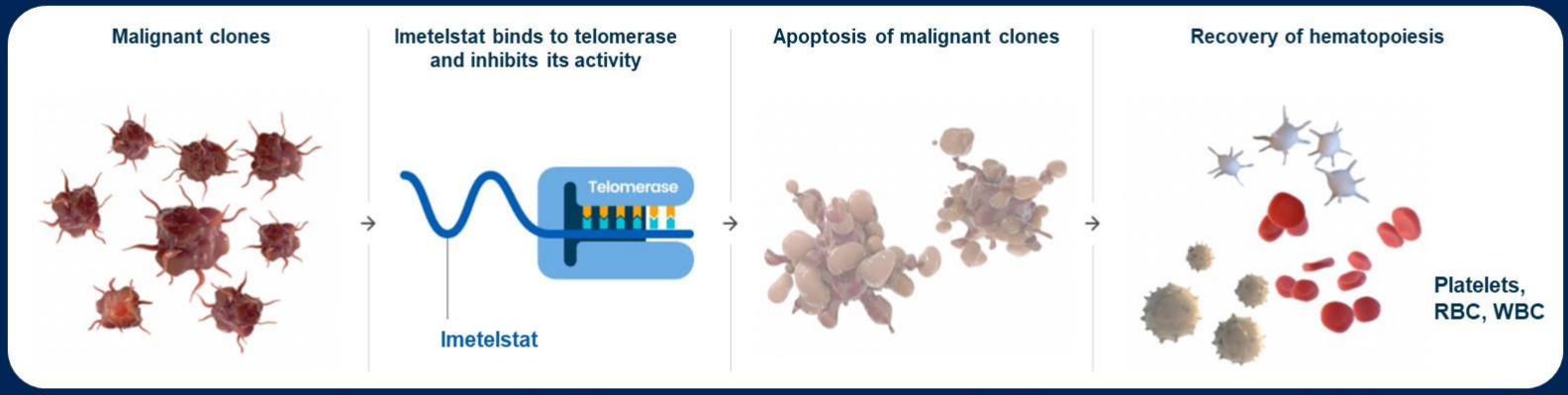
Amer Zeidan, MBBS, MHS,[1] Uwe Platzbecker, MD,[2] Valeria Santini, MD,[3] Pierre Fenaux, MD, PhD,[4] Mikkael A. Sekeres, MD,[5] Michael Robert Savona, MD,[6] Yazan F. Madanat, MD,[7] Maria Diez-Campelo, MD, PhD,[8] David Valcarcel-Ferreiras, MD, PhD,[9] Thomas Ilmer, MD,[10] Anna Jonasova, PhD,[11] Petra Belohlavkova, PhD,[12] Laurie Sherman, BSN,[13] Tymara Berry, MD,[13] Souria Dougherty, MBA,[13] Sheetal Shah, BS,[13] Libo Sun, PhD,[13] Ying Wan, MD, PhD,[13] Fei Huang, PhD,[13] and Rami Komrokji, MD[14]

[1]Section of Hematology, Department of Internal Medicine, Yale School of Medicine and Yale Comprehensive Cancer Center, Yale University, New Haven, CT, USA; [2]Department of Hematology, Cellular Therapy and Hemostaseology, Leipzig University Hospital, Leipzig, Germany; [3]MDS Unit, Azienda Ospedaliero Universitaria Careggi, University of Florence, Florence, Italy; [4]Service d'Hématologie Séniors, Hôpital Saint-Louis, Université de Paris 7, Paris, France; [5]Division of Hematology, Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; [6]Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, TN, USA; [7]Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA; [8]Hematology Department, The University Hospital of Salamanca, Salamanca, Spain; [9]Hematology Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [10]Hematology Private Practice, Dresden, Germany; [11]1st Medical Department - Hematology, General Hospital, Prague, Czech Republic; [12]4th Department of Internal Medicine - Haematology, Charles University Hospital, Hradec Kralove, Czech Republic; [13]Geron Corporation, Foster City, CA, USA; [14]Moffitt Cancer Center, Tampa, FL, USA

PRESENTED BY: Amer Zeidan, MBBS MHS, Associate Professor of Internal Medicine (Hematology)

Imetelstat in Lower Risk MDS

- Imetelstat is a first-in-class direct and competitive inhibitor of telomerase activity[1,2]
- Imetelstat specifically targets malignant clones with abnormally high telomerase activity, enabling recovery of effective hematopoiesis[3,4]



- In the phase 2 part of the IMerge study (NCT02598661), patients with LR-MDS who were heavily RBC transfusion dependent, ESA relapsed/refractory or ineligible, non-del(5q), and naive to lenalidomide and HMA achieved durable and continuous RBC-TI when treated with imetelstat, specifically 8-week RBC TI rates were 42% with a median TI duration of 86 weeks[5]
- This analysis reports phase 3 results from IMerge in the same patient population

ESA, erythropoiesis stimulating agent; HMA, hypomethylating agent; LR-MDS, lower risk myelodysplastic syndromes; RBC, red blood cell; TI, transfusion independence; WBC, white blood cell.

1. Asai A, et al. *Cancer Res.* 2003;63(14):3931-3939. 2. Herbert BS, et al. *Oncogene.* 2005;24(33):5262-5268. 3. Mosoyan G, et al. *Leukemia.* 2017;31(11):2458-2467. 4. Wang X at al. *Blood Adv.* 2018;25;2(18):2378-2388. 5. Steensma DP, et al. *J Clin Oncol.* 2021;39(1):48-56.

PRESENTED BY: Amer Zeidan, MBBS MHS, Associate Professor of Internal Medicine (Hematology)

IMerge Phase 3 Trial Design (MDS3001; NCT02598661)

Phase 3
Double-blind, randomized
77 Clinical sites in 17 countries

Patient Population (ITT N = 178):
- IPSS low- or intermediate 1- risk MDS
- Relapsed/refractory[a] to ESA or EPO >500 mU/mL (ESA ineligible)
- **Transfusion dependent: ≥4 units RBCs/8 weeks over 16-week pre-study**
- Non-deletion 5q
- No prior treatment with lenalidomide or HMAs

RANDOMIZE 2:1

Imetelstat
7.5 mg/kg IV/4 weeks
(N = 118)

Stratification:
- Transfusion burden (4-6 vs >6 units)
- IPSS risk category (low vs intermediate-1)

Supportive care, including RBC and platelet transfusions, myeloid growth factors (e.g., G-CSF), and iron chelation therapy administered as needed on study per investigator discretion

Placebo
(N = 60)

Safety population (treated) N = 177
Imetelstat N = 118
Placebo N = 59

Primary End Point:
- 8-week RBC-TI[b]

Key Secondary End Points:
- 24-week RBC-TI[b]
- Duration of TI
- Hematologic Improvement-Erythroid
- Safety

Key Exploratory End Point:
- VAF changes
- PRO (fatigue measured by FACIT-Fatigue)

[a]Received ≥8 weeks of ESA treatment (epoetin alfa ≥40,000 U, epoetin beta ≥30,000 U or darbepoetin alfa 150 µg or equivalent per week) without Hgb rise ≥1.5 g/dL or decreased RBC transfusion requirement ≥4 U/8 weeks *or* transfusion dependence or reduction in Hgb by ≥1.5 g/dL after hematologic improvement from ≥8 weeks of ESA treatment.

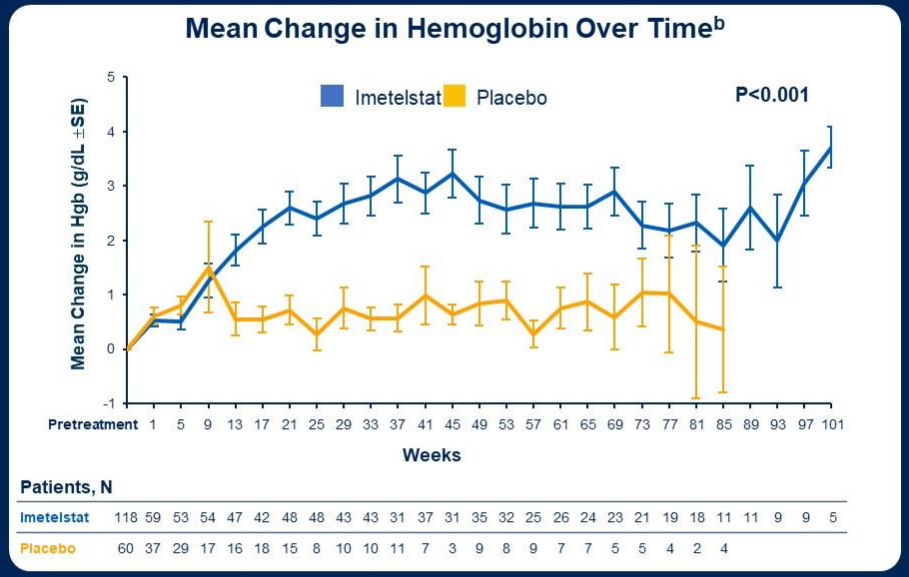
[b]Proportion of patients without any RBC transfusion for ≥8 consecutive weeks since entry to the trial (8-week TI); proportion of patients without any RBC transfusion for ≥24 consecutive weeks since entry to the trial (24-week TI)

EPO, erythropoietin; ESA, erythropoiesis stimulating agent; G-CSF, granulocyte colony-stimulating factor; Hgb, hemoglobin; HMA, hypomethylating agent; IPSS, International Prognostic Scoring System; ITT, intent-to-treat; IV, intravenous; MDS, myelodysplastic syndromes; PRO, patient-reported outcome; RBC, red blood cell; TI, transfusion independence, VAF, variant allele frequency.

PRESENTED BY: Amer Zeidan, MBBS MHS, Associate Professor of Internal Medicine (Hematology)

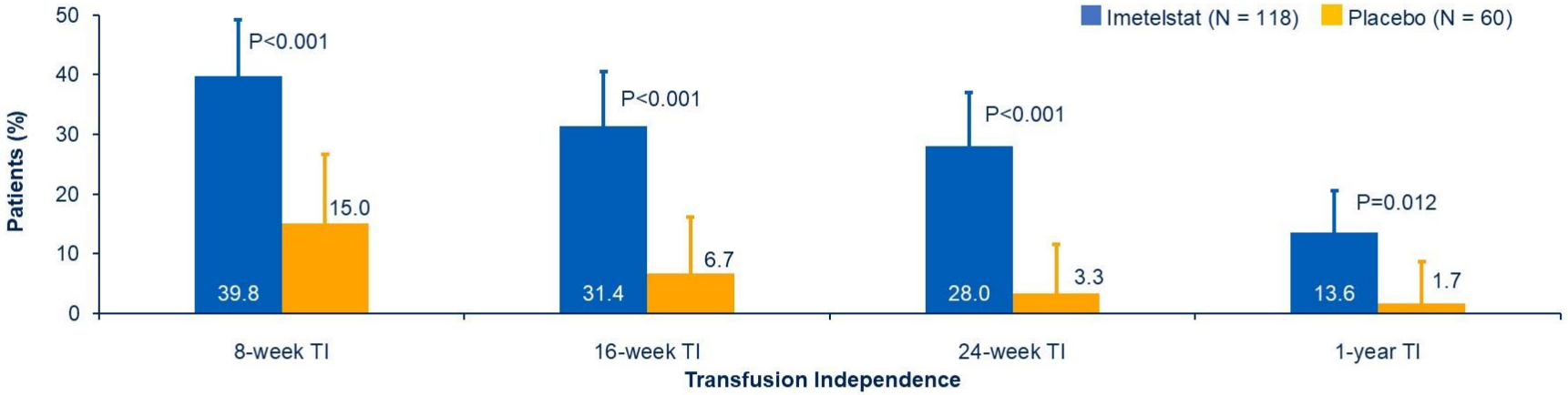
Significant and Sustained Increase in Hemoglobin Among Patients Treated With Imetelstat

8-Week TI Responders[a]	Imetelstat (N = 47)	Placebo (N = 9)
Median Hgb rise, g/dL (range)	3.6 (−0.1 to 13.8)	0.8 (−0.2 to 1.7)
Median Hgb peak, g/dL (range)	11.3 (8.0–21.9)	8.9 (7.9–9.7)



[a]Among patients achieving 8-week TI, analysis performed during TI. Hgb rise defined as the maximum Hgb value in the longest TI interval excluding the first 2 weeks minus the pretreatment Hgb level.
[b]Mean changes from the minimum Hgb of the values that were after 14 days of transfusions in the 8 weeks prior to the first dose date are shown. Data points that have <4 patients are not shown. P-value based on a mixed model for repeated measures with Hgb change as the dependent variable, week, stratification factors, minimum Hgb in the 8 weeks prior to the first dose date, treatment group, and treatment and week interaction term as the independent variables with autoregressive moving average (ARMA(1,1)) covariance structure.
Hgb, hemoglobin; RBC, red blood cell; SE, standard error; TI, transfusion independence.

Higher Rates of Longer-Term Duration of RBC TI Observed With Imetelstat vs Placebo[a]



Patients With Response, n (% [95% CI])

Imetelstat	47 (39.8 [30.9–49.3])	37 (31.4 [23.1–40.5])	33 (28.0 [20.1–37.0])	16 (13.6 [8.0–21.1])
Placebo	9 (15.0 [7.1–26.6])	4 (6.7 [1.9–16.2])	2 (3.3 [0.4–11.5])	1 (1.7 [0.0–8.9])

Data cutoff: October 13, 2022.

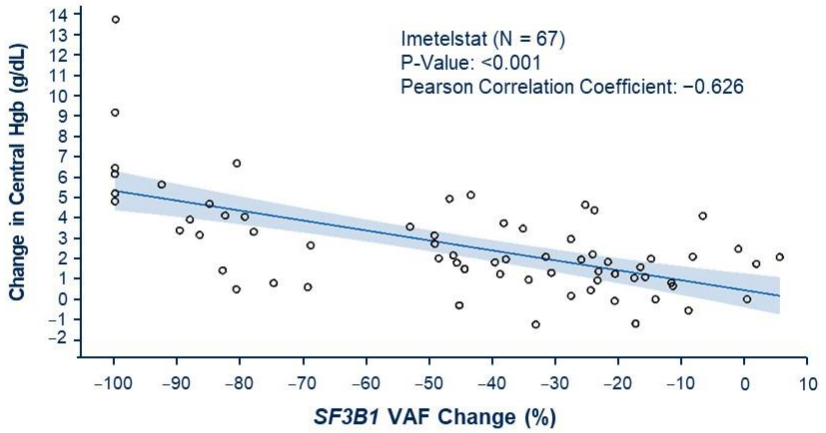
[a]Primary end point 8-week and the first secondary end point 24-week TI are statistically significant by study prespecified gatekeeping testing procedure. One-year TI represented a preliminary assessment. P-values determined by the Cochran-Mantel-Haenszel test, with stratification for prior RBC transfusion burden (≥4 to ≤6 vs >6 RBC units/8-weeks during a 16-week period prior to randomization) and baseline IPSS risk category (low vs intermediate-1) applied to randomization.

IPSS, International Prognostic Scoring System; RBC, red blood cell; TI, transfusion independence.

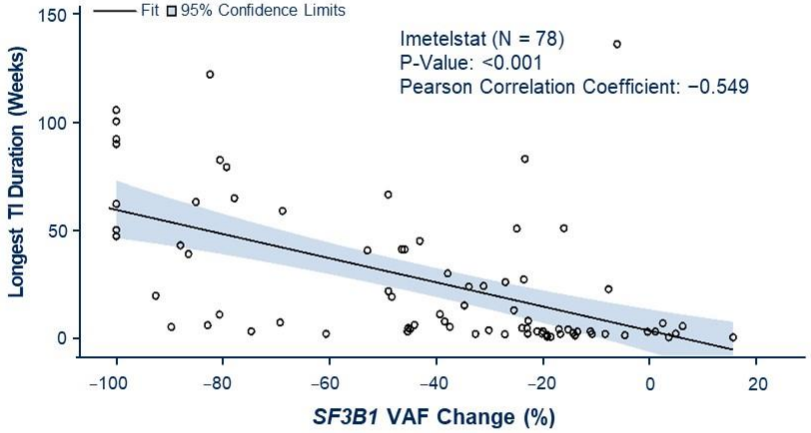
PRESENTED BY: Amer Zeidan, MBBS MHS, Associate Professor of Internal Medicine (Hematology)

SF3B1 VAF Reduction in Patients Treated With Imetelstat Correlated With Clinical Outcomes[a]

Maximum Increase in Hgb vs Maximum Reduction in *SF3B1* VAF[b,c]



Longest RBC-TI Duration vs Maximum Reduction in *SF3B1* VAF[c]



- With imetelstat, a greater reduction in *SF3B1* VAF correlated with a greater increase in Hgb and longer RBC-TI duration
- A greater VAF reduction in *TET2, DNMT3A* or *ASXL1* also correlated with longer RBC-TI duration

[a]Analyses included patients in imetelstat treatment group with detectable SF3B1 mutant allele (≥5%) pretreatment and any post-baseline mutation assessment. [b]Analysis included patients with post-baseline Hgb assessment, excluding assessments within 14 days post-RBC transfusion. [c]Fitted lines and P values based on linear regression with maximum increase in Hgb from pretreatment (left) and RBC-TI duration (right) as the dependent variable and the maximum percentage reduction from baseline in *SF3B1* VAF as independent variable.
ASXL1, additional sex combs like-1; DNMT3A, DNA (cytosine-5)-methyltransferase 3A; Hgb, hemoglobin; RBC, red blood cell; SF3B1, splicing factor 3b subunit 1; TET2, Tet methylcytosine dioxygenase 2; TI, transfusion independence; VAF, variant allele frequency.

Hematology

Hodgkin's Disease	Brentuximab Vedotin Nivolumab Pembrolizumab
Non Hodgkin Lymphoma	Axicabtagene Ciloleucel Brentuximab Vedotin Duvelisib Ibrutinib Idelalisib KTE-X19 Lisocabtagene maraleucel Loncastuximab tesirin Obinutuzumab Pixantrone Polatuzumab Vedotin Siltuximab Tafasitimab Tabelecleucel Tisagenlecleucel Zanubrutinib
CLL	Acalabrutinib Duvelisib Ibrutinib Idelalisib Obinutuzumab Venetoclax Zanubrutinib
Hairy cell leukemia	Moxetumomab Pasudotox
Multiple Myeloma	Belantamab Mafodotin Carfilzomib Ciltacabtagene Autoleucel Daratumumab Elotuzumab Idecabtagene Vicleucel Isatuximab Ixazomib Panobinostat Pomalidomide Selinexor
Sezary Syndrome/ Mycosis fungoides	Mogamulizumab
BPDCN	Tagraxofusp
ALL	Blinatumomab Clofarabin Inotuzumab Ozogamicin Tisagenlecleucel
AML	Daunorubicin / Cytarabine Decitabine Gemtuzumab Ozogamicin Gilterinib Glasdegib Midostaurin Venetoclax

since 2011

Ascimitinib Avapritinib Bosutinib Fedratinib Ponatinib Ruxolitinib	MPN, CML
Luspatercept	MDS
Damoctocog alfa pegol Efmoroctocog alfa Emicizumab Lonoctocog alfa Rurioctocog alfa Simoctcog alfa Turoctocog alfa Turoctocog alfa pegol Valoctocogene roxaparvovec	Hemophilia A
Albutrepenonacog alfa Eftrenonacog alfa Etranacogene Dezaparvovec Nonacog beta pegol	Hemophilia B
Andexanet alfa	Anticoagulation
Avatrombopag Fostamatinib	Immune Thrombocytopenia (ITP)
Lusutrombopag	Thrombocytopenia, chronic hepatic diseasse
Caplacizumab	Thrombotic Microangiopathy (TMA)
Ravulizumab	atypical Hemolytic Uremic Syndrome (aHUS)
Ravulizumab	Paroxysmal Nocturnal Hemoglobinuria (PNH)
Betibeglogene Autotemcel Luspatercept	Thalassemia, beta
Crizanlizumab Voxelotor	Sickle Cell Disease (SCD)
Mepolizumab	Hypereosinophilic syndrome
Sutimlimab	Hemolytic Anemia (CAD)
Roxadustat	Anemia, chronic kidney disease

2023 ASCO ANNUAL MEETING

Carfilzomib, lenalidomide, and dexamethasone (KRd) *versus* elotuzumab and KRd in transplant-eligible patients with newly diagnosed multiple myeloma: Post-induction response and MRD results from an open-label randomized phase 3 study

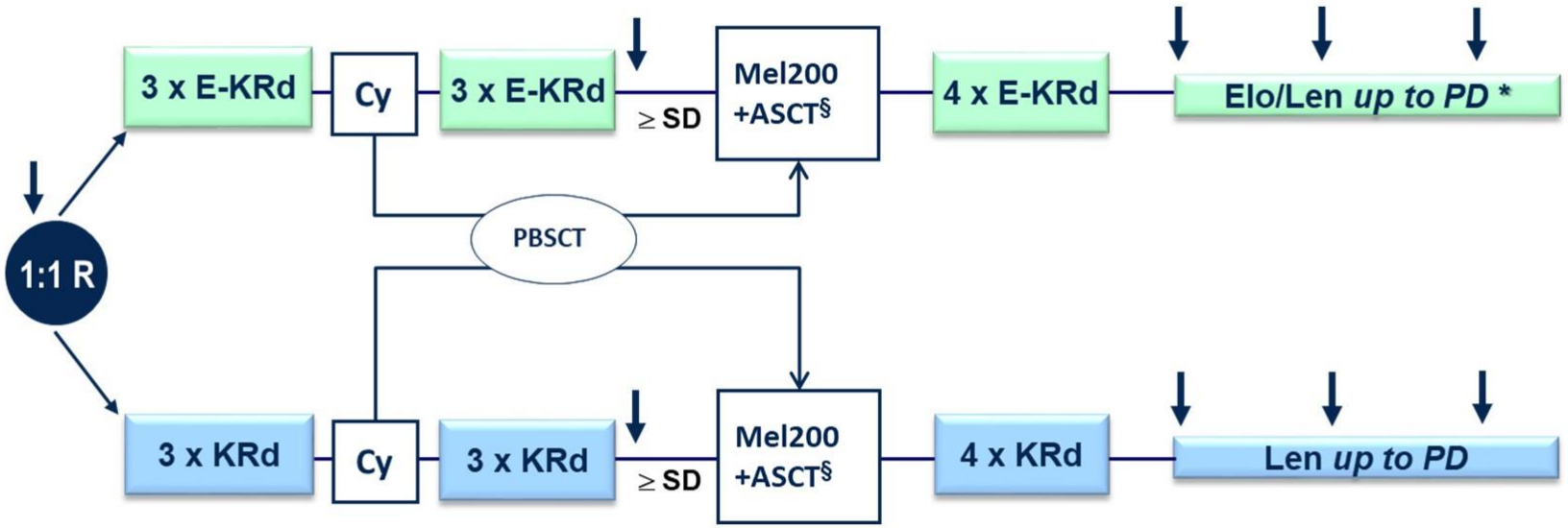
S Knop,[1] T Stuebig,[2] M Kull,[3] R Greil,[4] N Steiner,[5] F Bassermann,[6] A Nogai,[7] M von Lilienfeld-Toal,[8] S Janjetovic,[9] K Trautmann-Grill,[10] M Bittrichch,[1] MM Engelhardt,[11] A Hoferer,[12] S Theurich,[13] M Binder,[14] N Zojer,[15] HA Duerk,[16] M Brueggemann,[17] S Held,[18] and H Einsele[1] on behalf of *Deutsche Studiengruppe Multiples Myelom*

[1]Wuerzburg University Medical Center, Wuerzburg, Germany; [2]Schleswig-Holstein University Hospital, Kiel Campus, Kiel, Germany; [3]Ulm University Hospital, Dept. of Internal Medicine 3, Ulm, Germany; [4]University Hospital Salzburg Paracelus University, Salzburg, Austria; [5]Medical University Innsbruck, Dept. of Internal Medicine V, Innsbruck, Austria; [6]University Hospital rechts der Isar, Munich, Germany; [7]Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt Universität zu Berlin, Medizinische Klinik m.S. Hämatologie, Onkologie und Tumorimmunologie, Berlin, Germany; [8]Jena University Hospital, Dept. of Hematology and Oncology, Jena, Germany; [9]Helios Klinikum Berlin-Buch, Dept. of Hematology and Oncology, Berlin, Germany; [10]Department of Hematology and Oncology, Dresden University Hospital Carl Gustav Carus, Dresden, Germany; [11]University Hospital Medical Centre, Freiburg, Germany; [12]Robert Bosch Hospital, Dept. of Hematology and Oncology, Stuttgart, Germany; [13]Department of internal Medicine III, Hematology and Oncology, Gene Center, Cancer- and Immunometabolism Research Group, Ludwig-Maximilians University Munich, Mu, Munich, Germany; [14]Department of Internal Medicine IV, Oncology/Hematology, Martin-Luther-University Halle-Wittenberg, Halle, Germany; [15]Wilhelminen Cancer Research Institute, First Department of Medicine, Center for Oncology, Hematology, and Palliative Care, Clinic Ottakring, Vienna, Austria; [16]St Barbara Hospital Hamm, Dept. of Hematology and Oncology, Hamm, Germany; [17]Medical Department II, University Schleswig Holstein in the City Hospital Kiel, Kiel, Germany; [18]Clinassess GmbH, Leverkusen, Germany.

PRESENTED BY: Stefan Knop, M.D.

DSMM XVII Study: Elo-KRd versus KRd

Study Design; *N=576*



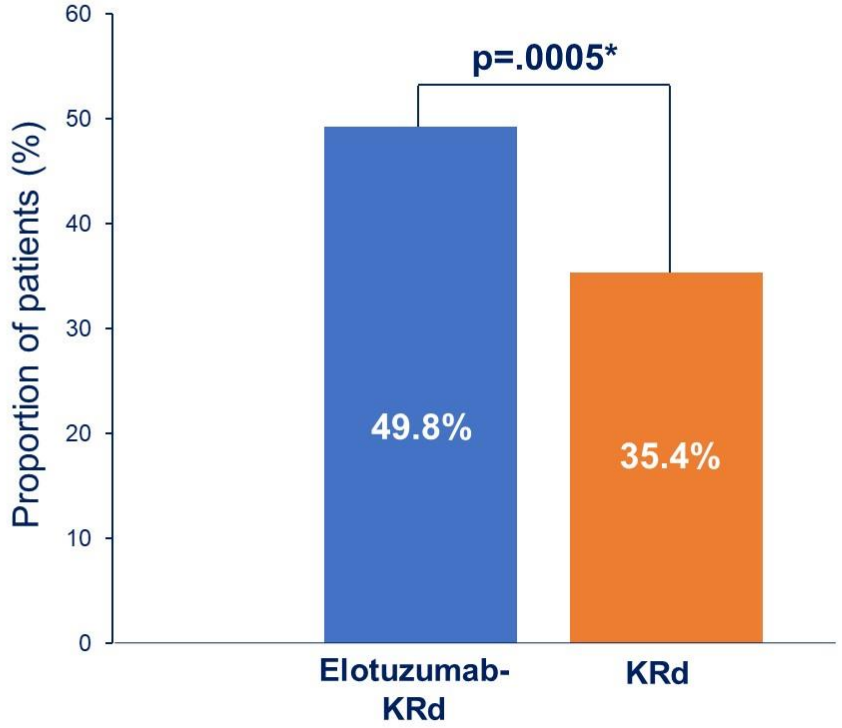
MRD assessment by NGF (EuroFlow) and NGS

* Elo maint. 20 mg/kg q28 days; § Tandem if no CR

clinicaltrials.gov: NCT03948035

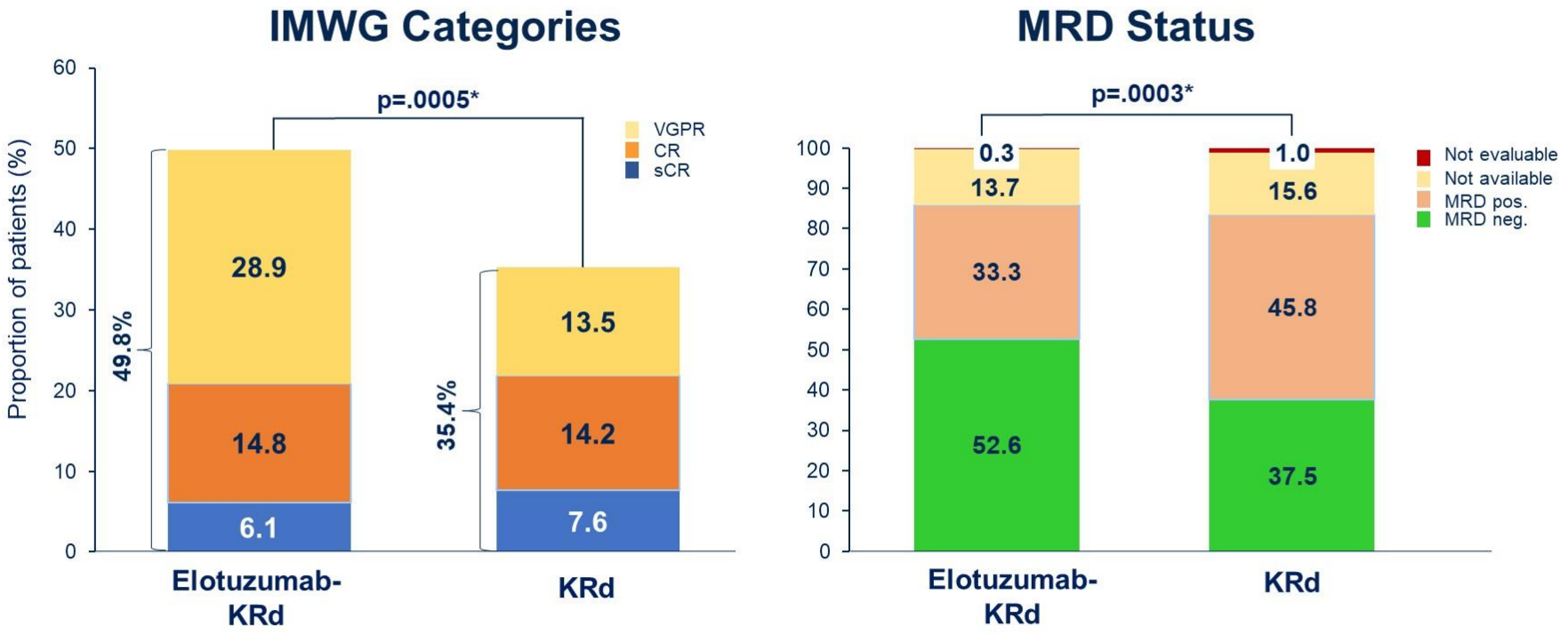
DSMM XVII Study: Post-induction Response

Patients with ≥ VGPR and MRD negativity; *N=576*

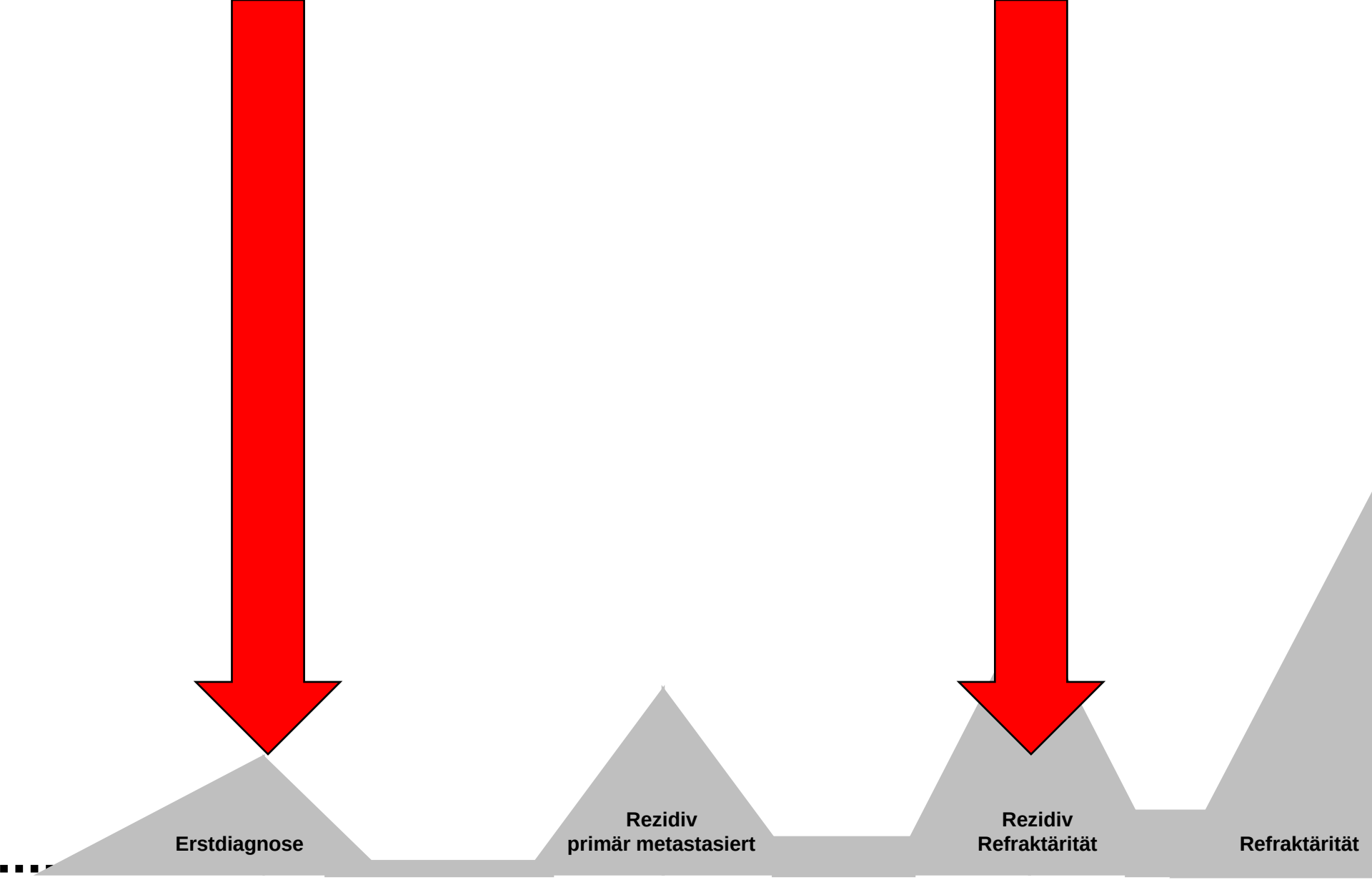


* Chi square; (2-sided, alpha=0.0253)

Primary Endpoint: Rate of ≥ VGPR *and* MRD–



* Chi square; (2-sided, alpha=0.0253)


Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität

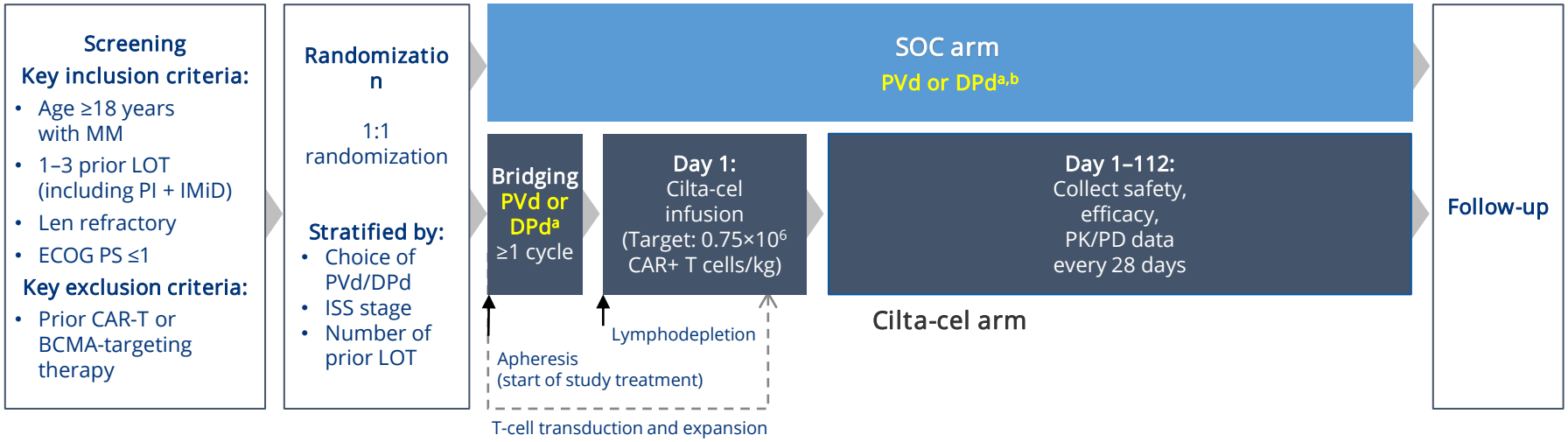
Phase 3 Results From CARTITUDE-4: Cilta-cel Versus Standard of Care (PVd or DPd) in Lenalidomide-Refractory Multiple Myeloma

Binod Dhakal[1], Kwee Yong[2], Simon Harrison[3], María-Victoria Mateos[4], Philippe Moreau[5], Niels WCJ van de Donk[6], Surbhi Sidana[7], Rakesh Popat[8], Nikoletta Lendvai[9], Carolina Lonardi[10], Ana Slaughter[11], Jordan M Schecter[9], Katherine Li[12], Enrique Zudaire[12], Diana Chen[13], Jane Gilbert[14], Lida Pacaud[15], Nitin Patel[15], Jesús San-Miguel[16], Hermann Einsele[17]

[1]Medical College of Wisconsin, Milwaukee, WI, USA; [2]University College London Cancer Institute, London, UK; [3]Peter MacCallum Cancer Centre and Royal Melbourne Hospital, Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia; [4]University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain; [5]Hematology Clinic, University Hospital Hotel-Dieu, Nantes, France; [6]Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, Netherlands; [7]Stanford University School of Medicine, Stanford, CA, USA; [8]University College London Hospitals, NHS Foundation Trust, London, UK; [9]Janssen Research & Development, Raritan, NJ, USA; [10]Janssen, Buenos Aires, Argentina; [11]Cilag GmbH International, Zug, Switzerland; [12]Janssen Research & Development, Spring House, PA, USA; [13]Janssen Research & Development, Shanghai, China; [14]Janssen Research & Development, High Wycombe, UK; [15]Legend Biotech USA Inc., Somerset, NJ, USA; [16]Cancer Center ClÍnica Universidad de Navarra (CCUN), CIMA; IDISNA, CIBERONC, Pamplona, Spain; [17]Universitätsklinikum Würzburg, Medizinische Klinik und Poliklinik II, Würzburg, Germany

Presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting; June 2–6, 2023; Chicago, IL, USA & Virtual

CARTITUDE-4 Study Design and Endpoints



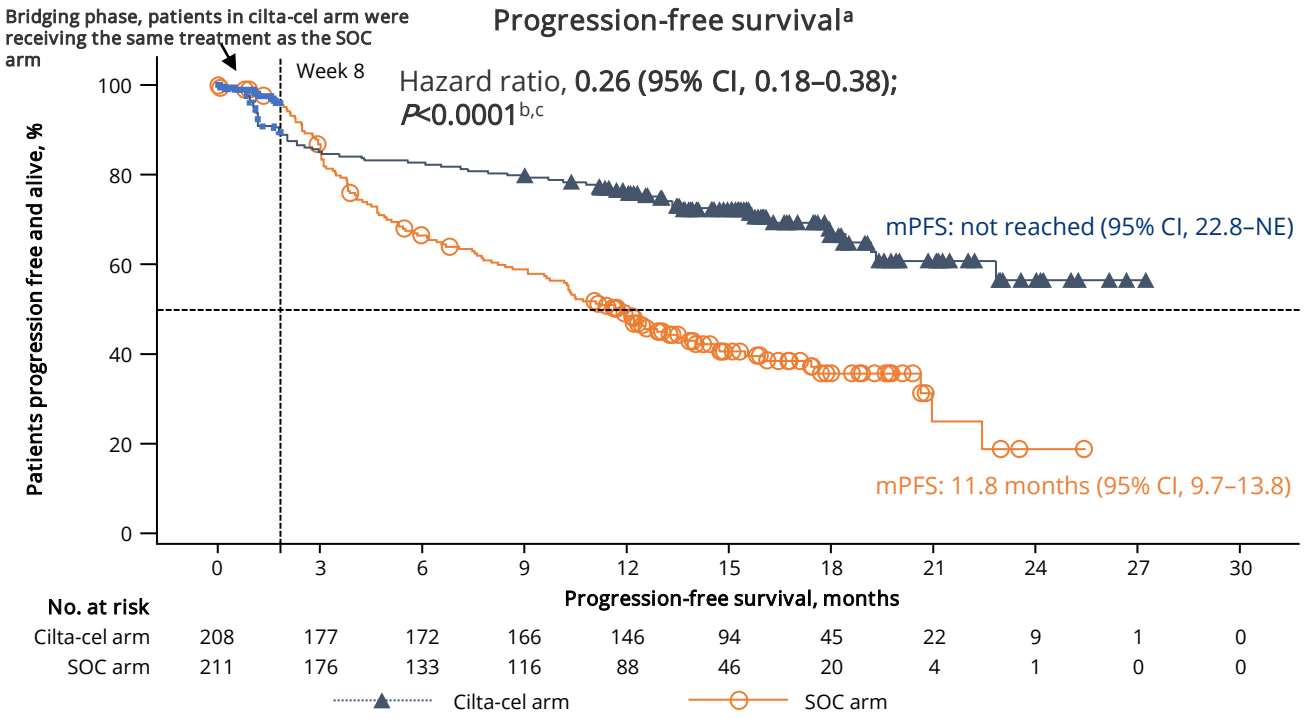
- **Primary endpoint**
- PFS[c]

- **Secondary endpoints**
- Efficacy: ≥CR, ORR, MRD negativity, OS
- Safety
- PROs

[a]Physicians' choice. [b]Administered until disease progression. [c]Time from randomization to disease progression/death.
BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor T cell; cilta-cel, ciltacabtagene autoleucel; CR, complete response; DPd, daratumumab, pomalidomide, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; Len, lenalidomide; LOT, line of therapy; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PD, pharmacodynamics; PFS, progression-free survival; PI, proteasome inhibitor; PK, pharmacokinetics; PRO, patient-reported outcome; PVd, pomalidomide, bortezomib, and dexamethasone; SOC, standard of care.

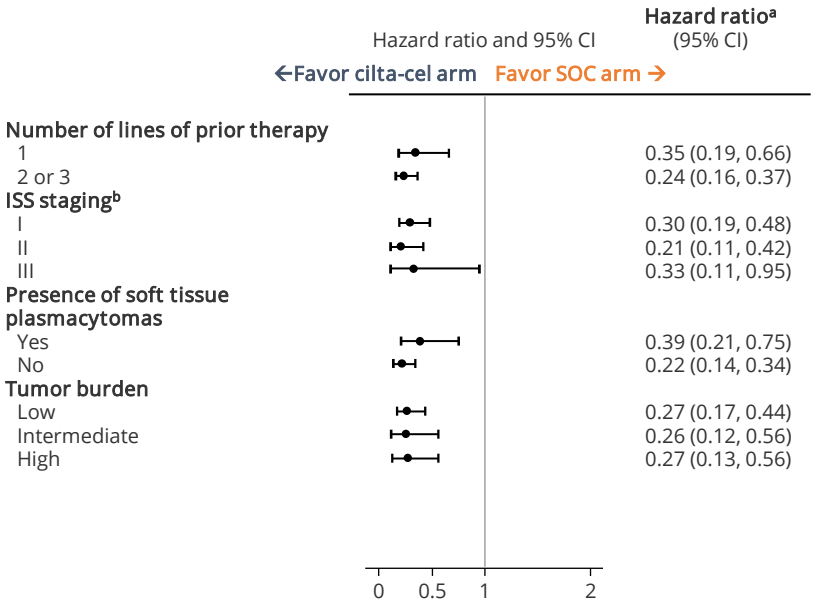
CARTITUDE-4: Primary Endpoint – PFS (ITT Population)

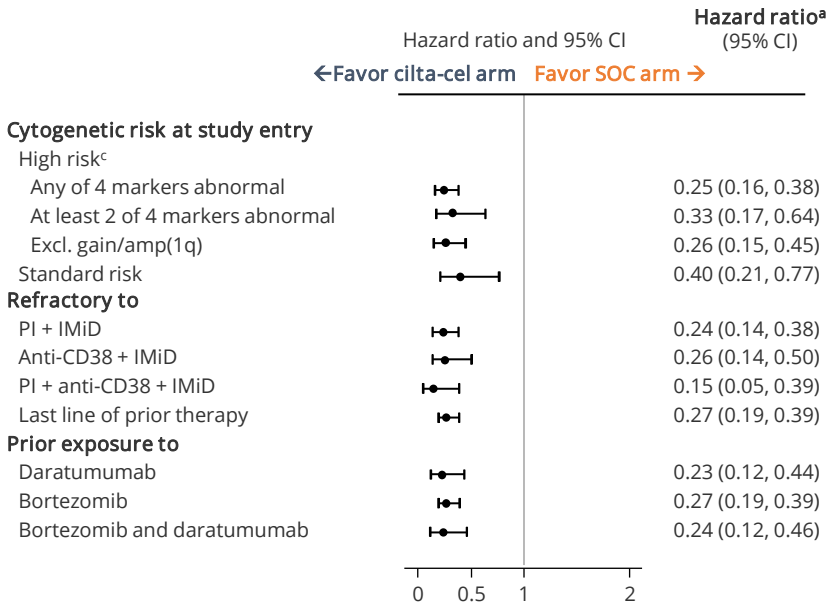
- **Cilta-cel vs SOC**
- 12-month PFS rate: 76% vs 49%
- SOC performed as expected



[a]Median follow-up, 15.9 months. [b]Constant piecewise weighted log-rank test. [c]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only progression-free survival events that occurred >8 weeks post randomization.
cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; mPFS, median progression-free survival; NE, not estimable; SOC, standard of care.

CARTITUDE-4: Key Subgroup Analysis (ITT)



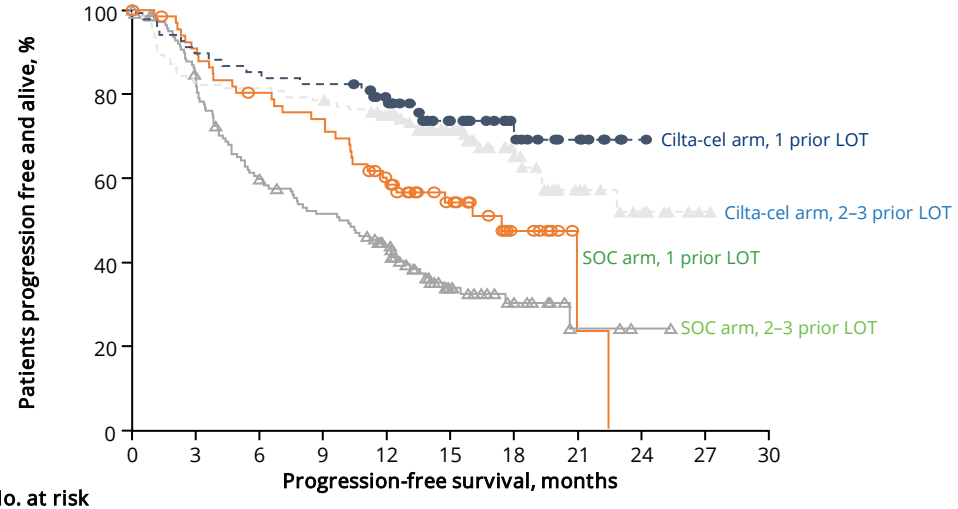


[a]Hazard ratio and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable, including only progression-free survival events that occurred >8 weeks post randomization. A hazard ratio <1 indicates an advantage for the cilta-cel arm. [b]Based on serum β_2-microglobulin and albumin. [c]Positive for del(17p), t(14;16), t(4;14), and/or gain/amp(1q) by fluorescence in situ hybridization testing. Protocol-defined high-risk cytogenetics refers to "Any of 4 markers abnormal."
cilta-cel, ciltacabtagene autoleucel; ECOG PS, Eastern Cooperative Oncology Group performance status; IMiD, immunomodulatory drug; ISS, International Staging System; PI, proteasome inhibitor; SOC, standard of care.

CARTITUDE-4: PFS by Prior Line of Therapy

- Cilta-cel improved PFS vs SOC whether patients had 1 or 2–3 prior LOT

Progression-free survival by treatment and number of prior lines in the ITT set



No. at risk											
Cilta-cel arm, 1 prior LOT	68	61	58	56	48	28	16	8	1	0	0
Cilta-cel arm, 2–3 prior LOT	140	116	114	110	98	66	29	14	8	1	0
SOC arm, 1 prior LOT	68	60	52	48	35	22	8	1	0	0	0
SOC arm, 2–3 prior LOT	143	116	81	68	53	24	12	3	1	0	0

cilta-cel, ciltacabtagene autoleucel; HR, hazard ratio; ITT, intent-to-treat; LOT, line of therapy; PFS, progression-free survival; SOC, standard of care.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma

J. San-Miguel, B. Dhakal, K. Yong, A. Spencer, S. Anguille, M.-V. Mateos, C. Fernández de Larrea, J. Martínez-López, P. Moreau, C. Touzeau, X. Leleu, I. Avivi, M. Cavo, T. Ishida, S.J. Kim, W. Roeloffzen, N.W.C.J. van de Donk, D. Dytfeld, S. Sidana, L.J. Costa, A. Oriol, R. Popat, A.M. Khan, Y.C. Cohen, P.J. Ho, J. Griffin, N. Lendvai, C. Lonardi, A. Slaughter, J.M. Schecter, C.C. Jackson, K. Connors, K. Li, E. Zudaire, D. Chen, J. Gilbert, T. Yeh, S. Nagle, E. Florendo, L. Pacaud, N. Patel, S.J. Harrison, and H. Einsele

Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma
New England Journal of Medicine

https://www.congresshub.com/Oncology/AM2023/Cilta-cel/Dhakal

Hämochromatose

HFE C282Y homozygot

Ergebnisse

Studie	Risikogruppe	Kohorte[1]	Homozygotie	Leber-erkrankung (HR)[2]	Herz-erkrankung (HR)[2]	Diabetes mellitus (HR)[2]
Dänemark	Allgemeinbevölkerung	17.688	422	2,16[3]	0,98[3]	1,66[3] 1,94[4]

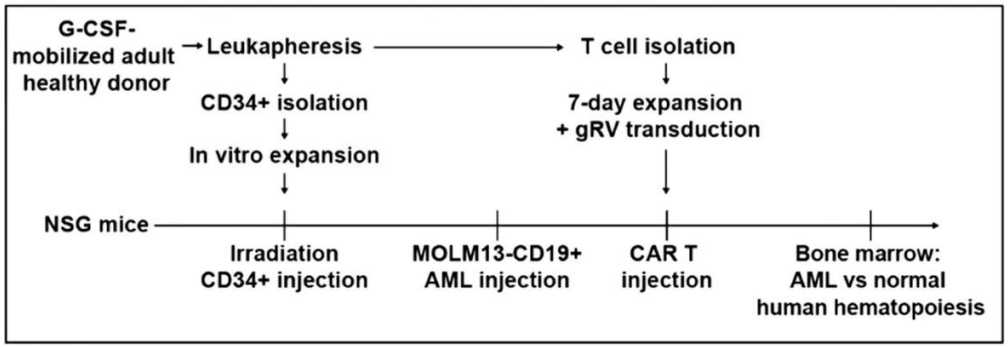
[1] N – Anzahl Personen; [2] HR – Hazard Ratio; [3] Erkrankungsrisiko; [4] Sterberisiko;

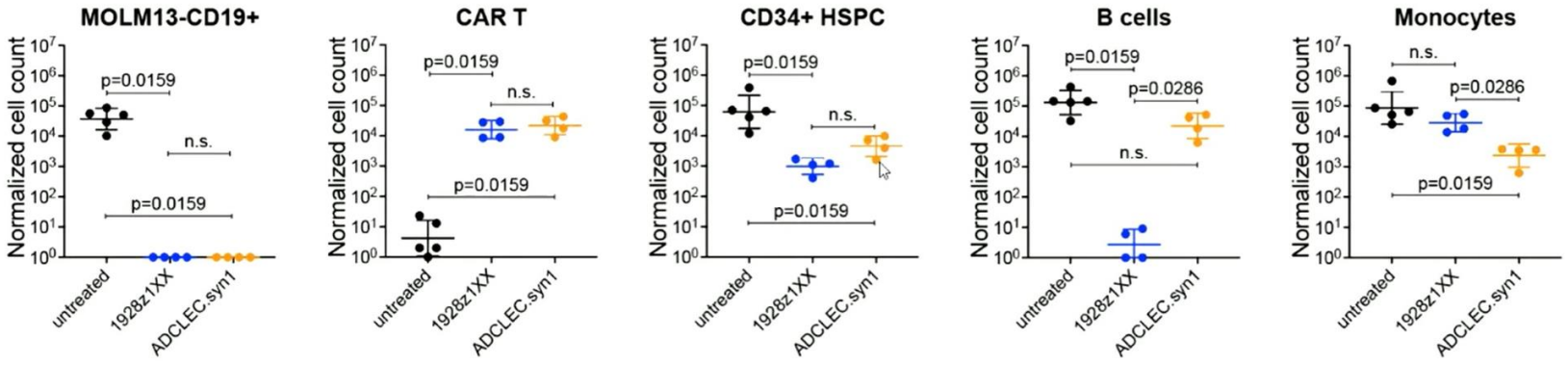
Mottelson et al., EHA Plenary Session 2023

Akute Myeloische Leukämie

CAR-T Zellen

ADCLEC.syn1 eliminates AML with limited on-target HSPC toxicity





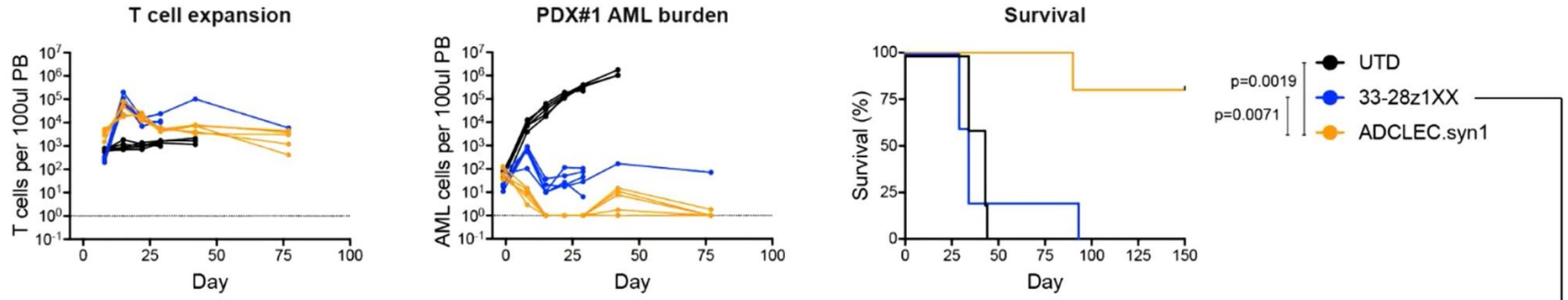
Haubner et al., in revision

EHA2023

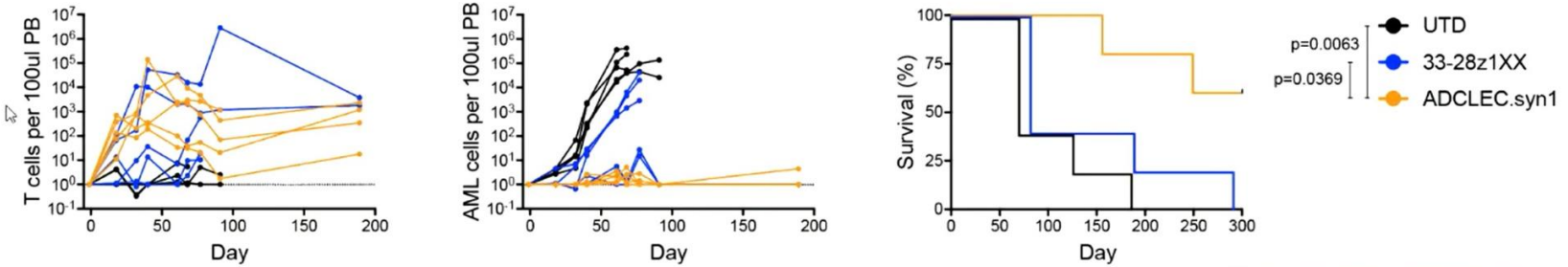
Haubner et et al., EHA Plenary Session 2023

ADCLEC.syn1 eliminates CD33-CAR-refractory AML LSC

Primary ("CAR-naïve") engraftment of AML PDX#1



Secondary (CD33-CAR-refractory) engraftment of AML PDX#1



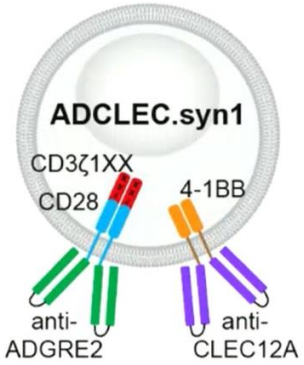
Haubner et al., in revision

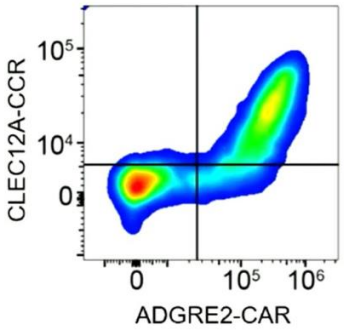
EHA2023

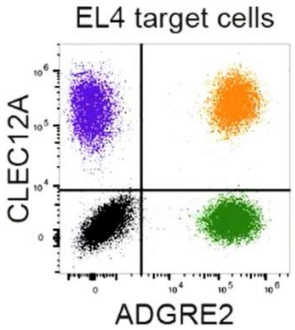
Haubner et et al., EHA Plenary Session 2023

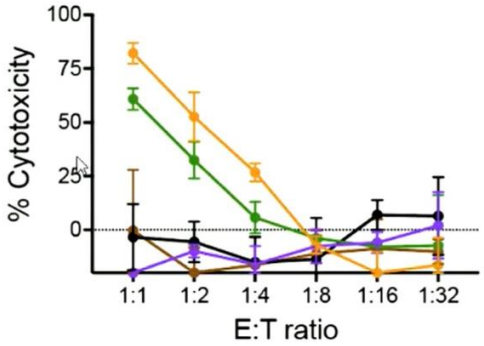
CCR-gated CAR sensitivity to prevent antigen-low AML escape

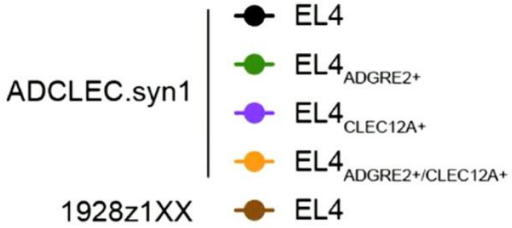
ADGRE2-1XX-CAR + **CLEC**12A-CCR
= ADCLEC.syn1











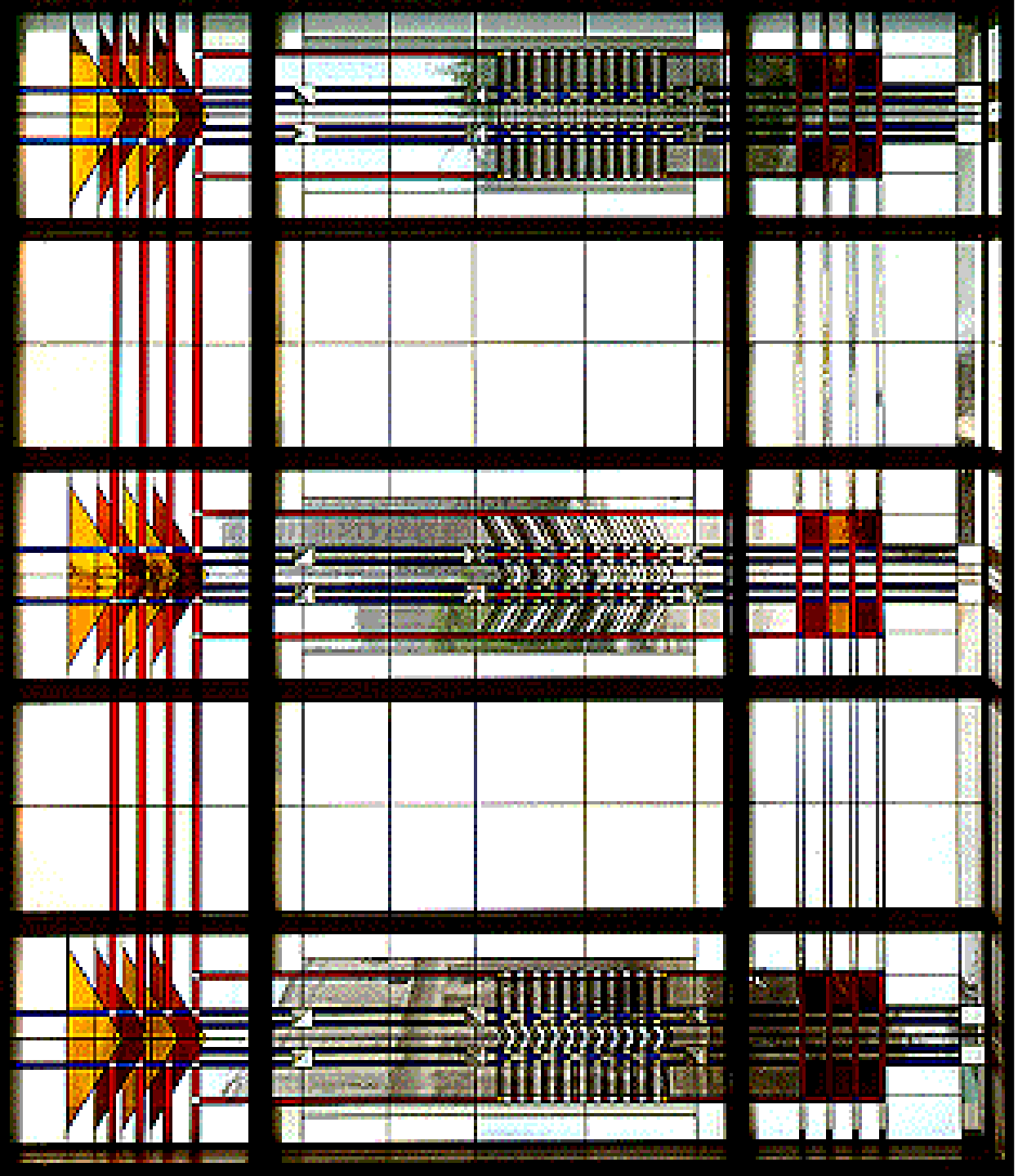
Haubner et al., in revision

EHA2023

Haubner et et al., EHA Plenary Session 2023

- Gliom
- Kolonkarzinom
- Lungenkarzinom
- Mammakarzinom
- Ovarialkarzinom
- Pankreaskarzinom
- Prostatakarzinom
- Rektumkarzinom
- Urothelkarzinom
- Weichgewebssarkom
- Zervixkarzinom

- Akute Myeloische Leukämie
- Hodgkin Lymphom
- Hämochromatose
- Multiples Myelom
- Myelodysplastische Neoplasien
- PMBCL



Vielen Dank für die Aufmerksamkeit!