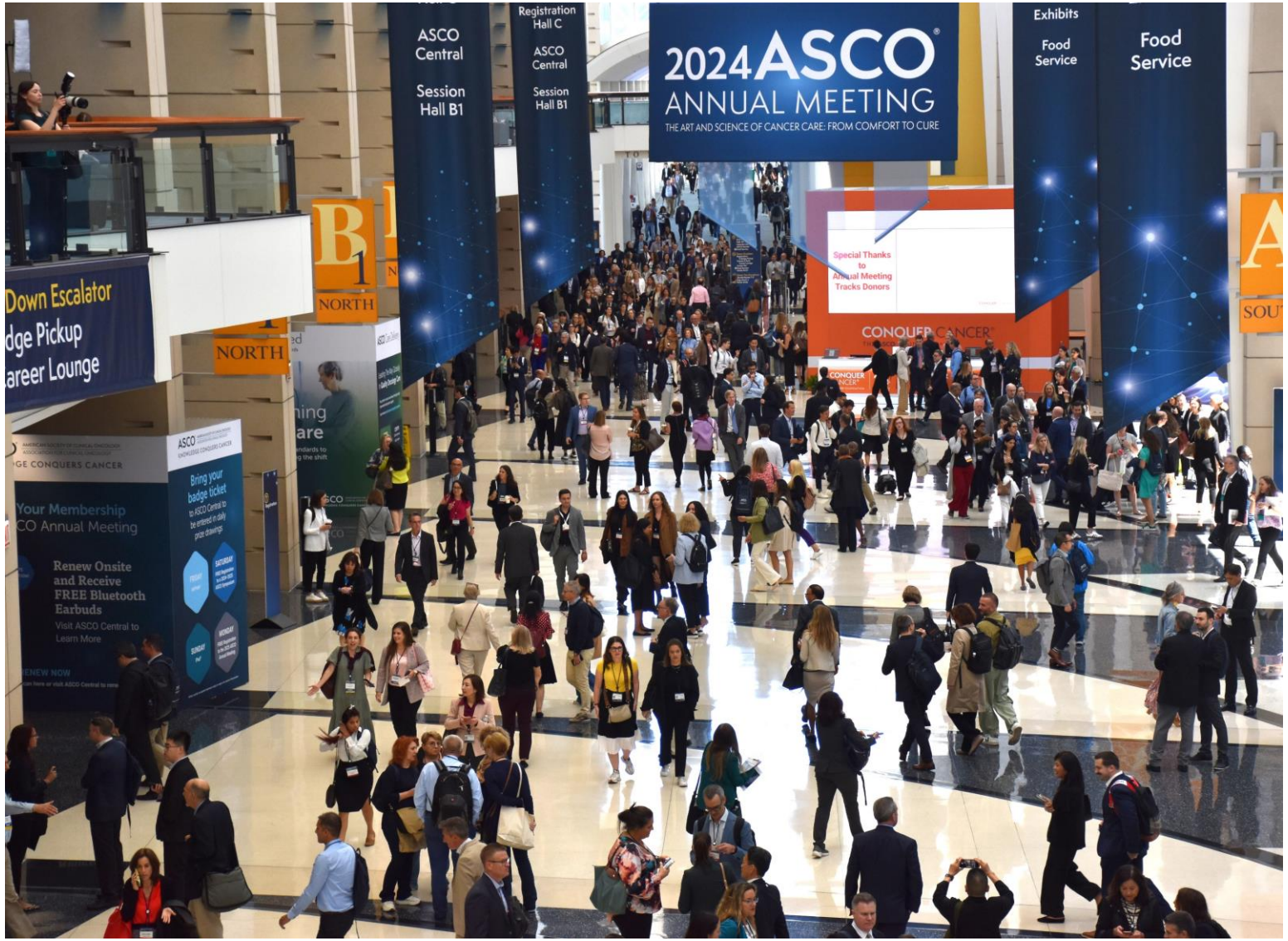
onkopedia



31. Mai – 3. Juni 2024


EHA
EUROPEAN
HEMATOLOGY
ASSOCIATION

- Kolorektales Karzinom
- Lungenkarzinom
- Mammakarzinom
- Melanom
- Ösophaguskarzinom
- Palliativmedizin
- Prostatakarzinom

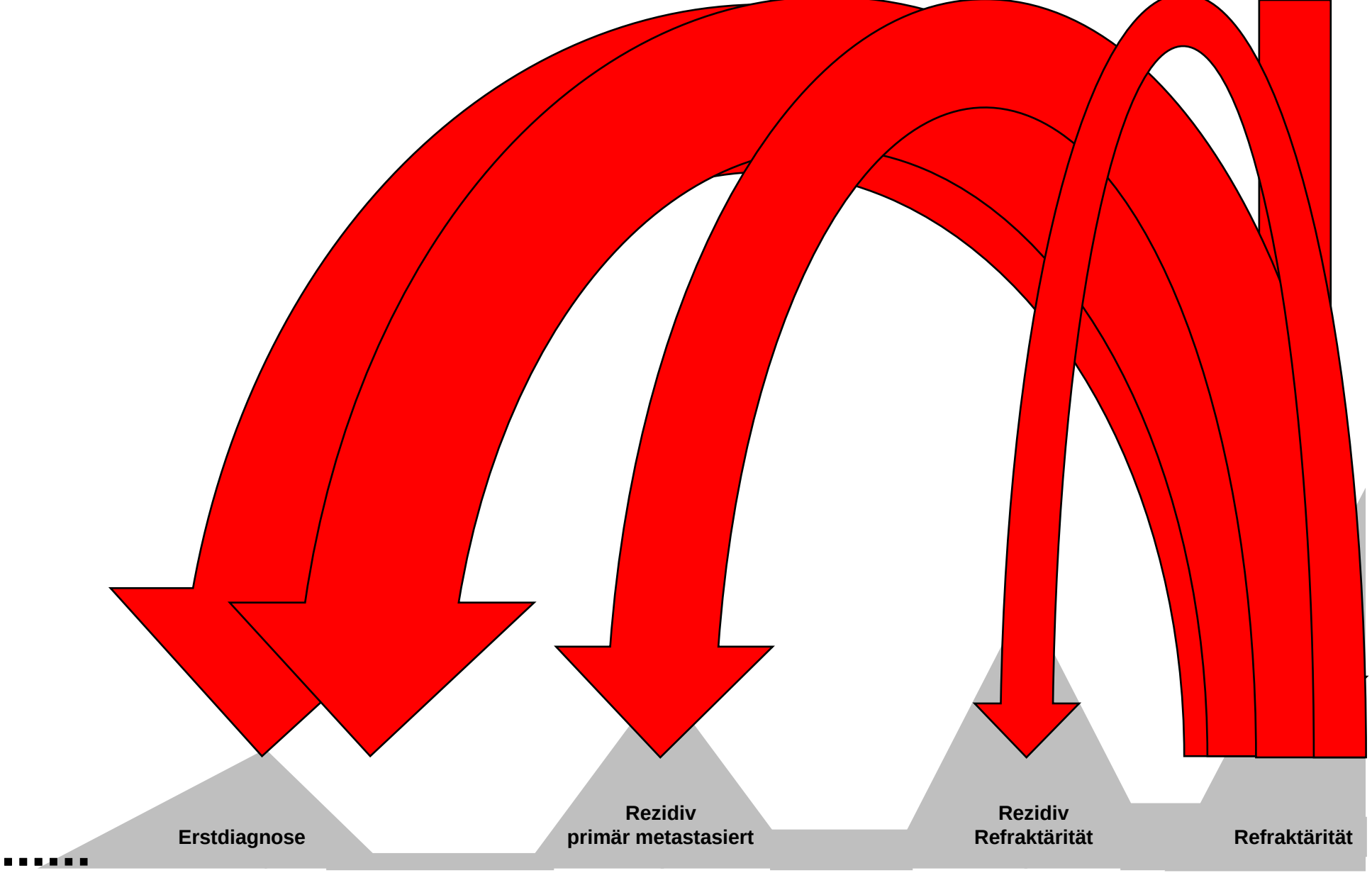
- Chronische Myeloische Leukämie
- Multiples Myelom

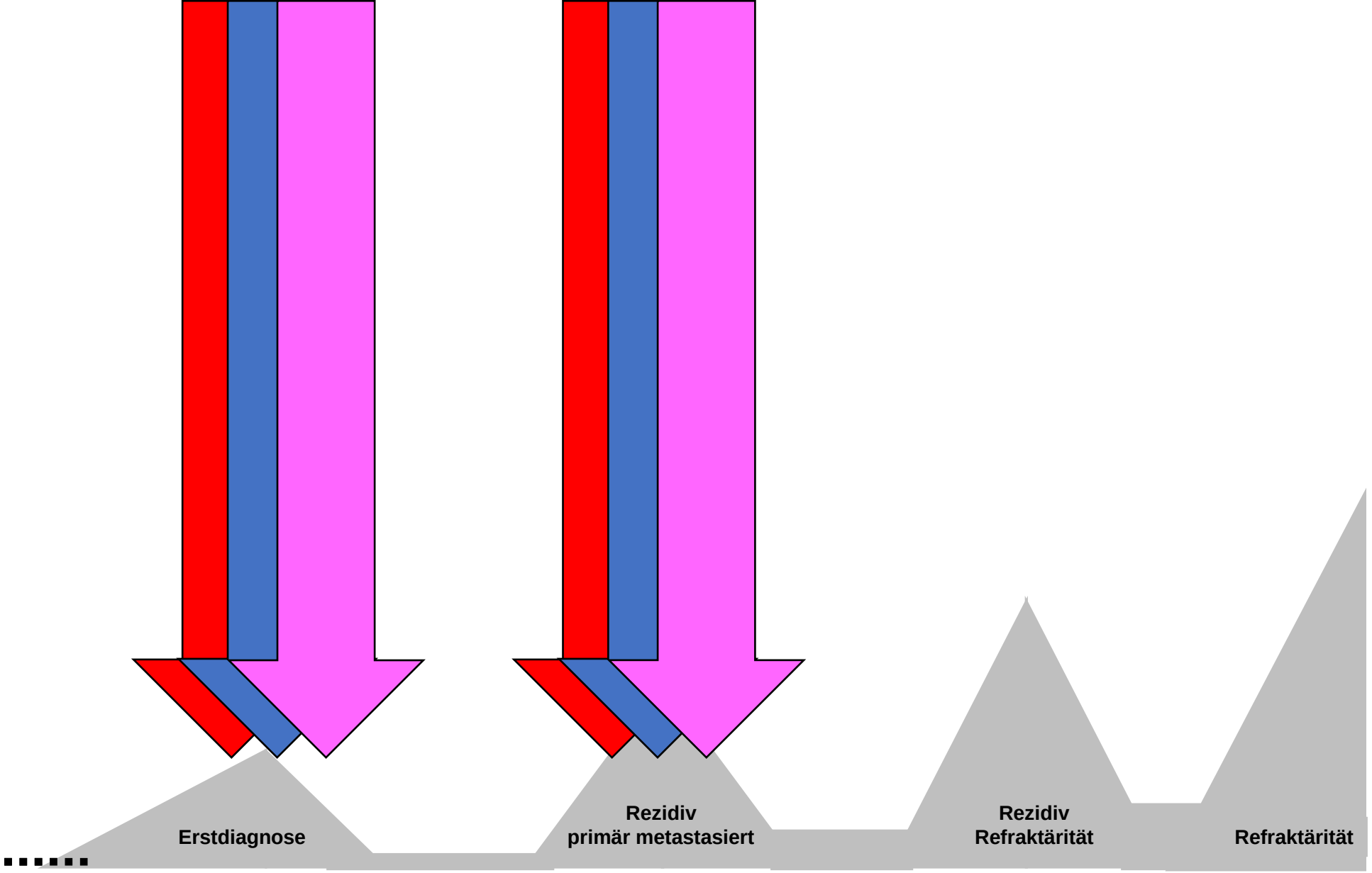
The NEW ENGLAND JOURNAL of MEDICINE

5 Vollpublikationen im NEJM

- **Kolorektales Karzinom**
- Lungenkarzinom (5)
- **Mammakarzinom**
- **Melanom**
- **Ösophaguskarzinom**
- **Palliativmedizin**
- **Prostatakarzinom**

- **Chronische Myeloische Leukämie**
- Multiples Myelom (4)


Erstdiagnose
Rezidiv
primär metastasiert
Rezidiv
Refraktärität
Refraktärität


Erstdiagnose
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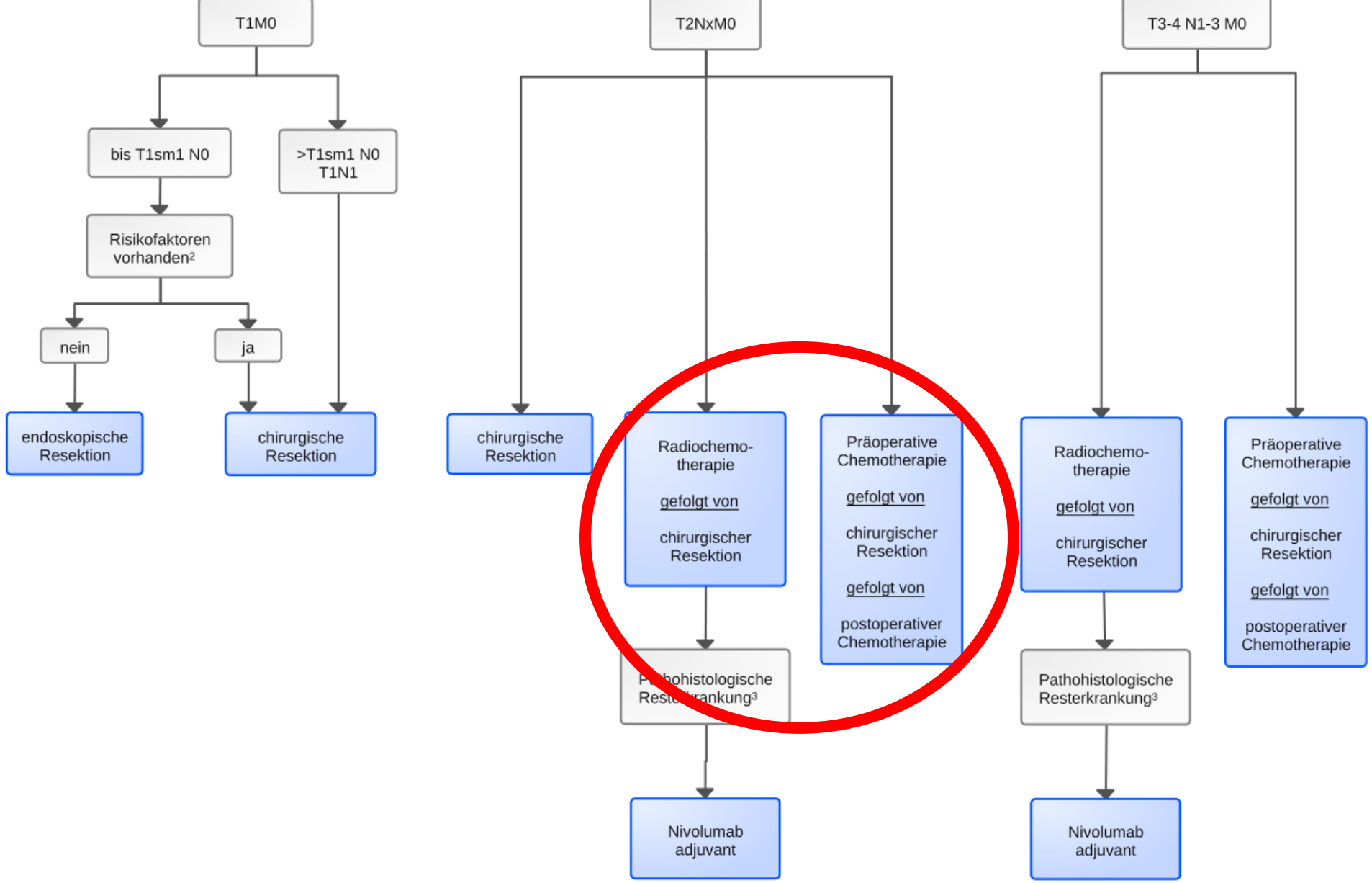
2024 ASCO ANNUAL MEETING

Perioperative Chemotherapy (FLOT) versus Neoadjuvant Chemoradiotherapy (CROSS) for Resectable Esophageal Adenocarcinoma

The ESOPEC Trial (NCT02509286)

J Hoeppner, F Lordick, T Brunner, C Schmoor, B Kulemann, UP Neumann, G Folprecht, T Keck, F Benedix, M Schmeding, E Reitsamer, CJ Bruns, JF Lock, B Reichert, M Ghadimi, K Wille, I Gockel, JR Izbicki, S Utzolino, P Grimminger

PRESENTED BY: Jens Hoeppner MD FACS FEBS



Legende:

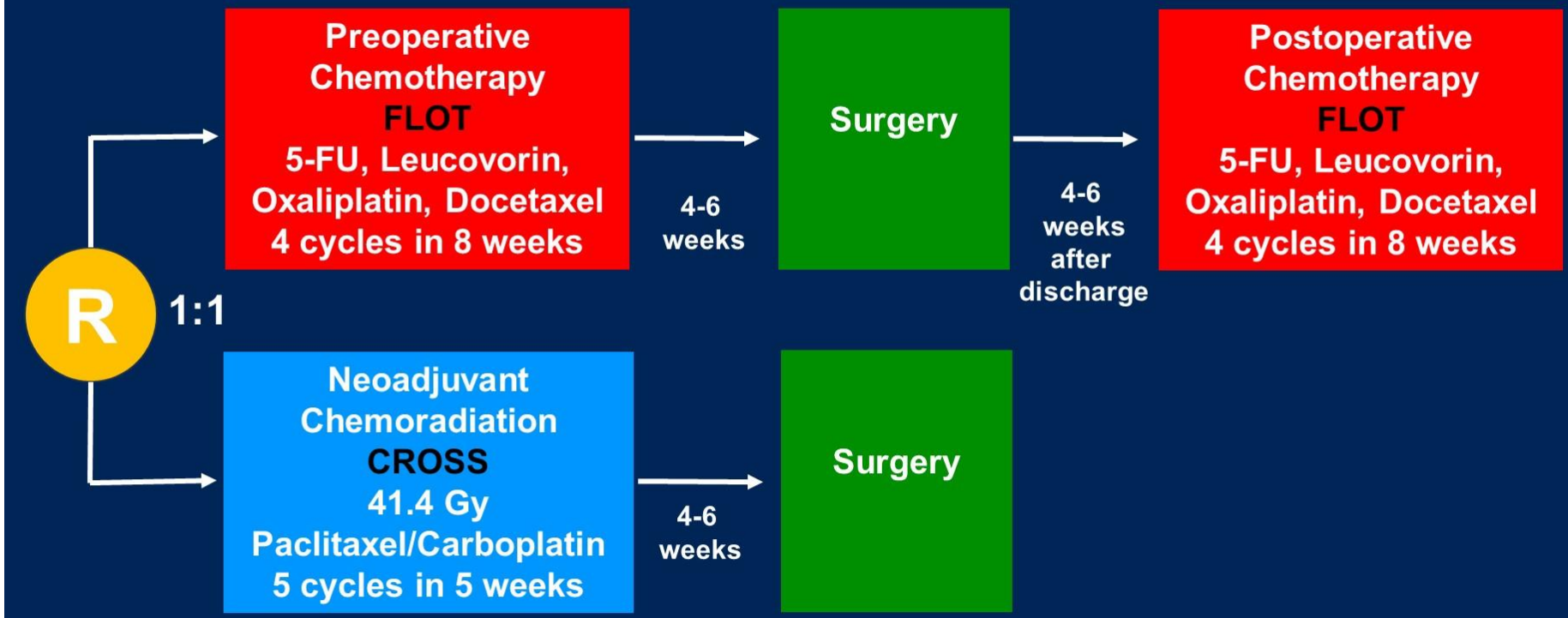
Therapie in kurativer Intention

[1] AEG: Adenokarzinom des ösophago-gastraler Übergangs

[2] Risikofaktoren: Ulceration, L1, V1, G3, R1 basal tiefe Submukosainfiltration, multifokale/nicht abtragbare Barrett-Läsionen

[3] R0-Resektion, wenn ypT ≥1 oder ypN ≥1

ESOPEC Trial Scheme



Main Eligibility Criteria

Inclusion Criteria

- Histology: Adenocarcinoma
- Esophageal cancer according UICC (TNM7)[1,*]
- Clinical stage cT1N+ or cT2-4a, cN0/+, cM0

Exclusion Criteria

- Squamous or other non-adenocarcinoma histology
- Gastric cancer
- Clinical Stage cT1cN0 and cT4b
- Metastatic disease

*Tumors of the esophagus and tumors of which the epicenter is within 5 cm of the esophagogastric junction and also extend into the esophagus.

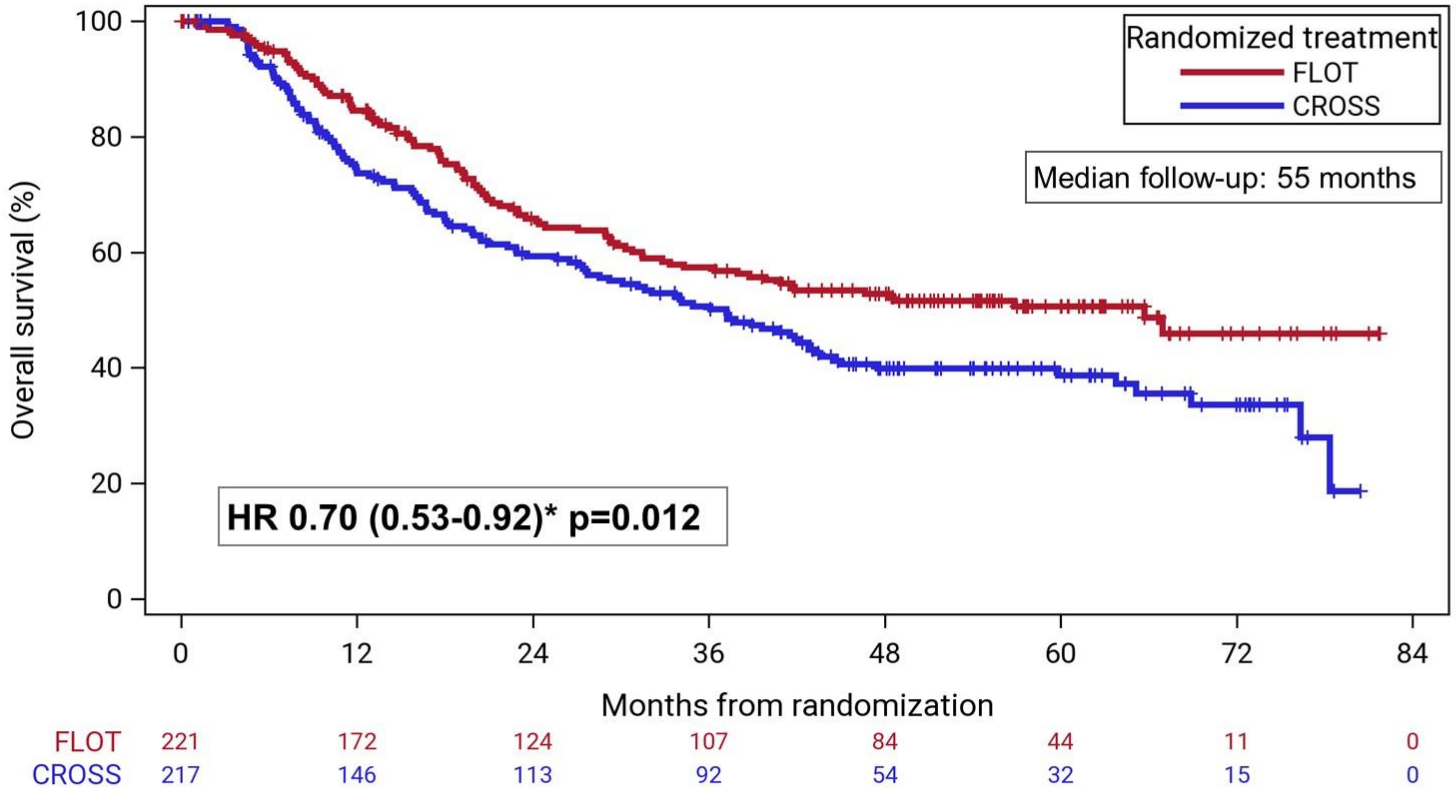
1. Sobin LH UICC TNM 7th edition 2009

Characteristics of ESOPEC Trial Patients

	FLOT Group	CROSS Group
N	221	217
Age mean (SD) in years	63.1 (8.6)	62.6 (9.8)
Sex male	89.1 %	89.4 %
ECOG		
> 0	26.7%	28.1%
Clinical T-stage		
cT1-2	19.5%	17.1%
cT3-4	79.1%	81.9%
Clinical N-stage		
cN0	22.2%	18.4%
cN+	77.8%	81.6%

1. Missing: 2 patients
2. Siewert BJS 1998
3. Tx:5 patients; Missing 2 patients

Overall Survival - ITT Population



	FLOT	CROSS
Events	97	121
Median OS time (months)	66 95% CI 36 – n.e	37 95% CI 28 – 43
3-year OS rate	57.4%	50.7%
5-year OS rate	50.6%	38.7%

2024 ASCO ANNUAL MEETING #ASCO24

PRESENTED BY: Jens Hoeppner MD FACS FEBS

*Two-sided 95% confidence interval; Cox regression adjusted for N stage and age, stratified for trial site

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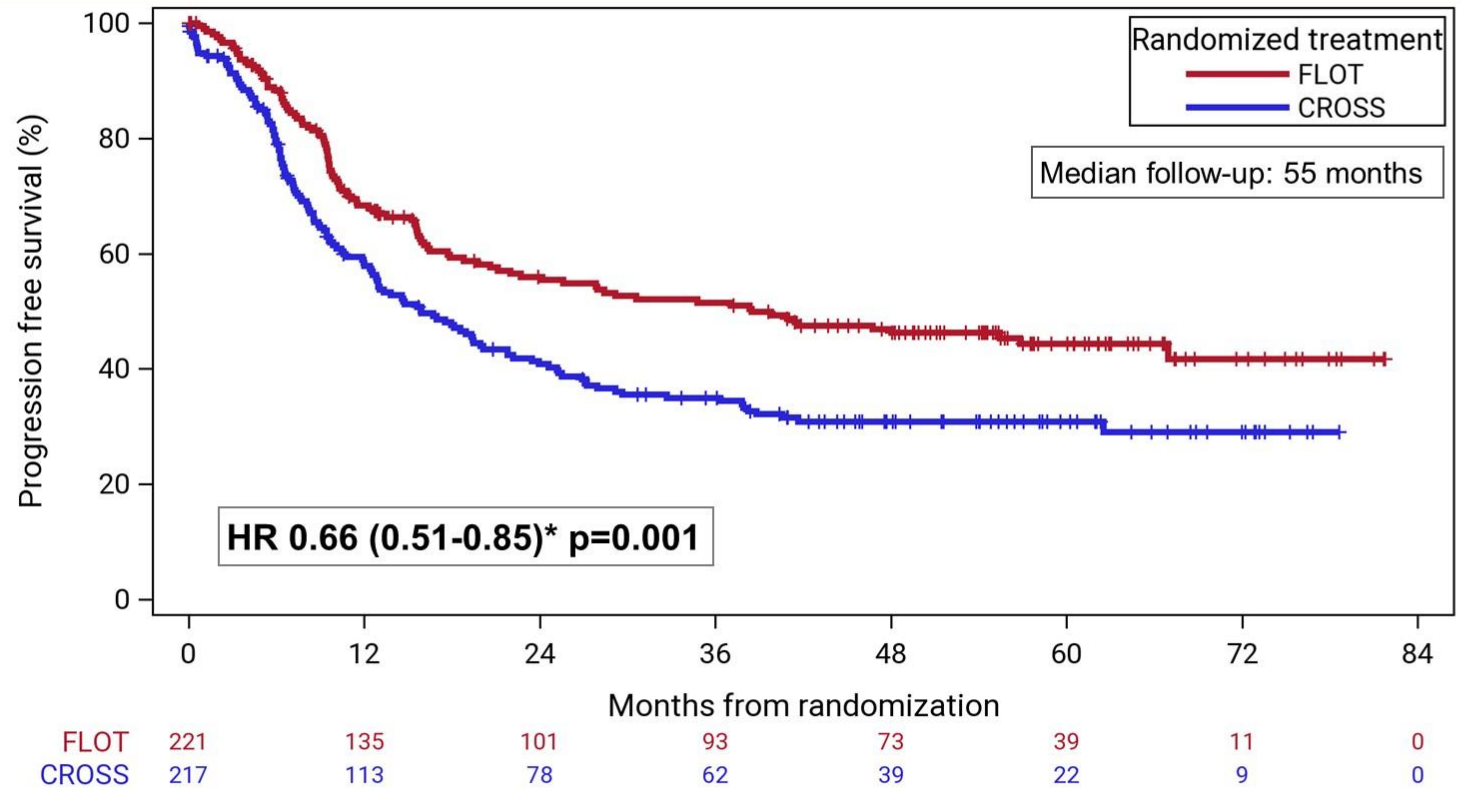
KNOWLEDGE CONQUERS CANCER

Progression Free Survival – ITT Population



	FLOT	CROSS
Events	107	137
Median PFS time (months)	38 95% CI 21 – n.e.	16 95% CI 12 – 22
3-year PFS rate	51.6%	35.0%
5-year PFS rate	44.4%	30.9%

2024 ASCO ANNUAL MEETING #ASCO24

PRESENTED BY: Jens Hoeppner MD FACS FEBS

*Two-sided 95% confidence interval; Cox regression adjusted for N stage and age, stratified for trial site

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

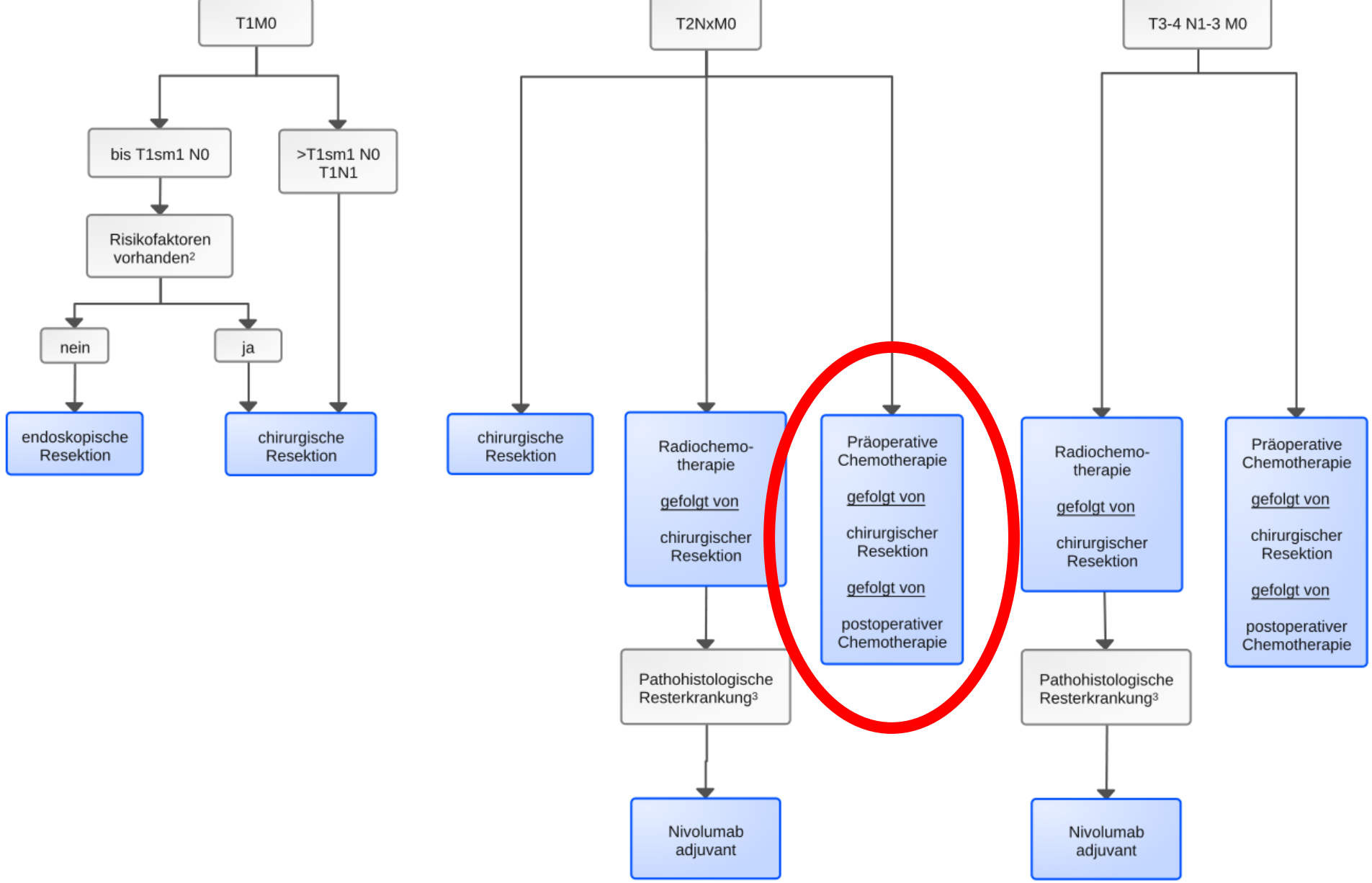
Postoperative Complications – Surgery Population

	FLOT Group	CROSS Group
N	191	180
Postoperative morbidity		
Clavien Dindo I	20.9%	20.0%
Clavien Dindo II	13.6%	15.0%
Clavien Dindo III	23.0%	23.3%
Clavien Dindo IV	6.8%	4.4%
Postoperative mortality		
30-days	1.0%	1.7%
90-days	3.2%	5.6%

Trial Summary & Recommendation

- Perioperative chemotherapy (FLOT) plus surgery improves overall survival compared to neoadjuvant chemoradiation (CROSS) plus surgery for patients with cT1cN+ and cT2-4a,cN-/+ M0 esophageal adenocarcinoma.

- Perioperative chemotherapy (FLOT) should be preferred over neoadjuvant chemoradiation (CROSS) for improving survival in resectable esophageal adenocarcinoma.



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3 R0-Resektion, wenn ypT ≥1 oder ypN ≥1

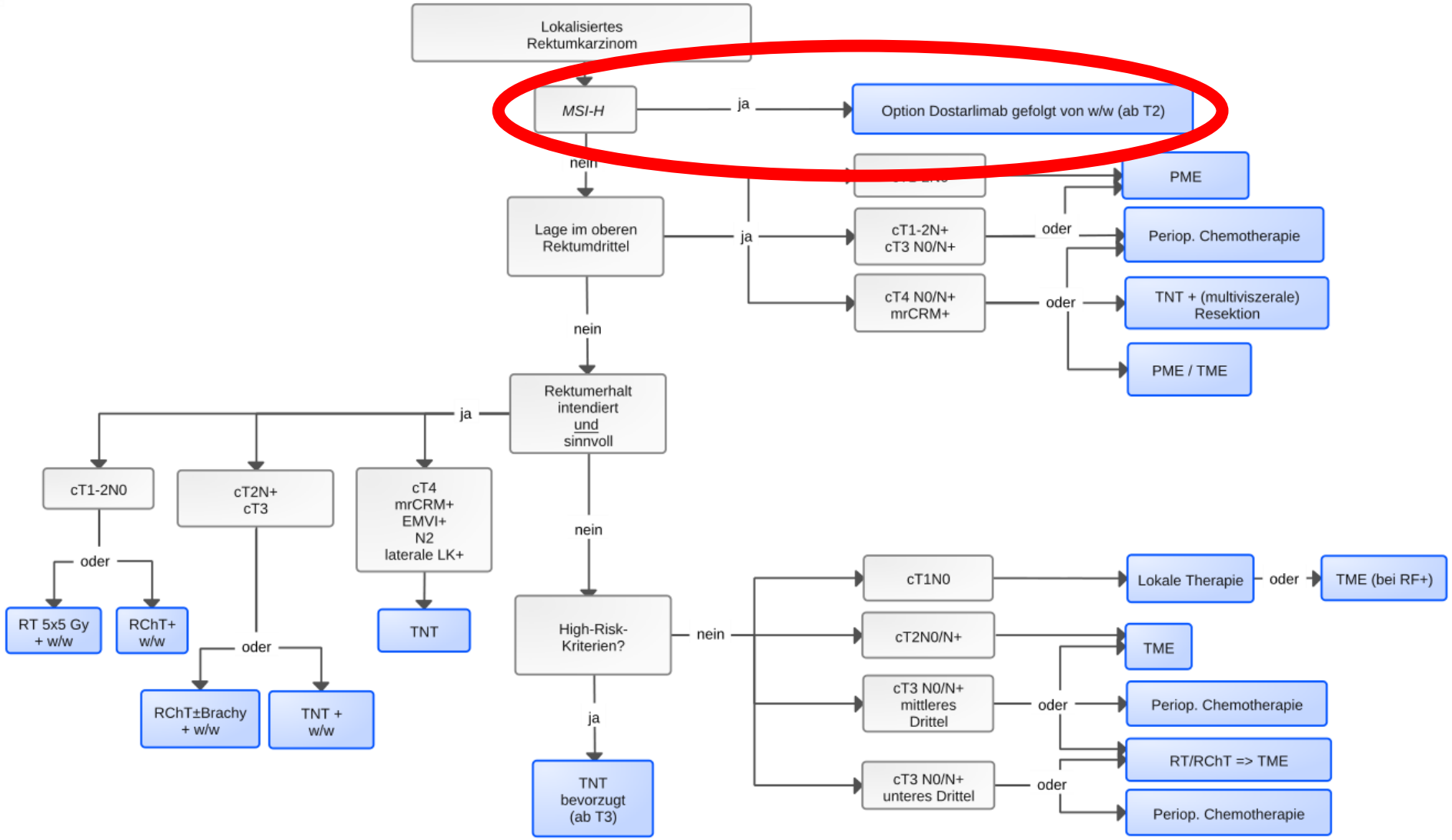
2024 ASCO ANNUAL MEETING

Durable complete responses to PD-1 blockade alone in dMMR locally advanced rectal cancer

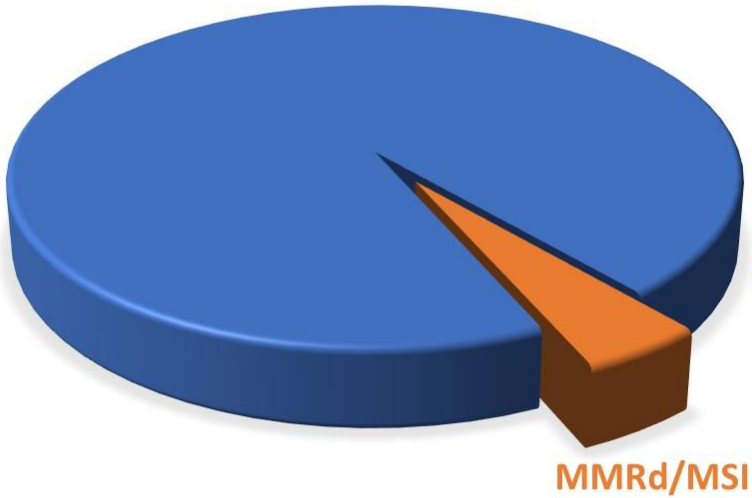
Andrea Cercek, M.D. , J. Joshua Smith, M.D., Ph.D. , Jinru Shia, M.D., Michael B. Foote, M.D., Jenna Sinoploi, N.P. Jill Weiss, B.A., Lindsay Temple, B.A., Henry Walch, M.S. , Miteshkumar Patel, M.S., Callahan Wilde, B.S., Leonard B. Saltz, M.D., Melissa Lumish, M.D., Benoit Rousseau, M.D., Ph.D., Guillem Argiles, M.D. , Zsofia Stadler, M.D. , Rona Yaeger, M.D. , Neil Segal, M.D., Philip Paty M.D., Marina Shcherba, M.D., Ryan Sugarman, M.D., Christopher Crane, M.D., Paul B. Romesser, M.D., Avni Desai, M.D., Imane El Dika, M.D., Maria Widmar, M.D., Iris Wei, M.D., Emmanouil Pappou, M.D., Ph.D., Gerard Fumo, M.D., Santiago Aparo, M.D., Mithat Gonen, M.D., Marc Gollub, M.D., Vetri S. Jayaprakasham, M.B.B.S., F.R.C.R., Tae-Hyung Kim, M.D., Julio Garcia Aguilar, M.D., Ph.D., Martin Weiser, M.D., and Luis A. Diaz, Jr., M.D.

Memorial Sloan Kettering Cancer Center
New York, NY

Stadienadaptierter Therapie-Algorithmus für die Stadien I-III



Rectal Cancer: Mismatch repair deficient (dMMR/MSI)



About 5-10% of all rectal cancers

Less sensitive to chemotherapy

Rectal cancer treated with total neoadjuvant therapy chemotherapy and chemoRT followed by TME

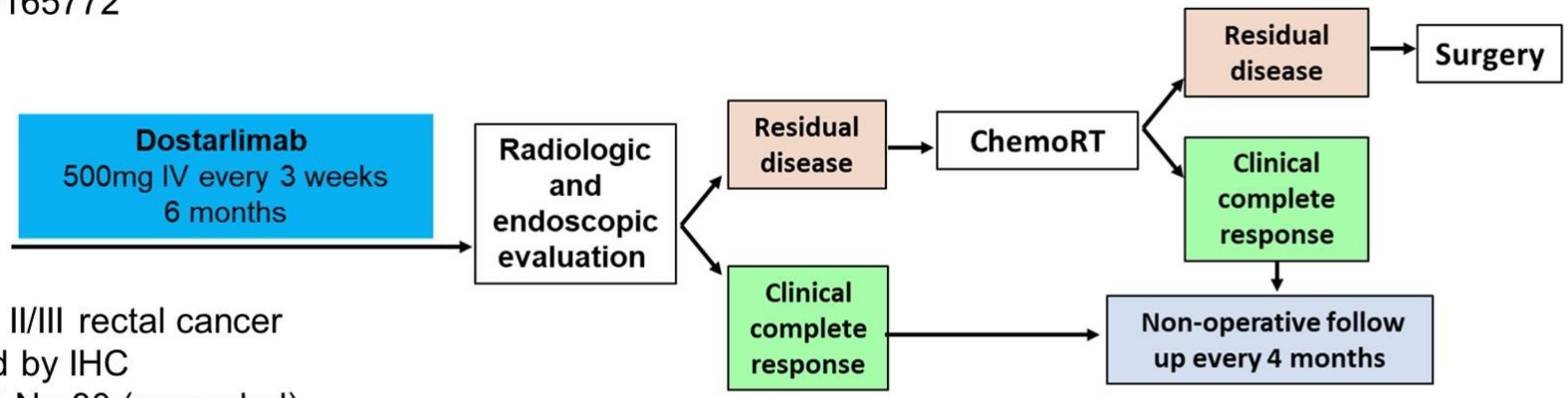
Outcome	No. of patients (%) dMMR	pMMR
FOLFOX as initial treatment	*n = 21*	*n = 63*
Progression of disease	6 (29)	0
Response or stable disease	15 (71)	63 (100)
Chemoradiation as initial treatment	*n = 16*	*n = 48*
Progression of disease	0	0
Complete pathologic response	2 (13)	8 (17)

dMMR/MSI mCRC sensitive to ICB in metastatic disease

Cercek, et al CCR 2020
Le, et al NEJM 2015

Neoadjuvant PD1 blockade in dMMR locally advanced rectal cancer

NCT04165772



Stage II/III rectal cancer
MMRd by IHC
Target N= 30 (expanded)

Primary Endpoints:

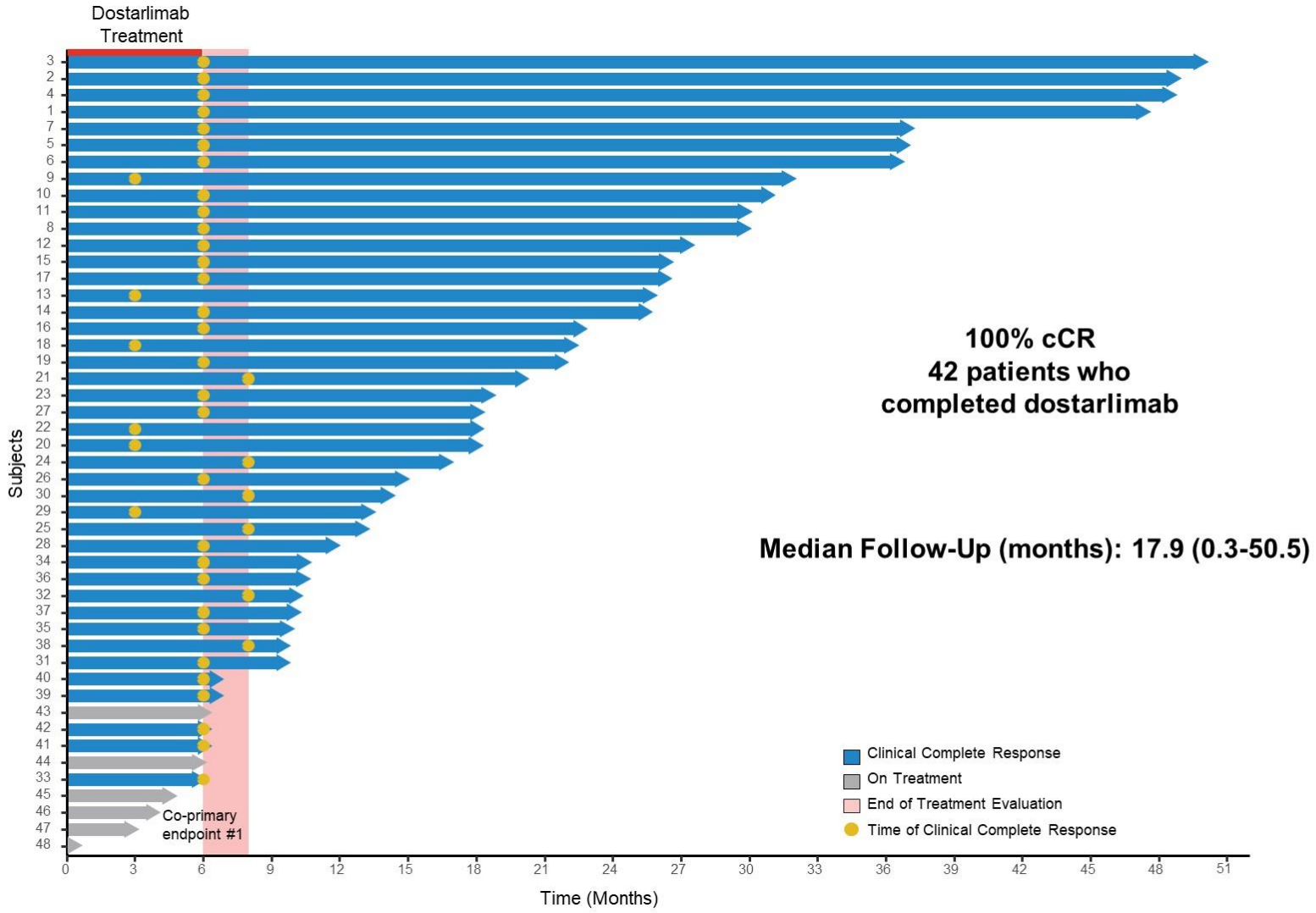
- ORR after completion of PD-1 alone or in combination with chemoRT
- pCR or sustained cCR for 12 mo after completion of PD1 alone or in combination with chemoRT

Sample Collection: ctDNA, biopsy, imaging

Baseline, 6 weeks, 3 mo, 6 mo and q4 mo during NOM

Cercek, et al. NEJM 2022

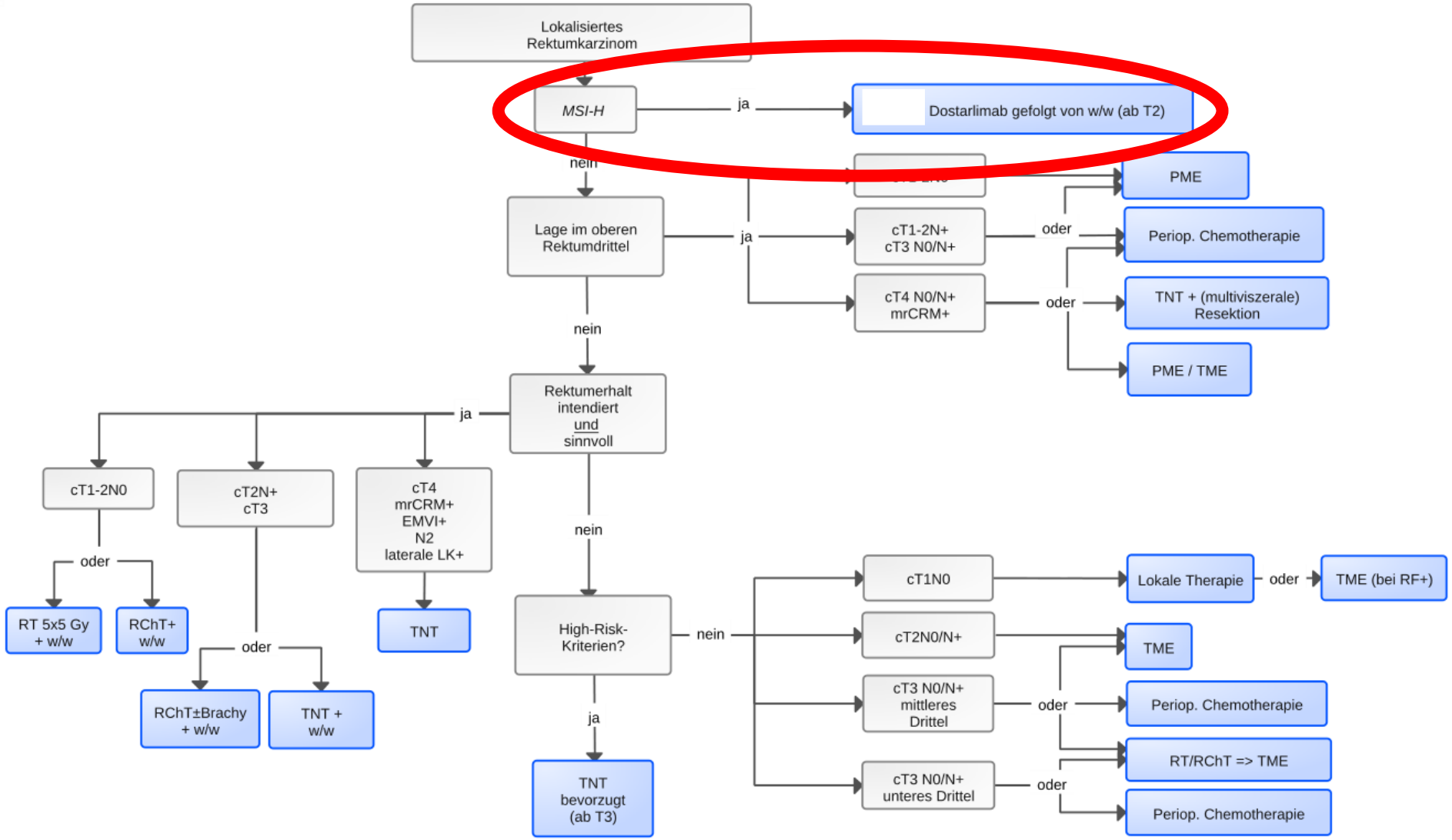
Patient Demographics N= 48	N (%)
Female Sex	**28 (58)**
Median Age (range)	**51 (26,78)**
Race	
White	**37 (77)**
Asian	**5(10)**
Black	**6 (13)**
Non Hispanic/Latino	**42 (85)**
Hispanic/Latino	**6 (13)**
Tumor Stage	
T 0/1/2	**10 (21)**
T 3	**23 (48)**
T 4	**15 (31)**
N +	**41 (85)**
Median Distance from anal verge (cm)	**5.1 (0, 14.8)**



Conclusions

- 100% clinical complete response in all 42 patients who completed dostarlimab
- Clinical complete responses are durable over 2 years
- No patients have required chemotherapy, radiation or surgery
- AZUR1 Global confirmatory study of dostarlimab in dMMR rectal cancer is ongoing

Stadienadaptierter Therapie-Algorithmus für die Stadien I-III



2024 ASCO ANNUAL MEETING

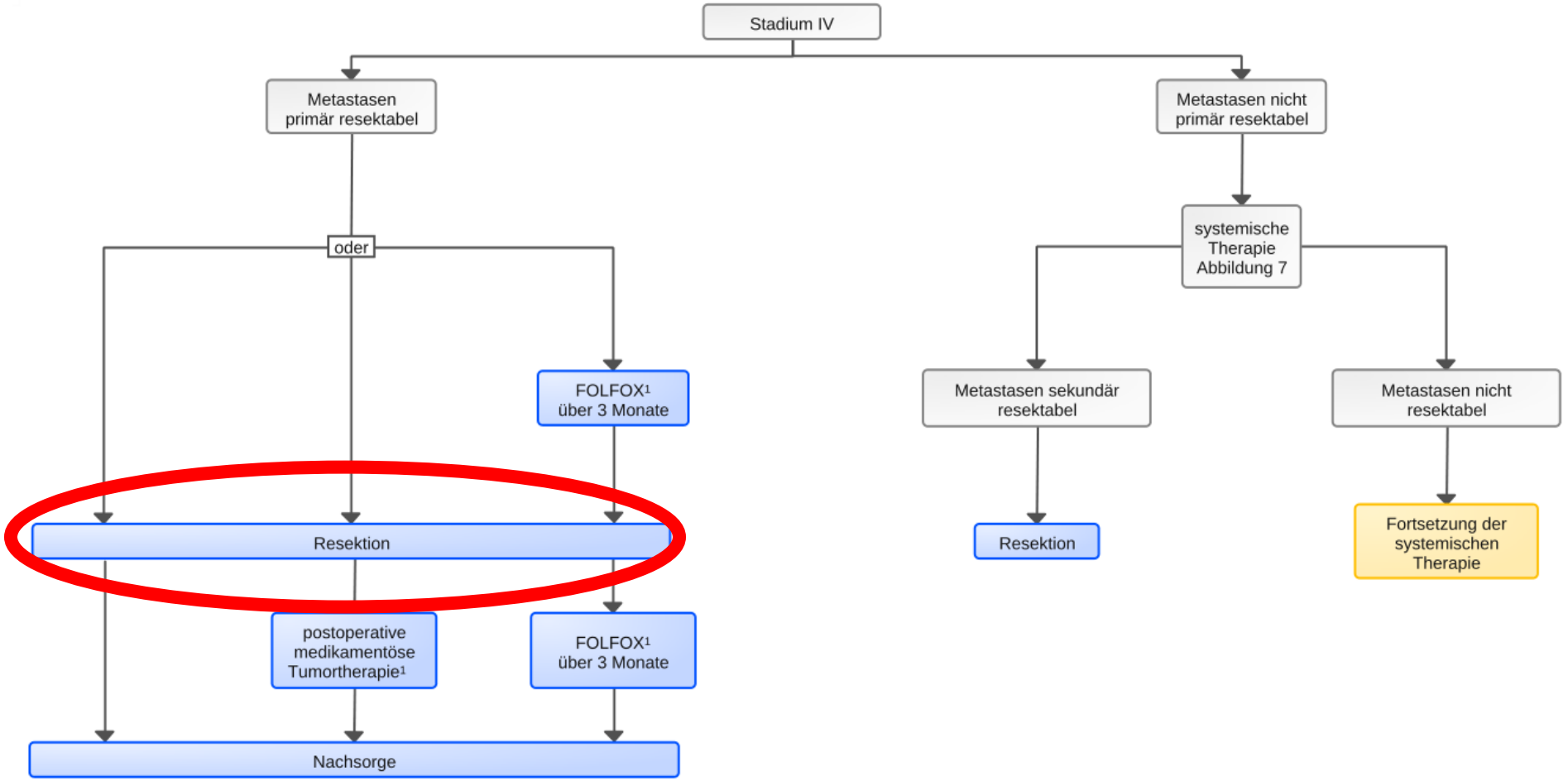
Liver Transplantation and Chemotherapy versus Chemotherapy alone in patients with definitively unresectable colorectal liver metastases : results from a prospective, multicentre, randomised trial (TransMet)

R Adam, C Piedvache, L Chiche, E Salamé, O Scatton, V Granger, M Ducreux, U Cillo, F Cauchy, JY Mabrut, C Verslype, L Coubeau, J Hardwigsen, E Boleslawski, F Muscari, J Lerut, L Grimaldi, F Levi, M Lewin, M Gelli

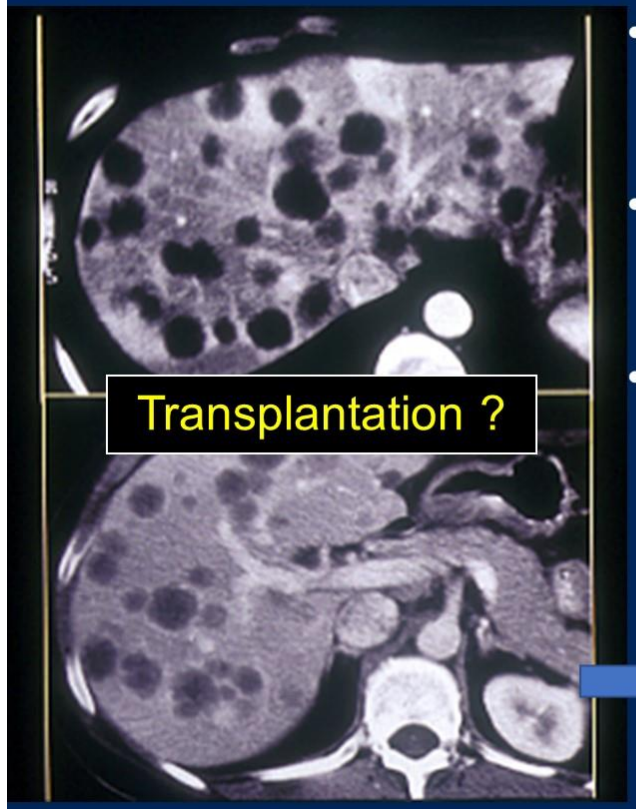
Paris-Saclay – Villejuif – Kremlin Bicêtre (France), Bordeaux (France), Tours (France), Paris (France), Grenoble (France), Villejuif (France), Padova (Italy), Clichy (France), Lyon (France), Leuven (Belgium), Louvain (Belgium), Marseille (France), Lille (France), Toulouse (France), Bruxelles (Belgium)

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Therapiestruktur im Stadium IV



Definitively Non Resectable Liver Metastases : Rationale



- Absolute contraindication in the 2000's because of the low 5-year survival (18%)[1]
- More recently : improved outcome with better patient selection and increased efficacy of chemotherapy (C) [2]
- However, strong evidence for clinical benefit : critical
  - Scarcity of organs
  - Perception "no role for local treatment in an advanced metastatic disease"

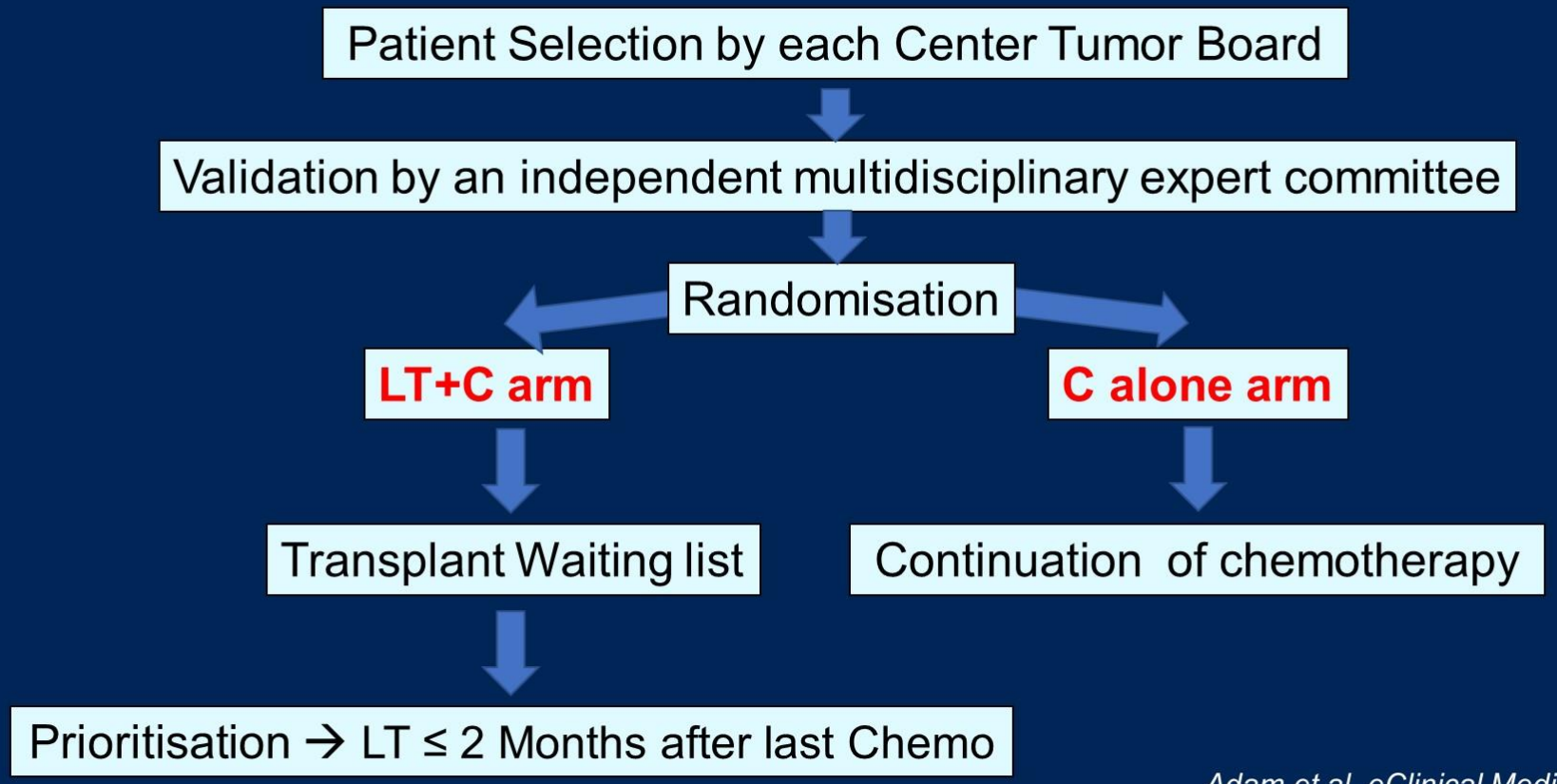
Randomised study to assess the efficacy of LT+C compared to C alone

(1) Foss et al, Tranplant Int 2010 *(2) Hagness et al, Ann Surg 2013*

TransMet Trial : Eligibility criteria

- ≤ 65 years
- Good performance status (ECOG 0 or 1)
- Confirmed unresectability of CLM by expert surgeons
- Gold standard Resection of the primary
- No extrahepatic disease
- Partial Response or Stability with Chemo : ≥ 3 months, ≤ 3 lines
- No BRAF mutation
- CEA < 80 ng/ml or 50% decrease from baseline
- Platelets count > 80.000 and white blood cell count > 2500

TransMet Trial : Study Design

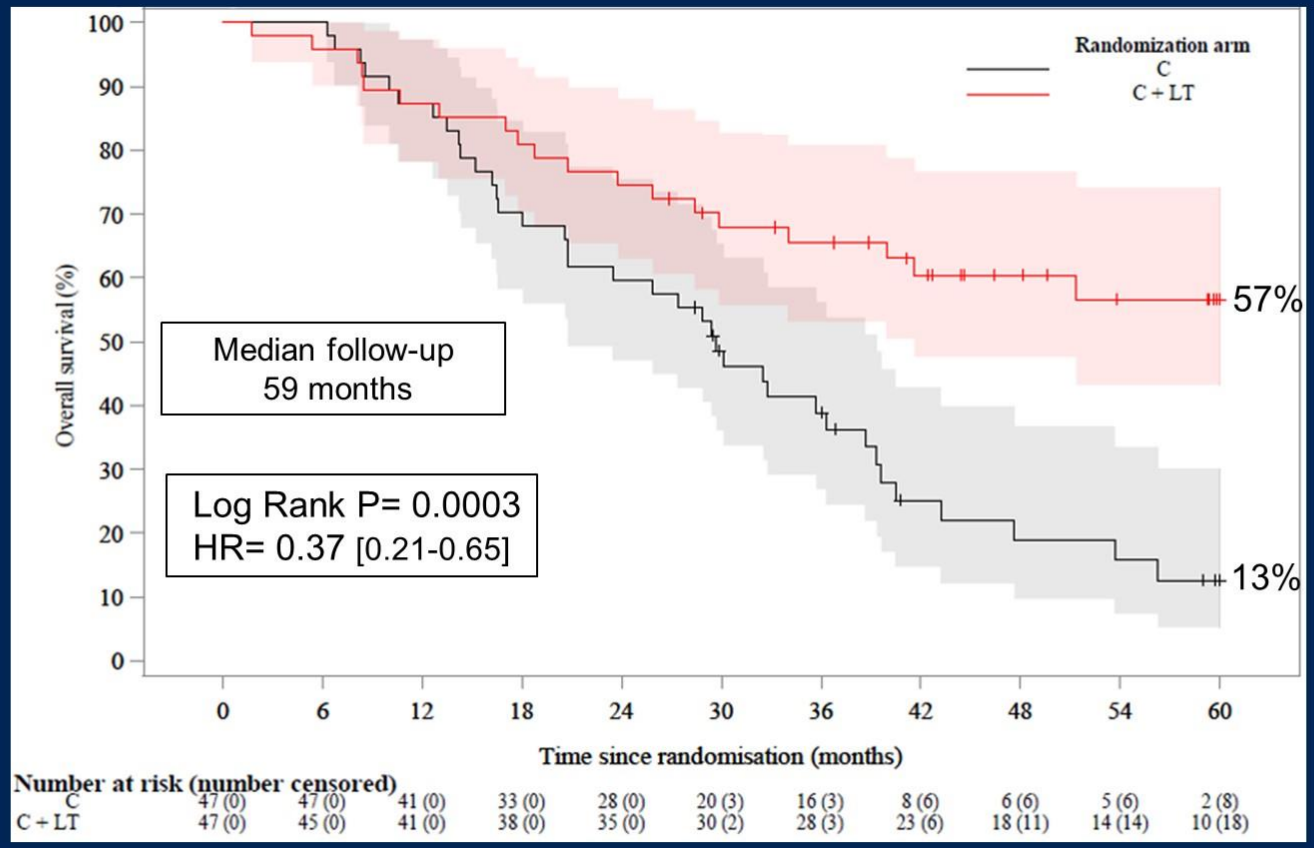


Adam et al, eClinical Medicine 2024

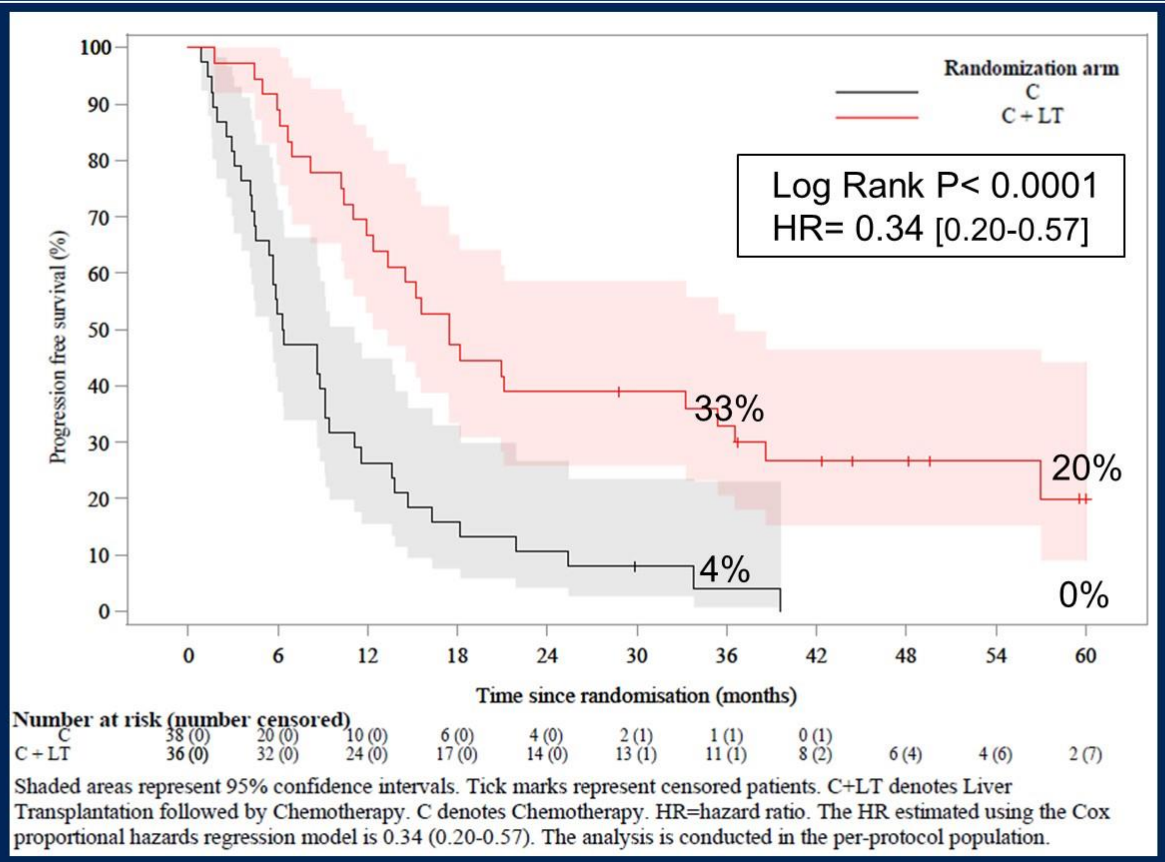
TransMet Trial : Patients Demographics at Randomisation

	LT+C group (n=47)	C alone group (n=47)
Type of chemotherapy		
5-FU alone	7 (15%)	1 (2%)
Oxaliplatin-based	12 (26%)	11 (23%)
Irinotecan-based	20 (43%)	27 (57%)
Triplet	8 (17%)	8 (17%)
Targeted therapy agent		
None	2 (4%)	4 (9%)
Anti-VEGF	17 (36%)	16 (34%)
Anti-EGFR	28 (60%)	27 (57%)
Total Number of lines		
1	18 (38%)	23 (49%)
2	21 (45%)	17 (36%)
3	8 (17%)	7 (15%)
Total Number of cycles (Median (IQR)	**21.0** (18.0, 29.0)	**17.0** (12.0, 24.0)
Tumour response		
Partial response	26 (55%)	21 (45%)
Stable disease	21 (45%)	26 (55%)
Delay primary resection – randomisation (Mo)	**16** (12 - 26)	**13·5** (9 - 19)
Delay randomization – LT (days)	51 (30 - 65)	-

TransMet Trial : Primary Endpoint 5-Yr OS (ITT)



TransMet Trial : Secondary Endpoint 3-5-Yr PFS (Per Protocol)



Shaded areas represent 95% confidence intervals. Tick marks represent censored patients. C+LT denotes Liver Transplantation followed by Chemotherapy. C denotes Chemotherapy. HR=hazard ratio. The HR estimated using the Cox proportional hazards regression model is 0.34 (0.20-0.57). The analysis is conducted in the per-protocol population.

Take Home messages from the TransMet trial

- Liver Transplantation + Chemotherapy significantly improves OS and PFS in selected patients with unresectable colorectal liver metastases compared to C alone
- These results were obtained through a rigorous patient selection and a prioritization for organ allocation
- Transplanted patients for CLM have similar survival (73% at 5 years) as those transplanted for established LT indications
- LT +C offers a potential of cure to cancer patients with otherwise poor long-term outcome

→ These results support LT as a new standard option that could change our practice in treating patients with liver-only, definitively unresectable CLM.

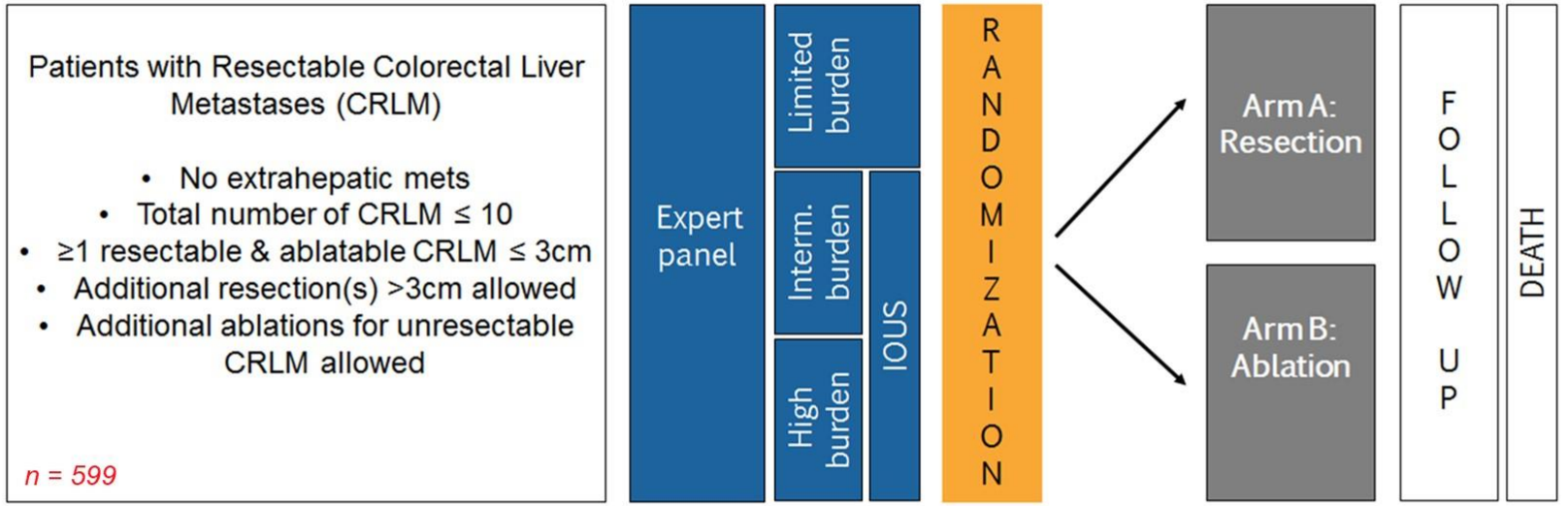
Amsterdam UMC
University Medical Centers

ASCO 2024 – Chicago, USA

Colorectal liver metastases: surgery versus thermal ablation: final results of the international phase 3 randomized controlled COLLISION trial

PROF. DR. MARTIJN R. MEIJERINK
Interventional Radiologist

COLLISION
Colorectal Liver Metastases: surgery vs thermal ablation

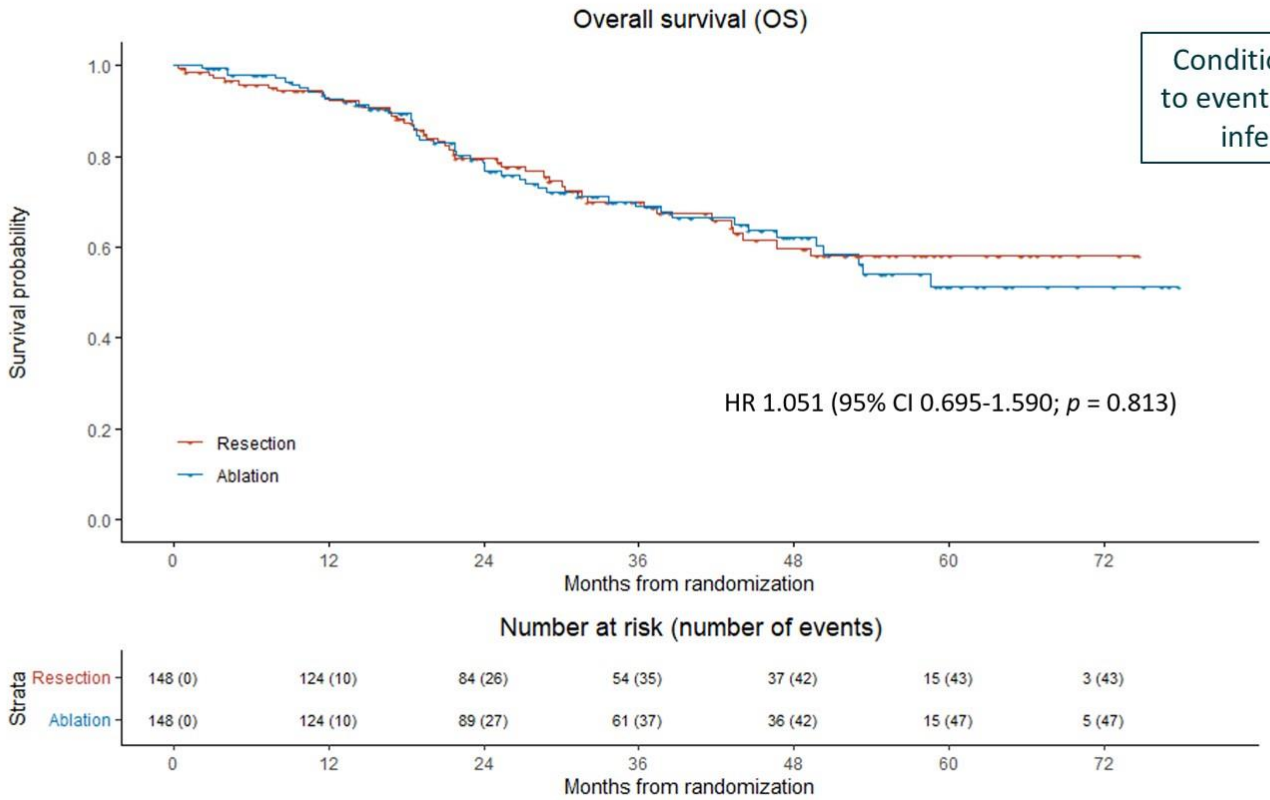


Phase III international multicenter randomized controlled trial to prove / disprove hypothesis of non-inferiority of thermal ablation compared to surgical resection for small-size colorectal liver metastases (CRLM)

- Approach (percutaneous, laparoscopic or open) according to local expertise
- If limited disease burden (max 3 CRLM ≤ 3cm) consider percutaneous / laparoscopic approach
- If intermediate or high disease burden randomize after eligibility check (after IOUS) during OR (single-blind)

RESULTS

OVERALL SURVIVAL – PRIMARY ENDPOINT



Conditional probability to eventually prove non-inferiority 91%!

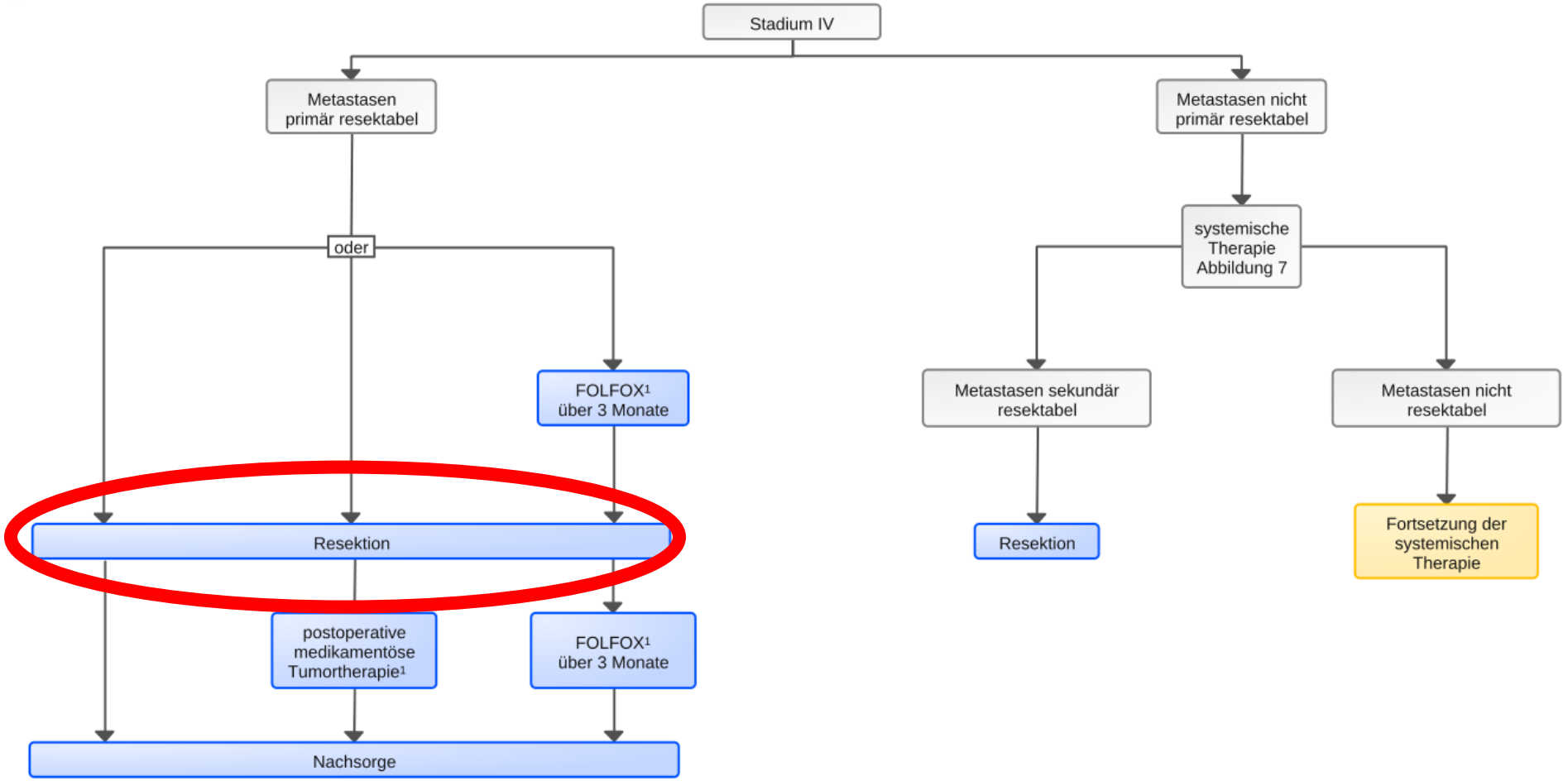
SUMMARY

COLLISION
Colorectal Liver Metastases: surgery vs thermal ablation

- **COLLISION stopped at halftime based on predefined stopping rules for**
  - Showing benefit of the experimental arm (ablation) over standard-of-care (resection)

- **For patients with small-size colorectal liver metastases, thermal ablation compared to standard-of-care surgical resection**
  - Substantially reduced morbidity and mortality
    - treatment related mortality 2.1% (resection) ⟶ 0.0% (ablation)
    - all-cause 90-day mortality 2.1% (resection) ⟶ 0.7% (ablation)
    - AEs rate 56% (resection) ⟶ 19% (ablation) and SAE rate 20% (resection) ⟶ 7% (ablation)
  - Was at least as good as surgical resection in locally controlling CRLM
    - no difference in *per-patient* local control: HR 0.131 (95% CI 0.016-1.064; p = 0.057)
    - superior *per-tumor* local control: HR 0.092 (95% CI 0.011-0.735; p = 0.024)
  - Showed no difference in local & distant tumor progression-free survival
  - Did not compromise overall survival (OS)

Therapiestruktur im Stadium IV

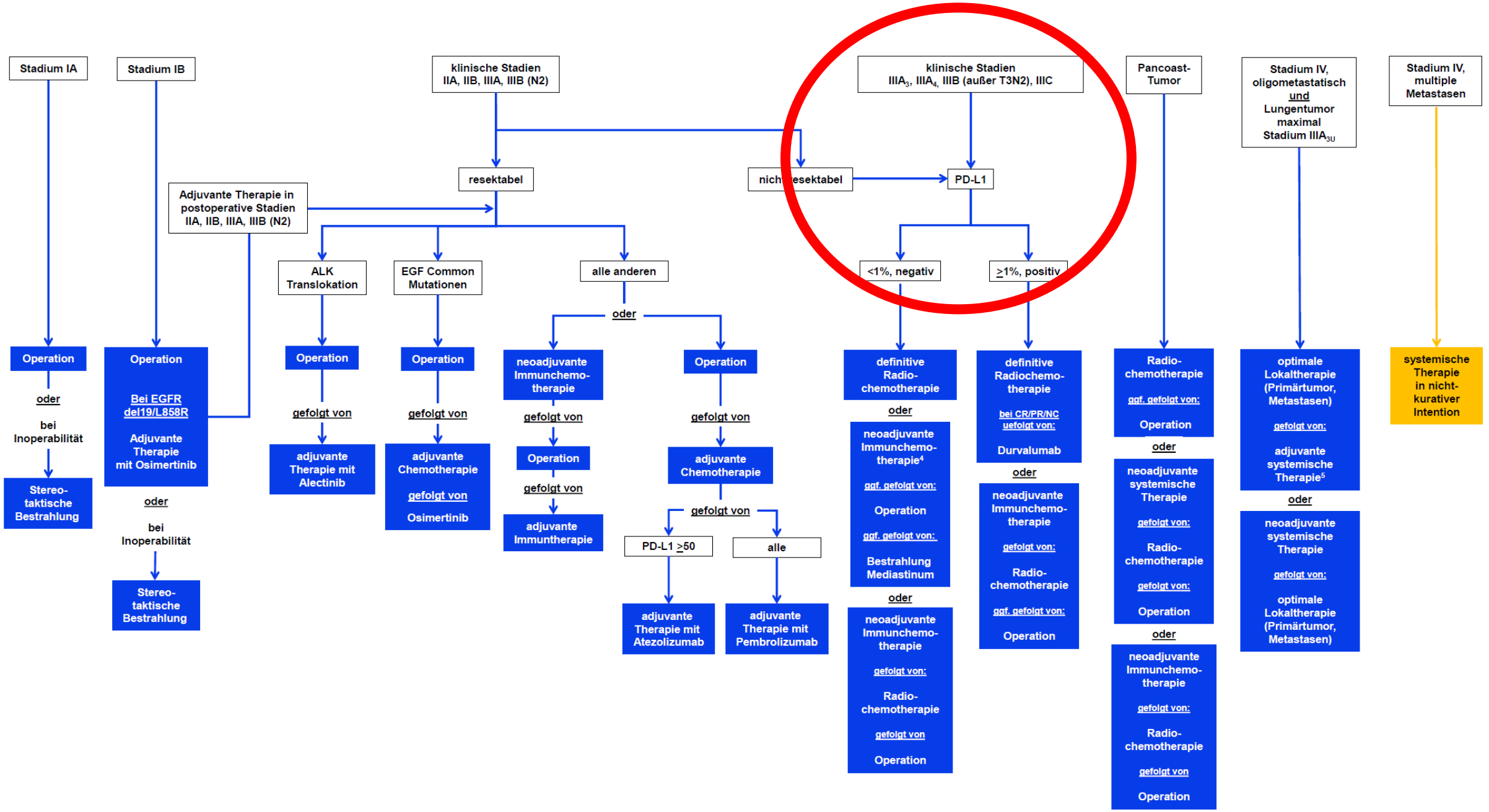


2024 ASCO ANNUAL MEETING

Osimertinib after definitive chemoradiotherapy in patients with unresectable stage III epidermal growth factor receptor-mutated (EGFRm) NSCLC: primary results of the Phase 3 LAURA study

Suresh S. Ramalingam,[1] Terufumi Kato, Xiaorong Dong, Myung-Ju Ahn, Le-Van Quang, Nopadol Soparattanapaisarn, Takako Inoue, Chih-Liang Wang, Meijuan Huang, James Chih-Hsin Yang, Manuel Cobo, Mustafa Özgüroğlu, Ignacio Casarini, Dang-Van Khiem, Virote Sriuranpong, Eduardo Cronemberger, Xiangning Huang, Toon van der Gronde, Dana Ghiorghiu, Shun Lu

[1]Emory University School of Medicine, Winship Cancer Institute, Atlanta, GA, USA


Stadium IA
Operation
oder
bei Inoperabilität
Stereo-taktische Bestrahlung
Stadium IB
Operation
Bei EGFR del19/L858R
Adjuvante Therapie mit Osimertinib
oder
bei Inoperabilität
Stereo-taktische Bestrahlung
Adjuvante Therapie in postoperative Stadien IIA, IIB, IIIA, IIIB (N2)
klinische Stadien IIA, IIB, IIIA, IIIB (N2)
resektabel
ALK Translokation
Operation
gefolgt von
adjuvante Therapie mit Alectinib
EGF Common Mutationen
Operation
gefolgt von
adjuvante Chemotherapie
gefolgt von
Osimertinib
alle anderen
oder
neoadjuvante Immunchemo-therapie
gefolgt von
Operation
gefolgt von
adjuvante Immuntherapie
Operation
gefolgt von
adjuvante Chemotherapie
gefolgt von
PD-L1 ≥50
adjuvante Therapie mit Atezolizumab
alle
adjuvante Therapie mit Pembrolizumab
nicht resektabel
klinische Stadien IIIA3, IIIA4, IIIB (außer T3N2), IIIC
PD-L1
<1%, negativ
definitive Radio-chemotherapie
oder
neoadjuvante Immunchemo-therapie4
ggf. gefolgt von:
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Bestrahlung Mediastinum
oder
neoadjuvante Immunchemo-therapie
gefolgt von:
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≥1%, positiv
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Durvalumab
oder
neoadjuvante Immunchemo-therapie
gefolgt von:
Radio-chemotherapie
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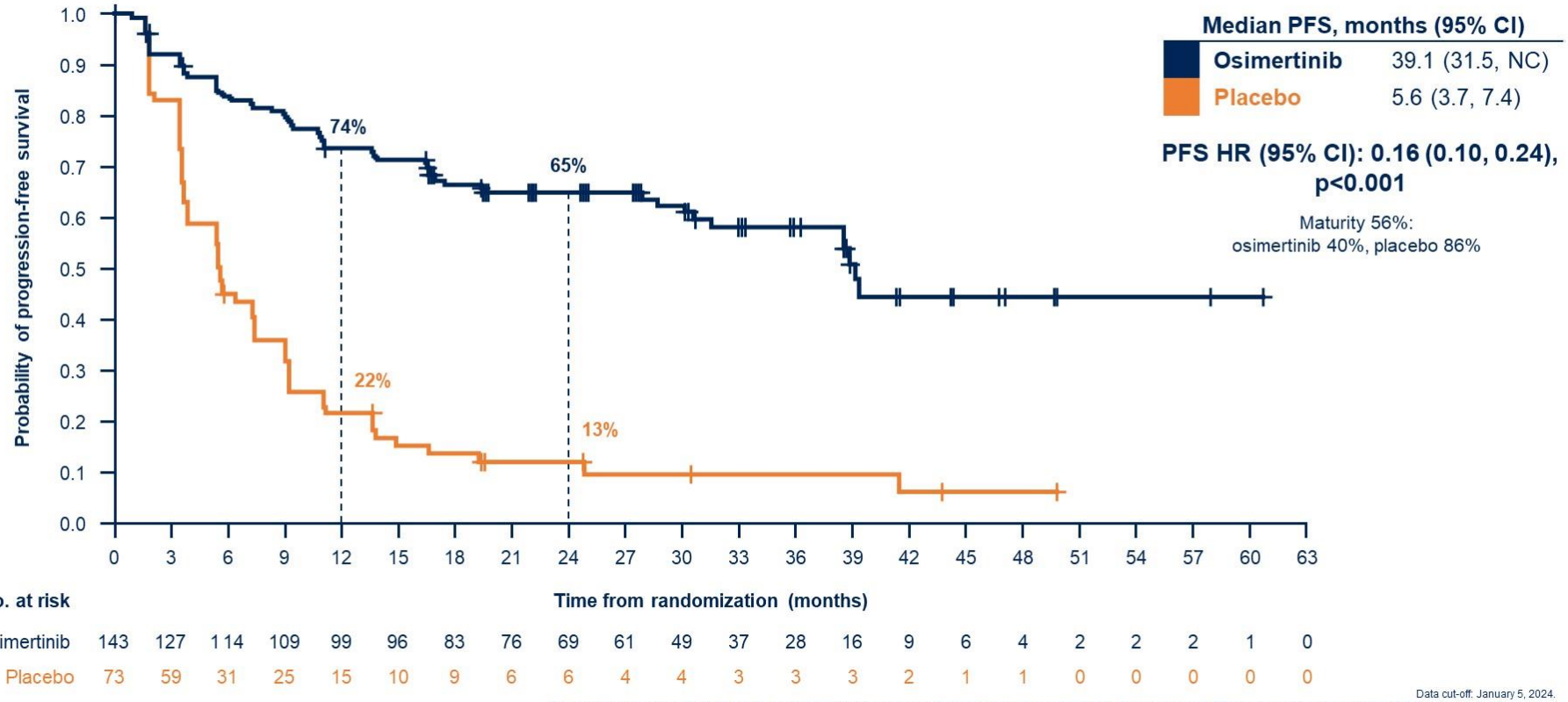
Pancoast-Tumor
Radio-chemotherapie
ggf. gefolgt von:
Operation
oder
neoadjuvante systemische Therapie
gefolgt von:
Radio-chemotherapie
gefolgt von:
Operation
oder
neoadjuvante Immunchemo-therapie
gefolgt von:
Radio-chemotherapie
gefolgt von
Operation
Stadium IV, oligometastatisch und Lungentumor maximal Stadium IIIA3U
optimale Lokaltherapie (Primärtumor, Metastasen)
gefolgt von:
adjuvante systemische Therapie5
oder
neoadjuvante systemische Therapie
gefolgt von:
optimale Lokaltherapie (Primärtumor, Metastasen)
Stadium IV, multiple Metastasen
systemische Therapie in nicht-kurativer Intention

Progression-free survival by BICR



No. at risk																						
Osimertinib	143	127	1 14	109	99	96	83	76	69	61	49	37	28	16	9	6	4	2	2	2	1	0
Placebo	73	59	31	25	15	10	9	6	6	4	4	3	3	3	2	1	1	0	0	0	0	0

Data cut-off: January 5, 2024.

Tick marks indicate censored data. Median follow-up for PFS (all patients): osimertinib 22.0 months, placebo 5.6 months. Median follow-up for PFS (censored patients): osimertinib 27.7 months, placebo 19.5 months.

BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; NC, not calculable; PFS, progression-free survival

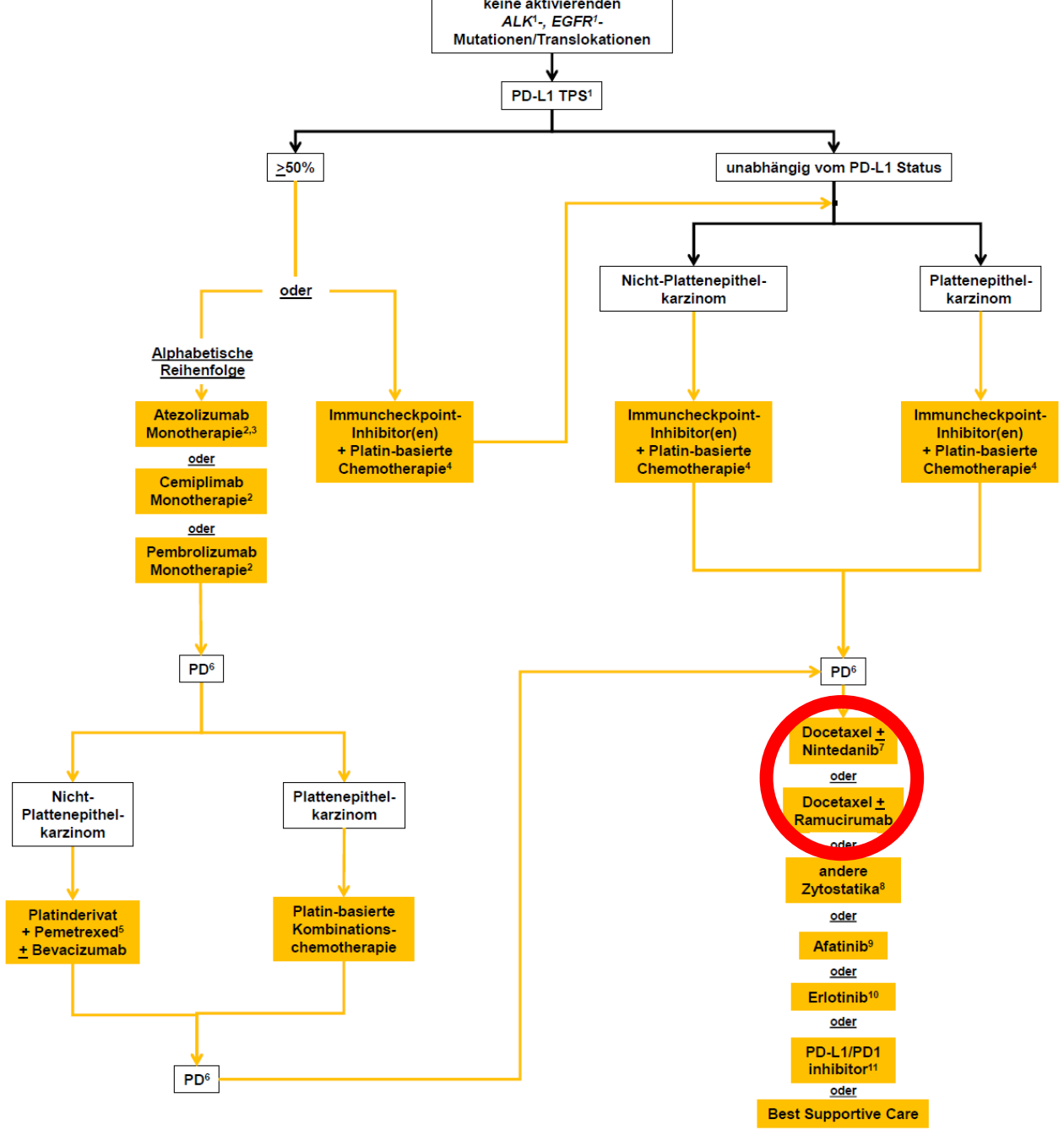
PRESENTED BY: Dr Suresh S. Ramalingam

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Osimertinib after Chemoradiotherapy in Stage III *EGFR*-Mutated NSCLC

Shun Lu, M.D., Terufumi Kato, M.D., Xiaorong Dong, M.D., Ph.D., Myung-Ju Ahn, M.D., Le-Van Quang, M.D., Nopadol Soparattanapaisarn, M.D., Takako Inoue, M.D., Chih-Liang Wang, M.D., Meijuan Huang, M.D., James Chih-Hsin Yang, M.D., Ph.D., Manuel Cobo, M.D., Mustafa Özgüroğlu, M.D., Ignacio Casarini, M.D., Dang-Van Khiem, M.D., Virote Sriuranpong, M.D., Ph.D., Eduardo Cronemberger, M.D., Toshiaki Takahashi, M.D., Ph.D., Yotsawaj Runglodvatana, M.D., Ming Chen, M.D., Ph.D., Xiangning Huang, Ph.D., Ellie Grainger, M.Sc., Dana Ghiorghiu, M.D., Ph.D., Toon van der Gronde, Pharm.D., Ph.D., and Suresh S. Ramalingam, M.D., for the LAURA Trial Investigators*


keine aktivierenden
ALK[1]-, EGFR[1]-
Mutationen/Translokationen
PD-L1 TPS[1]
≥50%
unabhängig vom PD-L1 Status
oder
Alphabetische Reihenfolge
Atezolizumab Monotherapie[2,3]
oder
Cemiplimab Monotherapie[2]
oder
Pembrolizumab Monotherapie[2]
Immuncheckpoint-Inhibitor(en) + Platin-basierte Chemotherapie[4]
Nicht-Plattenepithel-karzinom
Plattenepithel-karzinom
Immuncheckpoint-Inhibitor(en) + Platin-basierte Chemotherapie[4]
Immuncheckpoint-Inhibitor(en) + Platin-basierte Chemotherapie[4]
PD[6]
Nicht-Plattenepithel-karzinom
Plattenepithel-karzinom
Platinderivat + Pemetrexed[5] ± Bevacizumab
Platin-basierte Kombinations-chemotherapie
PD[6]
PD[6]
Docetaxel ± Nintedanib[7]
oder
Docetaxel ± Ramucirumab
oder
andere Zytostatika[8]
oder
Afatinib[9]
oder
Erlotinib[10]
oder
PD-L1/PD1 inhibitor[11]
oder
Best Supportive Care

2024 ASCO ANNUAL MEETING

Lorlatinib vs Crizotinib in Treatment-Naive Patients With Advanced *ALK*+ Non-Small Cell Lung Cancer: 5-Year Progression-Free Survival and Safety From the CROWN Study

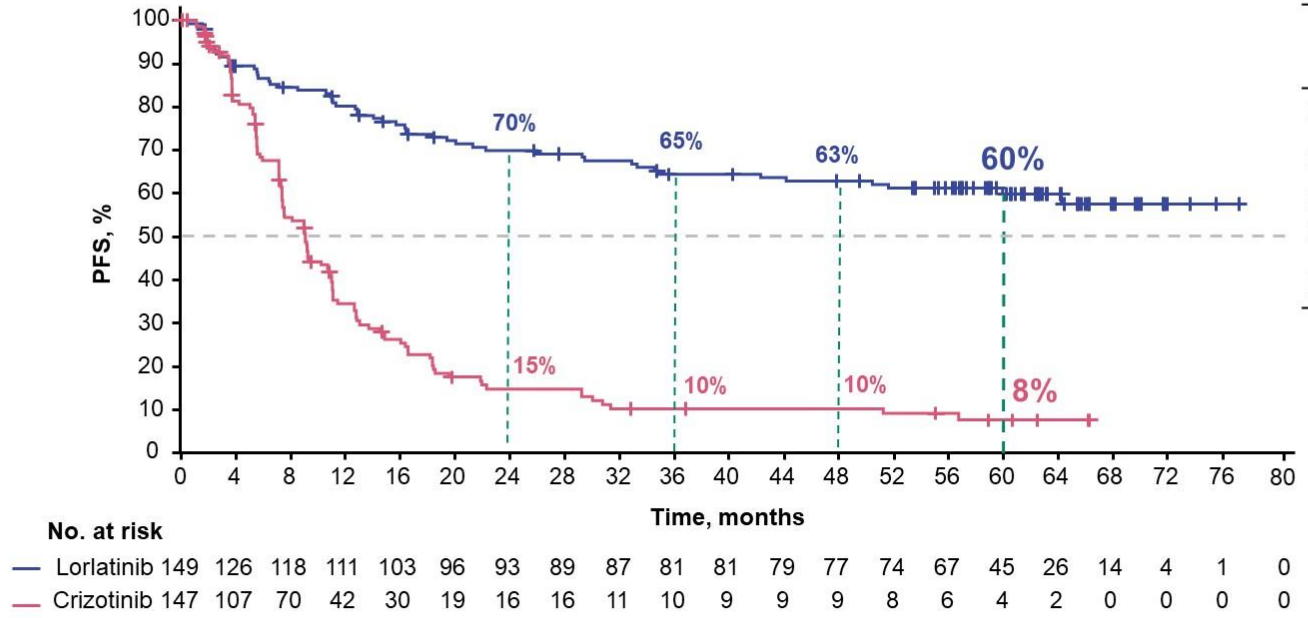
Benjamin J. Solomon,[1] Geoffrey Liu,[2] Enriqueta Felip,[3] Tony S. K. Mok,[4] Ross A. Soo,[5] Julien Mazieres,[6] Alice T. Shaw,[7] Filippo de Marinis,[8] Yasushi Goto,[9] Yi-Long Wu,[10] Dong-Wan Kim,[11] Jean-François Martini,[12] Rossella Messina,[13] Jolanda Paolini,[13] Anna Polli,[13] Despina Thomaidou,[14] Francesca Toffalorio,[13] Todd M. Bauer[15]

[1]Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; [2]Princess Margaret Cancer Centre, Toronto, ON, Canada; [3]Vall d'Hebron University Hospital and Vall d'Hebron Institute of Oncology, Barcelona, Spain; [4]State Key Laboratory of Translational Oncology, Chinese University of Hong Kong, Hong Kong; [5]National University Cancer Institute, Singapore; [6]Toulouse University Hospital and Centre de Recherche Cancérologie Toulouse CRCT, INSERM, France; [7]Massachusetts General Hospital Cancer Center, Boston, MA, USA; [8]European Institute of Oncology, IRCCS, Milan, Italy; [9]National Cancer Center Hospital, Tokyo, Japan; [10]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangdong, China; [11]Seoul National University College of Medicine and Seoul National University Hospital, Seoul, South Korea; [12]Pfizer, La Jolla, CA, USA; [13]Pfizer, Milan, Italy; [14]Pfizer, Athens, Greece; [15]Greco-Hainsworth Centers for Research/Tennessee Oncology, Nashville, TN, USA

Benjamin J. Solomon, MBBS, PhD
Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

PRESENTED BY: Benjamin J. Solomon (Ben.Solomon@petermac.org)

At 60.2 Months of Median Follow-Up, Median PFS by Investigator Was Still Not Reached With Lorlatinib



	Lorlatinib (n=149)	Crizotinib (n=147)
Events, n	55	115
PFS, median (95% CI), months	NR (64.3-NR)	9.1 (7.4-10.9)
HR (95% CI)	**0.19 (0.13-0.27)**	

At the time of this analysis, the required number of OS events for a protocol-specified second interim analysis **has not been reached**. OS follow up is ongoing

HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival.

PRESENTED BY: Benjamin J. Solomon (Ben.Solomon@petermac.org)

2024 ASCO ANNUAL MEETING

KRYSTAL-12: phase 3 study of adagrasib versus docetaxel in patients with previously treated locally advanced or metastatic non-small cell lung cancer (NSCLC) harboring a *KRAS*^{G12C} mutation

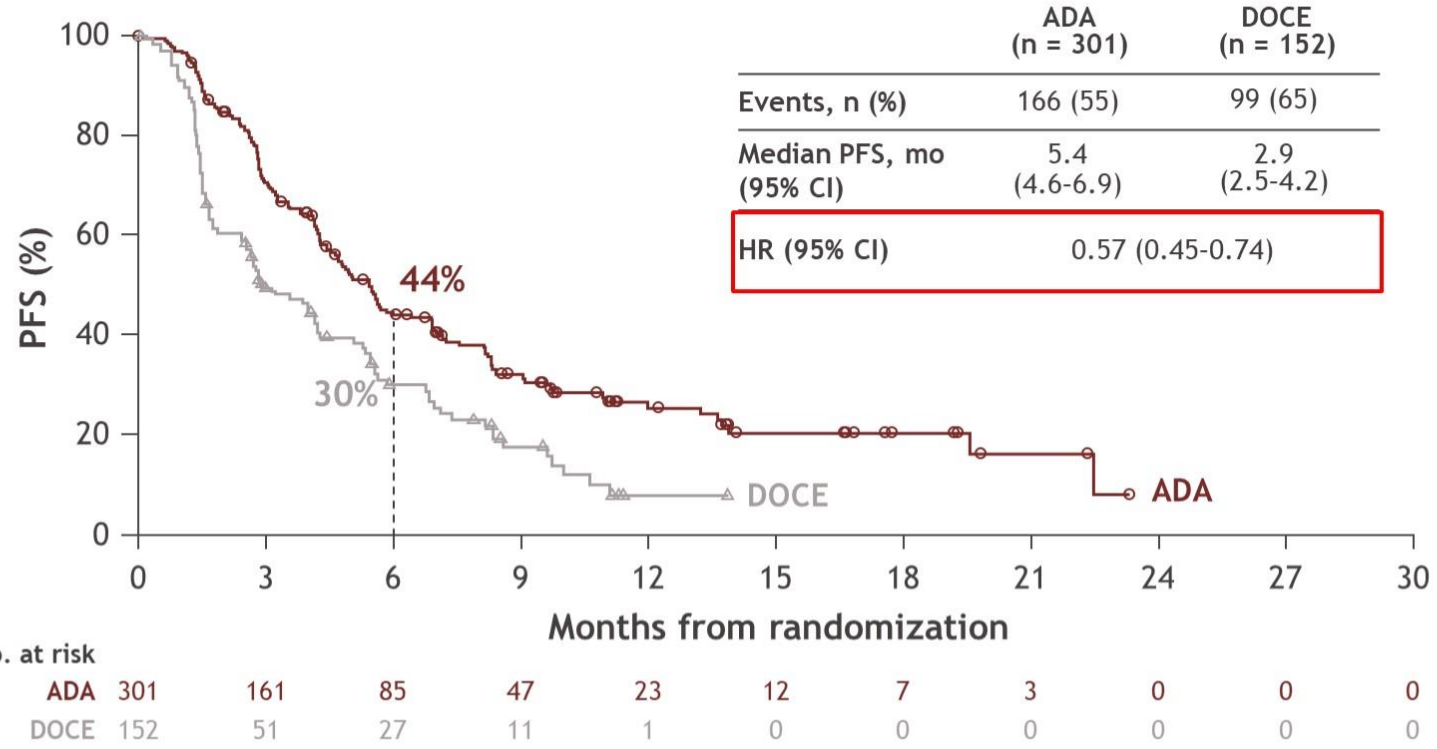
Tony S. K. Mok,[1] Wenxiu Yao,[2] Michaël Duruisseaux,[3-5] Ludovic Doucet,[6] Aitor Azkárate Martínez,[7] Vanesa Gregorc,[8] Oscar Juan-Vidal,[9] Shun Lu,[10] Charlotte De Bondt,[11] Filippo de Marinis,[12] Helena Linardou,[13] Young-Chul Kim,[14] Robert Jotte,[15] Enriqueta Felip,[16] Giuseppe Lo Russo,[17] Martin Reck,[18] Mary F. Michenzie,[19] Wenjing Yang,[19] Julie N. Meade,[19a] Fabrice Barlesi[20]

[1]Chinese University of Hong Kong, Hong Kong Special Administrative Region, China; [2]Sichuan Cancer Hospital & Institute, Chengdu, China; [3]Louis Pradel Hospital, Hospices Civils de Lyon Cancer Institute, Lyon, France; [4]Cancer Research Center of Lyon, UMR INSERM 1052, CNRS 5286, Lyon, France; [5]Université Claude Bernard Lyon 1, Université de Lyon, Lyon, France; [6]Institut de Cancérologie de l'Ouest, Nantes, France; [7]Hospital Universitario Son Espases, Mallorca, Spain; [8]Candiolo Cancer Institute, FPO-IRCCS, Candiolo, Italy; [9]Hospital Universitari i Politècnic La Fe, Valencia, Spain; [10]Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [11]Antwerp University Hospital, University of Antwerp, Antwerp, Belgium; [12]Istituto Europeo di Oncologia, IRCCS, Milan, Italy; [13]Fourth Oncology Department & Comprehensive Clinical Trials Center, Metropolitan Hospital, Athens, Greece; [14]Chonnam National University Medical School and CNU Hwasun Hospital, Hwasun-Gun, Republic of Korea; [15]Rocky Mountain Cancer Center, US Oncology Research, Denver, CO, USA; [16]Vall d'Hebron Institute of Oncology, Vall d'Hebron Barcelona Hospital Campus, Universitat Autonoma de Barcelona, Barcelona, Spain; [17]Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [18]Airway Research Center North, German Center for Lung Research, LungenClinic, Grosshansdorf, Germany; [19]Mirati Therapeutics, a Bristol Myers Squibb company, San Diego, CA, USA; [20]Gustave Roussy & Paris Saclay University, Villejuif, France

[a]Affiliation at the time of study

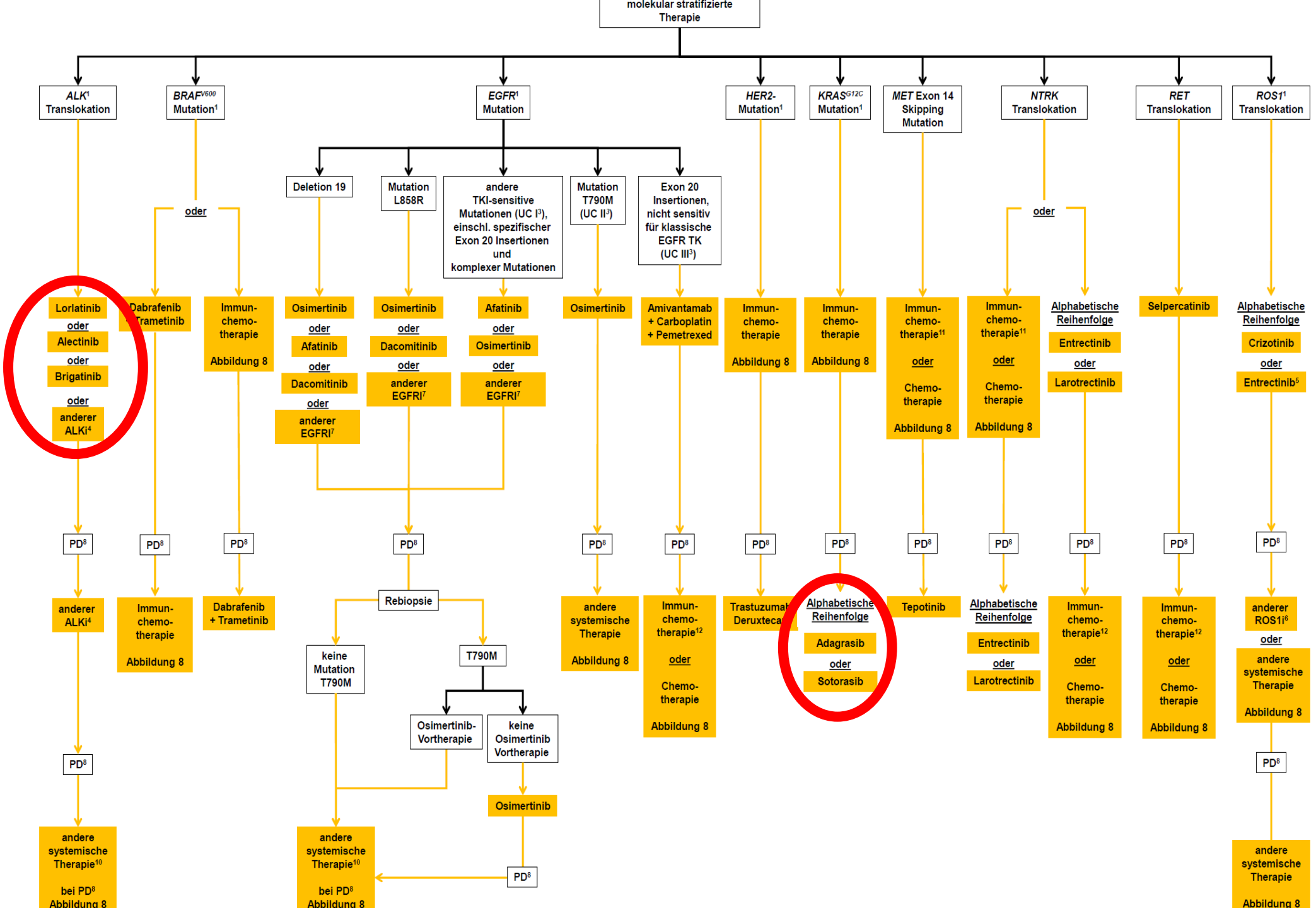
Abstract number LBA8509

PFS[a] per investigator assessment



	ADA (n = 301)	DOCE (n = 152)
Events, n (%)	166 (55)	99 (65)
Median PFS, mo (95% CI)	5.4 (4.6-6.9)	2.9 (2.5-4.2)
HR (95% CI)	0.57 (0.45-0.74)	

[a]Time from randomization to the date of disease progression or death due to any cause, whichever occurs first. For patients who started a subsequent anticancer therapy prior to disease progression or death, PFS was censored at the date of the last tumor assessment prior to the start of the new therapy.


molekular stratifizierte Therapie
ALK¹ Translokation
BRAF V600 Mutation¹
EGFR¹ Mutation
HER2-Mutation¹
KRAS G12C Mutation¹
MET Exon 14 Skipping Mutation
NTRK Translokation
RET Translokation
ROS1¹ Translokation
Deletion 19
Mutation L858R
andere TKI-sensitive Mutationen (UC I³), einschl. spezifischer Exon 20 Insertionen und komplexer Mutationen
Mutation T790M (UC II³)
Exon 20 Insertionen, nicht sensitiv für klassische EGFR TK (UC III³)
oder
Lorlatinib
Alectinib
Brigatinib
anderer ALKi⁴
Dabrafenib + Trametinib
Immun-chemo-therapie Abbildung 8
Osimertinib
Afatinib
Dacomitinib
anderer EGFRI⁷
Amivantamab + Carboplatin + Pemetrexed
Trastuzumab Deruxteca
Alphabetische Reihenfolge
Adagrasib
Sotorasib
Immun-chemo-therapie¹¹ oder Chemo-therapie Abbildung 8
Tepotinib
Entrectinib
Larotrectinib
Selpercatinib
Crizotinib
Entrectinib⁵
PD⁸
anderer ALKi⁴
Immun-chemo-therapie Abbildung 8
Rebiopsie
keine Mutation T790M
T790M
Osimertinib-Vortherapie
keine Osimertinib Vortherapie
andere systemische Therapie Abbildung 8
Immun-chemo-therapie¹² oder Chemo-therapie Abbildung 8
andere systemische Therapie¹⁰ bei PD⁸ Abbildung 8
anderer ROS1i⁶

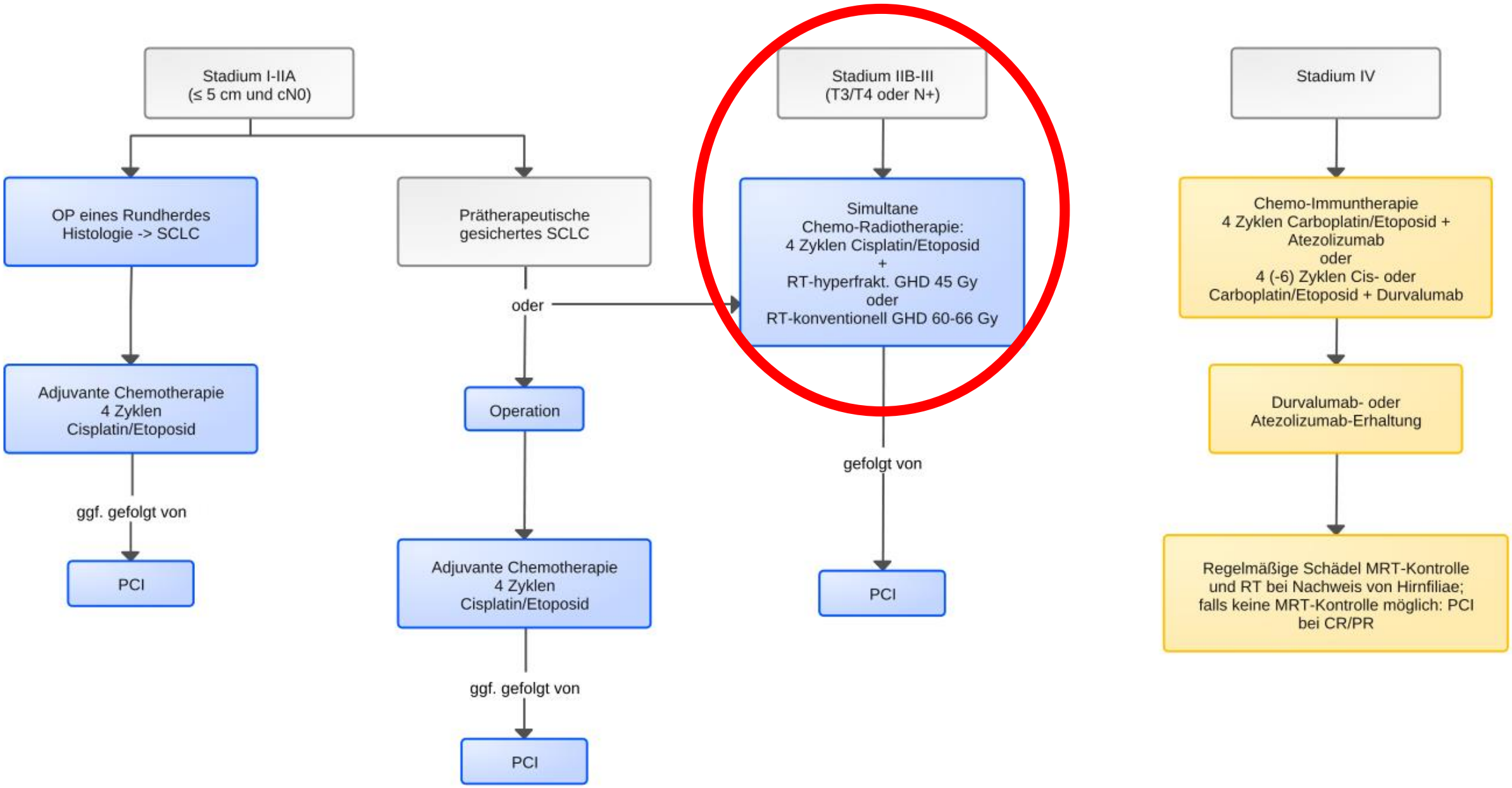
2024 ASCO ANNUAL MEETING

ADRIATIC: durvalumab as consolidation treatment for patients with limited-stage small-cell lung cancer (LS-SCLC)

David R. Spigel, Ying Cheng, Byoung Chul Cho, Konstantin Laktionov, Jian Fang, Yuanbin Chen, Yoshitaka Zenke, Ki Hyeong Lee, Qiming Wang, Alejandro Navarro, Reyes Bernabe, Eva Buchmeier, John Wen-Cheng Chang, Isamu Okamoto, Sema Sezgin Goksu, Andrzej Badzio, Bethany Gill, Hema Gowda, Haiyi Jiang, Suresh Senan

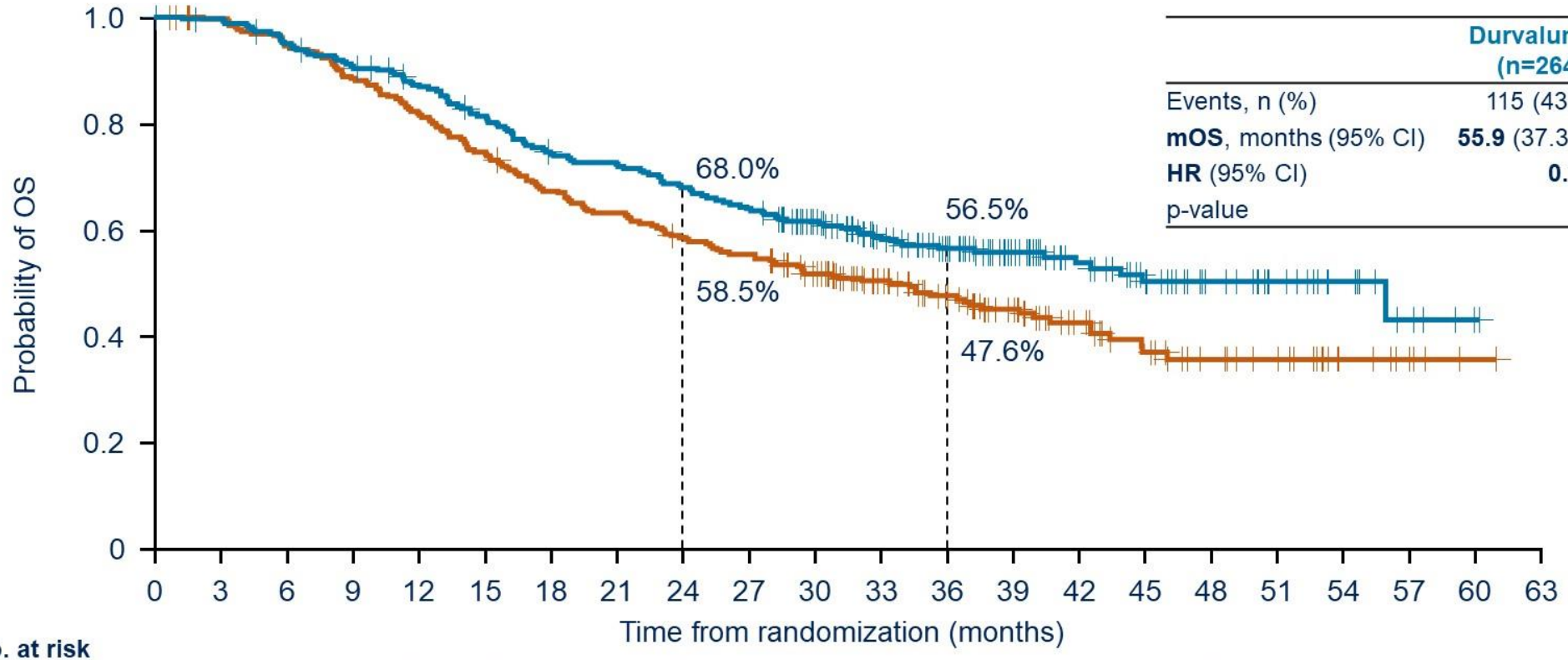
PRESENTED BY: Dr David R. Spigel, Sarah Cannon Research Institute, Nashville, TN, USA

Therapiestruktur für das kleinzellige Lungenkarzinom (SCLC)



Overall survival (dual primary endpoint)

- Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

No. at risk																						
Durvalumab	264	261	248	236	223	207	189	183	172	162	141	110	90	68	51	39	27	19	11	5	1	0
Placebo	266	260	247	231	214	195	175	164	151	143	123	97	80	62	44	31	23	19	8	5	1	0

OS was analyzed using a stratified log-rank test adjusted for receipt of PCI (yes vs no). The significance level for testing OS at this interim analysis was 0.01679 (2-sided) at the overall 4.5% level, allowing for strong alpha control across interim and final analysis timepoints.

PRESENTED BY: Dr David R. Spigel

CI, confidence interval; mOS, median OS; NE, not estimable.

2024 ASCO ANNUAL MEETING

Comparative Effectiveness Trial of Early Palliative Care Delivered via Telehealth versus In Person among Patients with Advanced Lung Cancer: The REACH PC Trial

Joseph A. Greer PhD & Jennifer S. Temel MD on behalf of:

Chardria Trotter MPH MBA, Vicki A. Jackson MD MPH, Simone Rinaldi APN-BC, Mihir Kamdar MD, Areej El-Jawahri MD, Nora Horick MS, Kedie Pintro MS, Dustin Rabideau PhD, Josephine Feliciano MD, Isaac Chua MD MPH, Konstantinos Leventakos MD, Stacy Fischer MD, Toby C. Campbell MD, Michael W. Rabow MD, Finly Zachariah MD, Laura C. Hanson MD, Sara F. Martin MD, Maria Silveira MD, and the REACH PC Investigators

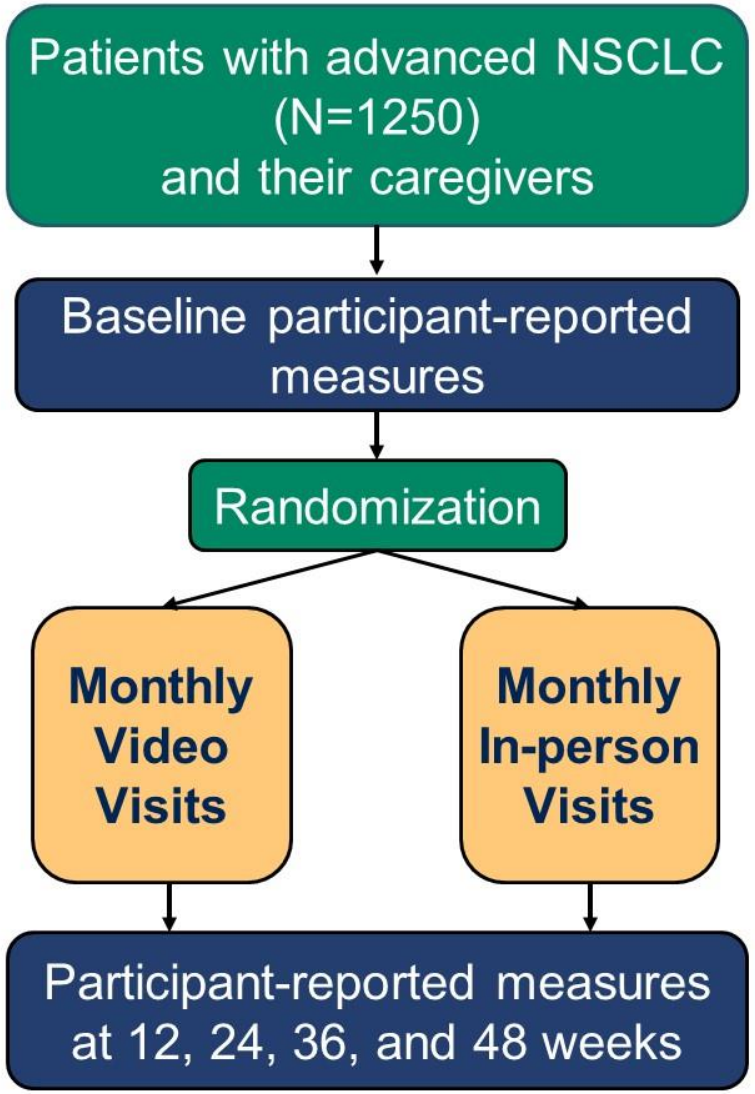
Study Aims and Design

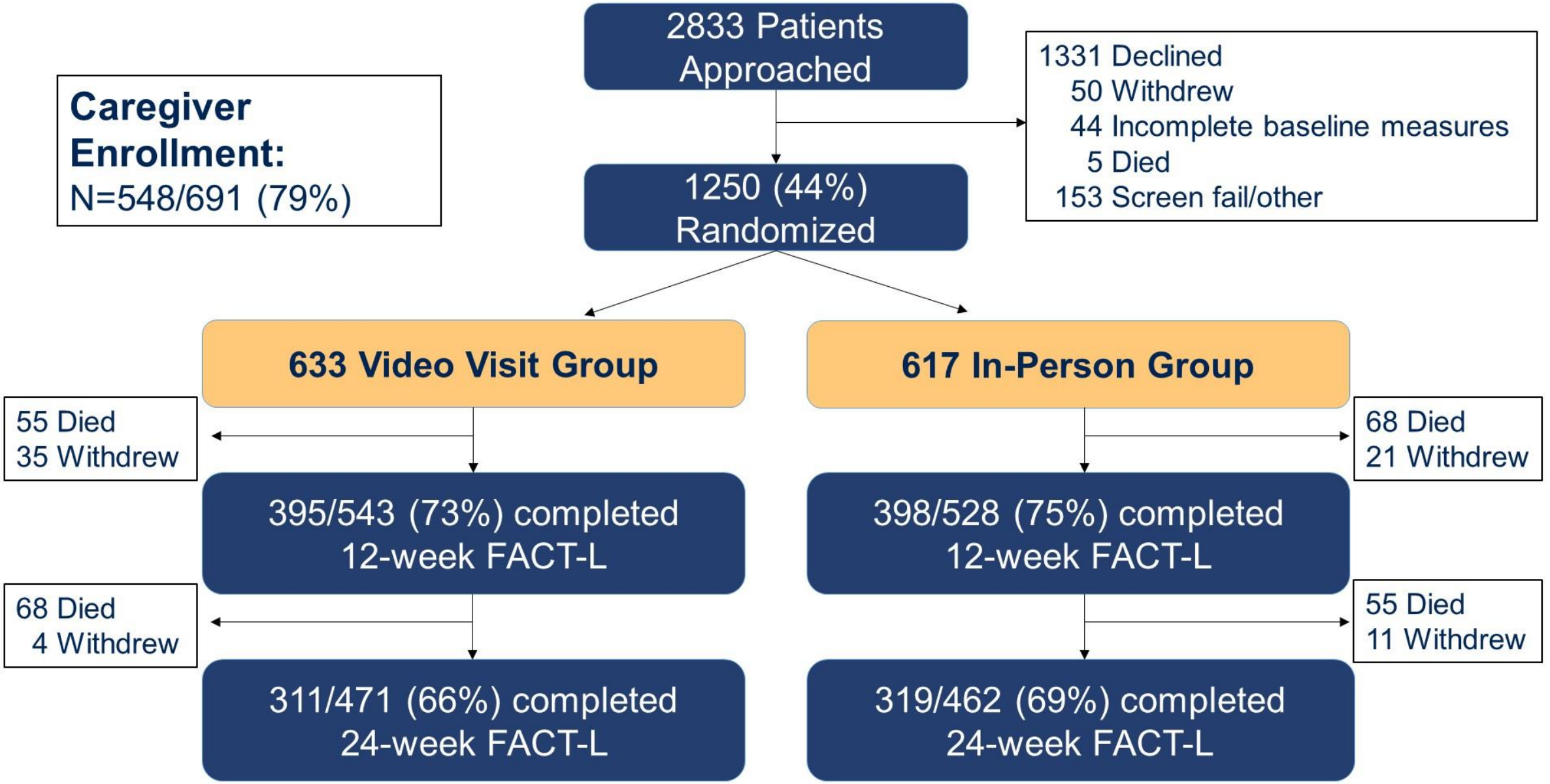
Primary Aim:

- To evaluate the equivalence of the effect of delivering early palliative care using video versus in-person visits on patient-reported quality of life

Secondary and Exploratory Aims:

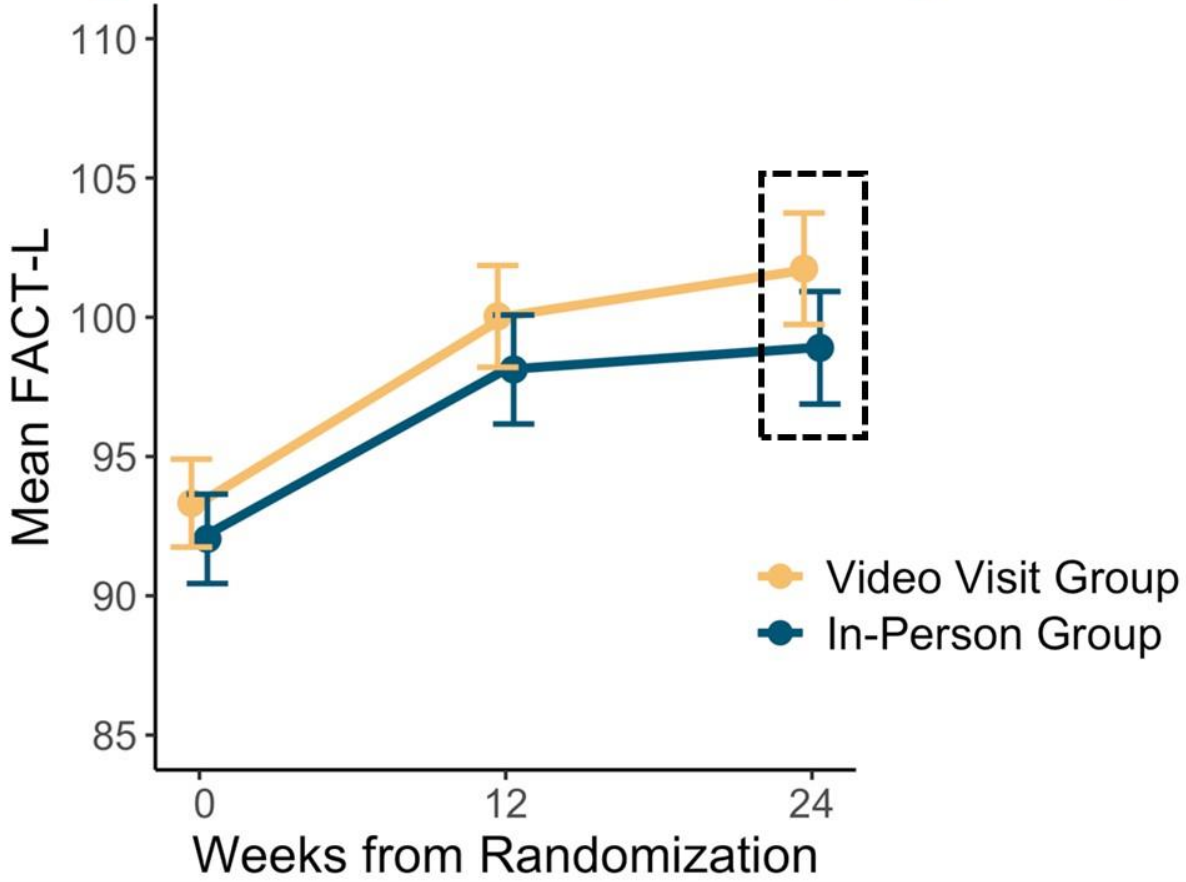
- Satisfaction with care
- Caregiver attendance at study visits
- Mood symptoms





Primary Outcome: Patient Quality of Life (QOL)

Higher scores indicate better QOL (range: 0-136)



Adjusted Mean FACT-L at 24 Weeks:

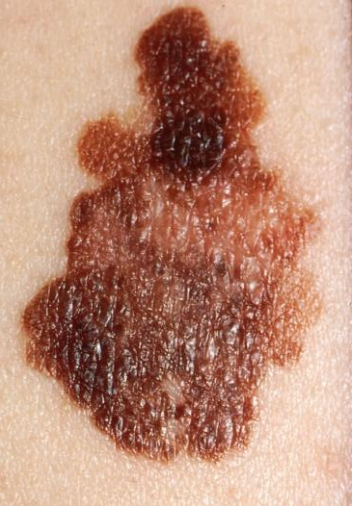
- Video Visit Group: **99.7**
- In-Person Group: **97.7**

Difference (90% CI): **2.0 (0.1, 3.9)**

p=**0.04 for equivalence**

Main Study Findings from the REACH PC Trial

- Palliative care led to equivalent benefits for patient-reported quality of life whether delivered via video or in-person visits among adults with advanced lung cancer.
- Findings underscore the potential to increase access to evidence-based early palliative care through telehealth delivery.



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

Patel et al., NEJM 3/2023

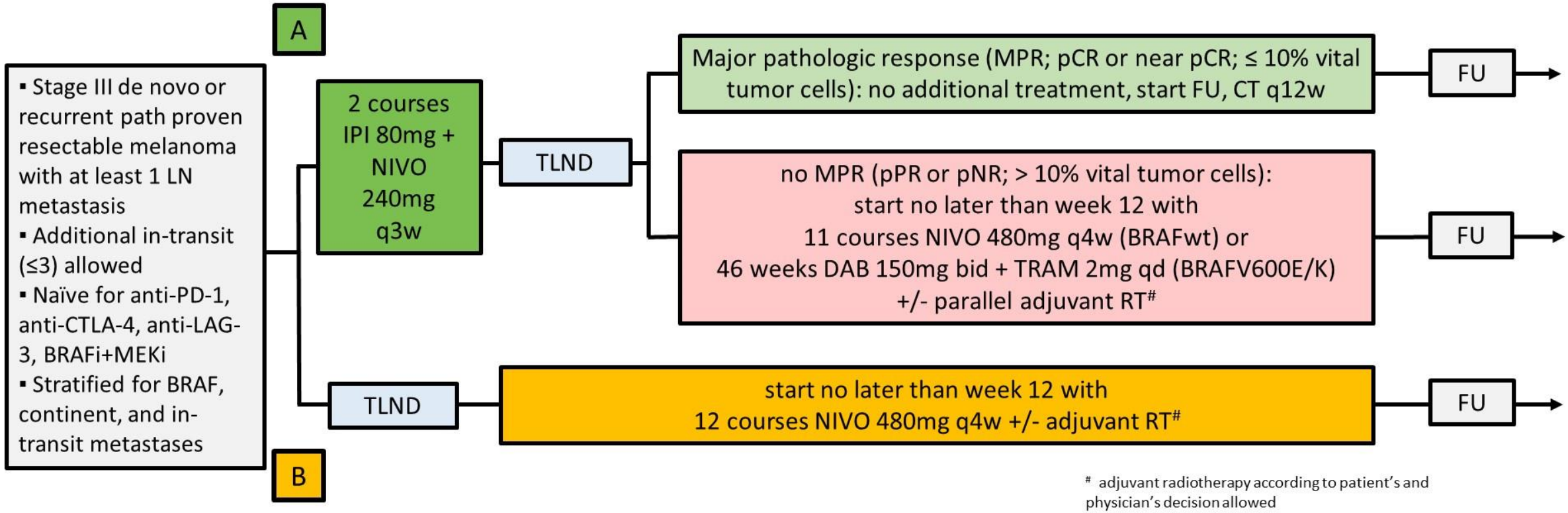
2024 ASCO ANNUAL MEETING

Neoadjuvant Nivolumab Plus Ipilimumab Versus Adjuvant Nivolumab in Macroscopic, Resectable Stage III Melanoma: The Phase 3 NADINA Trial

Christian U. Blank, M.W. Lucas, R.A. Scolyer, B.A. van de Wiel, A.M. Menzies, M. Lopez-Yurda, A.C.J. van Akkooi, W.J. van Houdt, R.P.M. Saw, A. Torres-Acosta, S.N. Lo, G.A.P. Hospers, M.S. Carlino, J.W.B. de Groot, E. Kapiteijn, K.P.M. Suijkerbuijk, P. Rutkowski, S. Sandhu, A.A.M. van der Veldt, G.V. Long

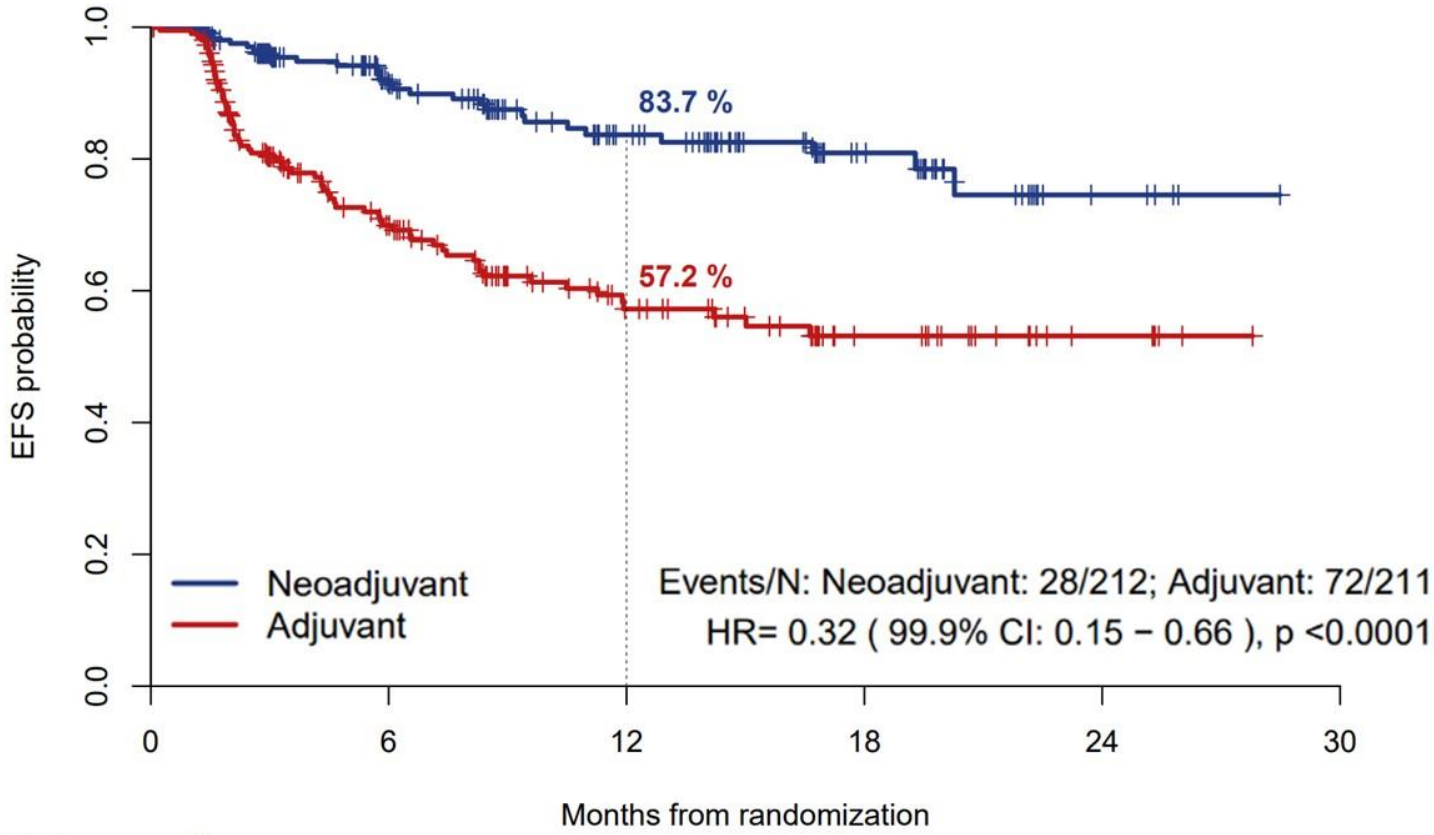
lay abstract

NADINA - Trial Design



PRESENTED BY: Christian U. Blank, MD PhD

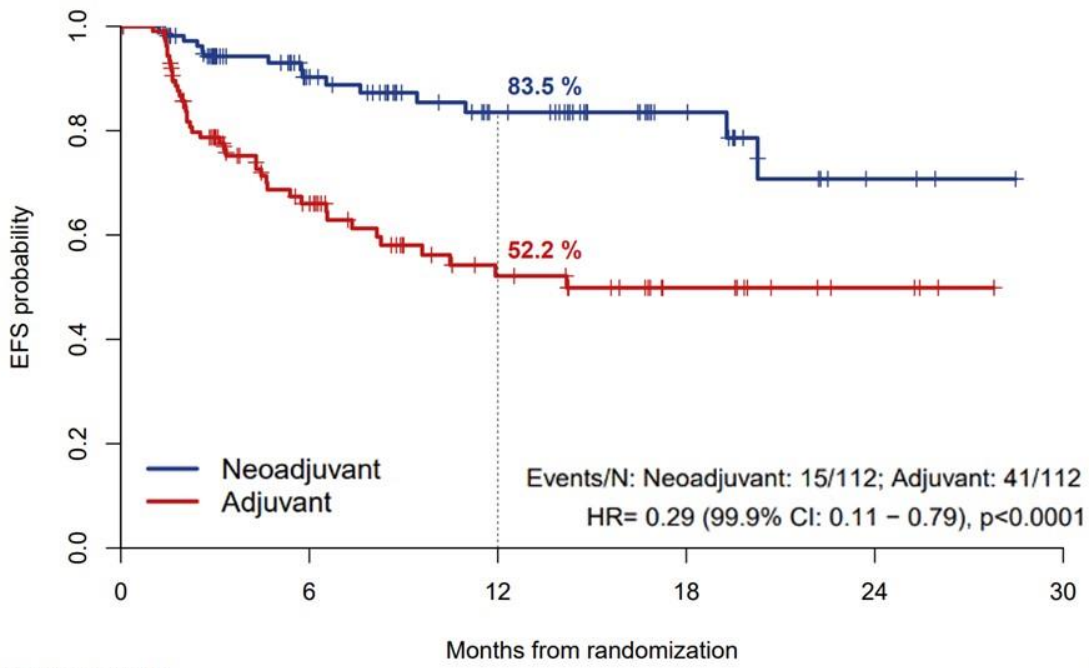
NADINA – Primary Endpoint: Event-Free Survival (EFS)



# at risk (censored)										
Neoadjuvant	212	(0)	126	(71)	77	(111)	34	(152)	5	(179)
Adjuvant	211	(0)	100	(57)	53	(89)	23	(116)	6	(133)

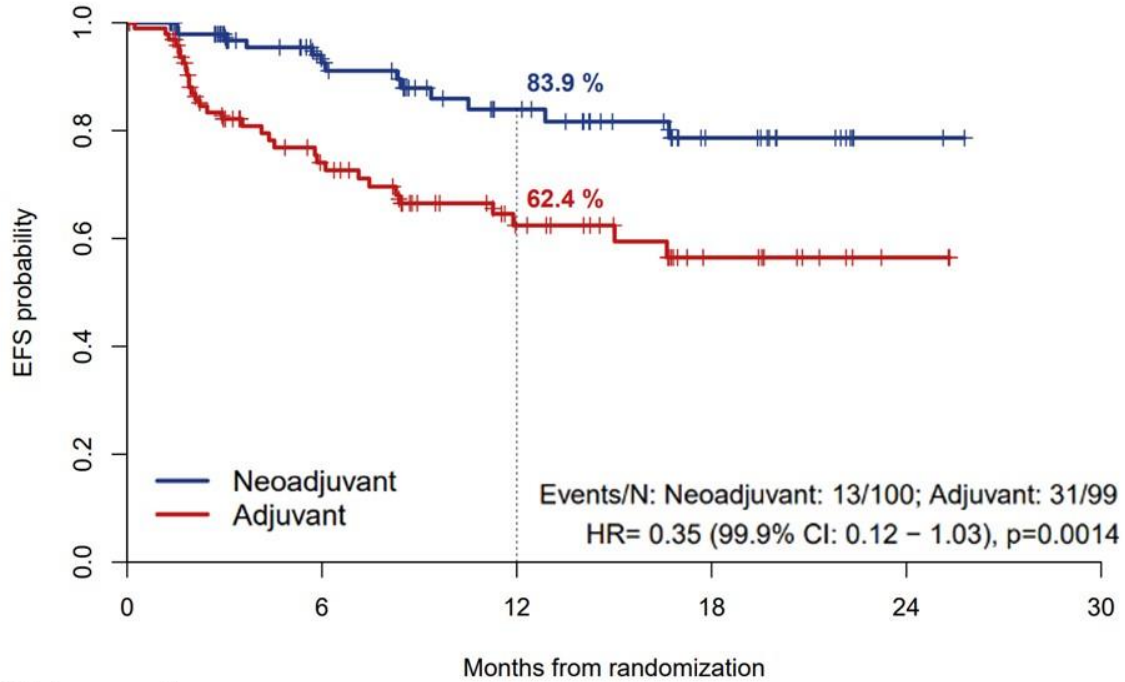
NADINA – EFS According to BRAF Mutational Status

BRAF$^{V600E/K}$ mutation



# at risk (censored)										
Neoadjuvant	112	(0)	63	(40)	38	(61)	18	(81)	3	(94)
Adjuvant	112	(0)	48	(32)	25	(47)	11	(60)	4	(67)

BRAF wildtype



# at risk (censored)										
Neoadjuvant	100	(0)	63	(31)	39	(50)	16	(71)	2	(85)
Adjuvant	99	(0)	52	(25)	28	(42)	12	(56)	2	(66)

PRESENTED BY: Christian U. Blank, MD PhD

NADINA – Main Findings

- NADINA shows a highly statistically significant **event-free survival (EFS) benefit for neoadjuvant combination of ipilimumab + nivolumab** as compared to standard of care adjuvant nivolumab in patients with macroscopic stage III melanoma

- **All patient subgroups benefit** from neoadjuvant ipilimumab + nivolumab (inclusive patients harbouring BRAF$^{V600E/K}$ mutation positive and negative tumors)

2024 ASCO ANNUAL MEETING

A-BRAVE-TRIAL

A-BRAVE Trial: a phase III randomised trial with Avelumab in early triple negative breast cancer with residual disease after neoadjuvant chemotherapy or at high risk after primary surgery and adjuvant chemotherapy

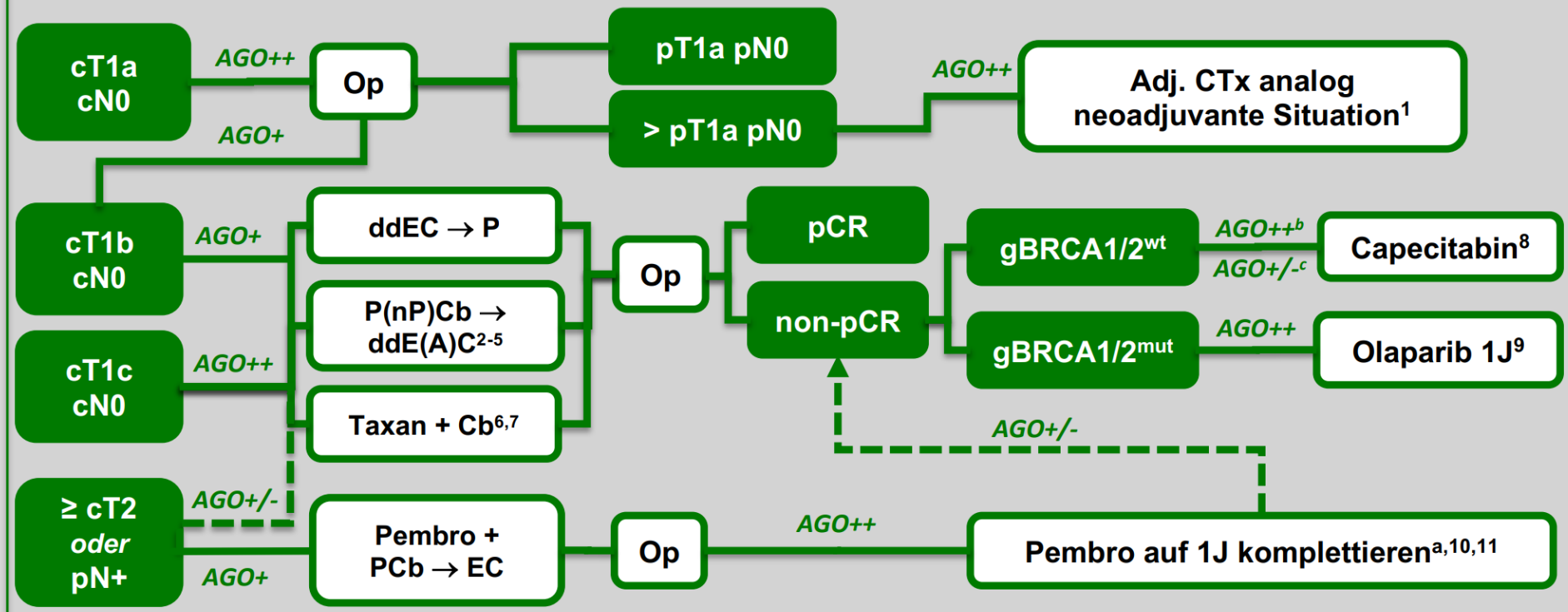
PierFranco Conte, Maria Vittoria Dieci, Giancarlo Bisagni, Peter Schmid, Vittoria Fotia, Federico Piacentini, Michelino de Laurentiis, Adolfo Favaretto, Stefano Tamberi, Giulia Bianchi, Claudio Zamagni, Saverio Cinieri, Domenico Corsi, Lucia Del Mastro, Antonella Ferro, Alessandra Gennari, Marta Mion, Antonino Musolino, Gian Luca De Salvo, Valentina Guarneri
on behalf of A-BRAVE study team

Medical Oncology 2, Istituto Oncologico Veneto IRCCS
DiSCOG-University of Padova, Italy

PRESENTED BY: Pierfranco Conte, MD

Therapie beim frühen triple-negativen Mammakarzinom

Guidelines Breast
Version 2024.1D



A, Doxorubicin; C, Cyclophosphamid; Cb, Carboplatin; CTx, Chemotherapie; dd, dosisdicht (alle 2 Wochen); E, Epirubicin; J, Jahr; mut, mutiert; nP, nab-Paclitaxel; Op, Operation; Pembro, Pembrolizumab; P, Paclitaxel; wt, wild type; [a] sofern Pembrolizumab neoadjuvant begonnen wurde; [b] nach A/T-haltiger Chemotherapie; [c] nach Chemotherapie mit Platin und/oder Pembrolizumab.

A-BRAVE Trial - Study Design

Investigator-driven study, sponsored by University of Padova.
Drug supply and Grant support by Merck KGaA.

High Risk TNBC patients who completed locoregional and systemic treatment with curative intent

Key eligibility criteria:
- Age ≥18 years
- ECOG PS 0-1
- TNBC (ER & PgR <10%, HER2 0-1+ or 2+ FISH-)^
- Anthracycline and taxane (neo)-adjuvant ChemoRx
- Tissue samples for central PD-L1 assessment
- Randomization <10 weeks from last chemo or surgery

- **Stratum A (Adjuvant): pT2N1, pT3-4 N0-3, pN2-3 anyT#**
- **Stratum B (Post-neoadjuvant): residual invasive carcinoma in the breast and/or axillary lymph nodes§***

R 1:1
N=477

Avelumab
10mg/kg, iv, q 2 weeks for 52 weeks

Observation

In case of ER 1-9%, adjuvant HT allowed at discretion of treating physicians.
Whenever indicated, radiotherapy allowed concomitantly with avelumab.

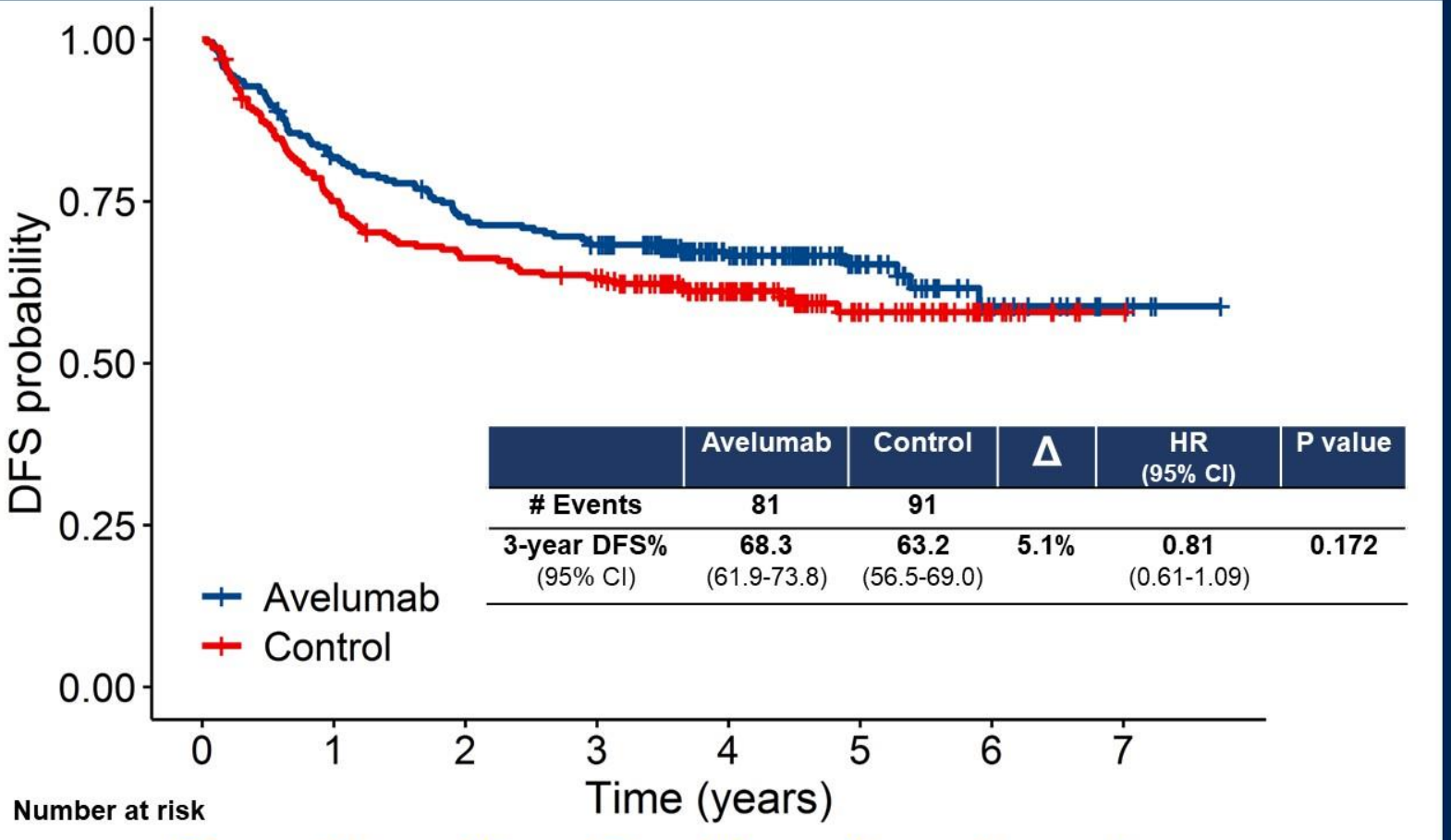
^for patients in the neoadjuvant stratum, TN status required in the preoperative and in the post-surgical specimen
 # trial initially limited to pN≥2; protocol amendment in 10/2017 to include patents with pT2N1 and pT3-4 N0-3 disease stage
§ excluding ypT1micN0, ypT1micN0i+, ypT0N0i+
*** After amendment on 06/2018, patients in stratum B were allowed to receive additional post-operative chemotherapy and were randomized at completion of treatment.**
Randomization balanced for Stratum A and Stratum B.

EUDRACT 2016-000189-45; NCT 02926196

PRESENTED BY: Pierfranco Conte, MD

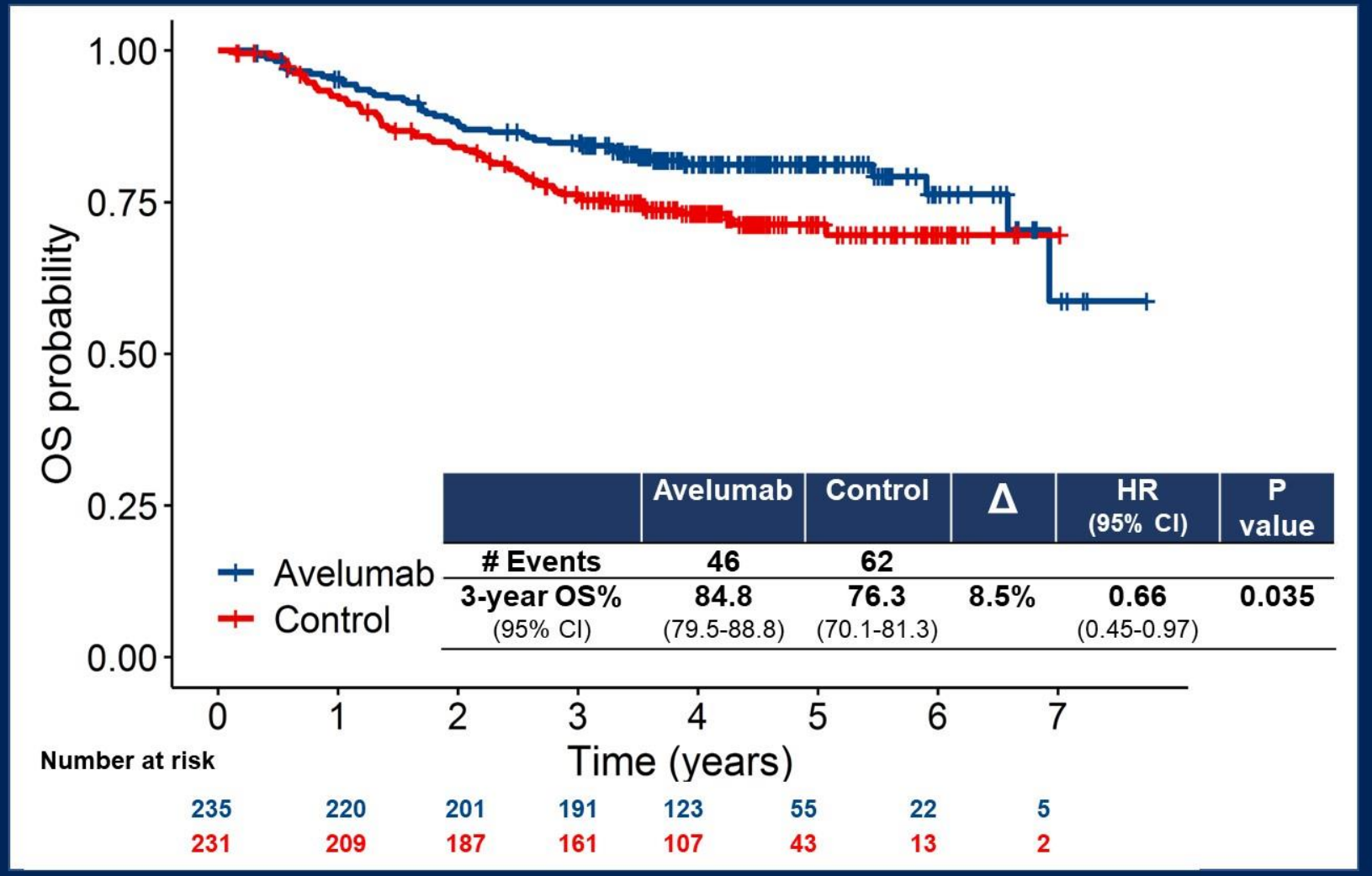
A-BRAVE Trial - Disease-Free Survival, ITT (co-primary end point)

median FUp: 52.1 months (95% CI: 49.8- 53.8)



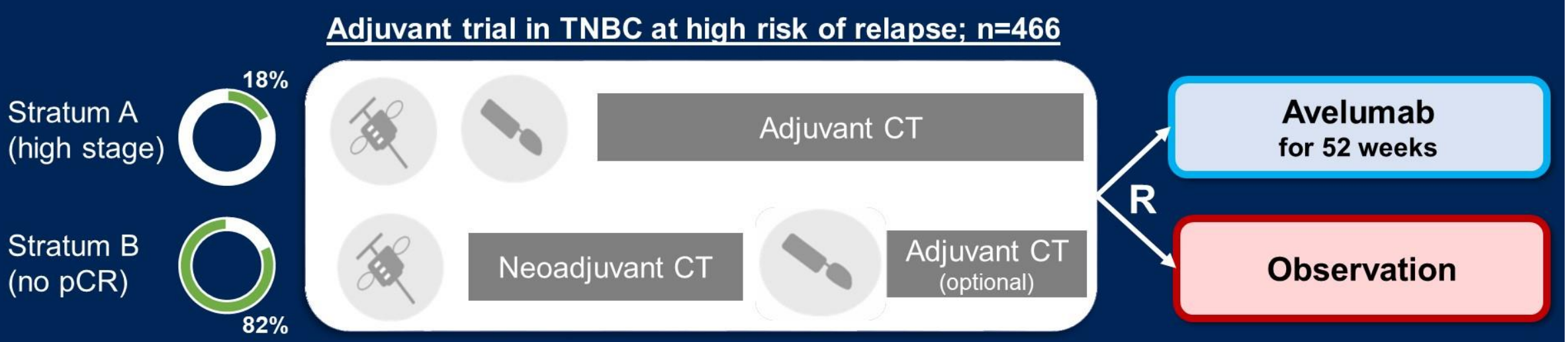
	Avelumab	Control	Δ	HR (95% CI)	P value
# Events	81	91			
3-year DFS% (95% CI)	68.3 (61.9-73.8)	63.2 (56.5-69.0)	5.1%	0.81 (0.61-1.09)	0.172

A-BRAVE Trial - Overall Survival, ITT (secondary endpoint)



	Avelumab	Control	Δ	HR (95% CI)	P value
# Events	46	62			
3-year OS% (95% CI)	84.8 (79.5-88.8)	76.3 (70.1-81.3)	8.5%	0.66 (0.45-0.97)	0.035

A-BRAVE Trial - Key findings



- **Primary endpoint DFS: *not met***
- **Secondary endpoint OS: *significant improvement with Avelumab***
- **Exploratory endpoint DDFS: *significant improvement with Avelumab***
- **Safety of Avelumab: no new safety signal; rare G ≥3 irAEs**

2024 ASCO ANNUAL MEETING

DESTINY BREAST06

Trastuzumab deruxtecan vs physician's choice of chemotherapy in patients with hormone receptor–positive, human epidermal growth factor receptor 2 (HER2)–low or HER2-ultralow metastatic breast cancer with prior endocrine therapy: primary results from DESTINY-Breast06

Giuseppe Curigliano
European Institute of Oncology, IRCCS, Milan, Italy;
Department of Oncology and Hematology-Oncology, University of Milan, Italy

Sunday, June 2, 2024

Additional authors: Xichun Hu, Rebecca Dent, Kan Yonemori, Carlos H Barrios, Joyce A O'Shaughnessy, Hans Wildiers, Qingyuan Zhang, Seock-Ah Im, Cristina Saura, Laura Biganzoli, Joohyuk Sohn, Christelle Lévy, William Jacot, Natasha Begbie, Jun Ke, Gargi Patel, Aditya Bardia

On behalf of the DESTINY-Breast06 investigators

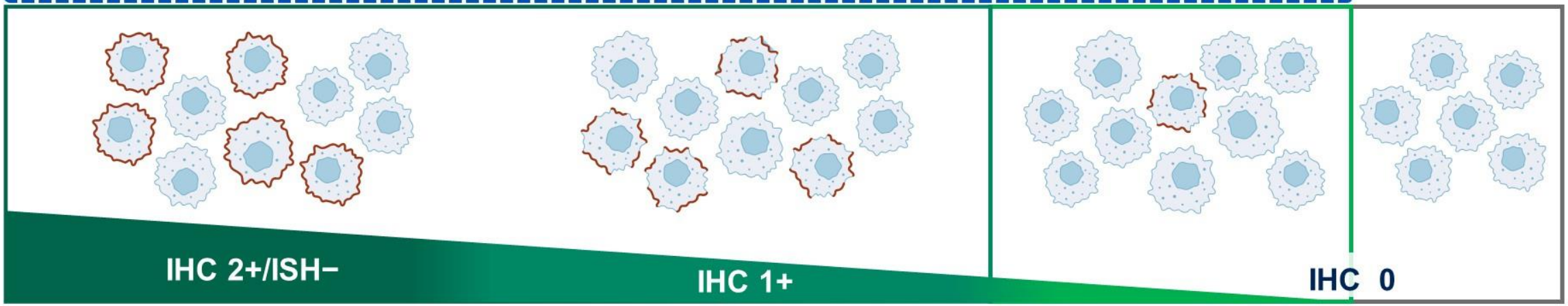
Targeting 'low' and 'ultralow' HER2-expressing tumors in mBC

HER2 IHC categories within HR+, HER2-negative (HER2−) mBC (per ASCO/CAP[1])

DESTINY-Breast06 patient population: ~85% of HR+, HER2− mBC

HER2-low ~60–65%[2,3]

HER2-ultralow ~20–25%[2–4]



IHC 2+/ISH−	IHC 1+	IHC 0	
Weak-to-moderate complete membrane staining in >10% tumor cells	Faint, incomplete membrane staining in >10% tumor cells	**Faint, incomplete membrane staining in ≤10% tumor cells**	Absent / no observable membrane staining

ASCO/CAP, American Society of Clinical Oncology / College of American Pathologists; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor–positive; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; T-DXd, trastuzumab deruxtecan

1. Wolff AC, et al. *J Clin Oncol*. 2023;41:3867–3872; 2. Denkert C, et al. *Lancet Oncol*. 2021;22:1151–1161; 3. Chen Z, et al. *Breast Cancer Res Treat*. 2023;202:313–323; 4. Mehta S, et al. *J Clin Oncol*. 2024;42(Suppl. 16):Abstract e13156

Study design

DESTINY-Breast06: a Phase 3, randomized, multicenter, open-label study (NCT04494425)

PATIENT POPULATION

- HR+ mBC
- HER2-low (IHC 1+ or IHC 2+/ISH−) or HER2-ultralow (IHC 0 with membrane staining)*
- **Chemotherapy naïve in the mBC setting**

Prior lines of therapy

- ≥2 lines of ET ± targeted therapy for mBC
  OR
- 1 line for mBC **AND**
  - Progression ≤6 months of starting first-line ET + CDK4/6i
    OR
  - Recurrence ≤24 months of starting adjuvant ET

Stratification factors

- Prior CDK4/6i use (yes vs no)
- HER2 expression (IHC 1+ vs IHC 2+/ISH− vs IHC 0 with membrane staining)
- Prior taxane in the non-metastatic setting (yes vs no)

R 1:1

T-DXd
5.4 mg/kg Q3W
(n=436)

HER2-low = 713
HER2-ultralow = 153†

TPC
(n=430)

Options: capecitabine, nab-paclitaxel, paclitaxel

ENDPOINTS

Primary

- PFS (BICR) in HER2-low

Key secondary

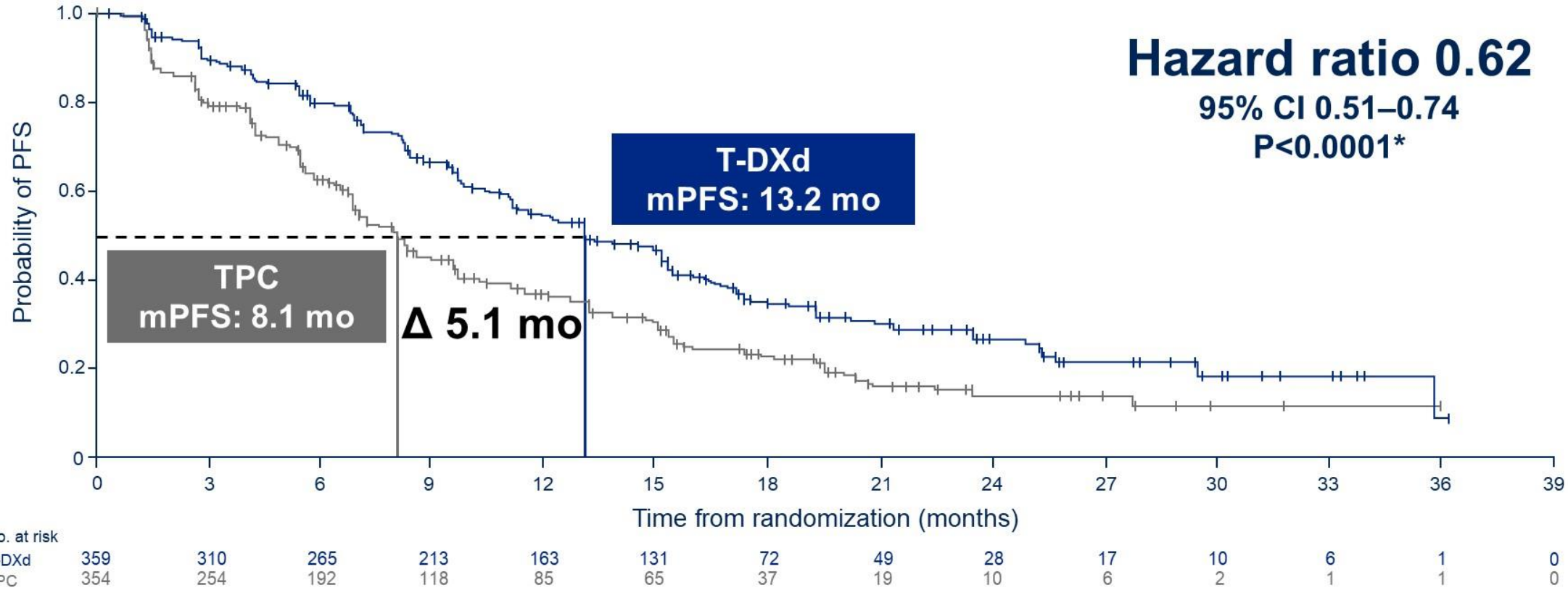
- PFS (BICR) in ITT (HER2-low + ultralow)
- OS in HER2-low
- OS in ITT (HER2-low + ultralow)

Other secondary

- PFS (INV) in HER2-low
- ORR (BICR/INV) and DOR (BICR/INV) in HER2-low and ITT (HER2-low + ultralow)
- Safety and tolerability
- Patient-reported outcomes‡

*Study enrollment was based on central HER2 testing. HER2 status was determined based on the most recent evaluable HER2 IHC sample prior to randomization. HER2-ultralow was defined as faint, partial membrane staining in ≤10% of tumor cells (also known as IHC >0<1+); †HER2-ultralow status as determined per IRT data (note: efficacy analyses in the HER2-ultralow subgroup were based on n=152 as determined per central laboratory testing data); ‡to be presented separately
BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor–positive; IHC, immunohistochemistry; INV, investigator assessed; IRT, interactive response technology; ISH, in situ hybridization; ITT, intent-to-treat; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice
NCT04494425. Updated. April 12, 2024. Available from: https://clinicaltrials.gov/study/NCT04494425 (Accessed May 13, 2024)

PFS (BICR) in HER2-low: primary endpoint



T-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with standard-of-care chemotherapy in HER2-low

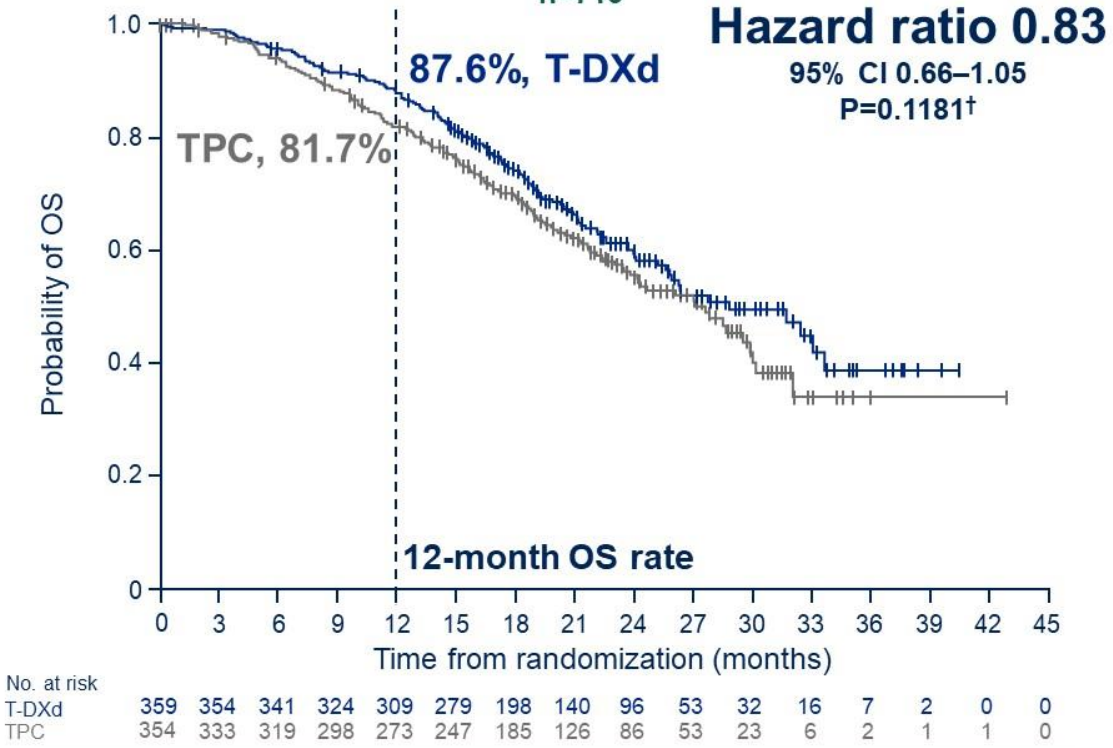
*P-value of <0.05 required for statistical significance
BICR, blinded independent central review; CI, confidence interval; HER2, human epidermal growth factor receptor 2; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

PRESENTED BY: Giuseppe Curigliano, MD, PhD

OS in HER2-low and ITT: key secondary endpoints (~40% maturity)

HER2-low*

n=713



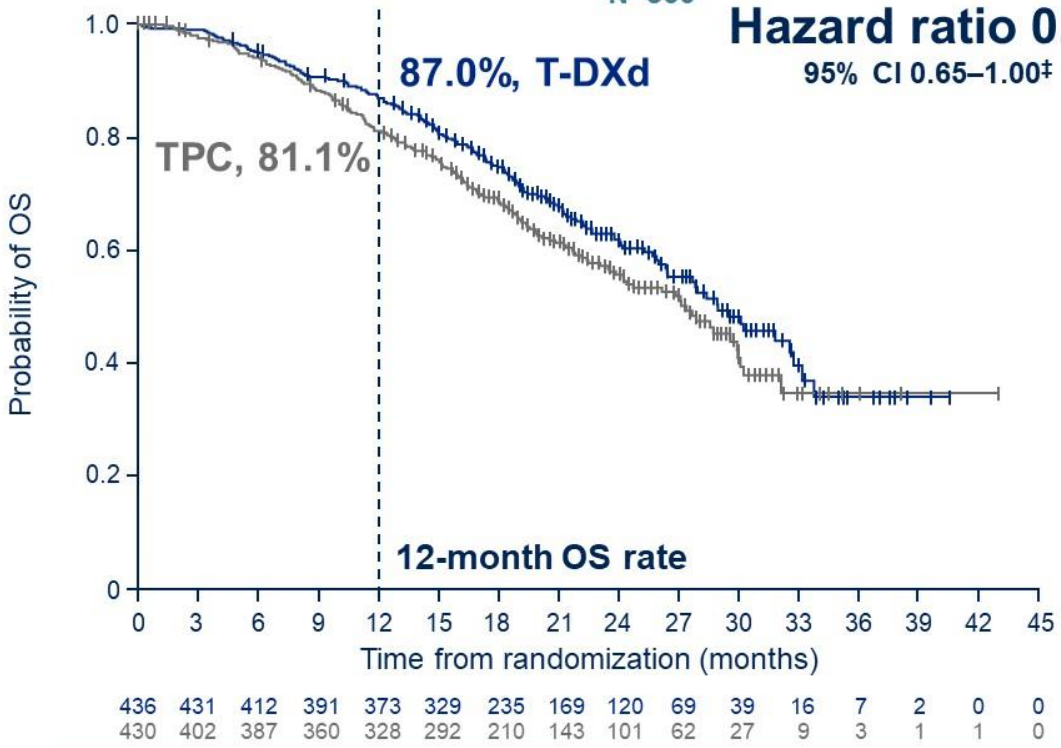
No. at risk

T-DXd	359	354	341	324	309	279	198	140	96	53	32	16	7	2	0	0
TPC	354	333	319	298	273	247	185	126	86	53	23	6	2	1	1	0

20.1% of patients in the TPC group received T-DXd post treatment discontinuation (HER2-low)

ITT (HER2-low + HER2-ultralow)

N=866



T-DXd	436	431	412	391	373	329	235	169	120	69	39	16	7	2	0	0
TPC	430	402	387	360	328	292	210	143	101	62	27	9	3	1	1	0

17.9% of patients in the TPC group received T-DXd post treatment discontinuation (ITT)

*39.6% maturity (of total N for population) at this first interim analysis; median duration of follow up was 18.6 months (HER2-low); †P-value of <0.0046 required for statistical significance; ‡no test of significance was performed in line with the multiple testing procedure; median duration of follow up was 18.2 months (ITT)

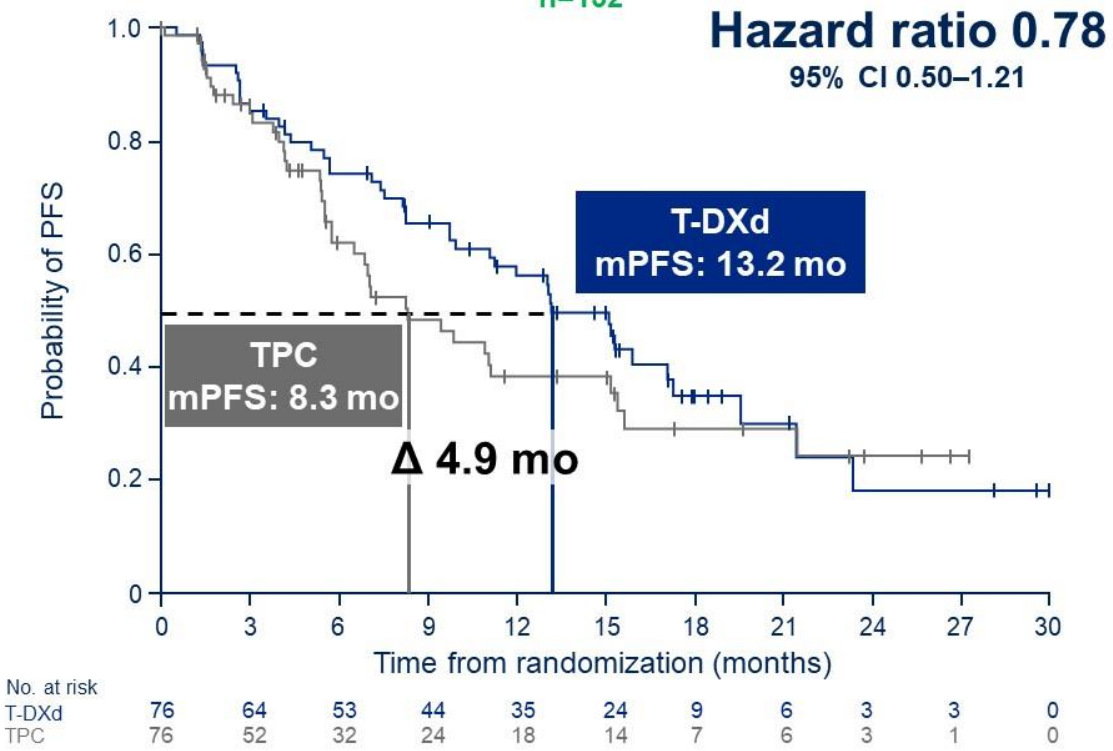
CI, confidence interval; HER2, human epidermal growth factor receptor 2; ITT, intent-to-treat; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

PRESENTED BY: Giuseppe Curigliano, MD, PhD

PFS and OS in HER2-ultralow: prespecified exploratory analyses

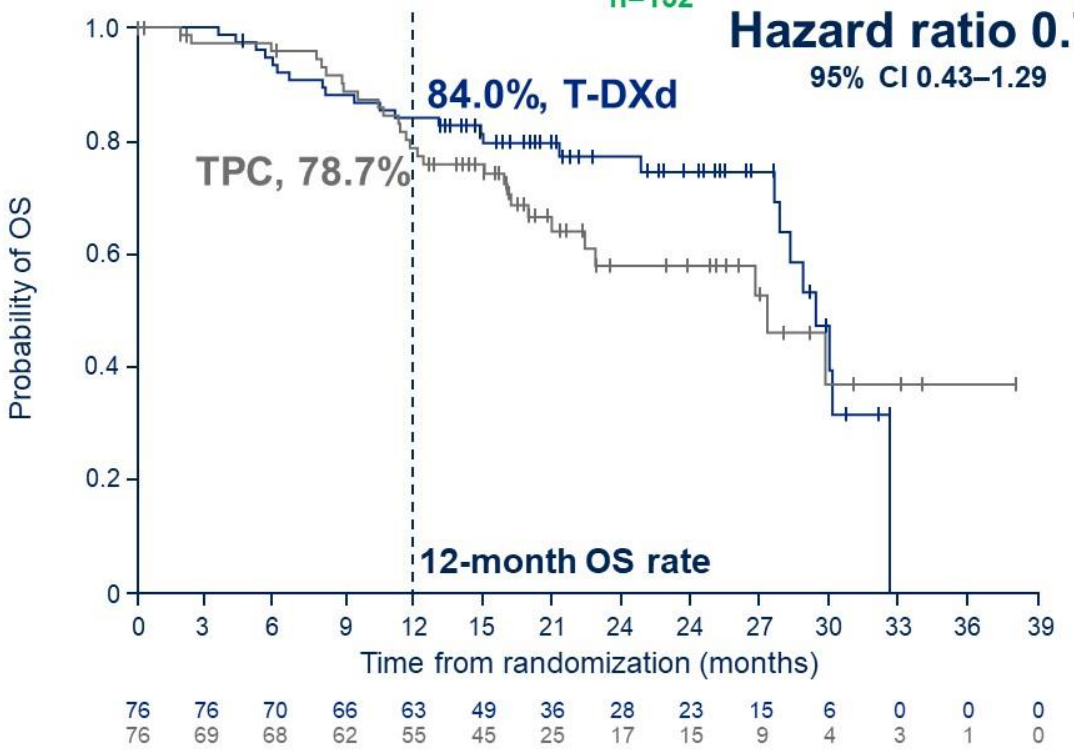
PFS (BICR)

n=152



OS*

n=152



PFS improvement with T-DXd vs TPC in HER2-ultralow was consistent with results in HER2-low

*34.9% maturity (of total N for population) at this first interim analysis; median duration of follow up was 16.8 months
BICR, blinded independent central review; CI, confidence interval; HER2, human epidermal growth factor receptor 2; OS, overall survival; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

PRESENTED BY: Giuseppe Curigliano, MD, PhD

2024 ASCO ANNUAL MEETING

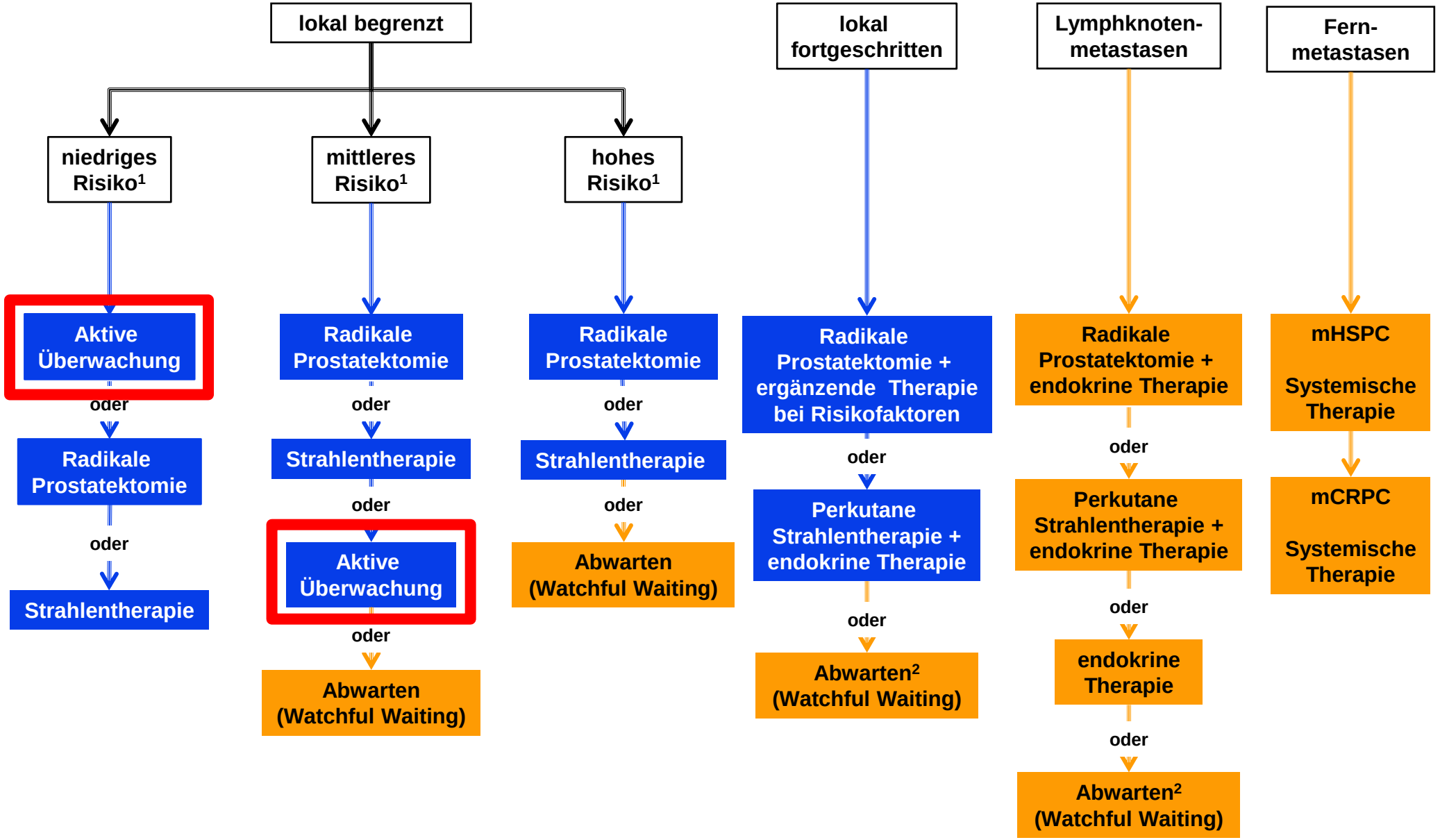
UHN Princess Margaret Cancer Centre

ABSTRACT LBA5002: A randomized, double-blind, placebo-controlled trial of metformin in reducing progression among men on expectant management for low-risk prostate cancer: The MAST (Metformin Active Surveillance Trial) study.

Neil E. Fleshner, Rui Miguel Bernardino, Katherine Lajkosz, Fred Saad, Jonathan Izawa, Darrel Drachenberg, Jeff W. Saranchuk, Simon Tanguay, Ricardo A. Rendon, Michael Leveridge, Bobby Shayegan, Adrian Fairey, Jessica Grace Cockburn, Doron Berlin, Robert James Hamilton, Tiiu Sildva, Rodney H. Breau, Patrick O. Richard, Laurence Klotz, Anthony M. Joshua

Prof. Anthony Joshua BSc(Med) MBBS PhD FRACP
Princess Margaret Cancer Centre, Toronto, Canada
Kinghorn Cancer Centre, St Vincents Hospital, Sydney, Australia

Anthony.Joshua@svha.org.au @AnthonyMJoshua @FleshnerNeil


lokal begrenzt
niedriges Risiko[1]
mittleres Risiko[1]
hohes Risiko[1]
Aktive Überwachung
oder
Radikale Prostatektomie
oder
Strahlentherapie
Radikale Prostatektomie
oder
Strahlentherapie
oder
Aktive Überwachung
oder
Abwarten (Watchful Waiting)
Radikale Prostatektomie
oder
Strahlentherapie
oder
Abwarten (Watchful Waiting)
lokal fortgeschritten
Radikale Prostatektomie + ergänzende Therapie bei Risikofaktoren
oder
Perkutane Strahlentherapie + endokrine Therapie
oder
Abwarten[2] (Watchful Waiting)
Lymphknoten-metastasen
Radikale Prostatektomie + endokrine Therapie
oder
Perkutane Strahlentherapie + endokrine Therapie
oder
endokrine Therapie
oder
Abwarten[2] (Watchful Waiting)
Fern-metastasen
mHSPC
Systemische Therapie
mCRPC
Systemische Therapie

BACKGROUND: Rationale

BIOLOGICAL	EPIDEMIOLOGICAL	CLINICAL
Importance of insulin, mTOR signaling[1]	Reduction of PCa mortality in diabetic men[4]	Reduction of Ki67 in neoadjuvant trial[7]
Overcomes NKX3.1 loss[2]	Associated with less BCR[5]	Improved OS with Abiraterone[8]
Improved immune micro-environment[3]	Improved OS in SEER[6]	Reduces progression and improves OS in HSPC[9]

1 White-Al Habeeb et al., 2016.2 Papachristodoulou et al., 2024. 3.Liu et al., 2018.4Margel et al., 2013. 5Zannella et al., 2013. 6 Scarton et al., 2022. Joshua et al., 2014 8 Wilson et al., 2022 9.Alghandour et al., 2021.7

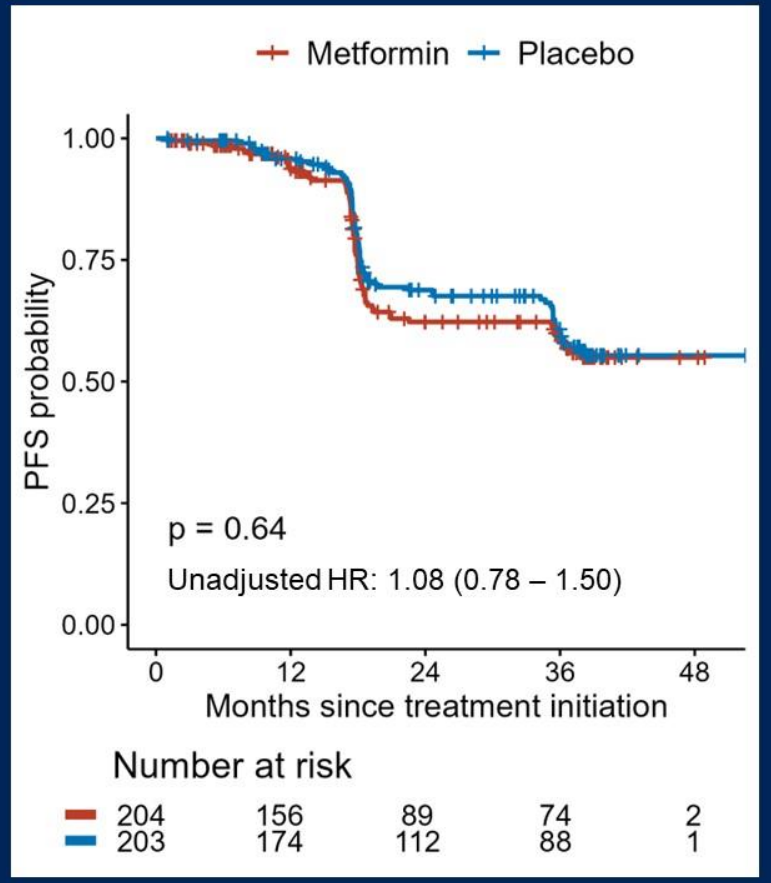
PRESENTED BY: Professor Anthony M.Joshua BSc (Med) (Hons) MBBS PhD (UToronto) FRACP

Baseline Demographics

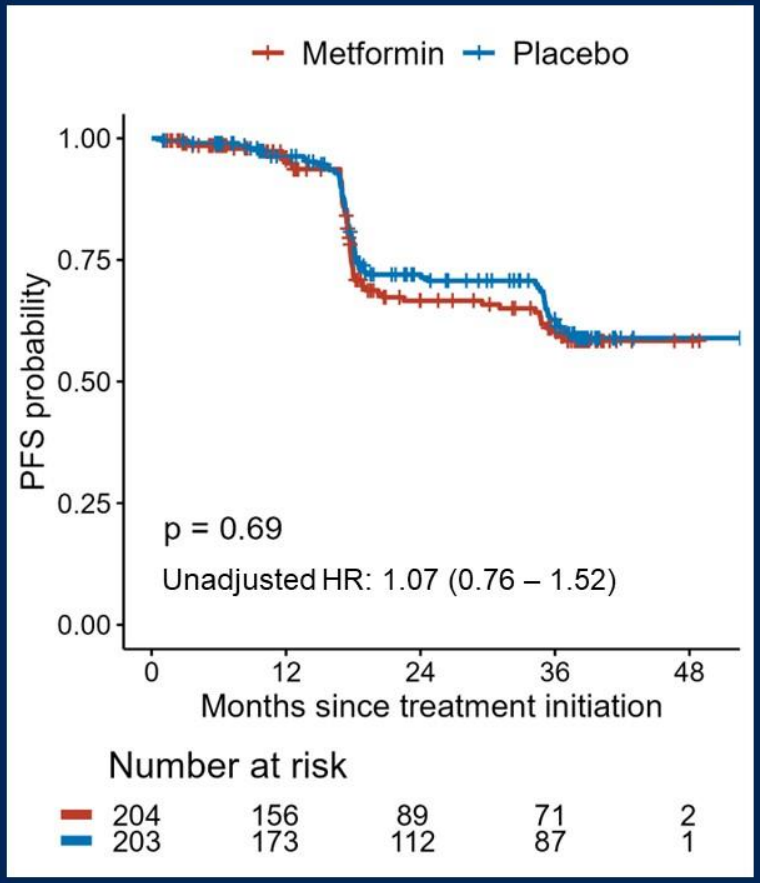
	Metformin (n=204)	Placebo (n=203)
Age		
Median (range)	62 (41 – 76)	63 (45 – 76)
Clinical Stage		
T1c (%)	189 (93.6)	185 (93.9)
T2a (%)	13 (6.4)	12 (6.1)
BMI		
Median (range)	27.4 (19.0 – 55.6)	27.7 (18.1 – 45.8)
PSA		
Median (range)	5.6 (0.8 – 31.4)	6.0 (0.4 – 16.1)
Positive Cores		
Median (range)	1 (0 – 7)	1 (0 – 6)
Tumour Volume		
Median (range)	43 (0 – 634)	44 (5.7 – 174)

Progression Free Survival

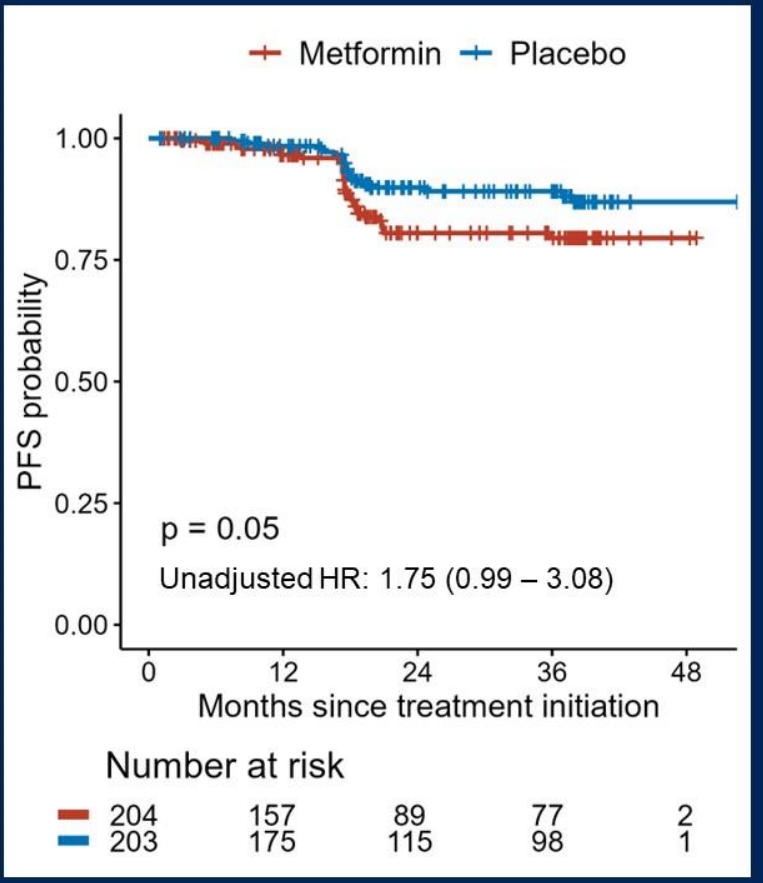
Therapeutic + Pathologic Progression



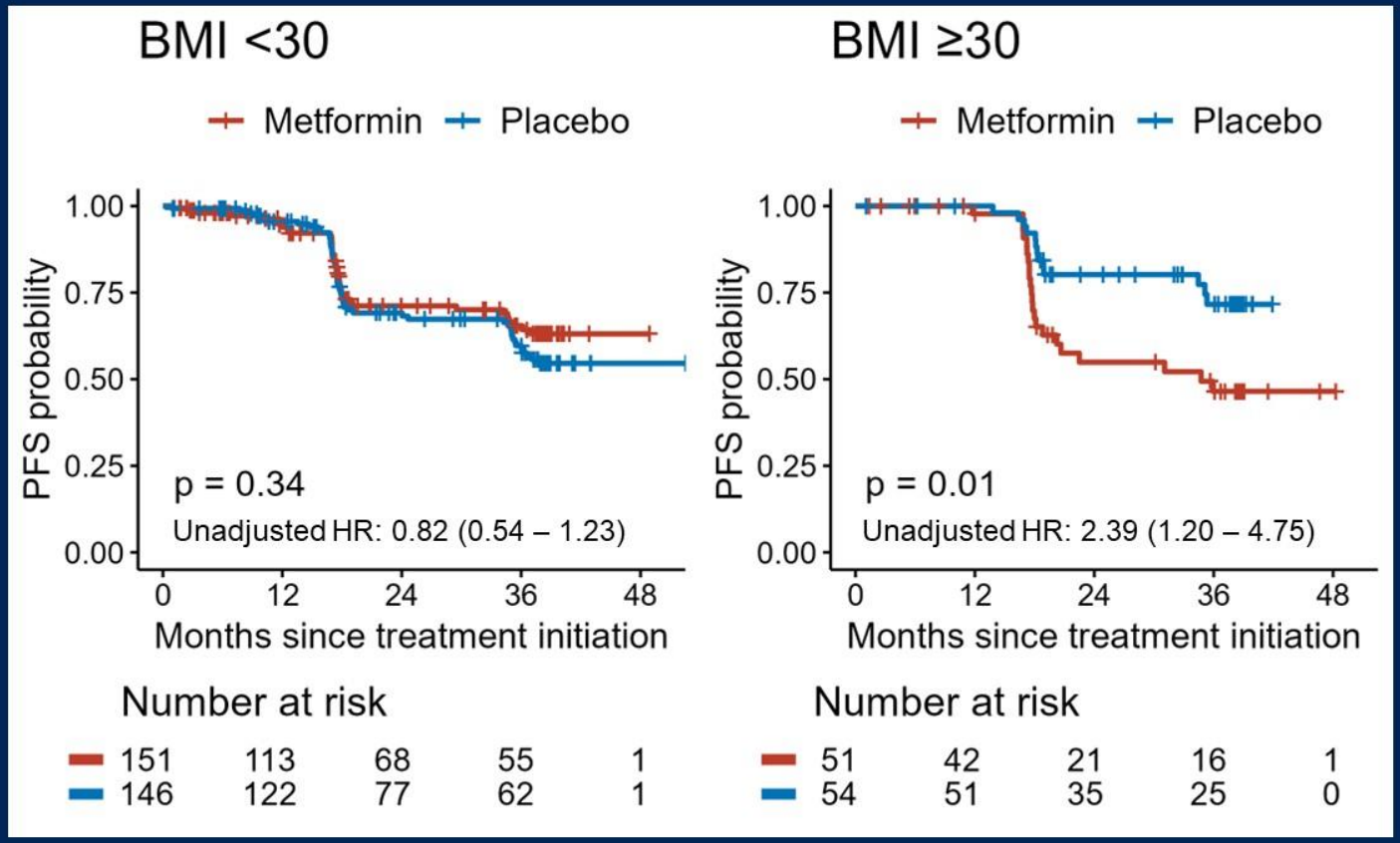
Pathologic Progression



Therapeutic Progression



BMI and Metformin with Pathologic Progression



Test for Interaction
Unadjusted p=0.012
Adjusted p=0.032

2024 ASCO ANNUAL MEETING

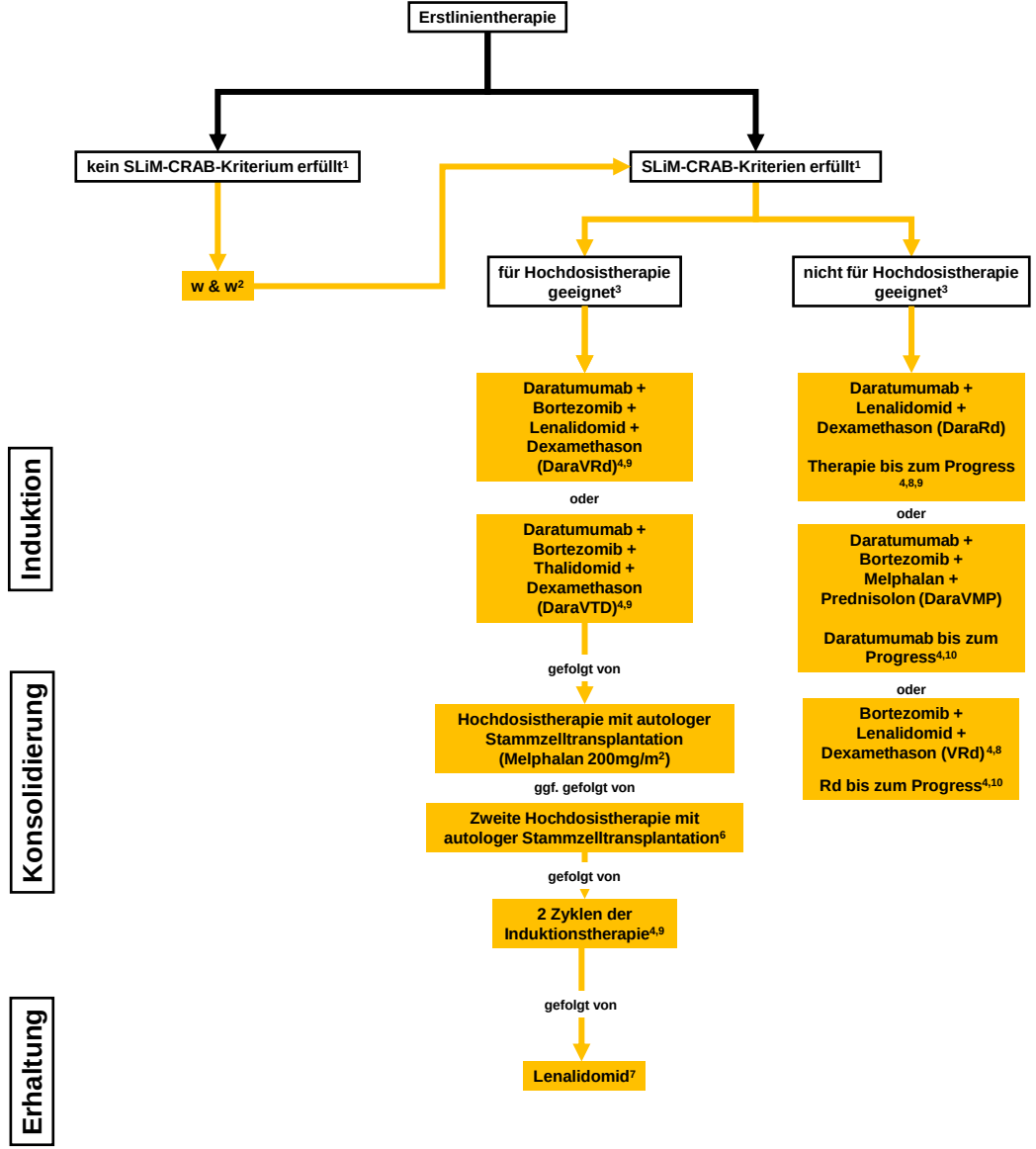
IMROZ

Phase 3 Study Results of Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone (Isa-VRd) Versus VRd for Transplant-Ineligible Patients With Newly Diagnosed Multiple Myeloma (IMROZ)

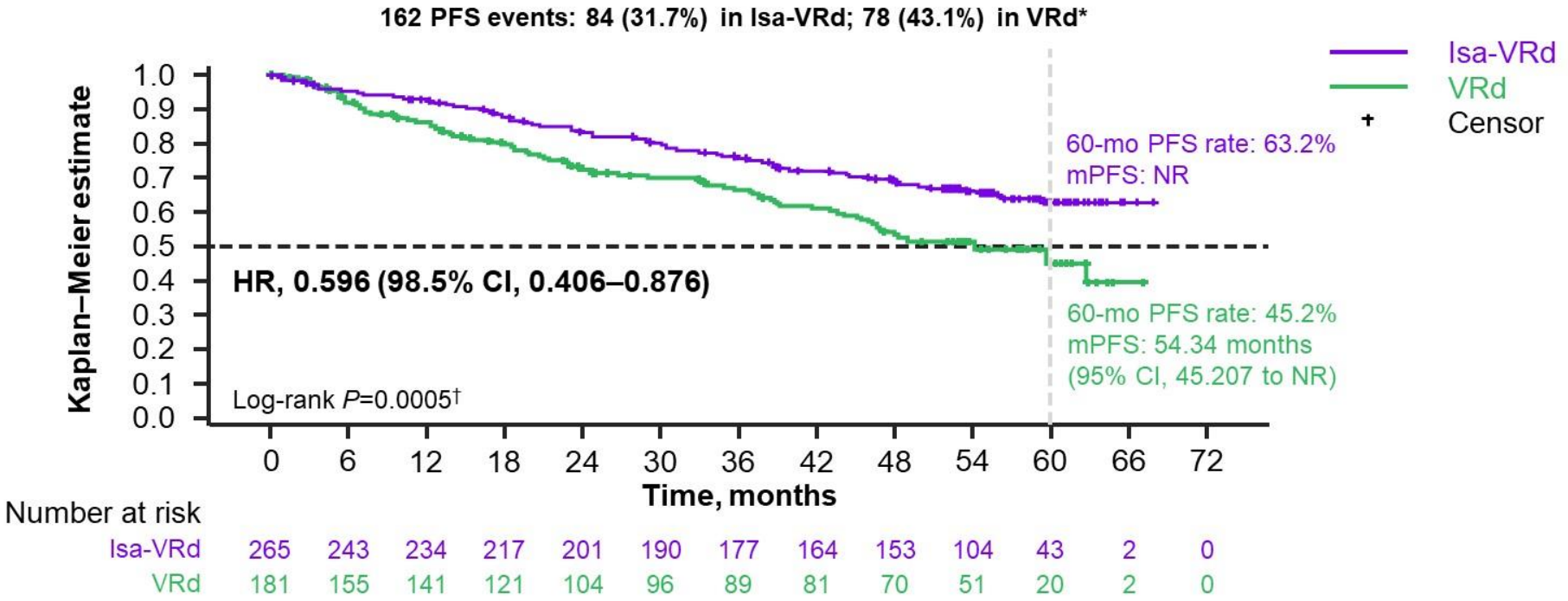
Thierry Facon,[1] Meletios-Athanasios Dimopoulos,[2] Xavier Leleu,[3] Meral Beksac,[4,5] Ludek Pour,[6] Roman Hajek,[7] Zhuogang Liu,[8] Jiri Minarik,[9] Philippe Moreau,[10] Joanna Romejko-Jarosinska,[11] Ivan Spicka,[12] Vladimir Vorobyev,[13] Michele Cavo,[14] Hartmut Goldschmidt,[15] Thomas Martin,[16] Salomon Manier,[17] Marie-France Brégeault,[18] Sandrine Macé,[18] Christelle Berthou,[18] Robert Z. Orlowski[19]

[1]Department of Haematology, University of Lille, and French Academy of Medicine, Paris, France; [2]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, Greece; [3]Service d'Hématologie et Thérapie Cellulaire, CHU and CIC Inserm 1402, Poitiers Cedex, France; [4]Department of Hematology, Ankara University, Ankara, Turkey; [5]Istinye University Ankara Liv Hospital, Ankara, Turkey; [6]Department of Internal Medicine, Hematology and Oncology, University Hospital Brno, Brno, Czech Republic; [7]Department of Hemato-Oncology, University Hospital Ostrava and Faculty of Medicine, University of Ostrava, Ostrava, Czech Republic; [8]Shengjing Hospital of China Medical University (Huaxiang Br), Shenyang, China; [9]Department of Hemato-Oncology, University Hospital Olomouc and Faculty of Medicine and Dentistry, Palacky University Olomouc, Olomouc, Czech Republic; [10]Department of Hematology, University Hospital Hôtel-Dieu, Nantes, France; [11]Department of Lymphoid Malignancies, Marie Sklowdoska-Curie National Research Institute of Oncology, Warszawa, Poland; [12]Charles University and General Hospital in Prague, Prague, Czech Republic; [13]SP Botkin Moscow City Clinical Hospital, Moscow, Russia; [14]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli," Università di Bologna, Bologna, Italy; [15]Department of Internal Medicine V, University of Heidelberg, Heidelberg, Germany; [16]Department of Hematology, University of California at San Francisco, San Francisco, California, USA; [17]Department of Hematology, University Hospital Center of Lille, Lille, France; [18]Sanofi, R&D, Vitry-sur-Seine, France; [19]Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA.

PRESENTED BY: Thierry Facon, MD


Erstlinientherapie
kein SLiM-CRAB-Kriterium erfüllt[1]
SLiM-CRAB-Kriterien erfüllt[1]
w & w[2]
für Hochdosistherapie geeignet[3]
nicht für Hochdosistherapie geeignet[3]
Induktion
Konsolidierung
Erhaltung
Daratumumab + Bortezomib + Lenalidomid + Dexamethason (DaraVRd)[4,9]
oder
Daratumumab + Bortezomib + Thalidomid + Dexamethason (DaraVTD)[4,9]
gefolgt von
Hochdosistherapie mit autologer Stammzelltransplantation (Melphalan 200mg/m²)
ggf. gefolgt von
Zweite Hochdosistherapie mit autologer Stammzelltransplantation[6]
gefolgt von
2 Zyklen der Induktionstherapie[4,9]
gefolgt von
Lenalidomid[7]
Daratumumab + Lenalidomid + Dexamethason (DaraRd)
Therapie bis zum Progress[4,8,9]
oder
Daratumumab + Bortezomib + Melphalan + Prednisolon (DaraVMP)
Daratumumab bis zum Progress[4,10]
oder
Bortezomib + Lenalidomid + Dexamethason (VRd)[4,8]
Rd bis zum Progress[4,10]

Primary endpoint met: Interim PFS analysis–IRC assessment in ITT population



At a median follow-up of 5 years (59.7 months), Isa-VRd followed by Isa-Rd led to a statistically significant reduction in the risk of progression or death by 40.4%

*Cutoff date for PFS analysis: September 26, 2023 (median follow-up, ~5 years). †Nominal one-sided *P* value.
NR, not reached.

The NEW ENGLAND JOURNAL of MEDICINE

IMROZ

ORIGINAL ARTICLE

Isatuximab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma

T. Facon, M.-A. Dimopoulos, X.P. Leleu, M. Beksac, L. Pour, R. Hájek, Z. Liu, J. Minarik, P. Moreau, J. Romejko-Jarosinska, I. Spicka, V.I. Vorobyev, B. Besemer, T. Ishida, W. Janowski, S. Kalayoglu-Besisik, G. Parmar, P. Robak, E. Zamagni, H. Goldschmidt, T.G. Martin, S. Manier, M. Mohty, C. Oprea, M.-F. Brégeault, S. Macé, C. Berthou, D. Bregman, Z. Klippel, and R.Z. Orlowski, for the IMROZ Study Group*

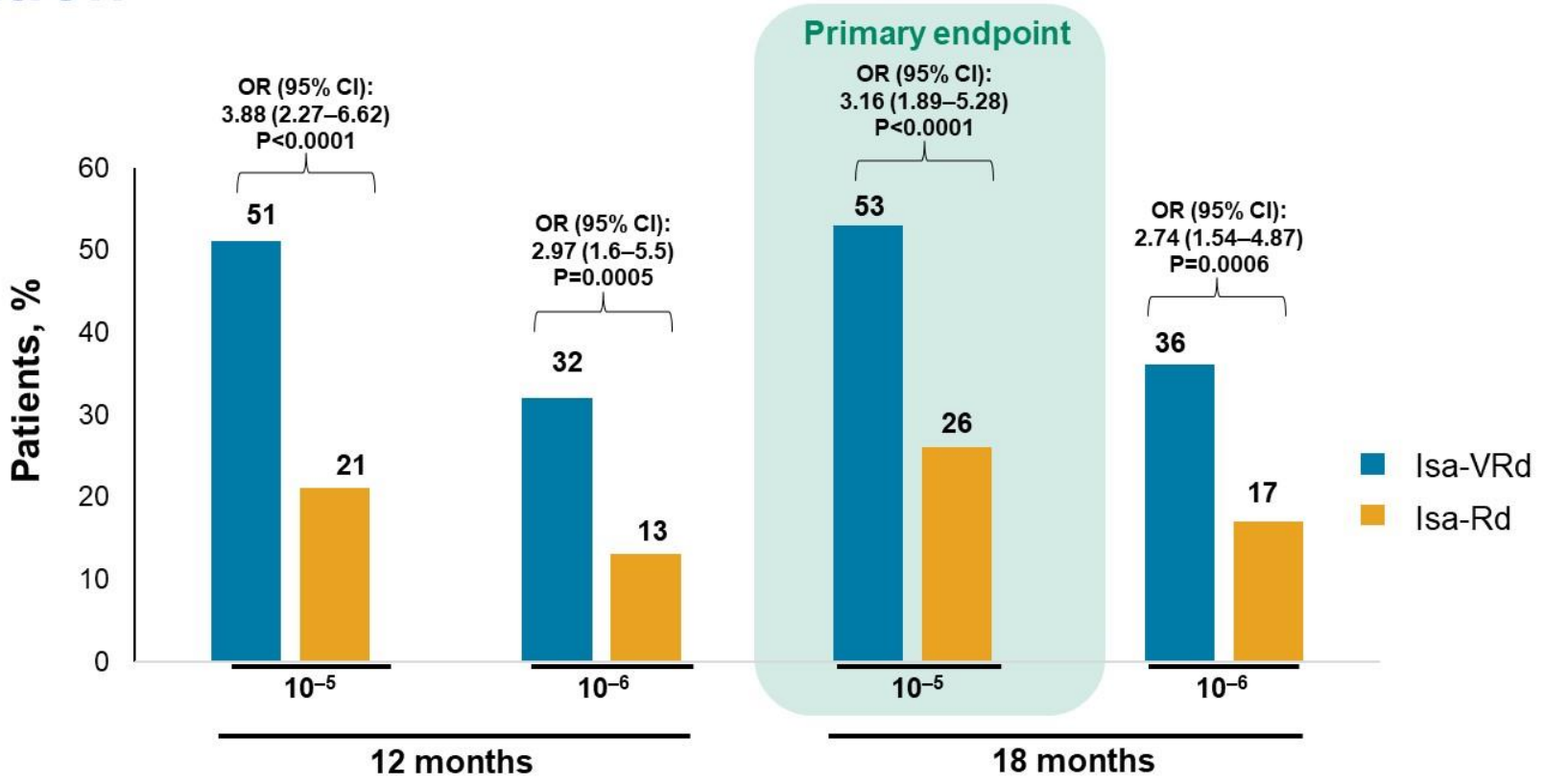
2024 ASCO ANNUAL MEETING

Isatuximab plus lenalidomide and dexamethasone with weekly bortezomib versus isatuximab plus lenalidomide and dexamethasone in newly diagnosed transplant ineligible Multiple Myeloma. The BENEFIT (IFM 2020-05) study

Xavier Leleu[1] and Cyrille Hulin[2], Lambert Jerome[3], Arthur Bobin[1], Aurore Perrot[4], Lionel Karlin[5], Roussel Murielle[6], Lydia Montes[7], Brieuc Cherel[8], Thomas Chalopin[9], Borhane Slama[10], Marie-Lorraine Chretien[11], Kamel Laribi[12], Claire Dingremont[13], Christophe Roul[14], Clara Mariette[15], Sophie Rigaudeau[16], Claire Calmettes[17], Mamoun Dib[18], Mourad Tiab[19], Laure Vincent[20], Jacques Delaunay[21], Alberto Santagostino[22], Margaret Macro[23], Emmanuelle Bourgeois[24], Frederique Orsini-Piocelle[25], Julie Gay[26], Benoit Bareau[27], Noemie Bigot[3], François Vergez[28], Pierre Lebreton[29], Reza Tabrizi[30], Agathe Waultier-Rascalou[31], Laurent Frenzel[32], Ronan Le Calloch[33], Emilie Chalayer[34], Thorsten Braun[35], Florence Lachenal[36], Selim Corm[37], Celine Kennel[38], Rakiba Belkhir[39], Jean-Sebastien Bladé[40], Bertrand Joly[41], Valentine Richez-Olivier[42], Helene Demarquette[43], Daniela Robu-Cretu[44], Laurent Garderet [45], Muriel Newinger-Porte[46], Amine Kasmi[47], Bruno Royer[48], Olivier Decaux[49], Bertrand Arnulf[48], Karim Belhadj[50], Cyrille Touzeau[51], Mohamad Mohty[52], Salomon Manier[53], Philippe Moreau[51], Hervé Avet-Loiseau[28], Jill Corre[28], Thierry Facon[53]

PRESENTED BY: Xavier Leleu, MD, PhD

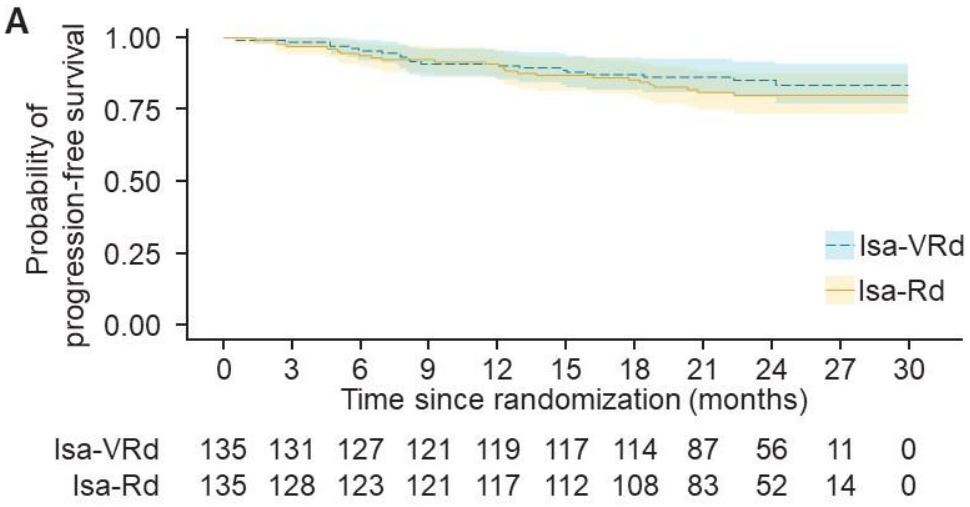
Primary endpoint: MRD–* rate at 18 months – ITT population

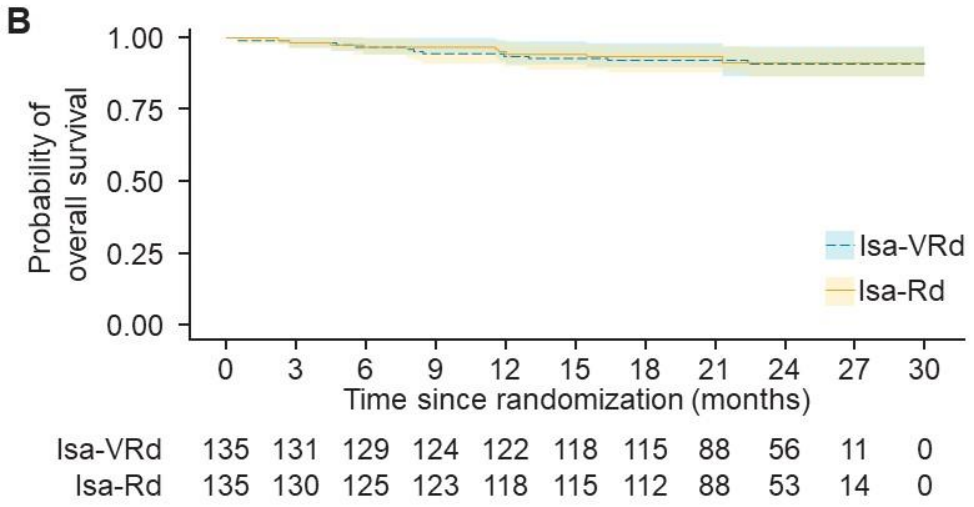


Isa-VRd resulted in deep response rates, with a significant improvement in the MRD at 12 and 18 months, and at 10^{-5} and 10^{-6} in the ITT population

*MRD was assessed on the basis of IMWG recommendations.[1]
CI, confidence interval; Isa, isatuximab; ITT, intent-to-treat; MRD–, minimal residual disease negativity; NGS, next generation sequencing; OR, odd ratio; R, lenalidomide; V, bortezomib.
1. Kumar S, et al. *Lancet Oncol* 2016;17:e328–e346.

Survival analysis-IRC assessment in ITT population





Estimated 24 months PFS
85.2% (95%CI 79.2–91.7) for Isa-VRd
80.0% (95% CI 73.3–87.4) for Isa-Rd

Estimated 24 months OS
91.1% (95%CI 86.1–96.4) for Isa-VRd
91.5% (95%CI 86.5–96.8) for Isa-Rd

At a median follow-up of 23.5 months, survival is still immature

d, dexamethasone; Isa, isatuximab; IRC, independent review committee; ITT, intent-to-treat; CI, confidence interval; OS, overall survival; PFS, progression-free survival; R, lenalidomide; V, bortezomib.

ORIGINAL ARTICLE

Belantamab Mafodotin, Bortezomib, and Dexamethasone for Multiple Myeloma

V. Hungria, P. Robak, M. Hus, V. Zherebtsova, C. Ward, P.J. Ho, A.C. Ribas de Almeida, R. Hajek, K. Kim, S. Grosicki, H. Sia, A. Bryant, M. Pitombeira de Lacerda, G. Aparecida Martinez, A.M. Sureda Balarí, I. Sandhu, C. Cerchione, P. Ganly, M. Dimopoulos, C. Fu, M. Garg, A.-O. Abdallah, A. Oriol, M.E. Gatt, M. Cavo, R. Rifkin, T. Fujisaki, M. Mielnik, N. Pirooz, A. McKeown, S. McNamara, X. Zhou, M. Nichols, E. Lewis, R. Rogers, H. Baig, L. Eccersley, S. Roy-Ghanta, J. Opalinska, and M.-V. Mateos, for the DREAMM-7 Investigators*

ABSTRACT

BACKGROUND

Belantamab mafodotin had single-agent activity in patients with relapsed or refractory multiple myeloma, a finding that supports further evaluation of the agent in combination with standard-care therapies.

METHODS

In this phase 3, open-label, randomized trial, we evaluated belantamab mafodotin, bortezomib, and dexamethasone (BVd), as compared with daratumumab, bortezomib, and dexamethasone (DVd), in patients who had progression of multiple myeloma after at least one line of therapy. The primary end point was progression-free survival. Key secondary end points were overall survival, response duration, and minimal residual disease (MRD)–negative status.

RESULTS

In total, 494 patients were randomly assigned to receive BVd (243 patients) or DVd (251 patients). At a median follow-up of 28.2 months (range, 0.1 to 40.0), median progression-free survival was 36.6 months (95% confidence interval [CI], 28.4 to not reached) in the BVd group and 13.4 months (95% CI, 11.1 to 17.5) in the DVd group (hazard ratio for disease progression or death, 0.41; 95% CI, 0.31 to 0.53; P<0.001). Overall survival at 18 months was 84% in the BVd group and 73% in the DVd group. An analysis of the restricted mean response duration favored BVd over DVd (P<0.001). A complete response or better plus MRD-negative status occurred in 25% of the patients in the BVd group and 10% of those in the DVd group. Grade 3 or higher adverse events occurred in 95% of the patients in the BVd group and 78% of those in the DVd group. Ocular events were more common in the BVd group than in the DVd group (79% vs. 29%); such events were managed with dose modifications, and events of worsening visual acuity mostly resolved.

CONCLUSIONS

As compared with DVd therapy, BVd therapy conferred a significant benefit with respect to progression-free survival among patients who had relapsed or refractory multiple myeloma after at least one line of therapy. Most patients had grade 3 or higher adverse events. (Funded by GSK; DREAMM-7 ClinicalTrials.gov number, NCT04246047; EudraCT number, 2018-003993-29.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Mateos can be contacted at mvmateos@usal.es or at Hospital Universitario de Salamanca, Paseo San Vicente, 58-182, 37007 Salamanca, Spain.

*A list of the DREAMM-7 Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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ORIGINAL ARTICLE

Belantamab Mafodotin, Pomalidomide, and Dexamethasone in Multiple Myeloma

Meletios Athanasios Dimopoulos, M.D., Meral Beksac, M.D., Ludek Pour, M.D., Sosana Delimpasi, M.D., Vladimir Vorobyev, M.D., Hang Quach, M.D., Ivan Spicka, C.Sc., Jakub Radocha, M.D., Ph.D., Pawel Robak, M.D., Ph.D., Kihyun Kim, M.D., Michele Cavo, M.D., Kazuhito Suzuki, M.D., Ph.D., Kristin Morris, Pharm.D., Farrah Pompilus, Ph.D., Amy Phillips-Jones, M.Sc., Xiaoou L. Zhou, M.D., Ph.D., Giulia Fulci, Ph.D., Neal Sule, M.B., B.S., M.D., Brandon E. Kremer, M.D., Ph.D., Joanna Opalinska, M.D., Ph.D., María-Victoria Mateos, M.D., Ph.D., and Suzanne Trudel, M.D., for the DREAMM-8 Investigators*

ABSTRACT

BACKGROUND

Triplet or quadruplet therapies incorporating proteasome inhibitors, immunomodulators, and anti-CD38 antibodies have led to prolonged survival among patients with newly diagnosed multiple myeloma; however, most patients have a relapse. Frontline lenalidomide therapy has increased the number of patients with lenalidomide-refractory disease at the time of the first relapse.

METHODS

In this phase 3, randomized, open-label trial, we evaluated belantamab mafodotin, pomalidomide, and dexamethasone (BPd), as compared with pomalidomide, bortezomib, and dexamethasone (PVd), in lenalidomide-exposed patients who had relapsed or refractory myeloma after at least one line of therapy. The primary end point was progression-free survival. Disease response and safety were also assessed.

RESULTS

A total of 302 patients underwent randomization; 155 were assigned to the BPd group, and 147 to the PVd group. At a median follow-up of 21.8 months (range, <0.1 to 39.2), the 12-month estimated progression-free survival with BPd was 71% (95% confidence interval [CI], 63 to 78), as compared with 51% (95% CI, 42 to 60) with PVd (hazard ratio for disease progression or death, 0.52; 95% CI, 0.37 to 0.73; P<0.001). Data on overall survival were immature. The percentage of patients with a response to treatment (partial response or better) was 77% (95% CI, 70 to 84) in the BPd group and 72% (95% CI, 64 to 79) in the PVd group; 40% (95% CI, 32 to 48) and 16% (95% CI, 11 to 23), respectively, had a complete response or better. Grade 3 or higher adverse events occurred in 94% of the patients in the BPd group and 76% of those in the PVd group. Ocular events occurred in 89% of the patients who received BPd (grade 3 or 4 in 43%) and 30% of those who received PVd (grade 3 or 4 in 2%); ocular events in the BPd group were managed with belantamab mafodotin dose modification. Ocular events led to treatment discontinuation in 9% of the patients in the BPd group and in no patients in the PVd group.

CONCLUSIONS

Among lenalidomide-exposed patients with relapsed or refractory myeloma, BPd conferred a significantly greater benefit than PVd with respect to progression-free survival, as well as deeper, more durable responses. Ocular events were common but were controllable by belantamab mafodotin dose modification. (Funded by GSK; DREAMM-8 ClinicalTrials.gov number, NCT04484623; EudraCT number, 2018-00434-21.)

The authors' affiliations are listed in the Appendix. Dr. Dimopoulos can be contacted at mdimop@med.uoa.gr or at 80 Vasilisis Sofias, 11528, Athens, Greece.

*A list of the DREAMM-8 Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Oral presentation #LBA6500

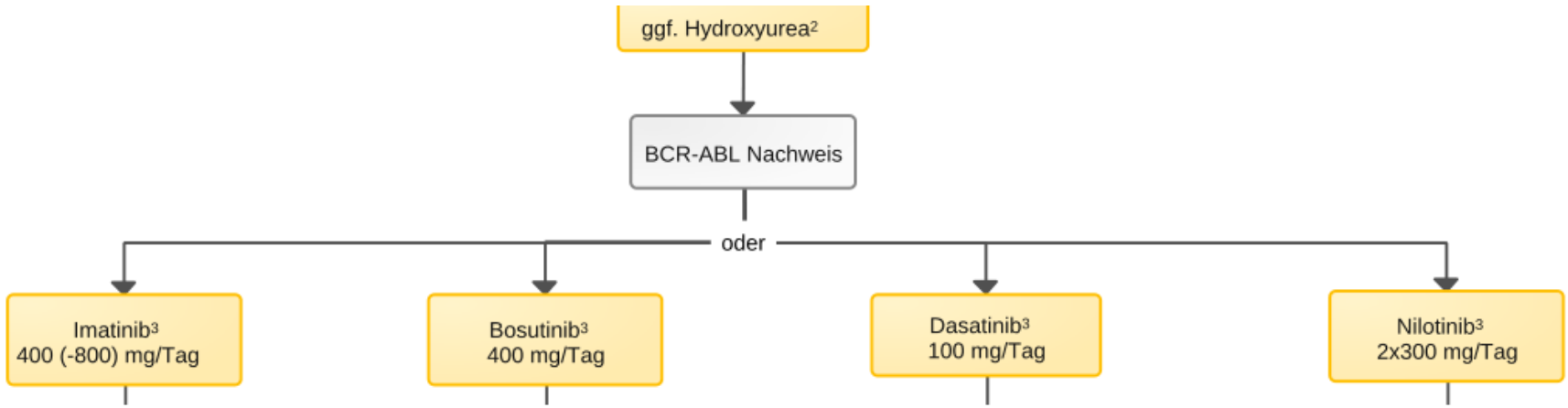
Timothy P. Hughes
Tim.Hughes@sahmri.com

ASC4FIRST, a Pivotal Phase 3 Study of Asciminib vs Investigator-Selected Tyrosine Kinase Inhibitors In Newly Diagnosed Patients with Chronic Myeloid Leukemia: Primary Results

Timothy P. Hughes, Andreas Hochhaus, Naoto Takahashi, Ghayas C. Issa, Richard A. Larson, Felice Bombaci, Jianxiang Wang, Dong-Wook Kim, Dennis Dong Hwan Kim, Jiri Mayer, Yeow-Tee Goh, Philipp Le Coutre, David J. Andorsky, Shruti Kapoor, Tracey McCulloch, Kamel Malek, Lillian Yau, Sophie Ifrah, Jorge E. Cortes

This study is sponsored by Novartis Pharmaceuticals Corporation. For more information, please refer to https://www.clinicaltrials.gov/study/NCT04971226.

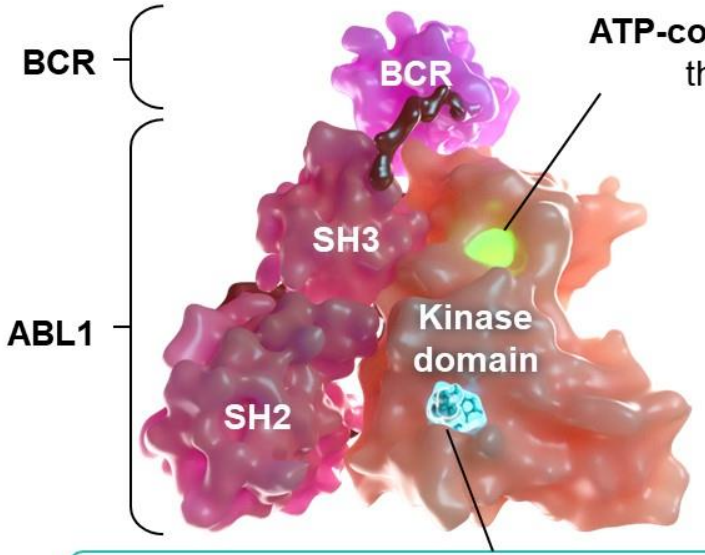
Oral presentation at: 2024 ASCO Annual Meeting; May 31-June 4, 2024; Chicago, Illinois, and virtual.


ggf. Hydroxyurea[2]
BCR-ABL Nachweis
oder
Imatinib[3]
400 (-800) mg/Tag
Bosutinib[3]
400 mg/Tag
Dasatinib[3]
100 mg/Tag
Nilotinib[3]
2x300 mg/Tag

Long-term therapeutic strategies for CML require treatments optimizing safety, tolerability, and efficacy

- Many newly diagnosed patients do not achieve optimal response with standard TKI therapy[1-3]
- Long-term use of 2G TKIs is associated with AEs, such as pleural effusion, GI events, and CV events.[4] Persistent AEs negatively affect patient adherence[5]

Asciminib: intentionally designed to improve efficacy and reduce off-target effects vs current ATP-competitive TKIs[6-8]



ATP-competitive TKIs target the ATP-binding site[8-10]

Frontline TKIs
- *Imatinib*
- *Nilotinib*
- *Dasatinib*
- *Bosutinib*

- *Ponatinib*
- *Olverembatinib*[a]
- *Radotinib*[b]

Asciminib Specifically Targets the ABL Myristoyl Pocket (STAMP)[6]

We report primary results from the phase 3 randomized ASC4FIRST trial of **asciminib vs investigator-selected (IS) TKIs** in patients with newly diagnosed CML-CP

AE, adverse event; ATP, adenosine triphosphate; CV, cardiovascular; GI, gastrointestinal; IS-TKI, investigator-selected TKI; SH, Src homology.
[a] Approved in China.
[b] Approved in South Korea.
Figure credit: Mauro MJ, et al. Presented at the 63rd American Society of Hematology Annual Meeting. Abstract 310. Reprinted with permission by the author.

Oral presentation at: 2024 ASCO Annual Meeting; May 31-June 4, 2024; Chicago, Illinois, and virtual.

ASC4FIRST, a head-to-head study comparing asciminib vs all standard-of-care TKIs in newly diagnosed patients with CML

NCT04971226

Key inclusion criteria

- Newly diagnosed Ph+ CML-CP with ***no*** prior TKIs[a]
- Age ≥18 years

Prerandomization TKI selection

- The TKI a patient will take if randomized to the investigator-selected (IS-TKI) arm
- Selected by the physician in consultation with the patient

Stratification by:

- Prerandomization TKI selection (IMA or 2G TKI)
- ELTS risk category (high, intermediate, low)

R 1:1

N=405

Asciminib (ASC) 80 mg QD

- Imatinib stratum: **ASC^{IMA}**
- 2G TKI stratum: **ASC^{2G}**

All IS-TKIs at label doses

- Imatinib stratum: **IS-TKI^{IMA}**
- 2G TKI stratum: **IS-TKI^{2G}**

End of study: LPFT + 5 years[b]

Data cutoff: Nov. 28, 2023

Primary endpoints:

- MMR at week 48 for asciminib vs all investigator-selected TKIs
- MMR at week 48 for asciminib vs investigator-selected TKI within the imatinib stratum

ASC, asciminib; ELTS, EUTOS long-term survival score; EUTOS, European Treatment and Outcome Study; IMA, imatinib; LPFT, last person first treatment; Ph, Philadelphia chromosome; QD, once daily; R, randomized.

[a] Either imatinib, bosutinib, dasatinib, or nilotinib is allowed for up to 2 weeks prior to randomization. Treatment with other TKIs prior to randomization was not permitted.

[b] Patients will remain on study for 5 years after the last patient first dose, unless they have discontinued early due to treatment failure, disease progression, pregnancy, intolerance, or investigator or patient decision.

Oral presentation at: 2024 ASCO Annual Meeting; May 31-June 4, 2024; Chicago, Illinois, and virtual.

Baseline characteristics were well balanced between asciminib and all IS-TKIs

Variable	Asciminib			IS-TKI		
	All asciminib (n=201)	Imatinib stratum (n=101)	2G TKI stratum (n=100)	All IS-TKI (n=204)	Imatinib stratum (n=102)	2G TKI stratum (n=102)
Median age (range), years	52.0 (18.0-79.0)	56.0 (21.0-79.0)	43.0 (18.0-76.0)	50.5 (19.0-86.0)	54.5 (20.0-86.0)	43.0 (19.0-83.0)
Age group, %						
18 to <65 years	77.1	68.3	86.0	76.0	68.6	83.3
65 to <75 years	17.9	23.8	12.0	16.7	21.6	11.8
≥75 years	5.0	7.9	2.0	7.4	9.8	4.9
Male, %	65.2	61.4	69.0	61.3	63.7	58.8
Framingham CV risk score, %[a]						
Low risk (<10%)	54.2	40.6	68.0	54.9	39.2	70.6
Intermediate risk (10%-20%)	15.9	20.8	11.0	21.6	28.4	14.7
High risk (≥20%)	29.9	38.6	21.0	23.5	32.4	14.7
ELTS, %[b]						
Low	60.7	61.4	60.0	61.3	62.7	59.8
Intermediate	27.9	29.7	26.0	27.9	29.4	26.5
High	11.4	8.9	14.0	10.8	7.8	13.7

[a] Framingham estimated 10-year cardiovascular disease risk categories.
[b] Based on randomization data.

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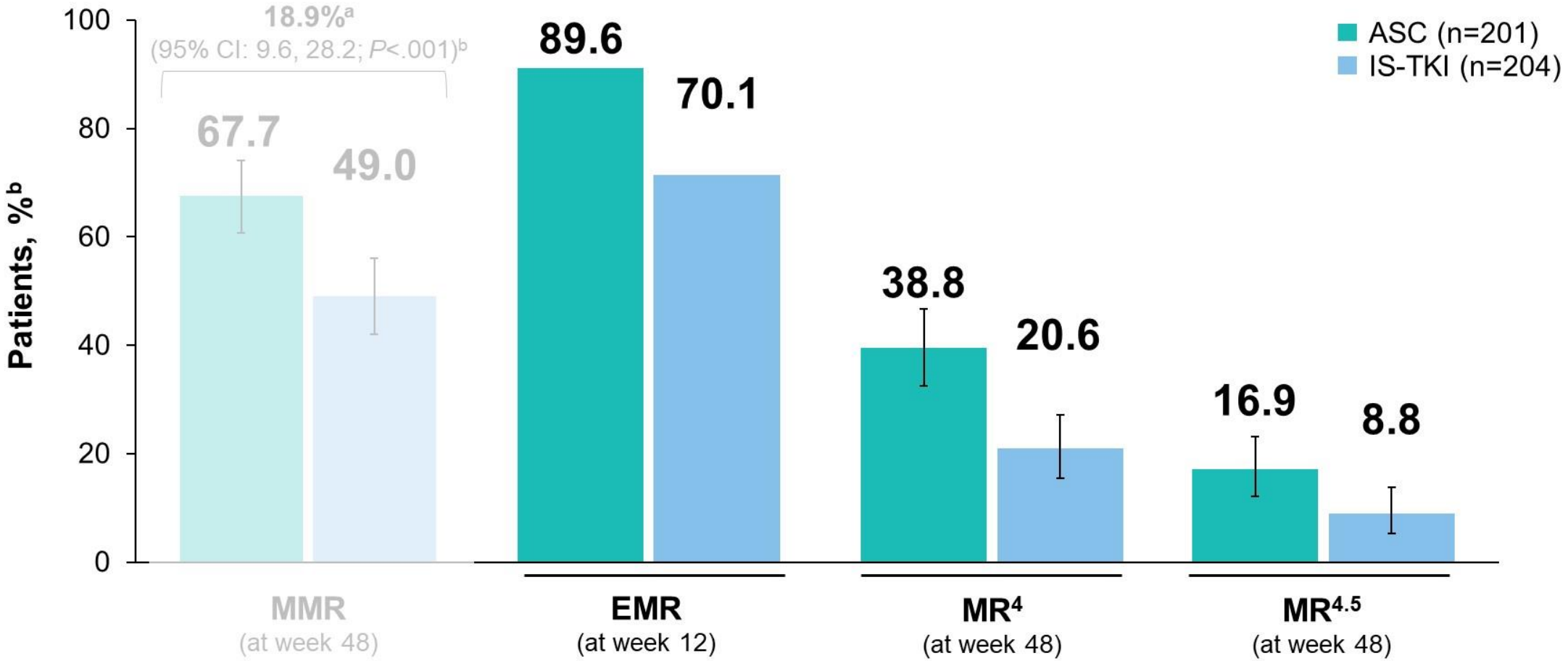
A higher proportion of patients achieved early and deep molecular responses with asciminib vs all IS-TKIs



IRT, interactive response technology.
Error bars represent 95% CIs.
[a] The common treatment difference and its 95% CI are estimated using the Mantel-Haenszel method after stratifying for (a) pre-randomization selected TKI, and (b) baseline ELTS risk groups (both IRT data).
[b] Adjusted 1-sided p-value calculated based on the graphical gatekeeping procedure. The null hypothesis is rejected if the adjusted p-value is ≤0.025.

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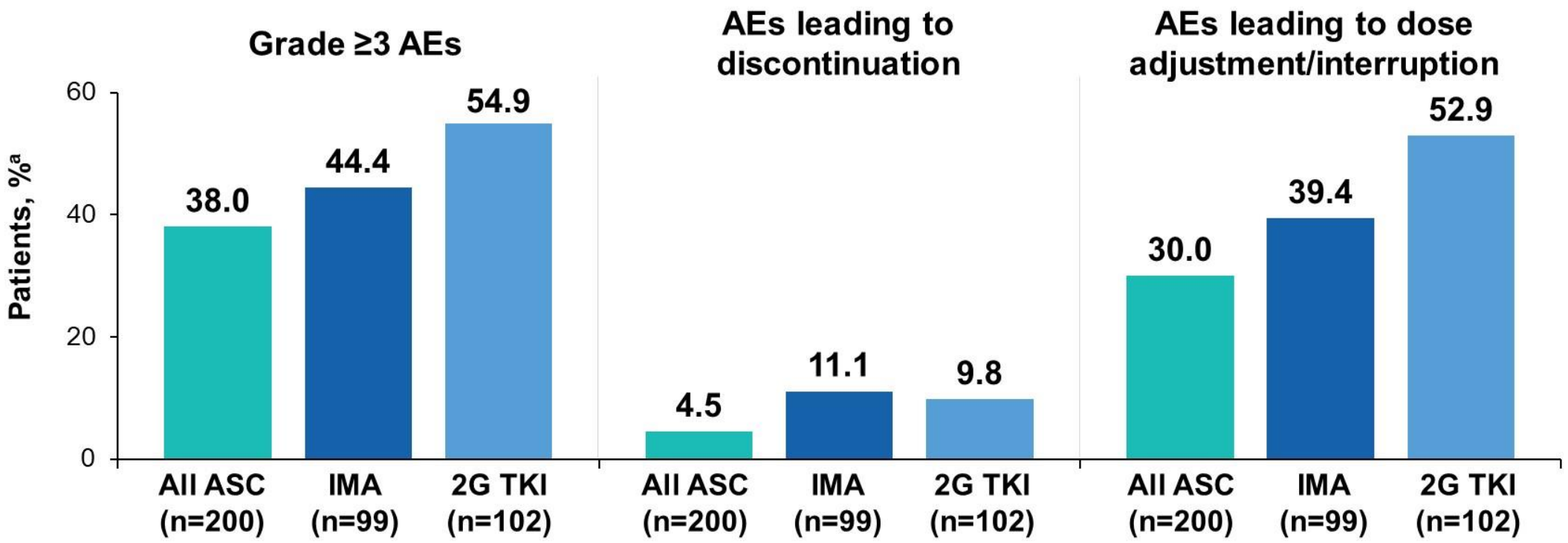
Asciminib demonstrated favorable safety and tolerability vs IMA and 2G TKIs



- The median dose intensity was 80.0 mg/day with ASC, 400.0 mg/day with IMA, 595.1 mg/day with NIL, 98.9 mg/day with DAS, and 341.8 mg/day with BOS
- The most common AEs leading to treatment discontinuation were increased lipase with ASC (1.5%), diarrhea and lymphopenia with IMA (2.0% each), and pleural effusion with 2G TKIs (2.0%)

BOS, bosutinib; DAS, dasatinib; NIL, nilotinib.
[a] Safety analyses consisted of patients who received ≥1 dose of study drug. Patients were analyzed according to the study treatment received. A patient with multiple severity grades for an AE is only counted under the maximum grade.

Oral presentation at: 2024 ASCO Annual Meeting; May 31-June 4, 2024; Chicago, Illinois, and virtual.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Asciminib in Newly Diagnosed Chronic Myeloid Leukemia

A. Hochhaus, J. Wang, D.-W. Kim, D.D.H. Kim, J. Mayer, Y.-T. Goh, P. le Coutre, N. Takahashi, I. Kim, G. Etienne, D. Andorsky, G.C. Issa, R.A. Larson, F. Bombaci, S. Kapoor, T. McCulloch, K. Malek, L. Yau, S. Ifrah, M. Hoch, J.E. Cortes, and T.P. Hughes, for the ASC4FIRST Investigators*

- Kolorektales Karzinom
- Lungenkarzinom
- Mammakarzinom
- Melanom
- Ösophaguskarzinom
- Palliativmedizin
- Prostatakarzinom

- Chronische Myeloische Leukämie
- Multiples Myelom

Vielen Dank für die Aufmerksamkeit!