Therapeutic Developments in GI Cancers

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Disclosures:

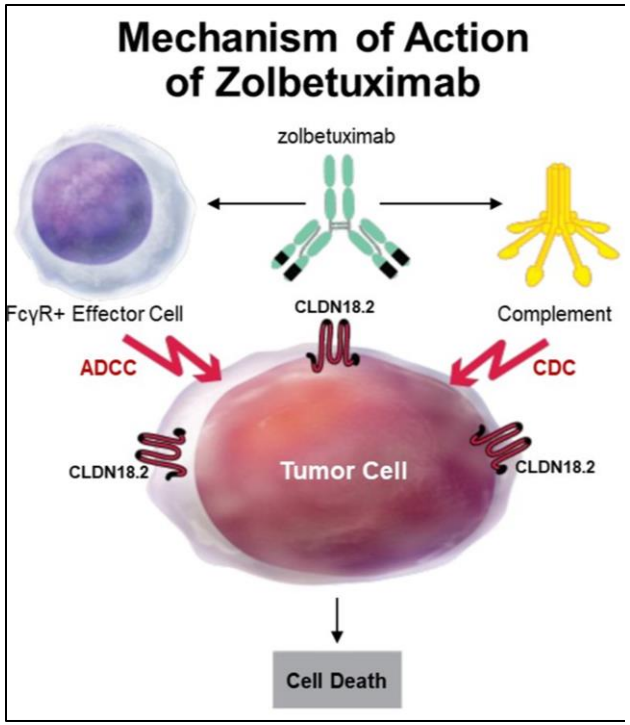
- Consultant:
  - Amgen
  - Elevation
  - General Electric
  - GSK
  - IGM
  - Merck
  - Natera
  - Pfizer
  - Seagen
  - Taiho

- Institutional Grants
  - Agenus
  - Elevar
  - Gritstone
  - Hutchmed
  - Janssen
  - Merck
  - Pfizer
  - Sumitomo

Discussion Points

- UGI
- Hepatobiliary
- Pancreatic
- Colorectal
- Anal

Phase III Trial of SPOTLIGHT in Gastric/GEJ Ca



Key Eligibility Criteria

- Previously untreated LA unresectable or mG/GEJ adenocarcinoma
- CLDN18.2+ (moderate-to-strong CLDN18 staining in ≥75% of tumor cells)[b]
- HER2–[c]
- ECOG PS 0–1

Stratification Factors

- Region (Asia vs non-Asia)
- Number organs w/ metastases (0–2 vs ≥3)
- Prior gastrectomy (yes vs no)

Planned (N ≈ 550)

R 1:1

(N = 283): Zolbetuximab 800/600[d] mg/m² IV Q3W + mFOLFOX6 IV Q2W, Cycles 1–4 (42 days/cycle) → Zolbetuximab 600 mg/m² IV Q3W + 5-FU + folinic acid IV Q2W, Cycles 5+

(N = 282): Placebo IV Q3W + mFOLFOX6 IV Q2W, Cycles 1–4 (42 days/cycle) → Placebo IV Q3W + 5-FU + folinic acid IV Q2W, Cycles 5+

Primary End Point
- PFS[e]

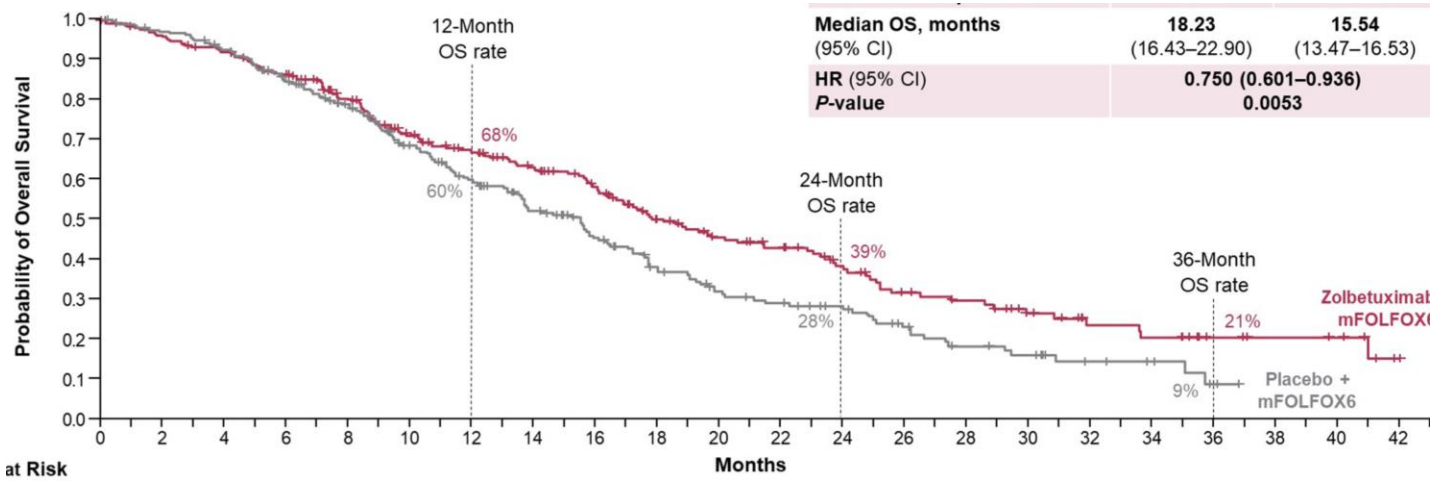
Key Secondary End Points
- OS
- TTCD in GHS/QoL, PF, and OG25-Pain

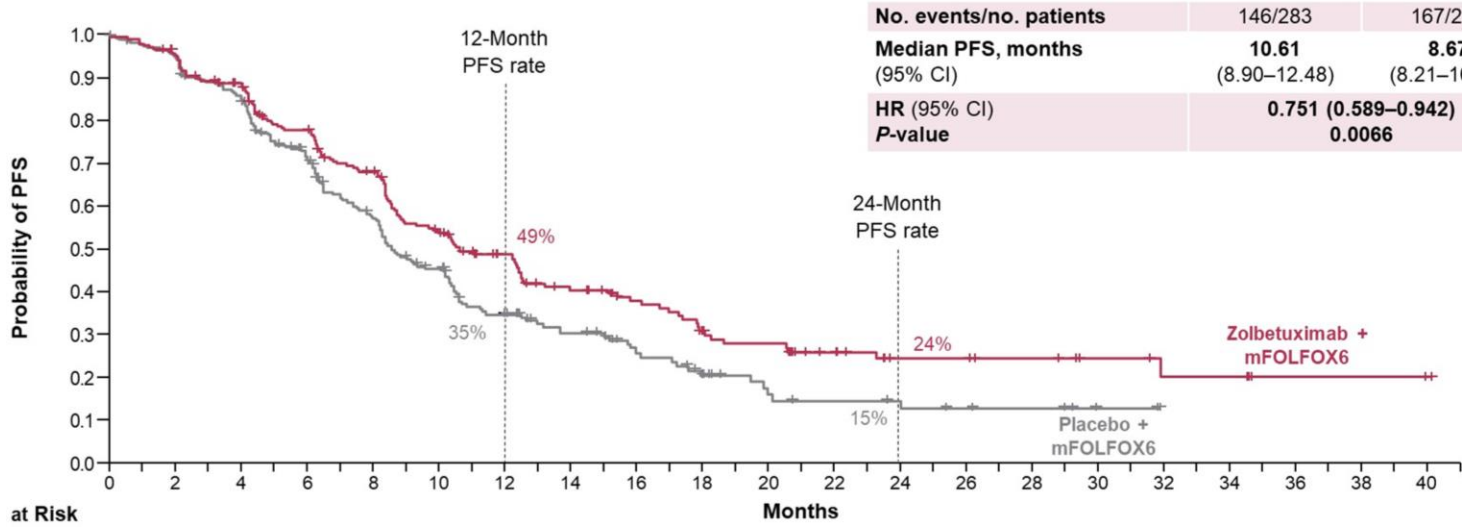
Secondary End Points
- ORR[e]
- DOR[e]
- Safety
- PROs

[a]Study was conducted at 215 sites in 20 countries across Australia, Asia, Europe, N. America, and S. America; [b]By central IHC using the analytically validated VENTANA CLDN18 (43-14A) RxDx Assay; [c]By central or local HER2 testing; [d]800 mg/m² at cycle 1 day 1 followed by 600 mg/m² on cycle 1 day 22 and days 1 and 22 of subsequent cycles; [e]Per RECIST v1.1 by independent review committee.

Shitara et al: ASCO GI 2023

SPOTLIGHT: PFS and OS



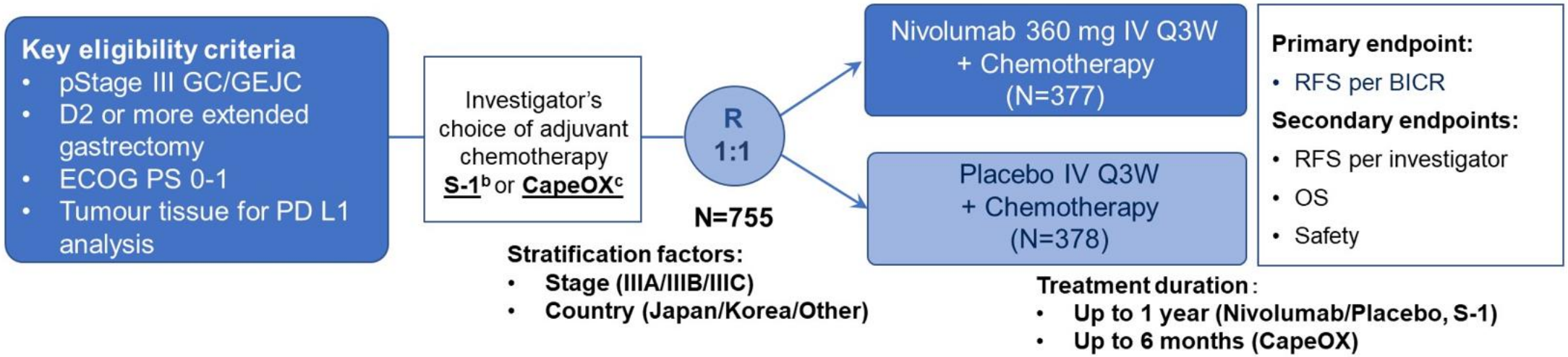


	Zolbetuximab + mFOLFOX6 (N = 211)	Placebo + mFOLFOX6 (N = 211)
Patients[a], n	128	131
ORR[b], % (95% CI)	60.7 (53.72–67.30)	62.1 (55.17–68.66)
BOR[c,d], n (%)		
CR	12 (5.7)	7 (3.3)
PR	116 (55.0)	124 (58.8)
SD	45 (21.3)	52 (24.6)
PD	14 (6.6)	14 (6.6)
Median DOR[b], months, (95% CI)	8.51 (6.80–10.25)	8.11 (6.47–11.37)
3rd quartile, months (95% CI)	29.9 (10.41–NE)	15.5 (13.27–NE)

Shitara et al: ASCO GI 2023

Attraction-5: Phase III trial of Adjuvant Nivo in Gastric/GEJ CA

- Phase 3, double-blind, placebo-controlled study of Asian patients (Japan, Korea, Taiwan, China)[a]



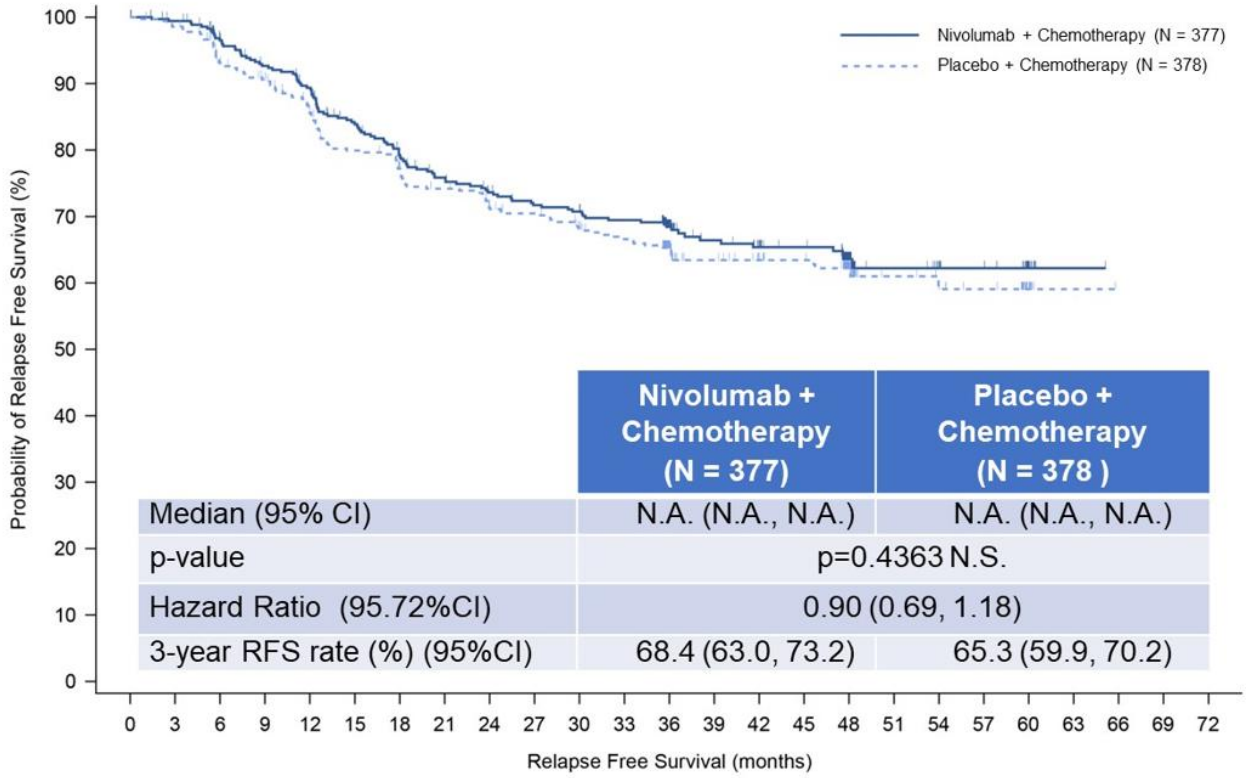
- Planned sample size: 700 patients (assuming HR=0.67; 3-year RFS, 71% vs 60%)
- Patients were randomized from February 2017 to August 2019
- All data are based on a clinical data cutoff of August 2022, at which point the minimum follow-up after the last patient randomized was 36 months

[a]ClinicalTrials.gov number, NCT03006705; [b]**S-1 therapy:** S-1 40 mg/m^2/dose orally twice daily (day1-28) , Q6W; [c]**CapeOX therapy:** Oxaliplatin 130 mg/m^2 IV once daily (day1), and Capecitabine 1000 mg/m^2/dose orally twice daily (day1-14), Q3W.

Abbreviations: BICR, blinded independent central review; CapeOX, capecitabine/oxaliplatin; GC, gastric cancer; GEJC, gastroesophageal junction cancer; IV, intravenous; Q3W, every 3 weeks; Q6W, every 6 weeks; S-1, tegafur/gimeracil/oteracil; BICR, blinded independent central review

Terashima et al: ASCO 2023

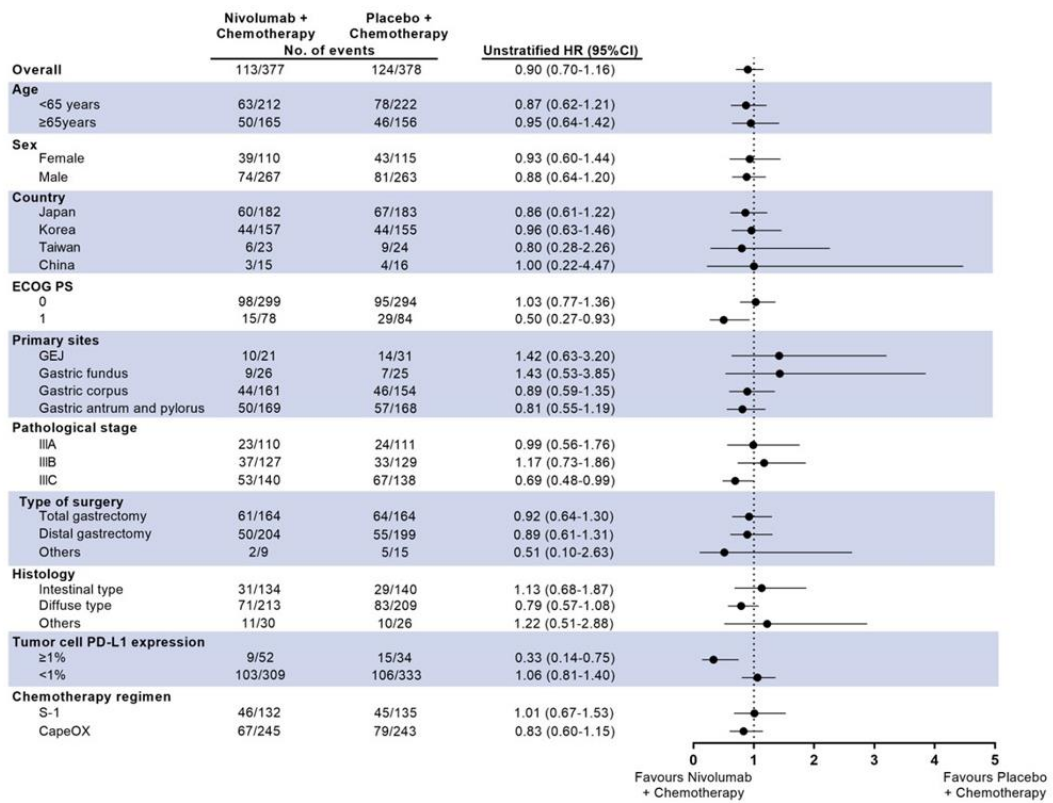
Results of ATTRACTION-5



	Nivolumab + Chemotherapy (N = 377)	Placebo + Chemotherapy (N = 378)
Median (95% CI)	N.A. (N.A., N.A.)	N.A. (N.A., N.A.)
p-value	p=0.4363 N.S.	
Hazard Ratio (95.72%CI)	0.90 (0.69, 1.18)	
3-year RFS rate (%) (95%CI)	68.4 (63.0, 73.2)	65.3 (59.9, 70.2)

At Risk

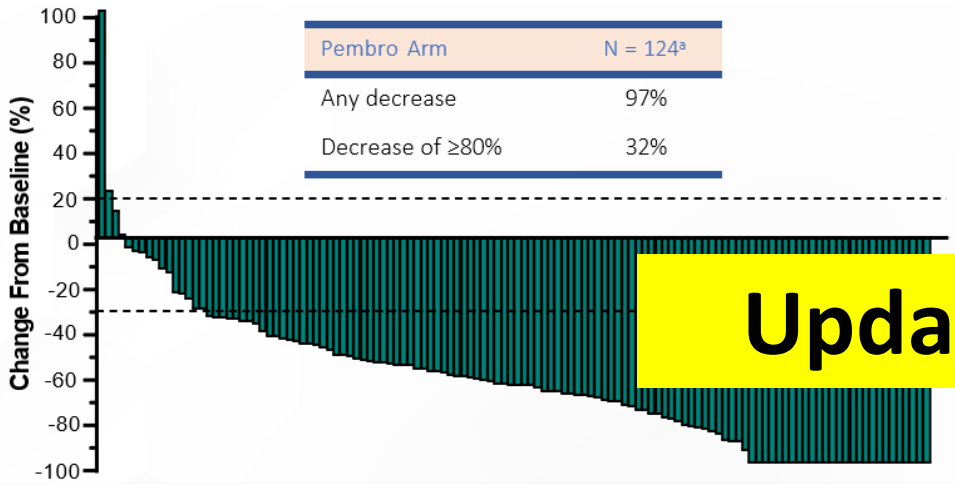
Nivolumab + Chemotherapy	377	349	326	310	297	273	255	241	231	223	219	214	162	127	120	114	58	33	28	24	9	1	0	0	0
Placebo + Chemotherapy	378	353	324	311	288	267	254	242	228	223	212	204	148	118	110	107	57	33	30	26	10	1	0	0	0

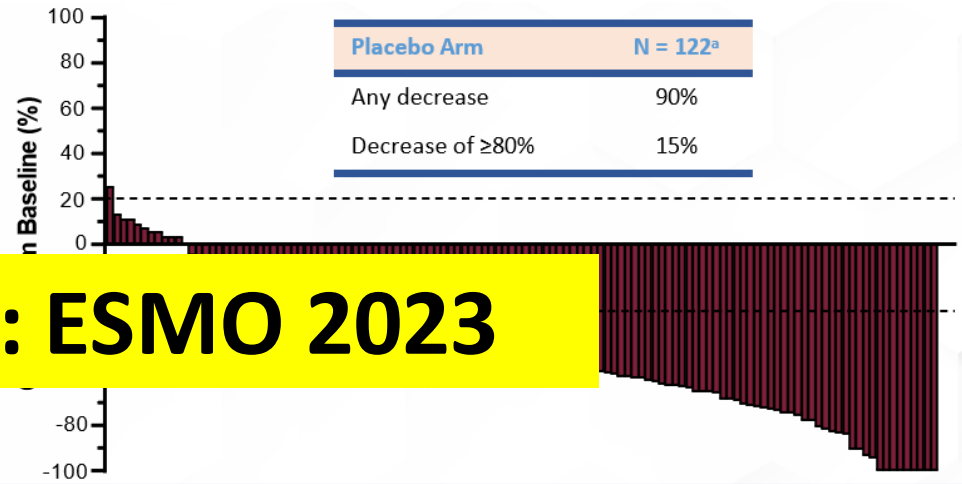


	Nivolumab + Chemotherapy No. of events	Placebo + Chemotherapy No. of events	Unstratified HR (95%CI)
Overall	113/377	124/378	0.90 (0.70-1.16)
Age			
<65 years	63/212	78/222	0.87 (0.62-1.21)
≥65years	50/165	46/156	0.95 (0.64-1.42)
Sex			
Female	39/110	43/115	0.93 (0.60-1.44)
Male	74/267	81/263	0.88 (0.64-1.20)
Country			
Japan	60/182	67/183	0.86 (0.61-1.22)
Korea	44/157	44/155	0.96 (0.63-1.46)
Taiwan	6/23	9/24	0.80 (0.28-2.26)
China	3/15	4/16	1.00 (0.22-4.47)
ECOG PS			
0	98/299	95/294	1.03 (0.77-1.36)
1	15/78	29/84	0.50 (0.27-0.93)
Primary sites			
GEJ	10/21	14/31	1.42 (0.63-3.20)
Gastric fundus	9/26	7/25	1.43 (0.53-3.85)
Gastric corpus	44/161	46/154	0.89 (0.59-1.35)
Gastric antrum and pylorus	50/169	57/168	0.81 (0.55-1.19)
Pathological stage			
IIIA	23/110	24/111	0.99 (0.56-1.76)
IIIB	37/127	33/129	1.17 (0.73-1.86)
IIIC	53/140	67/138	0.69 (0.48-0.99)
Type of surgery			
Total gastrectomy	61/164	64/164	0.92 (0.64-1.30)
Distal gastrectomy	50/204	55/199	0.89 (0.61-1.31)
Others	2/9	5/15	0.51 (0.10-2.63)
Histology			
Intestinal type	31/134	29/140	1.13 (0.68-1.87)
Diffuse type	71/213	83/209	0.79 (0.57-1.08)
Others	11/30	10/26	1.22 (0.51-2.88)
Tumor cell PD-L1 expression			
≥1%	9/52	15/34	0.33 (0.14-0.75)
<1%	103/309	106/333	1.06 (0.81-1.40)
Chemotherapy regimen			
S-1	46/132	45/135	1.01 (0.67-1.53)
CapeOX	67/245	79/243	0.83 (0.60-1.15)

Terashima et al: ASCO 2023

Phase III Keynote 811 Study: Trastuzumab/Chemotherapy +/- Pembrolizumab





Update: ESMO 2023

ORR and DCR, % (95% CI)	Pembro Arm (N = 133)	Placebo Arm (N = 131)
ORR	74.4% (66.2-81.6)	51.9% (43.0-60.7)
ORR difference[b]	22.7% (11.2-33.7) *P* = 0.00006	
DCR	96.2% (91.4-98.8)	89.3% (82.7-94.0)

Best Response, n (%)	Pembro Arm (N = 133)	Placebo Arm (N = 131)
CR	15 (11%)	4 (3%)
PR	84 (63%)	64 (49%)
SD	29 (22%)	49 (37%)
PD	5 (4%)	7 (5%)
Not evaluable	0	2 (2%)
Not assessed	0	5 (4%)

Duration of Response[c]	**Pembro Arm (N = 99)**	**Placebo Arm (N = 68)**
Median[d]	10.6 mo	9.5 mo
Range	1.1+ to 16.5+	1.4+ to 15.4+
≥6-mo duration[d]	70.3%	61.4%
≥9-mo duration[d]	58.4%	51.1%

Janjigian et al: Nature 2021

MATTERHORN: Neoadjuvant/adjuvant Durva+FLOT in Resectable Gastric/GEJ Cancer

Double-blind

Study Population

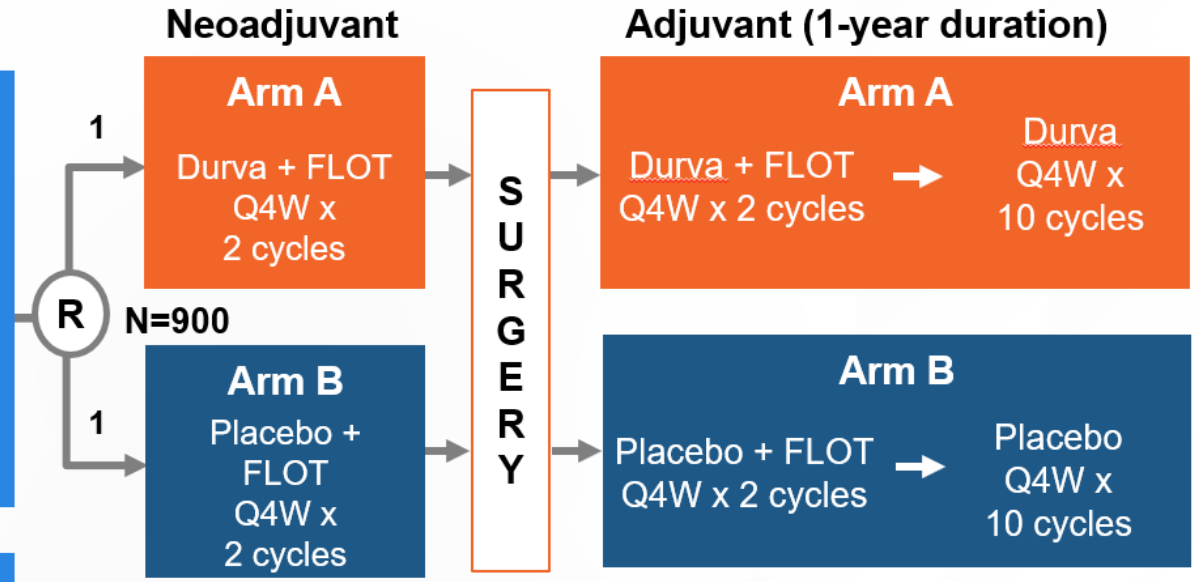
- Gastric or GEJ adenocarcinoma
- Stage II, III, and IVA (>T2 N0-3 M0 or T1-4 N+ M0)
- No evidence of metastasis
- No prior therapy
- ECOG PS 0 or 1

Stratification factors

- Geographic region (Asia vs non-Asia)
- Clinical lymph node status (positive vs negative)
- PD-L1 expression status*

*TIP<1% vs TIP≥1%.

†TIP<1% vs TIP≥1% vs TIP≥5%.



FLOT: 5-FU 2600 mg/m^2, oxaliplatin 85 mg/m^2, docetaxel 50 mg/m^2, leucovorin 200 mg/m^2 on days 1 and 15 Q4W
Durvalumab: 1500 mg on day 1 Q4W

Durvalumab (or placebo) monotherapy may be initiated if adjuvant chemo is discontinued before the 2-cycle completion

IDMC safety review: safety from the first dose of neoadjuvant therapy to recovery from surgery will be assessed in the first 60 patients or at 6 months from FSI, whichever occurs first (minimum of 20 patients)

Primary Endpoint

- EFS (ITT)

Key Secondary Endpoints

- pCR and OS

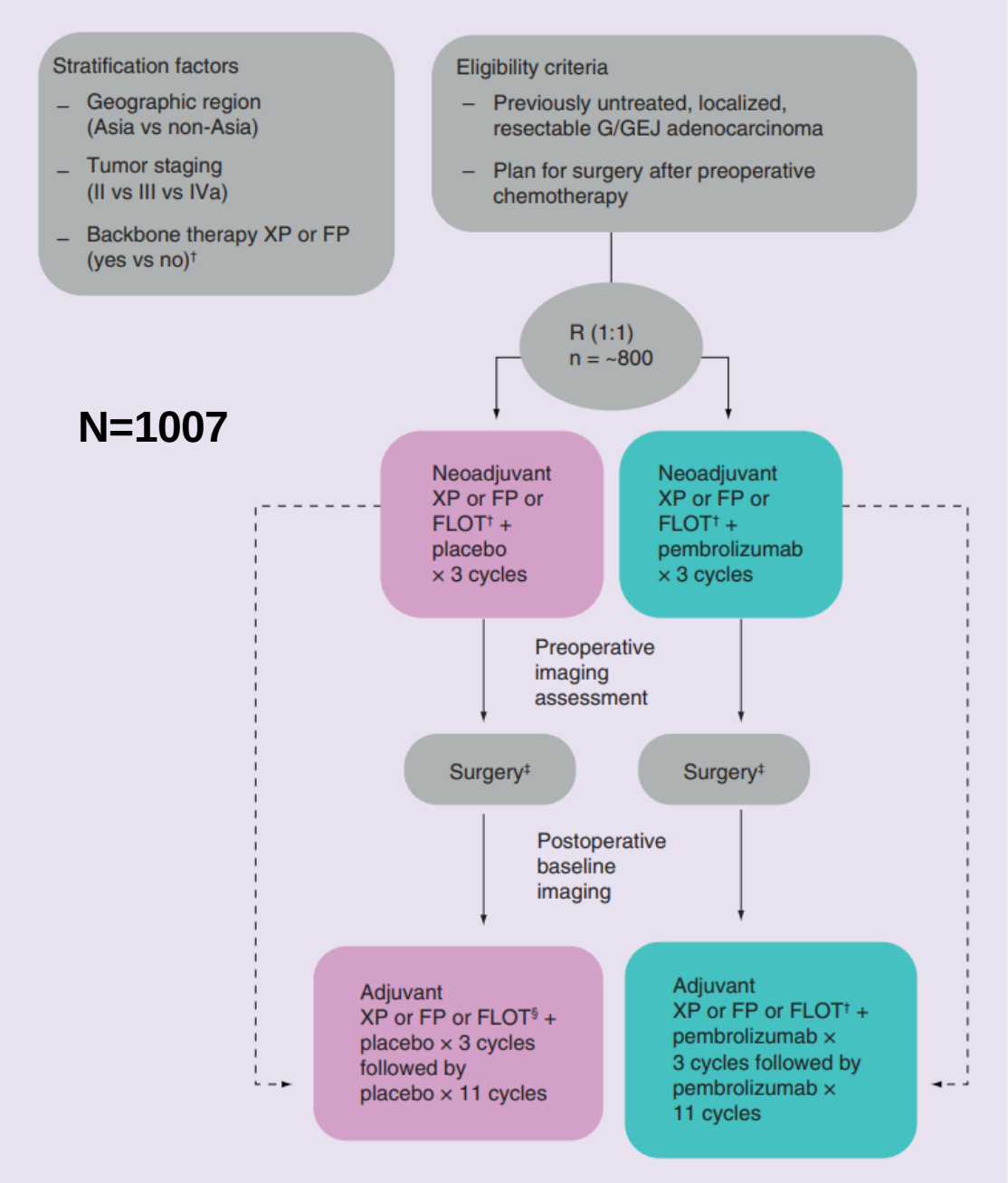
Secondary Endpoints

- OS24/36 and EFS24/36
- EFS (investigator)
- DFS and DFS24/36
- MFS and DSS
- R0 resection rate
- PROs
- All the efficacy endpoints in ITT and PD-L1 subgroups†

NCT04592913

Keynote 585:Double-blind study of perioperative pembrolizumab vs placebo plus chemotherapy in resectable gastric and GEJ adenocarcinoma

NCT03221426



Bang et al: Future Oncol. 2019

Press Releases: To be presented ESMO 2023

June 2023:

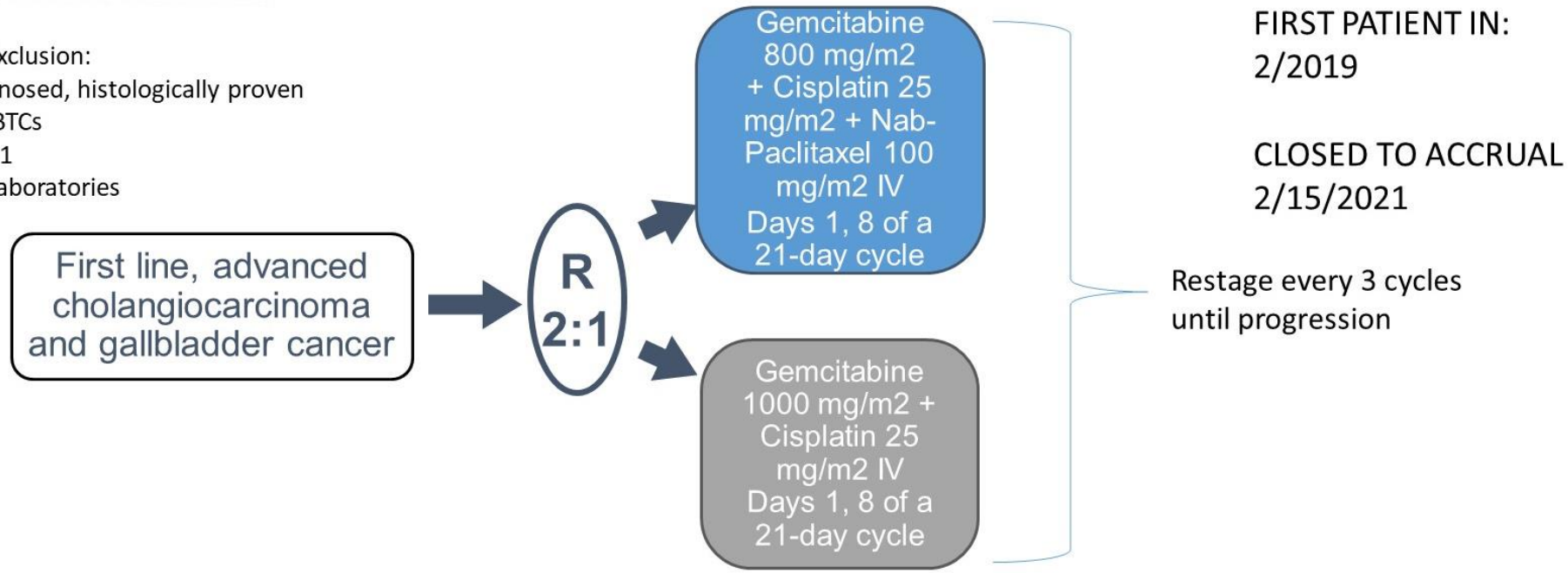
- **MATTERHORN**:
  - Durvalumab plus chemotherapy significantly improved pathologic complete response in gastric and gastroesophageal junction cancers in MATTERHORN Phase III trial
  - Trial will continue to assess event-free survival
- **Keynote 585**
  - At a pre-specified interim analysis conducted by an independent Data Monitoring Committee, the study met one of its primary endpoints of pathological complete response (pCR) rate and demonstrated a statistically significant improvement in pCR rates compared with chemotherapy alone
  - For the primary endpoint of event-free survival (EFS), there was an improvement in the KEYTRUDA arm; however, results did not meet statistical significance per the pre-specified statistical analysis plan

SWOG 1815: Gemcitabine/Cisplatin +/- Nab-Paclitaxel in Tx Naïve Advanced Biliary Cancers

Study Design

Prespecified stratifications factors: tumor type, PS, locally-advanced vs. metastatic

Key Inclusion/Exclusion:
- Newly diagnosed, histologically proven untreated BTCs
- ECOG PS 0-1
- Adequate laboratories



N = 441

FIRST PATIENT IN: 2/2019

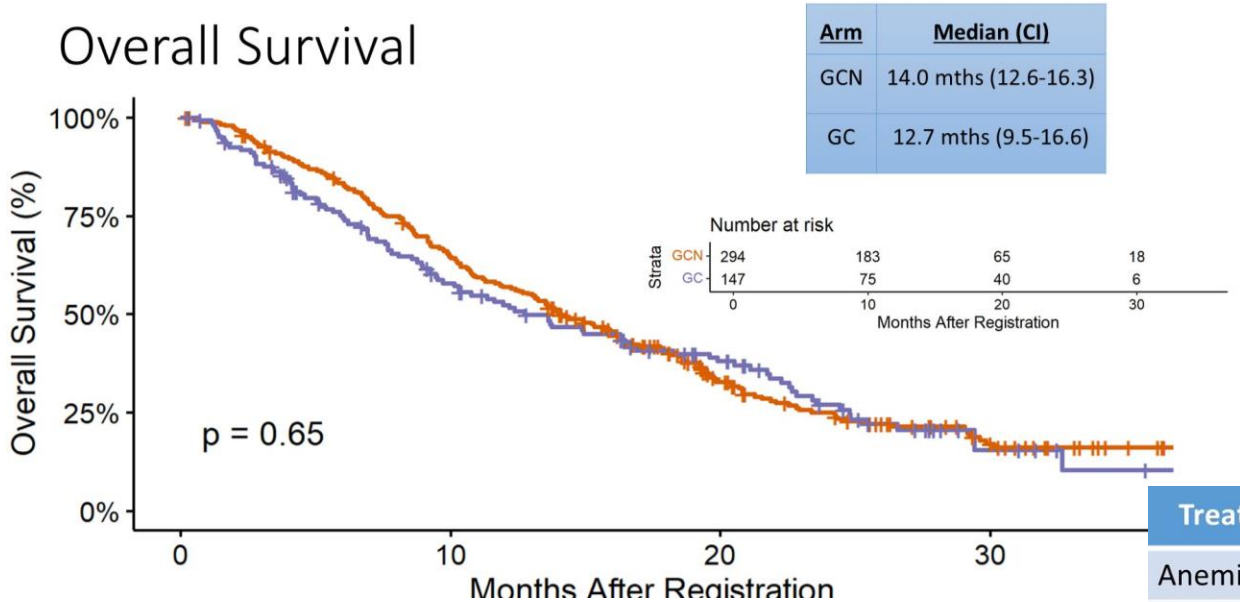
CLOSED TO ACCRUAL 2/15/2021

Primary EP: OS; **Target HR 0.7**
Secondary: ORR, PFS, DCR, safety, CA 19-9 changes

Archival blood and tissue specimens to be banked

Shroff R, et al. *J Clin Oncol*. 2023;41(4_Suppl):LBA490.

SWOG 1815: Gemcitabine/Cisplatin +/- Nab-Paclitaxel in Tx Naïve Advanced Biliary Cancers



Arm	Median (CI)
GCN	14.0 mths (12.6-16.3)
GC	12.7 mths (9.5-16.6)

Treatment-Related Adverse Event	GCN Grade 3-4 N (%)	GC Grade 3-4 N (%)
Anemia	95 (33%)	30 (22%)
Neutropenia	105 (37%)	37 (28%)
Thrombocytopenia	56 (20%)	20 (15%)
Leukopenia	72 (25%)	14 (10%)
Diarrhea	13 (5%)	1 (0.7%)
Fatigue	26 (9%)	8 (6%)
Sepsis	12 (4%)	3 (2%)
Peripheral Sensory Neuropathy	10 (4%)	1 (0.7%)

Shroff R, et al. *J Clin Oncol*. 2023;41(4_Suppl):LBA490.

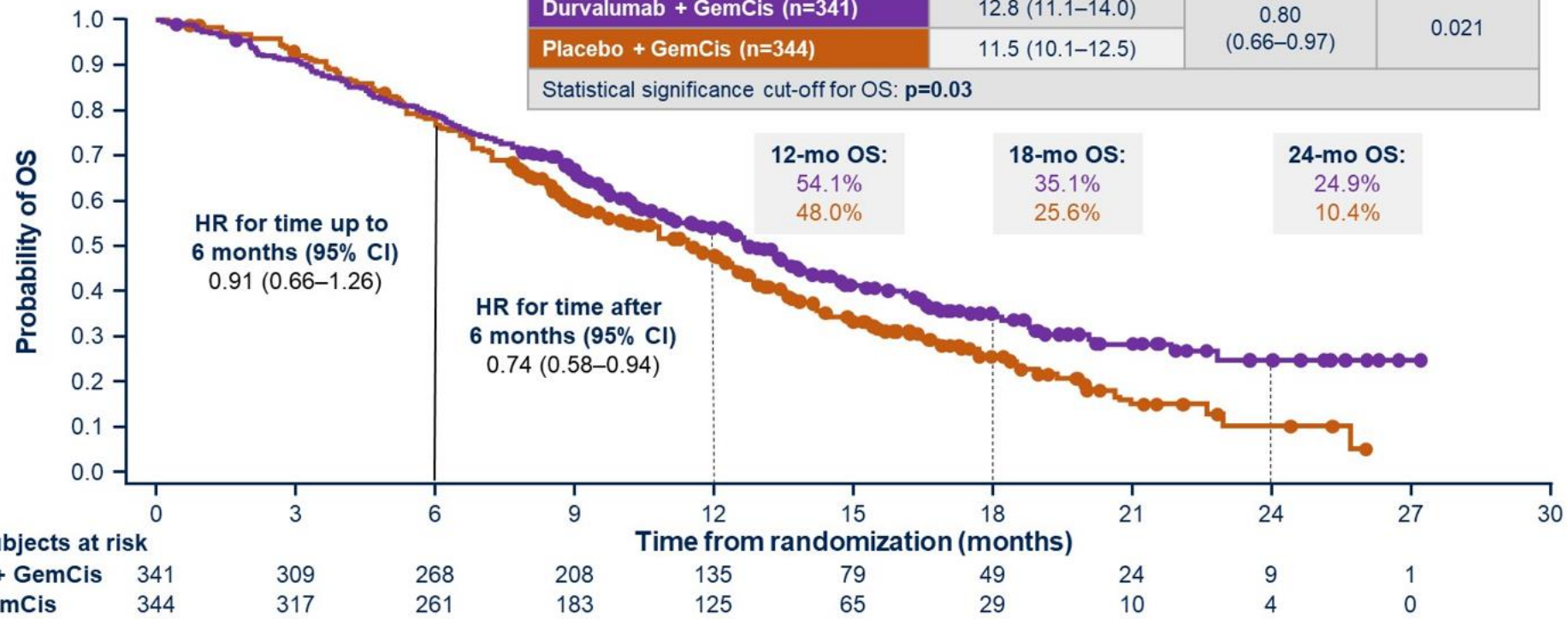
TOPAZ-1: Gem/Cis +/- Durvalumab

Key eligibility
- Locally advanced or metastatic BTC (ICC, ECC, GBC)
- Previously untreated if u
  metastatic at initial diagn
- Recurrent disease >6 m
  curative surgery or adjuv
- ECOG PS 0 or 1

Stratification factors
- Disease status
  - (initially unresectable ve
- Primary tumor location
  - (ICC versus ECC versus

Durvalumab 1500 mg Q3W + GemCis (up to 8 cycles) → **Durvalumab 1500 mg Q4W until PD**

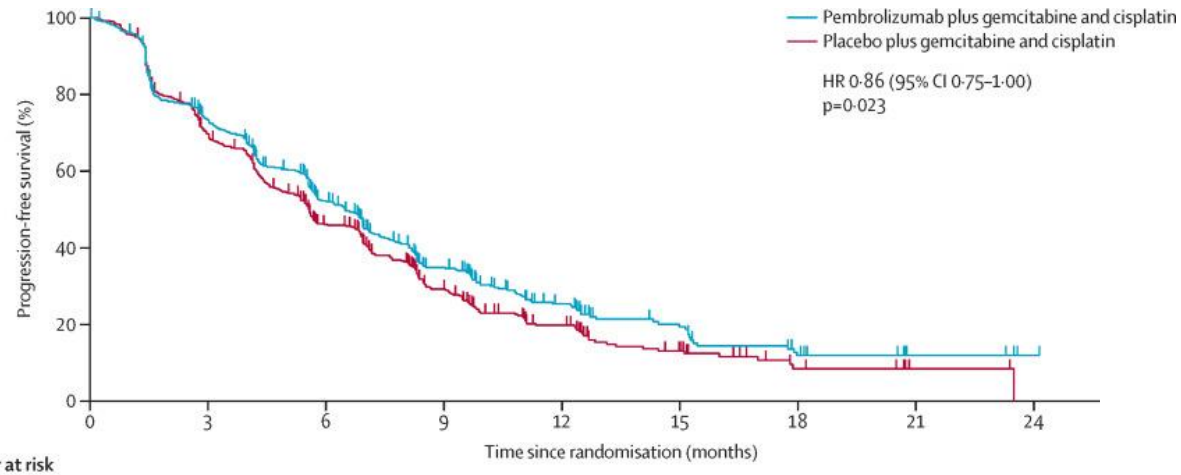
	Median OS (95% CI), months	Hazard ratio (95% CI)	p-value
Durvalumab + GemCis (n=341)	12.8 (11.1–14.0)	0.80 (0.66–0.97)	0.021
Placebo + GemCis (n=344)	11.5 (10.1–12.5)		
Statistical significance cut-off for OS: **p=0.03**			



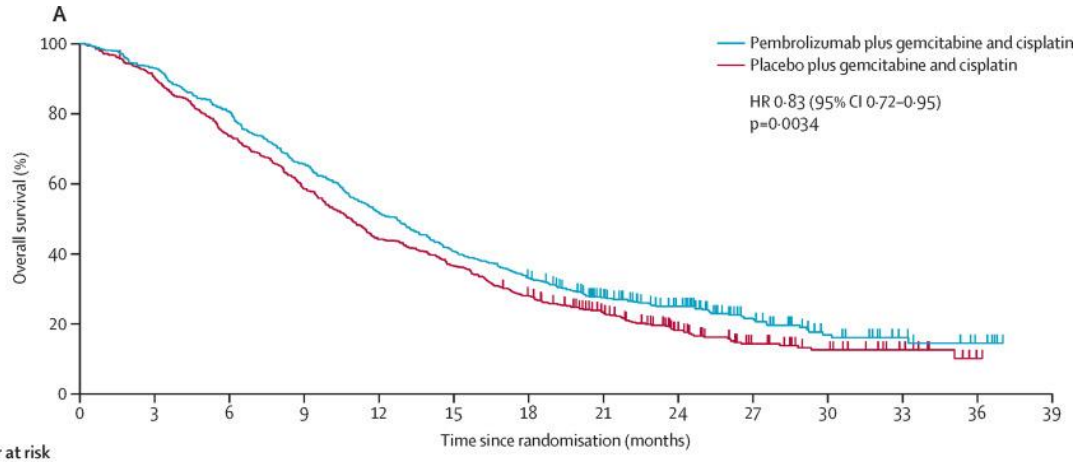
Number of subjects at risk										
Durvalumab + GemCis	341	309	268	208	135	79	49	24	9	1
Placebo + GemCis	344	317	261	183	125	65	29	10	4	0

Oh et al: NEJM, 2022

Keynote 966: Gem-cis with or without pembrolizumab



Number at risk (number censored)									
Pembrolizumab plus gemcitabine and cisplatin	533 (0)	368 (27)	238 (55)	121 (101)	62 (131)	29 (153)	14 (158)	5 (167)	1 (171)
Placebo plus gemcitabine and cisplatin	536 (0)	352 (25)	211 (50)	99 (94)	51 (113)	21 (130)	7 (139)	2 (144)	0 (145)



Number at risk (number censored)														
Pembrolizumab plus gemcitabine and cisplatin	533 (0)	496 (0)	430 (0)	350 (0)	275 (0)	217 (0)	175 (1)	122 (26)	88 (50)	46 (83)	21 (100)	11 (109)	5 (114)	0 (119)
Placebo plus gemcitabine and cisplatin	536 (0)	483 (1)	394 (1)	313 (1)	236 (1)	195 (1)	148 (3)	97 (30)	59 (49)	32 (65)	20 (74)	10 (84)	1 (92)	0 (93)

Kelley RK, et al. *Lancet*. 2023;401(10391):1853-1865.

ImBrave 151: Double Blinded Randomized Phase II of Gem/Cis/Atezo +/- Bev in Tx-Naïve Biliary Cancer

Advanced biliary tract cancer (n=162)

- Histologically confirmed intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma or gallbladder cancer
- ECOG PS 0/1
- Measurable disease per RECIST 1.1
- No prior systemic treatment for advanced BTC
- Screening EGD required for patients at high risk of esophageal varices

R 1:1

	Cycles 1-8 (21-day cycles)	Cycle 9 and beyond (21-day cycles)
Arm 1	Gemcitabine (1000 mg/m^2 IV on Days 1 and 8) Cisplatin (25 mg/m^2 IV on Days 1 and 8) Bevacizumab (15 mg/kg IV q3w) Atezolizumab (1200 mg IV q3w)	Bevacizumab (15 mg/kg IV q3w) Atezolizumab (1200 mg IV q3w)
Arm 2	Gemcitabine (1000 mg/m^2 IV on Days 1 and 8) Cisplatin (25 mg/m^2 IV on Days 1 and 8) Placebo (IV q3w)	Placebo (IV q3w) Atezolizumab (1200 mg IV q3w)

Treat until disease progression, unacceptable toxicity or loss of clinical benefit

No crossover

Stratification factors

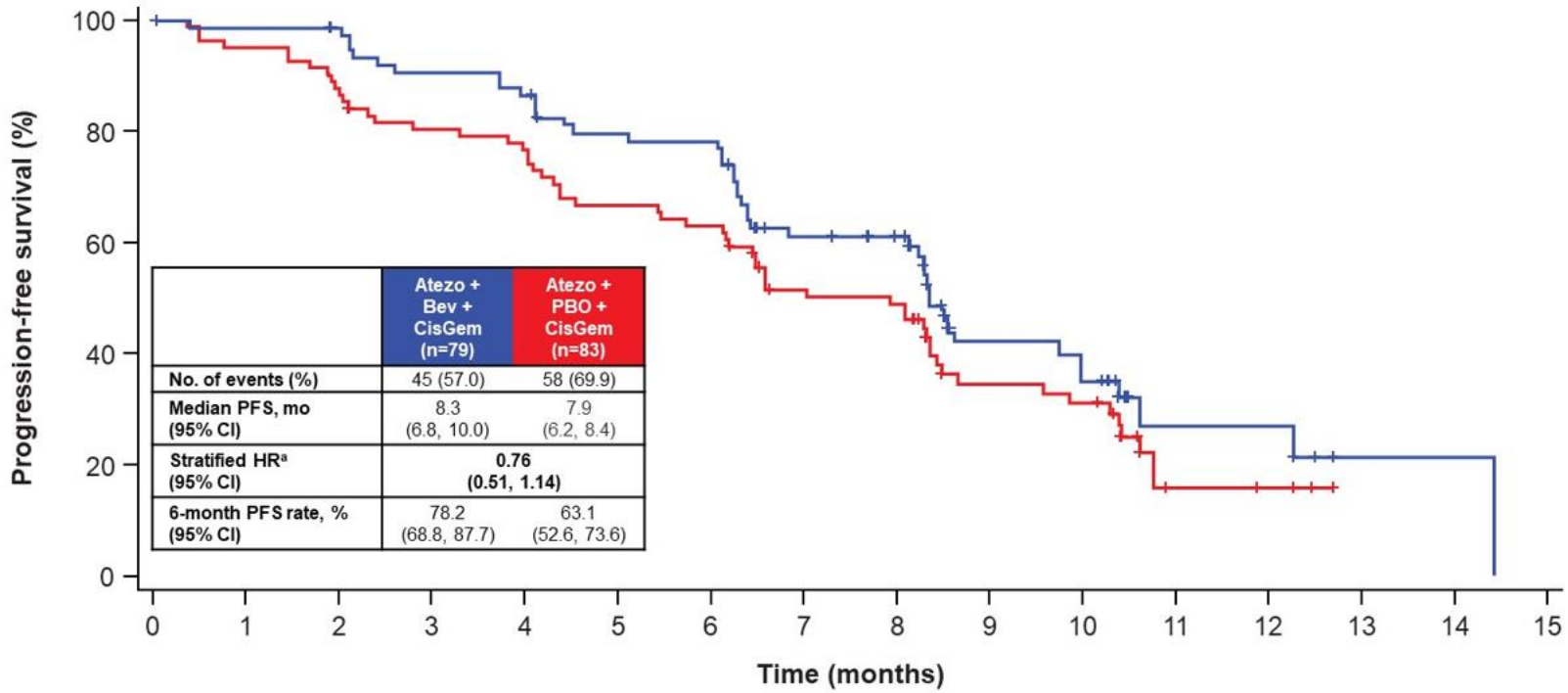
- Anatomical location of primary tumor (iCCA, eCCA or GBC)
- Metastatic disease (yes or no)
- Geographic region (Asia vs rest of world)

Key endpoints

- **Primary endpoint:** PFS[a]
- **Key secondary endpoints:** ORR,[a] duration of response,[a] DCR,[a] OS, safety, PRO/QOL
- **Exploratory endpoints:** 6-month PFS and OS rates, biomarkers, PRO-CTCAE

El-Khoueiry et al: ASCO GI 2023

Primary endpoint: PFS for ImBrave 151



	Atezo + Bev + CisGem (n=79)	Atezo + PBO + CisGem (n=83)
No. of events (%)	45 (57.0)	58 (69.9)
Median PFS, mo (95% CI)	8.3 (6.8, 10.0)	7.9 (6.2, 8.4)
Stratified HR[a] (95% CI)	0.76 (0.51, 1.14)	
6-month PFS rate, % (95% CI)	78.2 (68.8, 87.7)	63.1 (52.6, 73.6)

Number at risk																
Atezo + Bev + CisGem	79	75	73	67	64	57	56	41	38	18	15	5	5	1	1	NE
Atezo + PBO + CisGem	83	78	72	65	62	54	51	38	36	20	18	4	3	NE	NE	NE

Median follow-up duration: 10.8 months. CCOD: May 16, 2022. Atezo, atezolizumab; Bev, bevacizumab; CCOD, clinical cutoff date; CI, confidence interval; CisGem, gemcitabine plus cisplatin; eCCA, extrahepatic cholangiocarcinoma; GBC, gall bladder carcinoma; HR, hazard ratio; iCCA, intrahepatic cholangiocarcinoma; NE, not estimable; PBO, placebo; PFS, progression-free survival. [a]Stratified analysis. Stratification factors are location of primary tumor (iCCA vs eCCA vs GBC) and geographic region (Asia vs rest of world).

El-Khoueiry et al: ASCO GI 2023

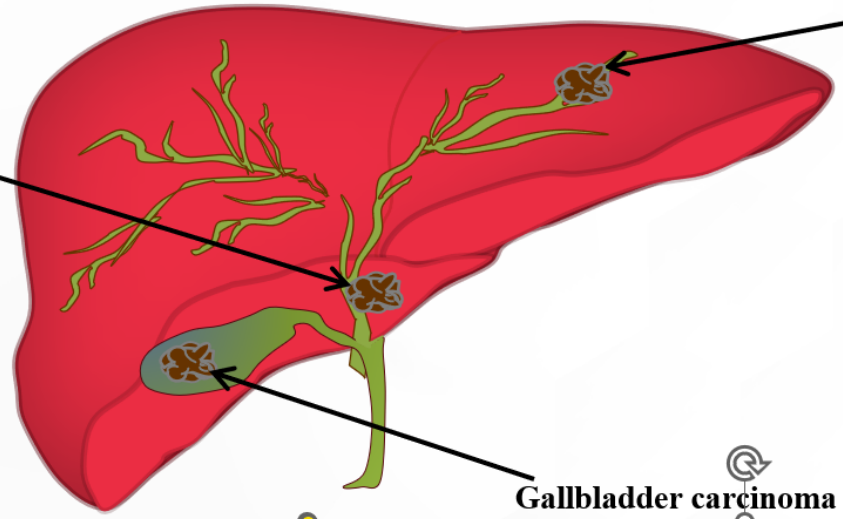
Molecular Alterations in Biliary Cancer

Intrahepatic Cholangiocarcinoma (ICC)

FGFR1-3 fusions, mutations & amplifications (11-17%)
IDH1/2 mutation (5-36%)
RNF43 mutation (9%)
PIK3CA mutations (3-9%)
BRAF mutations (3-7%)
HER2 amplification/mutation (7%)
MET amplification (2-7%)
MET mutation (5%)
EGFR mutation (1-2%)

Extrahepatic Cholangiocarcinoma (ECC)

IDH1/2 mutation (0-7%)
PIK3CA mutation (7%)
HER2 amplification/mutation (5-10%)
MET mutation (4%)
BRAF mutations (3%)
MET amplification (1%)



Gallbladder carcinoma (GBCA)

HER2 amplification/mutation (10-19%)
PIK3CA mutation (6-13%)
BRAF mutation (1-6%)
RNF43 mutation (4%)
MAP2K4 mutation (4%)
EGFR mutation (4%)
FGFR1-3 fusions, mutations & amplifications (3%)
IDH1/2 mutation (2%)

Valle JW, et al. *Cancer Discov.* 2017

2023 ASCO ANNUAL MEETING

Results from the Pivotal Phase 2b HERIZON-BTC-01 Study: Zanidatamab in Previously-treated HER2-amplified Biliary Tract Cancer (BTC)

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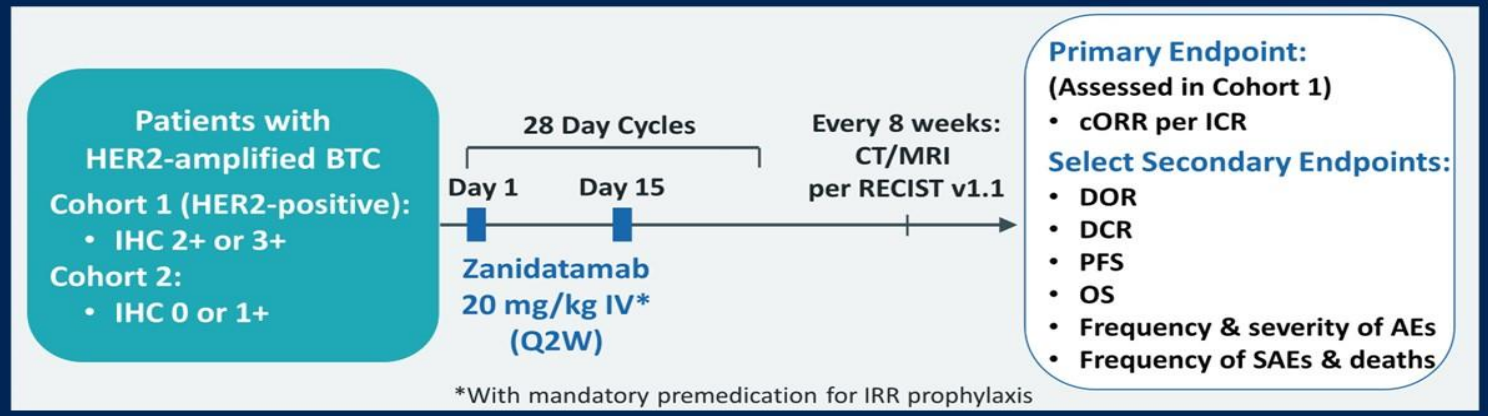
Pant S, et al. Presented at: ASCO;2023.

HERIZON-BTC-01 Study Design

- Phase 2b study of zanidatamab monotherapy in patients with HER2-amplified BTC

Key Eligibility Criteria

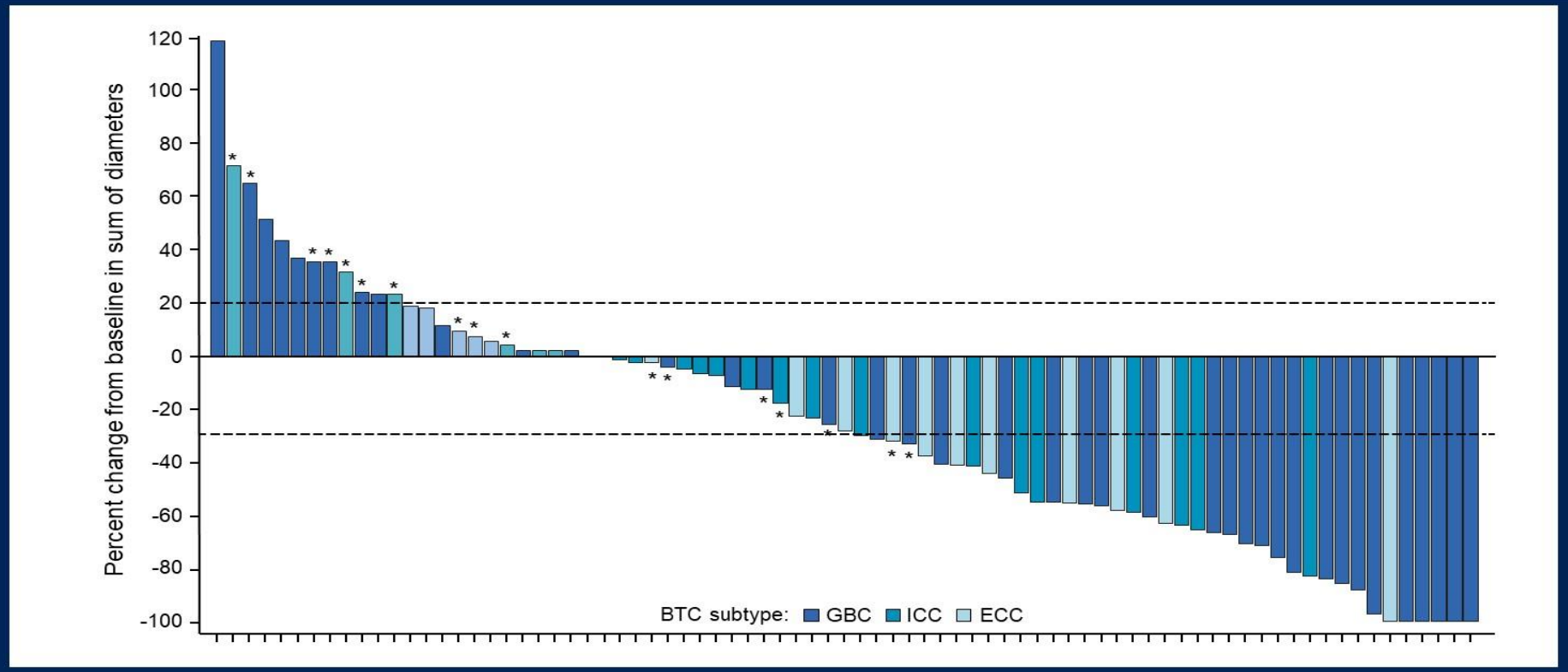
- Locally advanced or metastatic BTC[1]
- Tissue required to confirm HER2 status by central lab
- Progressed after treatment with a gemcitabine-containing regimen
- No prior HER2-targeted therapies
- ECOG PS of 0 or 1



[1] Excludes ampullary

AE = adverse event; cORR = confirmed objective response rate; CT = computed tomography scan; DCR = disease control rate; DOR = duration of response; ECOG PS = Eastern Cooperative Oncology Group performance status; ICR = independent central review; IHC = immunohistochemistry; IRR = infusion-related reaction; IV = intravenous; MRI = magnetic resonance imaging; OS = overall survival; Q2W = every two weeks; RECIST= Response Evaluation Criteria in Solid Tumors; SAE = serious adverse event.

Majority of evaluable patients (68.4%) had a decrease in target lesions (Cohort 1)



*Indicates patients with IHC 2+ status; all other patients had IHC status of 3+.
Dotted lines indicate 20% increase and 30% decrease in sum of diameters of target tumors.

Phase 2b HERIZON-BTC-01: Zanidatamab in Previously Treated HER-2 Amplified Biliary Tract Cancer

Key Eligibility Criteria

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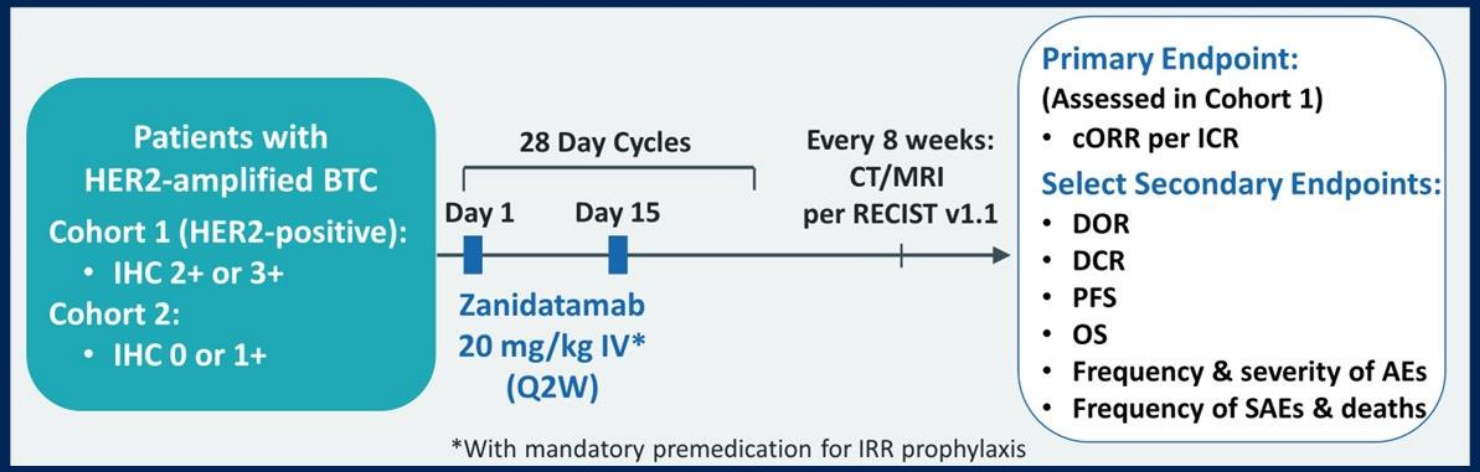

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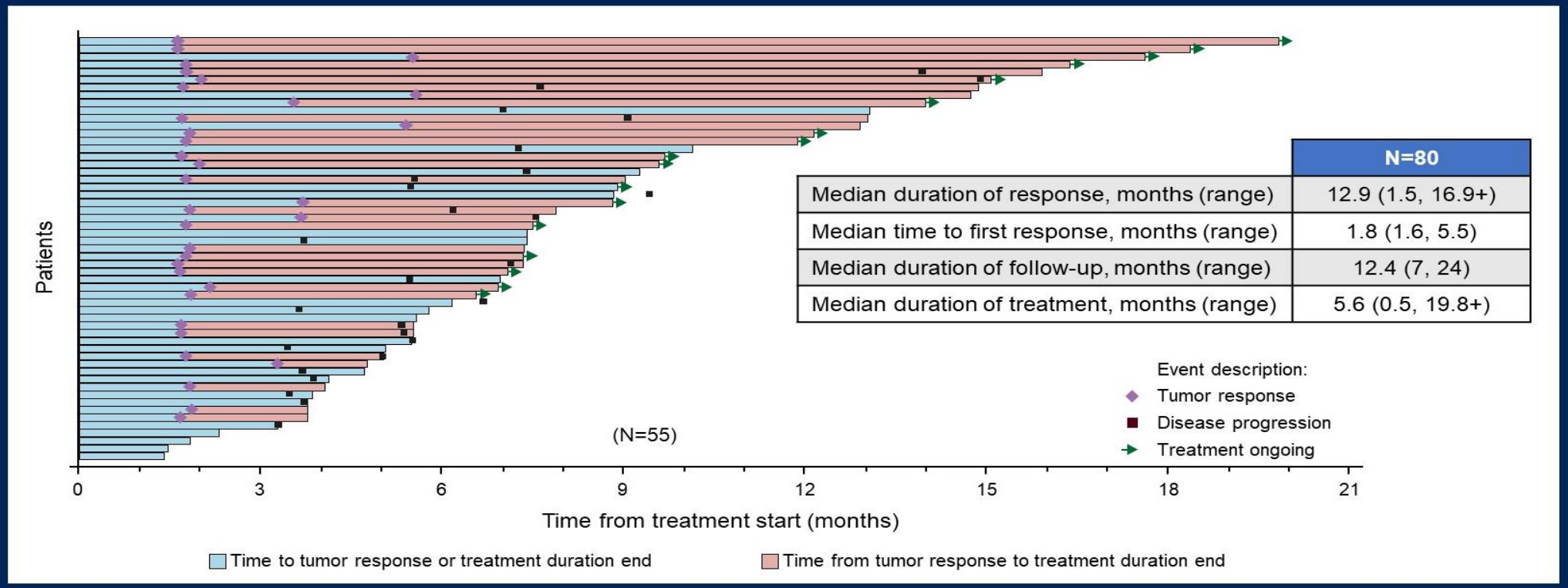
Pant et al: ASCO 2023

Phase 2b HERIZON-BTC-01: Zanidatamab in Previously Treated HER-2 Amplified BTC – Response

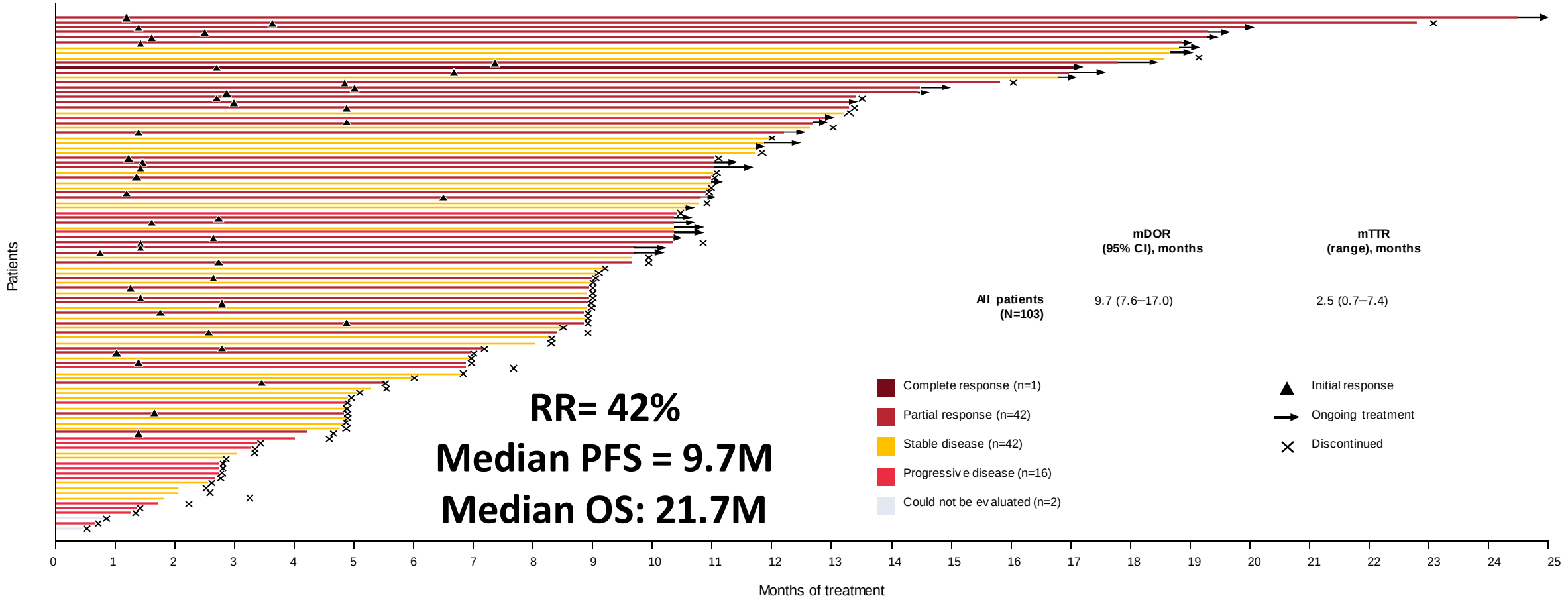


	N=80
Median duration of response, months (range)	12.9 (1.5, 16.9+)
Median time to first response, months (range)	1.8 (1.6, 5.5)
Median duration of follow-up, months (range)	12.4 (7, 24)
Median duration of treatment, months (range)	5.6 (0.5, 19.8+)

Note: Decisions to discontinue zanidatamab were based on investigator assessment. One patient with non-responding tumors was still on treatment.

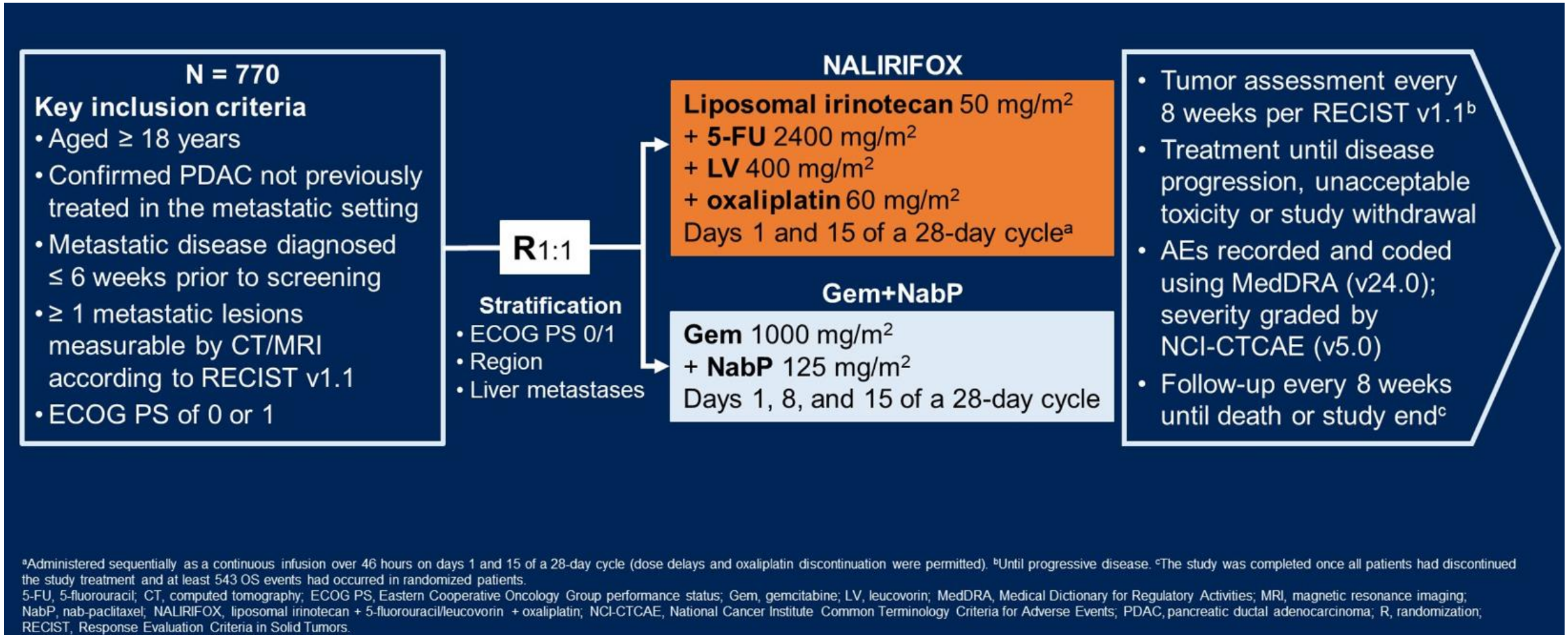
Pant et al: ASCO 2023

Futibatinib in FGFR2 Rearranged Intrahepatic Cholangio: FOENIX-CCA2 Study



Goyal L, et al. *N Engl J Med.* 2023;388:228–39.

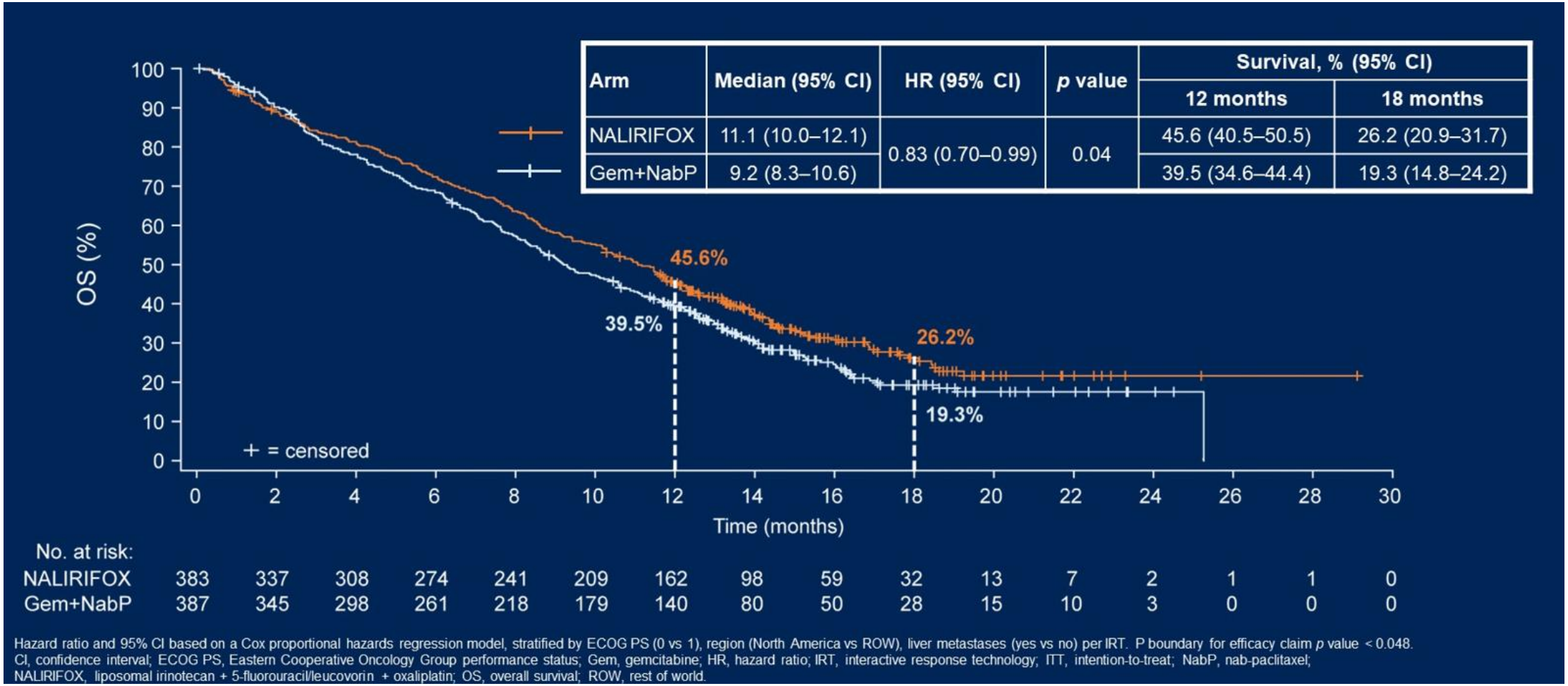
NAPOLI-3: NALIRIFOX vs. Gem/NabP in PDAC



[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.

O'Reilly et al: ASCO GI 2023

NAPOLI-3: Primary Endpoint for OS



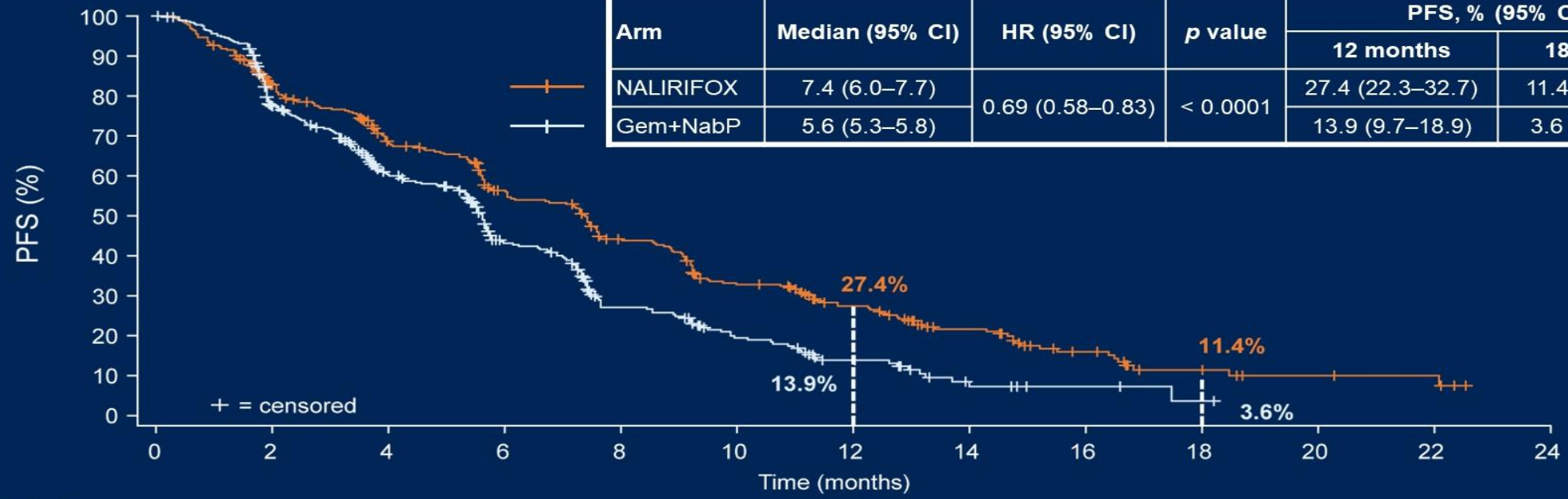
Arm	Median (95% CI)	HR (95% CI)	*p* value	Survival, % (95% CI)	
				12 months	18 months
NALIRIFOX	11.1 (10.0–12.1)	0.83 (0.70–0.99)	0.04	45.6 (40.5–50.5)	26.2 (20.9–31.7)
Gem+NabP	9.2 (8.3–10.6)			39.5 (34.6–44.4)	19.3 (14.8–24.2)

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.

O'Reilly et al: ASCO GI 2023

NAPOLI-3: PFS (ITT)

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)



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.
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O'Reilly et al: ASCO GI 2023

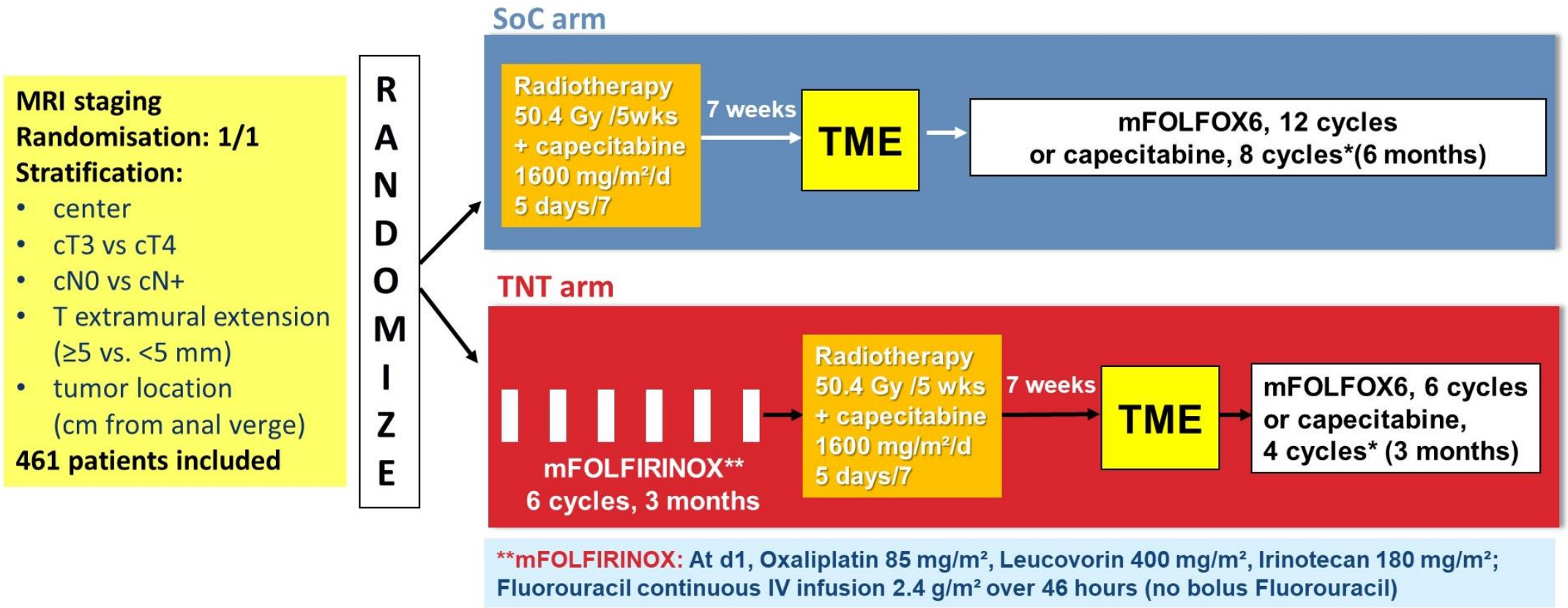
NAPOLI-3: SAE's

	NALIRIFOX (n = 370)		Gem+NabP (n = 379)	
Any-cause TEAEs in ≥10% of patients, %[a]	Any grade	Grade 3–4	Any Grade	Grade 3–4
Hematologic				
Neutropenia[b] / febrile neutropenia	50.0 / 2.4	23.8 / 2.4	50.6 / 2.6	38.0 / 2.4
Anemia	26.2	10.5	40.4	17.4
Thrombocytopenia[c]	24.0	1.6	40.6	6.1
Non-hematologic				
Diarrhea	70.5	20.3	36.7	4.5
Nausea	59.5	11.9	42.7	2.6
Vomiting	39.7	7.0	26.4	2.1
Hypokalemia	31.6	15.1	12.9	4.0
Peripheral neuropathy[d]	32.9	6.7	30.9	8.7
Paresthesia	11.9	0.3	8.7	0.5
Pyrexia	10.5	0.8	23.0	1.6

O'Reilly et al: ASCO GI 2023

Rectal Cancer: MSI-S

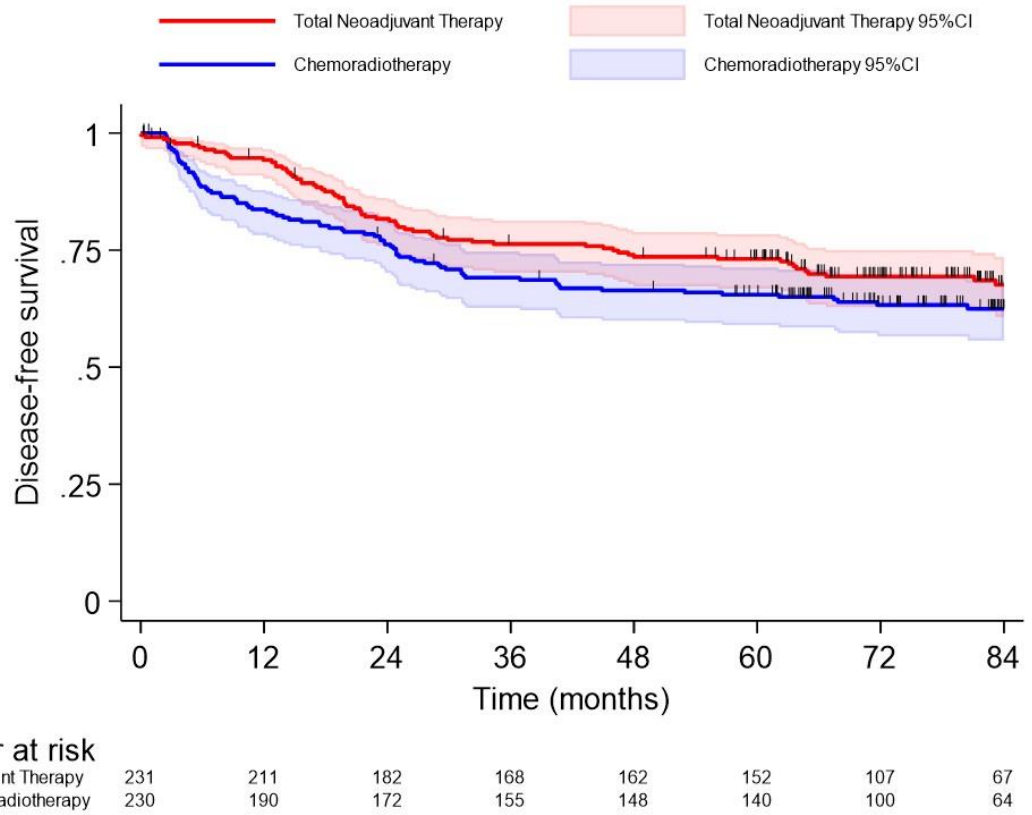
PRODIGE 23: Phase III Rectal CA



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

Conroy et al: ASCO 2023

PRODIGE 23: Phase III Rectal CA - DFS



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

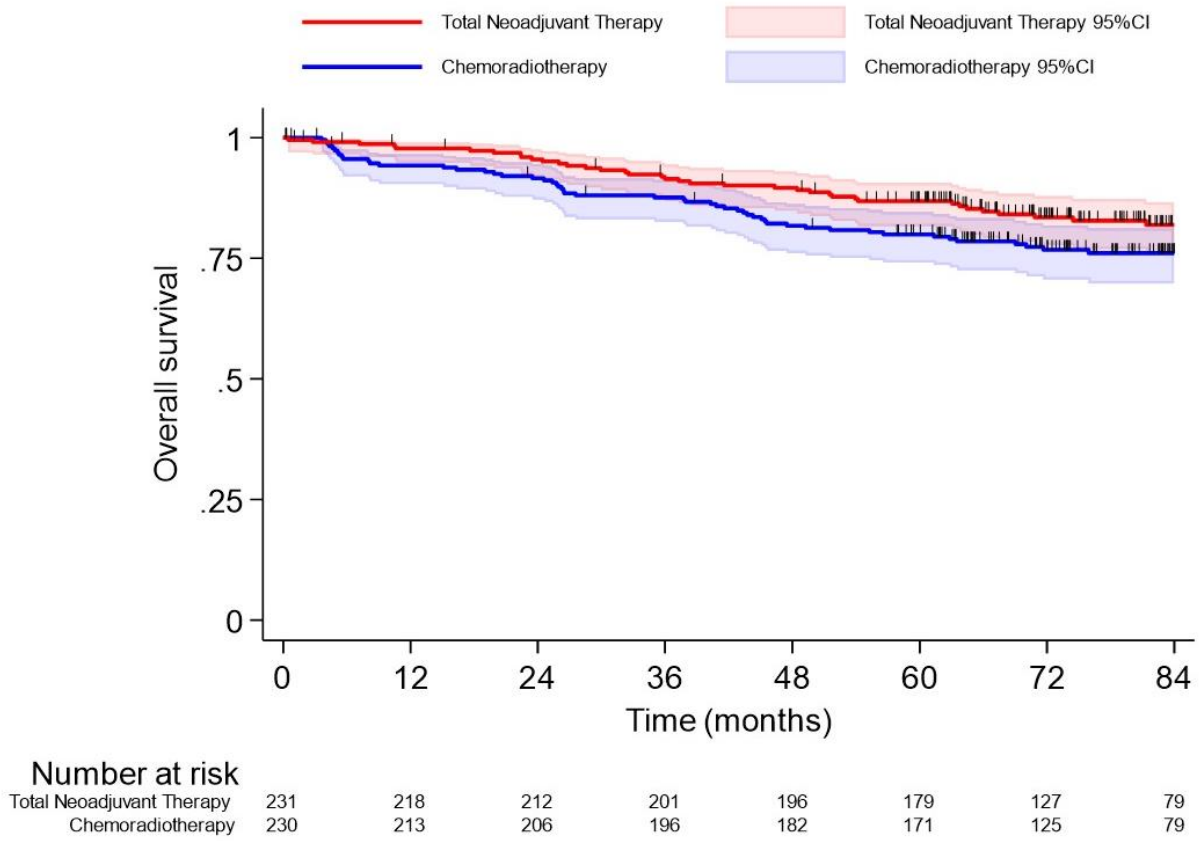
5-yr DFS rate:

- 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

Conroy et al: ASCO 2023

PRODIGE 23: Phase III Rectal CA - OS



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:

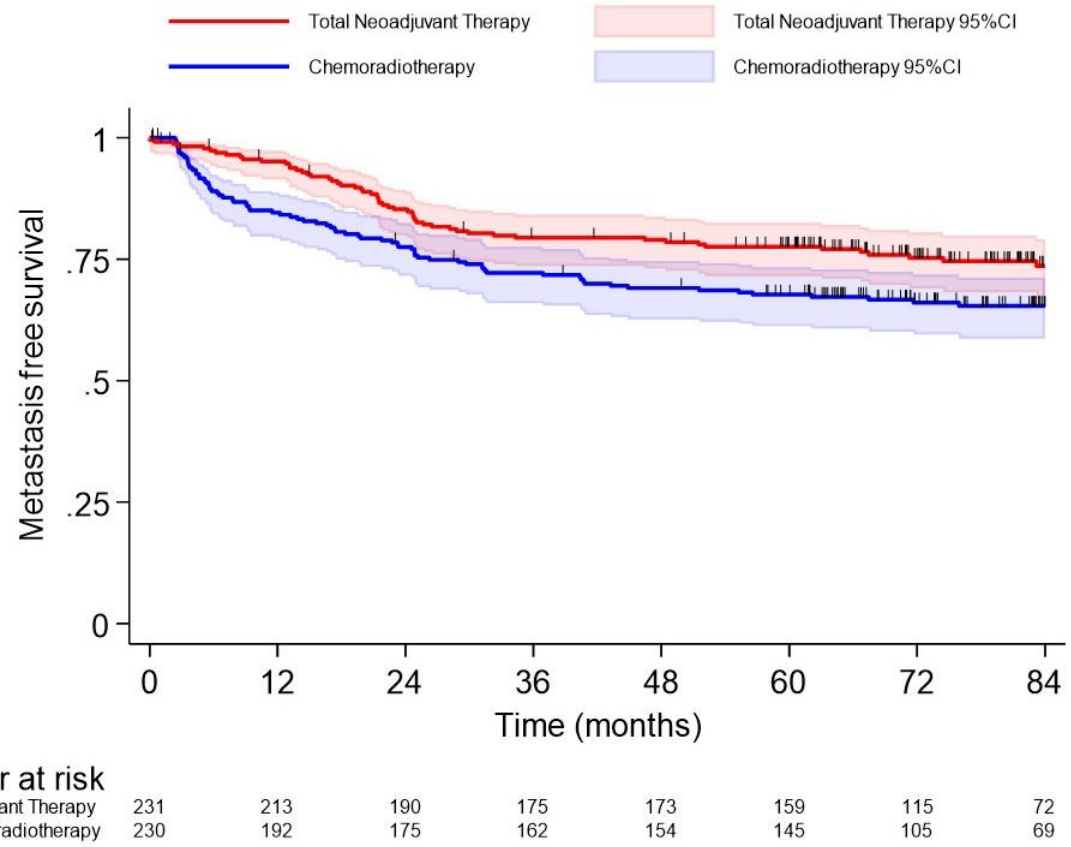
- 86.9% [95%CI: 81.6-90.7] TNT arm
- 80.0% [95%CI: 74.1-84.6] SoC arm

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

Conroy et al: ASCO 2023

PRODIGE 23: Phase III Rectal CA - MFS

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



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:

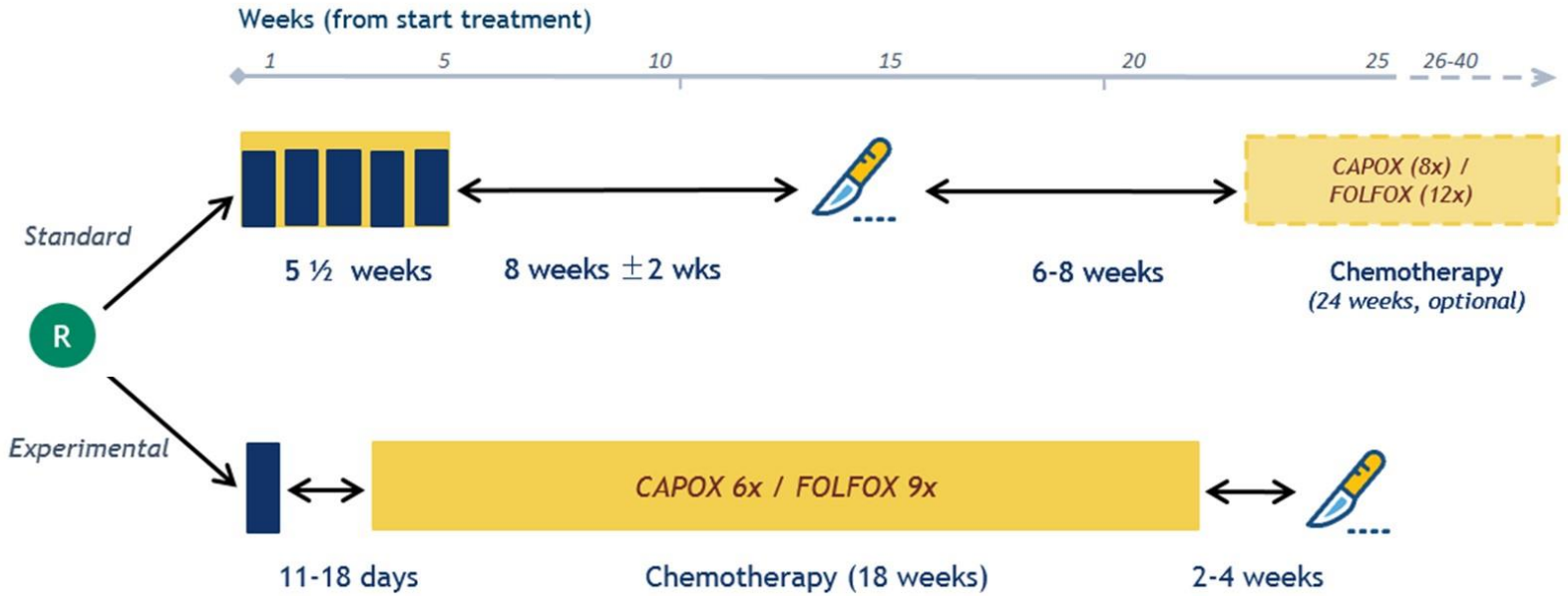
- 77.6% [95%CI: 71.5-82.5] TNT arm
- 67.7% [95%CI: 61.2-73.4] SoC arm

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

Conroy et al: ASCO 2023

RAPIDO: Short Course XRT

Study design



Standard: week 1-6: 28x1.8 Gy or 25x2 Gy at working days combined with capecitabine b.i.d. 825 mg/m^2 (twice daily) day 1-33-38.
Experimental: week 1: 5x5 Gy, week 3-20: 6x CAPOX (capecitabine b.i.d.1000 mg/m^2 (twice daily) day 1-14 every 3 weeks orally, oxaliplatin 130 mg/m^2 day 1 every 3 weeks iv or alternatively 9x FOLFOX4 (folinic acid, fluorouracil and oxaliplatin all iv every 2 weeks)

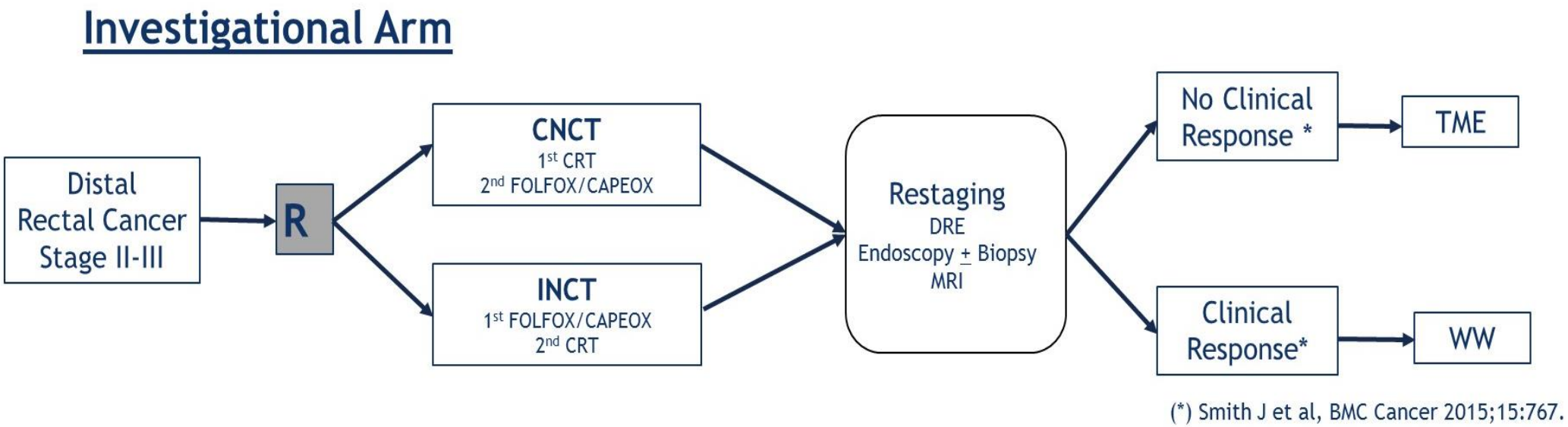
Bahadoer et al: Lanc Onc, 2020

RAPIDO Update

	RAPIDO	Standard of Care	P-value
Local regional failure (LRF)	12%	8%	0.07
Local regional recurrence (LRR)	10%	6%	**0.027**
Disease-related treatment failure (DrTF)	28%	34%	0.048
Distant Mets	23%	30%	**0.011**
Overall survival (OS)	82%	80%	0.50

Dikjstra, et al: Annals of Surg, 2023

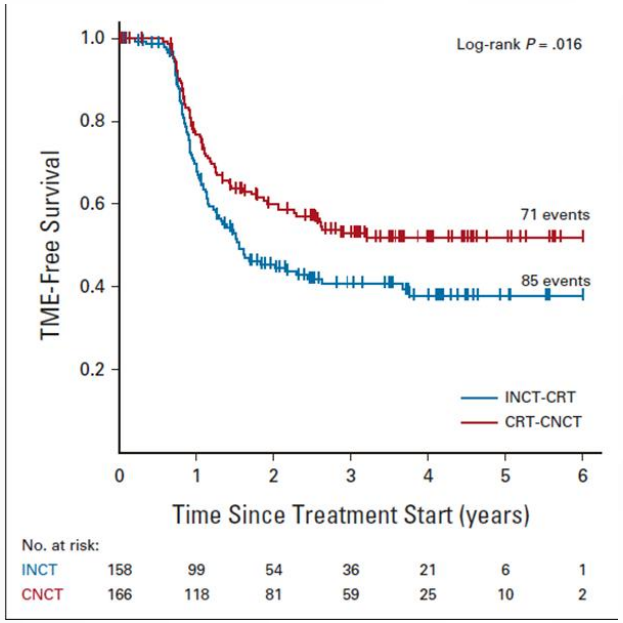
Organ Preservation in Rectal Cancer Trial (OPRA)

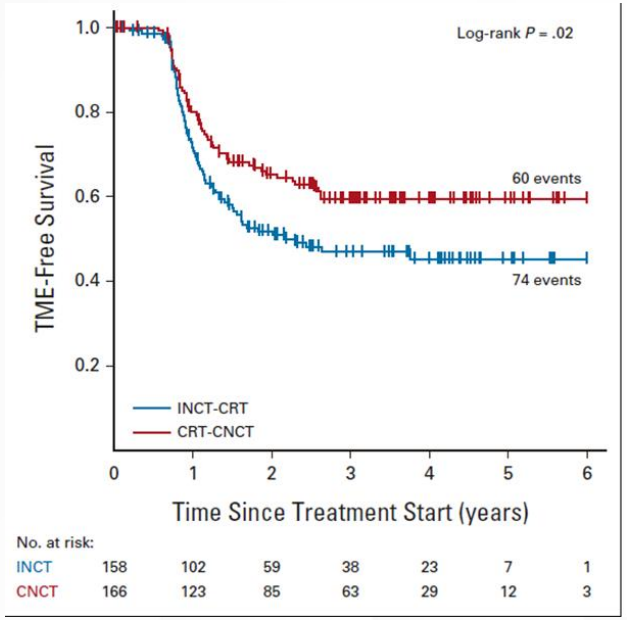


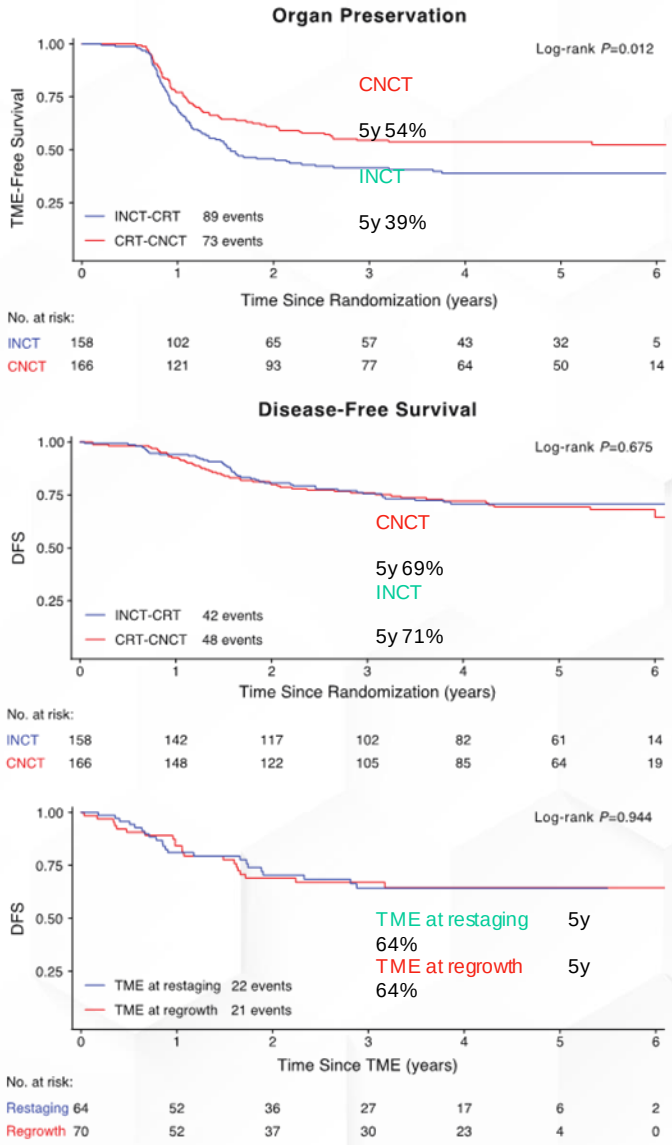
Garcia-Aguilar et al: JCO 2022

OPRA: 3-yr and 5-yr TME-Free Survival

- **Median follow-up 5.1 yrs.**
- 304 patients were restaged.
- 36% developed a regrowth:
  44% of INCT-CRT patients
  35/120 (29%) of CRT-CNCT patients.
- 94% of regrowths occurred within 2 years
- 99% occurred within 3 years after restaging.



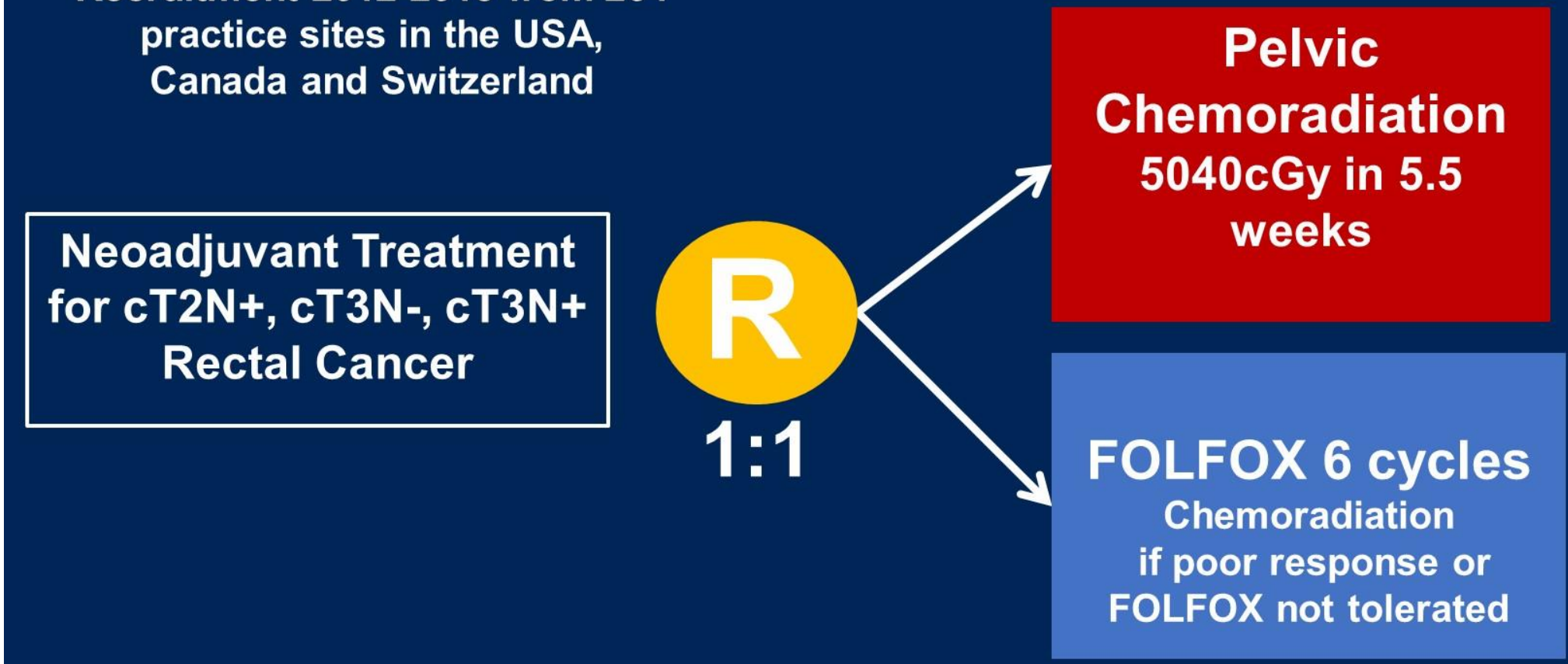




Garcia-Aguilar et al: JCO, 2022; Verheij et al: ASCO 2023

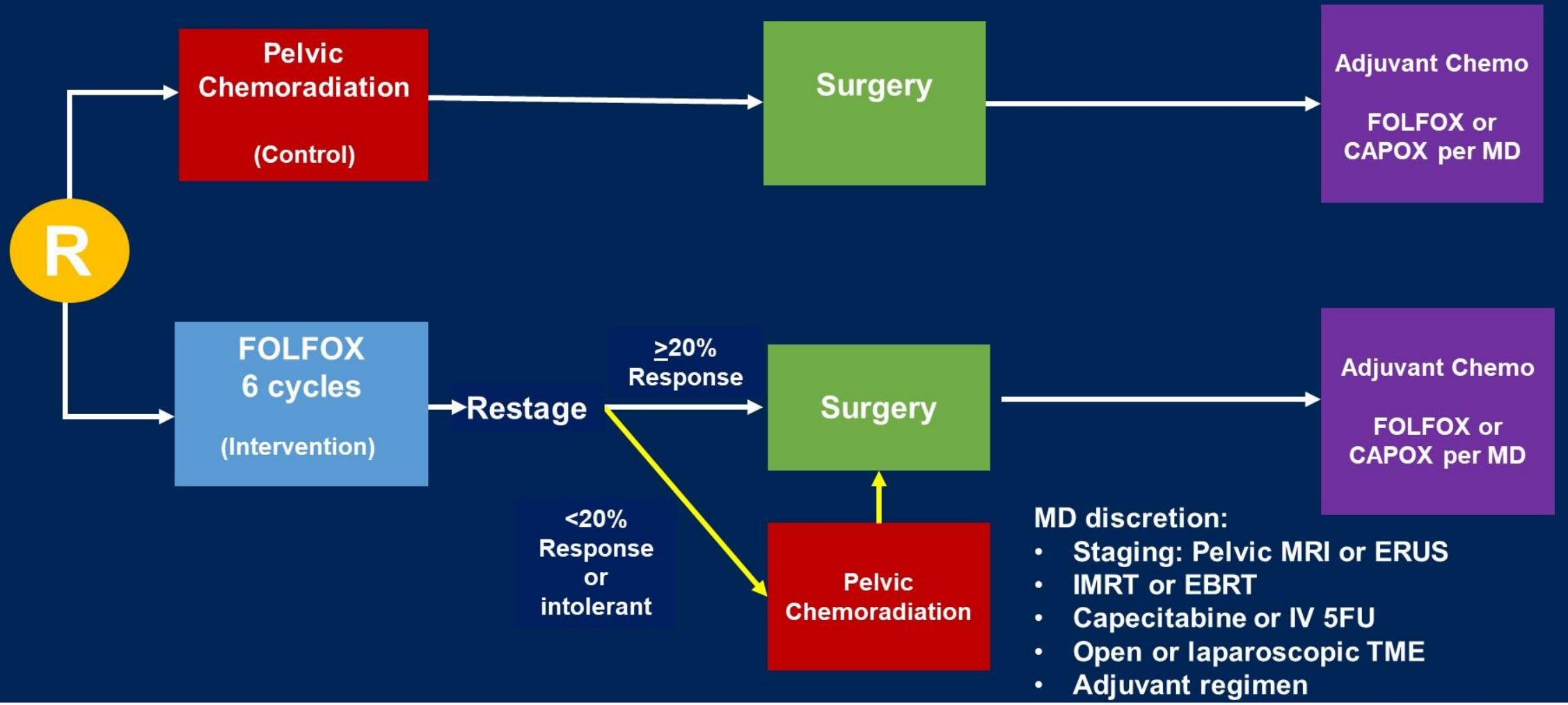
PROSPECT Study Summary

Recruitment 2012-2018 from 264 practice sites in the USA, Canada and Switzerland



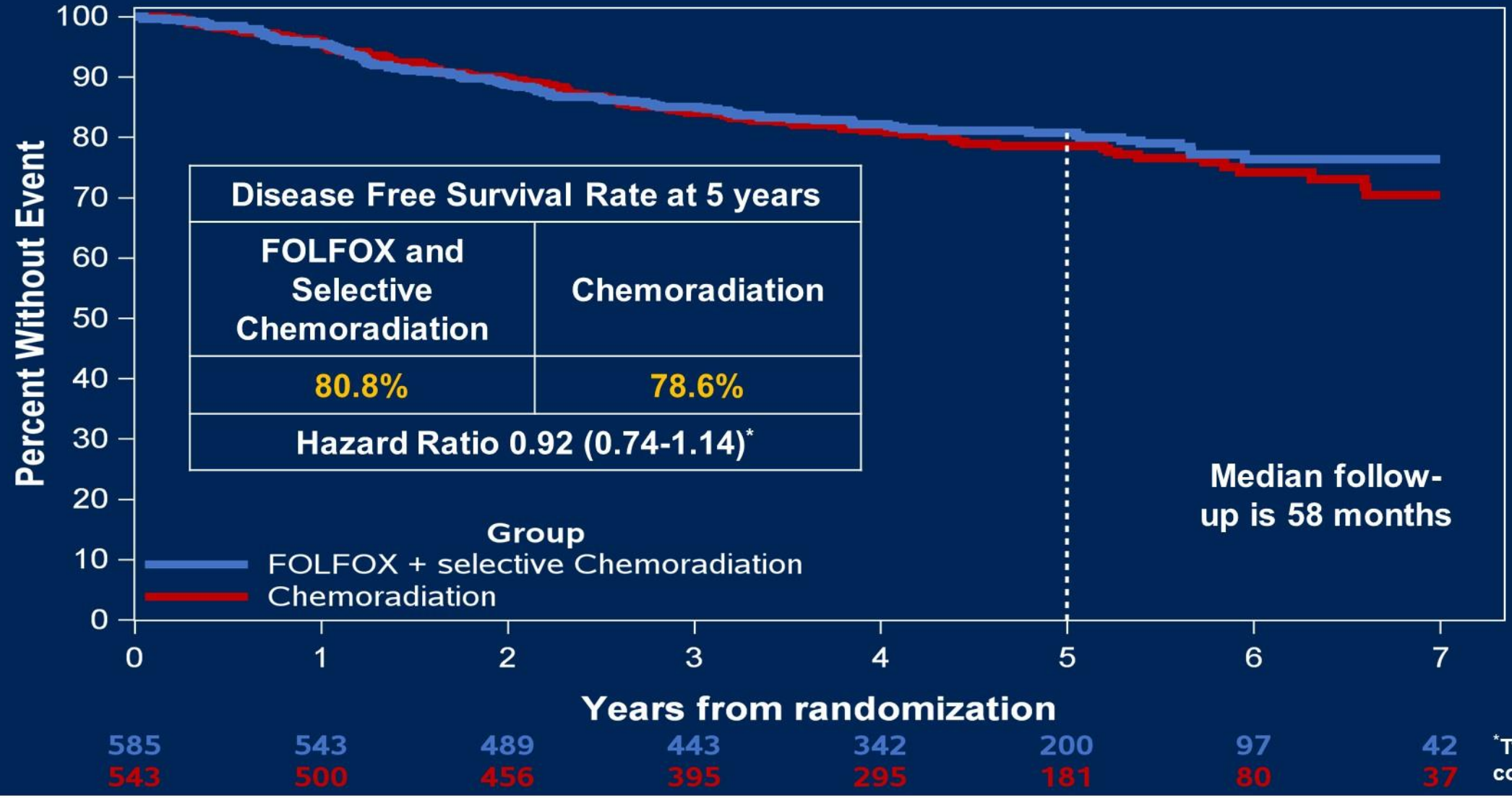
Schrag et al: NEJM, 2023

PROSPECT Study Full Schema



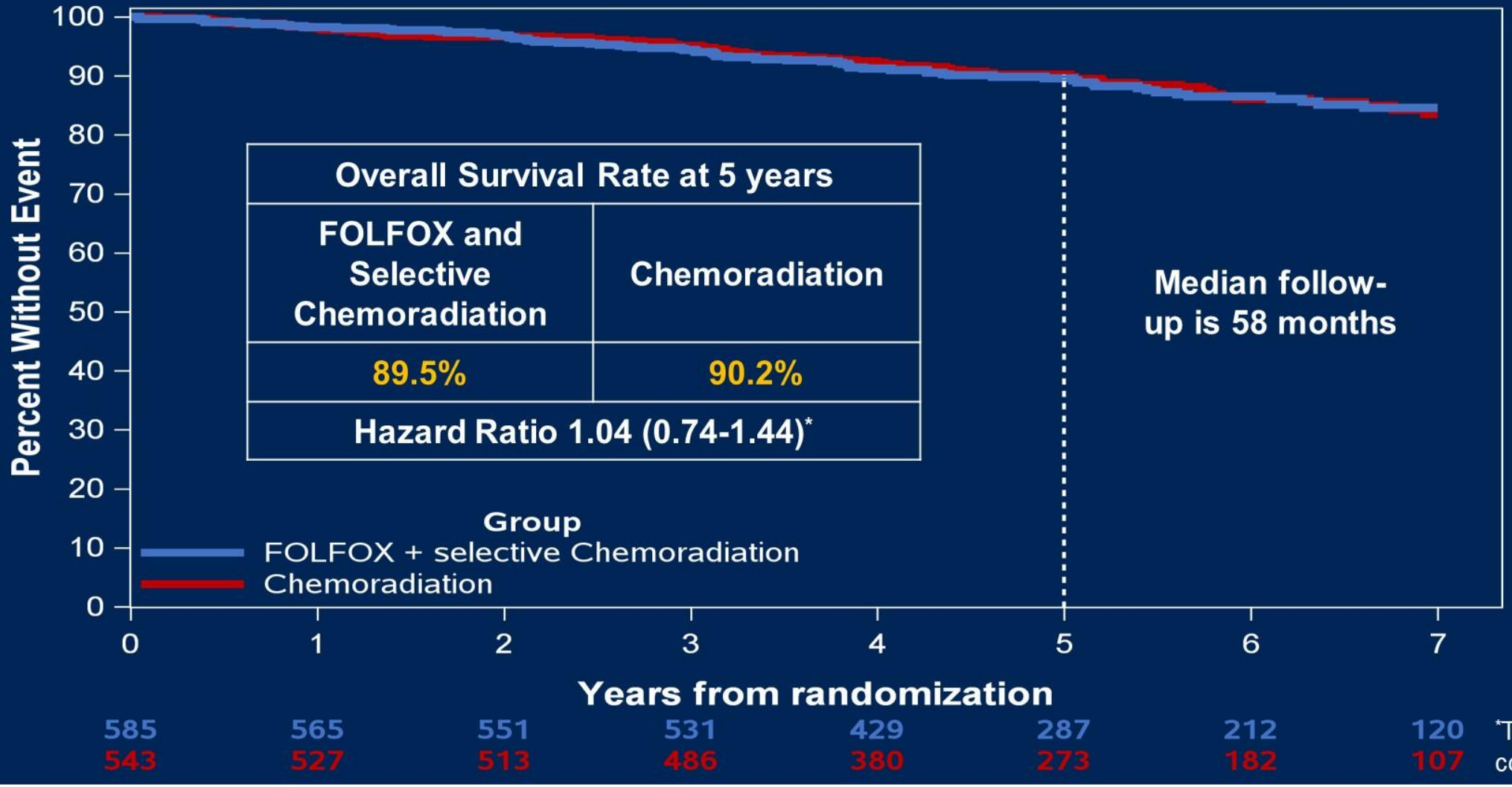
Schrag et al: NEJM, 2023

PROSPECT: Disease Free Survival



Schrag et al: NEJM, 2023

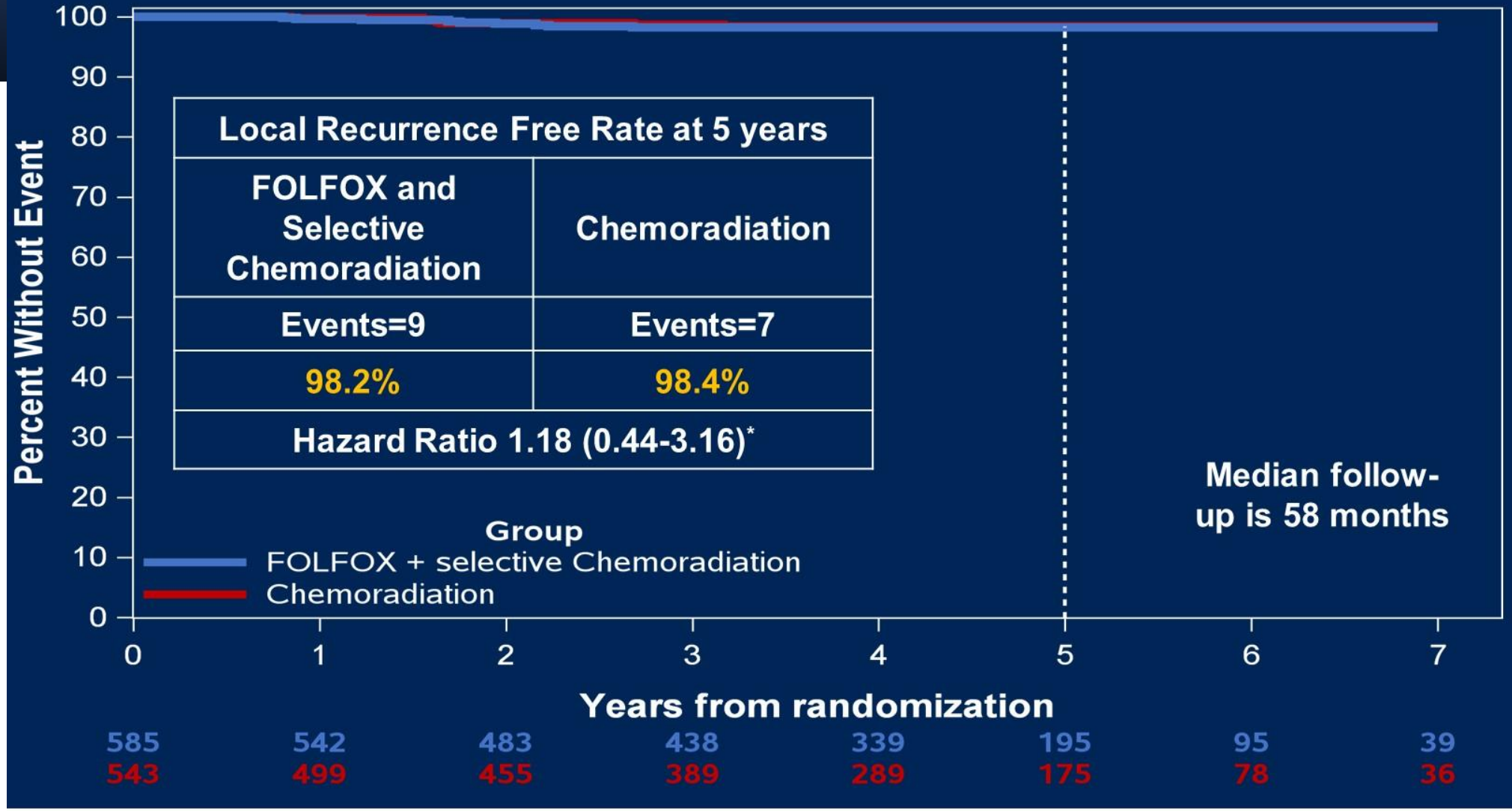
PROSPECT: Overall Survival



*Two-sided 95% confidence interval

Schrag et al: NEJM, 2023

PROSPECT: Freedom from Local Recurrence



*Two-sided 95% confidence interval

Schrag et al: NEJM, 2023

Watch and Wait Pioneer

Dr. Angelita Habr-Gama, MD, PhD
Professor
Sao Paulo, Brazil

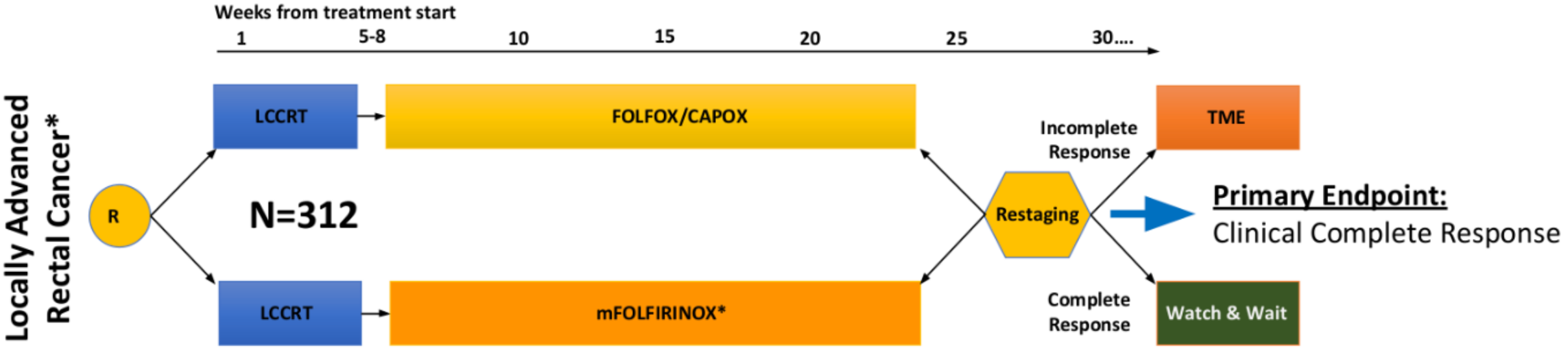
The Janus Rectal Cancer Study: A Randomized Phase II Trial

NCT05610163

A022104 An Alliance, NRG & SWOG Study



Opened: 9 Nov 2022!



PI's: J. Smith, A. Dasari, W. Hall

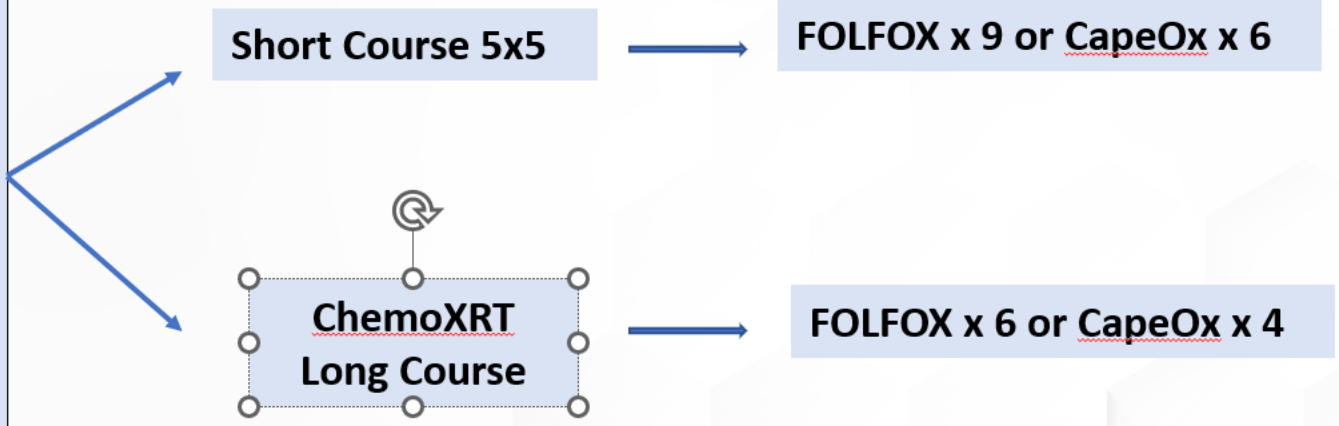
Schema Legend: Randomization = R; LCCRT = long-course chemoradiation; Restaging determination = endoscopy, MRI and clinical exam 8-12 weeks post-completion of assigned TNT regimen

* <=12cm, cT4N0, anyT, N+; T3N0 that would require APR or coloanal anastomosis

Short vs. Long-Course RT w/Organ Preservation for High-Risk Rectal Cancer Patients (ACO/ARO/AIO-18.1)

- Any cT3 < 6 cm
- cT3c/d in the middle third of the rectum (≥ 6-12 cm) with EMVI > 5 mm (>cT3b)
- cT3 with clear cN+
- cT4 tumors
- N+
- mrCRM+ (< 1mm)
- Extramural venous invasion (EMVI+)

N=712



Primary endpoint: Organ Preservation
PI: C. Roedel

NCT04246684

Rectal Cancer Trials: Summary

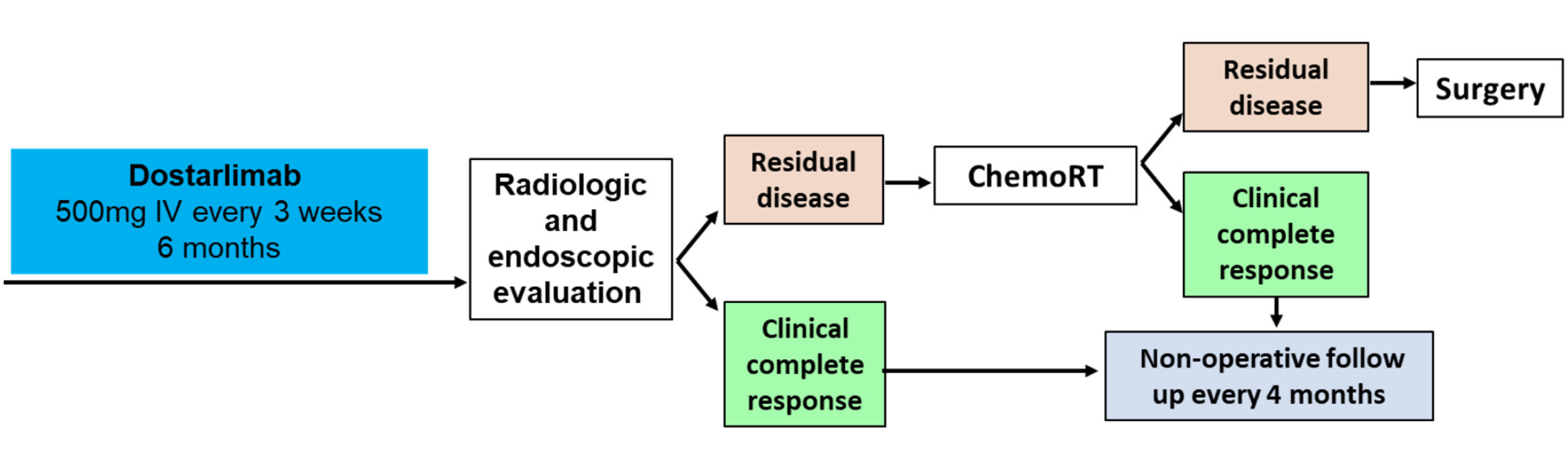
Name of Trial	Phase	AJCC Stage	Location of tumor	DFS	OS	Mets	Other	Findings
OPRA	II	T3/T4N0; TxN+	Low-Lying	Equivocal	Equivocal	N/A	Sequence; W+W	ChemoXRT first improves W+W
RAPIDO	III	T4a/b; N2	-	P= 0.048	P=0.50	P=0.011	5X5	Long-term: High-risk local recurrence
PRODIGE23	III	T3/T4N0; TxN+	-	-	P=0.033	P=0.011	FOLFOXIRI and not full TNT	Improved DFS and MFS
PROSPECT	III	T3N0 or TxN+	Mid to high	Equivocal	Equivocal	-	Non-inferior	Omission of XRT
JANUS NCT05610163	II/III(?)	T3/T4N0; TxN+	-	Pending	Pending	Pending	FOLFOXIRI	cCR
ACO/ARO/ AIO-18.1 NCT04495088	III	T3/T4N0; TxN+ EMVI	Low-mid	Pending	Pending	Pending	Pending	W+W

W+W = Active surveillance

Garcia-Aguilar et al: JCO, 2022; Bahadoer et al: Lanc Onc, 2021; Conroy et al: ASCO 2023; Schrag et al: NEJM, 2023

Rectal Cancer: MSI-H

PD-1 Blockade in Locally Advanced MSI-H Rectal Cancer



Patient population: Stage II and III mismatch repair deficient rectal cancer

Target Enrollment: 30 subjects

Study Design: Simon's two stage minimax design

Cercek et al: NEJM, 2022

NCT04165772

Demographic and disease characteristics of the patients at baseline

		Value (%)
Sex		
	Male	6 (33)
	Female	12 (67)
Age, median (range)		54 (26-78)
Race/Ethnicity		
	White non-Hispanic	11 (61)
	Hispanic	1 (6)
	Black or African American	3 (17)
	Asian-Far East/Indian Subcontinent	3 (17)
Tumor Staging		
	T1/2	4 (22)
	T3, T4	14 (78)
Nodal Staging		
	Node-positive	17 (94)
	Node-negative	1 (6)
Germline Mutation Status n=17		
	MSH2, MLH1, MSH6, or PMS2	10 (59)
	Negative	7 (41)
BRAF V600E wild type		18 (100)
Tumor Mutational Burden (mut/Mb), mean (range)		67 (36 -106)

Cercek et al: NEJM, 2022

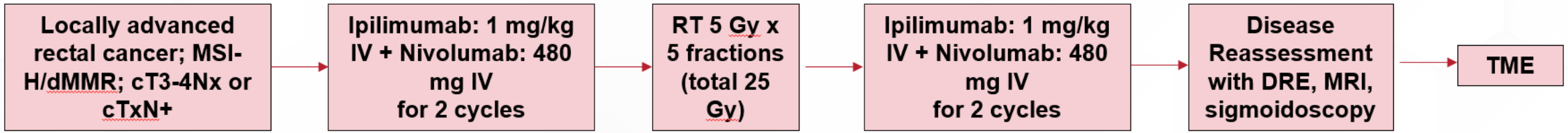
Individual responses to PD-1 blockade with dostarlimab

Patients who completed 6-months of dostarlimab

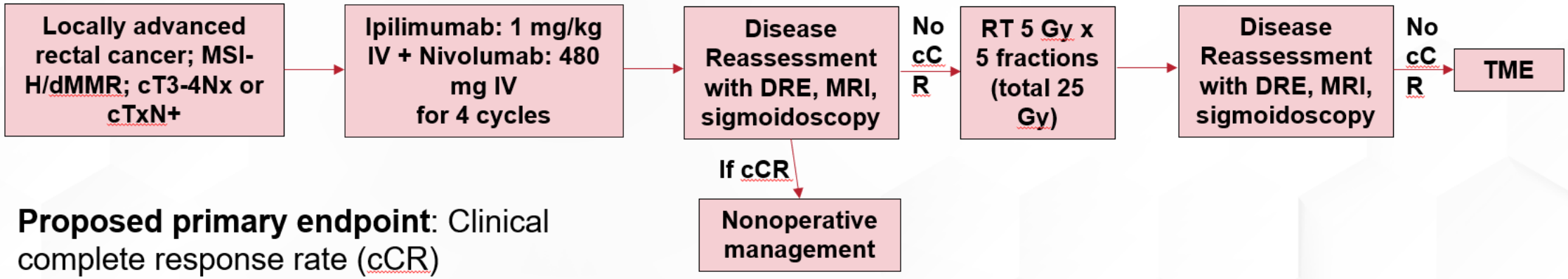
ID	Age	Stage T	Stage N	FU (months)	Digital rectal exam response	Endoscopic best response	Rectal MRI best response	Overall response 100%
1	38	T4	N+	23.8	CR	CR	CR	**cCR**
2	30	T3	N+	20.5	CR	CR	CR	**cCR**
3	61	T1/2	N+	20.6	CR	CR	CR	**cCR**
4	28	T4	N+	20.5	CR	CR	CR	**cCR**
5	53	T1/2	N+	9.1	CR	CR	CR	**cCR**
6	77	T1/2	N+	11.0	CR	CR	CR	**cCR**
7	77	T1/2	N+	8.7	CR	CR	CR	**cCR**
8	55	T3	N+	5.0	CR	CR	CR	**cCR**
9	68	T3	N+	4.9	CR	CR	CR	**cCR**
10	78	T3	N-	1.7	CR	CR	CR	**cCR**
11	55	T3	N+	4.7	CR	CR	CR	**cCR**
12	27	T3	N+	4.4	CR	CR	CR	**cCR**
13	26	T3	N+	0.8	CR	CR	CR	**cCR**
14	43	T3	N+	0.7	CR	CR	CR	**cCR**

Cercek et al. NEJM, 2022

EA2201: Current and Proposed Schema



Current primary endpoint: Pathologic complete response rate (pCR)



Proposed primary endpoint: Clinical complete response rate (cCR)

PI: Kristen Ciombor

Statistical design:

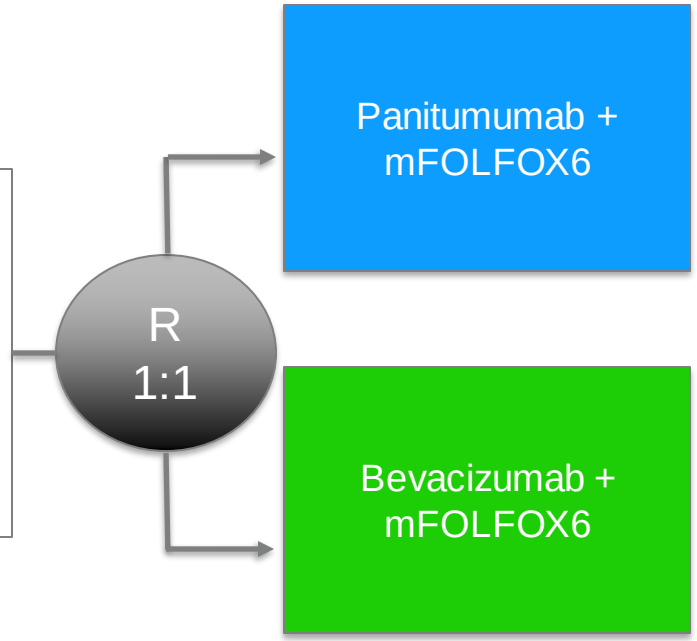
- Two-stage single-arm phase II study

Left sided all RAS WT mCRC

PARADIGM: 1st Prospective Phase III Trial (Lt-Sided All *RAS* WT mCRC- Amendment)

Patients with RAS WT metastatic CRC
- Unresectable disease
- No previous chemotherapy
- Age: 20-79 years
- ECOG performance status 0–1

N=823



Primary endpoint
- OS: left-sided population; overall population if significant

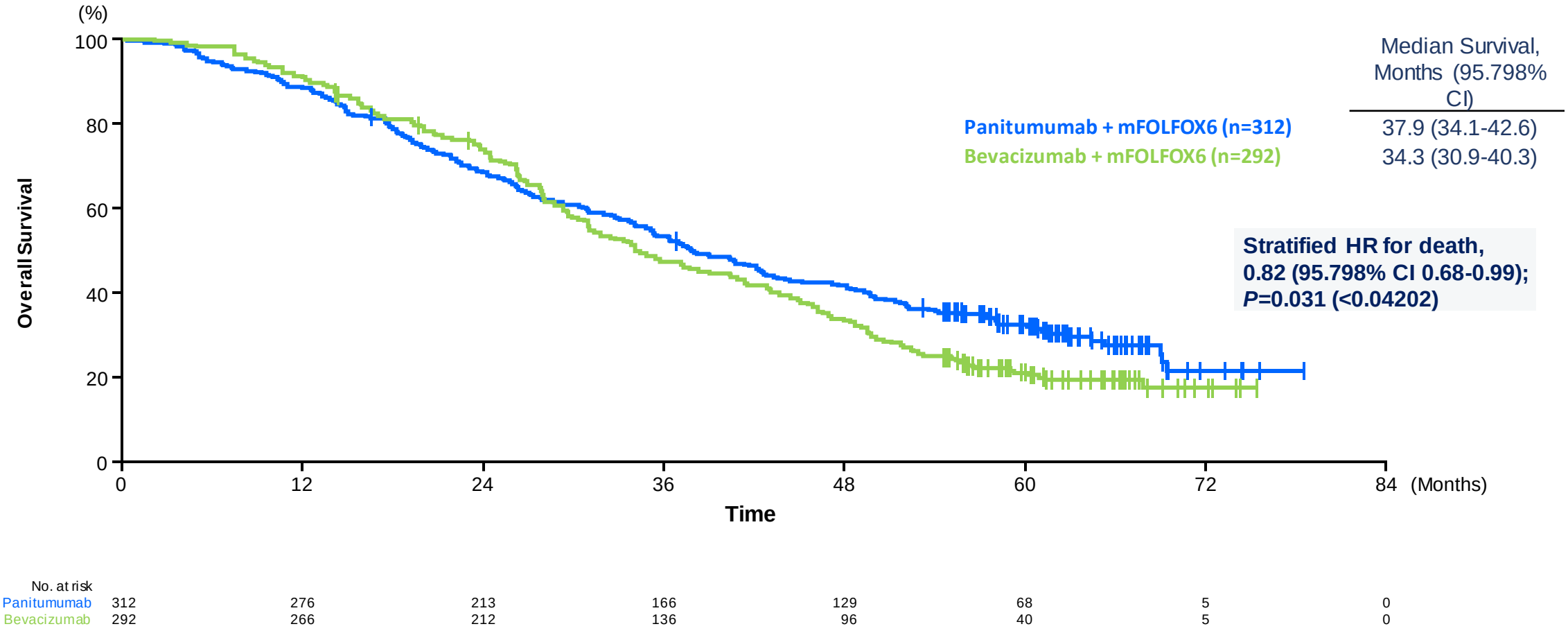
Secondary endpoints
- PFS, RR, DOR, R0 resection: left-sided and overall populations
- Safety: all treated patients

Exploratory endpoints
- ETS, depth of response, DCR: left-sided and overall populations

ECOG = Eastern Cooperative Oncology Group.

Yoshino T, et al. *J Clin Oncol.* 2022;40(Suppl 17):LBA1. Presented at: ASCO;2022. Watanabe J. *JAMA*. 2023;329:1271-82.

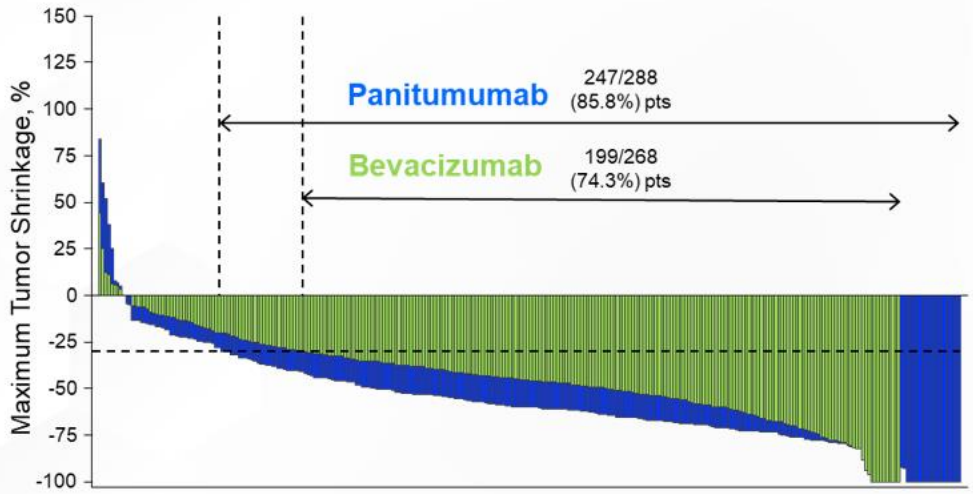
PARADIGM Primary Endpoint: OS in Left-Sided Population



- Yoshino T, et al. *J Clin Oncol.* 2022;40(Suppl 17):LBA1. Presented at: ASCO;2022. Watanabe J. *JAMA*. 2023.

PARADIGM: 1st Prospective Phase III Trial: RR and Depth of Response

Left-Sided Population



Horizontal dotted line at 30% indicates response per RECIST v1.1.

	Left-sided Population	
	Panitumumab + mFOLFOX6 (n=288)	Bevacizumab + mFOLFOX6 (n=268)
Median, %	-59.4	-43.6

Depth of response was assessed in patients with measurable lesions at baseline.

Parameter	Left-sided Population	
	Panitumumab + mFOLFOX6 (n=308)	Bevacizumab + mFOLFOX6 (n=287)
Response rate, % (95% CI)	80.2 (75.3–84.5)	68.6 (62.9–74.0)
Difference, % (95% CI)	11.2 (4.4–17.9)	
DCR, % (95% CI)	97.4 (94.9–98.9)	96.5 (93.7–98.3)
Median DOR,[a] months (95% CI)	13.1 (11.1–14.8)	11.2 (9.6–13.1)
R0 rate,[b] % (95% CI)	18.3 (14.1–23.0)	11.6 (8.2–15.9]

	No. (%) of Patients With Events	Median PFS, Months (95% CI)
Panitumumab + mFOLFOX6 (n=312)	245 (78.5)	13.7 (12.7–15.3)
Bevacizumab + mFOLFOX6 (n=292)	252 (86.3)	13.2 (11.4–14.5)

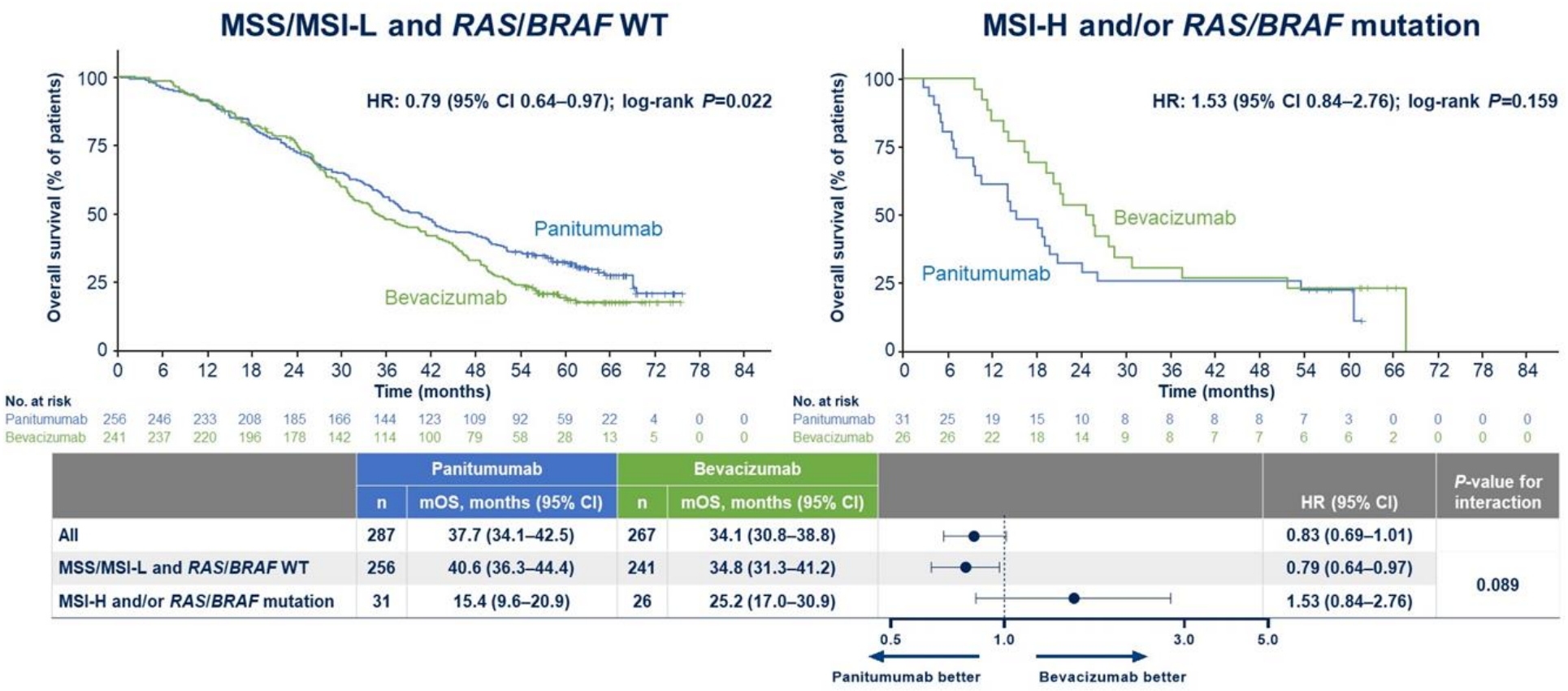
Stratified HR, 0.98 (95% CI, 0.82–1.17)

RR = relapsed/refractory.

Yoshino T, et al. *ASCO LBA 2022;* Watanabe J. *JAMA*. 2023.

PARADIGM Updated Molecular Analysis

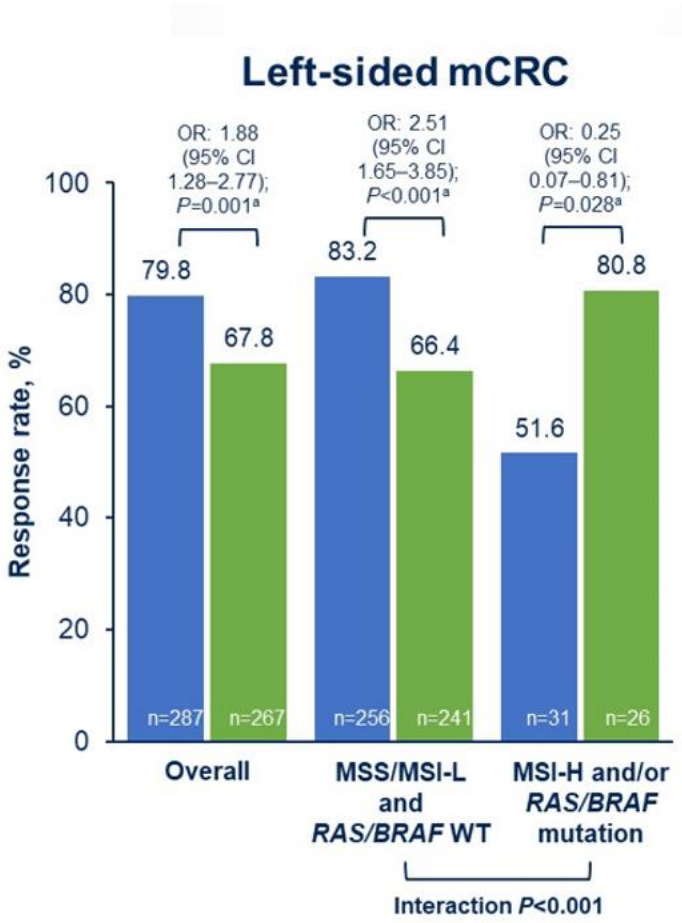
Overall survival by MSS/MSI and *RAS/BRAF* status in left-sided mCRC

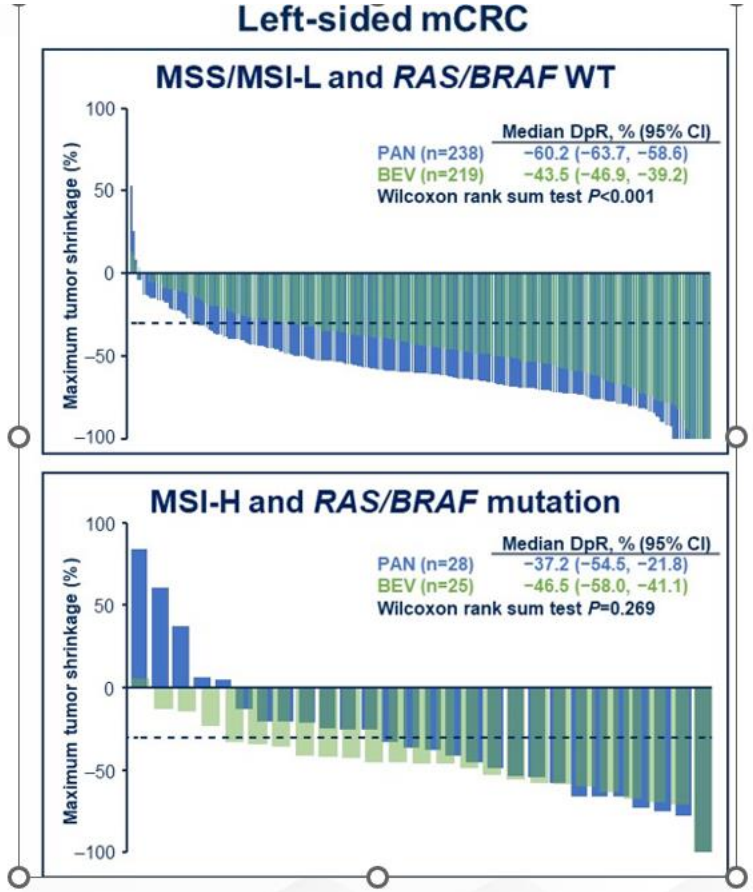


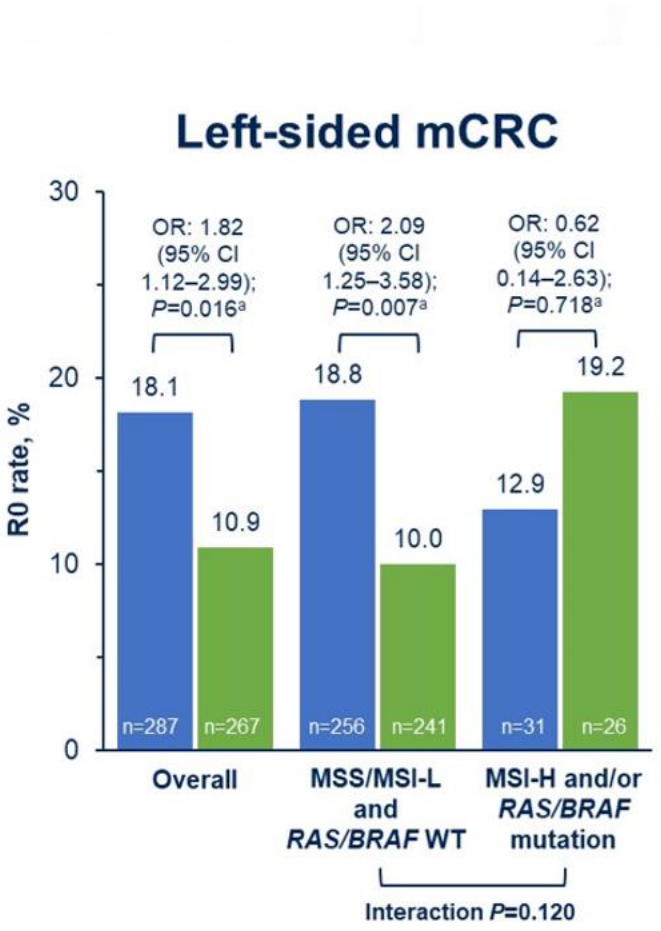
	Panitumumab		Bevacizumab		HR (95% CI)	*P*-value for interaction
	n	mOS, months (95% CI)	n	mOS, months (95% CI)		
All	287	37.7 (34.1–42.5)	267	34.1 (30.8–38.8)	0.83 (0.69–1.01)	
MSS/MSI-L and *RAS/BRAF* WT	256	40.6 (36.3–44.4)	241	34.8 (31.3–41.2)	0.79 (0.64–0.97)	0.089
MSI-H and/or *RAS/BRAF* mutation	31	15.4 (9.6–20.9)	26	25.2 (17.0–30.9)	1.53 (0.84–2.76)	

Yamazaki et al: ASCO 2023

PARADIGM Updated Molecular Analysis



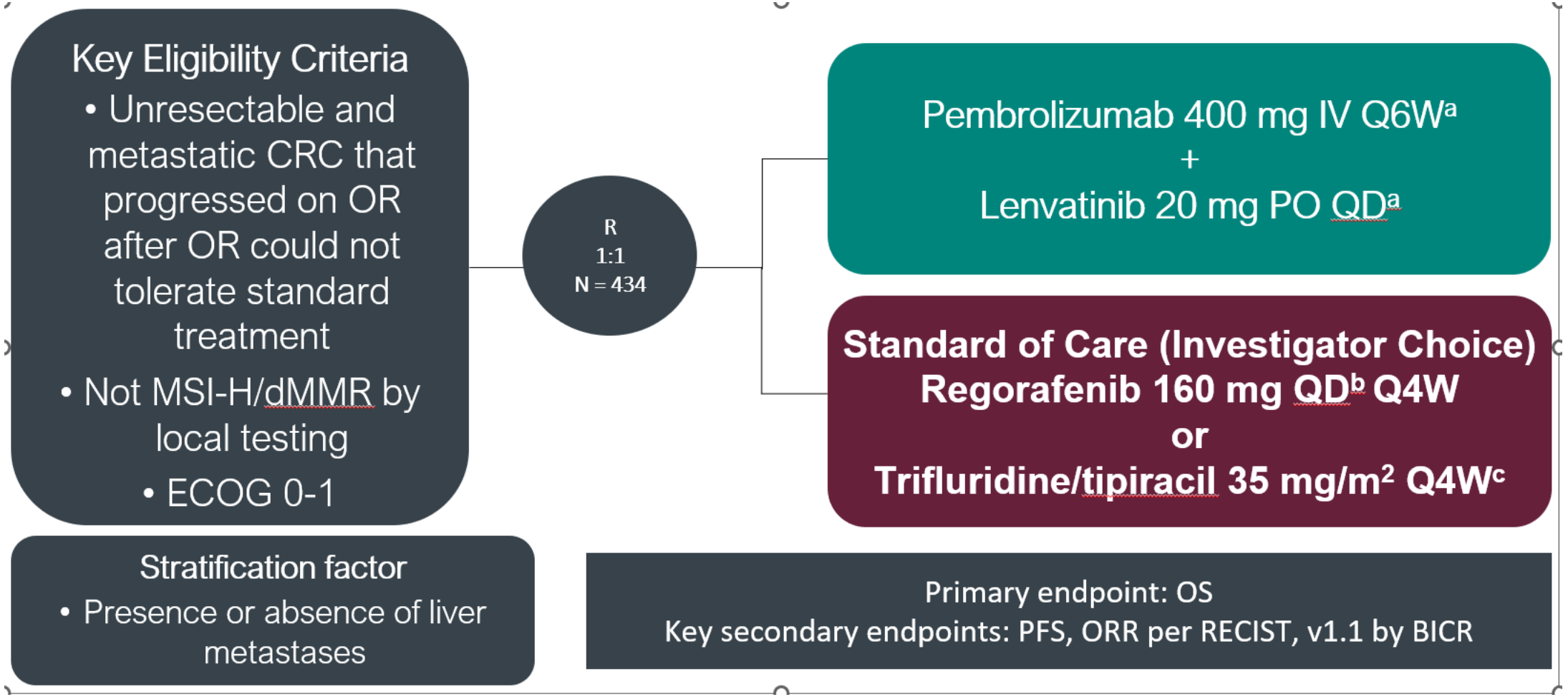




Yamazaki et al: ASCO 2023

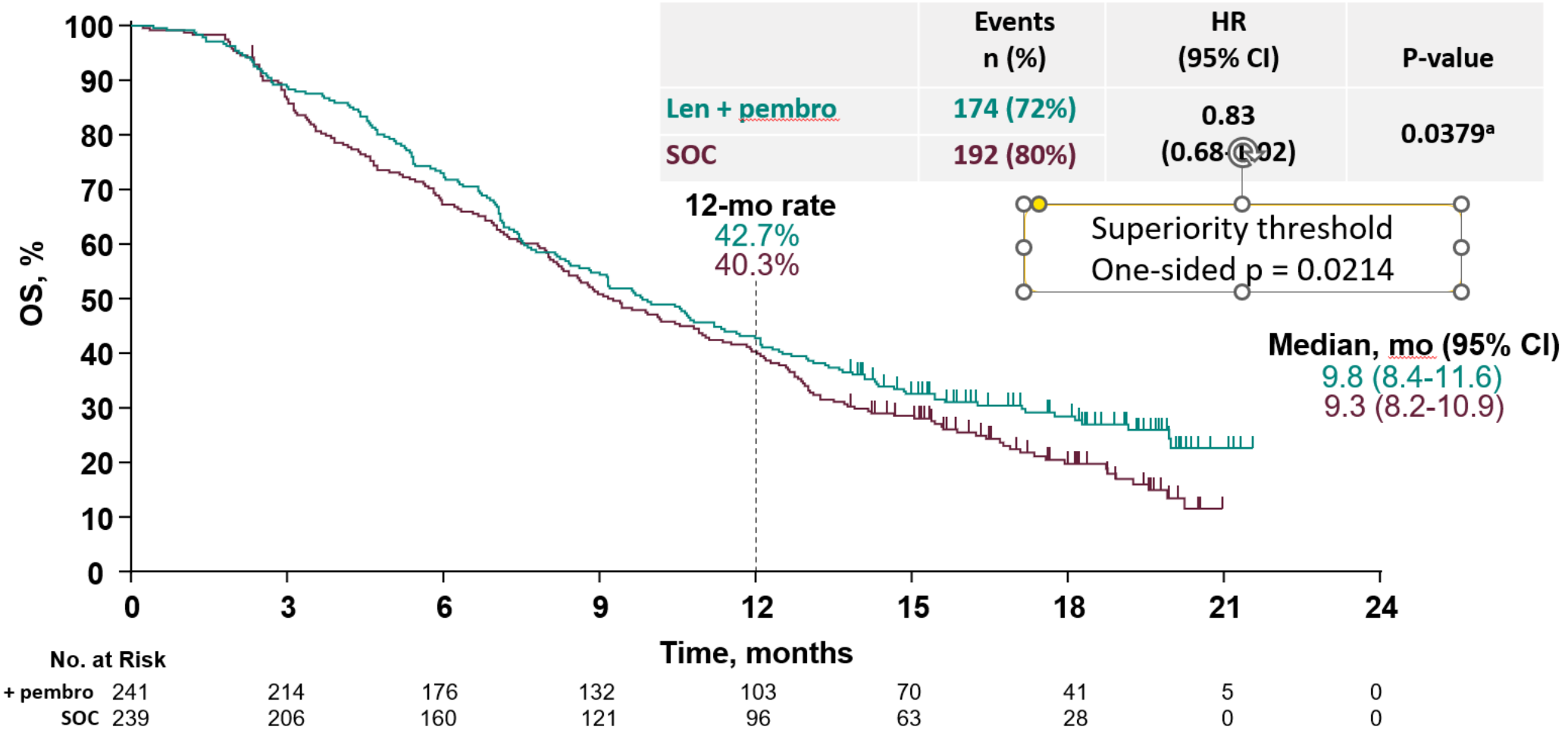
All comers mCRC

LEAP-017 Study Design



Kawazoe et al: WGIC, 2023

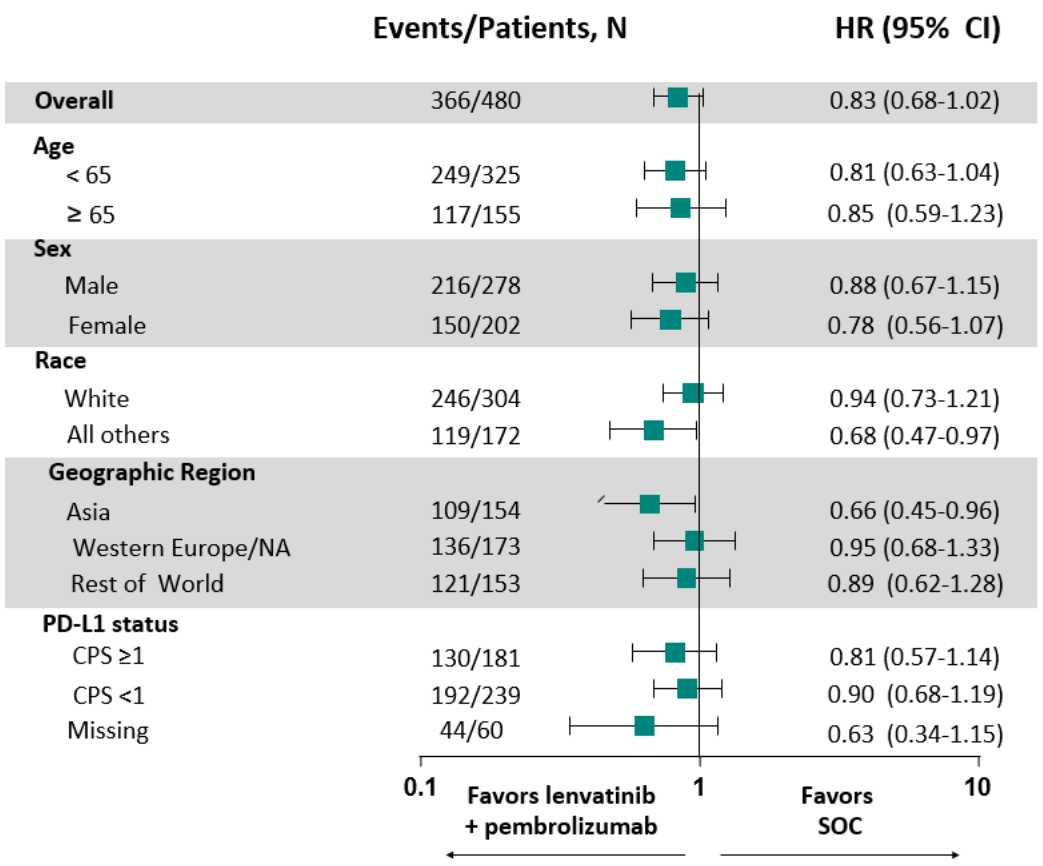
LEAP-017 Study Design

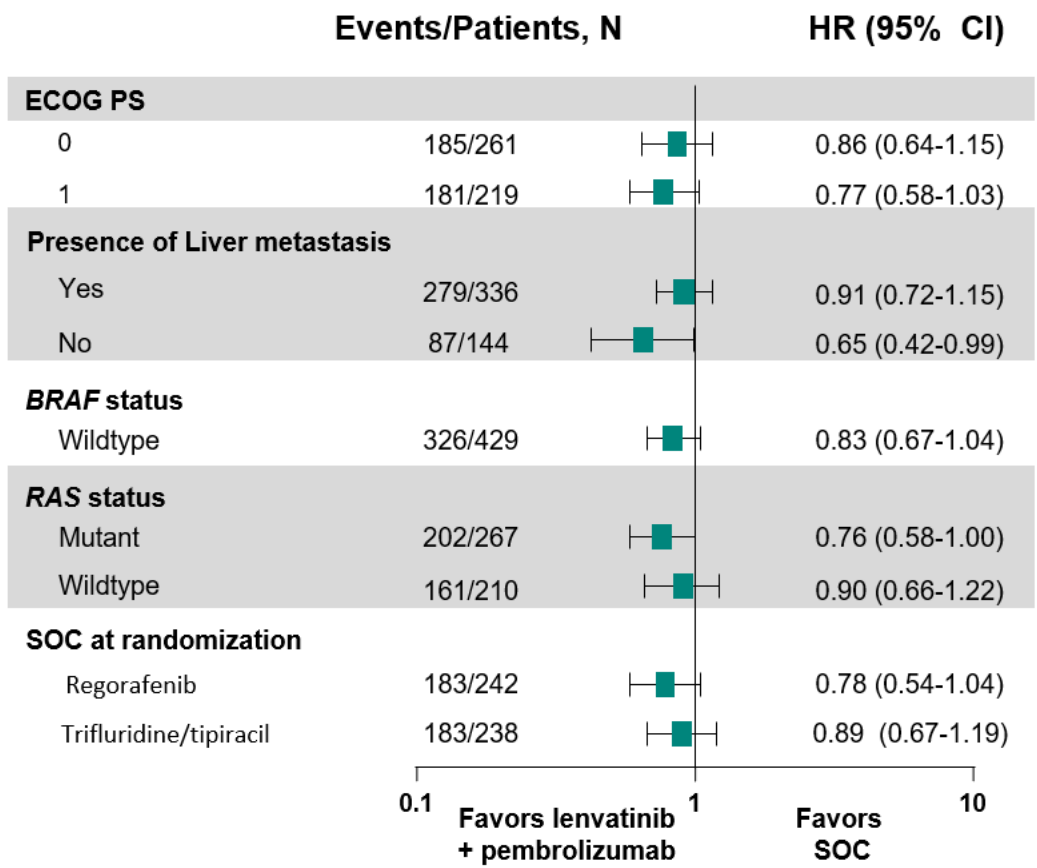


	Events n (%)	HR (95% CI)	P-value
Len + pembro	174 (72%)	0.83 (0.68-1.02)	0.0379[a]
SOC	192 (80%)		

Kawazoe et al: WGIC, 2023

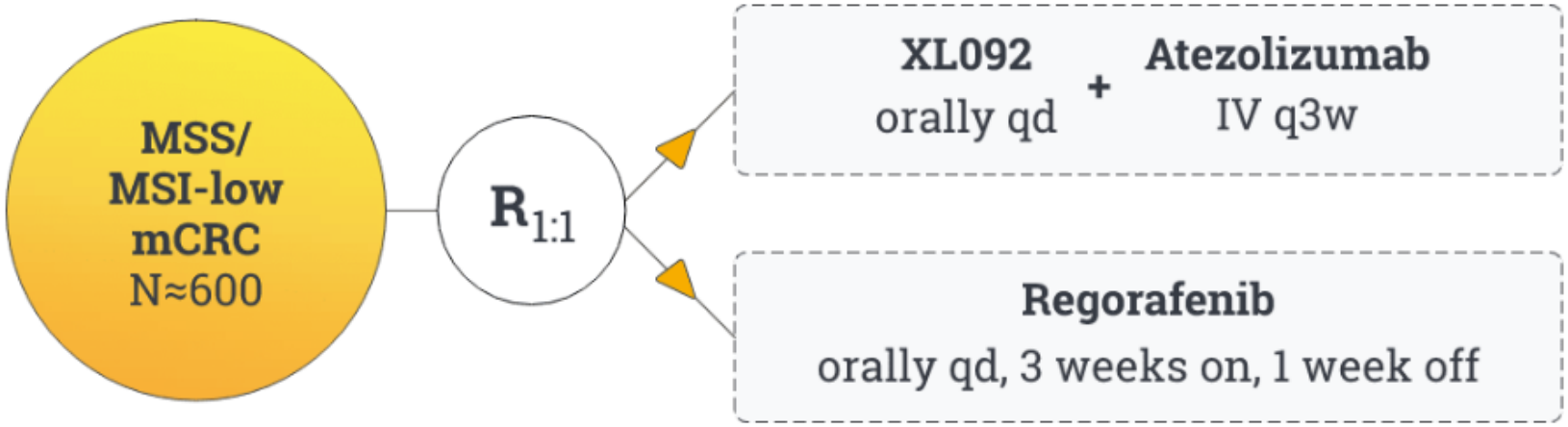
LEAP-017: Forest Plots for OS





Kawazoe et al: WGIC, 2023

Stellar 303:



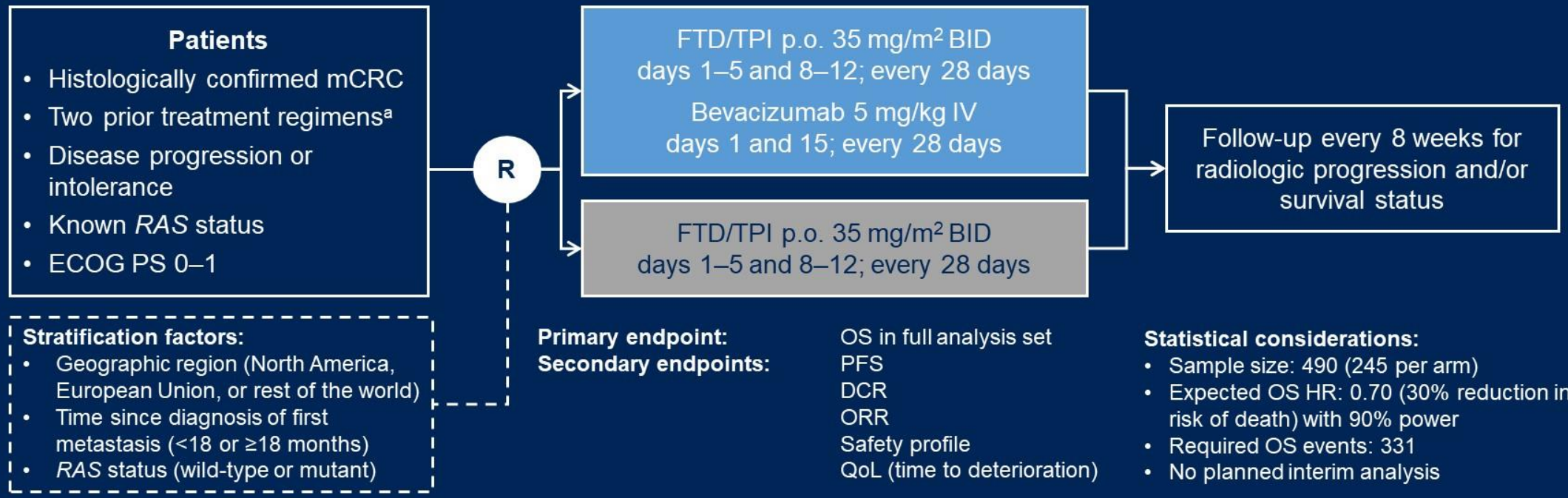
N= 600

- Known RAS status
- Progressed, refractory, or intolerant to all of the following SOC regimens for mCRC:
  - Fluoropyrimidine, irinotecan, and oxaliplatin, ± anti-VEGF mAb
  - Anti-EGFR mAb for RAS WT
  - BRAF inhibitor for known BRAF V600E mutations
- Progression ≤4 months following the last dose of SOC regimen
- No prior treatment with zanzalintinib (XL092), regorafenib, trifluridine/tipiracil, or PD-L1/PD-1–targeting ICIs

NCT05425940

SUNLIGHT study design

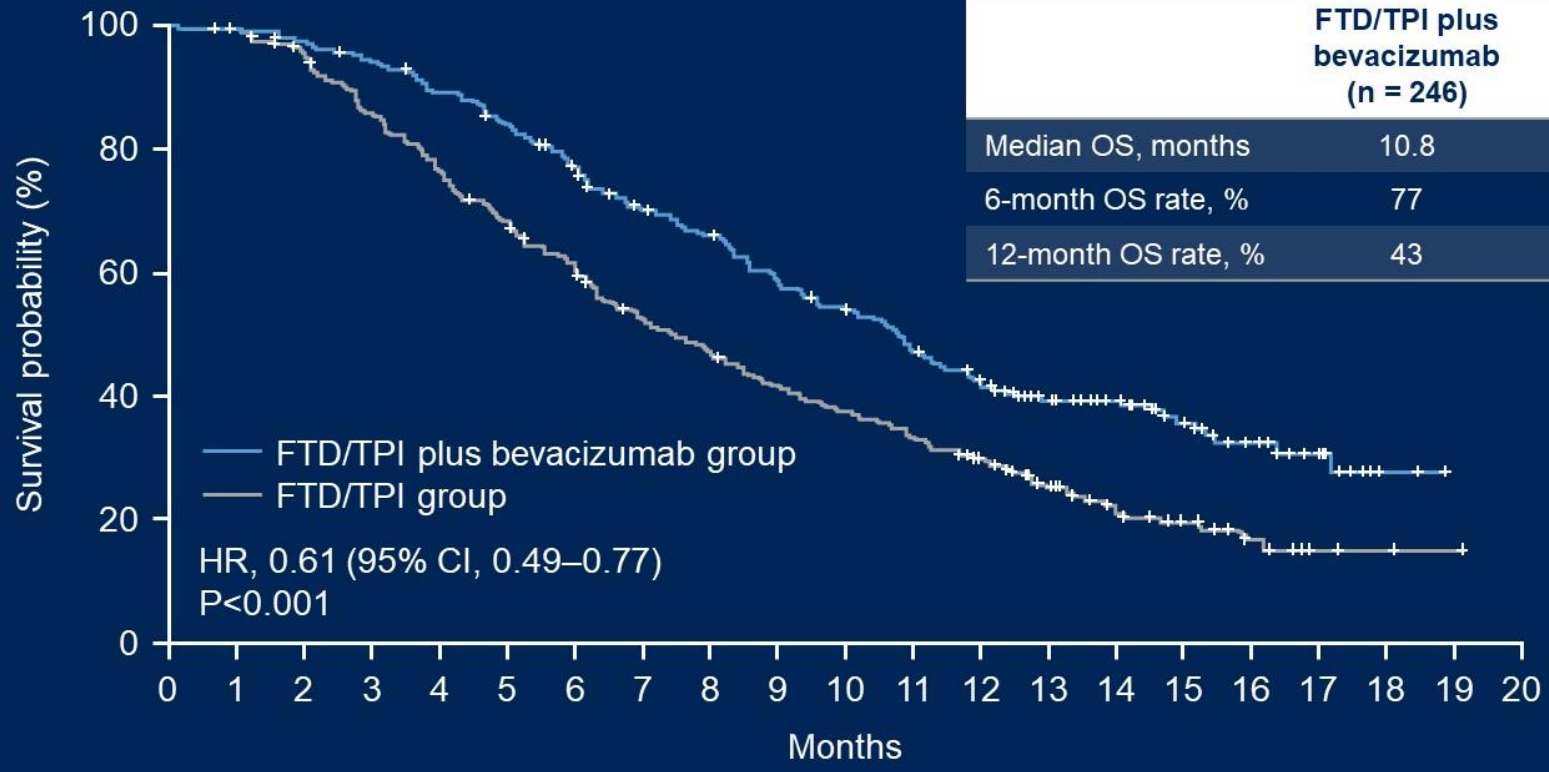
- An open-label, randomized, phase 3 study in patients with refractory mCRC (NCT04737187)



[a] Prior treatment must have included a fluoropyrimidine, irinotecan, oxaliplatin, an anti-VEGF monoclonal antibody (not necessarily bevacizumab), and/or an anti-EGFR monoclonal antibody for patients with *RAS* wild-type and could have included (neo)adjuvant chemotherapy if disease had recurred during treatment or within 6 months of the last administration of (neo)adjuvant therapy. BID, twice daily; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; EFGR, epidermal growth factor receptor; FTD/TPI, trifluridine/tipiracil; HR, hazard ratio; IV, intravenous; mCRC, metastatic colorectal cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; p.o., orally; QoL, quality of life; R, randomization; VEGF, vascular endothelial growth factor.

Tabanero et al: NEJM, 2023

OS in full analysis set (primary endpoint)



	FTD/TPI plus bevacizumab (n = 246)	FTD/TPI (n = 246)
Median OS, months	10.8	7.5
6-month OS rate, %	77	61
12-month OS rate, %	43	30

No. at risk

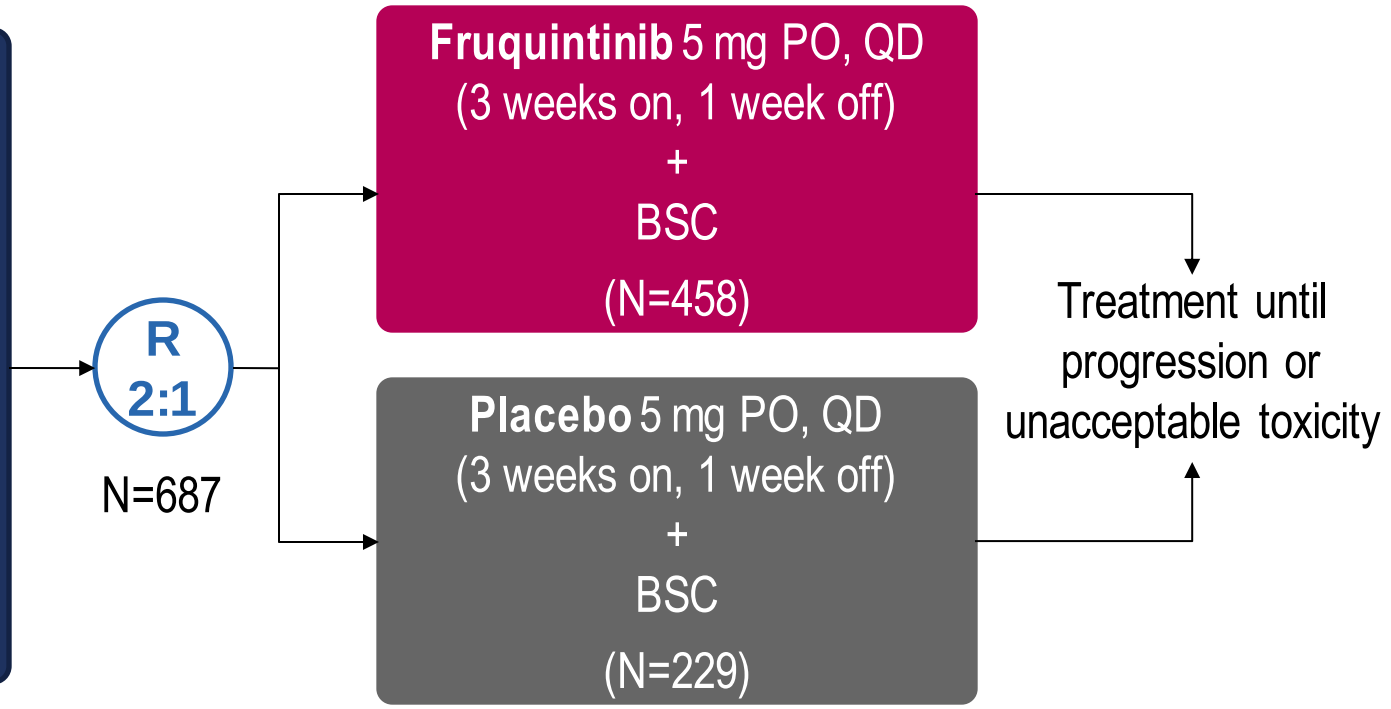
FTD/TPI plus bevacizumab group	246	244	239	230	217	203	183	160	149	131	119	104	88	69	52	37	24	13	2	0	0
FTD/TPI group	246	242	230	205	184	163	143	120	108	95	85	76	63	44	24	16	10	5	2	1	0

CI, confidence interval; FTD/TPI, trifluridine/tipiracil; HR, hazard ratio; OS, overall survival.

FRESCO-2 Study Design

Patient Eligibility

- Prior treatment with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and, if *RAS* wild type, an anti-EGFR therapy
- Progression on, or intolerance to, TAS-102 and/or regorafenib
- Prior treatment with an immune checkpoint inhibitor or BRAF inhibitor if indicated



Stratification Factors

- Prior therapy (TAS-102 vs regorafenib vs TAS-102 and regorafenib)
- *RAS* mutational status (wild-type vs mutant)
- Duration of metastatic disease (≤18 months vs >18 months)

Mechanism of action: Highly selective oral tyrosine kinase inhibitor of VEGFRs-1, -2, and -3

Note: To ensure the patient population is reflective of clinical practice, the number of patients treated with prior regorafenib was limited to 344 patients (50%)

BSC, best supportive care.
NCT04322539.

PARIS 2022 ESMO congress

Dasari A .....Eng et al. ESMO 2022; Dasari et al: Lancet, June 15, 2023

Patient and Disease Characteristics

ITT Population

Enrollment: Sep 2020 to Dec 2021

Data Cutoff: 24 June 2022

Characteristic, n (%)		Fruquintinib (N=461)	Placebo (N=230)
Age, y	Median (range)	64 (25, 82)	64 (30, 86)
	≥ 65	214 (46.4)	111 (48.3)
Sex	Female	216 (46.9)	90 (39.1)
	Male	245 (53.1)	140 (60.9)
Region	North America	82 (17.8)	42 (18.3)
	Europe	329 (71.4)	166 (72.2)
	Asia Pacific	50 (10.8)	22 (9.6)
ECOG PS	0	196 (42.5)	102 (44.3)
	1	265 (57.5)	128 (55.7)
Primary site at 1st diagnosis	Colon left	192 (41.6)	92 (40.0)
	Colon right	97 (21.0)	53 (23.0)
	Colon left and right	4 (0.9)	2 (0.9)
	Colon unknown	25 (5.4)	13 (5.7)
	Rectum only	143 (31.0)	70 (30.4)
Liver metastases	Yes	339 (73.5)	156 (67.8)

Characteristic, n (%)		Fruquintinib (N=461)	Placebo (N=230)
Duration of metastatic disease	≤ 18 mo	37 (8.0)	13 (5.7)
	> 18 mo	424 (92.0)	217 (94.3)
RAS status	WT	170 (36.9)	85 (37.0)
	Mutant	291 (63.1)	145 (63.0)
BRAF V600E mutation	No	401 (87.0)	198 (86.1)
	Yes	7 (1.5)	10 (4.3)
	Other/Unknown	5 (11.5)	22 (9.6)
Number of previous treatment lines in metastatic disease			
Median		4 (3–6)	4 (3–6)
≤3		125 (27%)	64 (28%)
>3		336 (73%)	166 (72%)
Previous therapies			
VEGF inhibitor		445 (97%)	221 (96%)
EGFR inhibitor		180 (39%)	88 (38%)
Immune checkpoint inhibitor		21 (5%)	11 (5%)
BRAF inhibitor		9 (2%)	7 (3%)
Previous trifluridine–tipiracil or regorafenib			
Trifluridine–tipiracil		240 (52%)	121 (53%)
Regorafenib		40 (9%)	18 (8%)
Both		181 (39%)	91 (40%)

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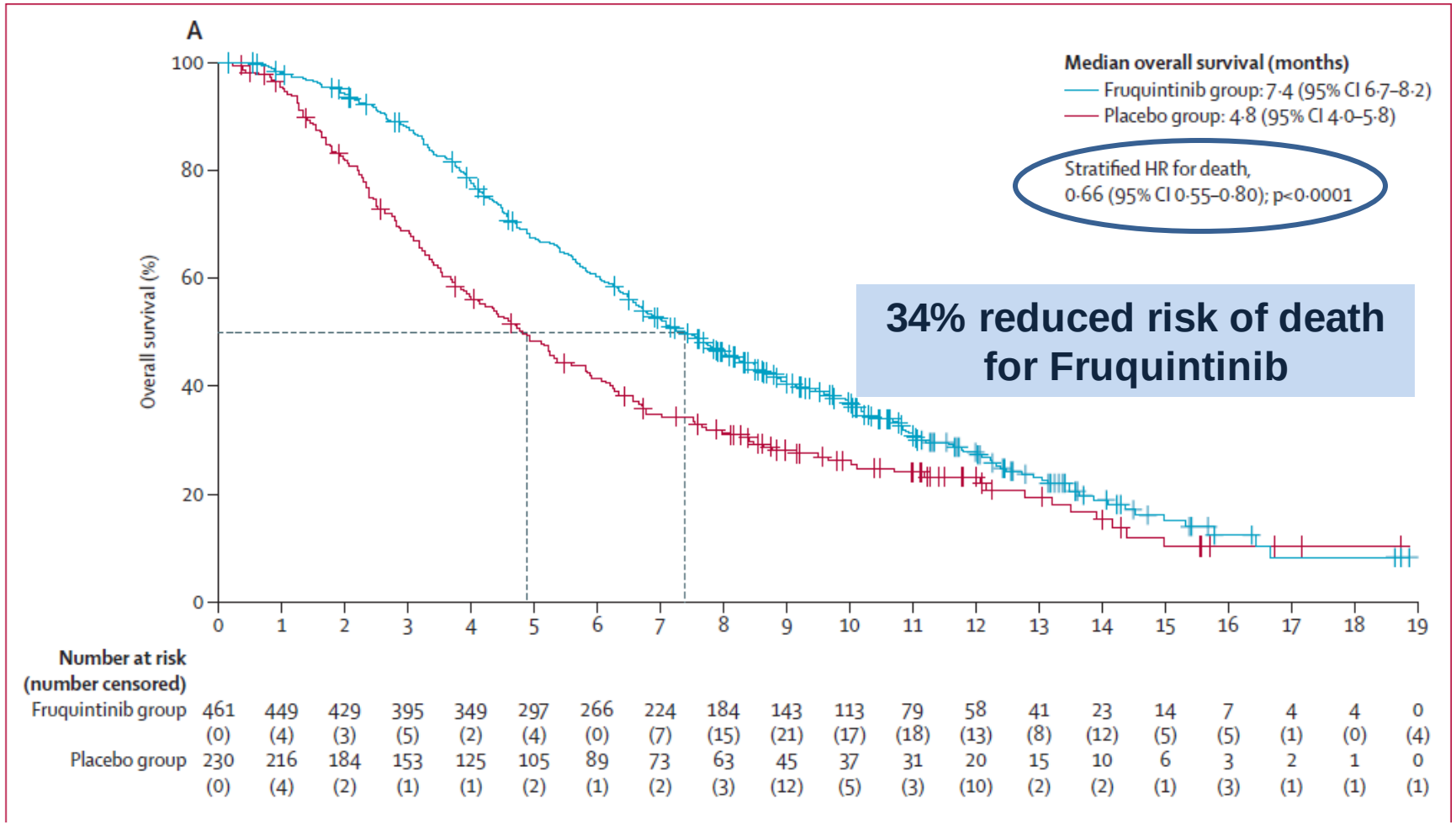
Dasari A .....Eng et al. ESMO 2022; Dasari et al: The Lancet, June 15, 2023

FRESCO-2: Primary Endpoint - OS

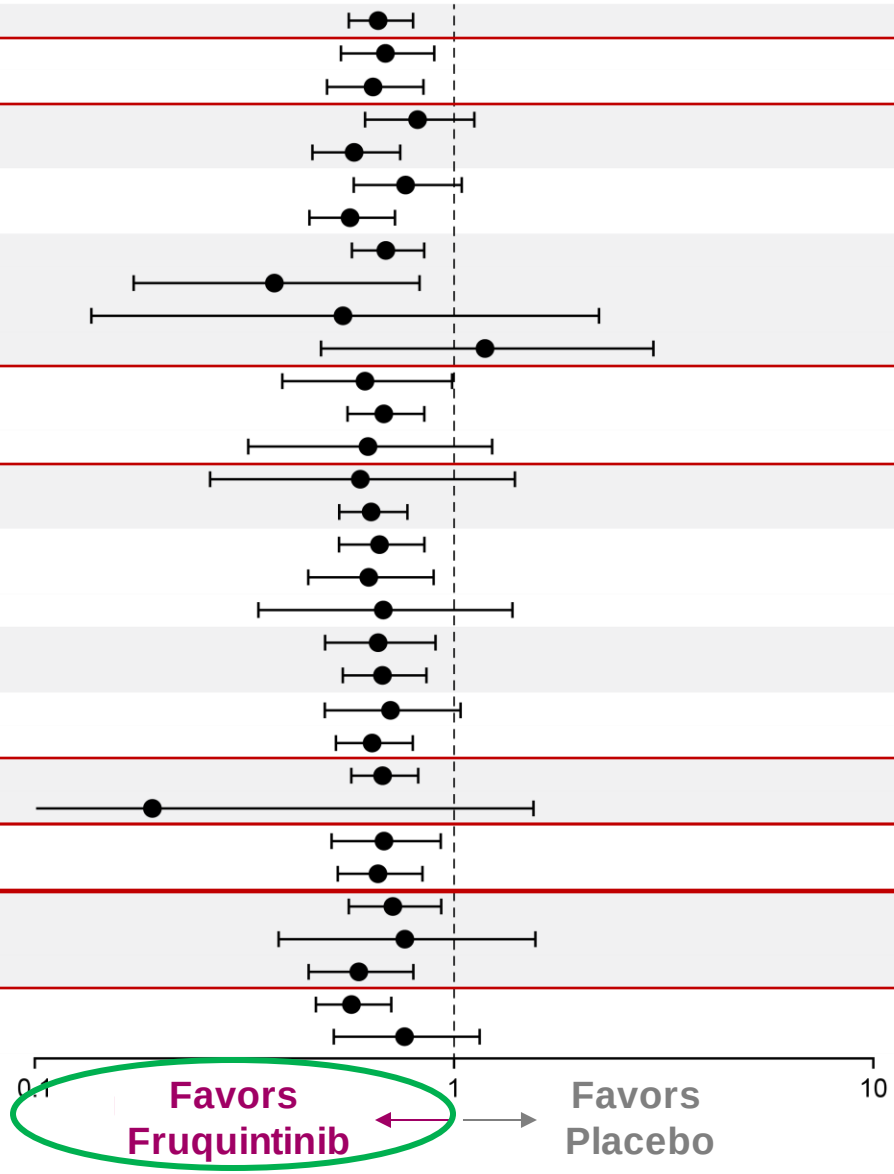


Dasari…Eng et al: The Lancet, 2023

OS Subgroup Analysis

ITT Population

Subgroup		Fruquintinib n/N	Placebo n/N	HR (95% CI)
ITT population		317/461	173/230	0.662 (0.549, 0.800)
Age	< 65	171/247	89/119	0.694 (0.534, 0.903)
	≥ 65	146/214	84/111	0.648 (0.494, 0.851)
Sex	Female	149/216	61/90	0.828 (0.609, 1.125)
	Male	168/245	112/140	0.584 (0.456, 0.749)
ECOG PS	0	121/196	67/102	0.775 (0.573, 1.050)
	1	196/265	106/128	0.571 (0.499, 0.728)
Race	Caucasian	260/367	145/192	0.696 (0.567, 0.854)
	Asian	24/43	14/18	0.377 (0.171, 0.833)
	African American	7/13	5/7	0.550 (0.135, 2.231)
	Other	26/38	9/13	1.199 (0.478, 3.008)
Region	North America	50/82	29/42	0.620 (0.387, 0.995)
	Europe	237/329	130/166	0.688 (0.554, 0.855)
	Asia Pacific	30/50	14/22	0.631 (0.321, 1.241)
Duration of metastatic disease	≤ 18 mo	30/37	8/13	0.605 (0.260, 1.406)
	> 18 mo	287/424	165/217	0.642 (0.529, 0.779)
Primary tumor site at 1st diagnosis	Colon	195/279	109/137	0.672 (0.528, 0.855)
	Rectum	99/143	49/70	0.633 (0.446, 0.900)
	Colon and Rectum	23/39	15/23	0.686 (0.339, 1.388)
RAS status	WT	119/170	62/85	0.667 (0.489, 0.909)
	Mutant	198/291	111/145	0.683 (0.539, 0.865)
# of prior treatment lines in metastatic disease	≤ 3	80/125	45/64	0.714 (0.488, 1.043)
	>3	237/336	128/166	0.645 (0.519, 0.802)
Prior VEGFi	Yes	306/445	167/221	0.683 (0.565, 0.827)
	No	11/16	6/9	0.193 (0.024, 1.557)
Prior EGFRi	Yes	127/180	64/88	0.689 (0.507, 0.936)
	No	190/281	109/142	0.666 (0.524, 0.846)
Prior TAS-102 and Regorafenib	TAS-102	165/240	88/121	0.723 (0.557, 0.938)
	Regorafenib	25/40	12/18	0.772 (0.379, 1.573)
	Both	127/181	73/91	0.600 (0.447, 0.805)
Liver metastases	Yes	255/339	132/156	0.576 (0.465, 0.713)
	No	62/122	41/74	0.771 (0.513, 1.158)



PARIS 2022 ESMO congress

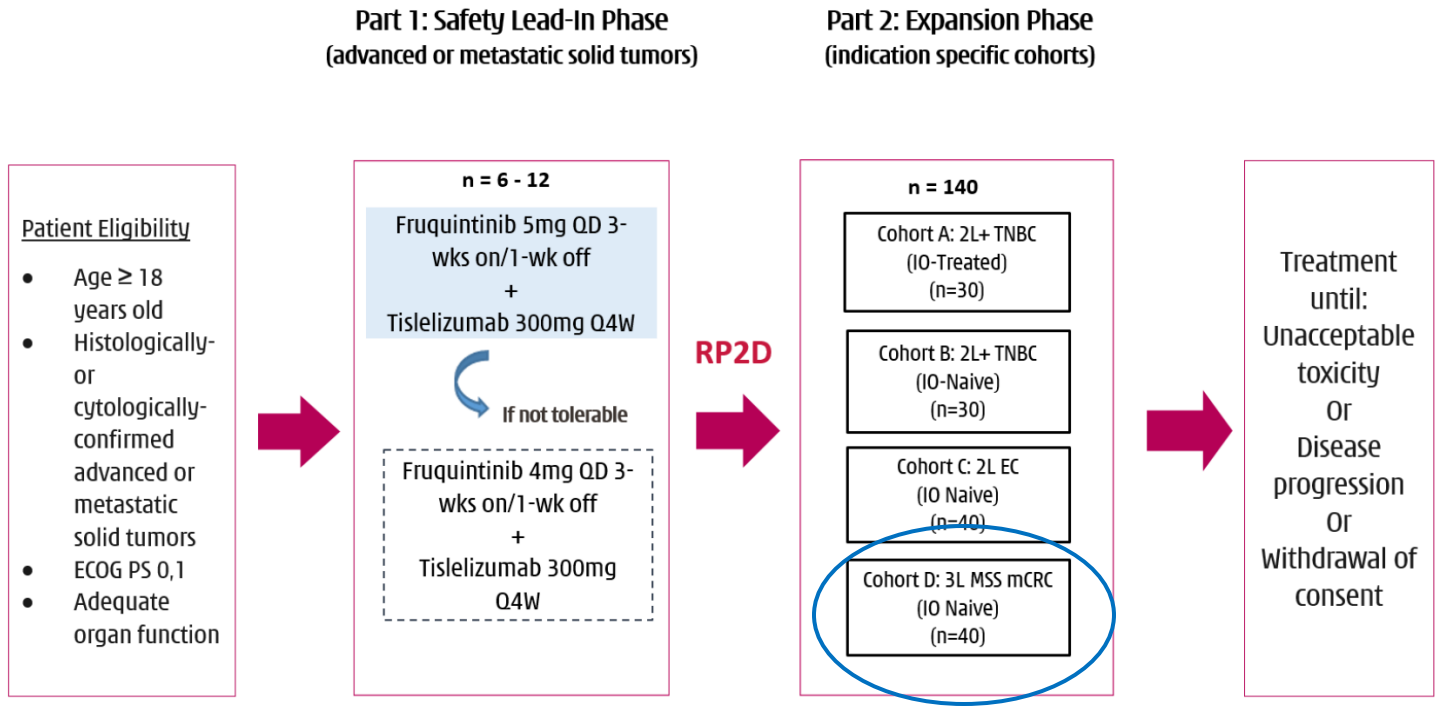
Dasari A .....Eng et al. ESMO 2022; Dasari et al: Lancet, June 15, 2023

Phase II Fruquintinib + Tislelizumab in MSI-S mCRC

Clinical Study Protocol

AN OPEN-LABEL, PHASE 1b/2 STUDY TO EVALUATE THE SAFETY AND EFFICACY OF FRUQUINTINIB IN COMBINATION WITH TISLELIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

Figure 1 Study Schematic

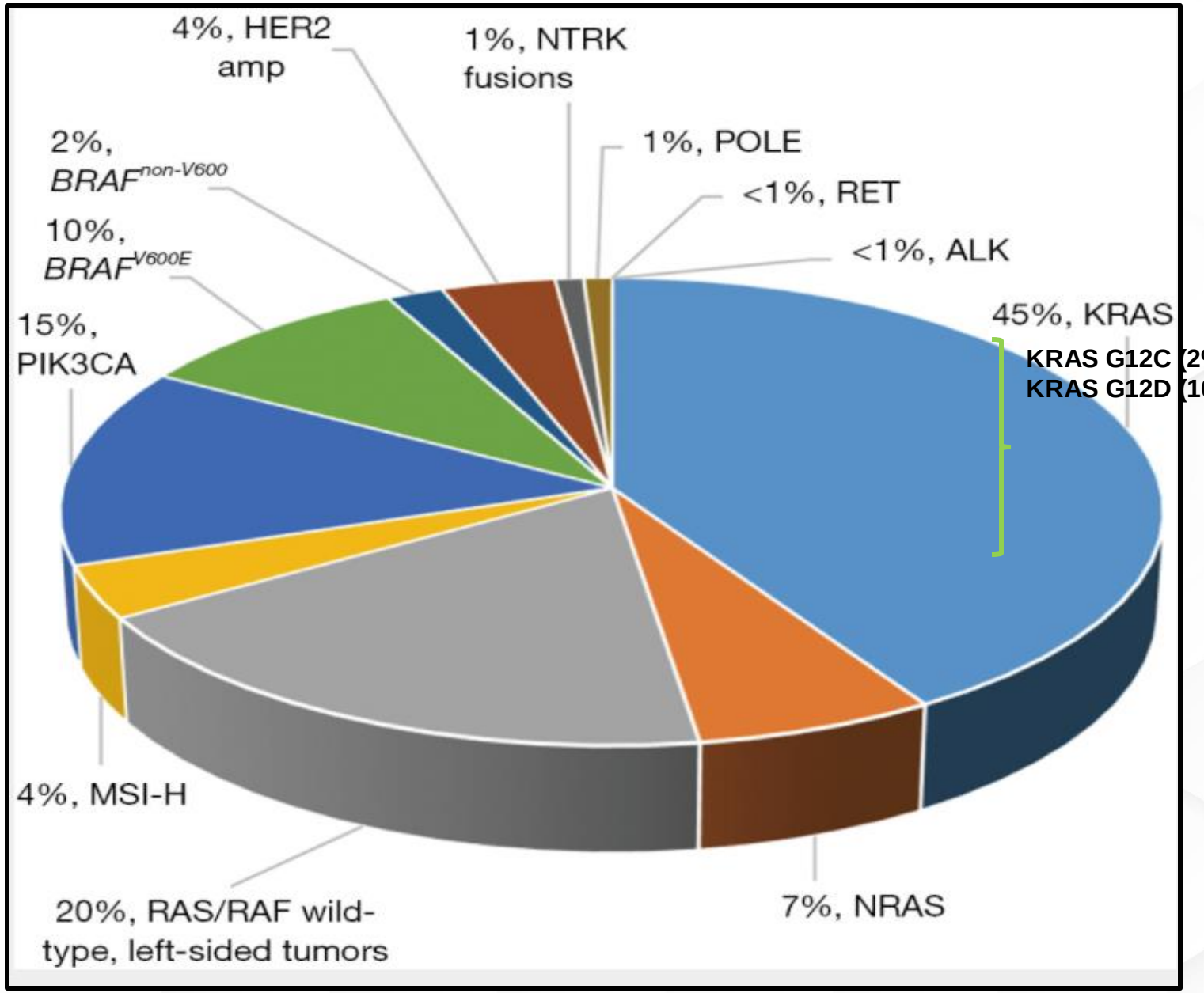


Completed enrollment in < 3 months)

NCT04577963

Precision Oncology

Molecular Subsets: Precision Oncology



Henry et al, CCO, 2019

Study Design: BREAKWATER

BREAKWATER (NCT04607421) is an ongoing, open-label, global, multicenter, randomized phase 3 study evaluating 1L EC ± chemotherapy vs SOC chemotherapy alone in participants with BRAF V600E-mutant mCRC

Safety Lead-In

Participants who have received ≤1 prior treatment for mCRC

Cohort 1 (n=30)
Encorafenib 300 mg QD
+ cetuximab 500 mg/m^2 Q2W
+ FOLFIRI Q2W in 28-day cycles

Cohort 2 (n=27)
Encorafenib 300 mg QD
+ cetuximab 500 mg/m^2 Q2W
+ mFOLFOX6 Q2W in 28-day cycles

Primary Endpoint

- Safety (frequency of DLTs)

Secondary Endpoints

- Safety (AEs, dose interruptions/ modifications/discontinuations)
- PKs
- Antitumor activity by investigator (ORR, DOR, TTR, PFS, OS)

Inclusion Criteria	Exclusion Criteria
• BRAF V600E-mutant mCRC (blood or tumor tissue) • ≤1 prior systemic treatment for mCRC • Evaluable disease (RECIST 1.1) • ECOG PS 0 or 1 • Adequate BM, hepatic, and renal function	• Prior treatment with BRAF or EGFR inhibitors or both oxaliplatin and irinotecan • Symptomatic brain metastases • MSI-H or dMMR tumors[a]

Phase 3

Participants who have not received prior systemic treatment for mCRC

R

Arm A (n≈235)
Encorafenib + cetuximab

Arm B (n≈235)
Encorafenib + cetuximab
+ mFOLFOX6

Control (n≈235)
mFOLFOX6/FOLFOXIRI/
CAPOX ± bevacizumab

Primary Endpoint

- PFS by BICR

Secondary Endpoints

- OS
- ORR, DOR, and TTR by BICR and by investigator
- PFS by investigator
- Safety
- PROs
- Biomarkers

Here we present an updated analysis from the BREAKWATER SLI, including updated safety and antitumor activity data by BICR, as well as preliminary biomarker data

Data cutoff: September 5, 2022.

[a]Unless patient ineligible to receive immune checkpoint inhibitors due to pre-existing medical condition.

BICR, blinded independent central review; BM, bone marrow; DLT, dose-limiting toxicity; dMMR, deficient mismatch repair; EC, encorafenib + cetuximab; MSI-H, microsatellite instability-high; PK, pharmacokinetic; Q2W, every 2 weeks; QD, once daily; SLI, safety lead-in; SOC, standard of care.

PRESENTED BY: Scott Kopetz, MD, PhD

Overview of Response by BICR

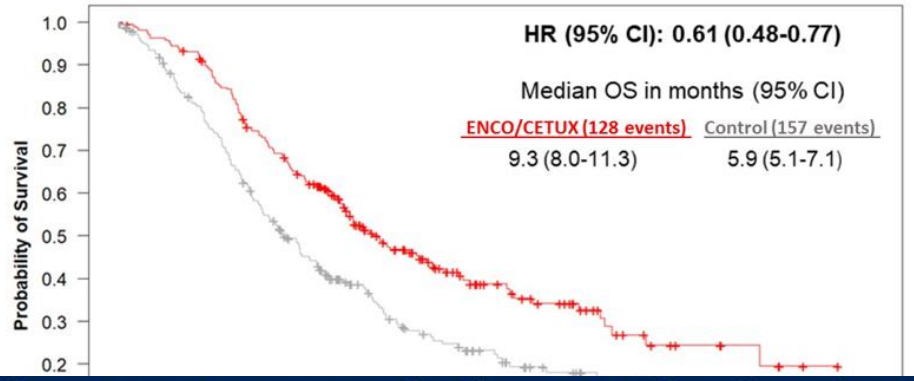
	1L		2L	
	EC + mFOLFOX6	EC + FOLFIRI	EC + mFOLFOX6	EC + FOLFIRI
Confirmed best overall response, n (%)	**n=19**	**n=12**	**n=8**	**n=18**
ORR, % (95% CI)	68.4 (46.0, 84.6)	75.0 (46.8, 91.1)	37.5 (13.7, 69.4)	44.4 (24.6, 66.3)
CR	1 (5.3)	2 (16.7)	0	1 (5.6)[a]
PR	12 (63.2)	7 (58.3)	3 (37.5)	7 (38.9)
SD	4 (21.1)	2 (16.7)	5 (62.5)	7 (38.9)
PD	1 (5.3)	0	0	0
Non-CR/non-PD[b]	0	1 (8.3)	0	2 (11.1)
Not evaluable[c]	1 (5.3)	0	0	1 (5.6)
Responders	**n=13**	**n=9**	**n=3**	**n=8**
mTTR, weeks (range)	6.9 (5.9–30.0)	7.0 (6.1–42.7)	6.9 (6.4–23.1)	13.0 (6.1–47.3)
mDOR, months (95% CI)	9.8 (6.9, NE)	12.4 (6.9, NE)	NE (5.6, NE)	9.9 (5.5, NE)
≥6 months, n (%)	7 (53.8)	6 (66.7)	1 (33.3)	4 (50.0)

Data cutoff: September 5, 2022.

[a]This participant with CR only had nontarget lesions at baseline. [b]Participants with only nontarget lesions at baseline. [c]Reasons included SD <6 weeks after treatment start date (1 patient in the EC + mFOLFOX6 cohort in the 1L setting) and early death (1 patient in the EC + FOLFIRI cohort in the 2L setting).

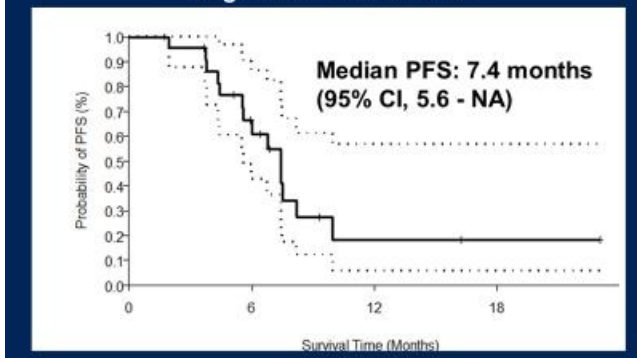
BICR, blinded independent central review; EC, encorafenib and cetuximab; NE, not estimable.

SWOG 2107: Previously Treated BRAF V600E MT

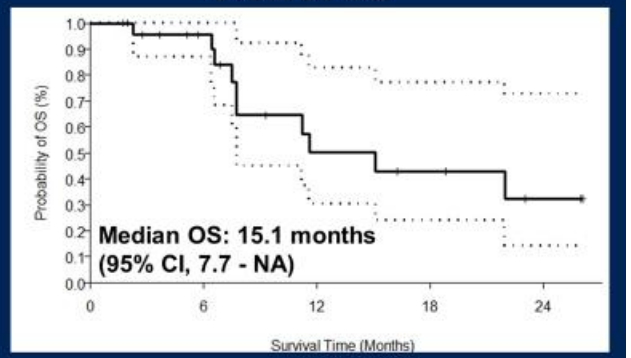


Survival outcomes: encorafenib + cetuximab + nivolumab

Progression-free survival



Overall survival



Median follow-up time: 16.3 months (95% CI, 6.9 –NA)
Median duration of response: 7.7 months (95% CI, 3.8 – NA)

Encorafenib + cetuximab: median PFS 4.2 months (95% CI, 3.7-5.4), median OS 8.4 months (95% CI, 7.5-11.0) [1]

[1]Kopetz S et al. NEJM 2019

SWOG 2107

Pts with MSS, *BRAF*^{V600E} metastatic CRC, AND
- 1-2 prior lines of systemic therapy
- ECOG PS 0-1
- No prior (1) BRAF, MEK, ERK; (2) anti-EGFR; or (3) immune checkpoint therapy

R

2:1

N=75

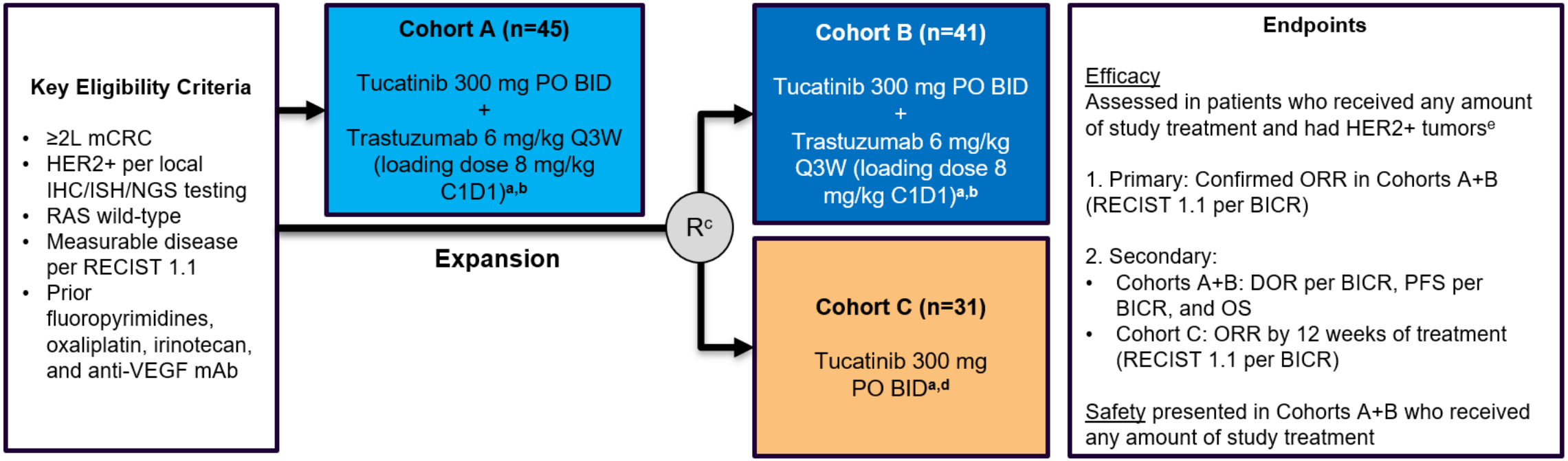
Encorafenib + cetuximab + nivolumab

Encorafenib + cetuximab

PI: V. Morris

SWOG
Leading cancer research. Together.

Mountaineer: Global, Open-Label, Phase 2 Trial



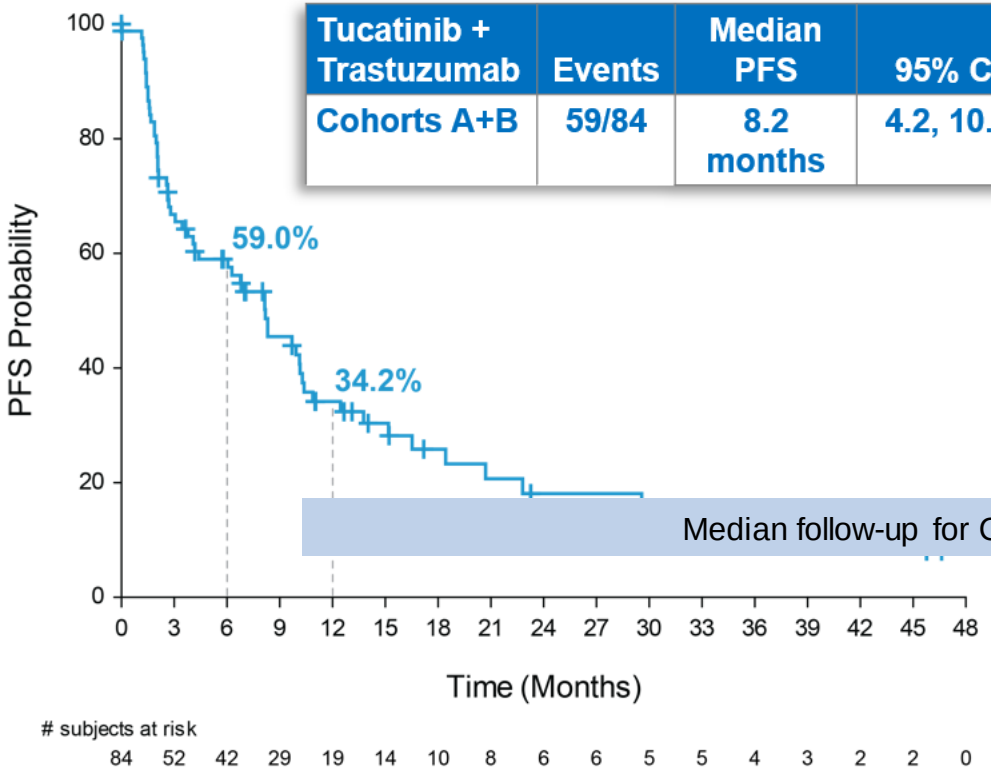
MOUNTAINEER began as a US Investigator-Sponsored Trial and initially consisted of a single cohort (Cohort A) and was expanded globally to include patients randomised to receive tucatinib + trastuzumab (Cohort B) or tucatinib monotherapy (Cohort C)

Strickler et al: NEJM 2023

Mountaineer: Global, Open-Label, Phase 2 Trial

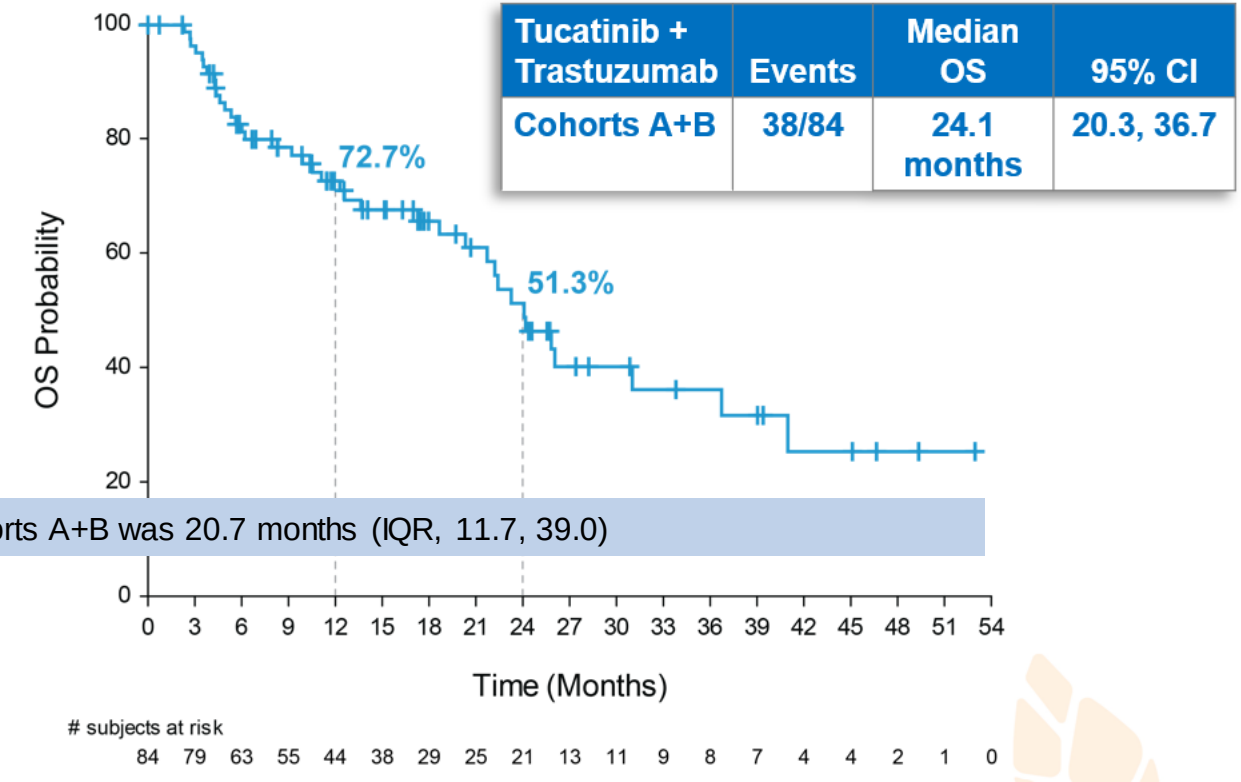
Progression-free Survival per BICR

Tucatinib + Trastuzumab	Events	Median PFS	95% CI
Cohorts A+B	59/84	8.2 months	4.2, 10.3



Overall Survival

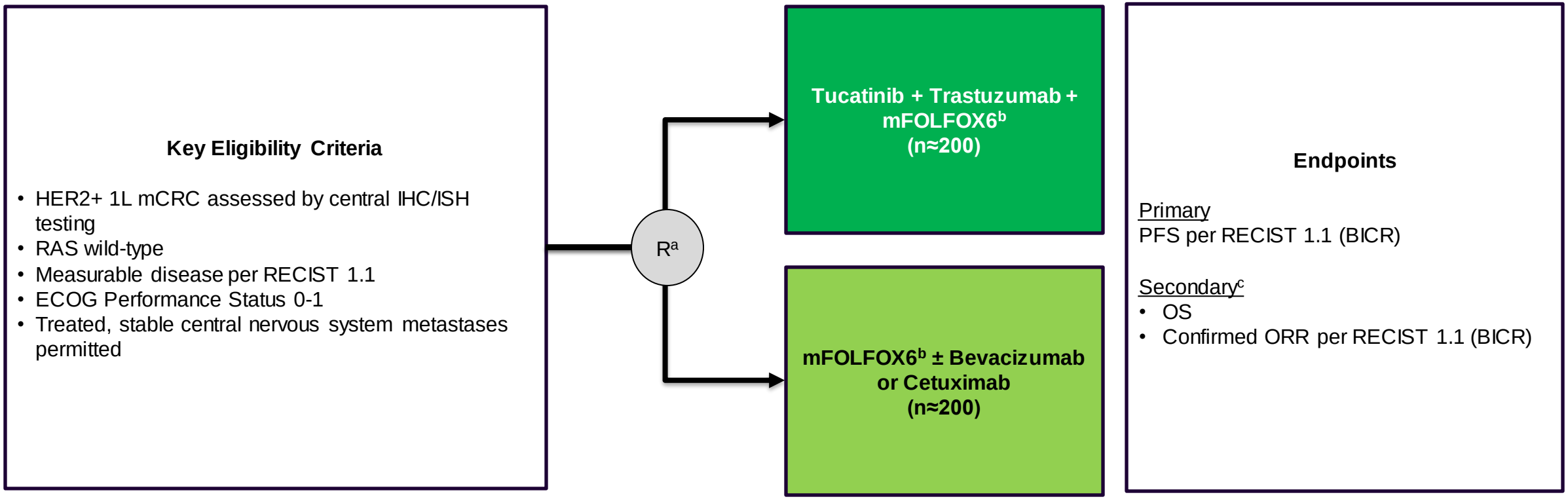
Tucatinib + Trastuzumab	Events	Median OS	95% CI
Cohorts A+B	38/84	24.1 months	20.3, 36.7



Median follow-up for Cohorts A+B was 20.7 months (IQR, 11.7, 39.0)

Strickler et al: NEJM 2023

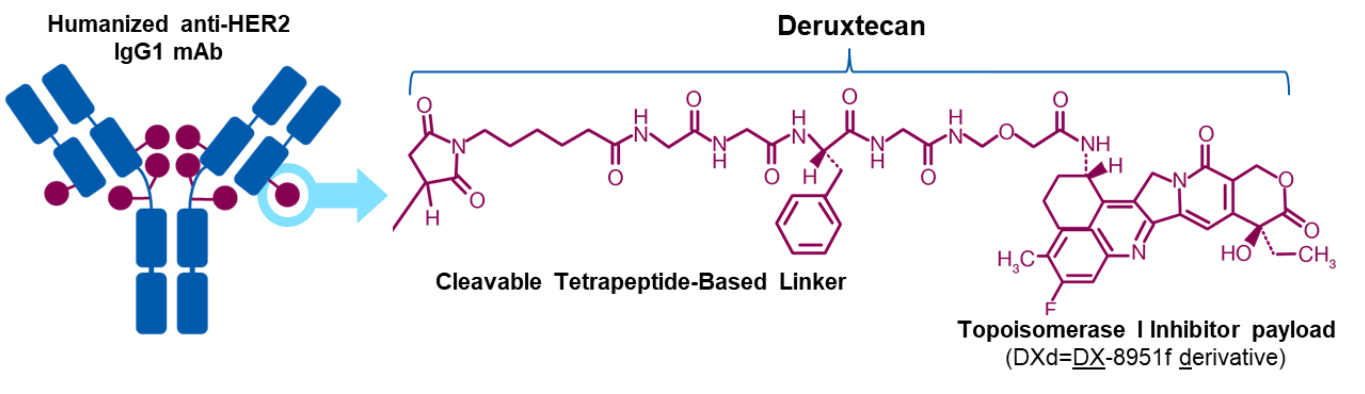
Mountaineer 3: Tx naïve mCRC



Strickler et al: NEJM 2023

Trastuzumab deruxtecan (T-DXd; DS-8201)

- Trastuzumab deruxtecan is an antibody-drug conjugate composed of a humanized monoclonal anti-HER2 antibody, a cleavable tetrapeptide-based linker, and a potent topoisomerase I inhibitor.
- Survival benefits of the drug have been proven in HER2-positive breast and gastric cancers.[1,2]

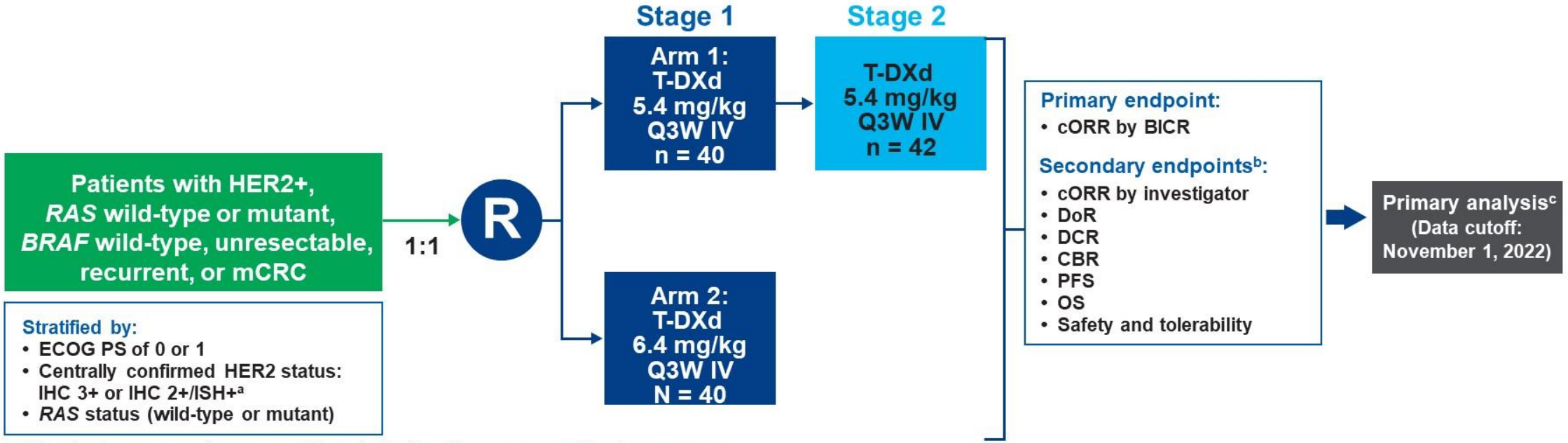


1. NEJM 2022;386:1143. 2. NEJM 2020;382:2419.

DESTINY-CRC02 Study Design

A randomized, blinded, 2-stage, 2-arm, multicenter, global, phase 2 study (NCT04744831)

- Stage 1 (randomized) was followed by Stage 2 (nonrandomized), which enrolled an additional 42 patients

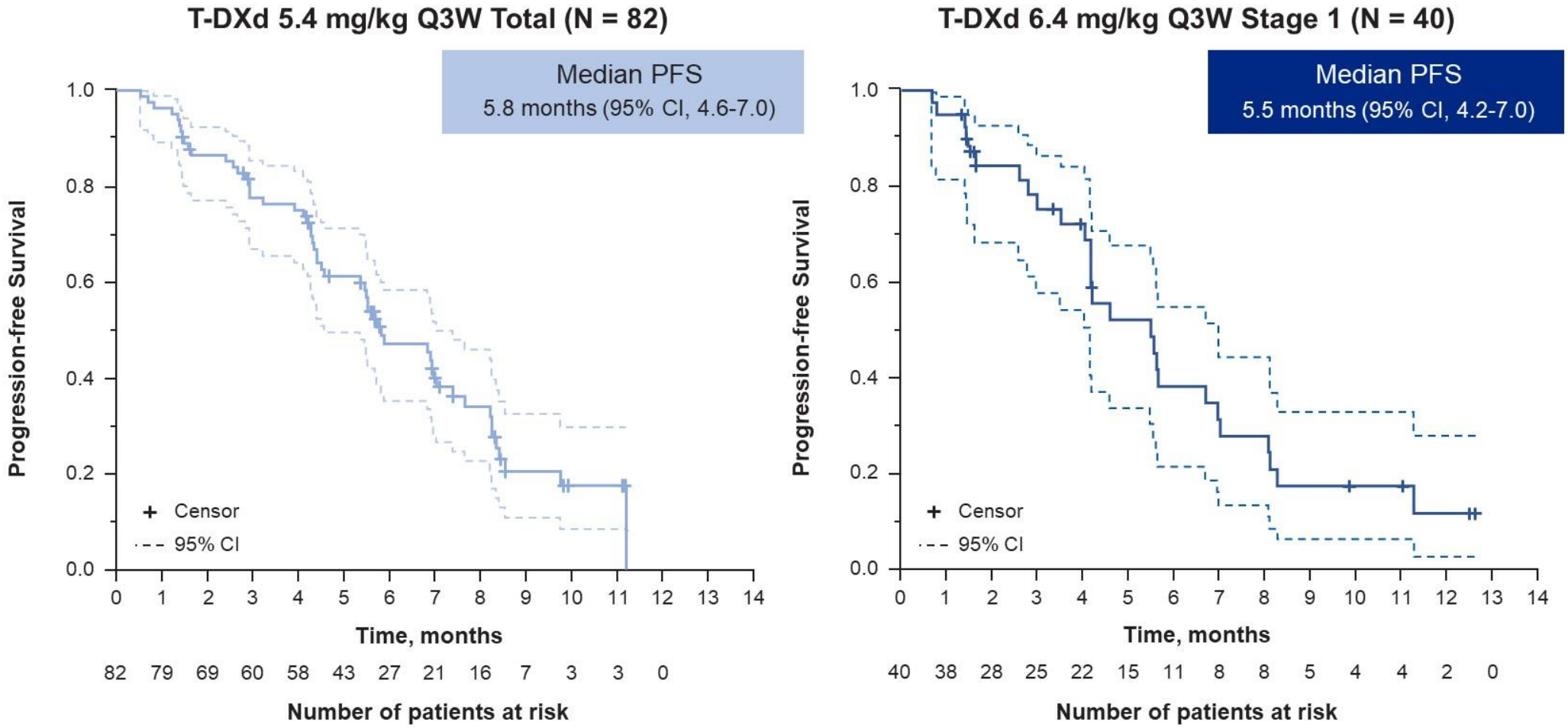


This study was not powered to statistically compare the two arms.

BICR, blinded independent central review; *BRAF*, v-raf murine sarcoma viral oncogene homolog B1; CBR, clinical benefit rate; cORR, confirmed objective response rate; DCR, disease control rate; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; IV, intravenously; mCRC, metastatic colorectal cancer; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; *RAS*, rat sarcoma; T-DXd, trastuzumab deruxtecan.
Both investigators and patients were blind to treatments.
[a]HER2 status was assessed with the Roche VENTANA HER2 Dual ISH DNA probe cocktail assay (IUO). [b]Exploratory endpoints included best percent change in the sum of diameters of measurable tumors based on BICR and investigator. [c]Primary analysis occurred ≥6 months after the last patient had been enrolled or when all patients discontinued from the study, whichever was earlier.

PRESENTED BY: Kanwal Raghav, MD

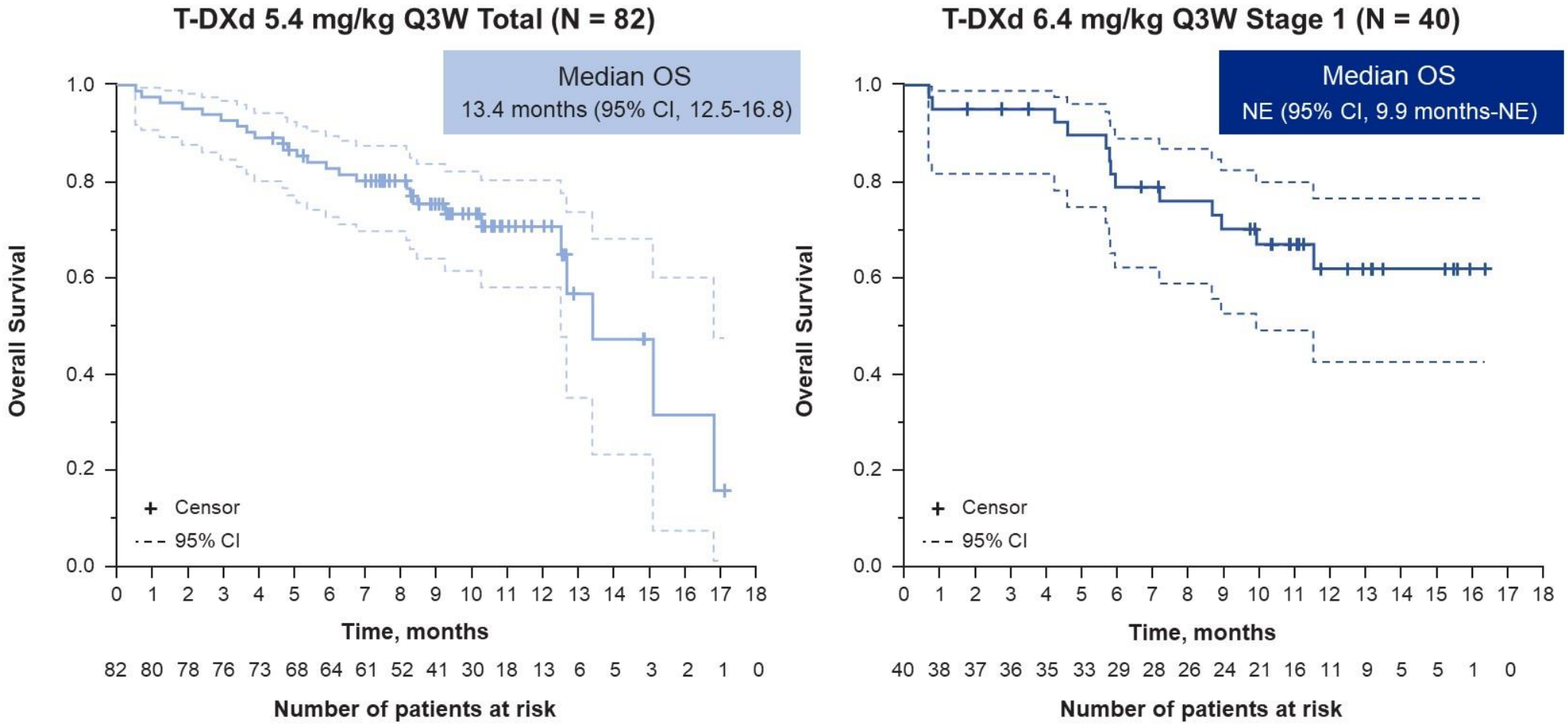
Median Progression-Free Survival by BICR



BICR, blinded independent central review; PFS, progression-free survival; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan.

PRESENTED BY: Kanwal Raghav, MD

Median Overall Survival



NE, not evaluable; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan.

Adjudicated Drug-Related ILD/Pneumonitis by Independent Adjudication Committee

Adjudicated as drug-related ILD/pneumonitis, n (%)	T-DXd 5.4 mg/kg Q3W			T-DXd 6.4 mg/kg Q3W
	Stage 1 n = 41[a]	Stage 2 n = 42	Total N = 83	Stage 1 N = 39
Any grade	4 (9.8)	3 (7.1)	7 (8.4)	5 (12.8)
Grade 1	1 (2.4)	0	1 (1.2)	2 (5.1)
Grade 2	3 (7.3)	3 (7.1)	6 (7.2)	2 (5.1)
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grade 5	0	0	0	1 (2.6)[b]

ILD, interstitial lung disease; Q3W, every 3 weeks; T-DXd, trastuzumab deruxtecan.
[a]1 patient randomized to receive T-DXd 6.4 mg/kg was mistakenly given T-DXd 5.4 mg/kg and counted in the 5.4 mg/kg arm safety analysis set. [b]There was 1 adjudicated, drug-related, grade 5 ILD/pneumonitis event, which was reported as respiratory failure, which was considered unrelated to study drug by investigator.

PRESENTED BY: Kanwal Raghav, MD

Ongoing KRAS G12C MT Phase I and III Trials

Phase 3: Sotorasib + Panitumumab

Patients

- > 1 prior line of treatment for mCRC
- KRAS G12C MT
- ECOG PS 0-2
- **N=193**
- ***Not yet recruiting**

NCT05198934

Arms A: Sotorasib 960 mg + Panitumumab or Arm B: Sotorasib (240 mg) + PMab

1:1 Randomization

Physician's Choice: Regorafenib or TAS-102

Primary Endpoint: PFS

- **Metastatic CRC**
- ***KRAS* G12C in tumor**
  - Local test acceptable for enrollment; central confirmation req'd w/in 30d
- **PD on 1L fluoropyrimidine + oxaliplatin or irinotecan**
- **No prior anti-EGFR or direct KRAS G12Ci**

1:1
N~420

Adagrasib 600 mg BID + Cetuximab 500 mg/m² Q2W

FOLFIRI or mFOLFOX6§

§Anti-VEGF/VEGFR allowed per Investigator discretion

Phase 1a

Dose escalation of LY3537982†

Primary endpoints:
Dose-limiting toxicities (DLTs), Adverse Events (AEs), and Serious Adverse Events (SAEs)

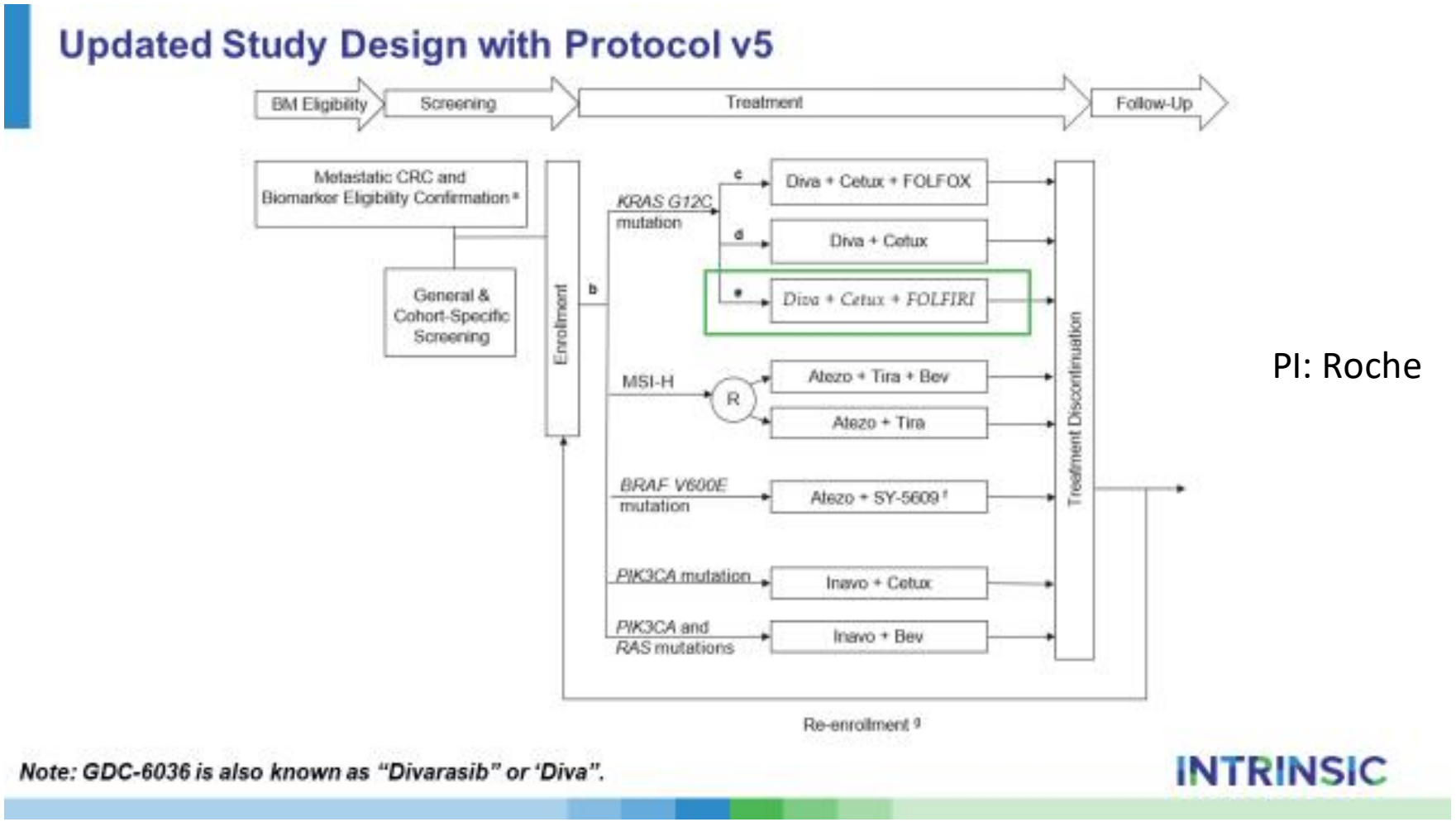
Phase 1b

Dose expansion:

- LY3537982† monotherapy
- LY3537982† + abemaciclib‡
- LY3537982† + erlotinib§
- LY3537982† + pembrolizumab||
- LY3537982† + temuterkib¶
- LY3537982† + LY3295668 (AurA inhibitor)#
- LY3537982† + cetuximab**
- LY3537982† + TNO155††

Primary endpoints:
DLTs, AEs, and SAEs

Intrinsic Trial: Biomarker Driven Trial



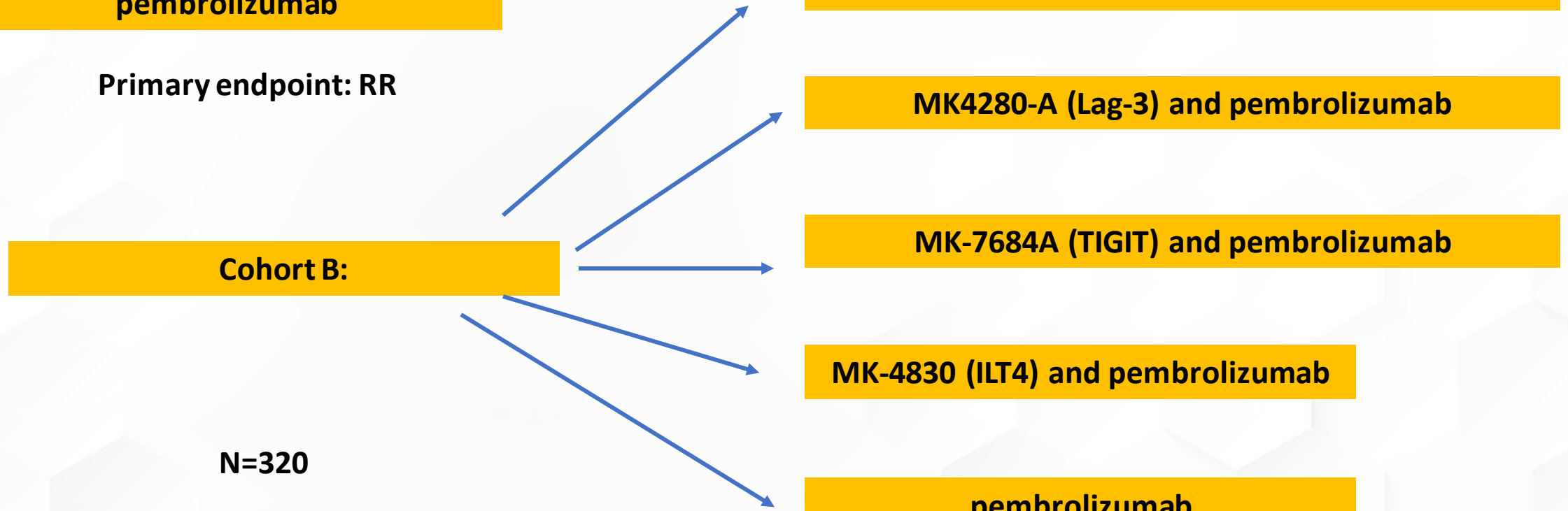
PI: Roche

NCT04929223

MK-1308A: MSI-H Treatment Naïve MCRC

Cohort A: MK-1308A and pembrolizumab

Primary endpoint: RR

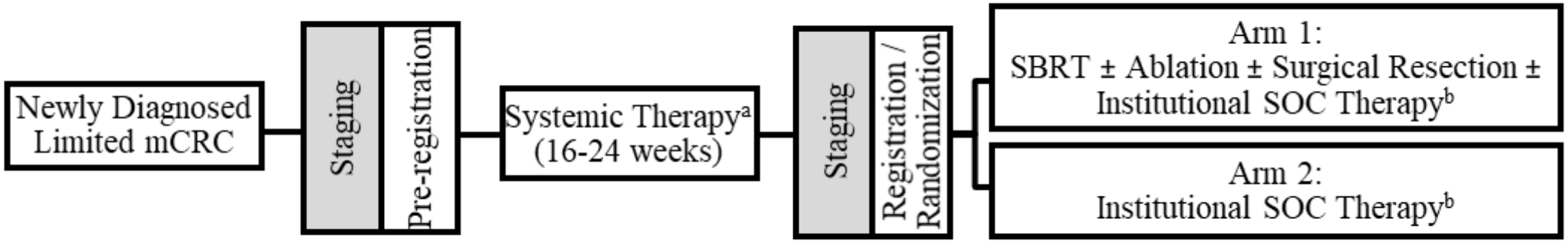


N=320

Primary Endpoint: RR

NCT04895722

Alliance A022101: A pragmatic, randomized phase III trial evaluating total ablative therapy for patients with limited metastatic colorectal cancer: Evaluating Radiation, Ablation, and Surgery (ERASur)



- N=364
- OS is primary endpoint
- There must be at least one other site of metastasis in addition to the liver
- Adjuvant must have been completed 12 months prior

ECOG-ACRIN cancer research group

Not for distribution

EA2222 - A Randomized Phase III Study of Systemic Therapy With or Without Hepatic Arterial Infusion for Unresectable Colorectal Liver Metastases: The PUMP Trial

Study Chair: Michael Lidsky, MD

Patient Eligibility

Adults, 18-80 years old

Persistently and technically unresectable liver-only metastatic CRC
(Allowed: Any calcified pulmonary nodule or ≤ 5 pulmonary nodules ≤ 6 mm and stable for ≥ 3 months on chemotherapy)

Prior systemic chemotherapy
≥ 6 ≤ 12 cycles (if cycle = 14 days) OR
≥ 4 ≤8 cycles (if cycle = 21 days)

New CRLM < 12 months after completing adjuvant therapy for stage II-III CRC

MDC Review

RANDOMIZE

Stratification:
RAS status
Primary tumor sidedness

Arm A
HAI/FUDR +
***SOC Chemo**

Arm B
***SOC Chemo**

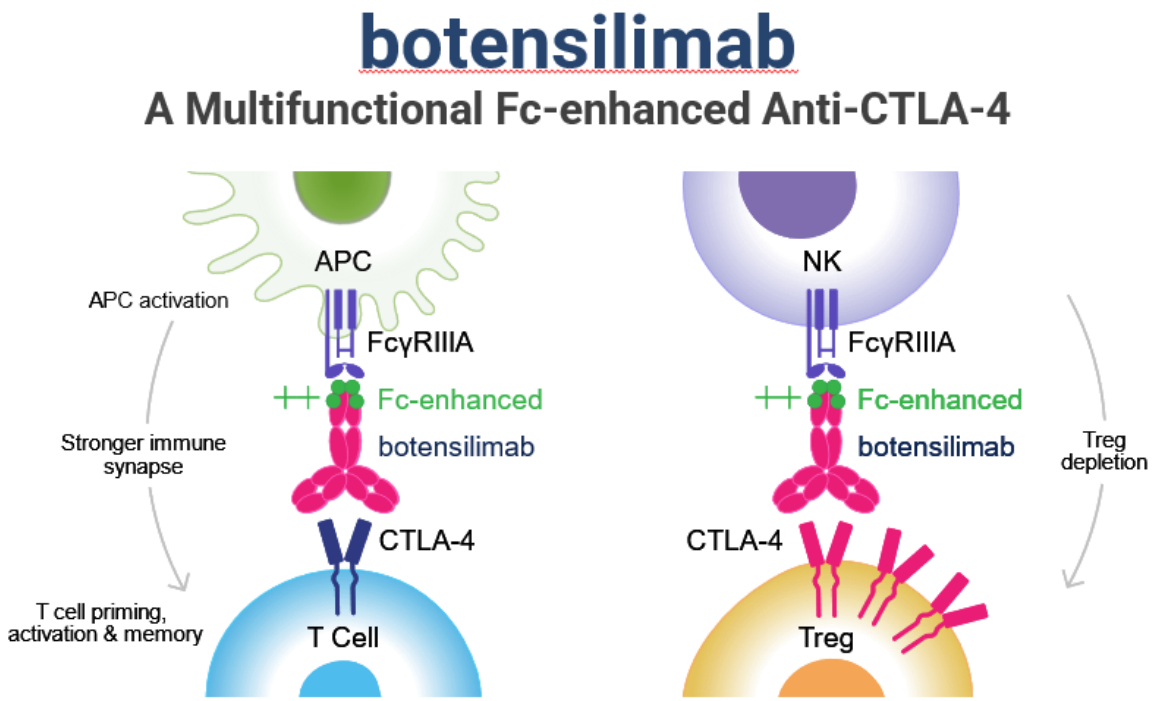
*per protocol

Primary endpoint = OS

Secondary endpoints: PFS, hPFS, ePFS, ORR, Conversion to resection, Toxicity

Correlatives – to improve patient selection and identify which patients may be at risk for short vs long term complications

Phase 1 trial of botensilimab, a multifunctional anti-CTLA-4, plus balstilimab (anti-PD-1) for metastatic MSI-S mCRC



Driving Activity in Cold or I-O Refractory Tumors[1-4]

- **Enhanced** T cell priming, expansion, memory[5,6]
- **Enhanced** frequency of APCs
- **Enhanced** Treg depletion
- **Reduced** complement mediated toxicity

BOTENSILIMAB IS A NOVEL INNATE & ADAPTIVE IMMUNE ACTIVATOR

Bullock et al: WGIC, 2023

PATIENT DISPOSITION

Intent-to-treat Population (ITT; All Treated Patients)
Safety Evaluable
101 Non-MSI-H patients received ≥1 dose
(1 or 2 mg/kg botensilimab Q6W + 3 mg/kg balstilimab Q2W)
- **77** with no active liver metastases
- **24** with active liver metastases

14 patients (including **6** with active liver metastases) did not receive ≥1 post-baseline 6-week imaging scan:
- **9** early progression
- **4** withdrew consent
- **1** related AE

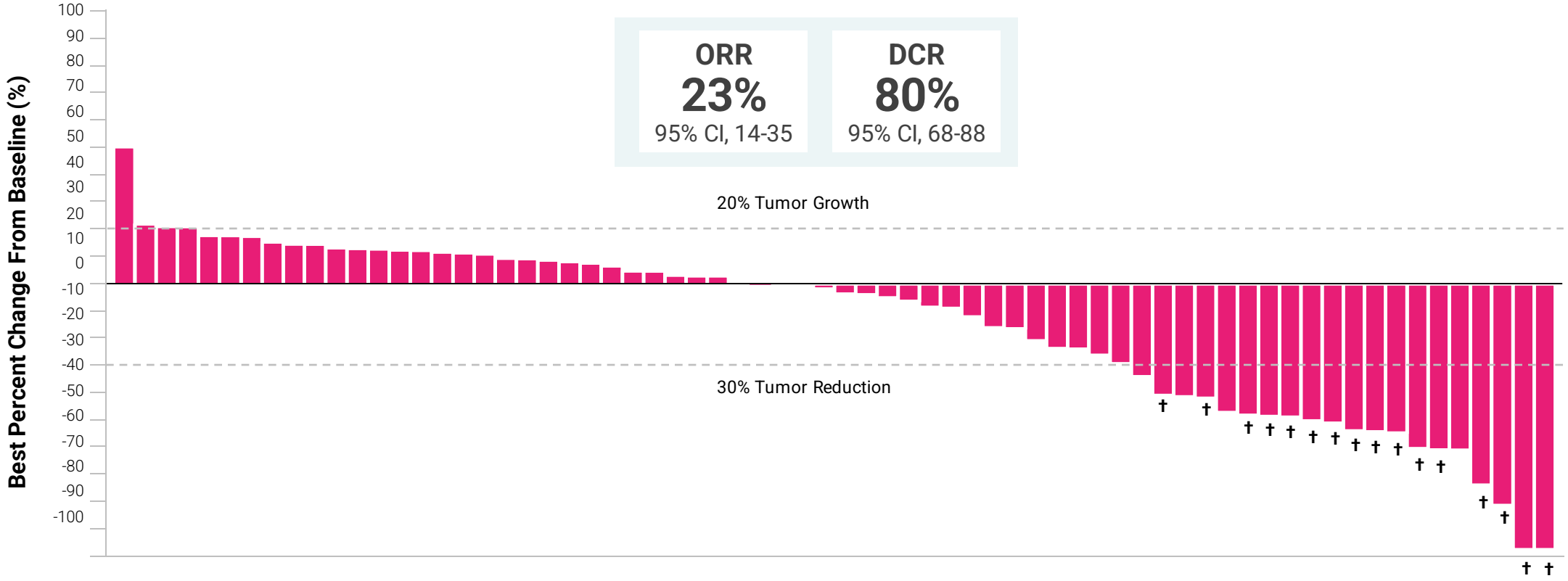
Efficacy Evaluable (EE)
87 had ≥1 post-baseline 6-week imaging scan
- **69** with no active liver metastases
- **18** with active liver metastases

Data cutoff: 26-MAY-2023

Bullock et al: WGIC, 2023

DEEP OBJECTIVE RESPONSES

No Active Liver Metastases (Efficacy Evaluable, n=69*)



Data cutoff: 26-MAY-2023

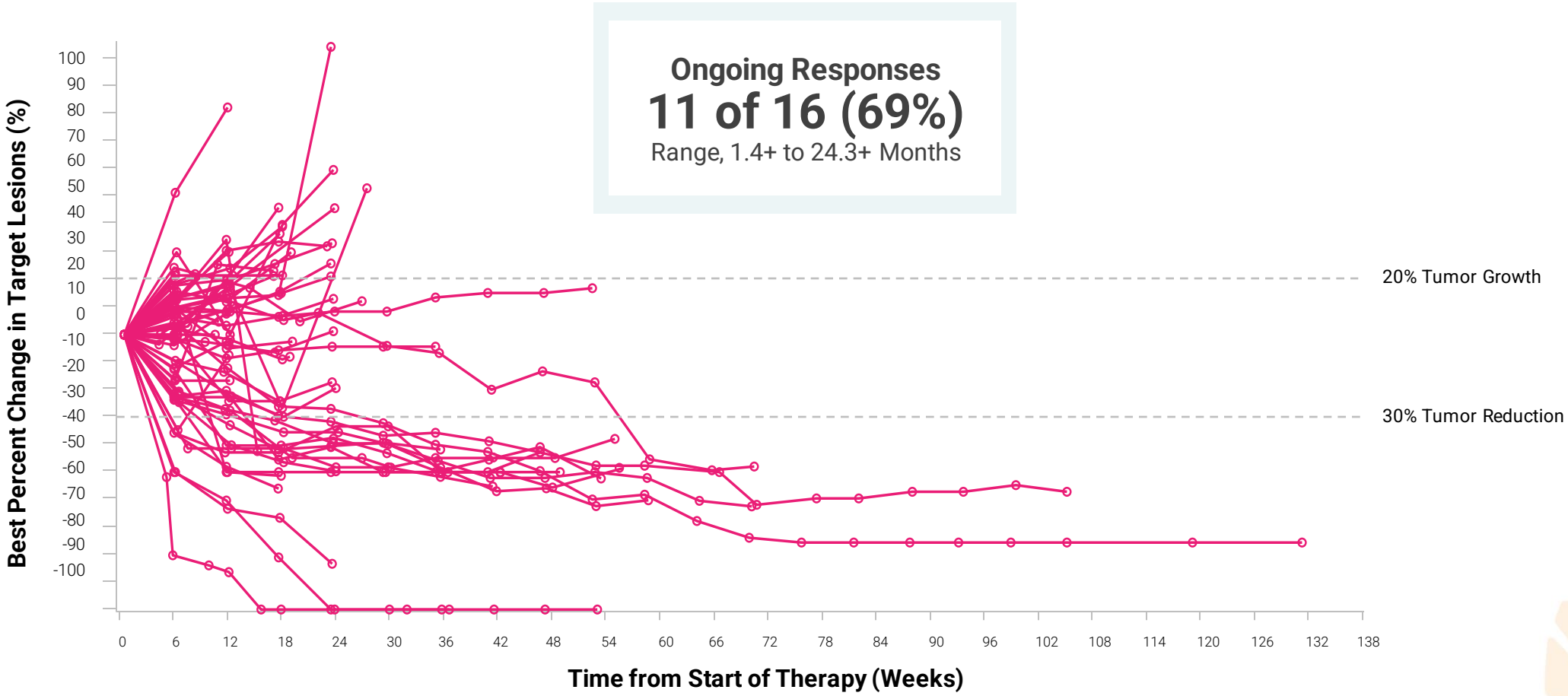
*69 patients were evaluable with ≥1 post-baseline scan. One patient out of the 69 is not included in the waterfall plot because RECIST was recorded as SD but no percent change was recorded as of the data cutoff.

†Confirmed response (CR or PR).

Bullock et al: WGIC, 2023

DURABLE OBJECTIVE RESPONSES

No Active Liver Metastases (Efficacy Evaluable, n=69*)



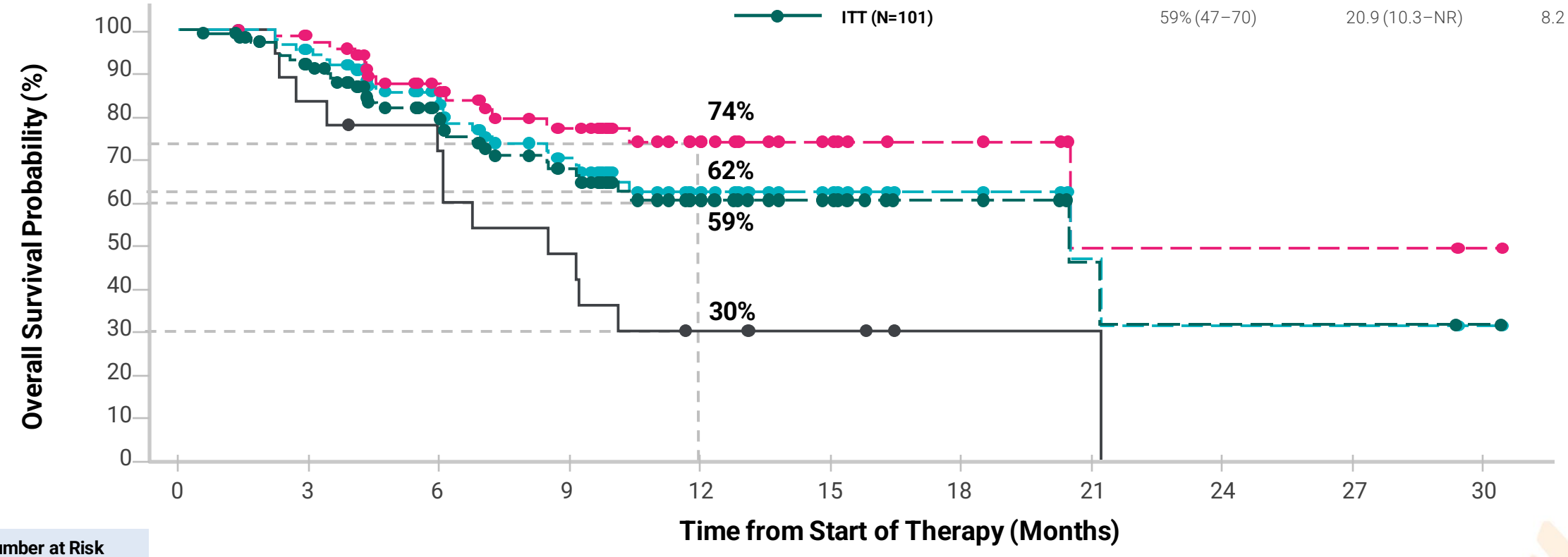
Data cutoff: 26-MAY-2023

*69 patients were evaluable with ≥1 post-baseline scan. One patient out of the 69 is not included in the spider plot because RECIST was recorded as SD but no percent change was recorded as of the data cutoff.

Bullock et al: WGIC, 2023

OVERALL SURVIVAL

	12-month OS, % (95% CI)	Median OS, Months (95% CI)	Median F/U, Months (Range)
No Active Liver Mets EE (n=69)	74% (59–84)	20.9 (20.9–NR)	9.8 (1.4–36.5)
Active Liver Mets EE (n=18)	30% (11–52)	8.7 (6.1–NR)	7.8 (2.3–21.7)
All EE (n=87)	62% (49–73)	20.9 (10.6–NR)	9.3 (1.4–36.5)
ITT (N=101)	59% (47–70)	20.9 (10.3–NR)	8.2 (0.5–36.5)



Number at Risk											
No Active Liver Mets EE	69	65	47	33	18	11	6	2	2	2	2
Active Liver Mets EE	18	15	13	8	4	3	1	1	0	0	0
All EE	87	80	60	41	22	14	7	3	2	2	2
ITT	101	85	60	41	22	14	7	3	2	2	2

Data cutoff: 26-MAY-2023

Bullock et al: WGIC, 2023

DEEP AND DURABLE OBJECTIVE RESPONSES

	All EE n=87*	No Active Liver Mets EE n=69†	Active Liver Mets EE n=18‡
Confirmed ORR, n % (95% CI)	18% (11–28)	23% (14–35)	0% (0–19)
BOR, n (%)			
CR	1 (1)	1 (1)	0
PR	15 (17)	15 (22)	0
SD	45 (52)	39 (57)	6 (33)
PD	26 (30)	14 (20)	12 (67)
DCR (CR + PR + SD), % (95% CI)	70% (59–80)	80% (68–88)	33% (13–59)
12-month OS, % (95% CI)	62% (49–73)	74% (59–84)	30% (11–52)
Ongoing responses§	11/16 (69%)		0

*Excludes patients with unconfirmed responses, among them one with a response in lung lesions who then became non-evaluable after a hemicolectomy which showed a pathologic CR, and another patient with a -60% reduction through week 60 who had a perisplenic nodule retrospectively identified as a new lesion at week 18.

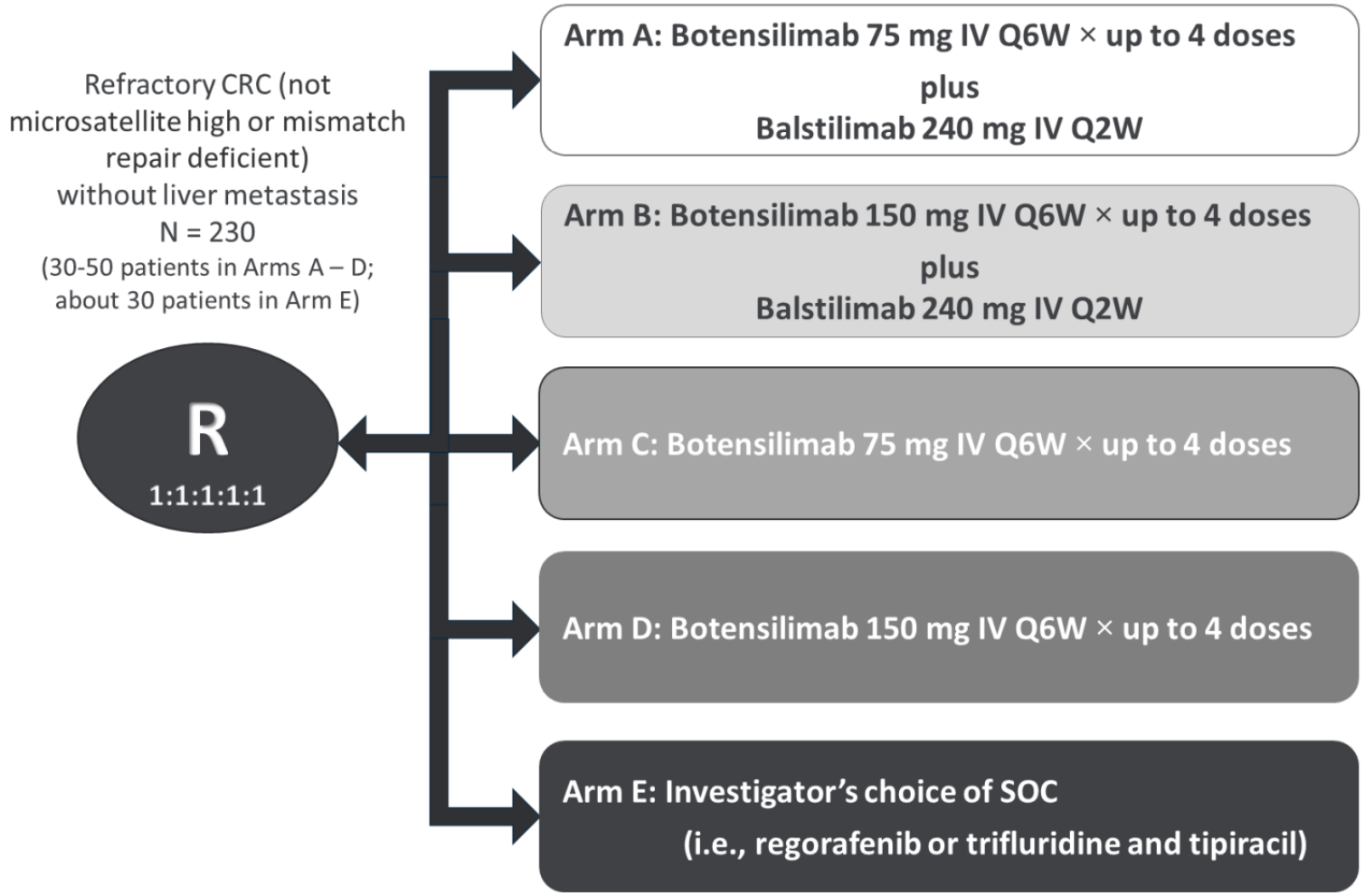
†In the ITT population with no active liver metastases (n=77), ORR was 21% (95% CI, 12–32) and DCR was 71% (95% CI, 60–81).

‡In the ITT population with active liver metastases (n=24), ORR was 0% (95% CI, 0–14) and DCR was 25% (95% CI, 10–47).

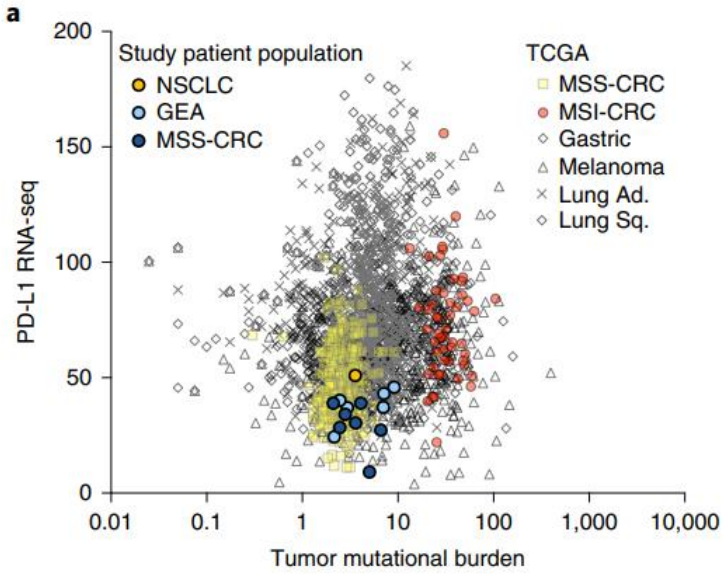
§Median DOR is immature as 11/16 (69%) patients are ongoing.

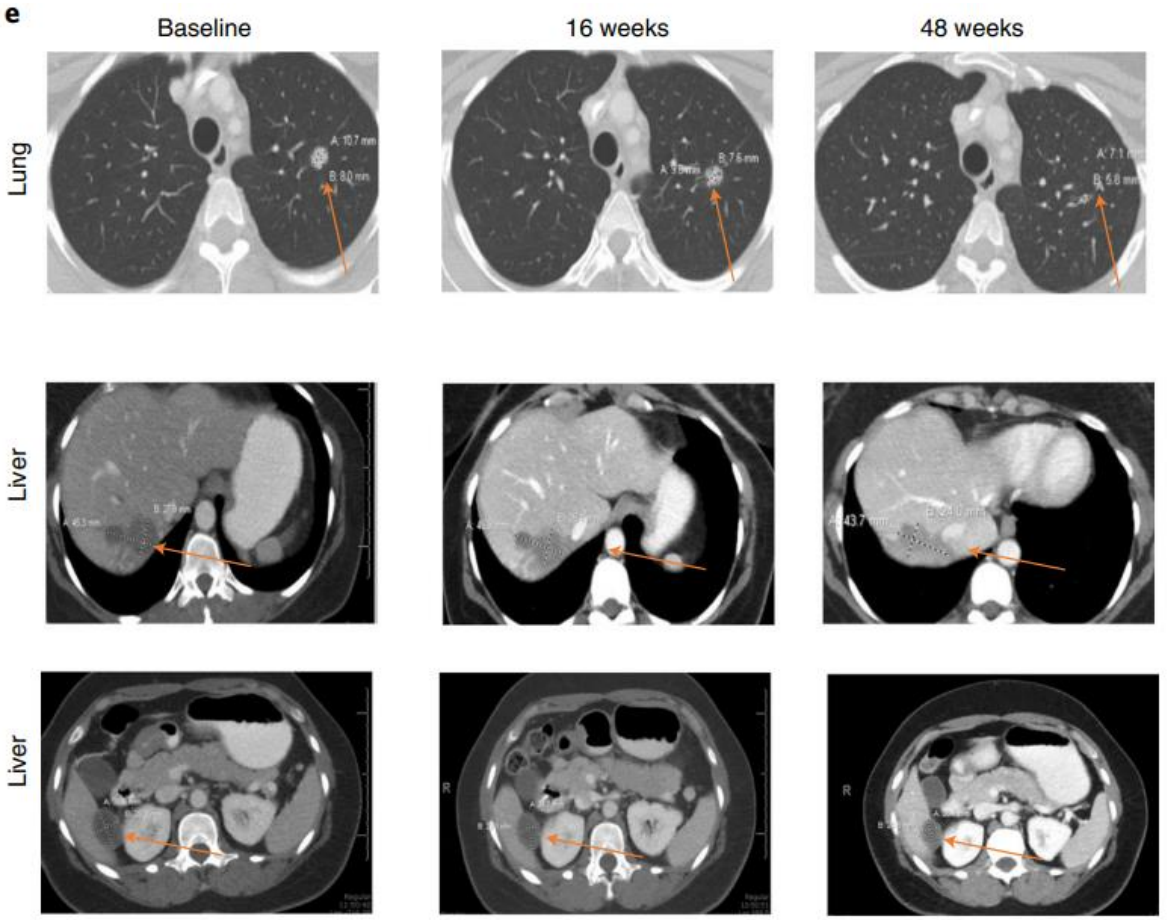
Bullock et al: WGIC, 2023

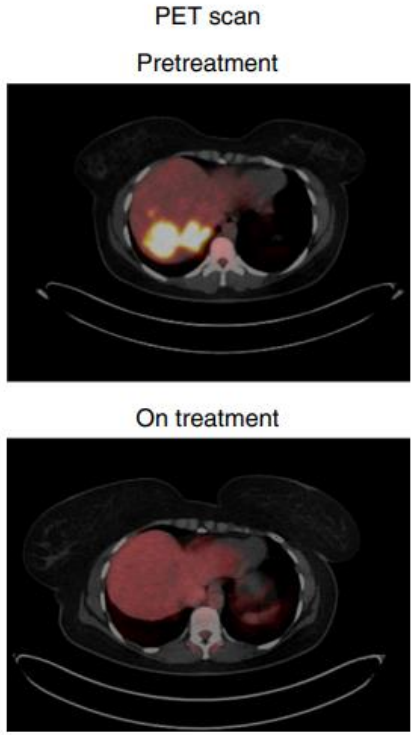
A Randomized, Open-Label, Phase 2 Study of Botensilimab (AGEN1181) as Monotherapy and in Combination With Balstilimab (AGEN2034) or Investigator's Choice Standard of Care (Regorafenib or Trifluridine and Tipiracil) for the Treatment of Refractory Metastatic Colorectal Cancer



Promising Neoantigen Vaccine

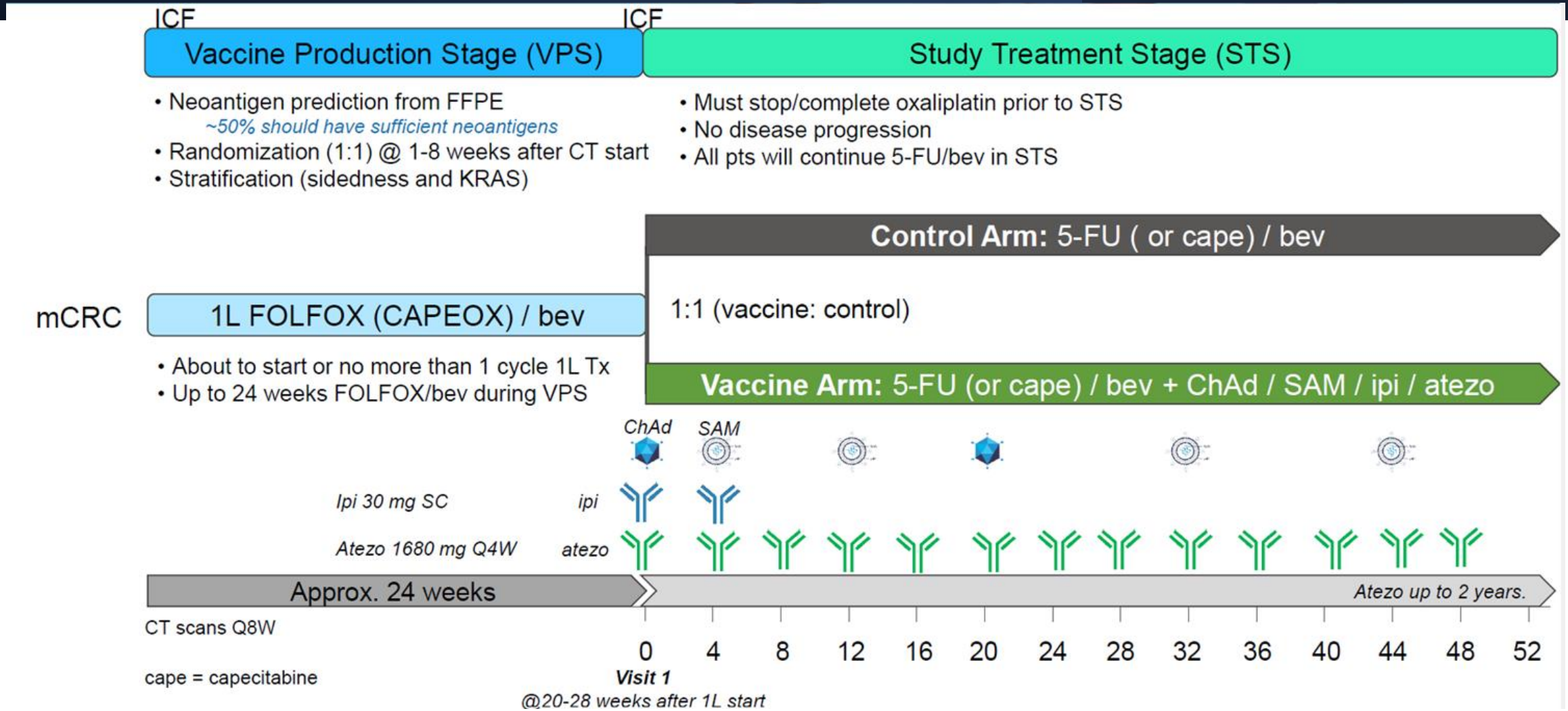






Palmer, Nature Med, 2023

A Phase 2/3, Randomized, Open-Label Study of Maintenance GRT-C901/GRT-R902, A Neoantigen Vaccine + Atezolizumab in mCRC



Anal Cancer

EA2182 (NCT04166318) A Randomized Phase II Study of De-Intensified ChemoRadiation for Early-Stage Anal Squamous Cell Carcinoma (DECREASE)

Eligibility:
T1-2N0M0 anal canal or anal margin squamous cell carcinoma (SCCA) measuring ≤4 cm (HIV+ allowed)

Accrual Goal
N = 71/252

PRE-REGISTRATION

Stratification Factors:
- Tumor stage: T1 vs T2
- HIV Status: HIV-positive vs. HIV-negative

Arm S: HIV-positive patients

Central Imaging Review Required

Arm R: HIV-negative patients

Central Imaging Review NOT Required

PI: J Dorth

RANDOMIZATION

2:1

Arm A: Standard-Dose Chemoradiation

Radiation:
- Primary tumor: 50.4 Gy in 28 fractions
- Elective nodal regions: full pelvis + inguinal 42 Gy in 28 fractions
- Mitomycin C (MMC) 12 mg/m^2 X 1; 5-fluorouracil (5-FU) CI X 2 cycles OR Capecitabine

Arm B: De-Intensified Chemoradiation

Radiation:
- Primary tumor:
  - T1: 36 Gy in 20 fractions
  - T2: 41.4 Gy in 23 fractions
- Elective nodal regions: true pelvis + inguinal
  - T1: 32 Gy in 20 fractions
  - T2: 34.5 Gy in 23 fractions
- MMC 10 mg/m^2 X 1; 5-FU CI X 1 cycle OR Capecitabine

Concurrent Chemo:
- MMC on day 1
- 5-FU CI 1000 mg/m^2/d days 1-4 (c1), days 29-32 (c2) OR
- Capecitabine 825 mg/m^{2}BID M-F on days of RT

*Cycle = 4 weeks (28 days)

LONG TERM FOLLOW-UP

Primary Endpoint:
2-year Disease Control

Eng et al: JCO, *in press*, 2022

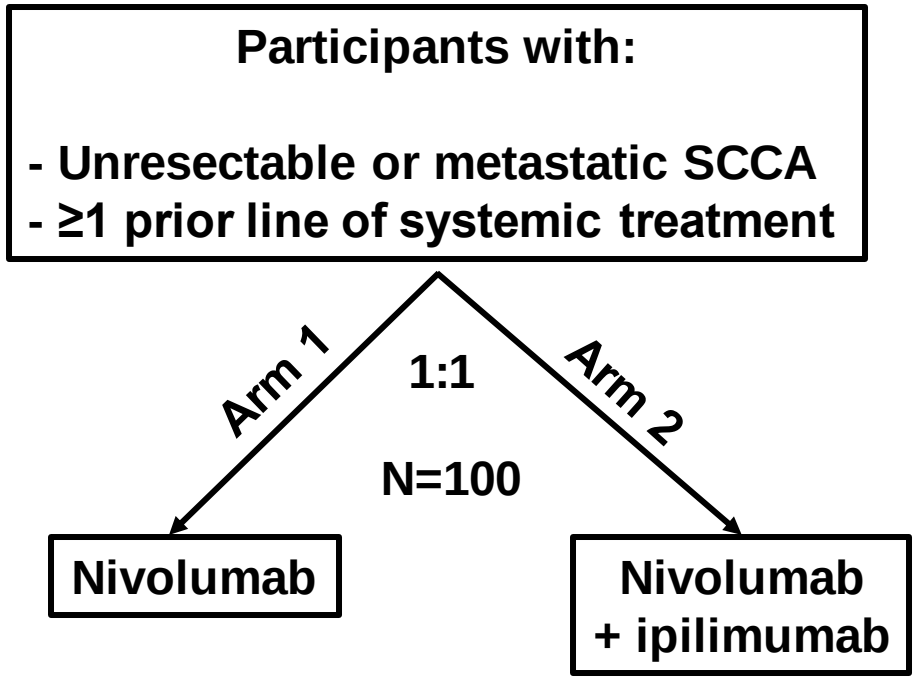
NCI9673 (Part B): A multi-institutional ETCTN randomized phase II study of nivolumab with or without ipilimumab in refractory, metastatic squamous cell carcinoma of the anal canal (NCT02314169)

V.K. Morris[1], K.K. Ciombor[2], B. Polite[3], S. Mukherjee[4], J.C. Krauss[5], T. Shields[6], O. Aranha[7], J. Hays[8], S. Kazmi[9], B. Weinberg[10], K. Nguyen[11], A.B. Benson[12], C. Lieu[13], S. Iqbal[14], H. Hochster[15], L. Xiao[1], C. Eng[2]

[1]University of Texas – MD Anderson Cancer Center; [2]Vanderbilt-Ingram Cancer Center; [3]University of Chicago; [4]Roswell Park Cancer Institute; [5]University of Michigan; [6]Karmanos Cancer Institute; [7]Washington University School of Medicine; [8]The Ohio State University; [9]The University of Texas Southwestern Medical Center; [10]Georgetown University; [11]Yale University; [12]Northwestern University; [13]University of Colorado; [14]University of Southern California; [15]Rutgers University

NCI9673 (Part B) Study Design

- **Primary Endpoint:**
  - **Progression-free survival (PFS)**
- **Secondary Endpoints:**
  - **Overall response (RECIST 1.1)**
  - **Overall survival (OS)**
  - **Safety/toxicity (CTCAE v5)**
- **Statistical Design:**
  - **H_0: Median $PFS_{Arm2} \leq PFS_{Arm1}$**
    H_a: Median $PFS_{Arm2} > PFS_{Arm1}$
  - **At a one-sided α=.10 and 90% power, 100 participants are needed to observe an improvement in median PFS from 4 to 7 months.**



Study Treatment:

- **Nivolumab: 480 mg IV every 4 weeks**
- **Ipilimumab 1 mg/kg IV every 8 weeks (Arm 2 only)**

NCT02314169; Morris et al, WGIC, 2023

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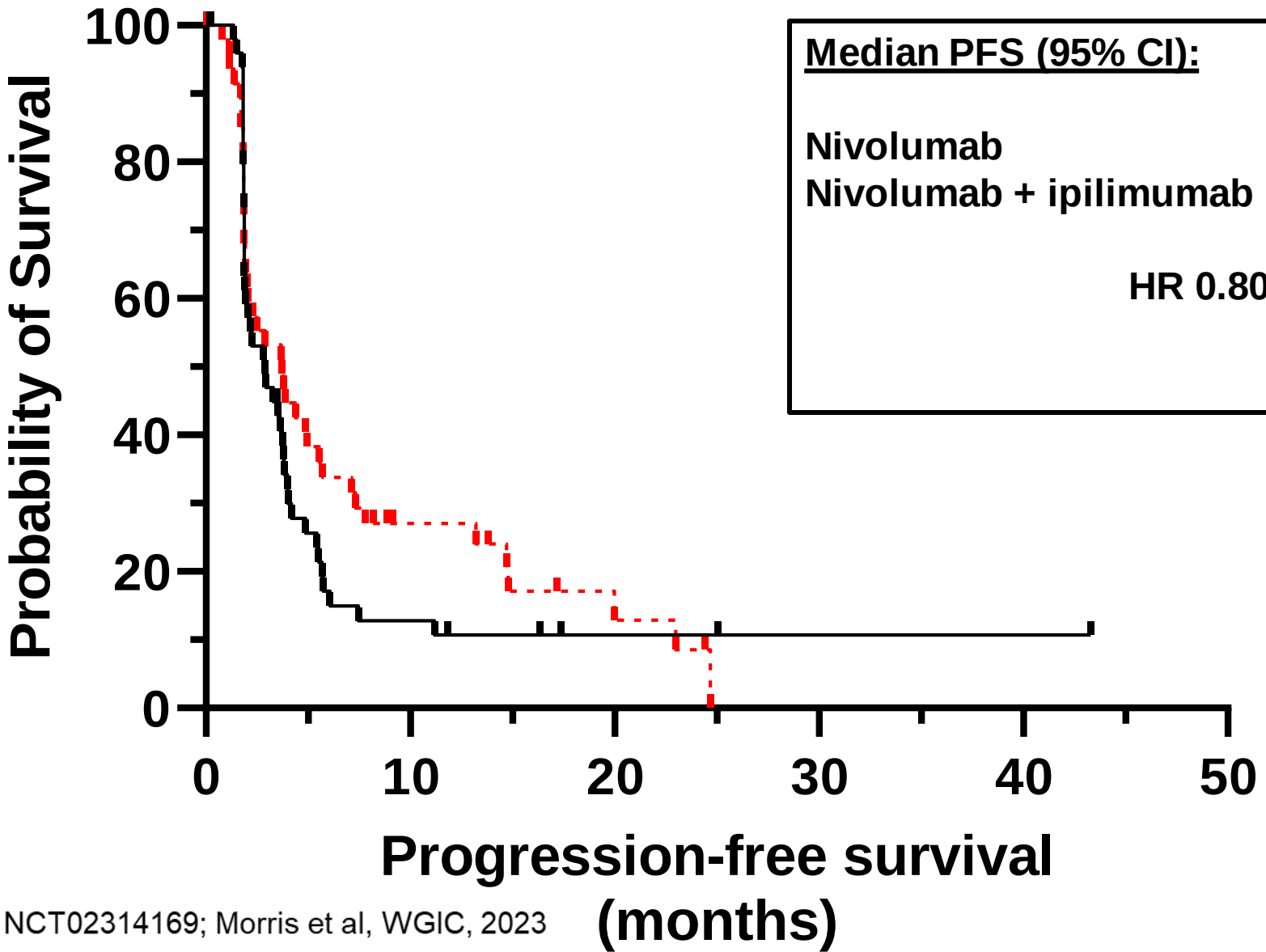
Progression-free survival



Median PFS (95% CI):

Nivolumab	2.9 months (1.9 – 4.0)
Nivolumab + ipilimumab	3.7 months (2.0 – 7.1)

HR 0.80 (95% CI, .52-1.2)
p= .16

Nivolumab
Nivolumab + ipilimumab

NCT02314169; Morris et al, WGIC, 2023

Median follow-up: 22 months

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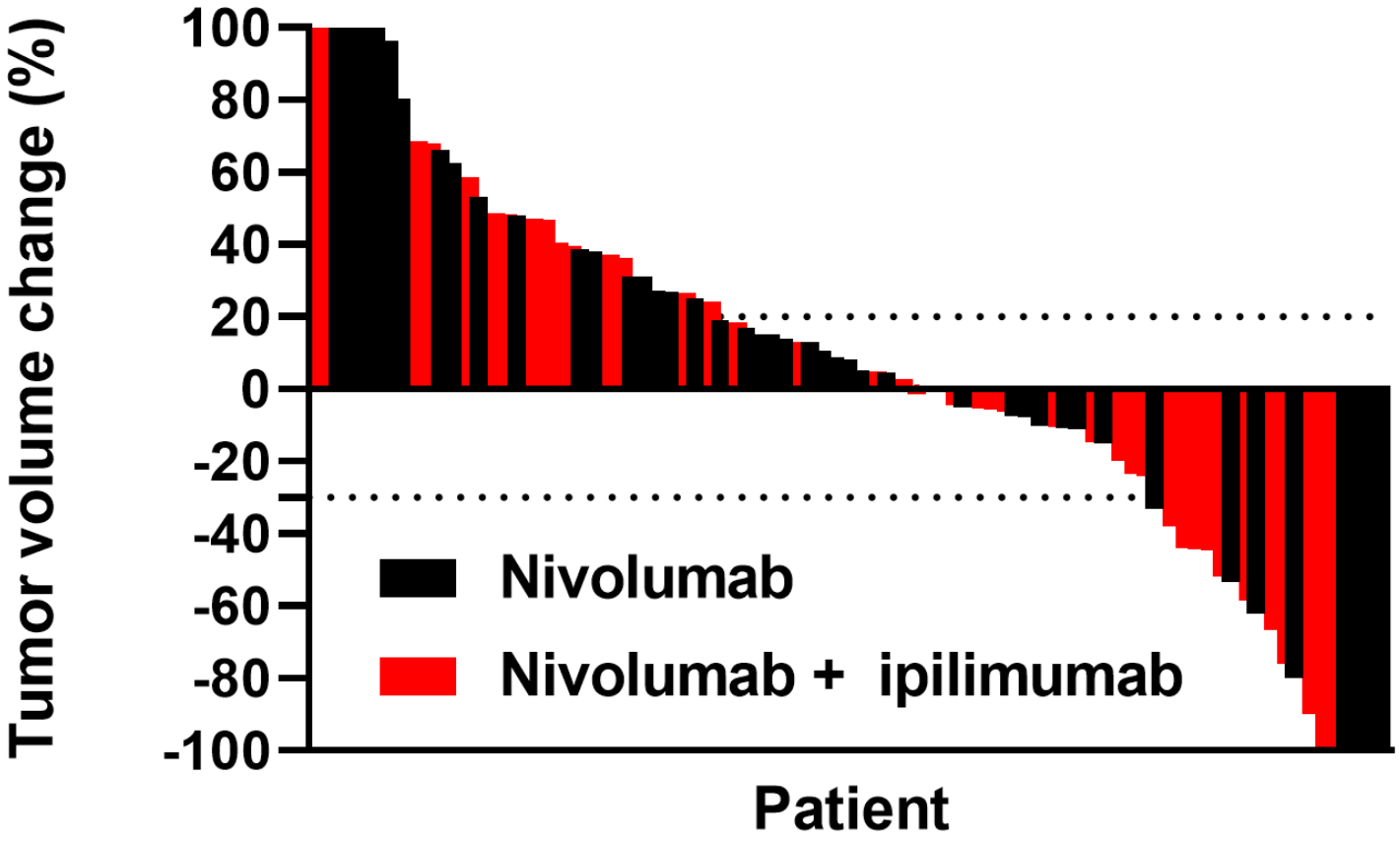
Response Assessment



Overall Response Rate (95% CI):

Nivolumab	17.4% (9.1-31)
Nivolumab + ipilimumab	21.5% (12-36)

Disease Control Rate (95% CI):

Nivolumab	43.5% (30-58)
Nivolumab + ipilimumab	47.6% (33-62)

	Nivolumab (%)	Nivolumab + Ipilimumab (%)
Complete Response	3 (6.5)	2 (4.8)
Partial Response	5 (10.9)	7 (16.7)
Stable Disease	12 (21.7)	11 (26.2)
Progressive Disease	26 (56.5)	22 (52.3)

NCT02314169; Morris et al, WGIC, 2023

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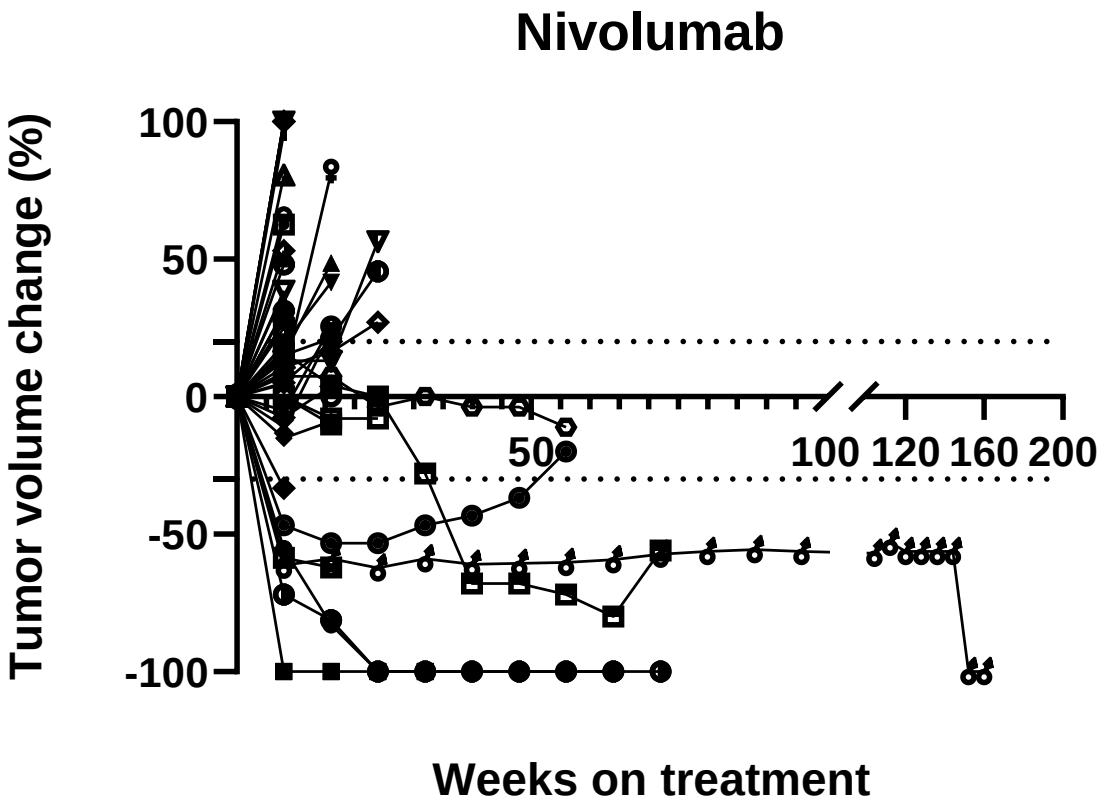
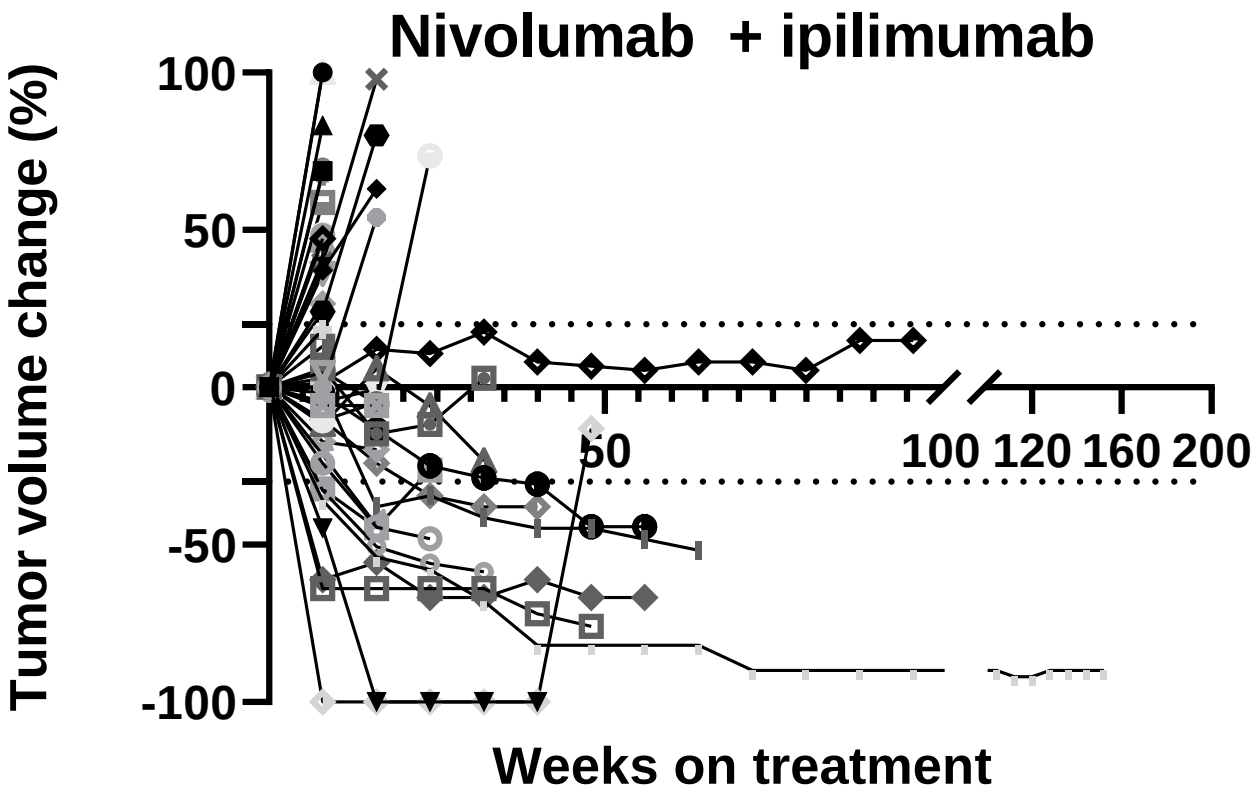
Spider Plots





	6-month PFS rate (95% CI)
Nivolumab	20 (10-30)
Nivolumab + ipilimumab	30 (20-50)

NCT02314169; Morris et al, WGIC, 2023

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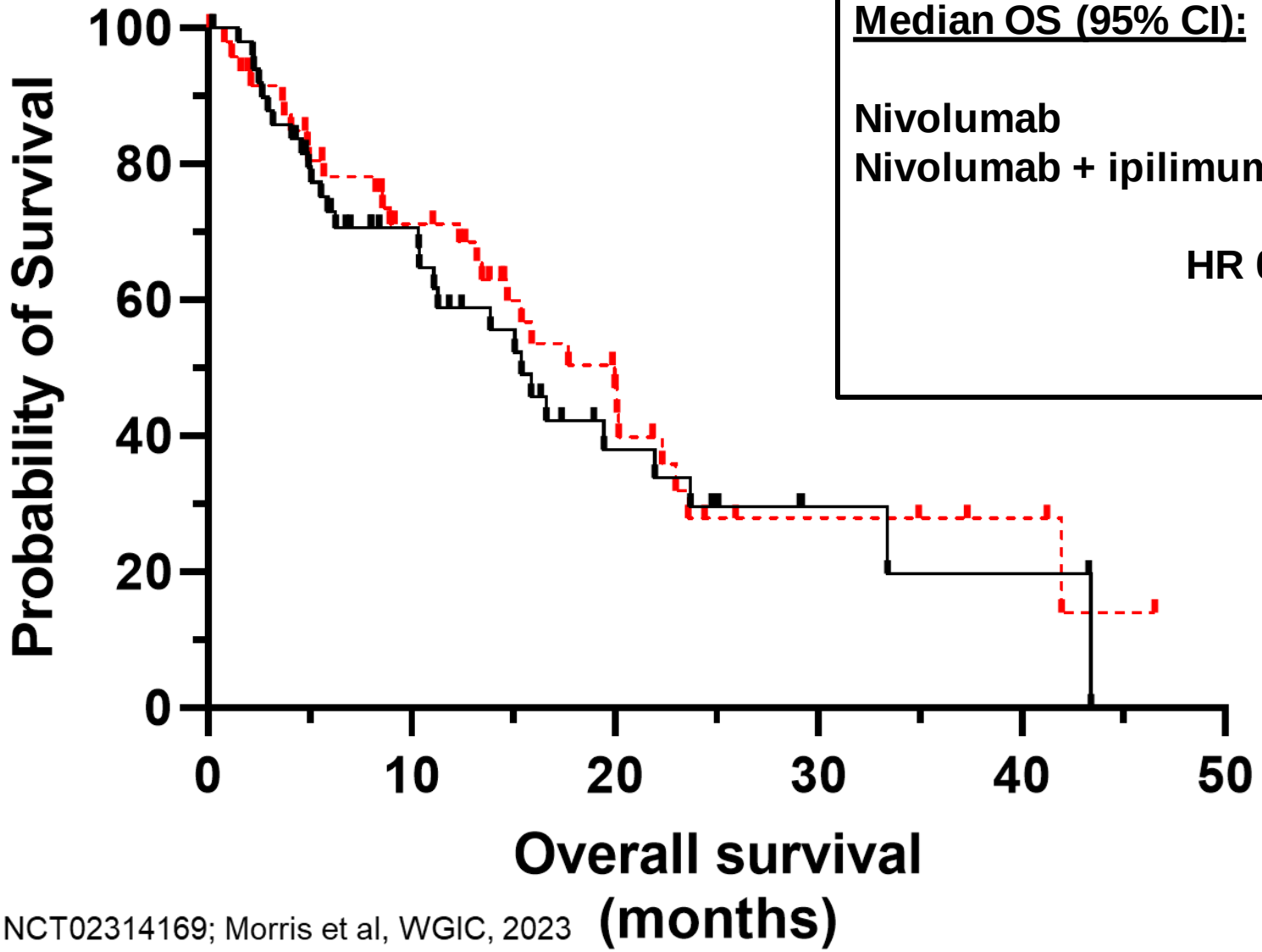
Overall survival

Median OS (95% CI):

Nivolumab	15.4 months (11.1 – NA)
Nivolumab + ipilimumab	20.0 months (13.5 – 23.6)

HR 0.86 (95% CI, .51-1.5)
p= .86



Nivolumab
Nivolumab + ipilimumab

NCT02314169; Morris et al, WGIC, 2023

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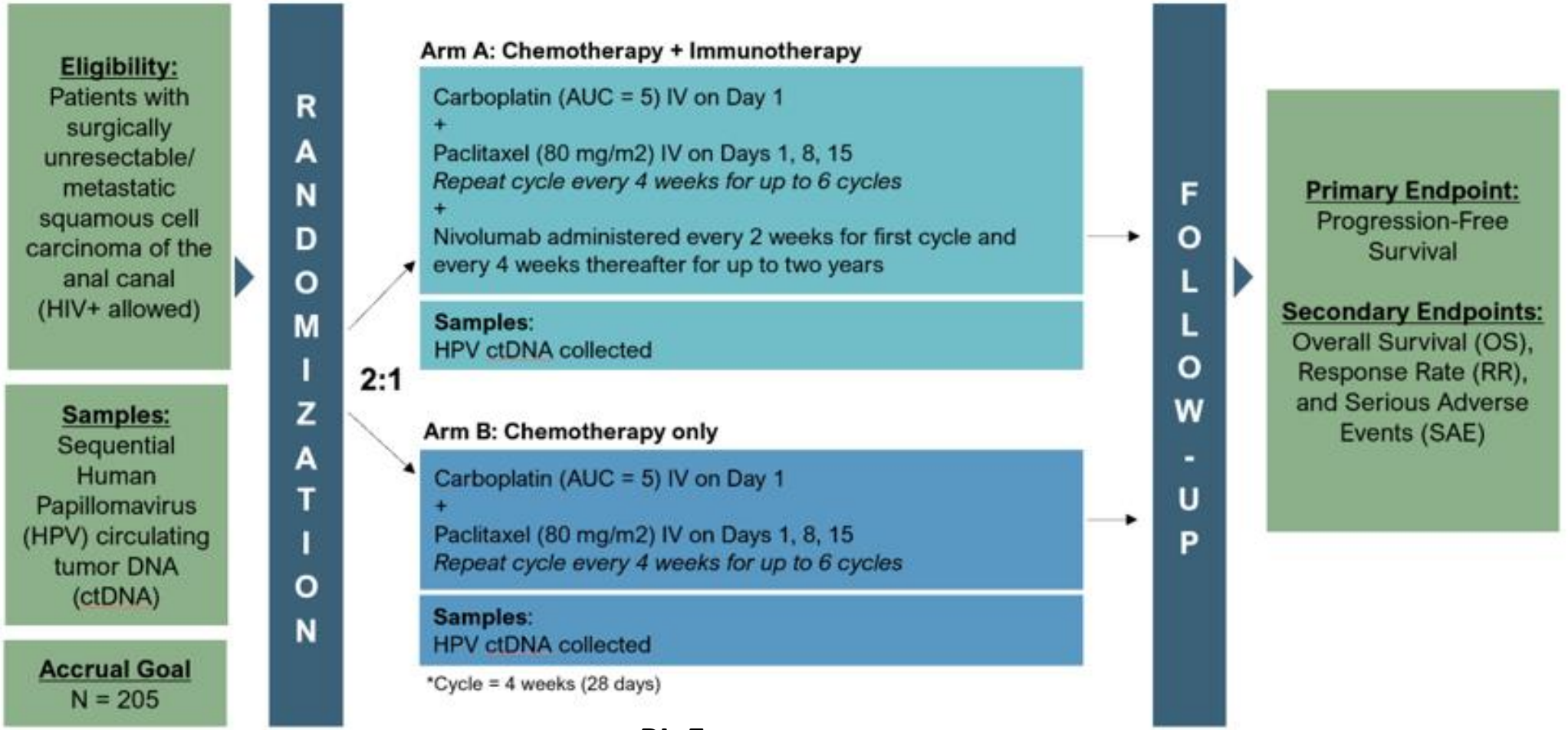
Safety/Toxicity Profile

- One grade 5 event (pneumonitis) occurred in a participant receiving nivolumab + ipilimumab.
- There were 4 grade 4 events in participants receiving nivolumab + ipilimumab: hyperglycemia (N=3) and diabetic ketoacidosis (N=1).
- There were 6 (12%) participants with grade 3 AEs attributed to nivolumab, and 12 (25%) participants with grades 3-5 AEs attributed to nivolumab + ipilimumab.

Grade ≥3 event	Nivolumab (N=52)	Nivolumab + ipilimumab (N=48)
Pneumonitis	0	4
Hyperglycemia	0	3
Hyponatremia	2	1
Abdominal pain	1	1
Elevated ALT	0	2
Adrenal insufficiency	0	1
Fatigue	0	1
Hypophysitis	0	1
Nephrotic syndrome	1	0

NCT02314169; Morris et al, WGIC, 2023

Figure 3B: ECOG EA2176 (NCT04444921): Phase 3 Clinical Trial of Carboplatin and Pacliitaxel +/- Nivolumab (2:1 randomization) in Treatment Naïve Metastatic Anal Cancer Patients

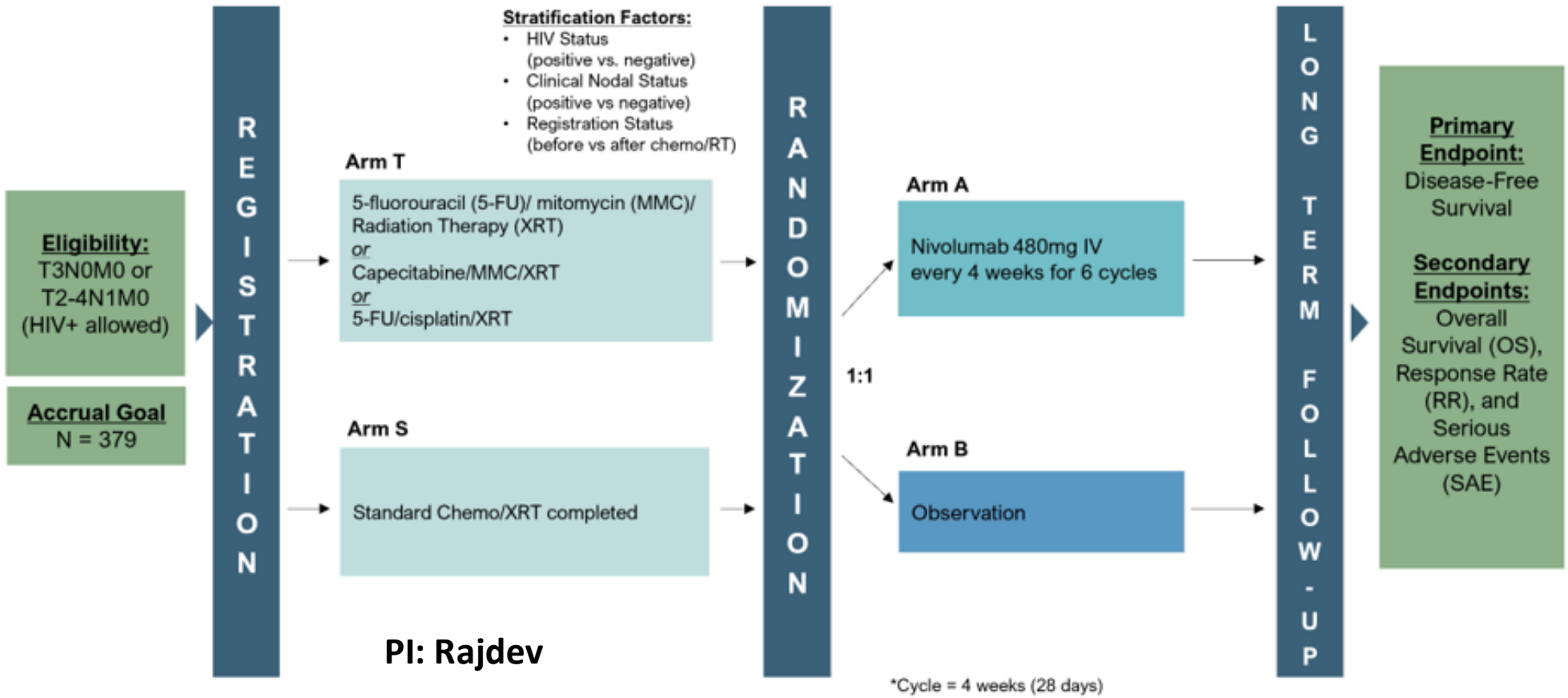


PI: Eng

*HIV pts are eligible

Eng et al: JCO, 2022

Figure 1B: EA2165 (NCT03233711): A Randomized Phase III Study of Nivolumab After Combined Modality Therapy (CMT) in High-Risk Anal Cancer



PI: Rajdev