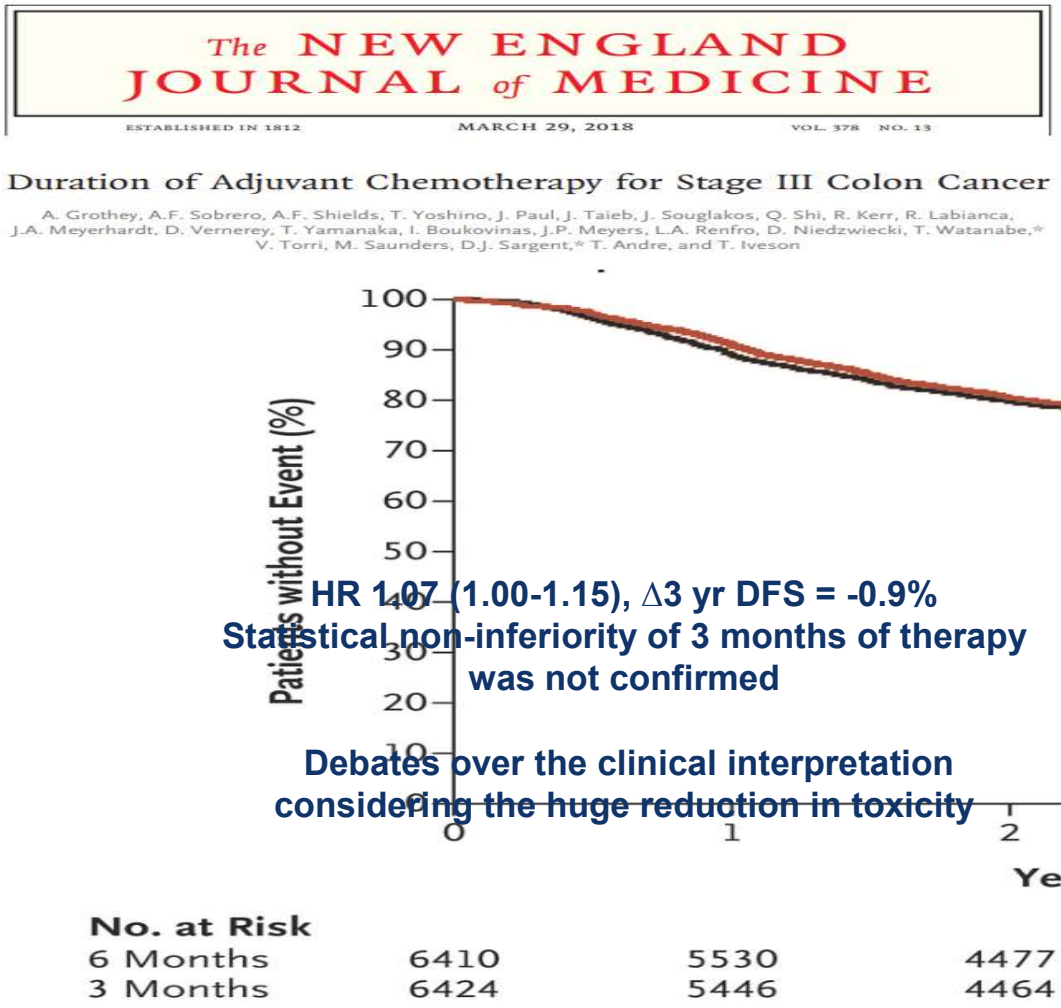
Colorectal Cancer: Where Are We? Focus on ASCO updates

Axel Grothey, MD

Director, GI Cancer Research

West Cancer Center and Research Institute



HR 1.07 (1.00-1.15), Δ3 yr DFS = -0.9%
Statistical non-inferiority of 3 months of therapy was not confirmed

Debates over the clinical interpretation considering the huge reduction in toxicity

6 trials, 12,834 pts

- TOSCA
- SCOT
- IDEA FRANCE
- ACHIEVE
- HORG
- CALGB/SWOG 80702

Objectives of updated analysis

1. To evaluate the non-inferiority (NI) of 3-month compared to 6-month treatment for patients with stage III colon cancer, for the secondary endpoint of overall survival (OS), with a pre-specified statistical hypothesis test

2. To update the results regarding the primary endpoint of disease-free survival (DFS) with mature data: median follow-up 6 yrs

3. To conduct pre-planned subgroup analyses regarding DFS and OS

Updated tumor characteristics

	Total (N=12,835)	
Tumor stage, %		
T1	3.9	
T2	9.4	
T3	65.8	
T4	20.8	range 12-30
Nodal stage, %		
N1	72.0	
N2	28.0	
Risk group, %		
low (T1, T2, or T3 N1)	58.7	
high (T4, N2, or both)	41.3	range 35-49
Primary tumor sidedness, %		
Proximal	29.4	
Distal	36.2	
Missing	34.4	
Chemotherapy regimen, %		
CAPOX	39.5	range 0, 10-75
FOLFOX	60.5	

The ranges shown refer to relevant differences among the 6 IDEA trials

Adverse Events

Adverse Events	FOLFOX				CAPOX			
	G0 - 1	G2	G3 - 4	p-value[1]	G0 - 1	G2	G3 - 4	p-value[1]
Overall				<.0001				<.0001
3 months	30%	32%	38%		35%	41%	24%	
6 months	11%	32%	57%		15%	48%	37%	
Neurotoxicity				<.0001				<.0001
3 months	83%	14%	3%		85%	12%	3%	
6 months	52%	32%	16%		55%	36%	9%	

[1]Chi-squared test for trend; Total of 19 grade 5 events; Adverse events only collected on first 617 patients enrolled to SCOT trial

Statistical Methods

NI margin determination for the current OS NI hypothesis testing

- **MOSAIC: 5-year OS rate: 4.3% increase (->76.0%); HR: 0.80 for oxaliplatin[1]**
- **The maximum acceptable loss of treatment efficacy was half of the above gain**
- **Upper 95% CI NI margin HR = 1/(0.8+(1-0.8)/2) = 1.11 (corresponding to 2.26% absolute reduction in OS rate)**
- **Similar compromise as for DFS**

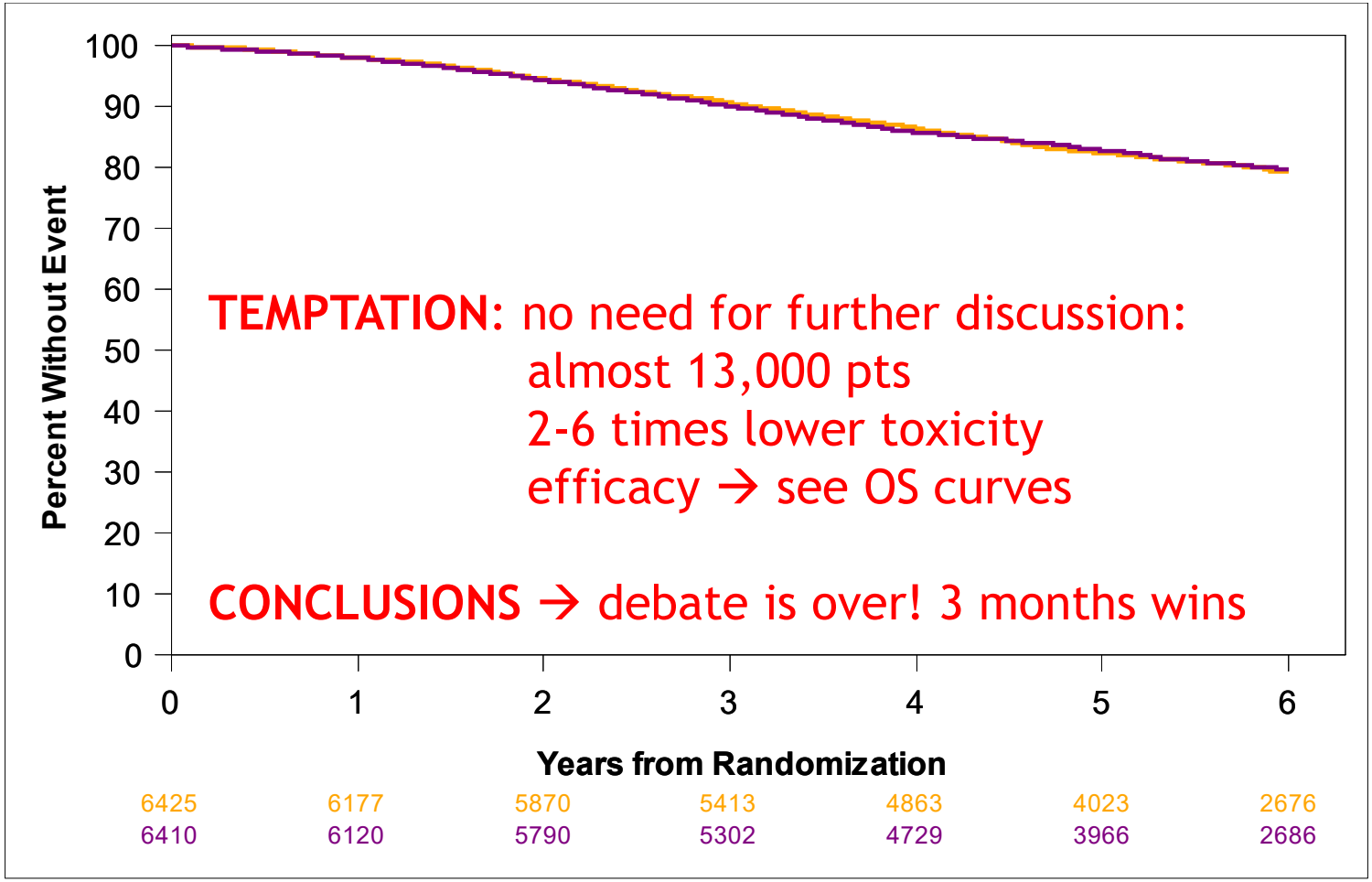
Pre-planned subgroup analysis for both OS and DFS endpoints with multiplicity adjustments

- **CAPOX vs. FOLFOX**
- **Low risk vs. High risk**

Claim 3m of treatment is NI to 6m regarding OS/DFS, if FDR (false discovery rate) adjusted one-sided p-value < 0.025

[1]Andre T, JCO 2015;

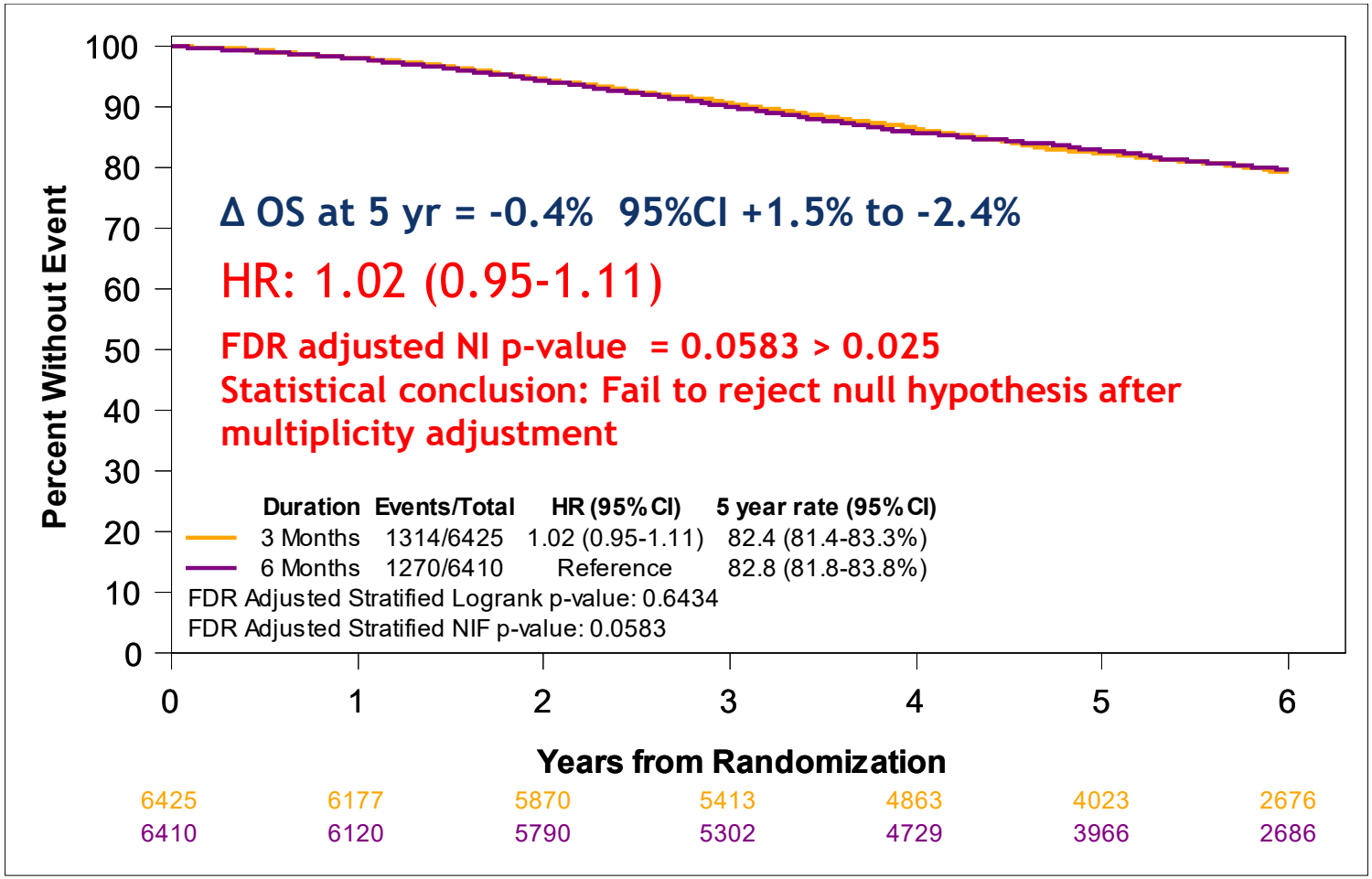
IDEA overall population OS



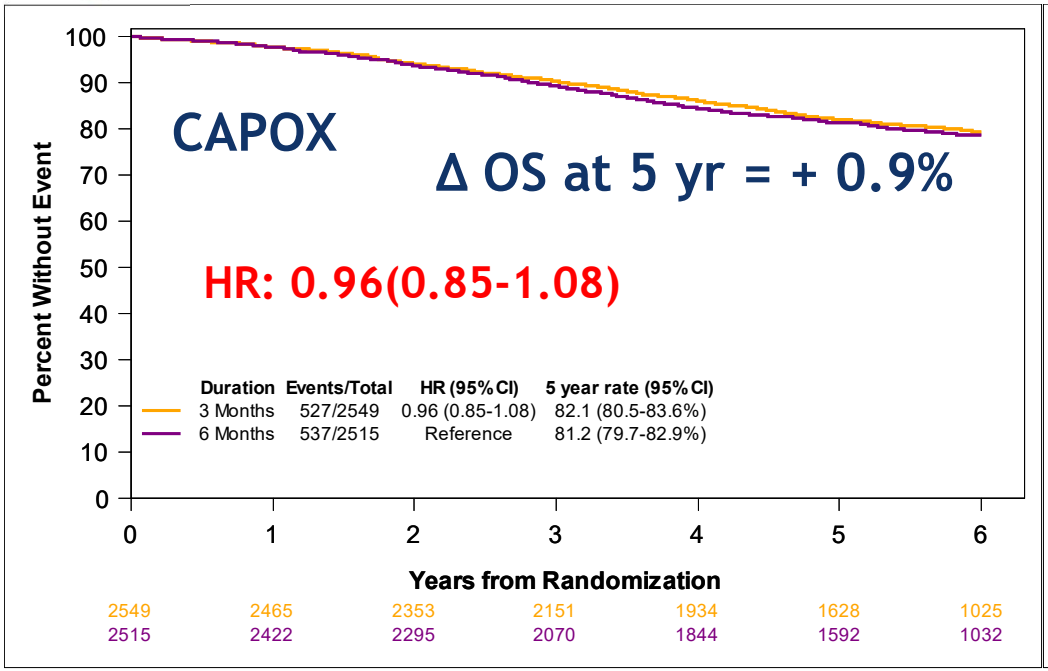
TEMPTATION: no need for further discussion:
almost 13,000 pts
2-6 times lower toxicity
efficacy → see OS curves

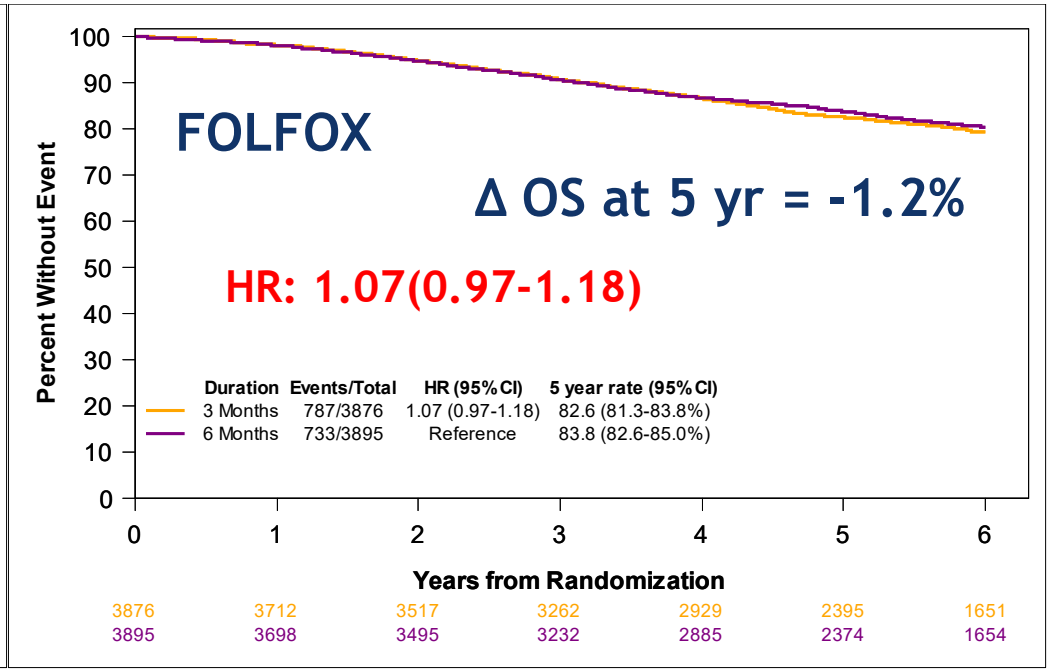
CONCLUSIONS → debate is over! 3 months wins

IDEA overall population OS



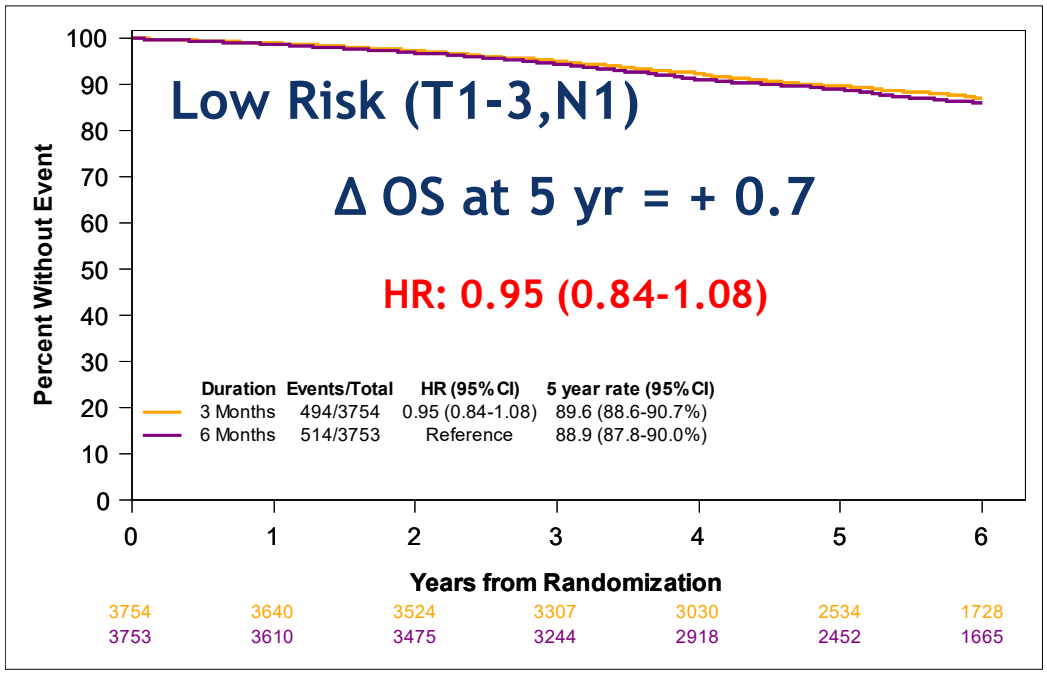
IDEA 5-yr OS by regimen

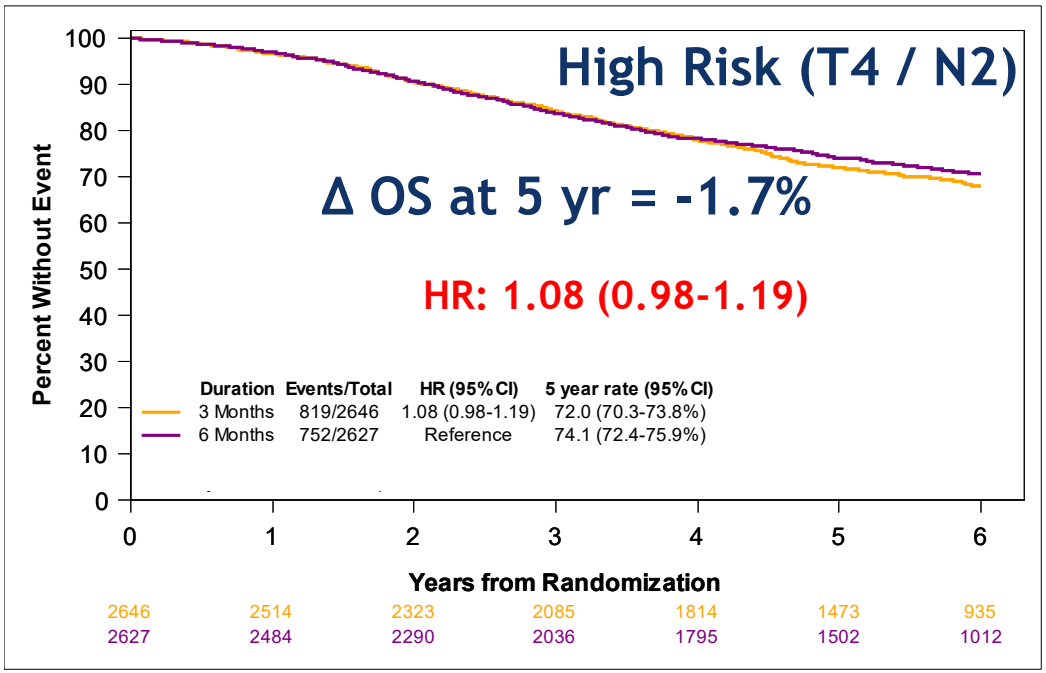




Interaction p-value = 0.2009

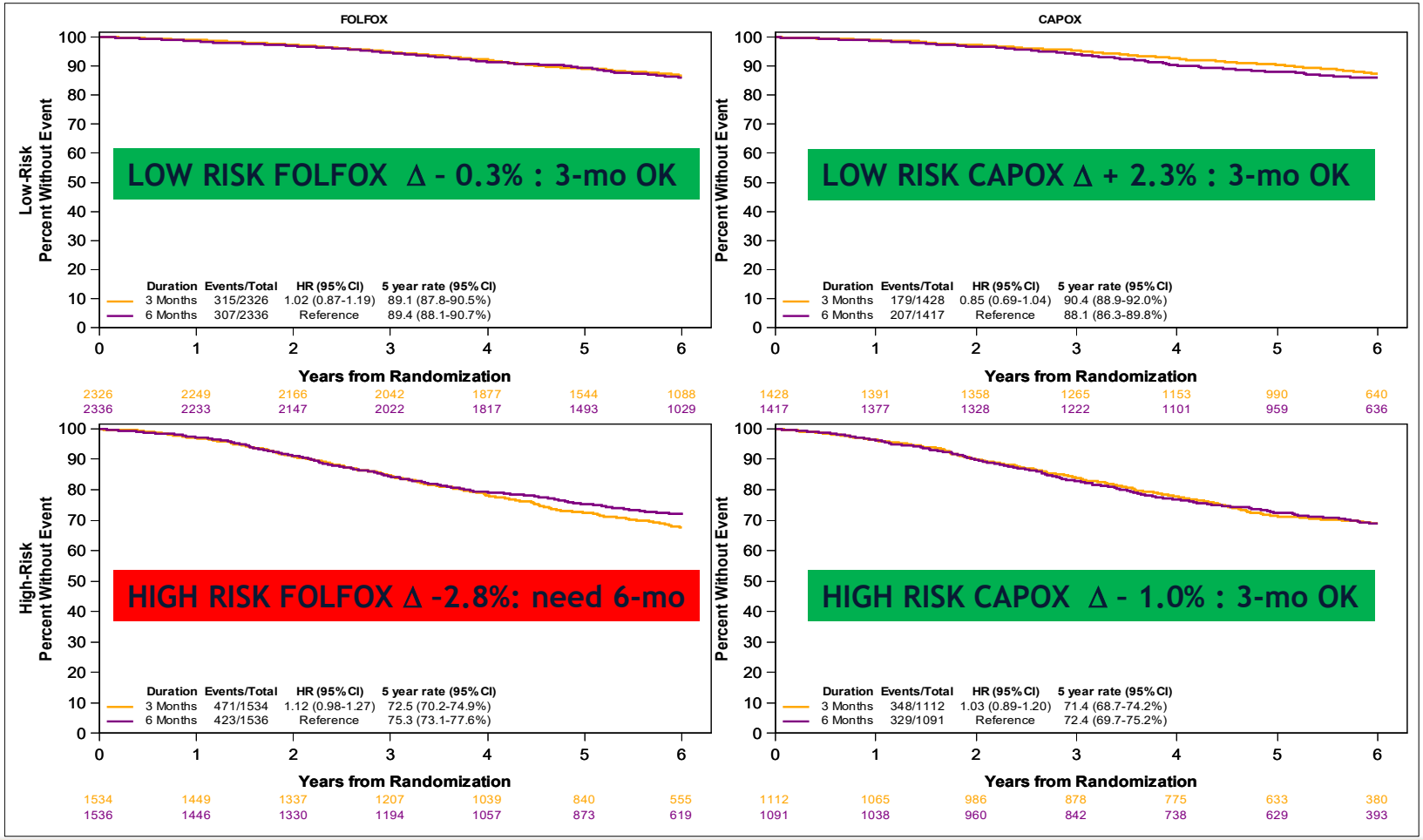
IDEA: 5-yr OS by risk group





Interaction p-value = 0.1512

IDEA 5-yr OS by regimen/risk



IMPLICATIONS FOR CLINICAL PRACTICE

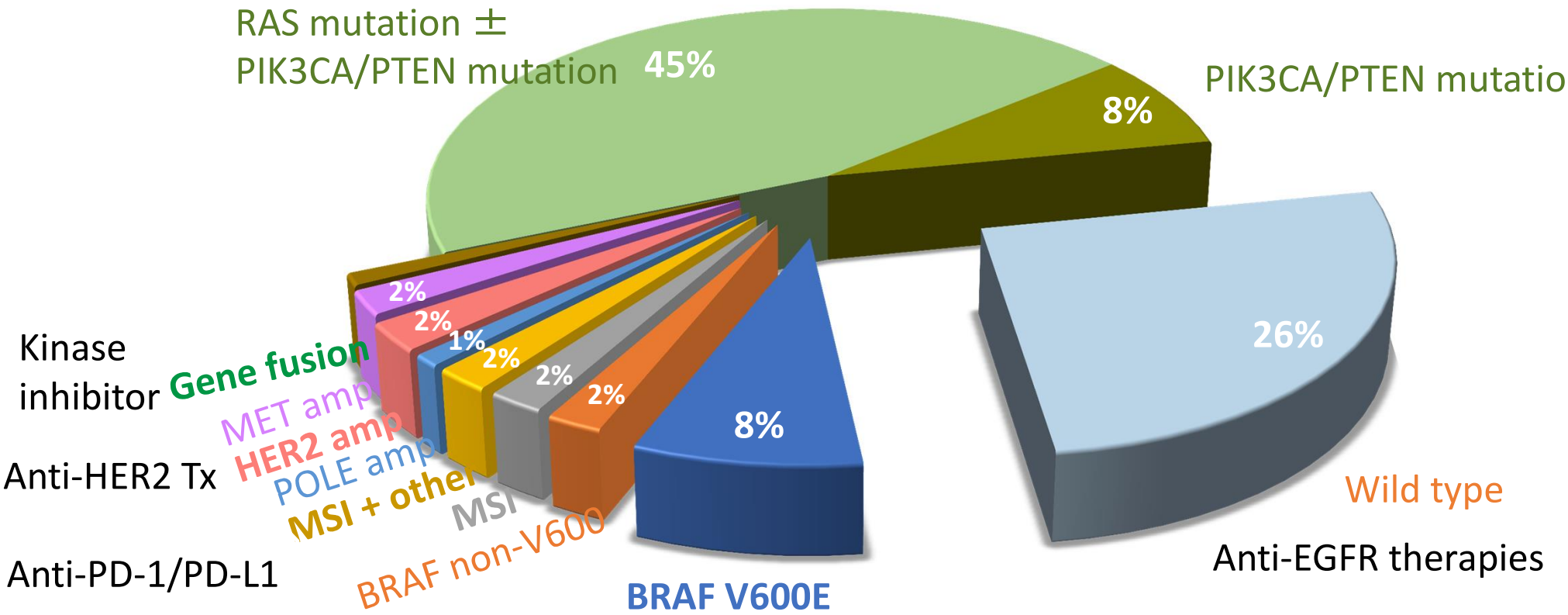
1. 60% of patients with stage 3 colon cancer are low risk and should receive 3 month of CAPOX

2. 40% of patients are high risk. For the majority of these, the risk-benefit assessment suggests 3 months of CAPOX as well. For those unwilling to loose even 1-2% of efficacy, 6 months of therapy is recommended.

3. For High risk cancers, novel prognostic factors including Immunoscore and/or ctDNA as marker for MRD, may help to define the best adjuvant therapy in the future[1-2]

[1]Pages F, Ann Oncol 2020; [2]Taieb J, ESMO 2019 (abstract, Ann Oncol 2019. 30, 867-867)

Genomic Markers in mCRC



Dienstmann. ASCO Ed Book. 2018.

BRAF mutations in CRC

- **Prognostic factor**
  - BRAF V600E mut with very poor prognosis
    - ➢ Intensification of first-line therapy = SOC (FOLFOXIRI + BEV)?
  - Non-V600E BRAF mut (Class 3!) with better prognosis than wild-type
    - ➢ Consider de-escalation of therapy
- **Predictive factor**
  - Negative predictive:
    - BRAF V600E mut cancers do not respond to EGFR antibodies
      - ➢ Data from meta-analysis support preclinical models
      - ➢ Non-V600E BRAF mut (Class 3) cancers can respond to EGFR antibodies
  - Positive predictive:
    - Targeted regimens for BRAF V600E mut cancers available
      - ➢ VIC, BEACON

BRAF V600E mutated mCRC

- 66 yo pt with PMH of HTN, GERD
- August 2019: Weight loss, anemia (Hb 7.9)
- September 15, 2019: CT abd/ pelvis shows liver mass in segm 6, retroperitoneal adenopathy, peritoneal implants, mass in ascending colon *with bowel obstruction*
- September 16, 2019: Right hemicolectomy. pT3 pN2b (15/16), M1c cancer
- CARIS profile: BRAF V600E mutation, MSS, TMB 10

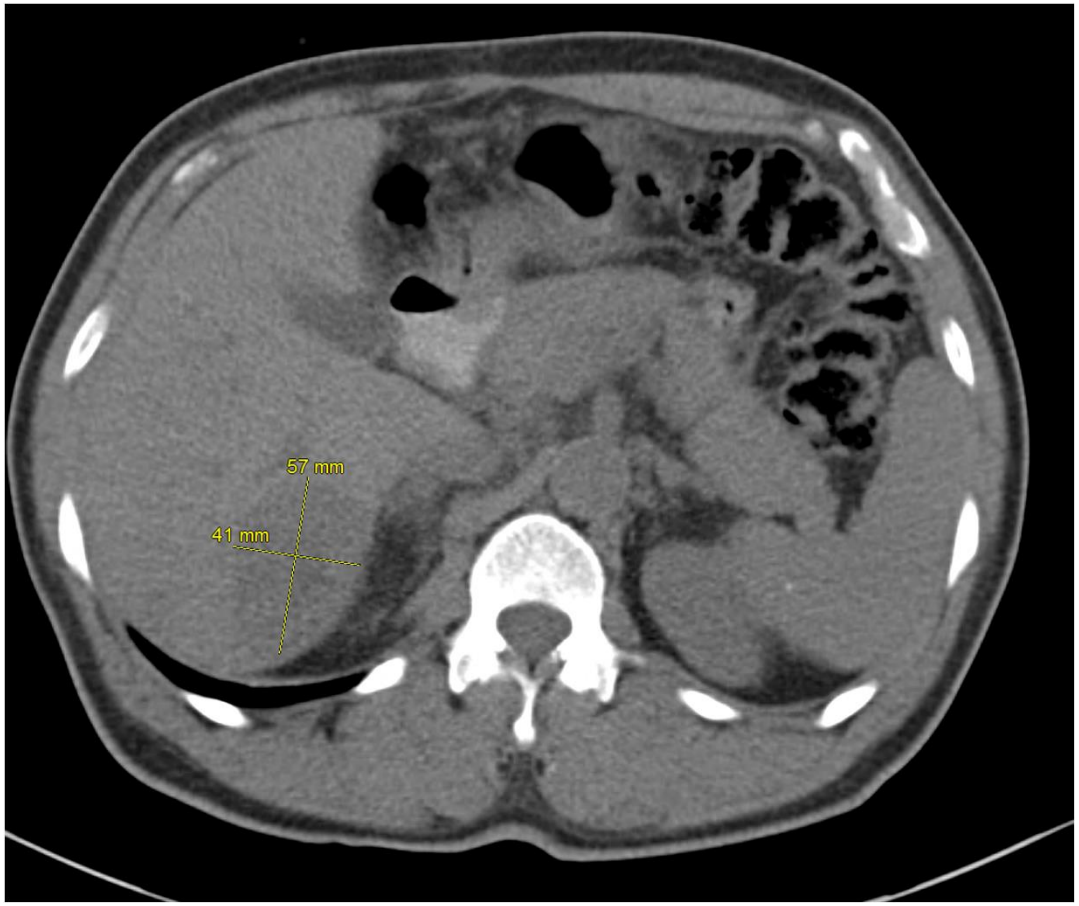
BRAF V600E mutated mCRC

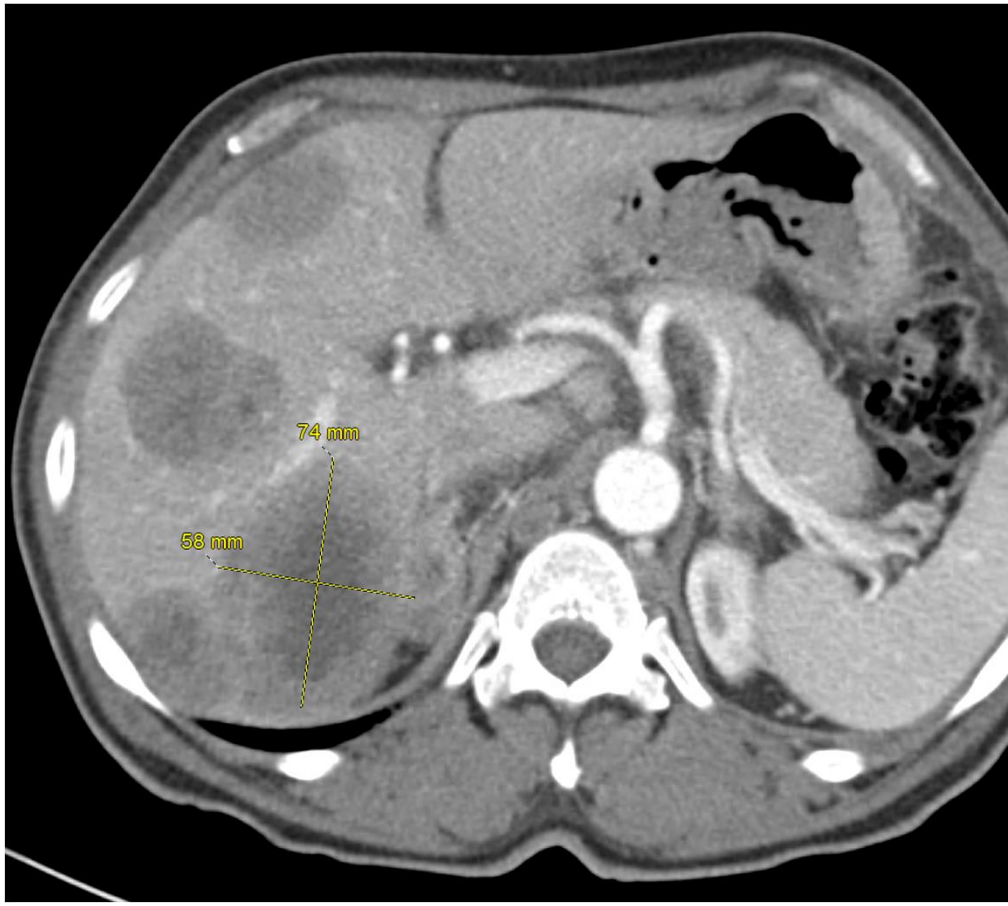
- October 31, 2019: CT scan before initiation of chemotherapy with progression of liver and peritoneal metastases, lymphadenopathy
- November 2019: Pt screen failure for ANCHOR study due to low EF (43%), start FOLFOXIRI + BEV -> rising CEA on therapy. Pt developed more pain in RUQ
- February 2020: CT after 4 cycles of chemo shows PD, patient increasingly symptomatic with RUQ pain and weight loss

OCT 2019 (w/o)

FOLFOXIRI + BEV

FEB 2020





BRAF V600E mutated mCRC

- **February 2020: Start BEACON triplet. Clinical response within 2 (!) days!**

BEACON: Phase 3 in 2nd/ 3rd Line BRAF V600E mut mCRC

Patients with *BRAF*^{V600E} mCRC with disease progression after 1 or 2 prior regimens; ECOG PS of 0 or 1; and no prior treatment with any RAF inhibitor, MEK inhibitor, or EGFR inhibitor

ENCORAFENIB + BINIMETINIB + CETUXIMAB
N = 30

Encorafenib 300 mg PO daily
Binimetinib 45 mg PO bid
Cetuximab standard weekly dosing

R 1:1:1

Triplet therapy
ENCORAFENIB + BINIMETINIB + CETUXIMAB
n = 205

Doublet therapy
ENCORAFENIB + CETUXIMAB
n = 205

Control arm
FOLFIRI + CETUXIMAB, or irinotecan + CETUXIMAB
n = 205

Primary Endpoints:

Triplet vs Control

OS
(All randomized Pts)

ORR – Blinded Central Review
(1st 331 randomized Pts)

Randomization was stratified by ECOG PS (0 vs. 1), prior use of irinotecan (yes vs. no), and cetuximab source (US-licensed vs. EU-approved)

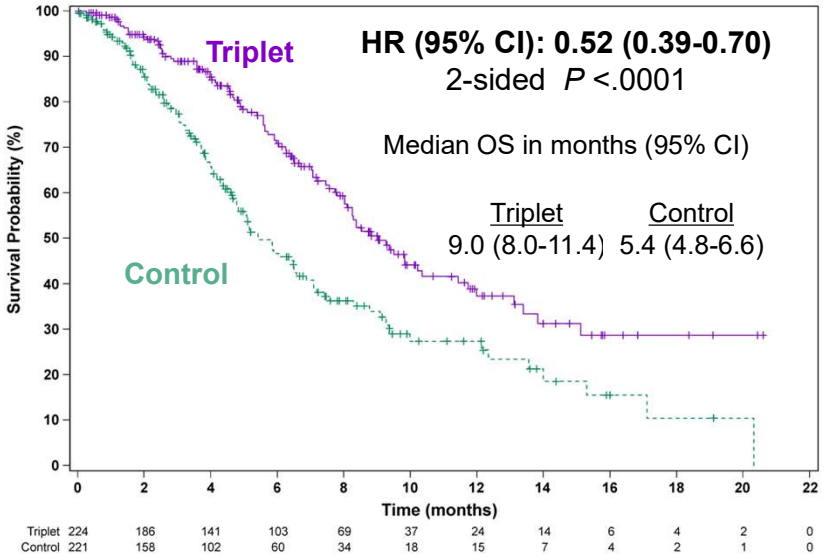
Secondary Endpoints: Doublet vs Control and Triplet vs Doublet - OS & ORR, PFS, Safety

QOL Assessments: EORTC QOL Questionnaire (QLQ C30), Functional Assessment of Cancer Therapy Colon Cancer, EuroQol 5D5L, and Patient Global Impression of Change).

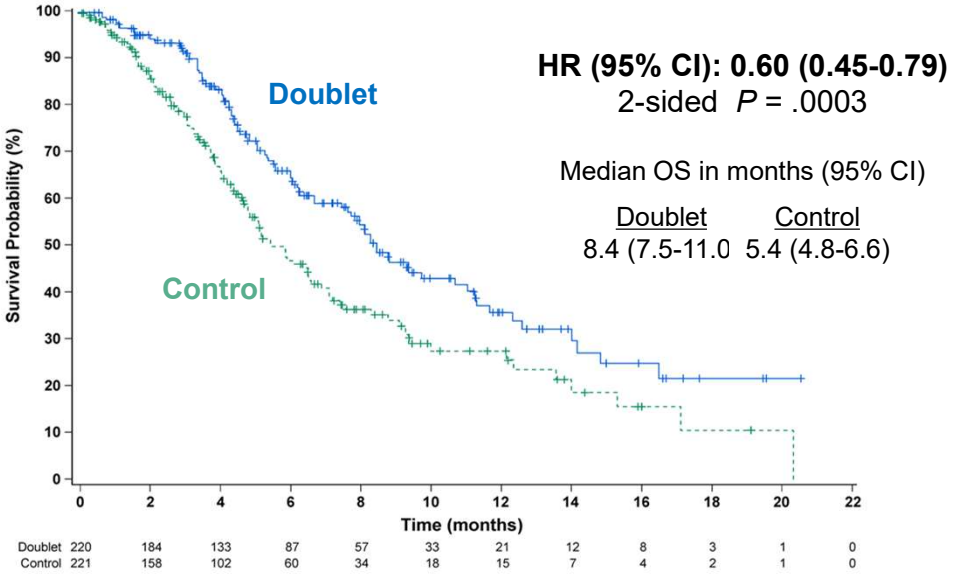
Kopetz et al., NEJM 2019

BEACON: Overall Survival and Objective Response Rate

Triplet vs Control



Doublet vs Control

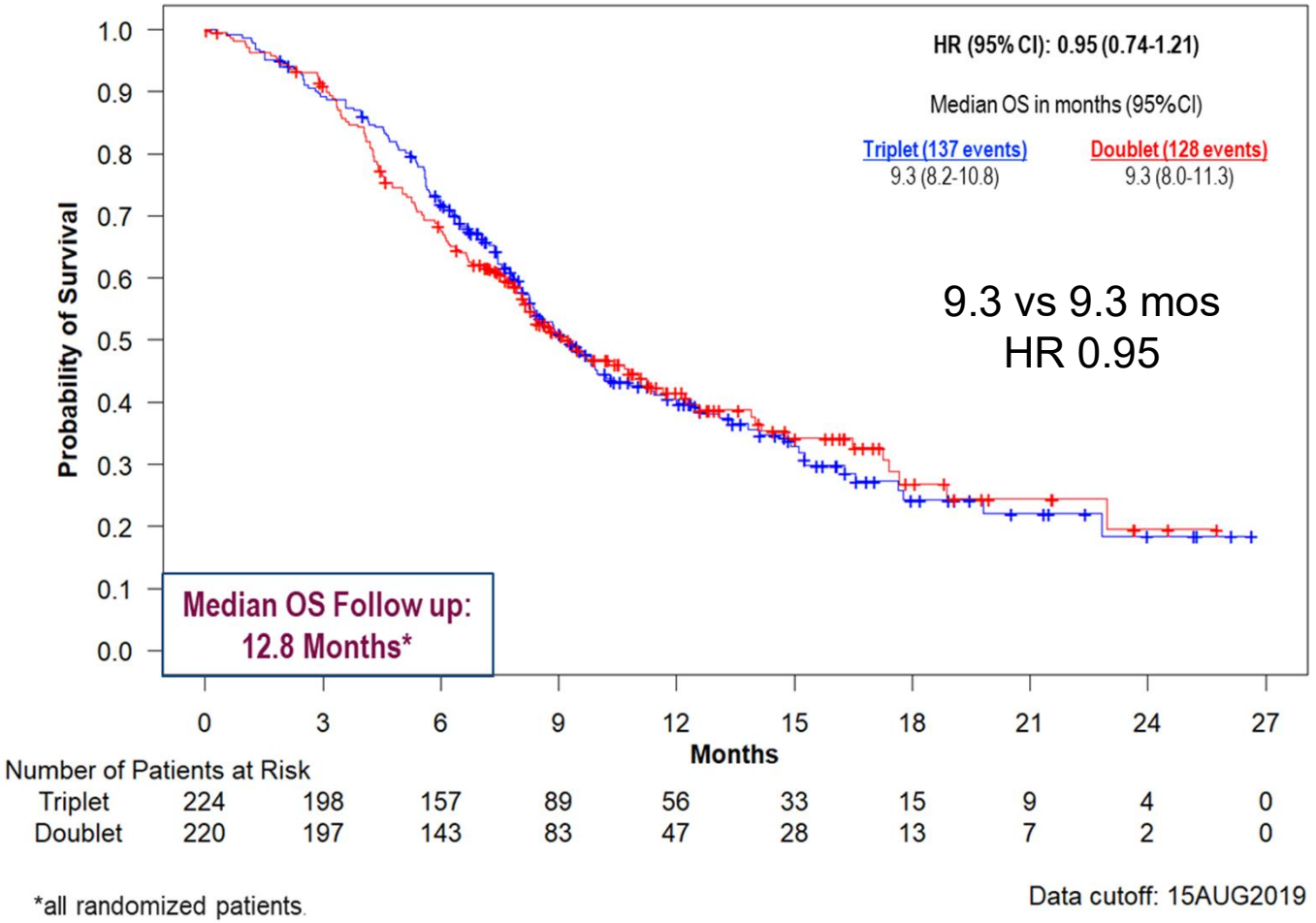


Objective Response Rate (first 331 randomized patients)

Confirmed Response by BICR	Triplet N = 111	Doublet N = 113	Control N = 107
Objective response rate	26%	20%	2%
(95% CI)	(18–35)	(13–29)	(<1–7)
P value vs control	<.0001	<.0001	

Kopetz S, Grothey A, et al. ESMO 2019. Abstract LBA-006; Kopetz S, Grothey A, et al. *N Engl J Med*. 2019;381:1632-1643.

BEACON CRC: Updated Analysis Triplet vs Doublet

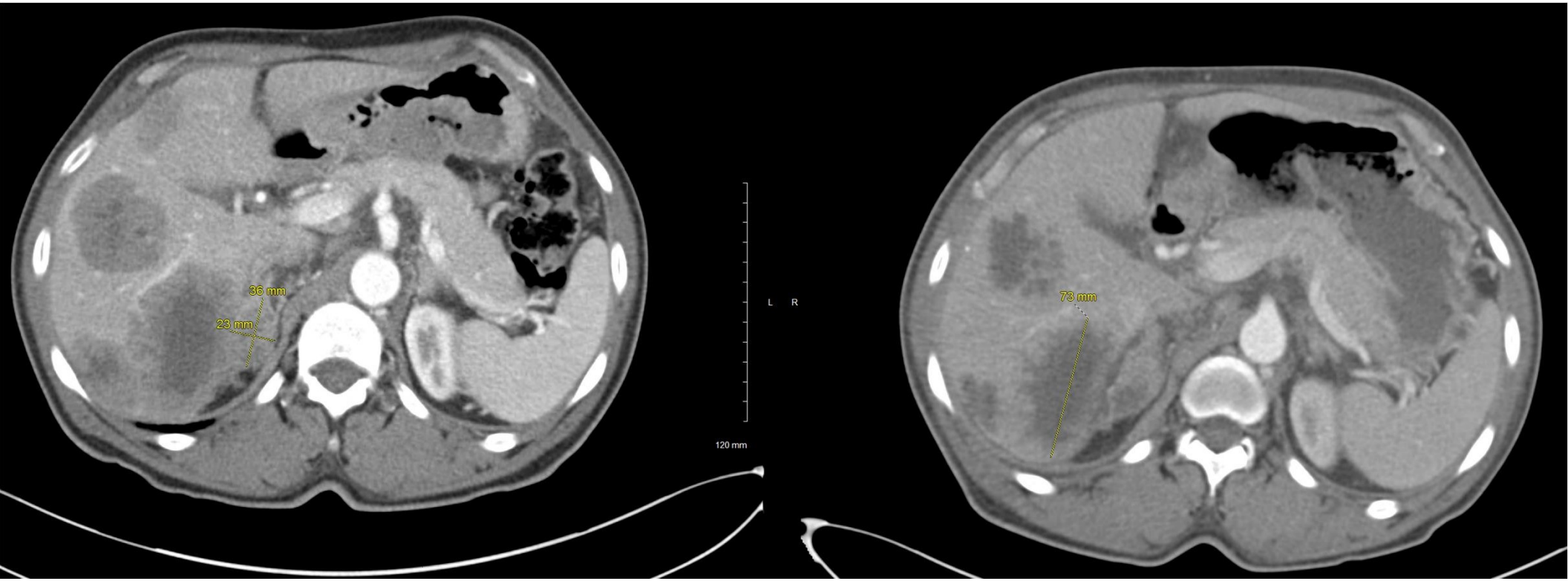


Kopetz S, Grothey A, et al. ASCO GI 2020.

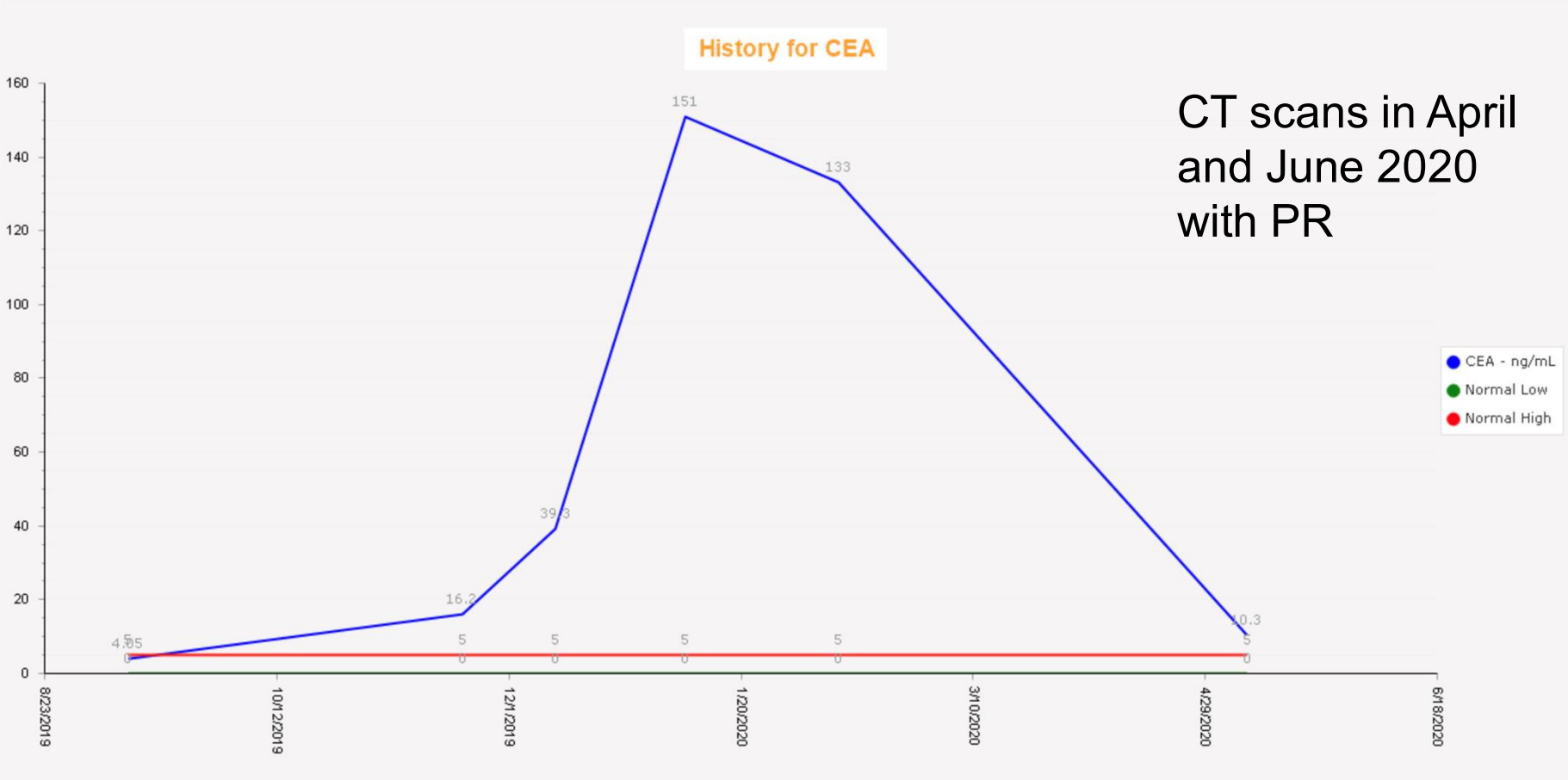
FEB 2020

BEACON

MAY 2020



CEA levels on therapy



CT scans in April and June 2020 with PR

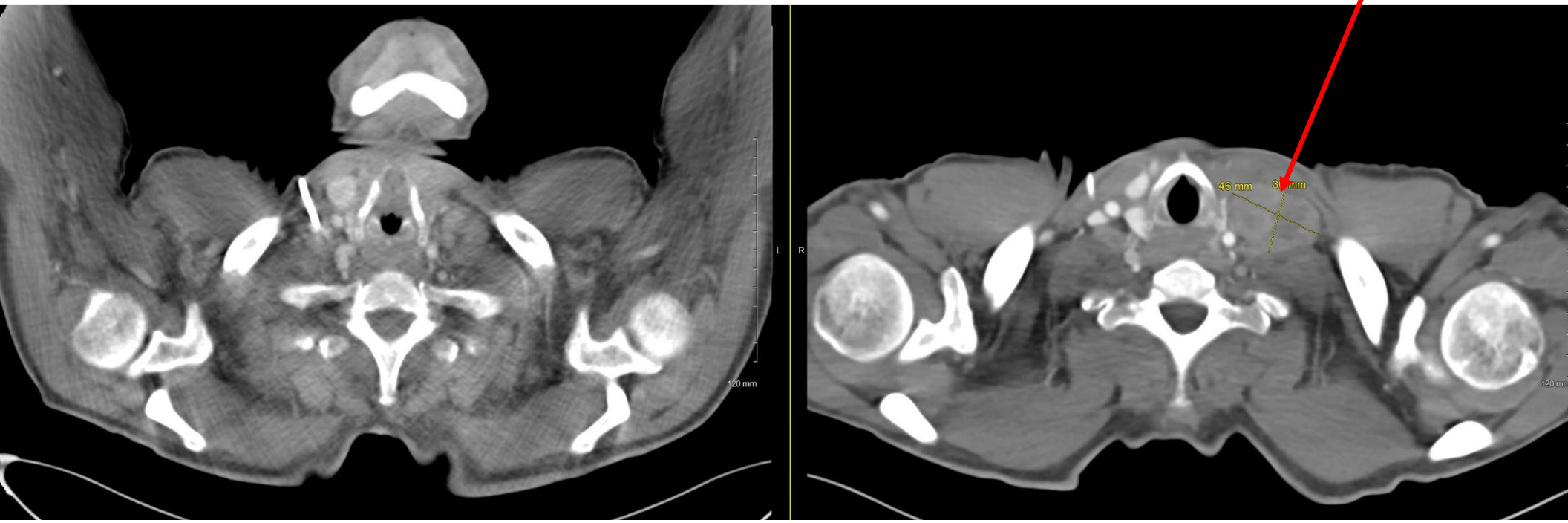
FOLFOXIRI-BEV

BEACON

MAY 2020

BEACON

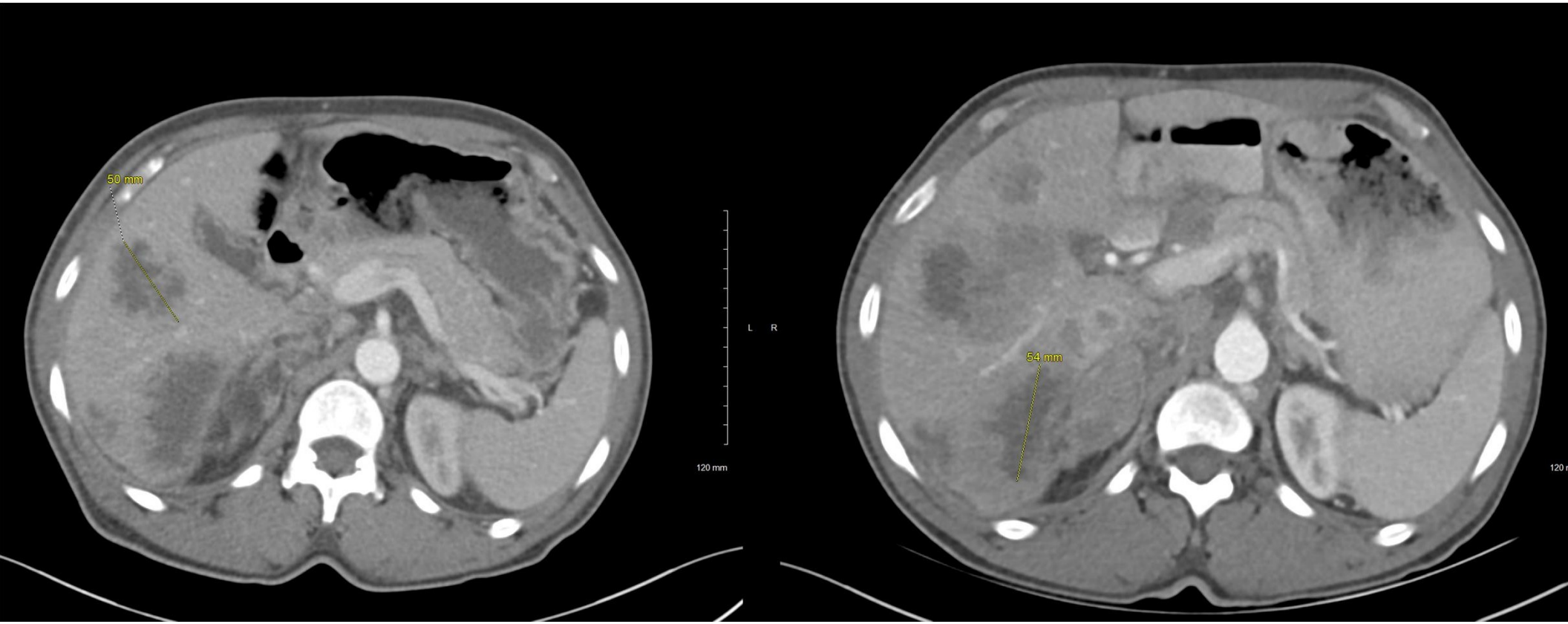
JUL 2020



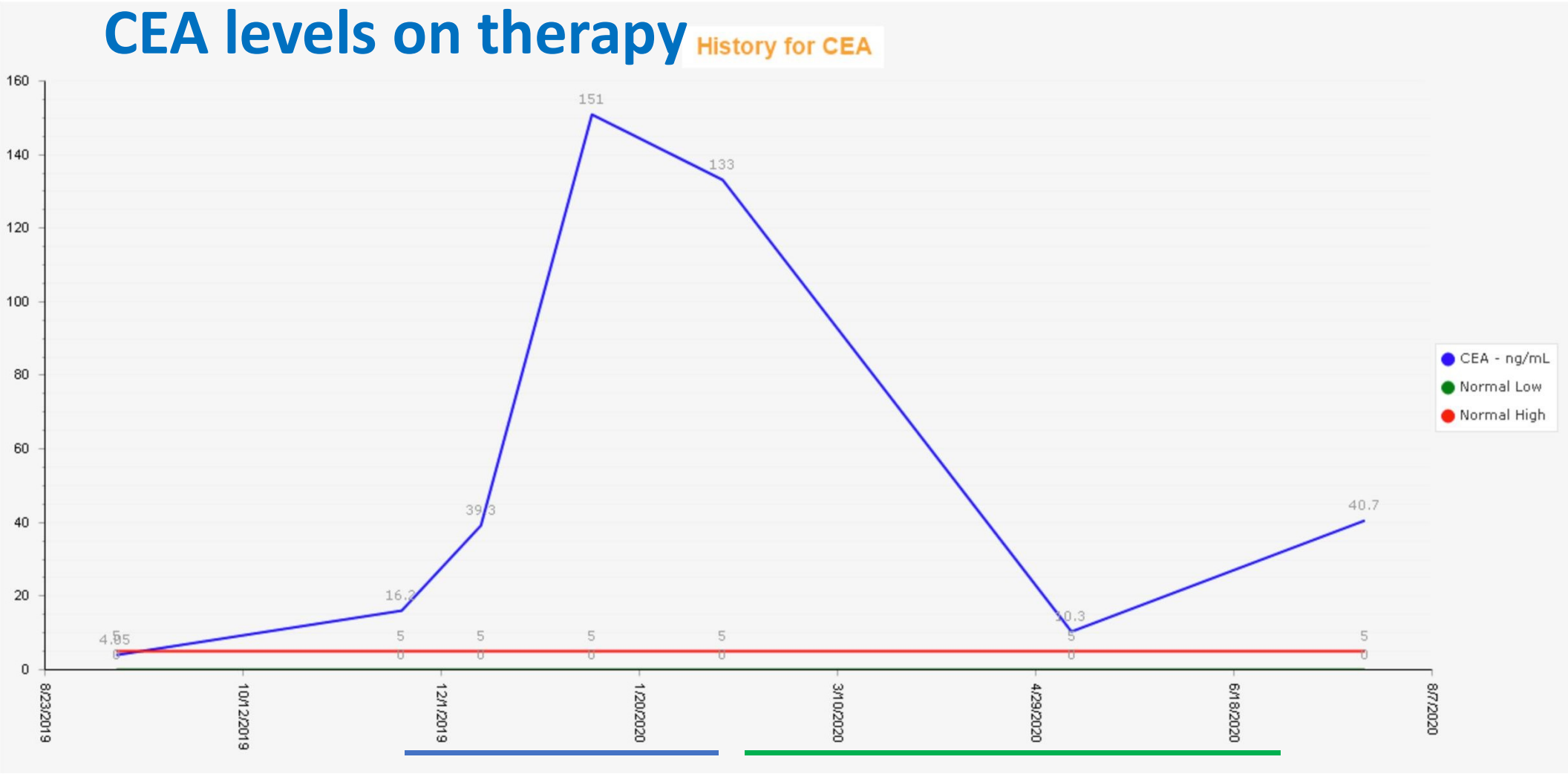
MAY 2020

BEACON

JUL 2020



CEA levels on therapy



FOLFOXIRI-BEV

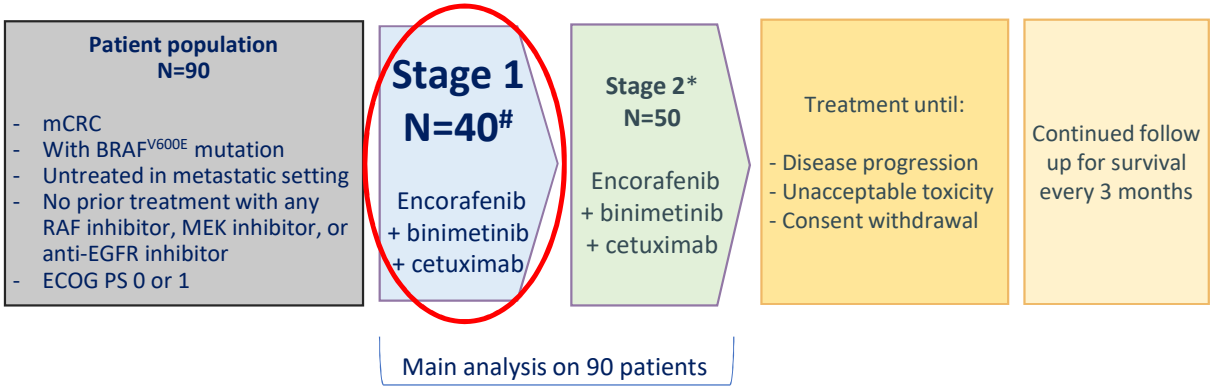
BEACON

BRAF V600E mutated mCRC

- **July 2020: CT scan with remarkable PD in LNs, lung, liver peritoneum.**
  PS drastically and rapidly decreased
- **July 30, 2020: Guardant360 assay shows**
  81.4% ctDNA (!), KRAS and MET amplification,
  BRAF V600E fraction 54.3%

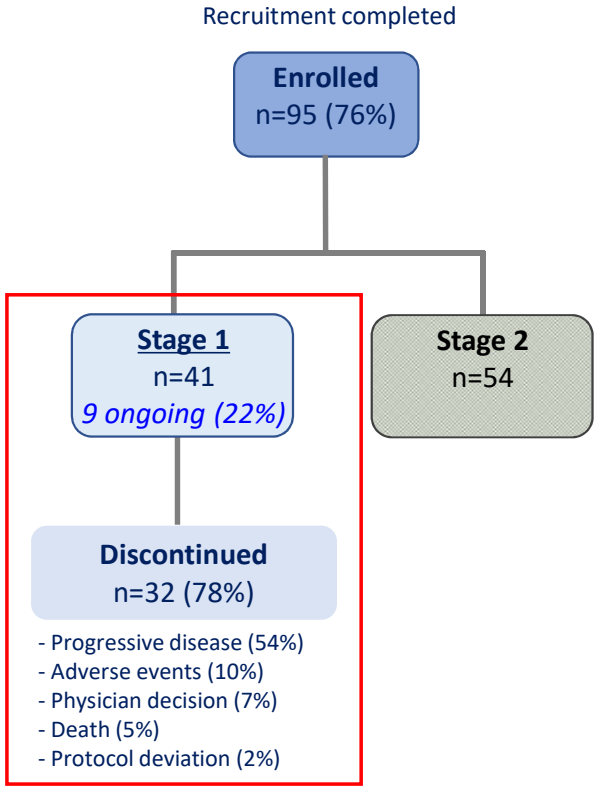
ANCHOR CRC, Phase 2 study in FIRST LINE BRAF^{V600E} mCRC

2-STAGE DESIGN[1]



Primary objective & endpoint: cORR (investigator assessed)

Secondary endpoints: PFS, OS, Safety, QoL, PK



1. Grothey A, et al. *Annals Oncol*. 2019;30(suppl 4):P-400
#Futility analysis
*Stage 2 enrolment only after ≥ 12 responses observed in stage 1
cORR=confirmed objective response rate, OS=overall survival, PK=pharmacokinetics, PFS=progression free survival, QoL=quality of life

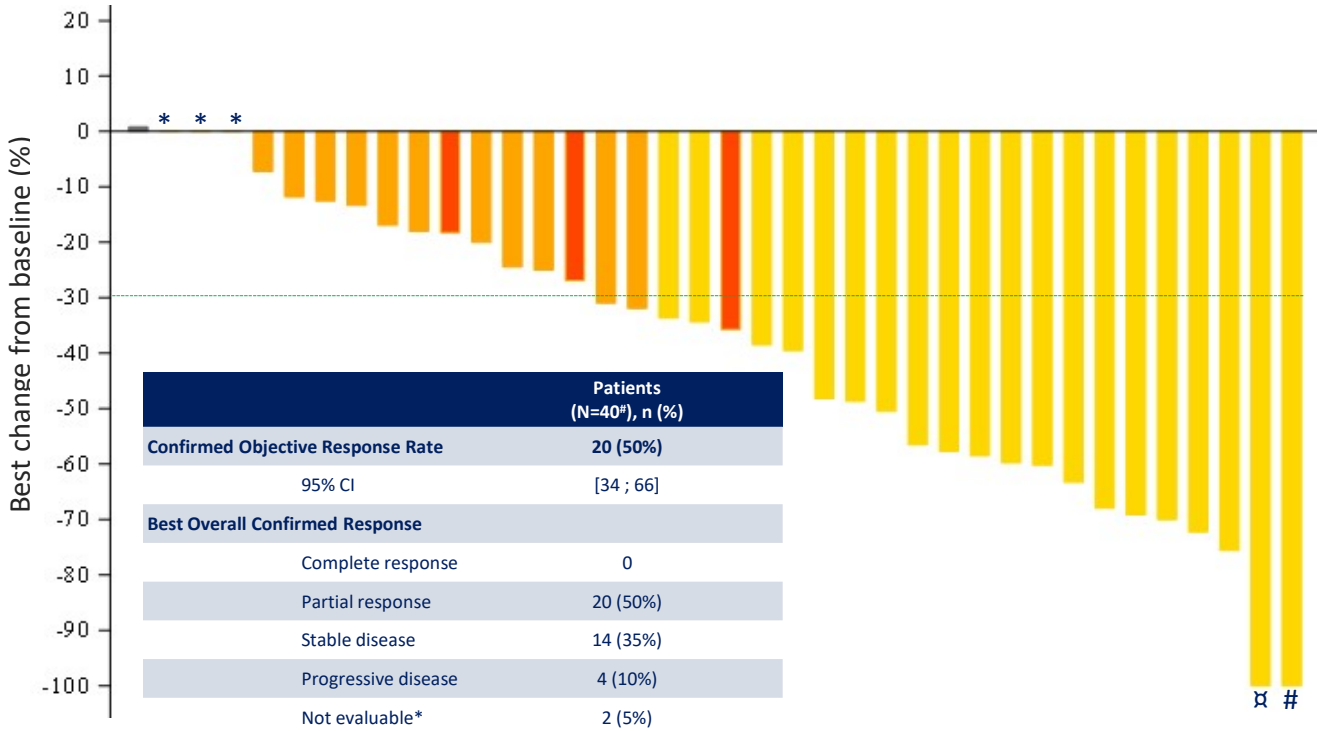
Cut-off date: 06-Feb-2020

Grothey et al., ESMO GI 2020

Note: the data have not been fully cleaned due to Covid-19 pandemic.

Best Percentage Change in Tumor Measurements for Stage 1

Investigator's assessment, patients evaluable for efficacy



	Patients (N=40#), n (%)
Confirmed Objective Response Rate	**20 (50%)**
95% CI	[34 ; 66]
Best Overall Confirmed Response	
Complete response	0
Partial response	20 (50%)
Stable disease	14 (35%)
Progressive disease	4 (10%)
Not evaluable*	2 (5%)

Partial Response
Stable Disease
Not evaluable
Progressive Disease

BUT:
Median PFS
Only 4.9 mos!

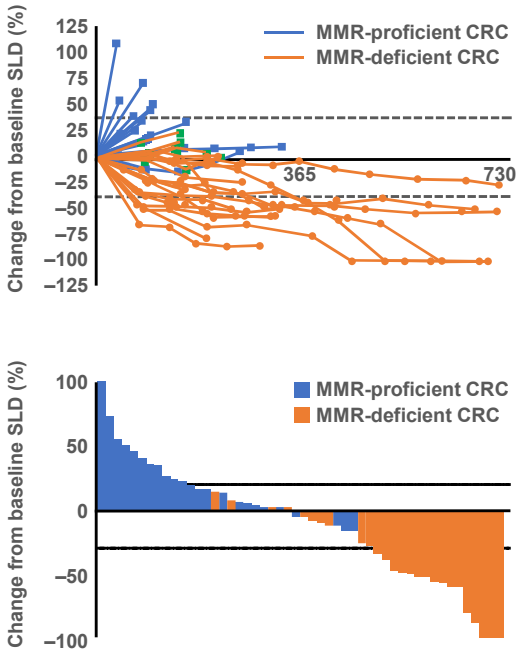
*3 patients with best percent change from baseline=0% and have Confirmed Best Overall Response=stable disease
¤ Complete Response on target lesion but non target lesion still present
Complete Response was not confirmed at the subsequent tumor evaluation

Grothey et al., ESMO GI 2020

Note: the data have not been fully cleaned due to Covid-19 pandemic.

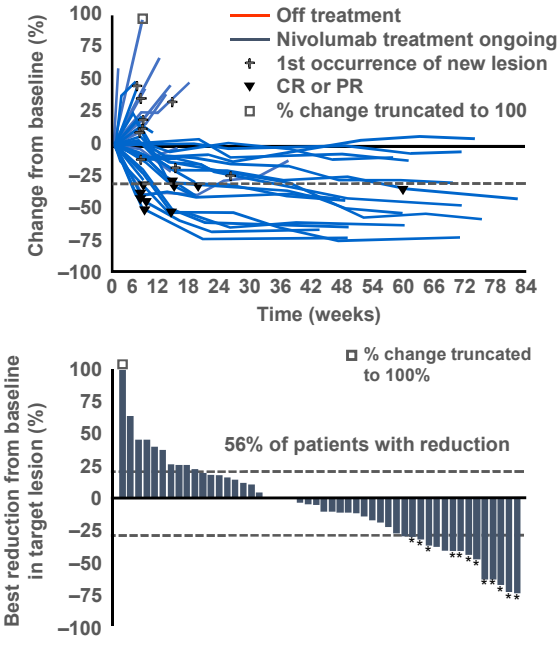
MSI-high Tumors are Responsive to PD-1 inhibitors

Pembrolizumab (KEYNOTE 016, phase II)[1,*]

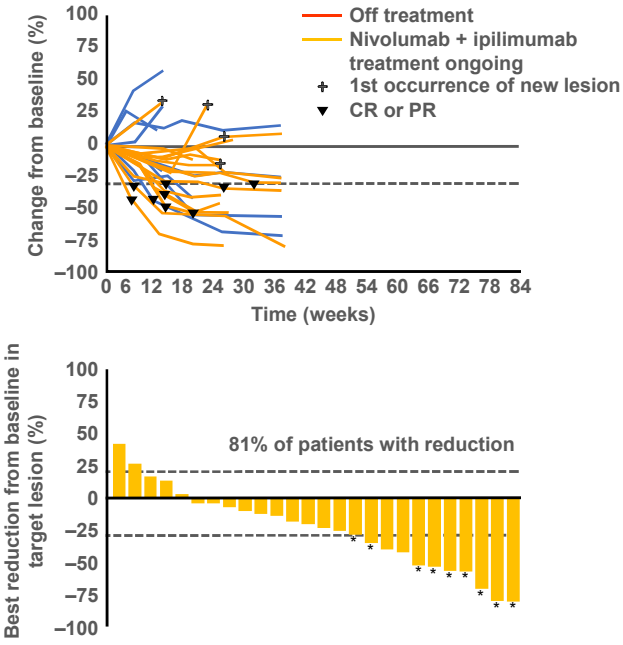


Nivolumab ± ipilimumab (CheckMate-142, phase II)[2]

Nivolumab 3mg/kg



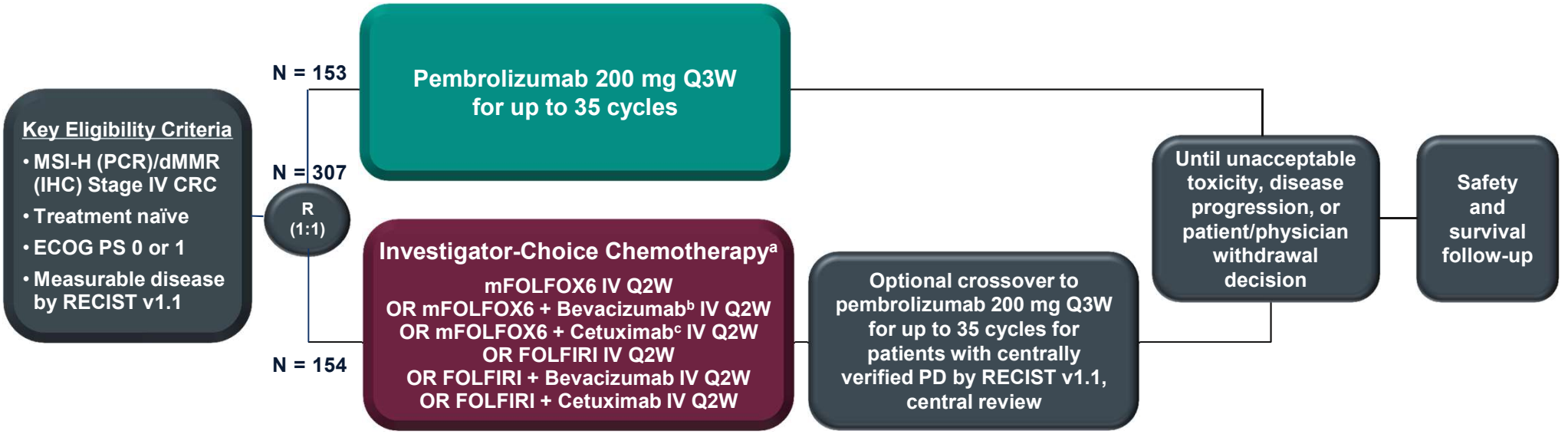
Nivolumab 3mg/kg + ipilimumab 1mg/kg



- ***Lynch Syndrome (yes/no/unknown): MMR-deficient CRC = 54/7/39; MMR-proficient CRC = 0/100/0**

1. Le et al. ASCO 2016; 2.Overman et al. ASCO 2016

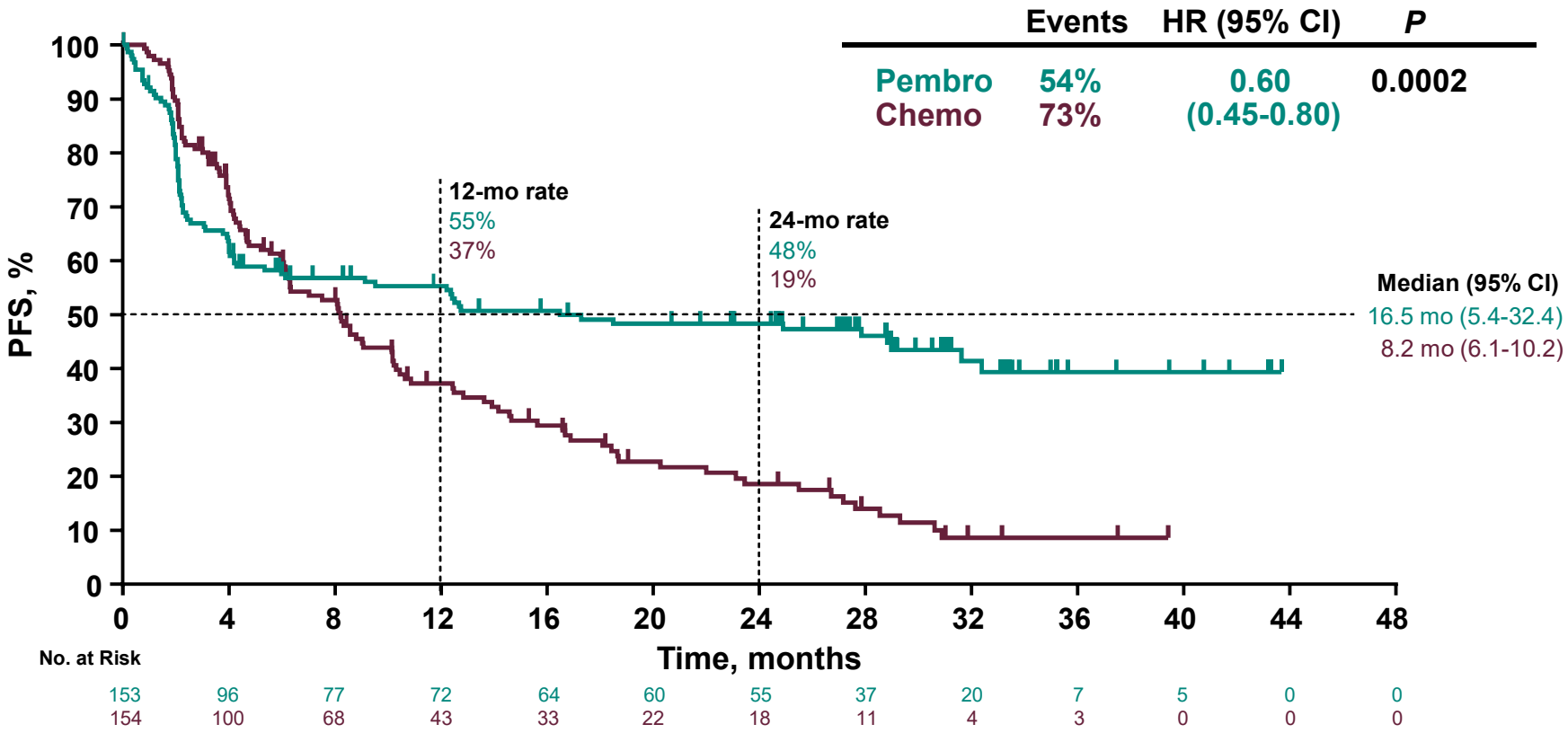
KEYNOTE-177 Study Design (NCT02563002)



- Dual-Primary endpoints: PFS per RECIST v1.1 per blinded independent central review (BICR) and OS
- Secondary endpoints: ORR per RECIST v1.1 by BICR, safety
- Tumor response assessed at week 9 and Q9W thereafter per RECIST v1.1 by BICR

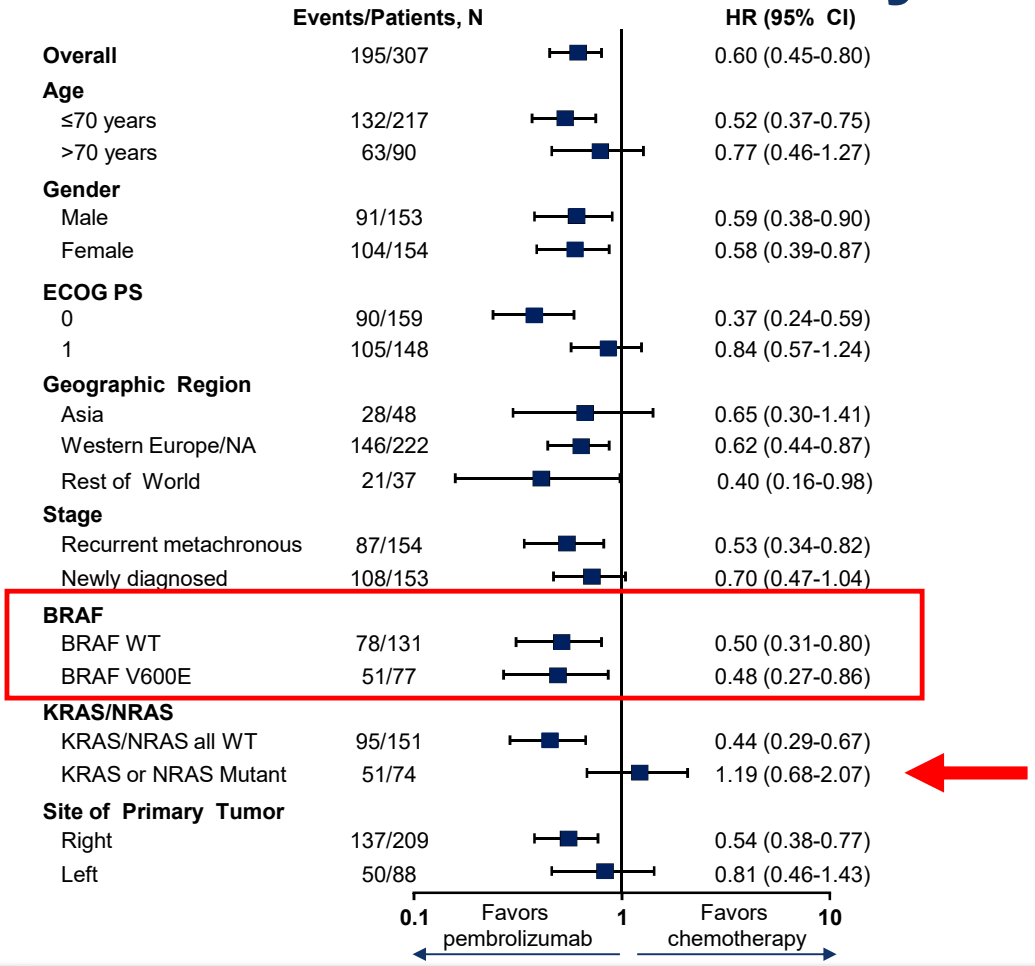
[a]Chosen before randomization; [b]Bevacizumab 5 mg/kg IV; [c]Cetuximab 400 mg/m2 over 2 hours then 250 mg/mg^2 IV over 1 hour weekly.
IHC: immunohistochemistry with hMLH1, hMSH2, hMSH6, PMS2; PCR: polymerase chain reaction; PFS, progression-free survival; OS: overall survival; ORR: overall response rate; Q9W: every 9 weeks.

Progression-Free Survival



Median study follow-up: 32.4 months (range, 24.0 – 48.3); PFS (time from randomization to first documented disease progression or death) assessed per RECIST v1.1 by BICR; Superiority of pembrolizumab vs chemotherapy for PFS was demonstrated at the pre-specified one-sided α = 0.0117; Data cut-off: 19Feb2020.

Progression-Free Survival in Key Subgroups



NA, North America; Data cut-off: 19Feb2020.

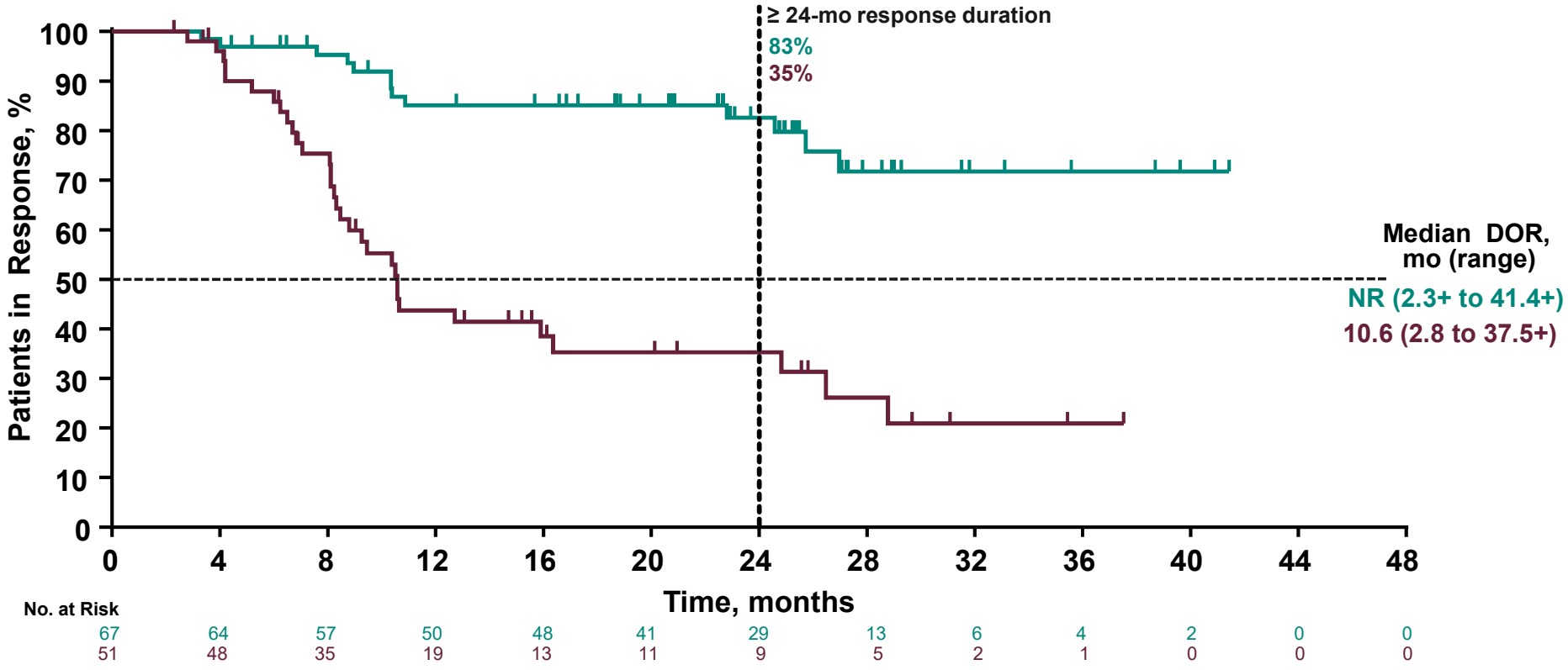
Antitumor Response

	Pembrolizumab N = 153	Chemotherapy N = 154
ORR, n (%)	**67 (43.8)**	**51 (33.1)**
Difference, estimate (95% CI)		10.7 (0.2, 21.3)
P-value		
Best Overall Response, n (%)		
Complete response	17 (11.1)	
Partial response	50 (32.7)	
Stable disease	32 (20.9)	
Disease control rate (CR+PR+SD)	99 (64.7)	
Progressive disease	45 (29.4)	19 (12.3)
Not evaluable	3 (2.0)	2 (1.3)
No assessment	6 (3.9)	17 (11.0)
Median time to response (range), mo	2.2 (1.8-18.8)	2.1 (1.7-24.9)

Correlation with:
- TMB
- MMR protein signature
- RAS mut
- Sidedness
- PD-L1 expression

Data cut-off: 19Feb2020; Response assessed per RECIST v1.1 by BICR.

Duration of Response



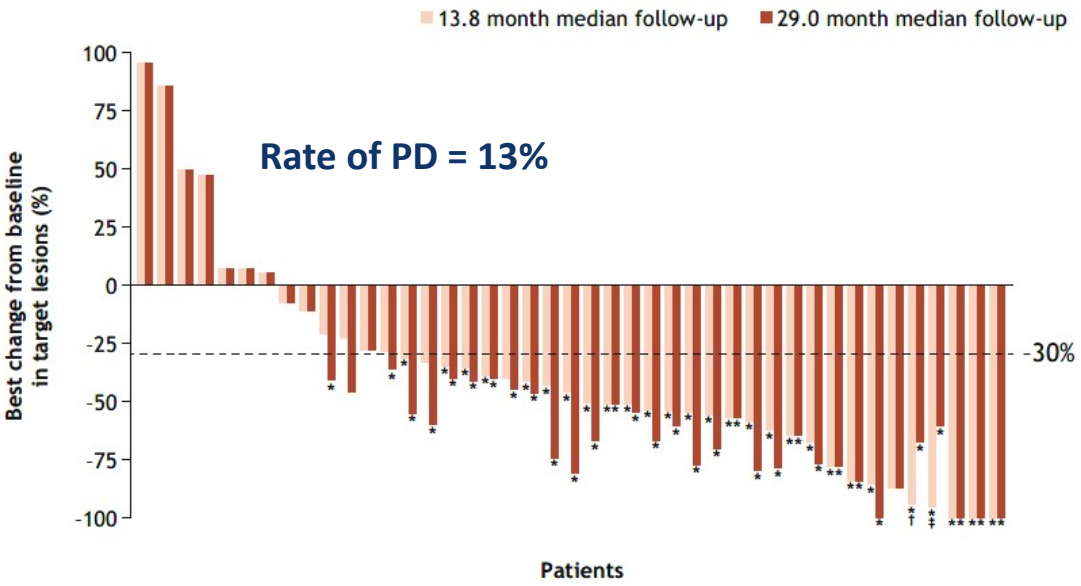
Duration of Response assessed per RECIST v1.1 by BICR; Data cut-off: 19Feb2020.

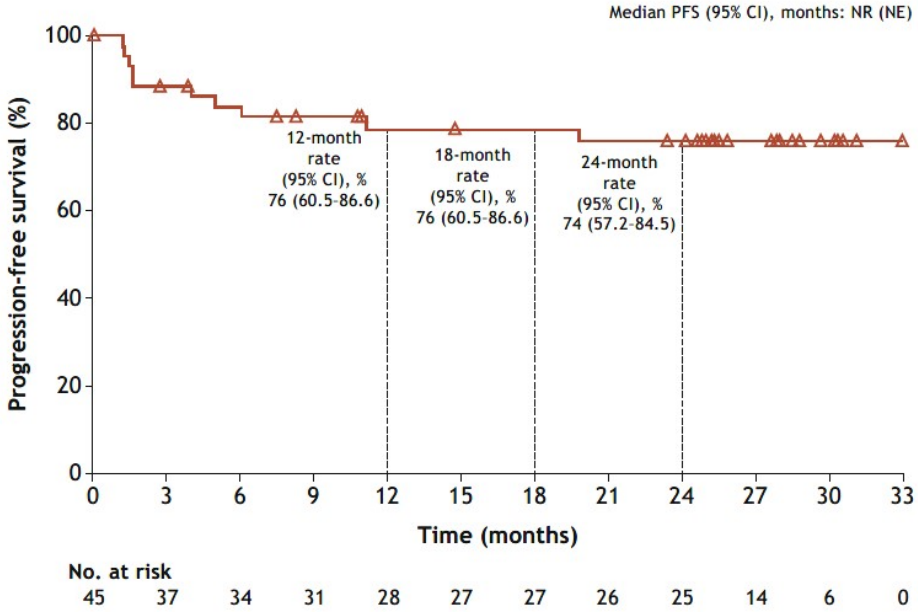
Adverse Events (AEs) in All Treated Patients

	Pembrolizumab N = 153		Chemotherapy N = 143	
All AEs	97%		99%	
Treatment-related	80%		99%	
Grade ≥3	**22%**		**66%**	
Death	0		1%[a]	
Discontinued	10%		6%	
Incidence ≥20%[b] in any group	**All**	**Grade ≥3**	**All**	**Grade ≥3**
Diarrhea	25%	2%	52%	10%
Fatigue	21%	2%	44%	9%
Nausea	12%	0	55%	2%
Decreased appetite	8%	0	34%	2%
Stomatitis	5%	0	30%	4%
Alopecia	3%	0	20%	0
Vomiting	3%	0	28%	4%
Decreased neutrophil count	1%	0	23%	17%
Neutropenia	0	0	21%	15%
Peripheral sensory neuropathy	0	0	20%	2%

[a]One grade 5 event of intestinal perforation; [b]Treatment-related adverse events; Data cut-off: 19Feb2020.

Front-line Immunotherapy Context: Nivolumab/Ipilimumab





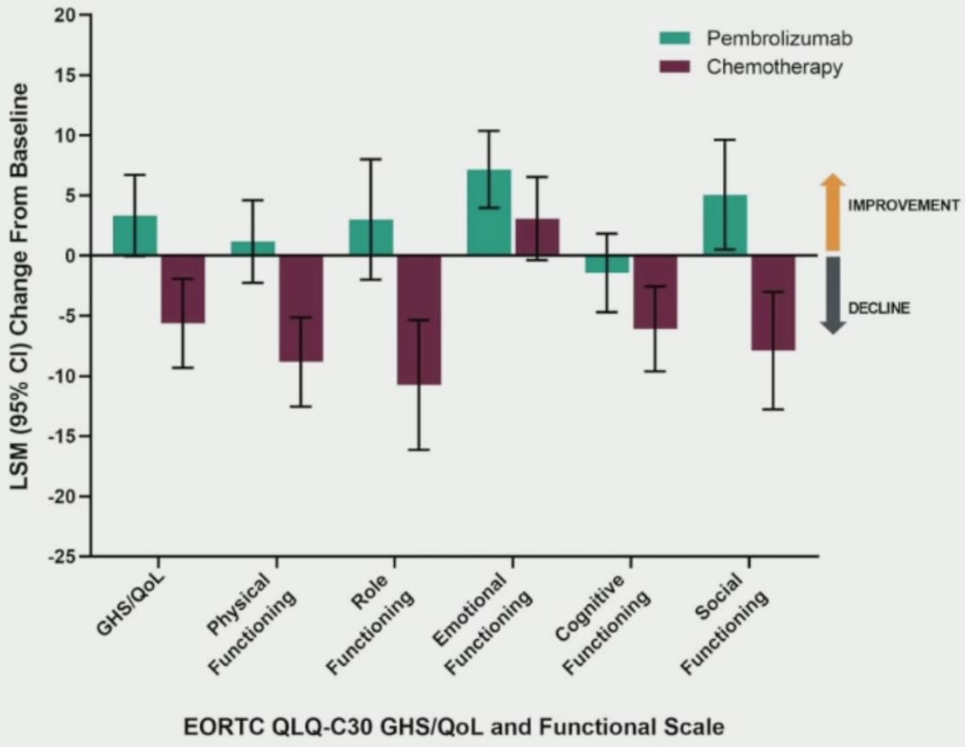
- **Major limitation: Small 45 patient single arm cohort**

Lenz et al., ASCO 2020

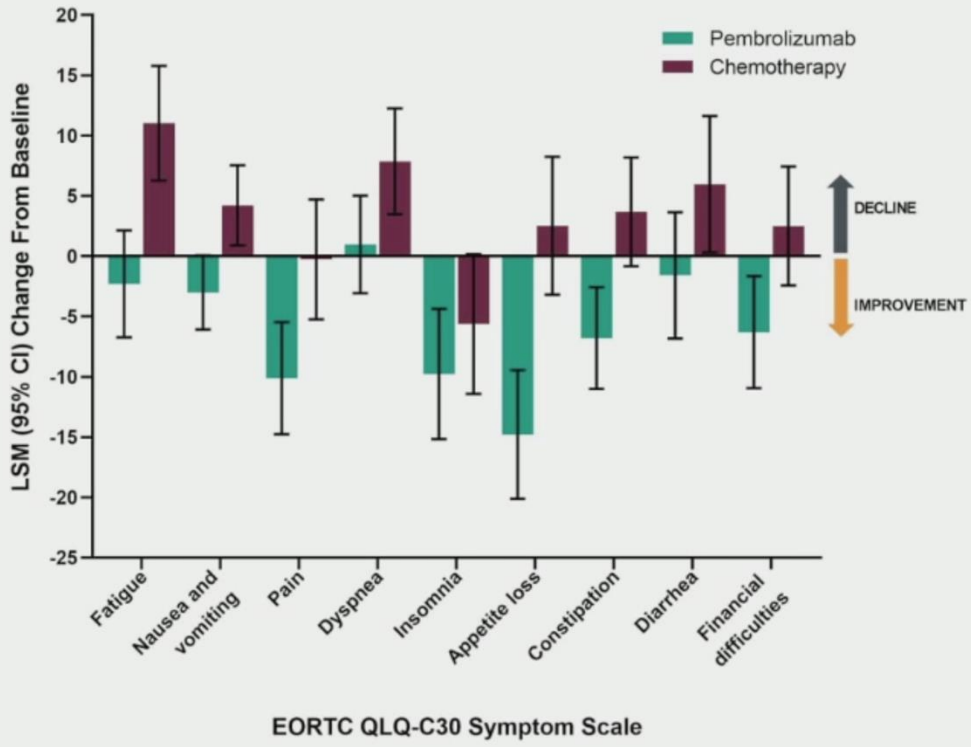
Change in Score From Baseline to Prespecified Week 18

EORTC QLQ-C30 GHS/QoL, Functional, and Symptom Scales/Items

GHS/QoL and Functional Scales[a]



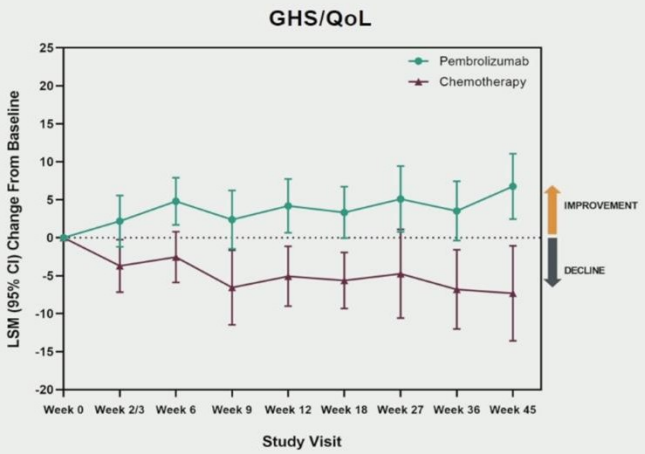
Symptom Scales/Items[a]



[a]Error bars indicate 95% CIs around the mean. Data cutoff: February 19, 2020.

Change in Score From Baseline Over Time[a]

EORTC QLQ-C30 GHS/QoL, Physical Functioning, Social Functioning, and Fatigue



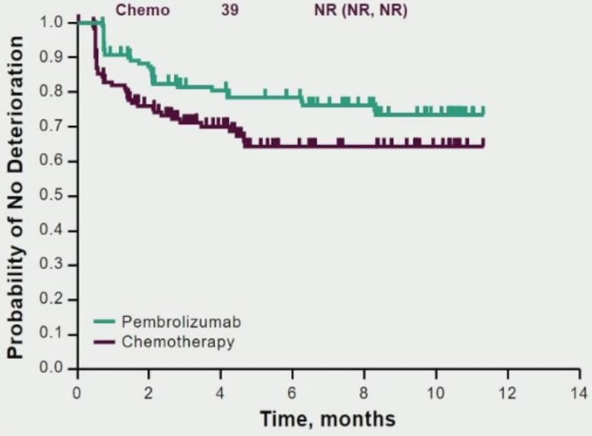
[a]Based on a constrained longitudinal data analysis model with PRO scores as the response vari
Data cutoff: February 19, 2020.

Time to Deterioration

EORTC QLQ-C30 GHS/QoL and Physical Functioning

GHS/QoL[a]

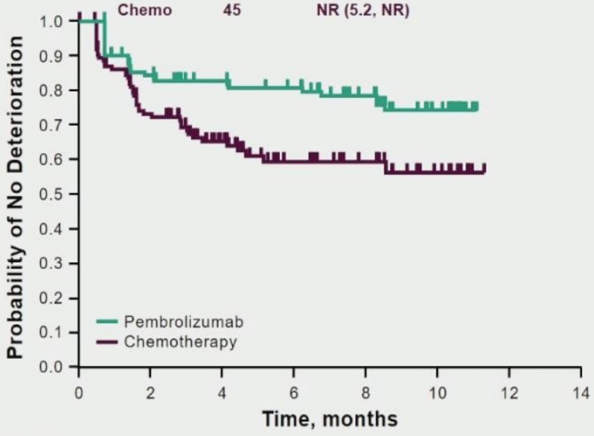
	Events, n	Median (95% CI), mo	HR (95% CI)	*P* Value[b]
Pembro	30	NR (NR, NR)	0.61 (0.38-0.98)	0.0195
Chemo	39	NR (NR, NR)		



No. at risk								
Pembrolizumab	141	104	82	71	58	42	0	0
Chemotherapy	131	85	57	32	25	10	0	0

Physical Functioning[a]

	Events, n	Median (95% CI), mo	HR (95% CI)	*P* Value[b]
Pembro	29	NR (NR, NR)	0.50 (0.32-0.81)	0.0016
Chemo	45	NR (5.2, NR)		

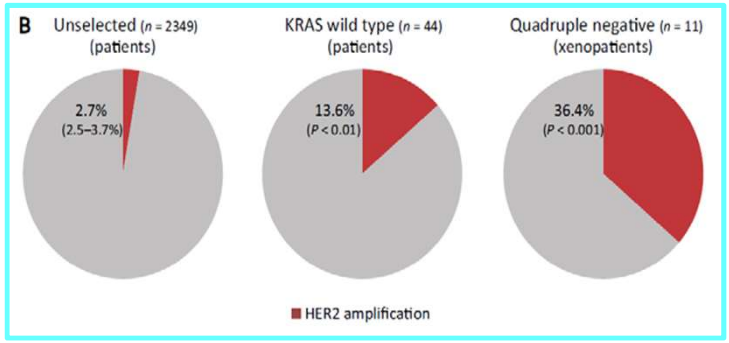


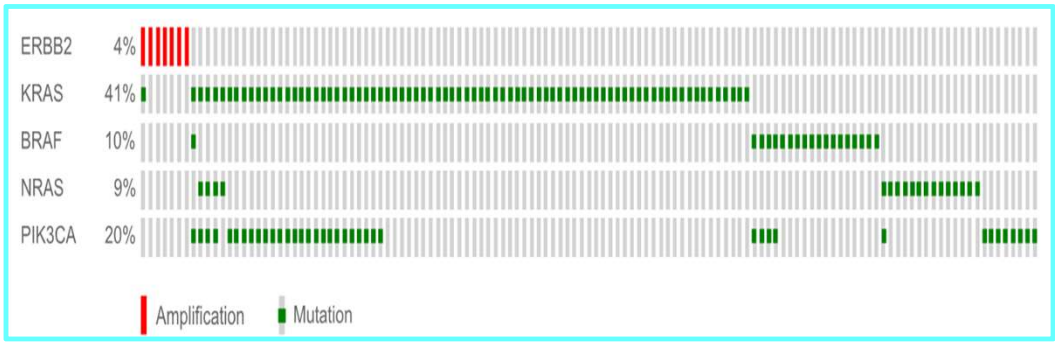
No. at risk								
Pembrolizumab	141	101	84	74	60	43	0	0
Chemotherapy	131	83	54	31	23	10	0	0

[a]Time to deterioration was defined as first onset of a ≥10-point change in score from baseline. [b]*P* values are 1-sided and nominal with no adjustment for multiplicity.
Data cutoff: February 19, 2020.

HER-2 Amplification in CRC

Study	N	Positive Rate	IHC 2+	IHC 3+	FISH Concordance
Nathanson et al. Int J Cancer '03	139	IHC: 5 (4%) FISH: 4 (3%)	2	3	K = 0.85
Ooi et al. Mod Pathol '04	244	IHC: 8 (3%) FISH: 8 (3%)	2	6	100%
Marx et al. Human Path '10	1439	IHC: 39 (3%) FISH: 36 (3%)	12	27	100%
Summary IHC	**1822**		**16**	**36**	**Good**





- 5.3% HER2 amplification seen in HERACLES Study (screened = 836)[1]
- HER2 amplification enriched in KRAS, NRAS, BRAF, and PIK3CA WT tumors[2]

[1]Siena et al. GI ASCO 2015 [2]Bertotti et al. Cancer Discovery 2011;1:508-523. [2]Kuwada et al. Int. J. Cancer: 109, 291–301 (2004)

HER-2 Amplification in CRC

- **Resistance marker for EGFR antibodies**
- **Defines patients who are candidates for HER-2 targeted therapy**

HERACLES: Trastuzumab + Lapatinib

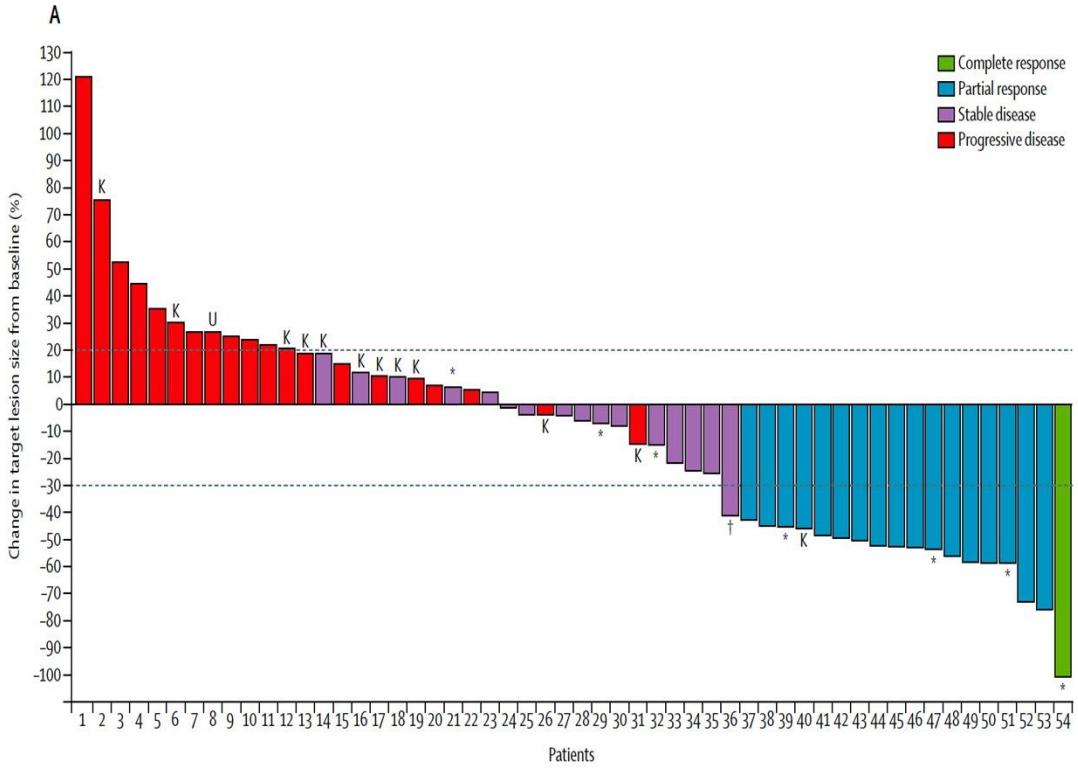
Best Response (RECIST 1:1 by Central Rev)	N	%
Responses (PR + CR)	**8**	**30**
Complete response	1	4
Partial response	7	26
Stable disease ≥4 mos	**8**	**30**
Stable disease <4 mos	4	15
Progressive disease	7	25
Total	27	100

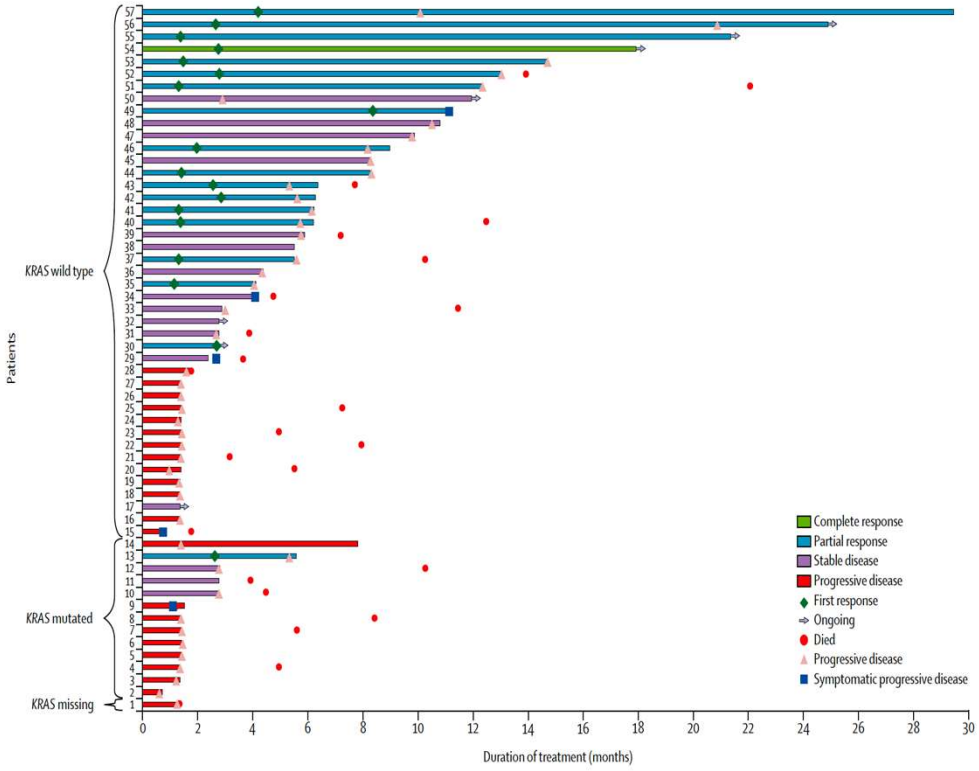
60% DCR

Primary endpoint met in advance with 8/27 objective responses (as per protocol, 6/27 needed to declare the study positive)

Sartore-Bianchi, et al. Lancet Oncol 2016

MyPathway: Trastuzumab + Pertuzumab in HER-2 pos CRC





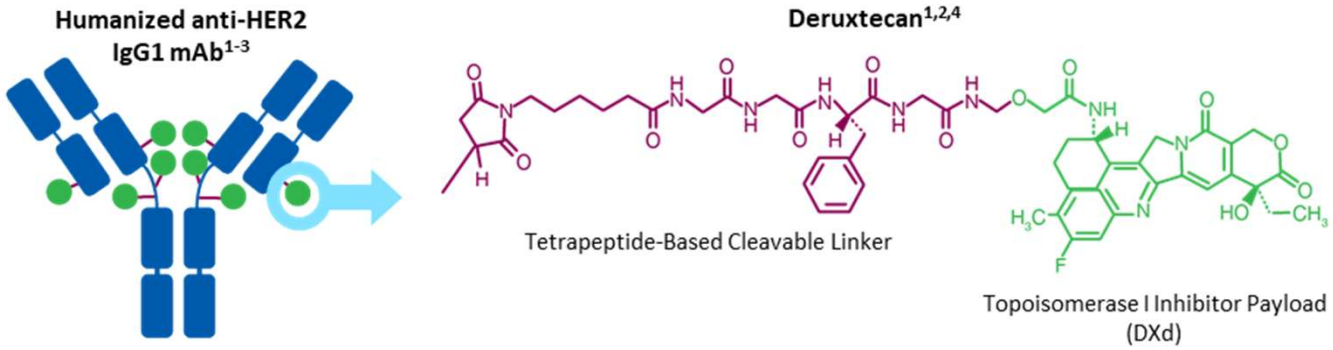
Response: 18/57 (32%)

Merik-Bernstam, et al., Lancet Oncol 2019

T-DXd is a Novel ADC Designed to Deliver an Antitumor Effect

T-DXd is an ADC with 3 components:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab
- A topoisomerase I inhibitor payload, an exatecan derivative
- A tetrapeptide-based cleavable linker



- Payload mechanism of action: topoisomerase I inhibitor
- High potency of payload
- High drug to antibody ratio ≈ 8
- Payload with short systemic half-life
- Stable linker-payload
- Tumor-selective cleavable linker
- Membrane-permeable payload

The clinical relevance of these features is under investigation.
ADC, antibody-drug conjugate.
1. Nakada T, et al. *Chem Pharm Bull* (Tokyo). 2019;67(3):173-185. 2. Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. 3. Trail PA, et al. *Pharmacol Ther*. 2018;181:126-142. 4. Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046.

PRESENTED BY: Prof Salvatore Siena; Università degli Studi di Milano, Milan, Italy; salvatore.siena@unimi.it

DESTINY-CRC01 Study Design

An open-label, multicenter, phase 2 study (NCT03384940)

Patients

- Unresectable and/or metastatic CRC
- HER2 expressing (central confirmation)
- RAS/BRAF wild type
- ≥2 prior regimens
- Prior anti-HER2 treatment was allowed
- Excluded patients with a history of or current/suspected interstitial lung disease

T-DXd 6.4 mg/kg q3w

Cohort A (n = 53)
HER2 Positive (IHC 3+ or IHC 2+/ISH+)

A futility monitoring was done after ≥20 patients in Cohort A had 12 weeks of follow-up to inform opening of Cohorts B and C

Cohort B (n = 7)
HER2 IHC 2+/ISH−

Cohort C (n = 18)
HER2 IHC 1+

Primary endpoint

- Confirmed ORR by independent central review (ICR) in Cohort A

Data cutoff: August 9, 2019

- 38.5% (30/78) remained on treatment
- 61.5% discontinued, primarily for progressive disease (41.0%) and clinical progression (9.0%)

PRESENTED BY: Prof Salvatore Siena; Università degli Studi di Milano, Milan, Italy; salvatore.siena@unimi.it

Efficacy

	HER2+ Cohort A (N = 53)
Confirmed ORR by ICR	**45.3% (n = 24)** (95% CI, 31.6%-59.6%)
CR	1.9% (n = 1)
PR	43.4% (n = 23)
SD	37.7% (n = 20)
PD	9.4% (n = 5)
Not evaluable	7.5% (n = 4)[a]
Disease control rate	83.0% (95% CI, 70.2%-91.9%)
Duration of response, median	Not reached (95% CI, 4.2 months-NE)

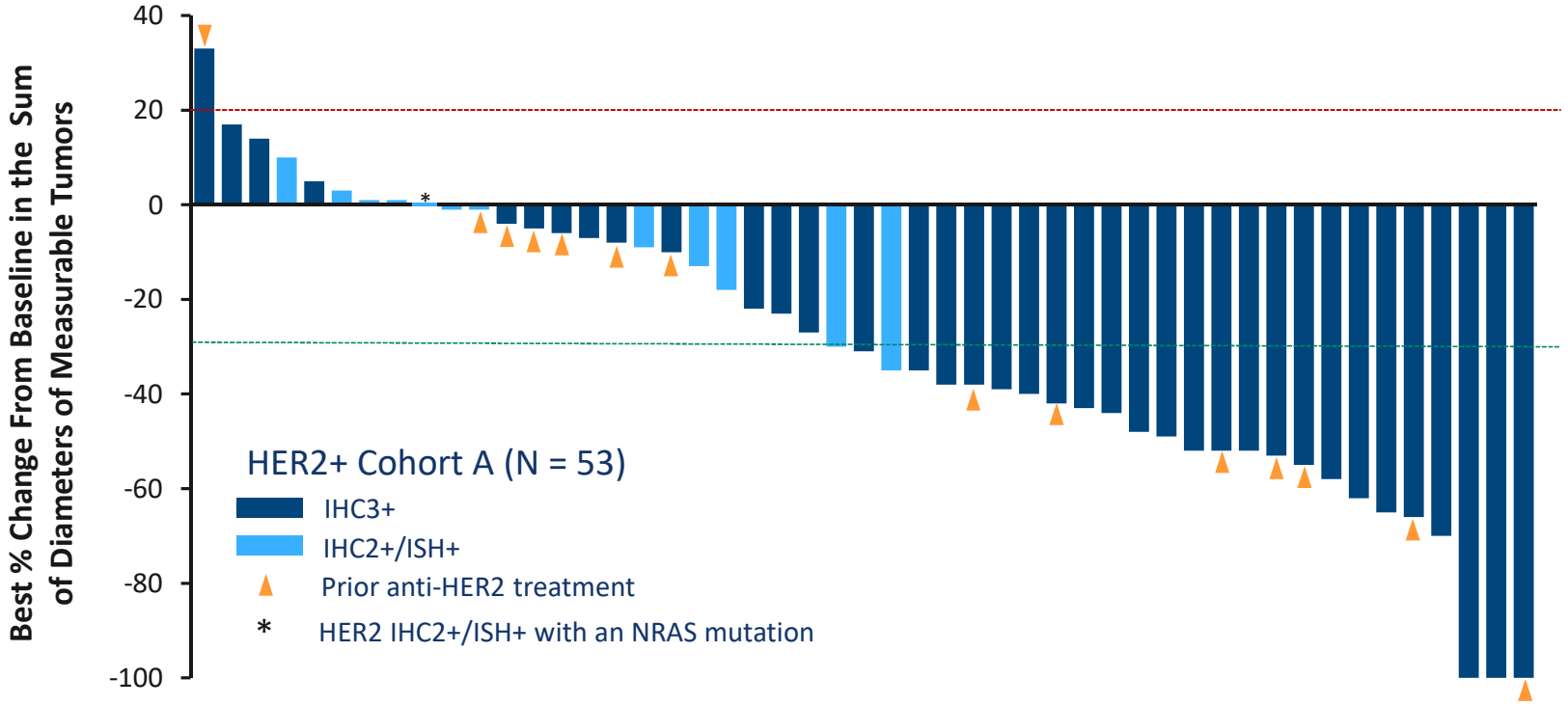
- There were no confirmed responses by ICR in Cohort B or C

[a] Patients were missing postbaseline scans.
Median study duration, 5.0 months (range, 0.6-10.5 months).

PRESENTED BY: Prof Salvatore Siena; Università degli Studi di Milano, Milan, Italy; salvatore.siena@unimi.it

DESTINY-CRC01

Best Change in Tumor Size



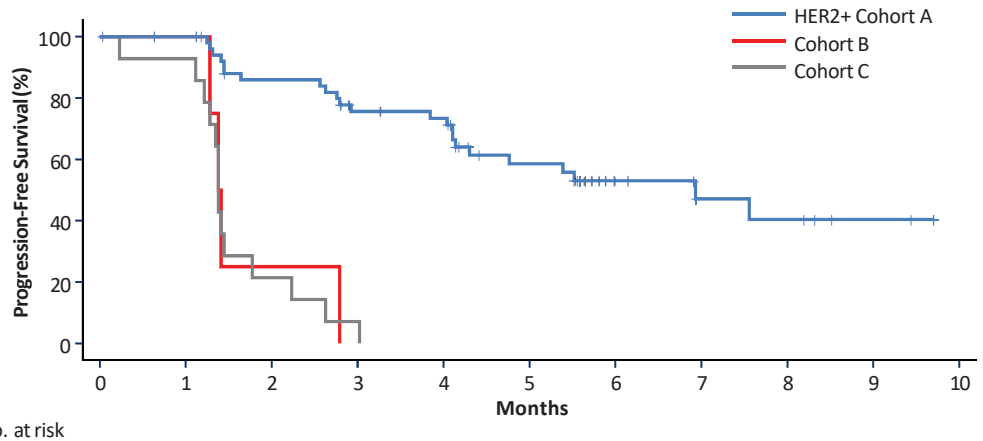
PRESENTED BY: Prof Salvatore Siena; Università degli Studi di Milano, Milan, Italy; salvatore.siena@unimi.it

DESTINY-CRC01

Progression-Free and Overall Survival

Progression-Free Survival

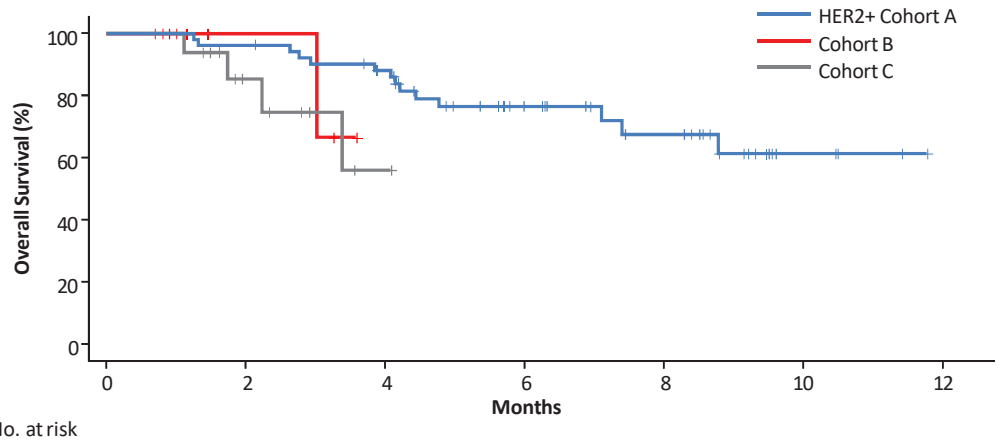
Median: 6.9 months in HER2+ Cohort A
(95% CI, 4.1-NE)



No. at risk											
Cohort A	53	50	42	35	33	21	11	7	6	2	0
Cohort B	7	6	1	0	0	0	0	0	0	0	0
Cohort C	18	13	3	1	0	0	0	0	0	0	0

Overall Survival

Median: Not reached in any cohort
(overall 95% CI, 0.74-NE)



No. at risk							
Cohort A	53	49	42	23	14	4	0
Cohort B	7	3	0	0	0	0	0
Cohort C	18	9	1	0	0	0	0

Per protocol, Cohorts B and C opened for enrollment after Cohort A and therefore have less follow-up at the time of data cutoff.
Median follow-up for OS was 4.1 month (range, 0.7-11.8 months).

PRESENTED BY: Prof Salvatore Siena; Università degli Studi di Milano, Milan, Italy; salvatore.siena@unimi.it

AEs of Special Interest: Interstitial Lung Disease

	All Patients (N = 78)					
Preferred Term, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial Lung Disease	0	2 (2.6)	1 (1.3)	0	2 (2.6)	5 (6.4)

Among the 5 total events:

- Median time to investigator-reported onset was 80 days (range, 22-132)
- 5 of 5 patients with grade ≥ 2 ILD received corticosteroids
- 2 patients recovered, 1 did not recover (later died due to disease progression), and 2 died
- In the 2 fatal cases, onset was from 40-126 days, both received steroids as part of treatment, and death occurred 6-18 days after diagnosis

Protocol recommendations: Monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected

Drug related; ILD was determined by an Independent ILD Adjudication Committee based on 44 preferred terms.
One additional grade 5 ILD case in Cohort B was reported after the data cutoff. This case was adjudicated after data cutoff as drug-related ILD.

PRESENTED BY: Prof Salvatore Siena; Università degli Studi di Milano, Milan, Italy; salvatore.siena@unimi.it

Rectal Cancer Management post-ASCO 2020

- Intensification
  - TNT – **RAPIDO, PRODIGE 23, OPRA**, NRG-GI002
  - Additional systemic agents – **PRODIGE 23**, NRG-GI002
  - RT escalation (dose, sensitizers) – NRG-GI002
- De-Intensification
  - Less surgery (LE, NOM) – **OPRA**
  - Less RT (omission, SCRT) – **RAPIDO**, PROSPECT
  - Less chemo (duration, intensity) – IDEA (SCOT)

Modified from Hallemeier, ASCO 2020

LARC: Personalized therapy

- **Tuning dials and switches to clinical scenario to achieve the optimal outcome**

PRESENTED AT: 2020 ASCO ANNUAL MEETING #ASCO20

PRESENTED BY: