Our Journey of ctDNA in Resected Colon Cancer

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Disclosure

- Consultant/Honorarium: Boston Scientific, AstraZeneca, Exelixis, Pfizer, Bristol Myers Squibb, Ipsen, Merus, BeOne
- Speaker: Ipsen, Exelixis
- Research funding (institution): Compass Therapeutics, IGM Biosciences, Genentech, Boston Scientific, Pfizer, Novartis, Incyte, Jazz Pharmaceuticals

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Disclosure!

- More questions have been generated than those have been answered

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CIRCULATE JAPAN

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- Observational study
- GALAXY utilized a personalized, tumor-informed ctDNA assay (Signatera). Blood samples collected before surgery and 4, 12, 24, 36, 48, 72 and 96 weeks after surgery.
- Patients with stage I-IV colon cancer (stage IV eligible for resection) were enrolled
- Median follow up time 11.4 months

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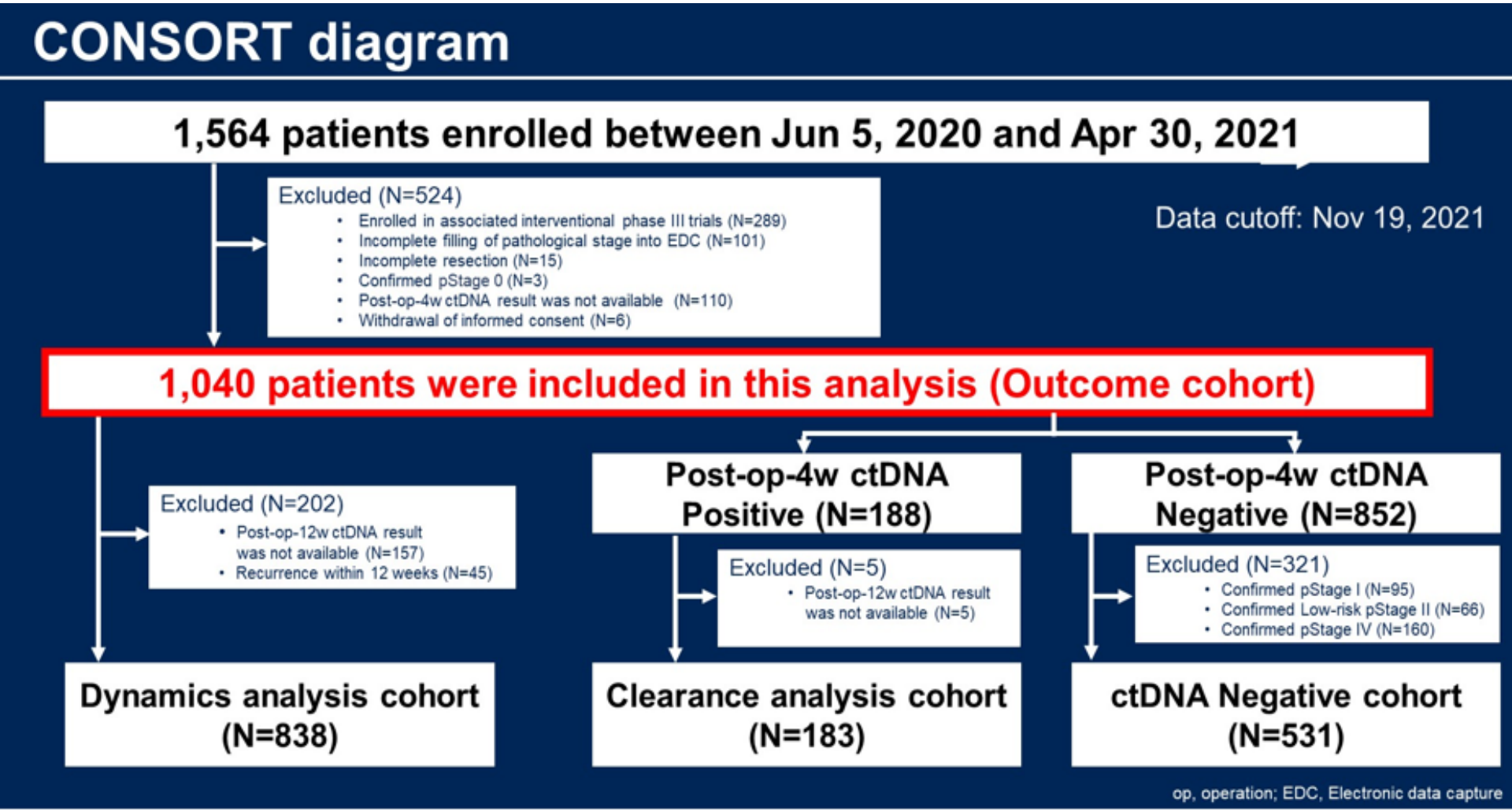
CONSORT diagram



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Patient characteristics in short outcome cohort

	Patients with post-op-4w negative ctDNA (N=852)		Patients with post-op-4w positive ctDNA (N=188)		P-value
Sex					
Male/Female	433/419	51%/49%	117/71	62%/38%	< 0.01
Performance status					
0/1	744/108	87%/13%	166/22	88%/12%	0.81
pStage[1]					
pStage I	95	11%	2	2% 1%	
pStage II	291	34%	24	8% 13%	
pStage III	306	36%	91	23% 48%	
pStage IV	160	19%	71	31% 38%	< 0.001
RAS/BRAF* mutational status Central assessment				*Excluded 5 cases with unknown *RAS/BRAF* status	
Double wt	420	49%	94	50%	0.87
RAS mt	351	41%	86	46%	0.25
BRAF V600E mt	78	9%	6	3%	< 0.01
MSI status** Central assessment				**Excluded 4 cases with undetectable MSI status	
MSI-High	100	12%	5	3%	< 0.001

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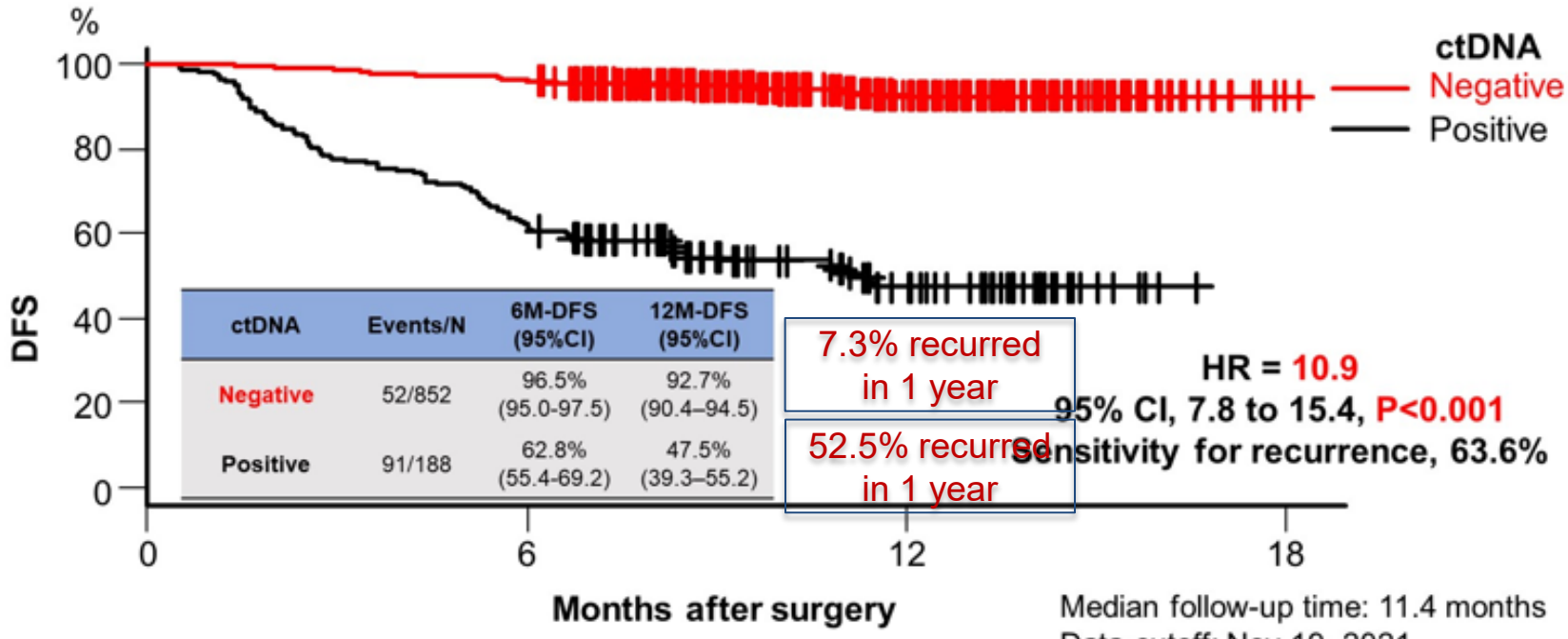
DFS by post-op-4w ctDNA status in overall population (pStage I-IV)



ctDNA	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
Negative	52/852	96.5% (95.0-97.5)	92.7% (90.4–94.5)
Positive	91/188	62.8% (55.4-69.2)	47.5% (39.3–55.2)

Number at risk

Negative	852	822	310	1
Positive	188	118	38	0

DFS, disease-free survival; HR, hazard ratio; CI, confidential interval DFS curve was estimated by the Kaplan-Meier method. HR and 95%CI were calculated by the Cox proportional hazard model.

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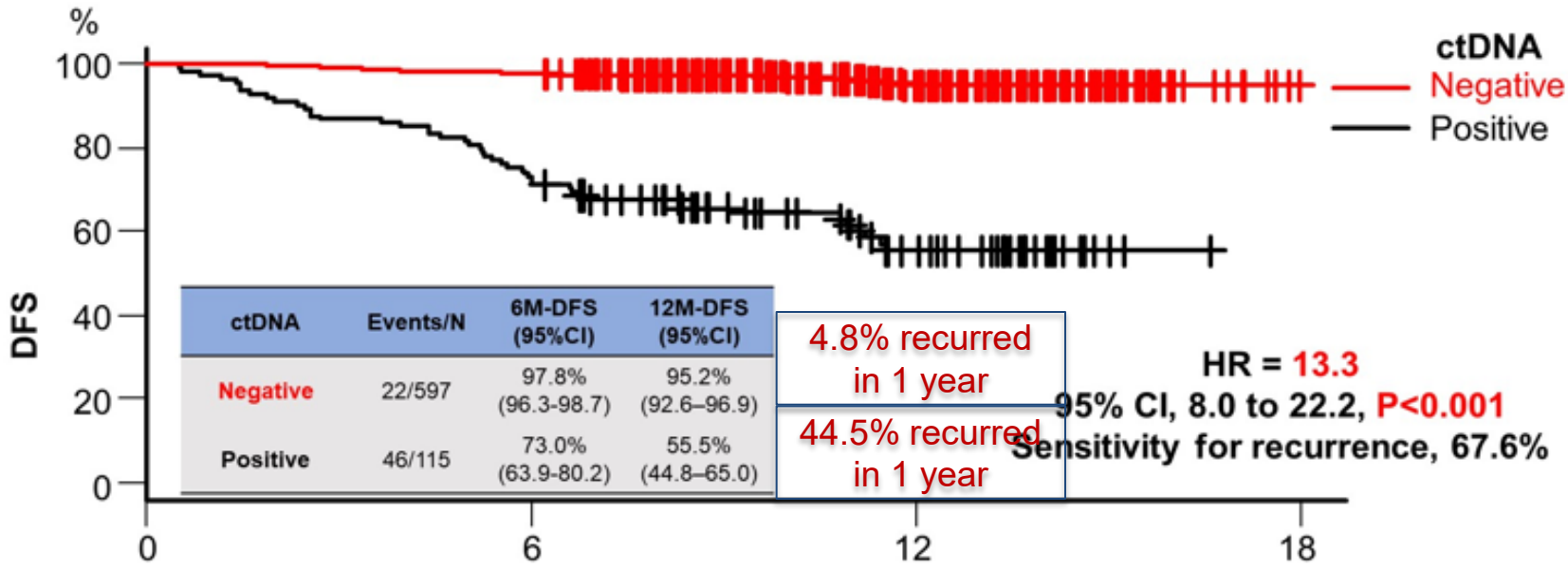
DFS by post-op-4w ctDNA status in overall population (pStage II-III)



ctDNA	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
Negative	22/597	97.8% (96.3-98.7)	95.2% (92.6–96.9)
Positive	46/115	73.0% (63.9-80.2)	55.5% (44.8–65.0)

Median follow-up time: 11.4 months
Data cutoff: Nov 19, 2021

Number at risk

Negative	597	584	223	0
Positive	115	84	31	0

DFS, disease-free survival; HR, hazard ratio; CI, confidential interval DFS curve was estimated by the Kaplan-Meier method. HR and 95%CI were calculated by the Cox proportional hazard model.

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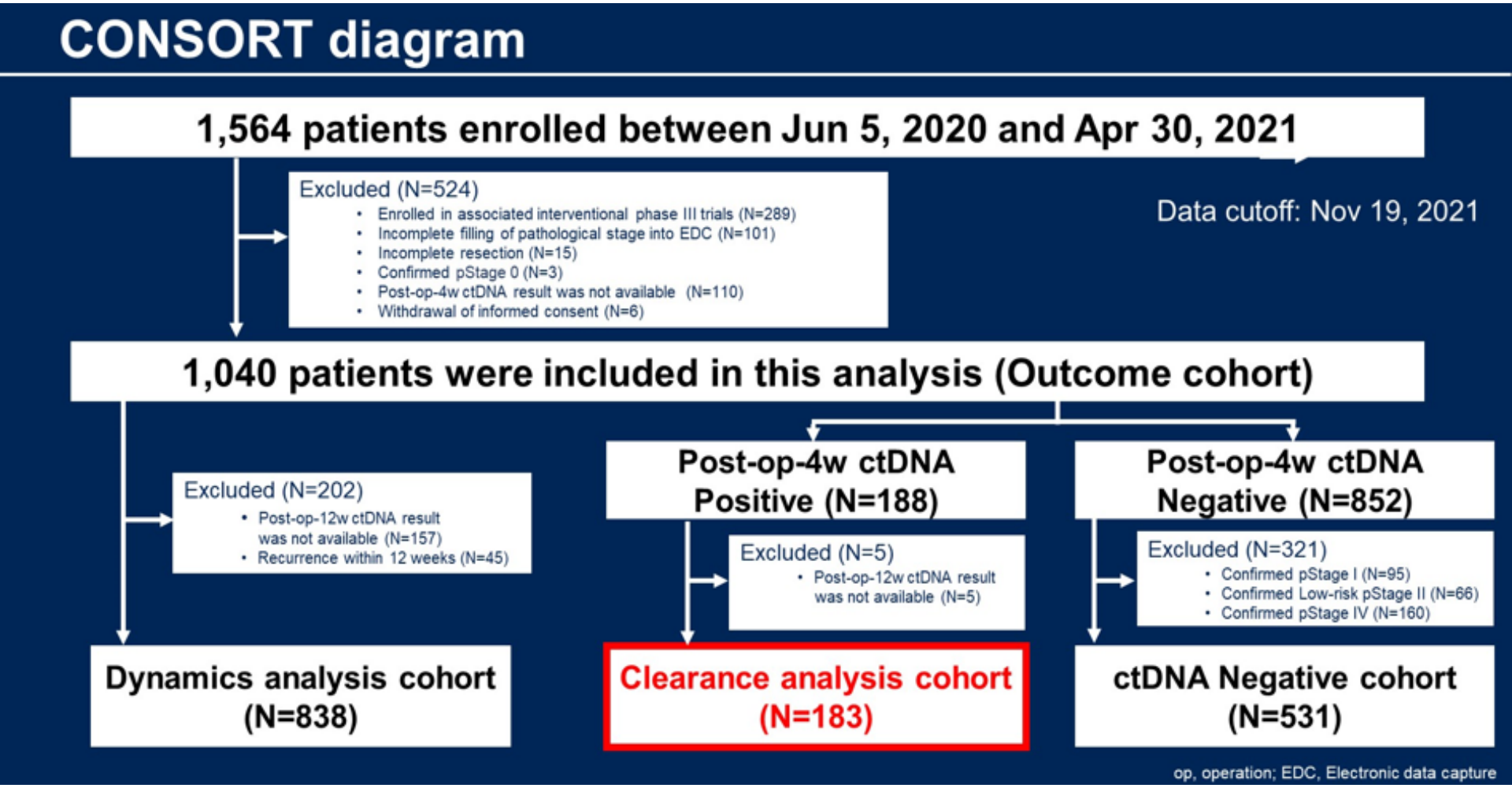
CONSORT diagram



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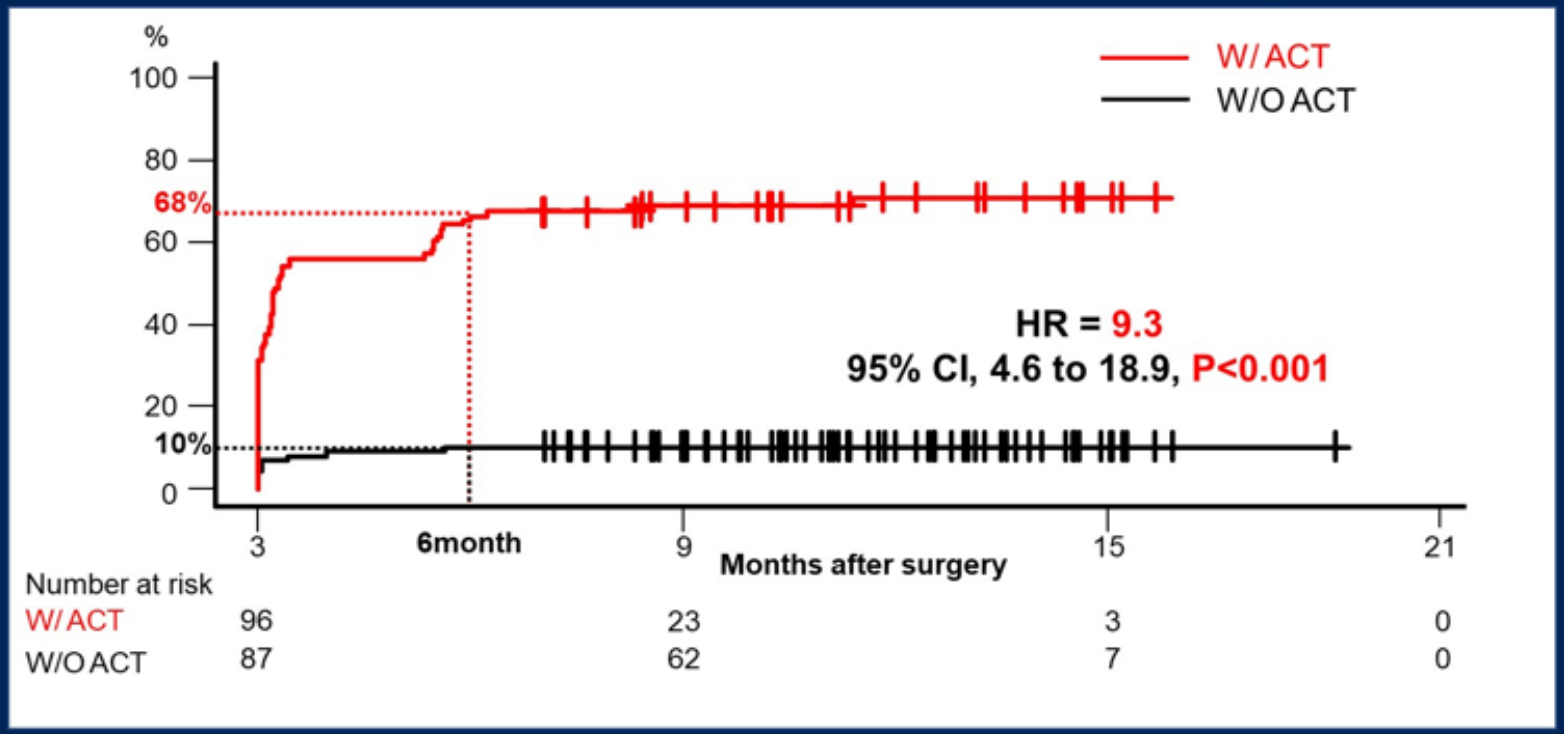
ctDNA clearance rate

Cumulative Incidence of ctDNA clearance pStage I-IV



Landmark analysis at the post-op-12w was performed. HR was adjusted by sex, performance status, and pStage.
ACT, adjuvant chemotherapy; HR, hazard ratio, cumulative curve was estimated by the gray`s test. HR and 95%CI were calculated by Fine-Gray sub-distribution hazard model.

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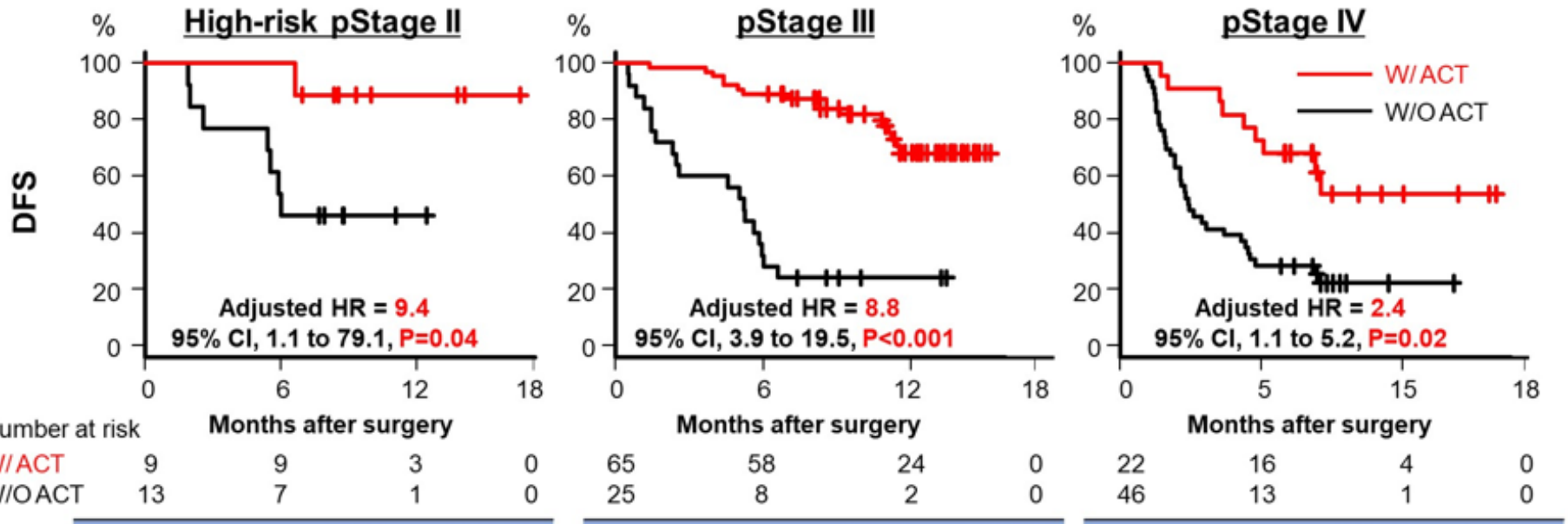
DFS by pStage in post-op-4w ctDNA positive population



	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
W/ ACT	1/9	100% (100–100)	88.9 (43.3–98.4)
W/O ACT	7/13	53.8% (24.8–76.0)	46.2 (19.2–69.6)

	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
W/ ACT	17/65	89.2% (78.7–94.7)	68.3 (53.4–79.2)
W/O ACT	19/25	32.0% (15.2–50.2)	24.0 (9.8–41.7)

	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
W/ ACT	9/22	72.7% (49.1–86.7)	53.7% (28.4–73.6)
W/O ACT	35/46	28.3% (16.2–41.6)	22.3% (11.2–35.7)

HR was adjusted by sex, and performance status. ACT, adjuvant chemotherapy; DFS, disease-free survival; HR, hazard ratio; CI, confidential interval. DFS curve was estimated by the Kaplan-Meier method. HR and 95%CI were calculated by the Cox proportional hazard model.

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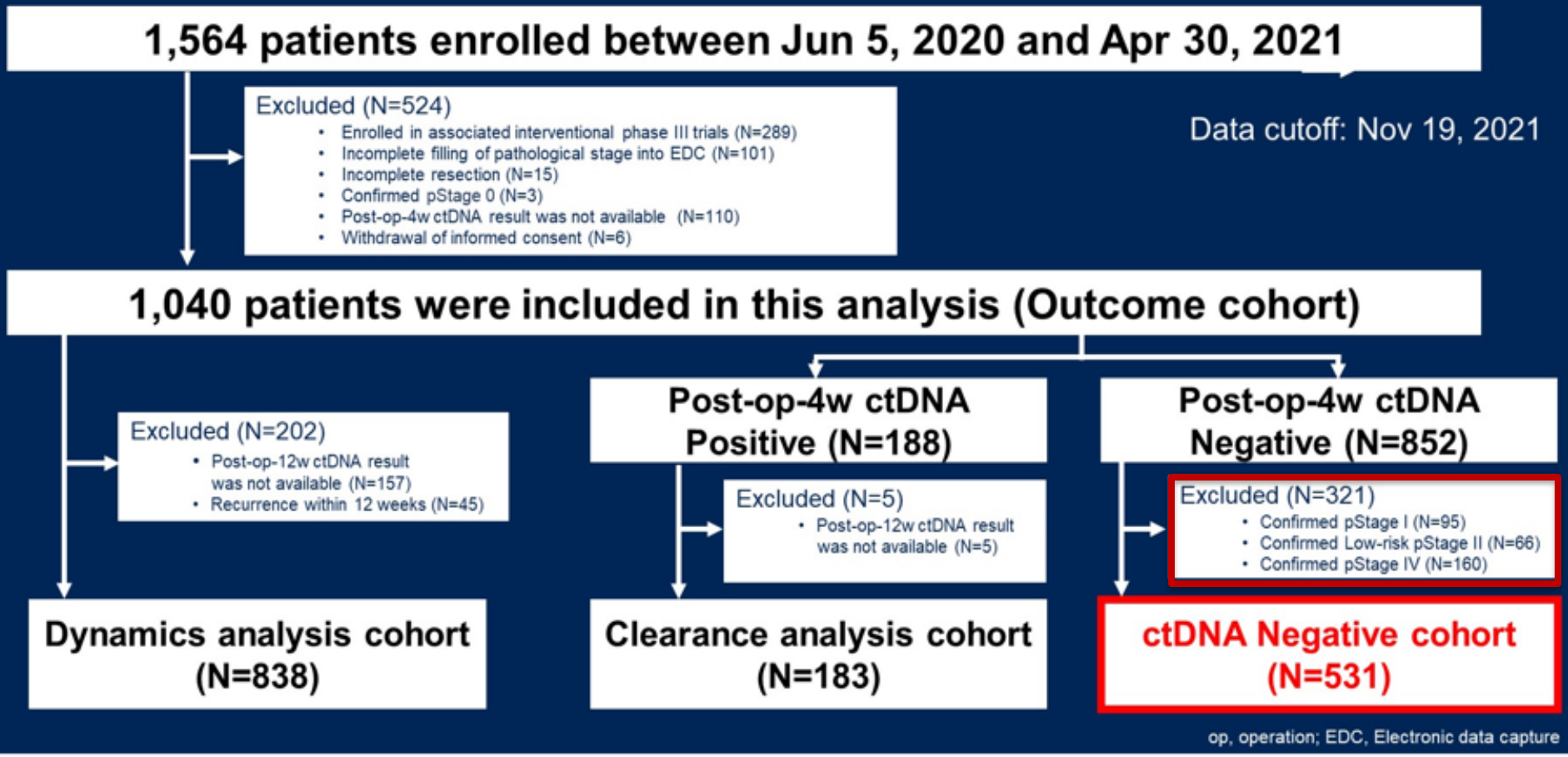
CONSORT diagram



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Patient characteristics in ctDNA negative cohort

	Patients W/ ACT (N=214)		Patients W/O ACT (N=317)		P
Sex					
Male/Female	106/108	50%/50%	159/158	50%/50%	0.93
Performance status					
0/1	196/18	92%/8%	258/59	81%/19%	**0.001**
pStage[1]					
pStage II (high-risk)	37	17%	188	59%	**<0.001**
pStage III	177	83%	129	41%	
ACT regimen: FP+Oxa / FP					
FP+Oxa / FP (High-risk pStage II)	24/13	65%/35%	-	-	-
FP+Oxa / FP (pStage III)	152/25	86%/14%	-	-	-

16% adjuvant chemo

58% adjuvant chemo

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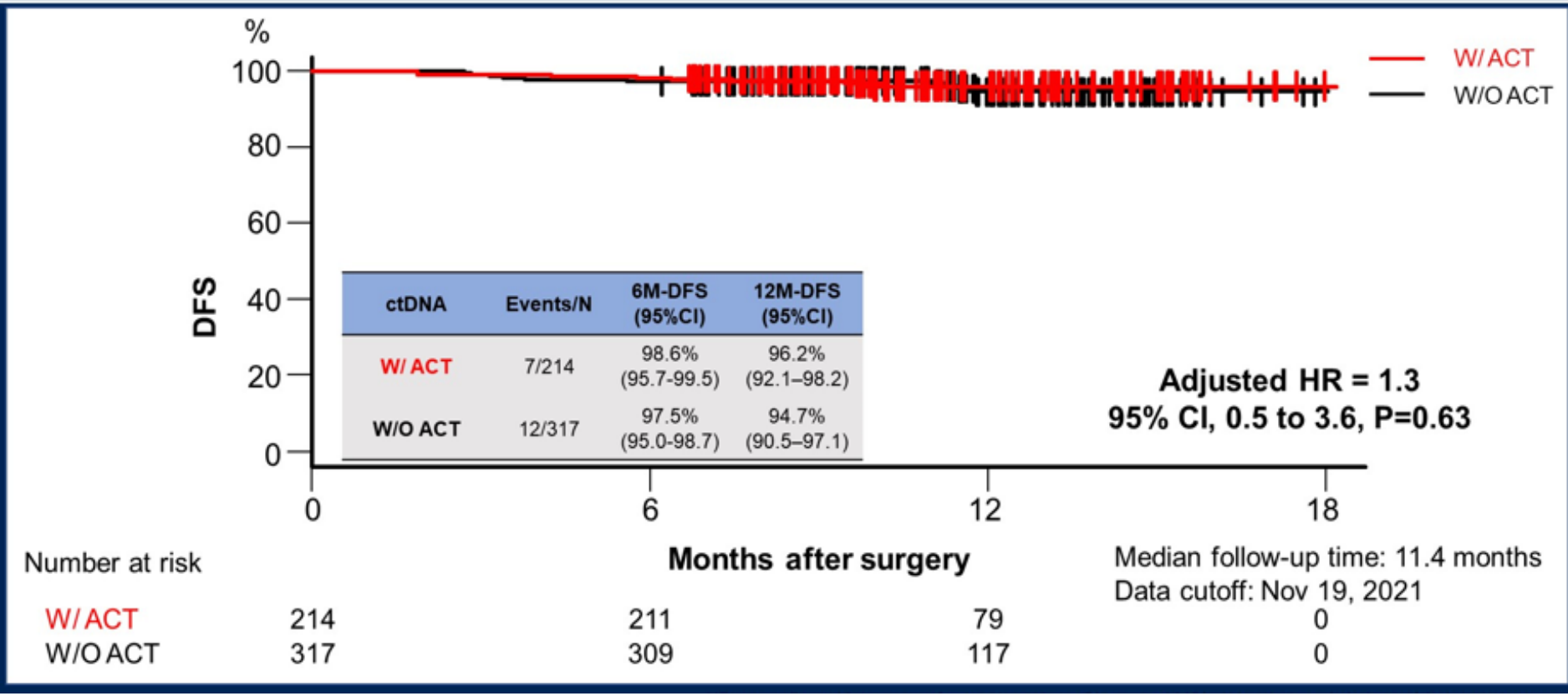
DFS by ACT in post-op-4w ctDNA negative population (High-risk pStage II-III)



ctDNA	Events/N	6M-DFS (95%CI)	12M-DFS (95%CI)
W/ ACT	7/214	98.6% (95.7-99.5)	96.2% (92.1–98.2)
W/O ACT	12/317	97.5% (95.0-98.7)	94.7% (90.5–97.1)

Median follow up less than 1 year

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ASCO Gastrointestinal Cancers Symposium

Circulating tumor DNA (ctDNA) dynamics in colorectal cancer (CRC) patients with molecular residual disease: Updated analysis from GALAXY study in the CIRCULATE-JAPAN

Presenting Author: Hiroki Yukami, MD, PhD

Co-authors: Yoshiaki Nakamura, Saori Mishima, Koji Ando, Hideaki Bando, Jun Watanabe, Keiji Hirata, Naoya Akazawa, Masataka Ikeda, Mitsuru Yokota, Kentaro Kato, George Laliotis, Vasily N. Aushev, Adham A. Jurdi, Minetta C. Liu, Daisuke Kotani, Eiji Oki, Ichiro Takemasa, Takeshi Kato, Takayuki Yoshino

- Updated 24-month DFS analysis in stage I-IV patients with radically resected CRC participating in the prospective, observational GALAXY study

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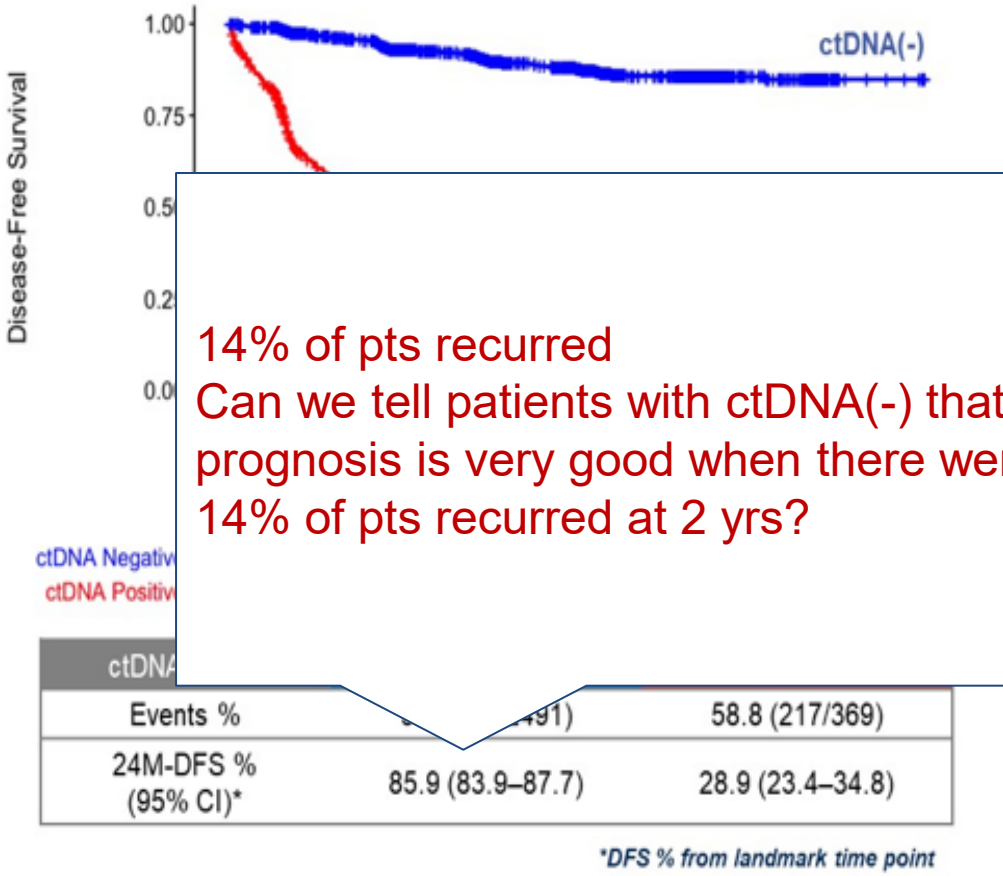
DFS according to status in the MRD window in all stage



14% of pts recurred
Can we tell patients with ctDNA(-) that the prognosis is very good when there were 14% of pts recurred at 2 yrs?

ctDNA		
Events %	[illegible]491)	58.8 (217/369)
24M-DFS % (95% CI)*	85.9 (83.9–87.7)	28.9 (23.4–34.8)

*DFS % from landmark time point

MRD window: 2-10 weeks post surgery, prior to start of any adjuvant therapy - Landmark 10 weeks post-surgery

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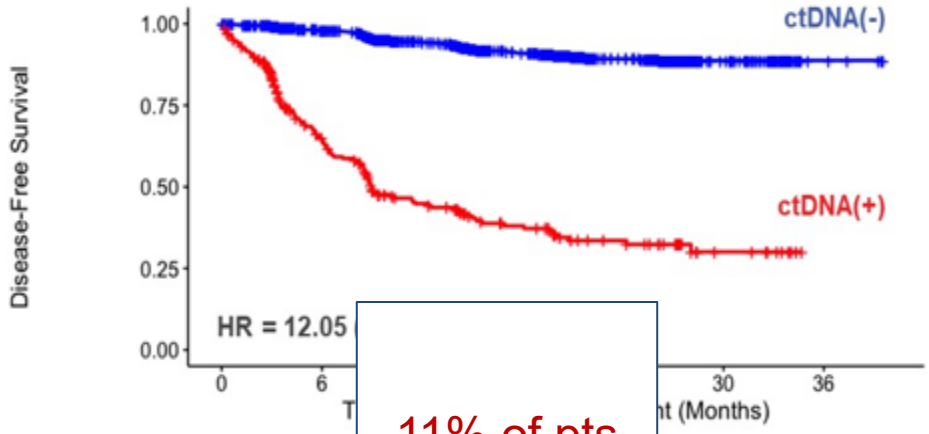
DFS according to status in the MRD window in pStage II/III



Dynamics	ctDNA Positive
Events %	56.5 (143/275)
24M-DFS % (95% CI)*	89.3 (87.2–91.1) 33.5 (26.5–40.7)

*DFS % from landmark time point

MRD window: 2-10 weeks post surgery, prior to start of any adjuvant therapy - Landmark 10 weeks post-surgery

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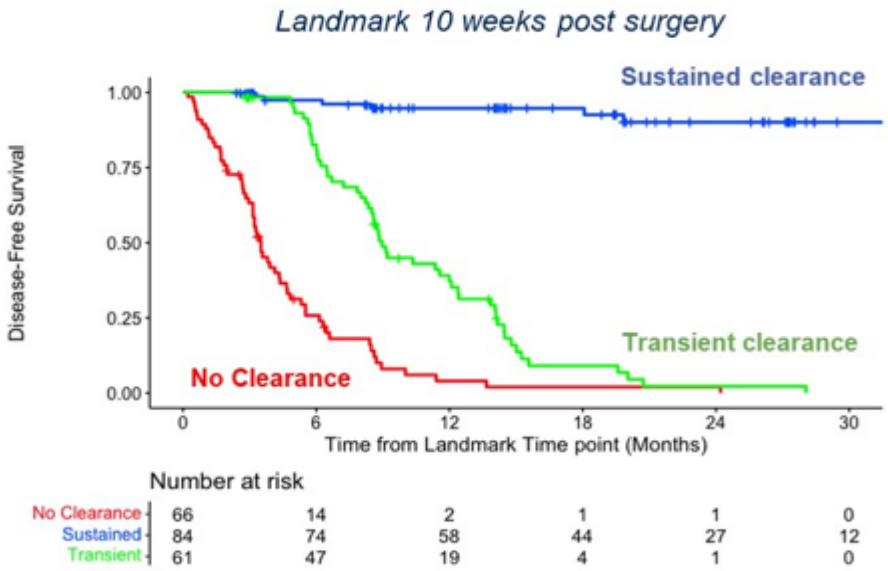
DFS according to ctDNA clearance in pts with ctDNA positive in the MRD window



ctDNA Clearance	Sustained Clearance	Transient Clearance	No Clearance
Events %	7.1 (6/84)	85.2 (52/61)	89.4 (59/66)
Median DFS months (95% CI)	NR	9 (8.5–12.4)	3.5 (3.2–4.7)
24M-DFS % (95% CI)*	90.1 (78.6–95.6)	2.3 (0.02–10.3)	2 (0.02–9.2)
HR	**Reference**	**25.13**	**87.08**
95% CI	Not applicable	10.57–59.73	36.14–209.84
P	Not applicable	<0.0001	<0.0001

**DFS % from landmark time point*

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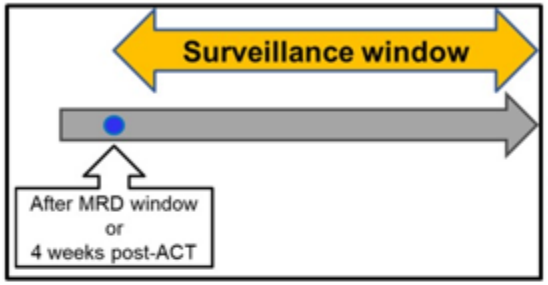
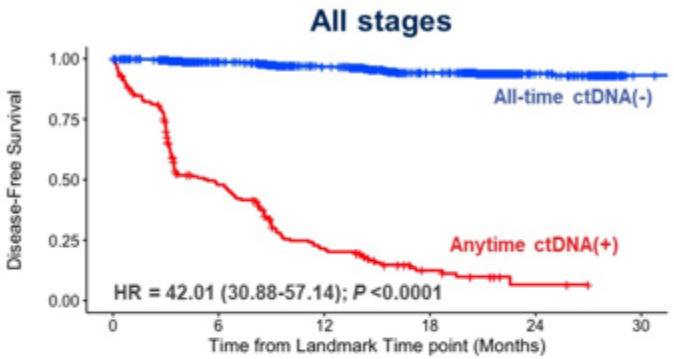
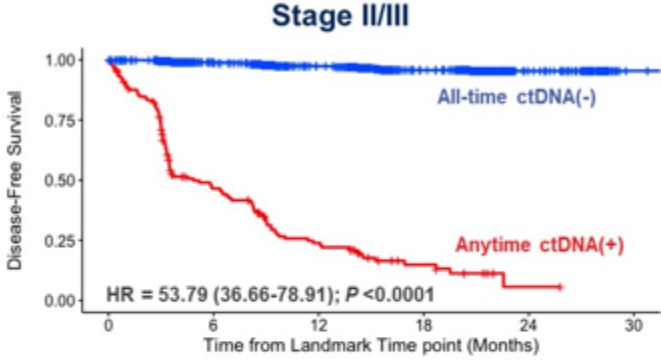
DFS according to ctDNA status in the Surveillance window







2,998 stage I-IV patients included in the outcome cohort

Excluded (N=1,212)
- No subsequent timepoints available (n=858)
- DFS event prior to the 8 months landmark timepoint (n=354)

Surveillance Window analysis cohort (n=1,786)

Number at risk

ctDNA Negative	1582	1211	885	432	125	8
ctDNA Positive	204	84	33	10	2	0

Number at risk

ctDNA Negative	1326	1022	737	355	97	5
ctDNA Positive	146	57	26	9	1	0

ctDNA status	All-time Negative	Anytime Positive
Events %	3.7 (58/1582)	77.5 (158/204)
24M-DFS % (95% CI)*	93.9 (92–95.4)	6.6 (2–14.9)

ctDNA status	All-time Negative	Anytime Positive
Events %	2.7 (36/1326)	75.3 (110/146)
24M-DFS % (95% CI)*	95.4 (93.5–96.8)	5.6 (0.8–18.3)

*DFS % from landmark time point

I know

- *Surveillance window starts from 4 weeks post-ACT or at the end of MRD window [illegible] no ACT, until the last follow up or relapse.*
- *Landmark 8 months post-surgery (2 months for ACT initiation + 6 months of ACT d[illegible]tion)*

ctDNA-positive in the surveillance window is predictive of inferior DFS

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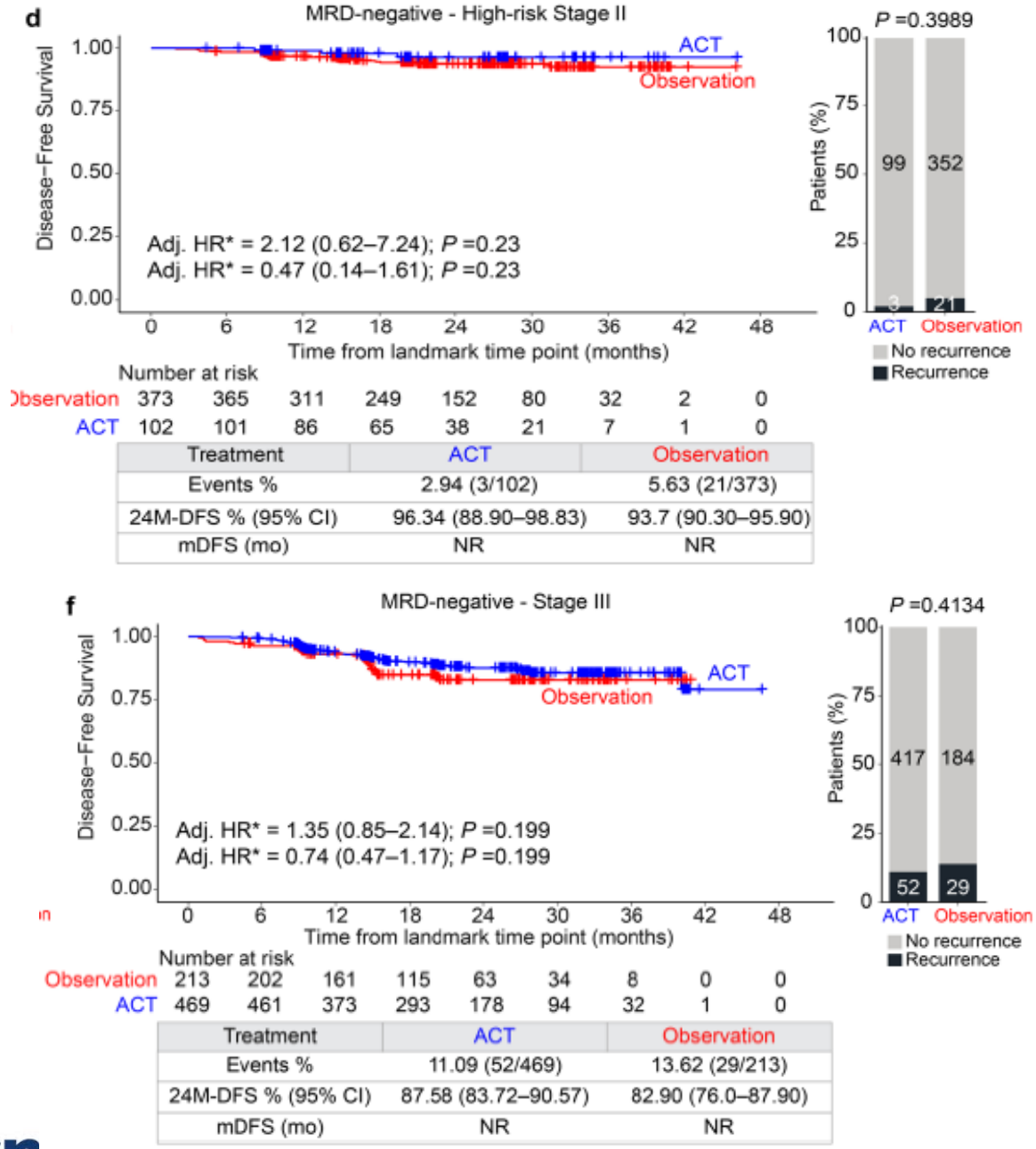

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Nakamura Y, et al. Nature Medicine Vol 30, 2024: 3272-3283

Messages conveyed (to me)

- Post-op ctDNA (-) is great.

  - Clinical risk?

  - lack of benefit from adjuvant chemo in high-risk stage II/III pts with post-op ctDNA (-) with median follow up of 2 years – observational study, await longer follow up

- Post-op ctDNA (+) predicts poor prognosis. But, if adjuvant chemo can clear ctDNA, prognosis does not seem to be that bad.
- Lack of randomization

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DYNAMIC II

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2022 ASCO ANNUAL MEETING

Adjuvant Chemotherapy Guided by Circulating Tumor DNA Analysis in Stage II Colon Cancer

The Randomized DYNAMIC Trial

Stage II Colon Cancer

- R0 resection
- ECOG 0 – 2
- Staging CT within 8 weeks
- Provision of adequate tumor tissue within 4 weeks post-op
- No synchronous colorectal cancer

Plasma Collections
Week 4 + 7 post-op

ctDNA-Guided Management

- **ctDNA-Positive → Adjuvant Chemo** (oxaliplatin-based or single agent FP)
- **ctDNA-Negative → Observation**

ctDNA-Positive = Positive result at week 4 and/or 7

Standard Management

Adjuvant treatment decisions based on conventional clinico-pathologic criteria

Endpoints

Primary
- RFS rate at 2 years

Key Secondary
- Proportion receiving adjuvant chemo

Secondary
- RFS by ctDNA status for ctDNA-guided arm
- TTR
- OS

Stratification Factors
- T stage (T3 vs T4)
- Type of participating center (metropolitan vs regional)

Surveillance:
- CEA → 3-monthly for 24M, then 6-monthly for 36M
- CT C/A/P → 6-monthly for 24M, then at 36M

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Background: Stage II Colon Cancer

- Benefit of adjuvant chemotherapy controversial in average-risk stage II colon cancer
- Adjuvant chemo generally considered for pts with high-risk features: T4, <12 LN removed, perforation/obstruction, LVI, PNI, poorly differentiated history.

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Adjuvant Treatment Delivery

Treatment Information	ctDNA-Guided N = 294	Standard Management N = 147	P-value
Adjuvant Chemotherapy received, n	45 **(15%)**	41 **(28%)**	0.0017
Chemotherapy regimen received, n Oxaliplatin-based doublet Single agent fluoropyrimidine	 28/45 **(62%)** 17/45 **(38%)**	 4/41 **(10%)** 37/41 **(90%)**	 <.0001
Time from surgery to commencing chemotherapy, median (IQR), days	83 (76, 89)	53 (49, 61)	<.0001
Treatment duration, median (IQR), weeks	24 (19, 24)	24 (21, 24)	0.9318
Completed planned treatment, n	38 (85%)	32 (78%)	0.7036
Percentage of full dose delivered, median (IQR)	78 (56, 100)	84 (64, 100)	0.6194

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Statistical Considerations

- **Primary Analysis Population: Intention-To-Treat (ITT)**
  - Eligible patients who were randomized and had both blood draws (week 4 and 7)
  - Primary analysis when the last patient reached a minimum follow-up of 2 years
- **Statistics / Sample Size**
  - 80% power, $\alpha = 0.05$, 10% drop-out rate → 450 patients needed to show non-inferiority of 2-year RFS rate with a margin of 8.5%
  - Non-inferiority accepted if lower bound of 95% CI of difference lies above -8.5%
  - Key secondary endpoint: reduction in proportion treated with adjuvant chemotherapy from 30% to 10% (> 99% power, $\alpha = 0.05$)

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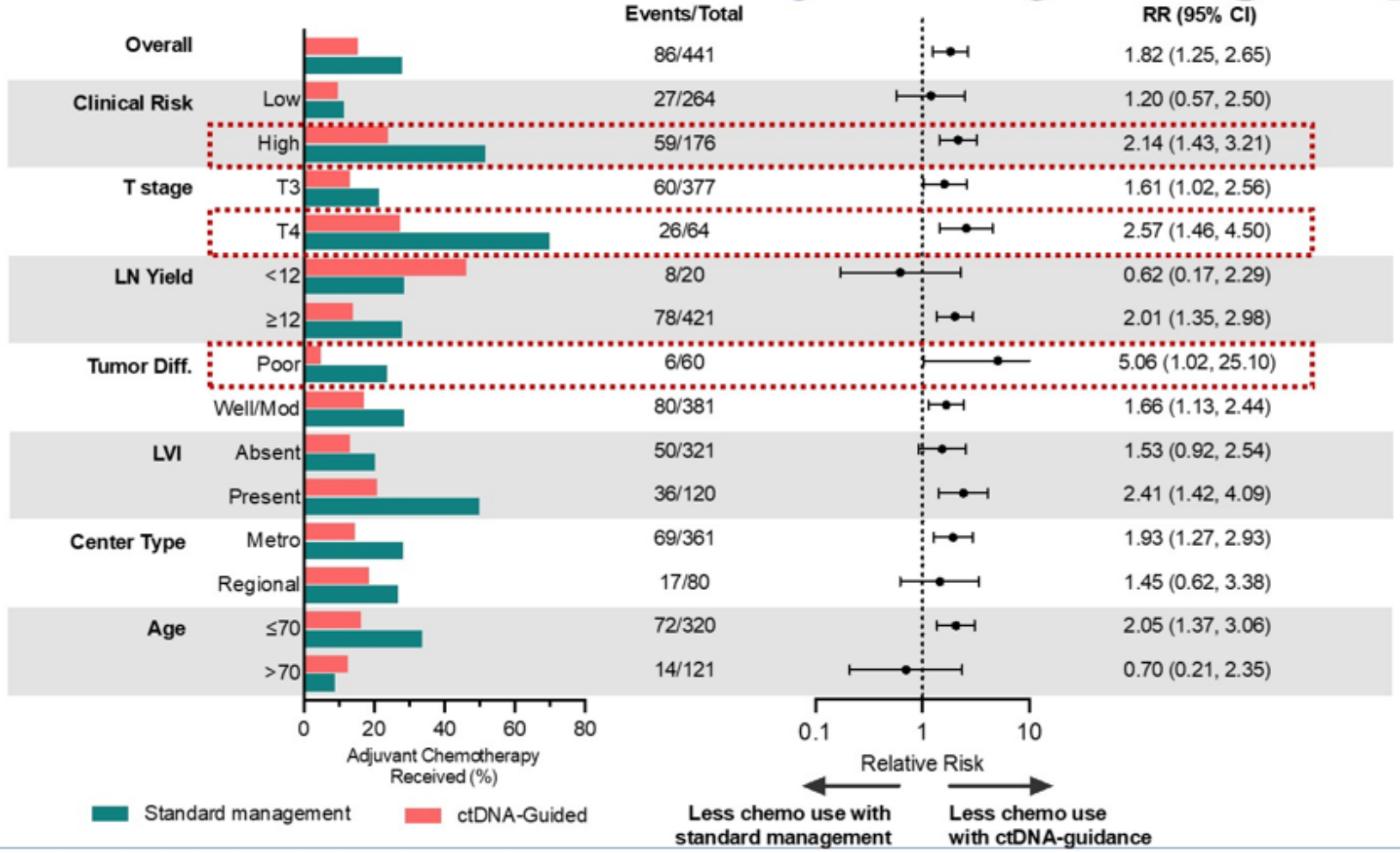
Adjuvant Treatment Delivery in Key Subgroups



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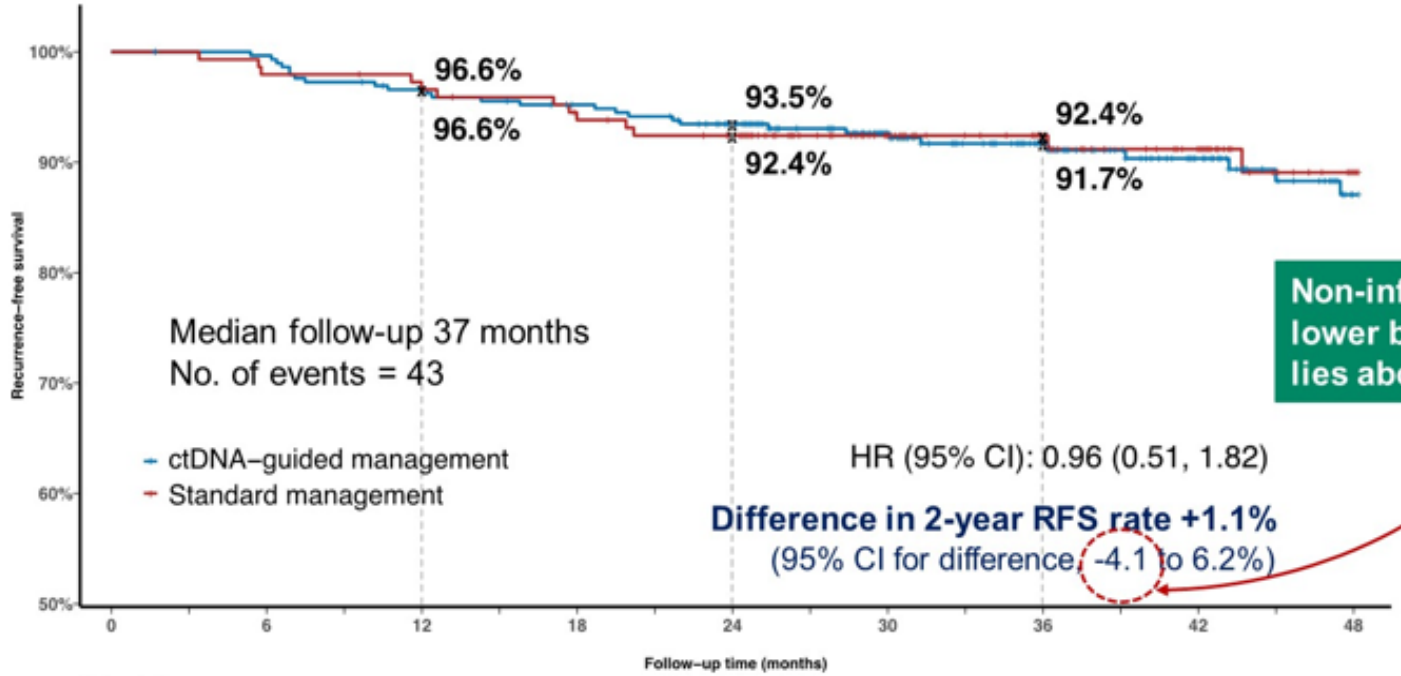
Recurrence-Free Survival



Numbers at risk

ctDNA-guided	294	292	281	273	259	207	155	109	64
Standard	147	144	142	136	128	97	78	57	33

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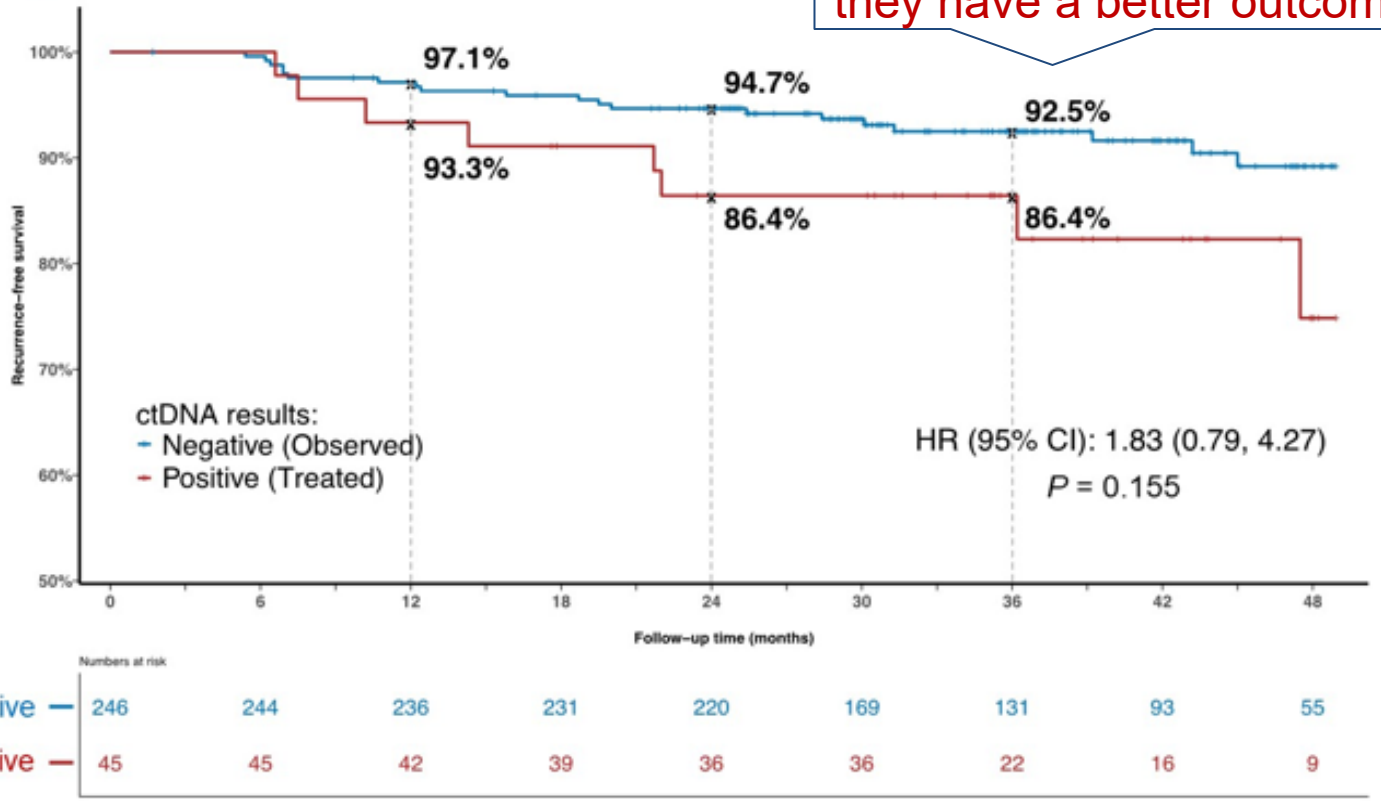
Recurrence-Free Survival: ctDN

ctDNA Negative vs Positive

7.5 % of pts recurred
How many of these pts had high risk features? If these pts w high-risk features received chemo, would they have a better outcome?



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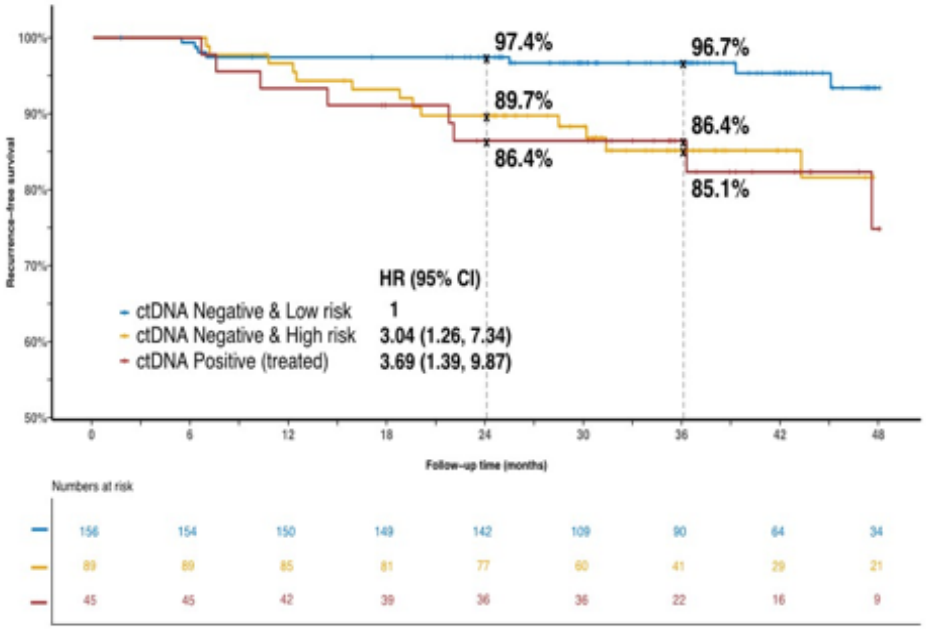
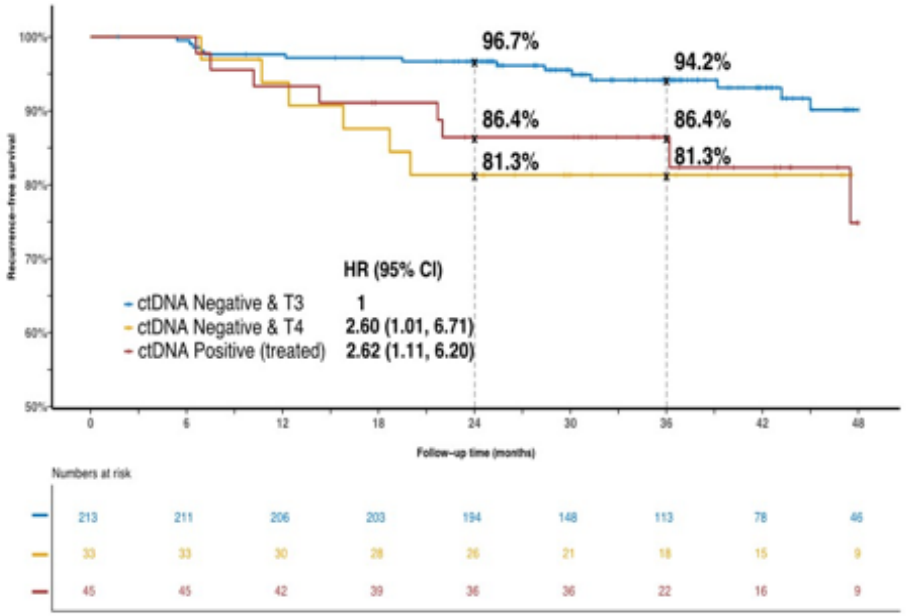
For high-risk pts, ctDNA (-), 14% recurred

For T4 pts, ctDNA (-), 19% recurred





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My interpretation

- In ctDNA-guided management arm, adjuvant chemo was started beyond 8 weeks after surgery.
- In ctDNA-guided management arm, even in pts with neg ctDNA, if they have high risk features, 14-19% of them still recurred. These pts did not receive adjuvant chemo. Would adjuvant chemo change this outcome?
- Ultimately, the answer I want to know is, if pts are ctDNA neg, is it safe to skip chemo even if these are clinically high-risk pts? – not addressed by this study design.

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NRG ONCOLOGY

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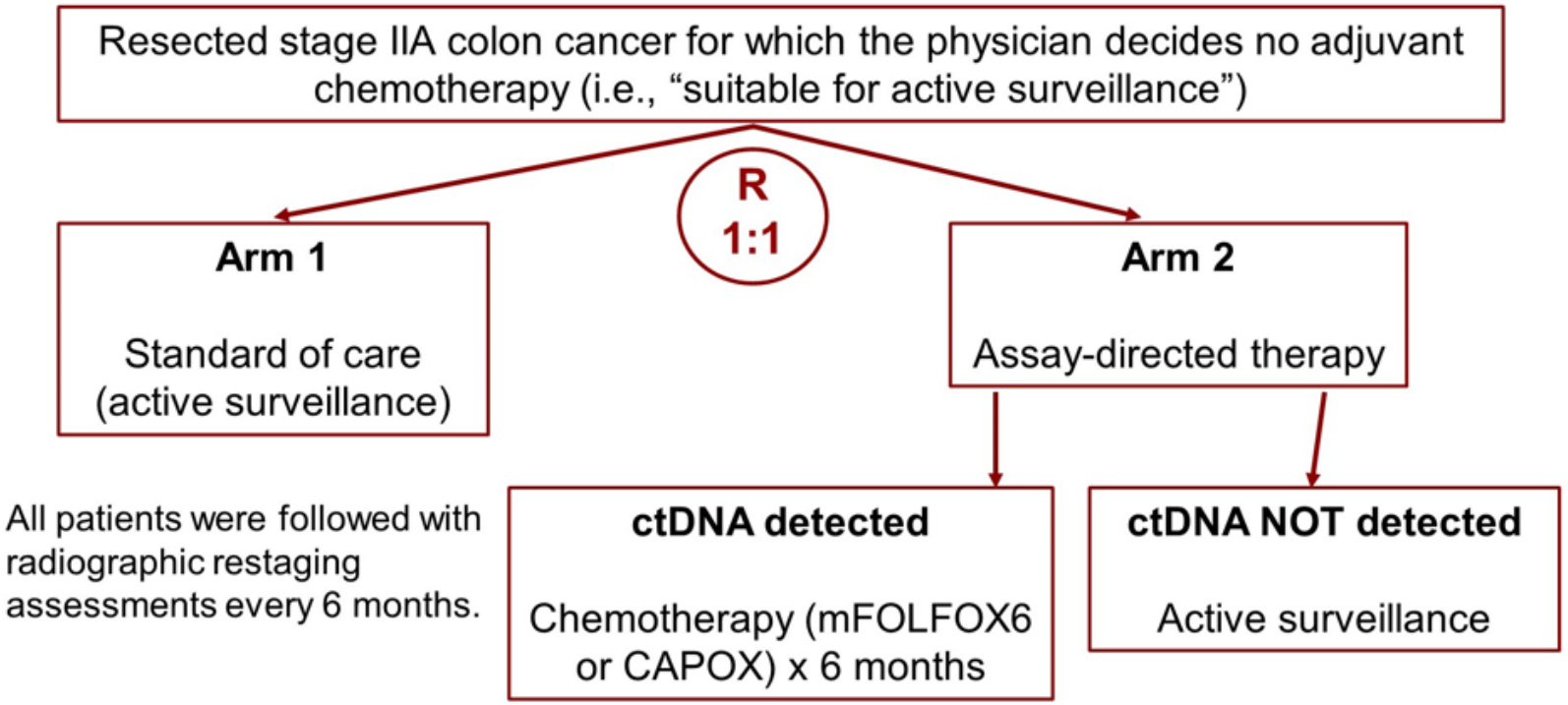
Phase II results of circulating tumor DNA as a predictive biomarker in adjuvant chemotherapy in patients with stage II colon cancer: NRG-GI005 (COBRA) phase II/III study

Van K. Morris[1], Greg Yothers[2], Scott Kopetz[1], Shannon L. Puhalla[3], Peter C. Lucas[2], Atif Iqbal[4], Patrick M Boland[5], Dustin A. Deming[6], Aaron J. Scott[7], Howard J Lim[8], Theodore S. Hong[9], Norman Wolmark[2], Thomas J. George[10]



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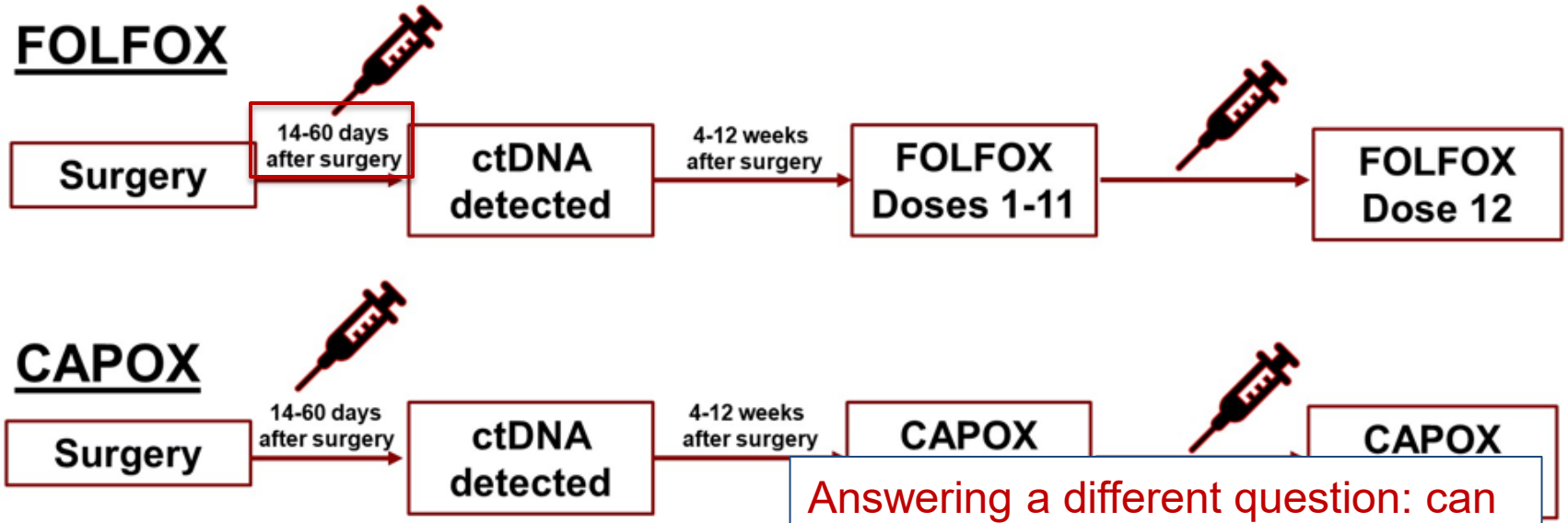
Morris VK, et al. ASCO GI 2024 Abstract 433174

Treatment schema: Arm 2 “ctDNA detected”



The 6-month timepoint was collected two weeks
prior to the administration of the last dose of che

Answering a different question: can adjuvant chemo lead to ctDNA clearance better than observation in these average/low risk stage II but ctDNA (+) pts

Guardant LUNAR Assay was used

Primary objective: compare rates of ctDNA clearance between ctDNA (+) cohorts at 6 months after randomization

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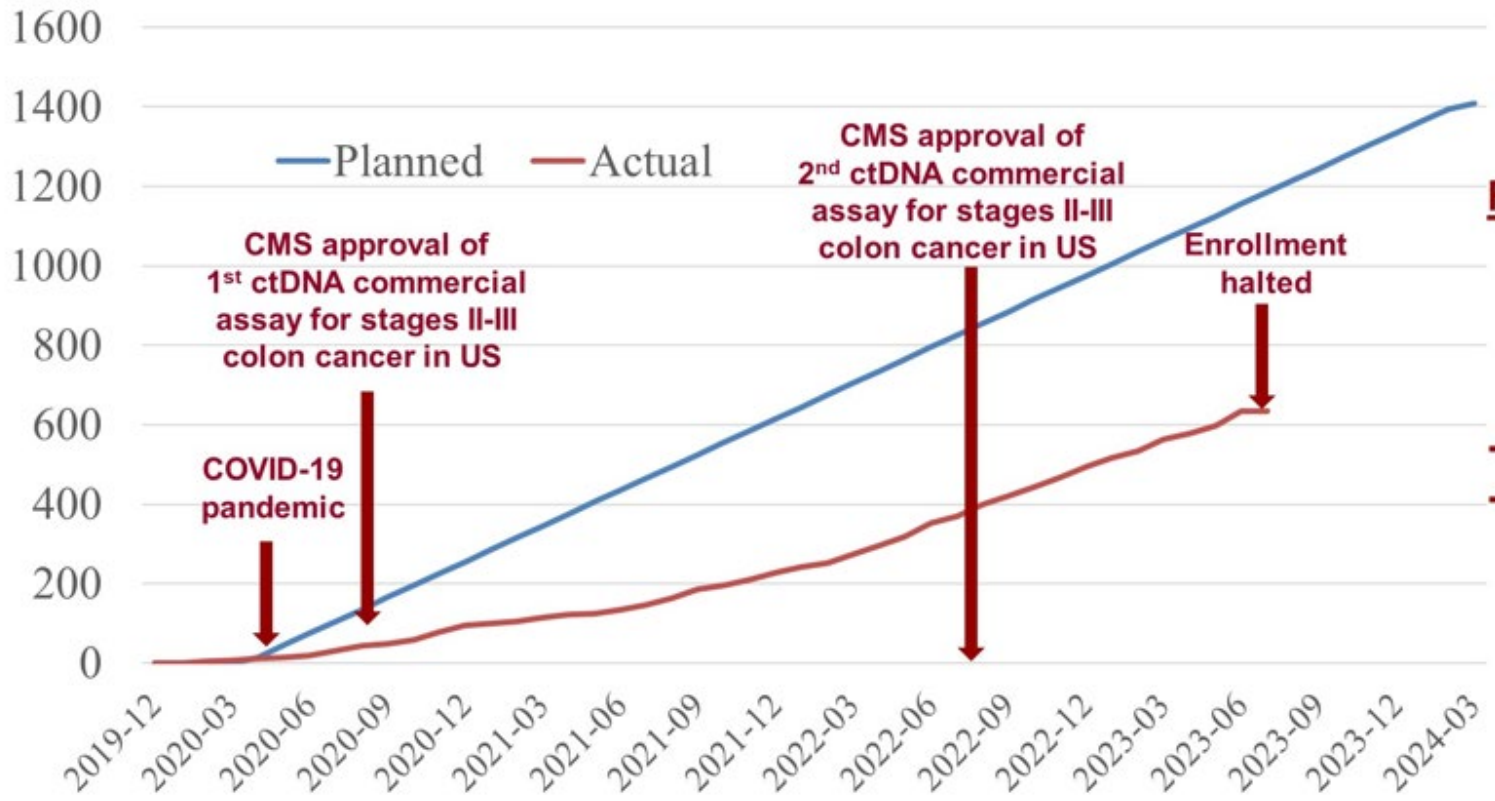
Morris VK, et al. ASCO GI 2024 Abstract 433174

Patient Accrual



Final accrual:

635/1408 participants

- **US: 458**
- **Canada: 177**

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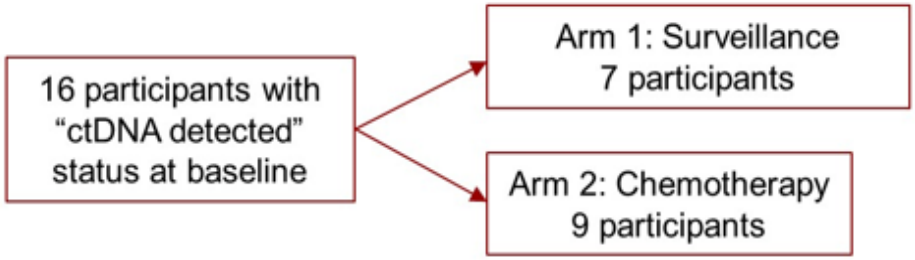
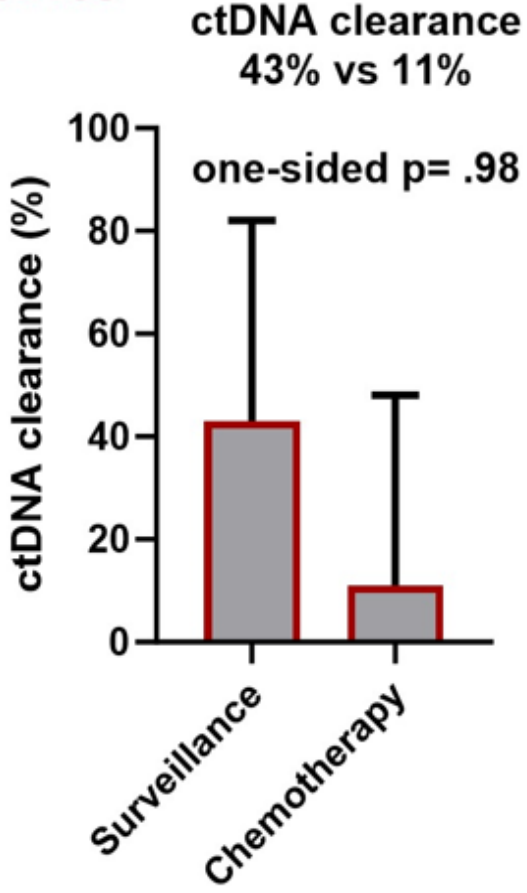
Phase II Endpoint Analysis: ctDNA(+) baseline participants

- Among 596 participants with baseline ctDNA status available, ctDNA(+) detection was observed in 33 (5.54%).



- Clearance of ctDNA at 6 months among ctDNA(+) participants at baseline was observed in:
  - **Arm 1 (surveillance):** 3 of 7 (43%, 95% CI 10 - 82%) participants
  - **Arm 2 (chemotherapy):** 1 of 9 patients (11%, 95% CI 0.3 - 48%) participants

- **Because the 1-sided Fisher's Exact Test yields p = 0.98 exceeded 0.35, H_o was not rejected, and the decision rule calls for early stopping due to futility.**



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My Interpretation

- Eligible patients have stage IIA (T3N0) colon adenocarcinoma with no risk features. Outside of a clinical trial, adjuvant chemotherapy is not usually recommended for this group of patients
- 2% of pts were ctDNA+ at baseline. Another 3% of pts became ctDNA+ later
- First draw could be false-positive if drawn within 4 weeks after surgery
- Selected assay was tumor-agnostic

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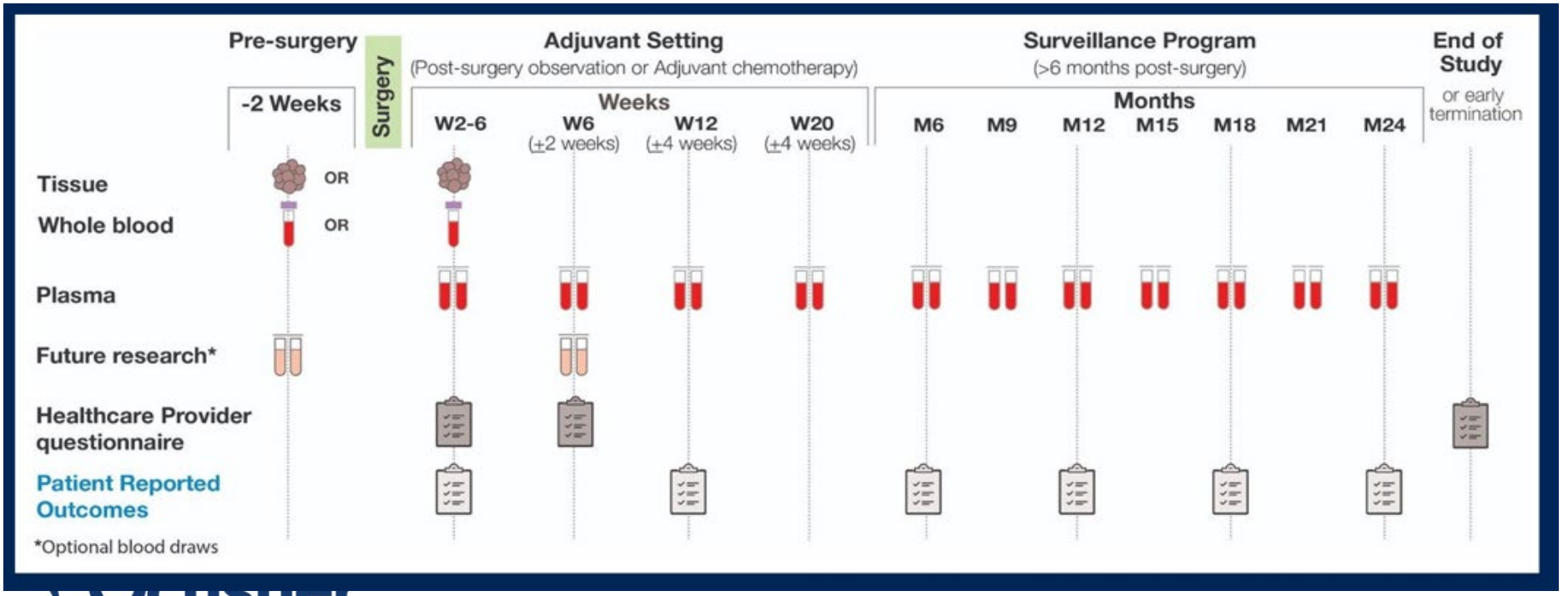
ASCO Gastrointestinal Cancers Symposium

Circulating Tumor DNA for Detection of Molecular Residual Disease (MRD) in Patients with Stage II/III Colorectal Cancer (CRC): Final Analysis of the BESPOKE CRC Sub cohort.

Presenting author: Purvi K. Shah, MD[1]

- Multicenter, prospective, observational study evaluating the ability of ctDNA to inform adjuvant chemo decisions in pts with stage II/III CRC
- Signatera



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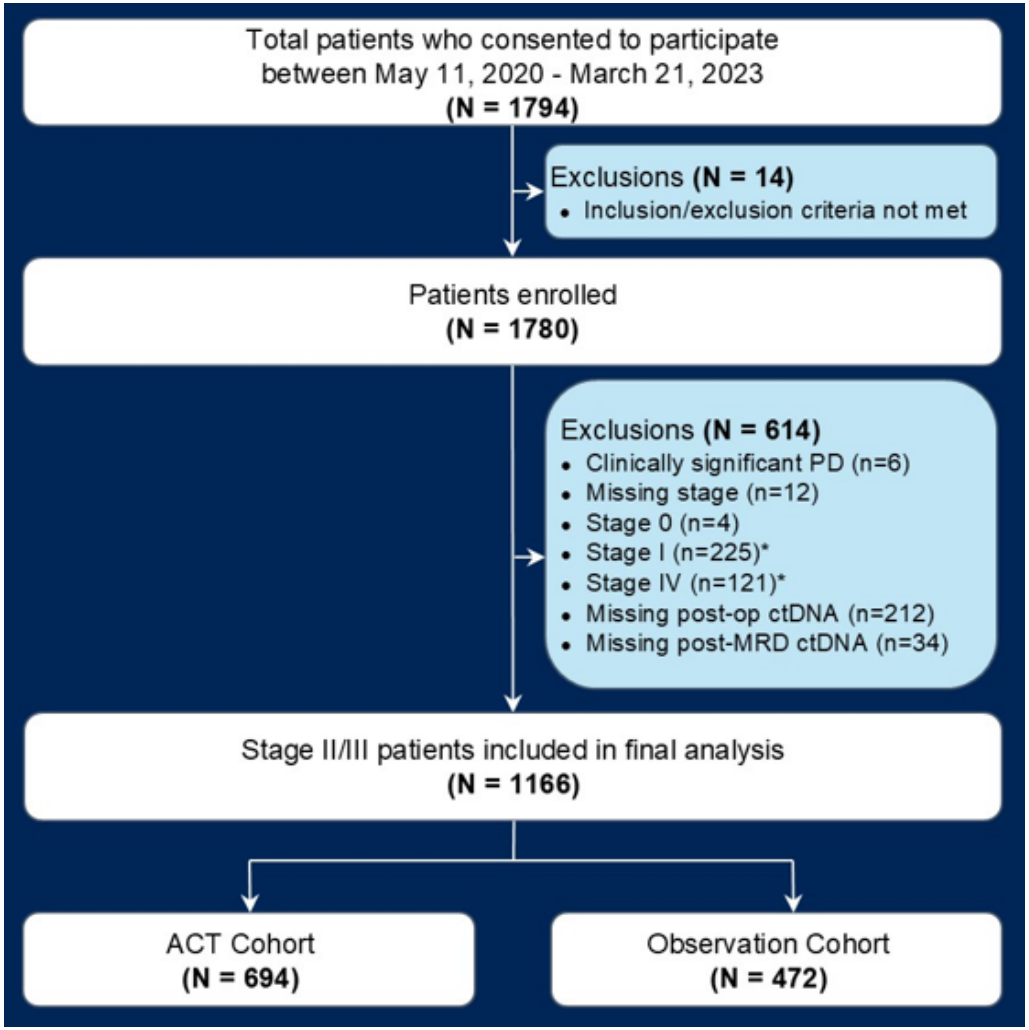
Consort Diagram



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Patient characteristics and prevalence of ctDNA

Characteristic (n, %)	N = 1166
Age (median, range)	61.8 (22 - 94)
Median follow-up (months, range)	23.9 (0.5-36.5)
Gender	
Male	661 (56.7%)
Female	505 (43.3%)
Pathologic Stage	
II	517 (44.3%)
III	649 (55.7%)
Age Group	
< 65	674 (57.8%)
65 +	491 (41.4%)
Missing	1 (0.1%)
Race and Ethnicity	
White	844 (72.4%)
Black or African American	137 (11.7%)
Asian	42 (3.6%)
Native Hawaiian/Pacific Islander	8 (0.7%)
Native American/Alaskan	4 (0.3%)
Not Reported/Missing	123 (10.5%)
Other	25 (2.1%)

Characteristic (n, %)	N = 1166
Hispanic Origin	
Hispanic or Latino	123 (10.5%)
Not Hispanic or Latino	956 (82.0%)
Unknown	87 (7.5%)
ECOG	
0	743 (63.7%)
1	355 (30.4%)
2	52 (4.5%)
Missing	16 (1.4%)
Adjuvant chemotherapy (ACT)	
Yes	694 (59.5%)
No	472 (40.5%)
Recurrence	
Yes	188 (16.1%)
No	978 (83.9%)

Stage	Total N	MRD-positive n (%)	95% CI for positivity rate
Stage II	517	39 (**7.54%**)	5.57 - 10.15
Stage III	649	184 (**28.35%**)	25.02 - 31.94

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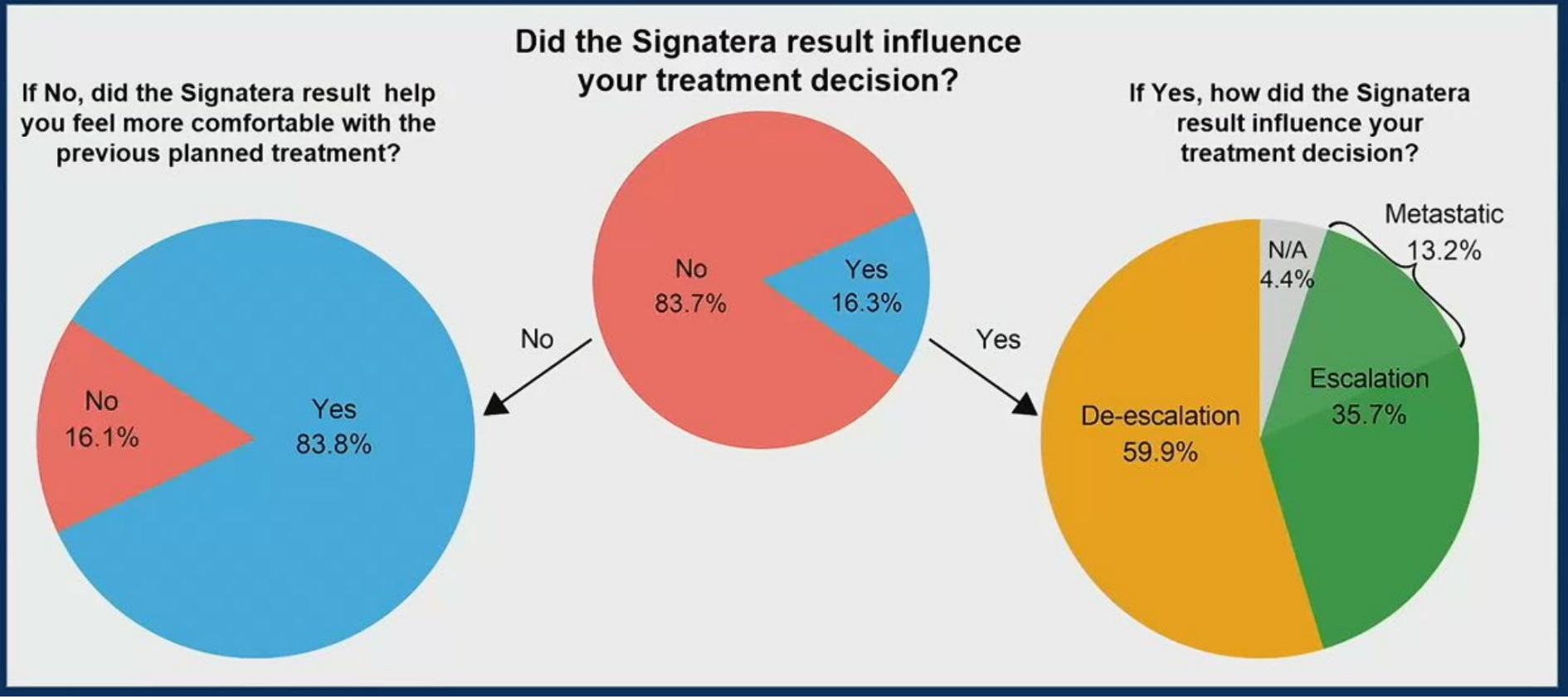
Impact of Signatera on adjuvant treatment decisions



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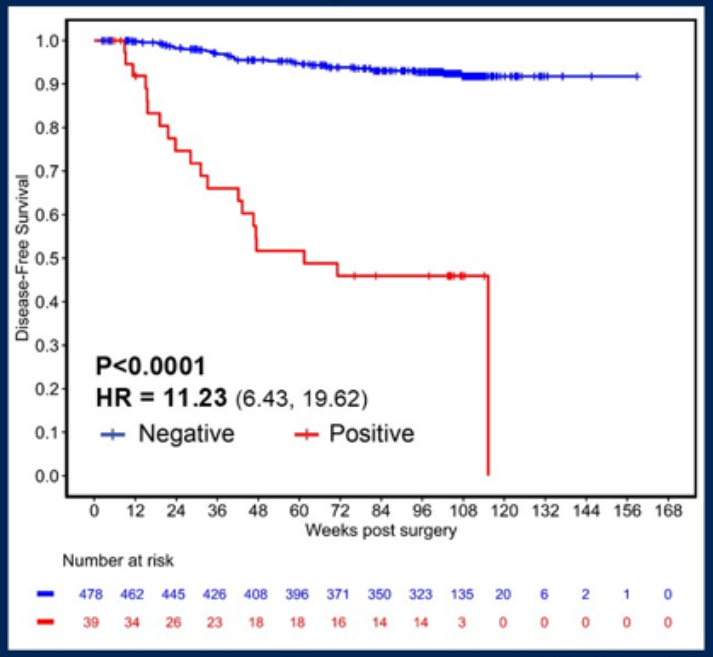
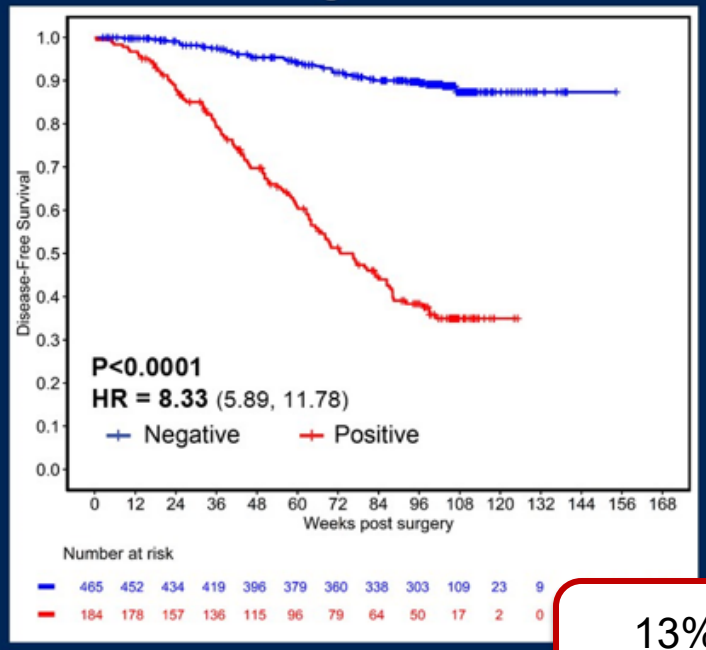
Post-operative ctDNA positivity predicts inferior DFS

Stage II



ctDNA Status	Events	Median DFS post surgery, months (95%)	2-year DFS post surgery,% (95% CI)
Negative	33	NE (NE-NE)	**91.8** (NE-NE)
Positive	20	12.7 (8.3-NE)	**45.9** (32.1-65.8)

Stage III



ctDNA Status	# Events	Median DFS post surgery, months (95%)	
Negative	47	NE (NE-NE)	**87.4** (83.8-91.1)
Positive	105	16.2 (13.6-18.9)	**35.5** (28.6-44.2)

13% recurred

Landmark DFS Analysis at 6 weeks (42 Days). NE: Not Estimable

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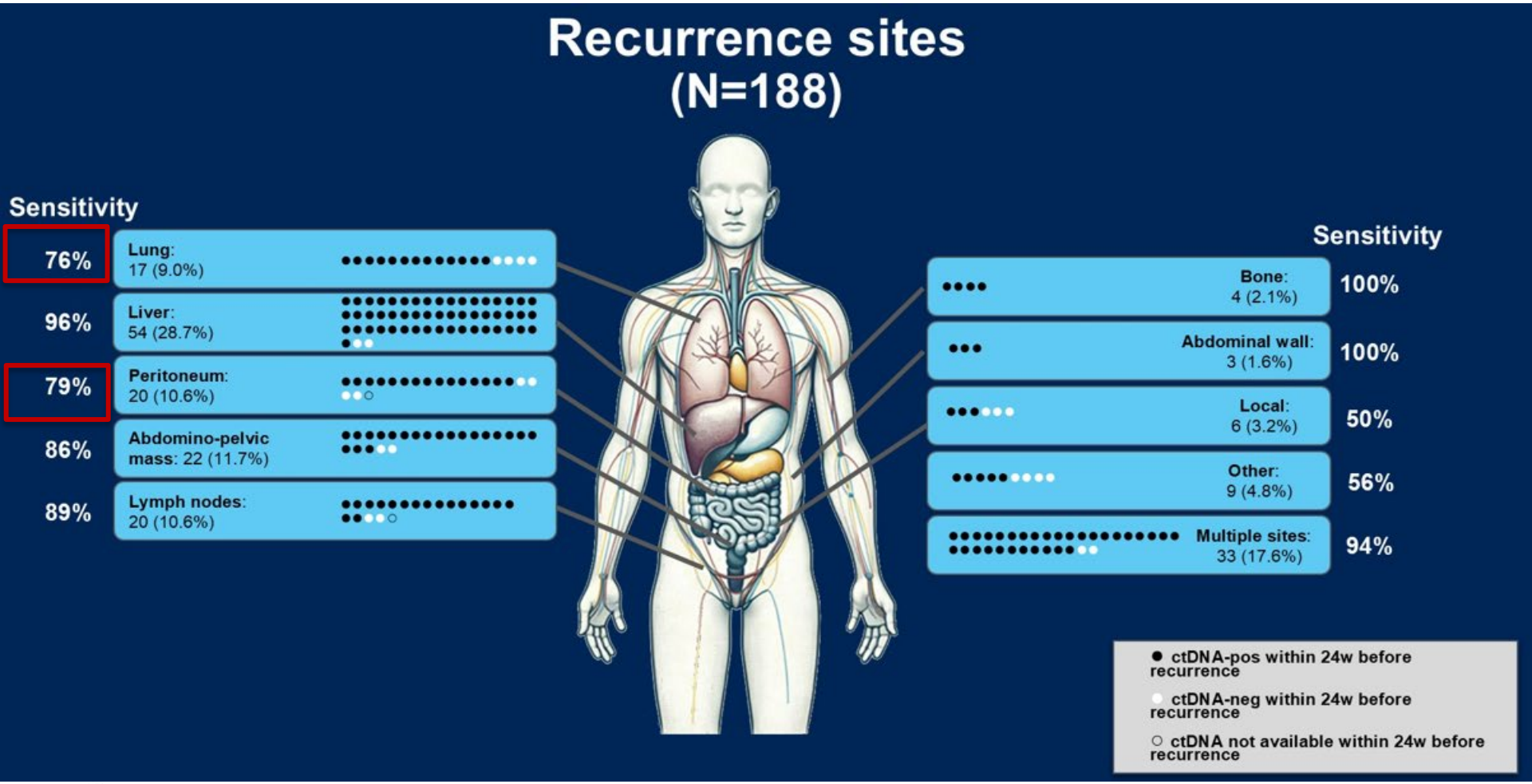

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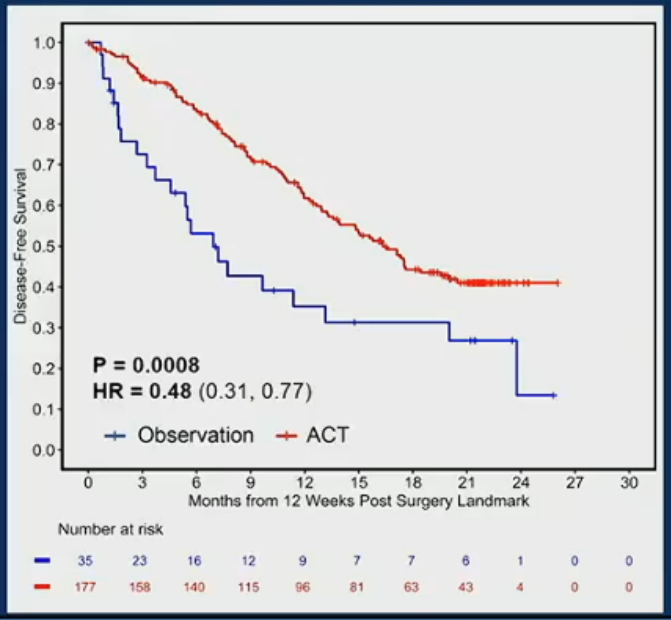
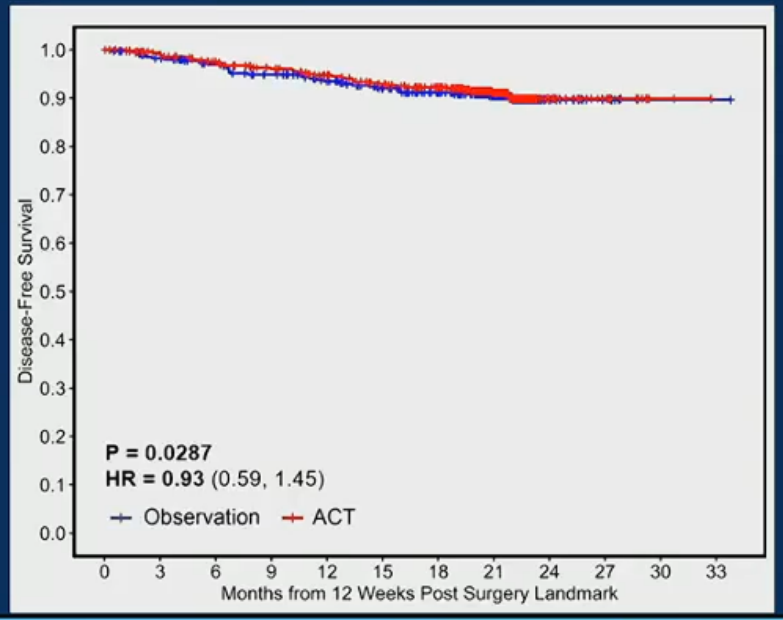
ctDNA MRD testing is predictive of the benefit of ACT

MRD-positive patients



Adjuvant strategy	ACT	Observation
Numbers of events (%)	96/177 (54.24)	29/35 (82.86)
2-year DFS post surgery, % (95% CI)	**40.3** (33.3 - 48.9)	**24.7** (13.2 - 46.3)
Median DFS post surgery, months (95%)	17.7 (14.6 - 21.4)	7.1 (4.6 - 21.4)

MRD-negative patients



Adjuvant strategy	ACT	Observation
Numbers of events (%)	43/506 (8.50)	37/408 (9.07)
2-year DFS post surgery, % (95% CI)	**89.7** (86.7- 92.9)	**89.5** (86.2- 92.9)
Median DFS post surgery, months (95%)	Not reached	Not reached

- Clinical risk of these patients (stage II vs III, T3 vs T4, N0/1 vs N2, risk factors)?

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My interpretation

- If ctDNA positive, high risk of recurrence. Tumors sensitive to FOLFOX probably derived benefits.
- If ctDNA negative, ~10% of patients recurred. FOLFOX not helping - are these tumors happen to be those that don't respond to FOLFOX; need better/different drugs? Do we have better drugs?
- For a high-risk patient (T4, N2/3) and ctDNA negative, do I feel comfortable not offering chemo?
- Observational study

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- 54 yo F w/stage IIIC (T4aN2aM0) poorly differentiated adenocarcinoma of the cecum, +LVI and PNI), high tumor budding score, MMR-proficient, s/p R colectomy on 8/19/24.
- Patient declined further chemo after 1 dose of oxaliplatin.
- ctDNA results:

10/19/24 neg

12/30/24 neg

3/31/25 pos 0.99 – PET followed by MRI pelvis showed a new 7 cm R ovarian mass

6/26/25 pos 19.06 – TAH-BSO 7/14/25. Path showed a 10 cm metastatic carcinoma involving the right ovary.

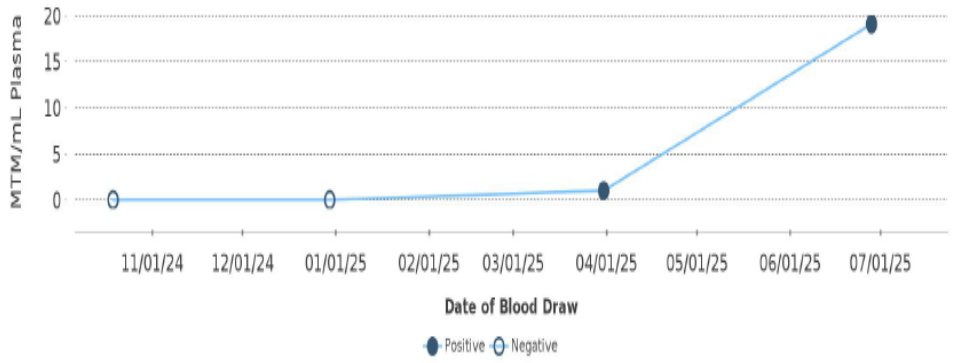
FINAL RESULTS SUMMARY

Signatera Positive

Date: 06/28/2025
MTM/mL: 19.08

Mean tumor molecules per mL is calculated based on the mean of ctDNA molecules detected per mL of the patient's plasma. See Limitations section below.

Historical Results



Date	Reported MTM/mL
Jun 28, 2025	19.08
Mar 31, 2025	0.99
Dec 30, 2024	0.00
Oct 19, 2024	0.00

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DYNAMIC III

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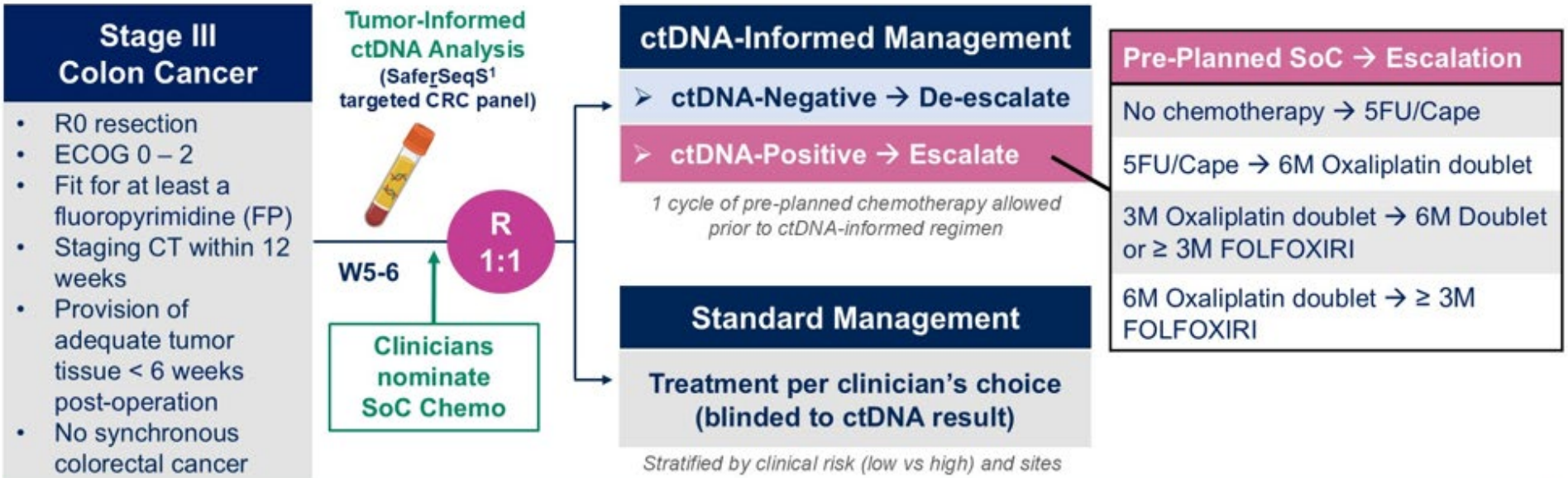
2025 ASCO ANNUAL MEETING

ctDNA-Guided Adjuvant Chemotherapy Escalation in Stage III Colon Cancer

Primary Analysis of the ctDNA-Positive Cohort from the Randomized AGITG DYNAMIC-III Trial (Intergroup Study of AGITG and CCTG)



Primary Analysis of ctDNA-Positive Cohort: Endpoints to be Presented	
Primary: 2 years RFS	**Secondary:** safety, end-of-treatment (EoT) ctDNA clearance
	Exploratory: post-operative ctDNA levels

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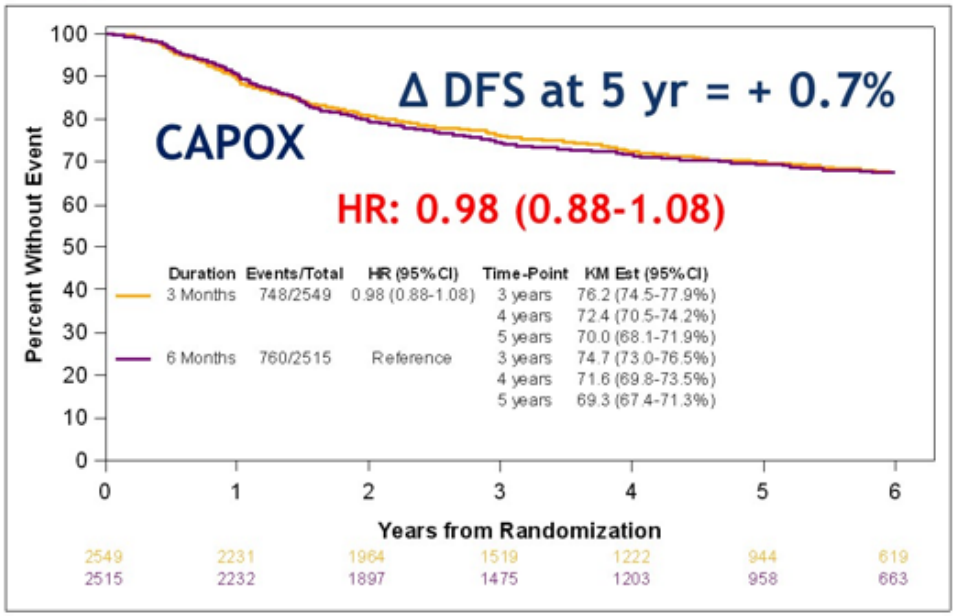
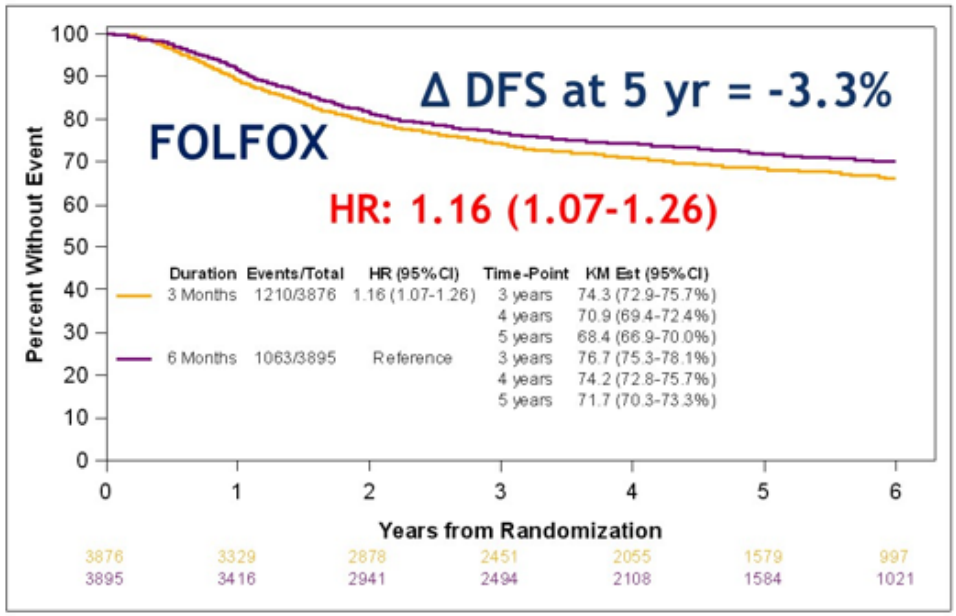
Tie J, et al. ASCO 2025 Abstract 3503

IDEA 5-yr DFS by regimen





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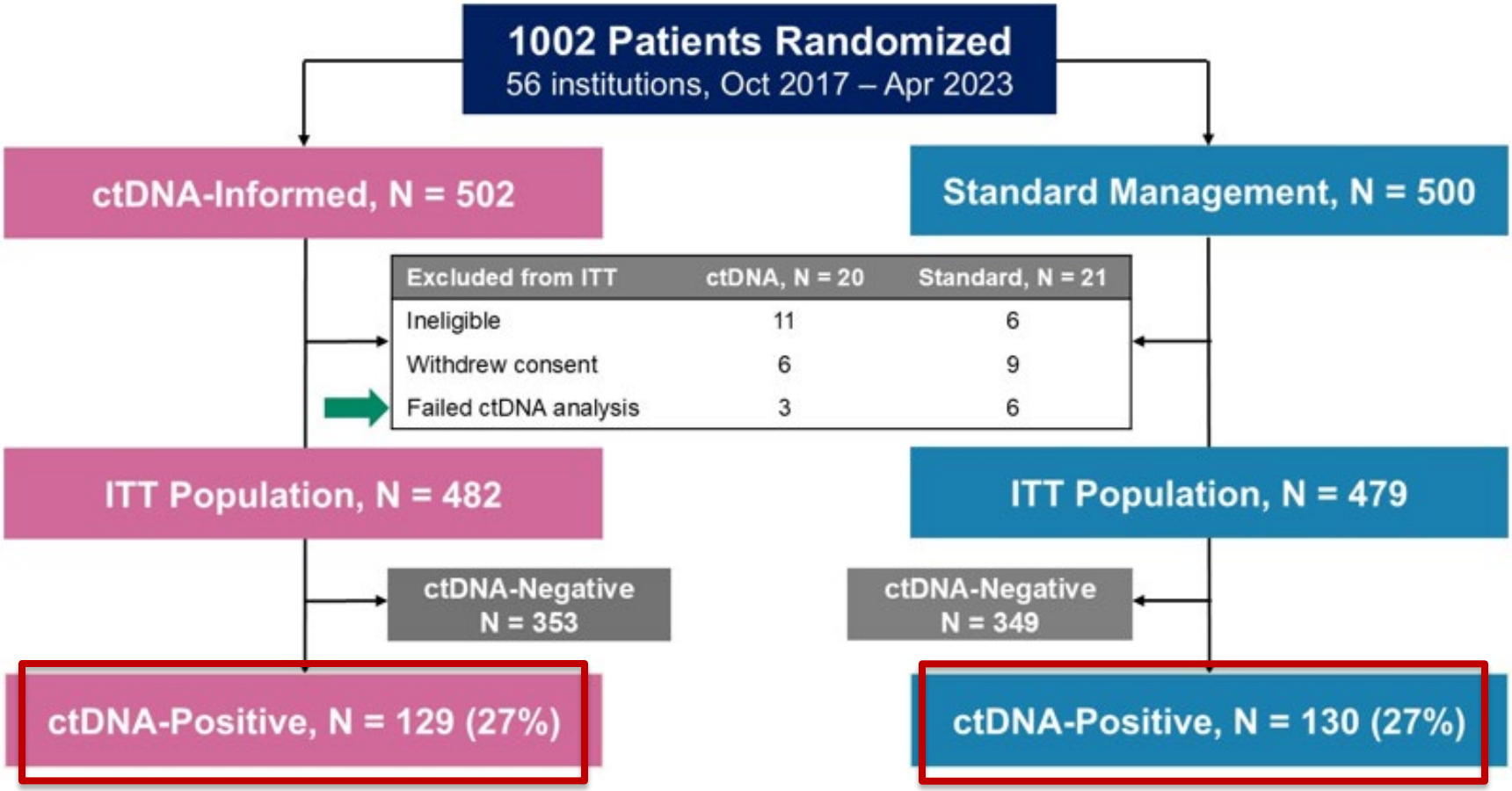
Sobreno AF, et al. ASCO 2020 Abstract 4004



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Tie J, et al. ASCO 2025 Abstract 3503

Key Baseline Characteristics

Characteristics	ctDNA-Informed Escalation N = 129, N (%)	Standard Management N = 130, N (%)
Age, median (range), years	64 (30, 87)	61 (30, 90)
Sex, Male	82 (64)	80 (62)
ECOG, 0	107 (83)	99 (76)
Primary tumor location, right-sided	63 (49)	53 (41)
Clinical risk, high (T4 or N2)	77 (60)	69 (53)
T stage, T4	48 (38)	49 (38)
N stage, N2	54 (42)	45 (35)
Nodes examined, median (IQR)	22 (17-29)	20 (15-26)
Extramural tumor deposits, yes	51 (39)	40 (31)
Obstruction/Perforation, yes	25 (19)	25 (19)
Mismatch repair, deficient	14 (11)	12 (9)

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Treatment Exposure: ITT Population

Treatment Information		ctDNA-Informed Escalation N = 129, N (%)	Standard Management N = 130, N (%)
Commenced protocol treatment escalation		115 (89)	--
Chemotherapy received	No Chemotherapy	4 (3)	4 (3)
	Single agent FP	3 (2)	14 (11)
	3M Oxaliplatin doublet	1 (1)	59 (45)
	6M Oxaliplatin doublet	56 (44)	53 (41)
	≥ 3M FOLFOXIRI	65 (50)	0 (0)
Time from surgery to commencing chemotherapy, median (IQR), days		59 (52-68)	53 (49-61)
Treatment duration, median (IQR), days		150 (126-161)	147 (76-161)
Completed planned treatment		95 (74)	86 (68)

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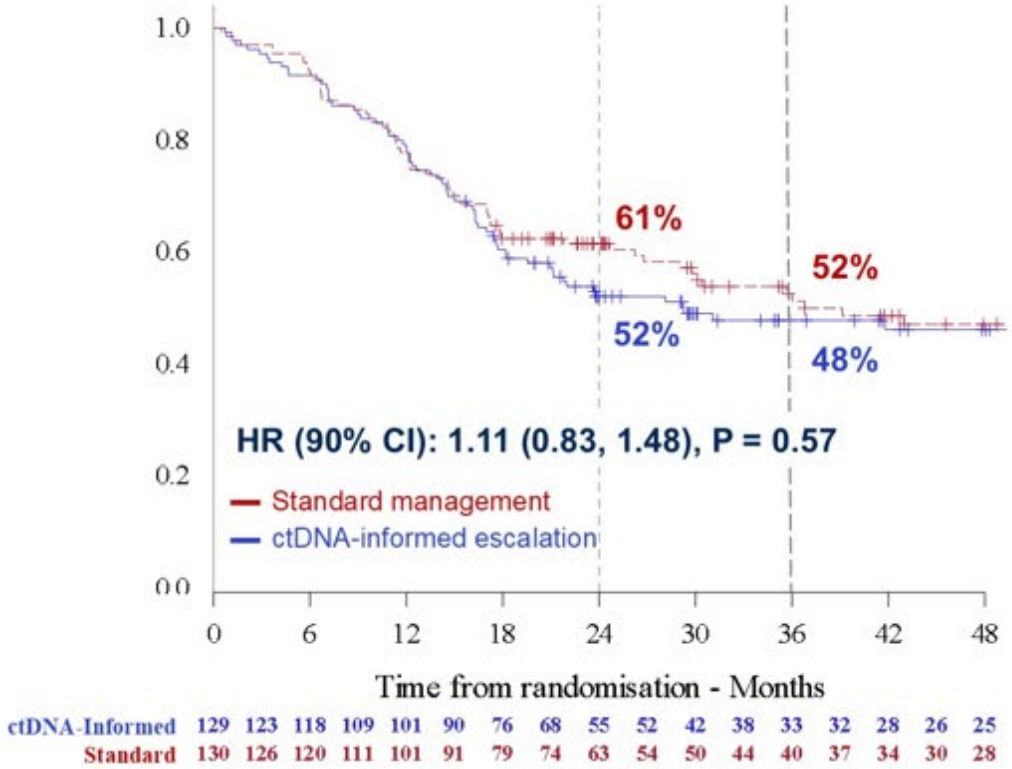
Recurrence-Free Survival



	Total	Events	Median RFS (mths)	2-year RFS (90% CI)	3-year RFS (90% CI)
ctDNA	129	66	29.24	52% (44, 59)	48% (40, 55)
SoC	130	62	36.80	61% (54, 68)	52% (44, 60)

Median follow-up 42.2 months (0.78 - 63.0)

Data cut-off: 14 Nov 2024

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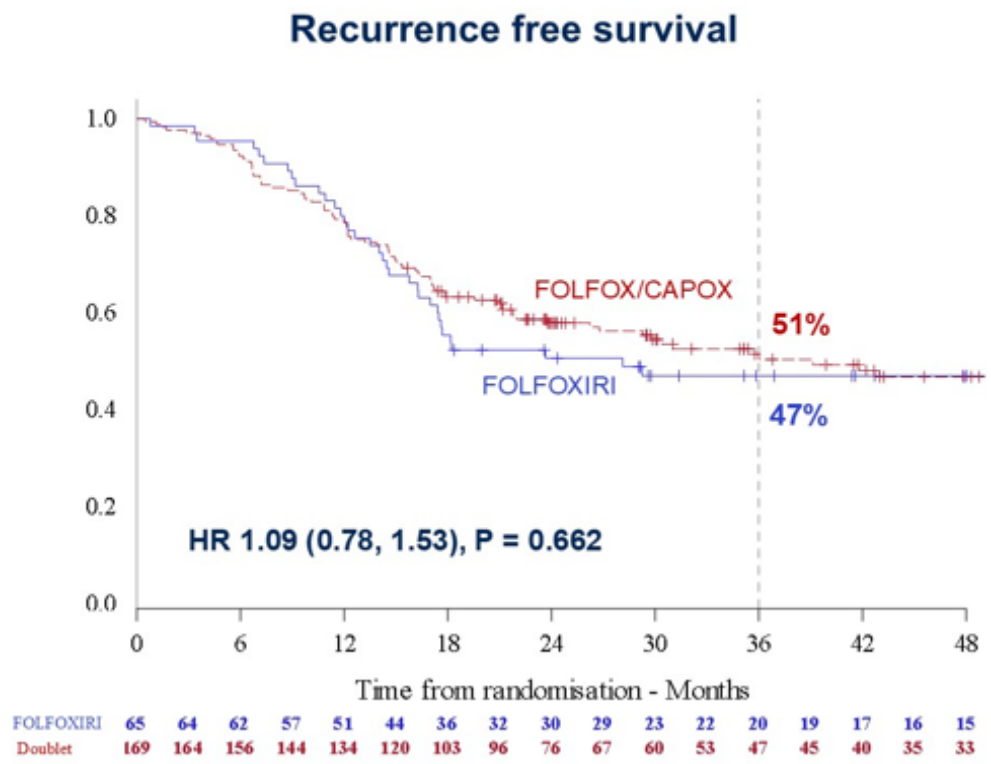
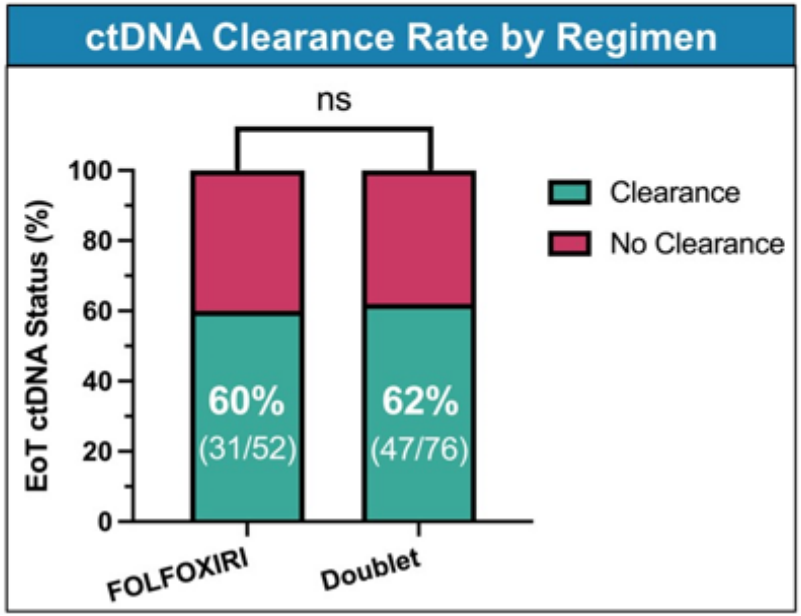
Post-Hoc Analysis: FOLFOXIRI vs FOLFOX/CAPOX



	TDMM/mL, median (IQR)	P
FOLFOXIRI	0.28 (0.06, 1.78)	0.236
Doublet	0.15 (0.06, 0.97)	



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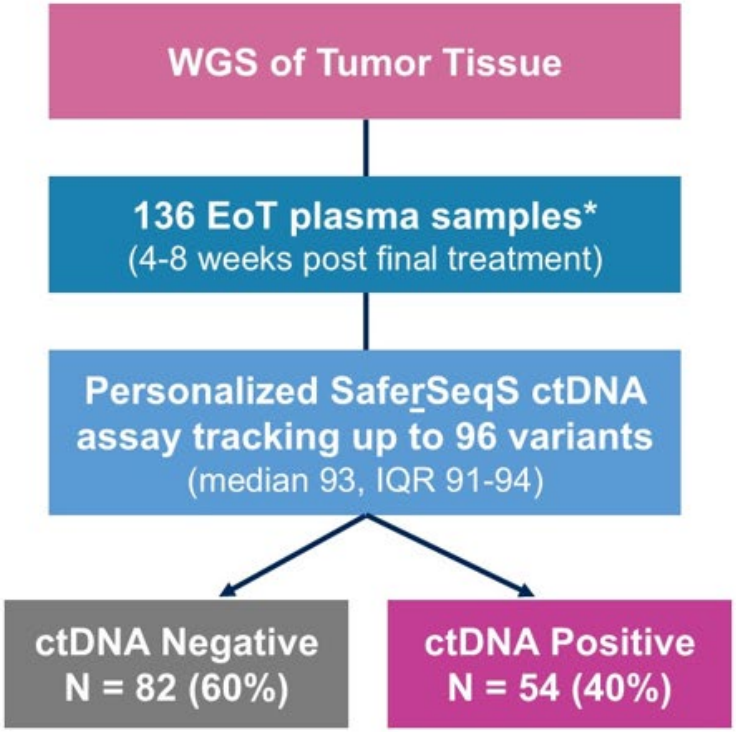
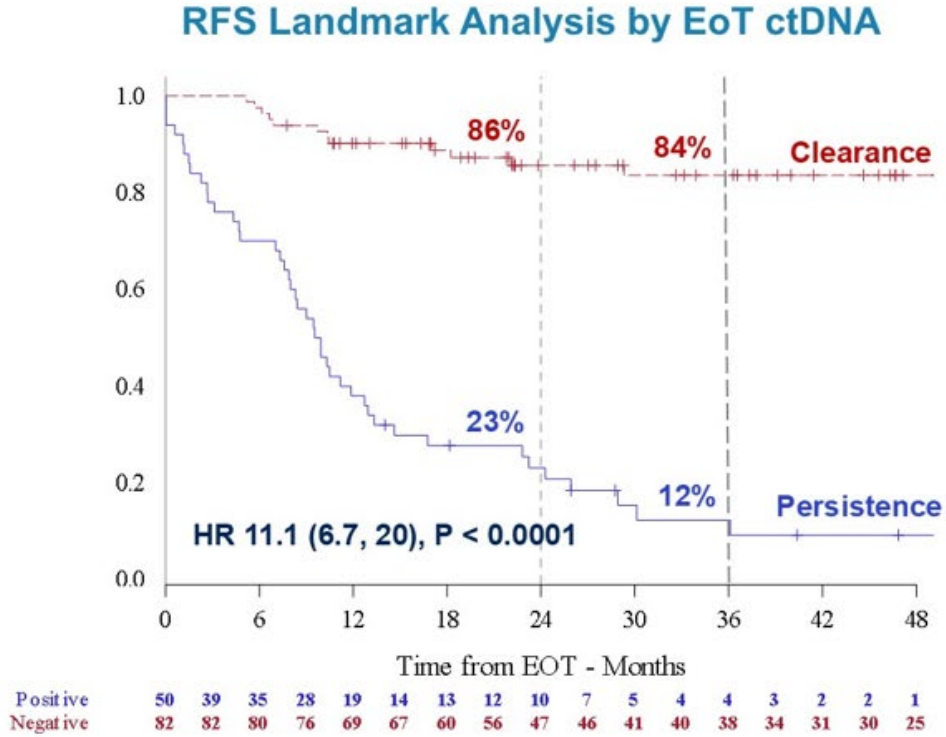
End of Treatment (EoT) ctDNA Clearance and RFS



*from both study arms: 98 ctDNA-informed, 38 standard (optional collection)



4 EoT-positive cases excluded from landmark analysis due to EoT blood draw occurring after documented recurrence

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Tie J, et al. ASCO 2025 Abstract 3503

My interpretation of DYNAMIC III

- Post-op ctDNA (+) is a poor prognostic sign
- If adjuvant chemo can clear ctDNA, patients do better – obviously
- Does chemo escalation help? Does not seem like it
- Curious to know the data in ctDNA negative groups – can we safely de-escalate or omit chemo in patients with stage III colon cancer and post-op ctDNA negative?

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- Does a negative ctDNA right now predict serial negative ctDNA in the future?

    - for average risk stage II colon cancer, I would not expect cancer to come back for the majority of patients. Post-op negative ctDNA is reassuring (but do I need that?)

    - for high-risk patients, does a negative ctDNA postop predict serial negative ctDNA in the future?

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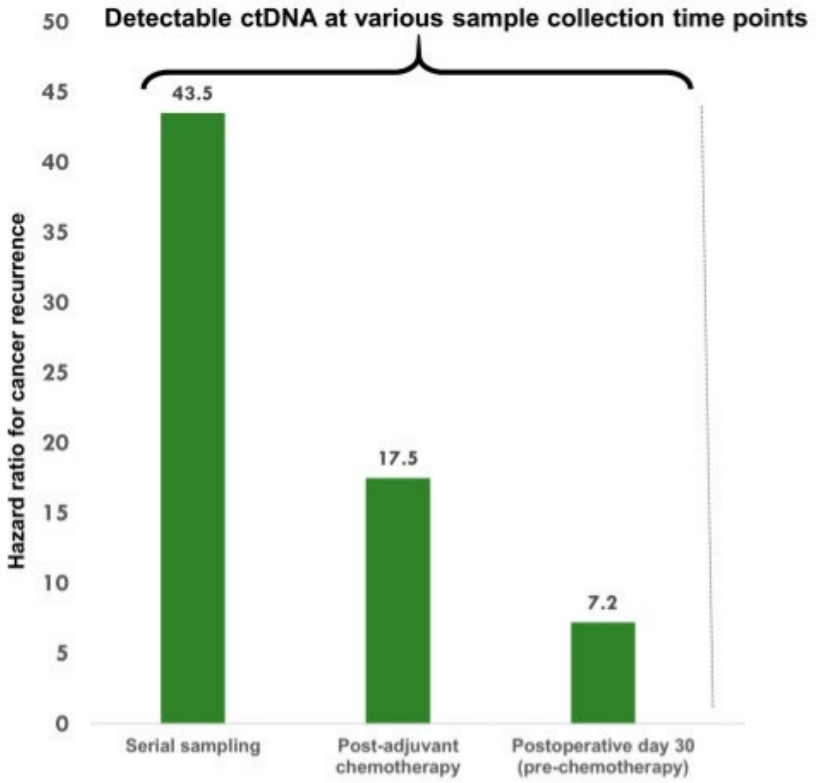

- Single post-op sensitivity 41%. Serial monitoring sensitivity 88%

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Parikh AR. ASCO GI 2024
Chkrabarti S, et al. Cancers (Basel).2020 Sep 29;12(1):2808

- For high-risk patients who are ctDNA (-), my decision on adjuvant chemo still depends on the clinical risks.

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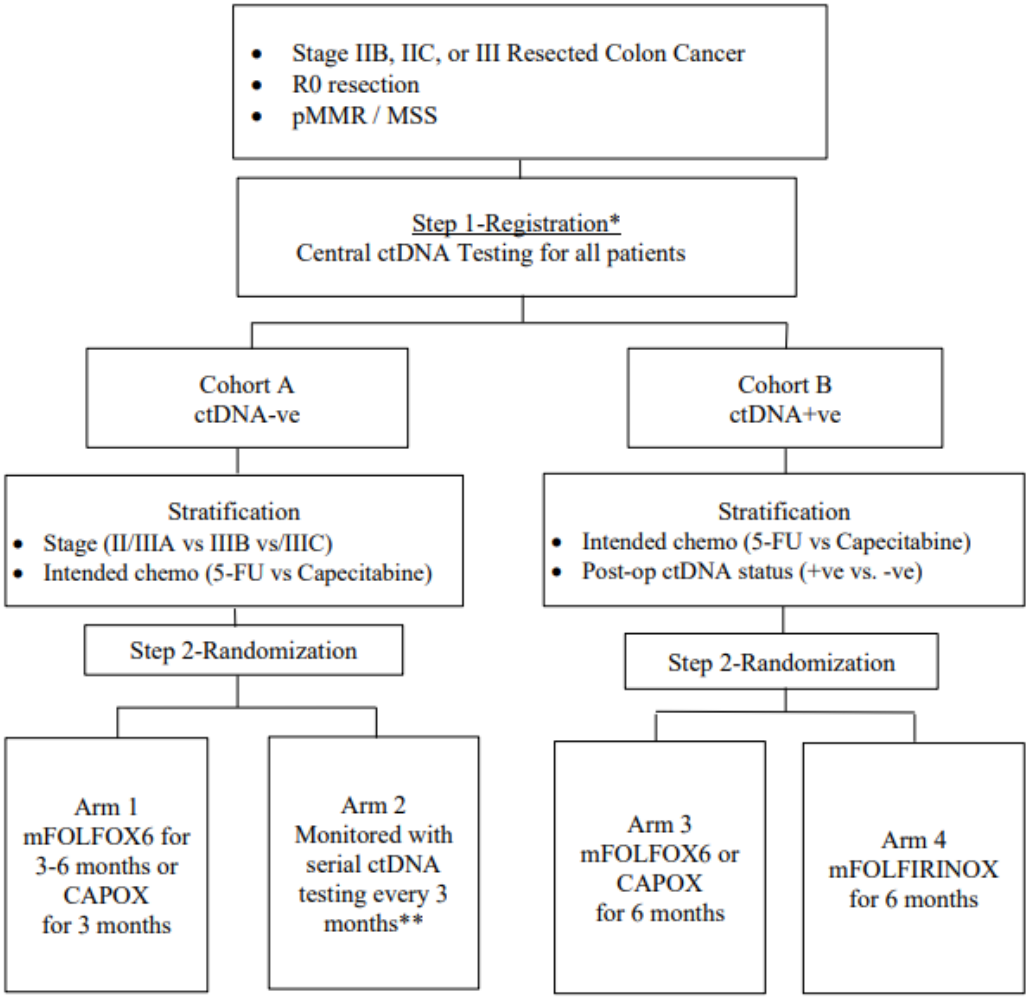
Ongoing NRG-GI008 trial in patients with resected stage III colon cancer

Figure 1.
NRG-GI008 SCHEMA



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- What do we do with post-op positive ctDNA that is not being cleared by adjuvant chemo? – bad tumor biology, lack of effective chemotherapy when colon cancer don't respond to FOLFOX/FOLFIRINOX
- Molecular targeted treatment (RAS, BRAF V600E, NTRK, etc)? Vaccine? Immunotherapy?
- After pts finish adjuvant chemo, if they remain ctDNA (+) but NED on scans, does starting/extending treatment prolong OS?

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- Phase IB study of immunotherapy with ex vivo pre-activated and expanded CB-NK cells in combination with cetuximab, in colorectal cancer patients with minimal residual disease

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Our journey of ctDNA in resected colon cancer

Post-op ctDNA (+) is a bad prognostic sign. Sustained clearance with adjuvant chemotherapy in some patients are possible. If not, prognosis is very poor.

Single post-op ctDNA has limited sensitivity. Serial monitoring can improve the sensitivity.

Sensitivity of ctDNA is higher in pts with liver, bone, abdominal wall mets, and lower in lung and peritoneal mets

More questions need to be answered. Can we safely de-escalate chemo in ctDNA (-) pts? What should we do for pts who are ctDNA (+) and cannot be cleared by adjuvant chemo? Ongoing trials.

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Thank You