Baptist Health

Miami Cancer Institute

Updates in Colorectal Cancer 2024

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ASCO Gastrointestinal Cancers Symposium

Circulating tumor DNA (ctDNA) for informing adjuvant chemotherapy (ACT) in stage II/III colorectal cancer (CRC): Interim analysis of BESPOKE CRC study

Presenting author: Pashtoon Kasi[1], MD, MS

Co-authors: Vasily N Aushev[2], Joe Ensor[2], Nathan Langer[3], Christopher Wang[4], Timothy Cannon[5], Lyudmyla Berim[6], Trevor Feinstein[7], Axel Grothey[8], Joseph McCollom[9], Sujith Kalmadi1[0], Ahmed Zakari[11], Farshid Dayyani[12], Don Gravenor[13], Janelle Meyer[14], Saima Sharif[15], Adham Jurdi[2], Minetta C Liu[2], Alexey Aleshin[2], Scott Kopetz[16]

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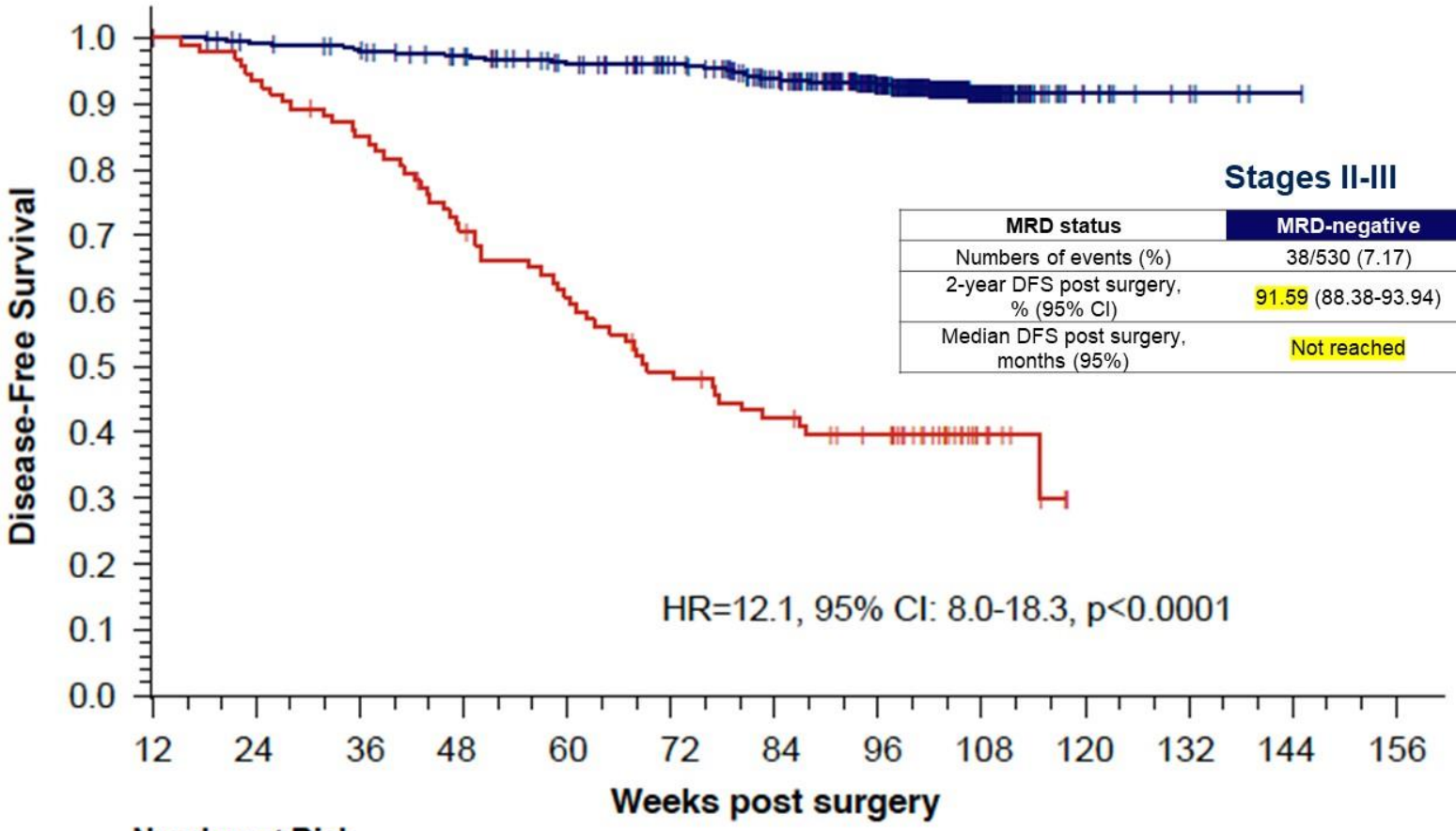
Prospective Study

154 Stage 2 patients, 193 Stage 3 patients.

ctDNA-positivity at MRD time point is predictive of inferior DFS

-6.5% +MRD Stage 2

-22% +MRD Stage 3



Stages II-III

MRD status	MRD-negative	MRD-positive
Numbers of events (%)	38/530 (7.17)	55/93 (59.14)
2-year DFS post surgery, % (95% CI)	91.59 (88.38-93.94)	29.86 (13.26-48.54)
Median DFS post surgery, months (95%)	Not reached	15.98 (13.77-20.22)

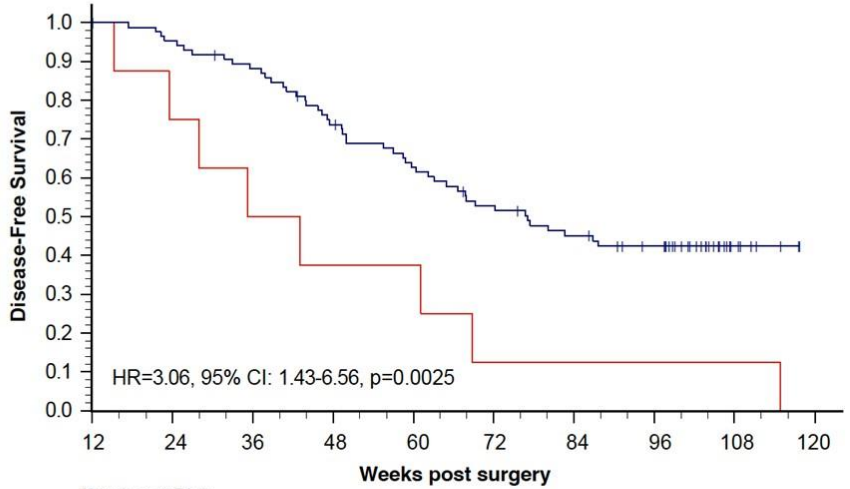
Number at Risk

MRD-negative	530	522	513	499	482	464	429	353	101	12	5	1	0
MRD-positive	93	87	78	64	54	43	36	30	8	0			

PRESENTED BY: Pashtoon Kasi, MD, MS

Benefit from ACT observed in MRD-positive but not MRD-negative patients

MRD-positive patients

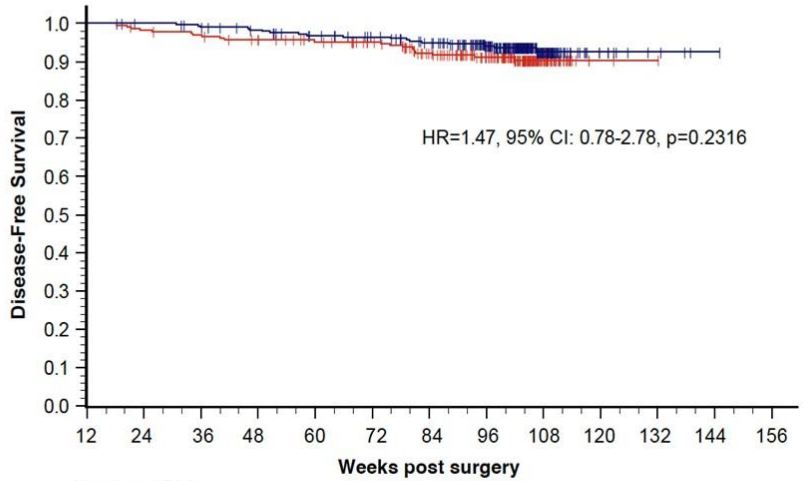


Number at Risk

ACT	85	80	72	56	48	39	32	18	2	0
Observation	8	6	4	3	2	1	1	1	0	

Adjuvant strategy	ACT	Observation
Numbers of events (%)	47/85 (55.29)	8/8 (100)
2-year DFS post surgery, % (95% CI)	42.44 (31.55-52.91)	12.50 (0.66-42.27)
Median DFS post surgery, months (95%)	17.78 (14.37-not reached)	7.52 (3.52-15.88)

MRD-negative patients



Number at Risk

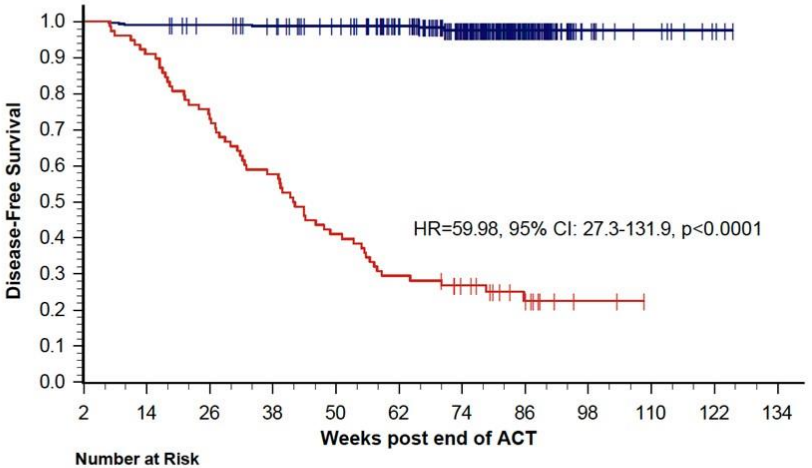
ACT	296	293	288	281	271	263	251	207	61	10	4	1	0
Observation	234	229	225	218	211	201	178	146	40	2	1	0	

Adjuvant strategy	ACT	Observation
Numbers of events (%)	18/296 (6.08)	20/234 (8.55)
2-year DFS post surgery, % (95% CI)	93.70 (90.03-96.05)	90.39 (85.38-93.75)
Median DFS post surgery, months (95%)	Not reached	Not reached

PRESENTED BY: Pashtoon Kasi, MD

ctDNA-positivity during surveillance is predictive of inferior DFS regardless of adjuvant therapy (ACT or observation)

Patients receiving ACT

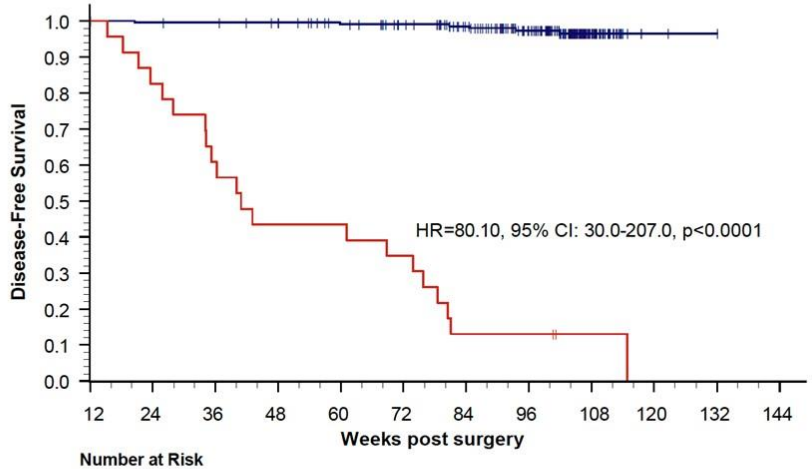


Number at Risk

ctDNA-negative	329	326	321	315	305	278	213	87	16	9	3	0
ctDNA-positive	78	71	57	45	32	23	17	8	2	0		

ctDNA status (surveillance)	ctDNA-negative	ctDNA-positive
Numbers of events (%)	7/329 (2.13)	59/78 (75.64)
2-year DFS post end of ACT, % (95% CI)	97.58 (94.96-98.84)	22.56 (13.49-33.08)
Median DFS post end of ACT, months (95%)	Not reached	9.70 (7.43-12.32)

Patients on observation



Number at Risk

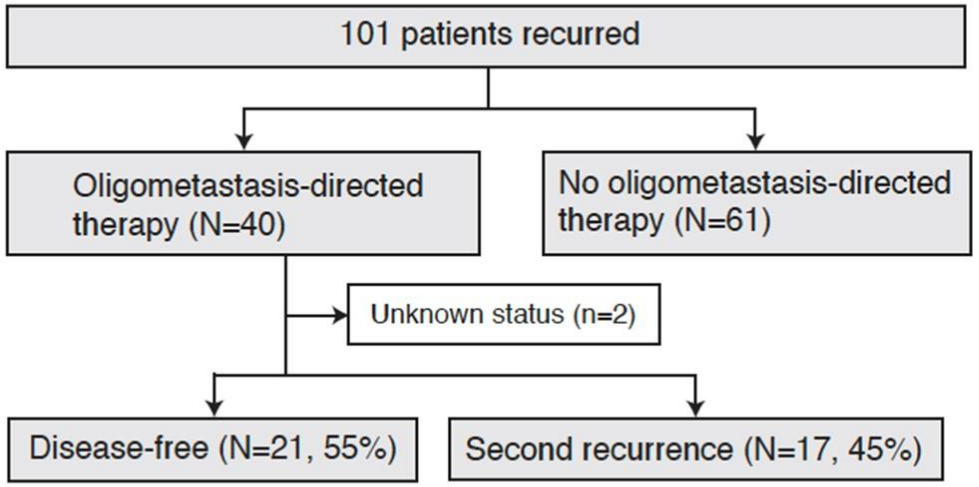
ctDNA-negative	225	224	223	219	211	201	183	151	42	2	1	0
ctDNA-positive	23	19	14	10	10	8	3	3	1	0		

ctDNA status (surveillance)	ctDNA-negative	ctDNA-positive
Numbers of events (%)	6/225 (2.67)	21/23 (91.30)
2-year DFS post surgery, % (95% CI)	96.60 (92.44-98.49)	13.04* (3.27-29.72)
Median DFS post surgery, months (95%)	Not reached	9.44 (7.86-17.03)

*Most recurrences occurred within the1st year.

*85% of molecular recurrences by 15 months

ctDNA testing was associated with higher oligometastasis-directed therapy



Oligometastasis-directed therapy type	N
Surgery	30
Radiofrequency Ablation (RFA)	3
Microwave Ablation (MWA)	2
Stereotactic Body Radiation Therapy (SBRT)	2
Y90 radiotherapy	2
Chemoradiation	1

ASCO Gastrointestinal Cancers Symposium

AGITG
AUSTRALASIAN GASTRO-INTESTINAL TRIALS GROUP

Circulating Tumor DNA Analysis Informing Adjuvant Chemotherapy in Locally Advanced Rectal Cancer

The Randomized AGITG DYNAMIC-Rectal Study

Jeanne Tie

Peter MacCallum Cancer Centre and Walter & Eliza Hall Institute of Medical Research, Melbourne, Australia

On behalf of the DYNAMIC-RECTAL Investigators

Joshua D Cohen, Yuxuan Wang, Chris Brown, Rachel Wong, Jeremy Shapiro, Rob Campbell, Fiona Day, Theresa Hayes, Morteza Aghmesheh, Christos Karapetis, Maria Popoli, Lisa Dobbyn, Janine Ptak, Natalie Silliman, Christopher Douville, Nickolas Papadopoulos, Kenneth Kinzler, Bert Vogelstein, Peter Gibbs

DYNAMIC-Rectal Study Design (Phase 2 Study)

ACTRN12617001560381

Locally Advanced Rectal Cancer

- cT3-4 and/or N+
- Pre-op LCCRT
- R0 TME surgery
- ECOG 0 – 2
- No metastasis on CT CAP at diagnosis
- Provision of adequate tumor tissue within 5 weeks post-op

ctDNA Analysis
Week 4 + 7 post-op

R
2:1

Stratification
ypN stage
Participating site

ctDNA-Informed Management

- **ctDNA-Pos → 4M Adjuvant Chemo** (oxaliplatin-based or single agent FP)
- **ctDNA-Neg + ypN0 → Observation**
- **ctDNA-Neg + ypN+ → Clinician's choice**

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

Standard Management

Adjuvant treatment decisions at clinician's discretion

Endpoints

Primary
- Proportion receiving adjuvant chemo

Key Secondary
- 3-year RFS (non-inferiority)

Secondary
- OS
- ctDNA dynamics

- Target sample size 408: 80% power with 95% confidence to demonstrate non-inferiority margin of at most 10%
- Ceased recruitment early (due to COVID-19 and increasing adoption of TNT) → **230 eligible patients analyzed**

PRESENTED BY: Jeanne Tie, MBChB FRACP MD

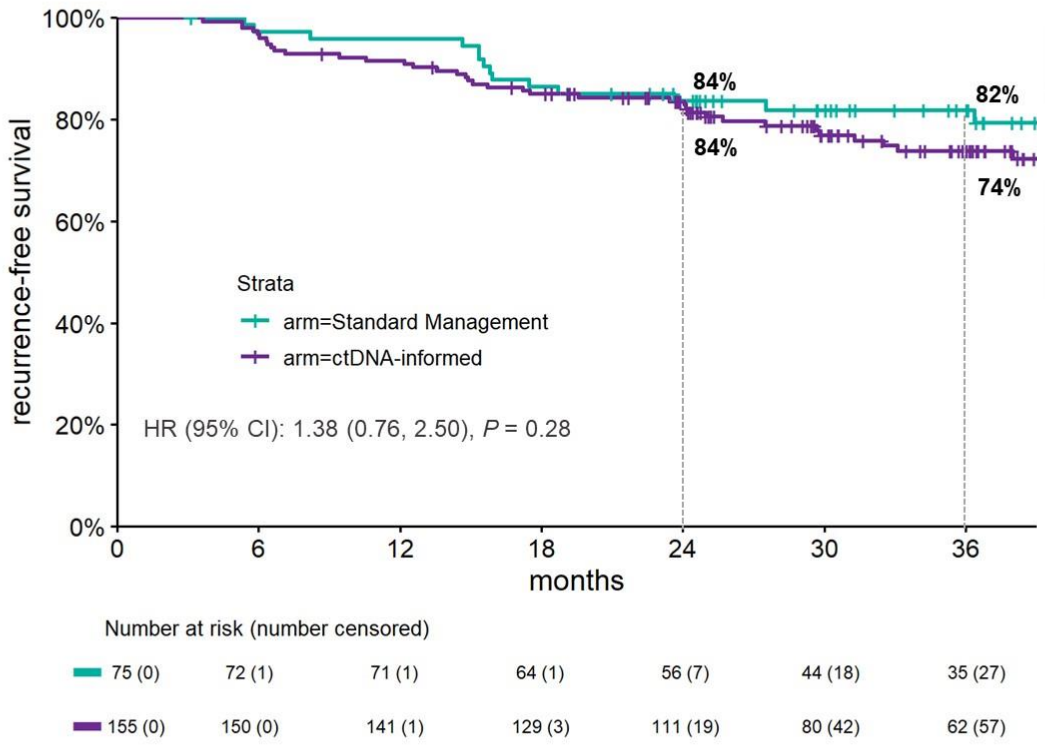
Recurrence-Free Survival

Median follow-up 36 months

-23% with cN2

-30% with pN+

-15% pCR

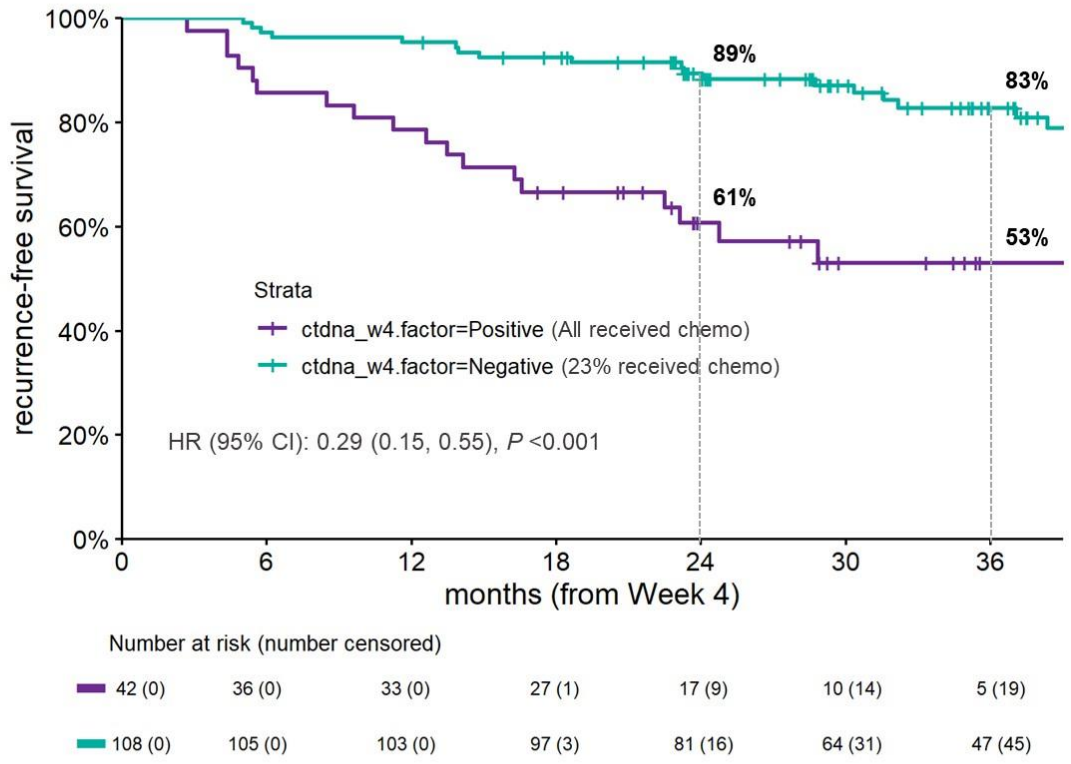


Adjuvant Treatment Delivery

Treatment Information	ctDNA-Informed N = 155	Standard N = 75	P
Adjuvant chemo commenced, n	71 **(46%)**	58 **(77%)**	<0.001
ctDNA +ve ctDNA –ve ctDNA unknown	42 (27%) 25 (16%) 4 (3%)		
Chemo regimen, n Oxaliplatin-based doublet Single agent	 43/155 **(28%)** 28/155 **(18%)**	 19/75 **(25%)** 39/75 **(52%)**	 --
Time to commencing chemotherapy, median (IQR), days	69 (54, 80)	56 (49, 62)	--
Treatment duration, median (IQR), weeks	15 (11, 18)	14 (11, 17)	--
Completed planned treatment, n	57/71 (80%)	41/58 (71%)	--

PRESENTED BY: Jeanne Tie, MBChB FRACP MD

Recurrence-Free Survival and ctDNA Status



DYNAMIC-Rectal Summary

- ctDNA-informed approach to adjuvant therapy for locally advanced rectal cancer following neoadjuvant chemoradiation and surgery was associated with a reduced rate of chemotherapy administration (46% vs 77%, p <0.001)
- A significant proportion of ctDNA-negative patients (23%) received adjuvant chemotherapy
- Small sample size precludes any conclusions to be drawn about the non-inferiority in recurrence-free survival of ctDNA-informed vs standard management
- Risk of recurrence was lower in post-op ctDNA-negative patients compared to ctDNA-positive patients (3-year RFS 83% vs 53%)
- The most common site of relapse in ctDNA-negative patients was the lung (83%) whilst liver (69%) was the dominant site of relapse in ctDNA-positive patients

ASCO Gastrointestinal Cancers Symposium

Nivolumab plus ipilimumab vs chemotherapy as first-line treatment for microsatellite instability-high/ mismatch repair-deficient metastatic colorectal cancer: first results of the CheckMate 8HW study

Thierry Andre,[1] Elena Elez,[2] Eric Van Cutsem,[3] Lars Henrik Jensen,[4] Jaafar Bennouna,[5] Guillermo Ariel Mendez,[6] Michael Schenker,[7] Christelle de la Fouchardiere,[8] Maria Luisa Limon,[9] Takayuki Yoshino,[10] Jin Li,[11] Heinz-Josef Lenz,[12] Jose Manzano Mozo,[13] Giampaolo Tortora,[14] Rocio Garcia-Carbonero,[15] Elvis Cela,[16] Yingsi Yang,[16] Ming Lei,[16] Lixian Jin,[16] Sara Lonardi[17]

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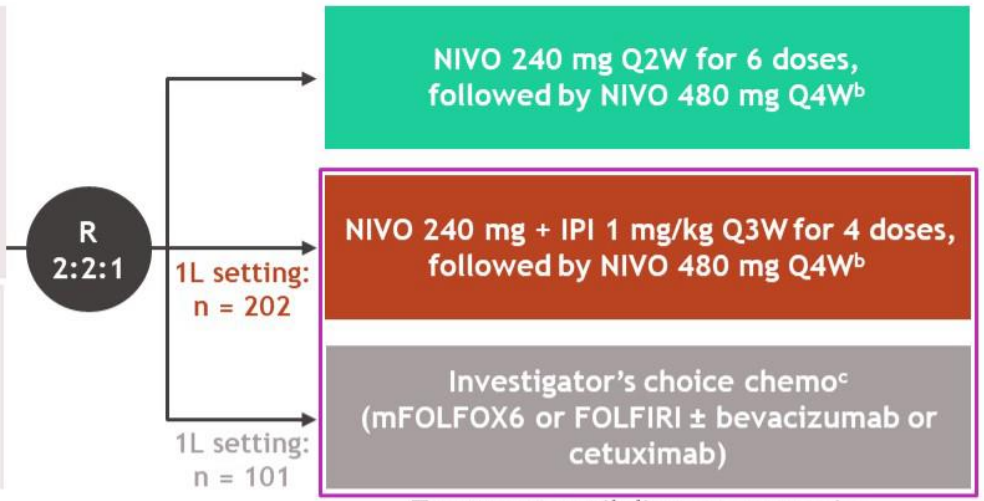
Abstract number LBA768

CheckMate 8HW study design (Validation for CheckMate 142)

- CheckMate 8HW is a randomized, multicenter, open-label phase 3 study[a]

Key eligibility criteria:
- Histologically confirmed unresectable or metastatic CRC
- MSI-H/dMMR status by local testing
- ECOG PS 0 or 1

Stratification factors:
- Prior lines of treatment (0 vs 1 vs ≥ 2)
- Primary tumor location (right vs left)



Treatment until disease progression, unacceptable toxicity, withdrawal of consent (all arms), or a maximum treatment duration of 2 years (NIVO and NIVO + IPI arms only)

Dual primary endpoints in patients with centrally confirmed MSI-H/dMMR status[d]:
- PFS by BICR[e] (NIVO + IPI vs chemo in the 1L setting)
- PFS by BICR[e] (NIVO + IPI vs NIVO across all lines)

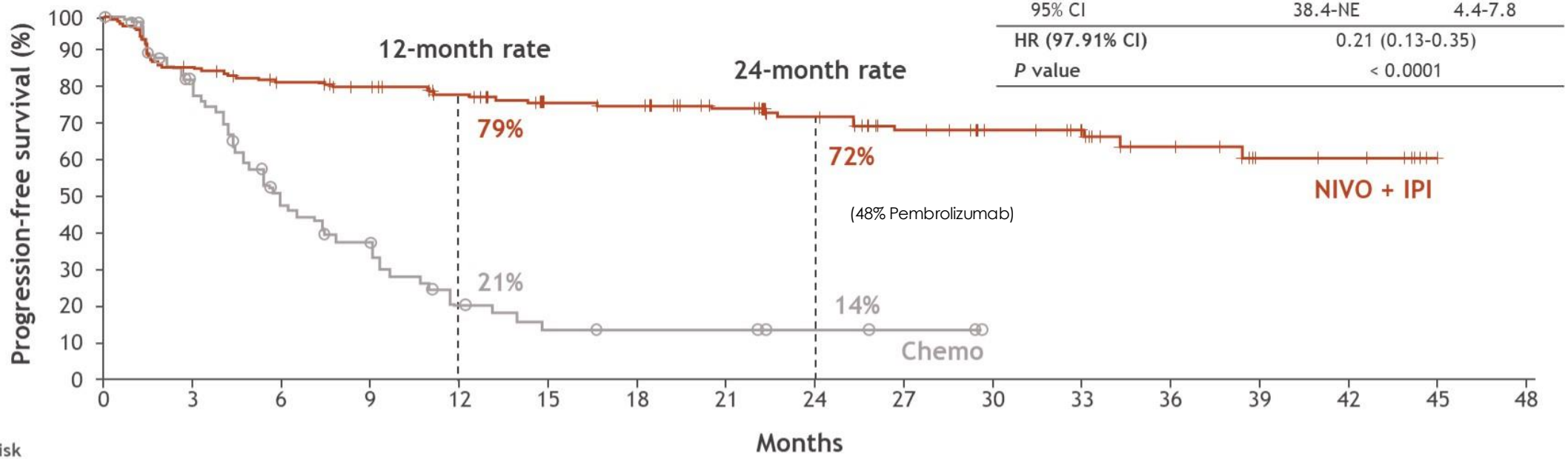
Other select endpoints:
- Safety
- OS; ORR by BICR[e]; PROs

- At data cutoff (October 12, 2023), the median follow-up[f] was 24.3 months

[a]ClinicalTrials.gov. NCT04008030. [b]Patients with ≥ 2 prior lines are randomized only to the NIVO or NIVO + IPI arms. [c]Patients receiving investigator's choice of chemotherapy are eligible to receive NIVO + IPI upon progression (crossover treatment). [d]Confirmed using either immunohistochemistry and/or polymerase chain reaction-based tests. [e]Evaluated using RECIST v1.1. [f]Time between randomization and last known date alive or death.

Progression-free survival

1L centrally confirmed MSI-H/dMMR	NIVO + IPI (n = 171)	Chemo (n = 84)
Median PFS,[a,b] mo	NR	5.9
95% CI	38.4-NE	4.4-7.8
HR (97.91% CI)	0.21 (0.13-0.35)	
P value	< 0.0001	



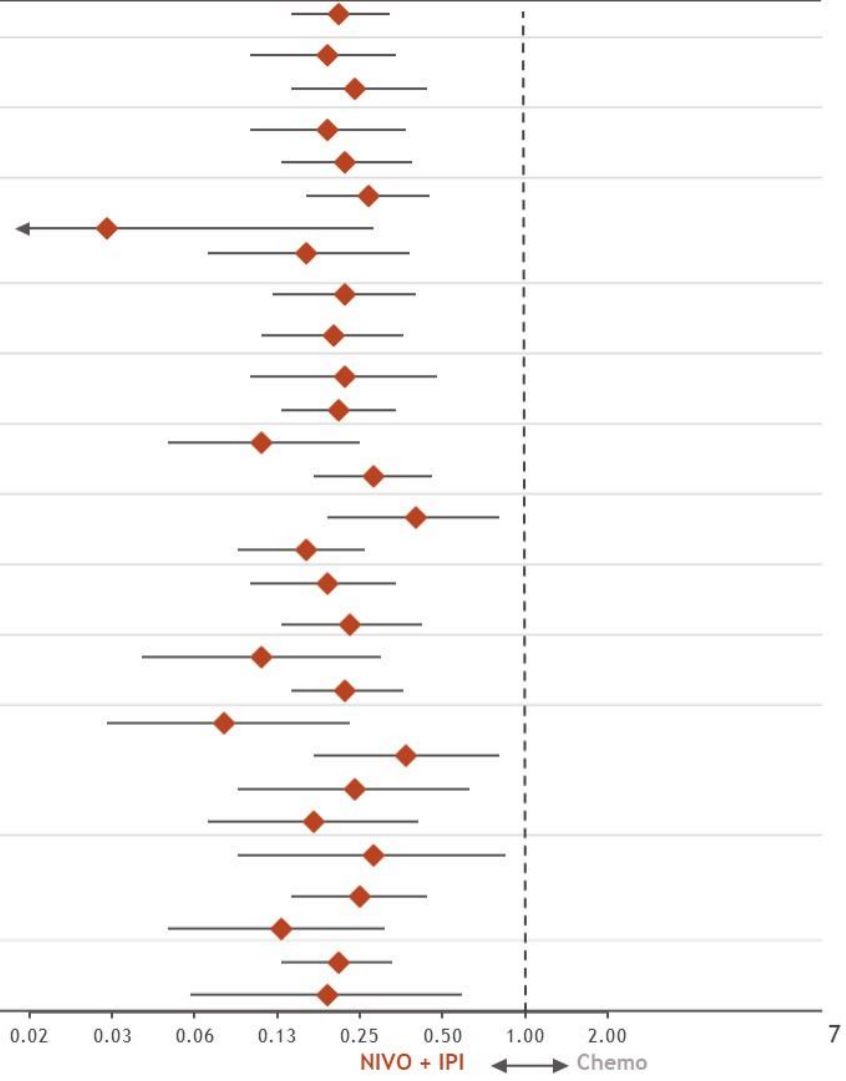
No. at risk																	
NIVO + IPI	171	144	132	122	108	95	92	77	64	53	42	37	22	10	9	1	0
Chemo	84	53	29	20	10	6	5	5	3	2	0	0	0	0	0	0	0

- PFS benefit with NIVO + IPI vs chemo was robust and consistent across the sensitivity analyses, including PFS by BICR in 1L all randomized patients (HR, 0.32; 95% CI, 0.23-0.46)

[a]Per BICR. [b]Median follow-up, 24.3 months.

Progression-free survival subgroup analysis

Category (1L centrally confirmed MSI-H/dMMR)	Subgroup	Median PFS,[a] mo		Unstratified HR
		NIVO + IPI	Chemo	
Overall (N = 255)		NR	5.9	0.21
Age, years	< 65 (n = 138)	NR	5.7	0.19
	≥ 65 (n = 117)	NR	5.9	0.24
Sex	Male (n = 117)	NR	5.9	0.19
	Female (n = 138)	NR	6.2	0.22
Region	US/Canada/Europe (n = 167)	NR	5.7	0.27
	Asia (n = 28)	NR	7.4	0.03
	Rest of world (n = 60)	NR	6.2	0.16
ECOG PS	0 (n = 142)	NR	9.0	0.22
	≥ 1 (n = 113)	NR	4.2	0.20
Tumor sidedness	Left (n = 70)	NR	4.4	0.22
	Right (n = 185)	NR	7.1	0.21
Liver metastases[a]	Yes (n = 87)	NR	5.9	0.11
	No (n = 166)	NR	5.4	0.28
Lung metastases[a]	Yes (n = 53)	13.2	4.9	0.40
	No (n = 200)	NR	6.2	0.16
Peritoneal metastases[a]	Yes (n = 115)	NR	4.4	0.19
	No (n = 138)	NR	7.4	0.23
Tumor cell PD-L1 expression	≥ 1% (n = 55)	NR	3.4	0.11
	< 1% (n = 191)	NR	6.5	0.22
BRAF/KRAS/NRAS mutation status	*BRAF/KRAS/NRAS* all wild type (n = 58)	34.3	5.4	0.08
	BRAF mutant (n = 72)	NR	9.2	0.37
	KRAS or *NRAS* mutant (n = 45)	NR	5.7	0.24
	Unknown (n = 74)	NR	4.9	0.17
Lynch syndrome	Yes (n = 31)	NR	7.4	0.28
	No (n = 152)	NR	6.2	0.25
	Unknown (n = 66)	NR	5.5	0.13
Prior surgery related to current cancer	Yes (n = 222)	NR	7.1	0.21
	No (n = 33)	NR	3.0	0.19



[a]Per BICR.

Summary

- NIVO + IPI demonstrated superior PFS vs chemo ± bevacizumab or cetuximab in previously untreated patients with centrally confirmed MSI-H/dMMR mCRC (HR, 0.21 [97.91% CI, 0.13–0.35]; *P* < 0.0001)
  - 79% reduction in the risk of disease progression or death
  - Early and sustained separation of PFS curves starting at approximately 3 months
  - 24-month PFS rates for NIVO + IPI vs chemo: 72% vs 14%
  - PFS benefit across all prespecified subgroups, including patients with *KRAS* or *NRAS* mutations and those with baseline liver, lung, or peritoneal metastases
- NIVO + IPI had a different safety profile compared with chemo, with fewer grade 3/4 TRAEs, and safety was consistent with the established profiles of each individual drug
  - No new safety signals were identified
- The study is ongoing to assess the other dual primary endpoint of PFS by BICR (NIVO + IPI vs NIVO across all lines), as well as secondary endpoints including OS
- **These results support NIVO + IPI as a standard-of-care 1L treatment option for patients with MSI-H/dMMR mCRC**

2024 ASCO ANNUAL MEETING

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

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

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

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PRESENTED BY:

TransMet Trial : Eligibility criteria

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

TransMet Trial : Endpoints

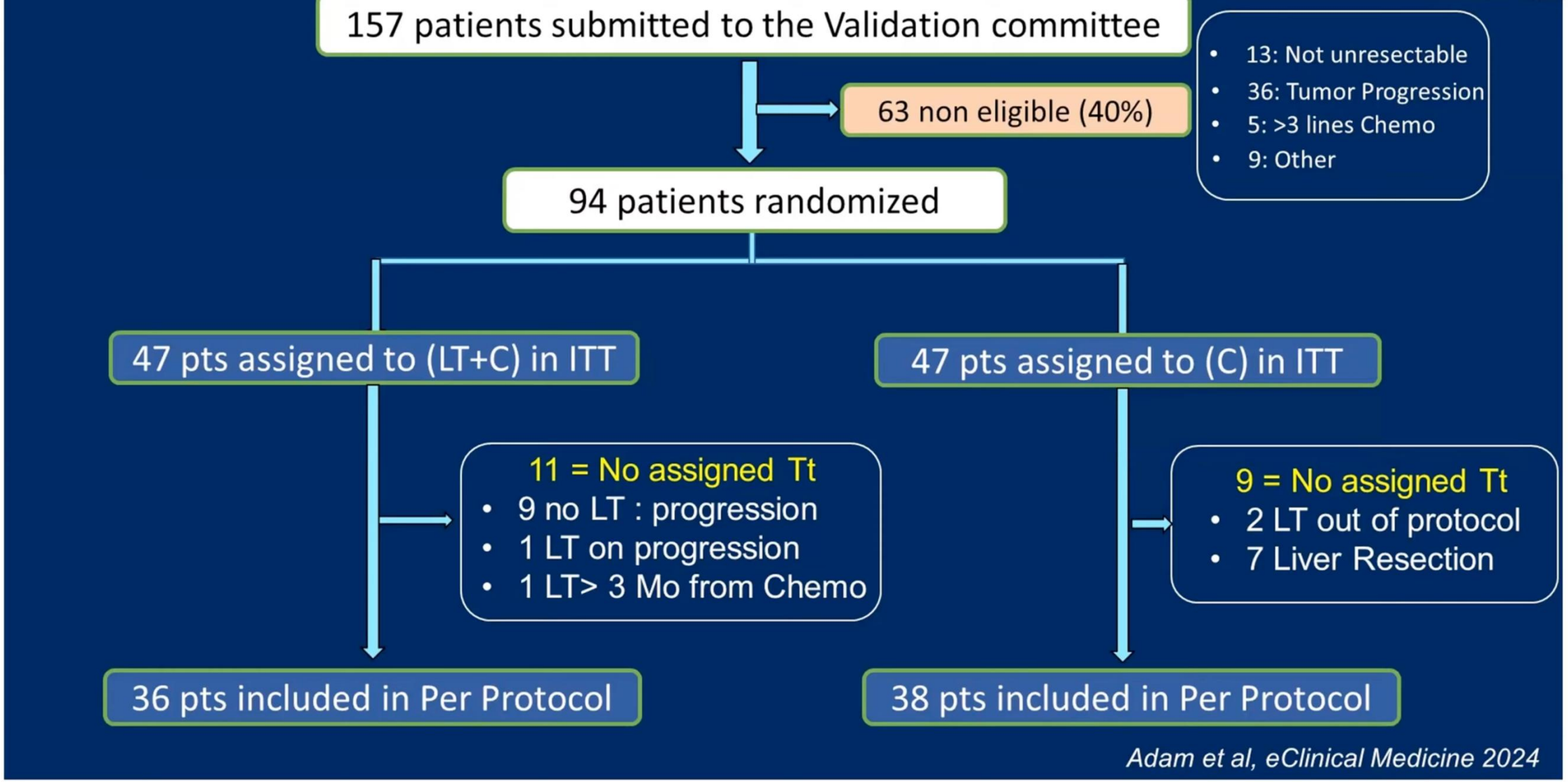
Primary Endpoint

- **Overall Survival (OS) at 5 years**

Secondary Endpoints

- OS at 3 years
- Progression-Free Survival (PFS) at 3 and 5 years*
- Recurrence rate at 3 and 5 years

* Progression : Recurrence in the LT+C group / Progression in the C group



2024 ASCO ANNUAL MEETING #ASCO24

PRESENTED BY: Prof René Adam

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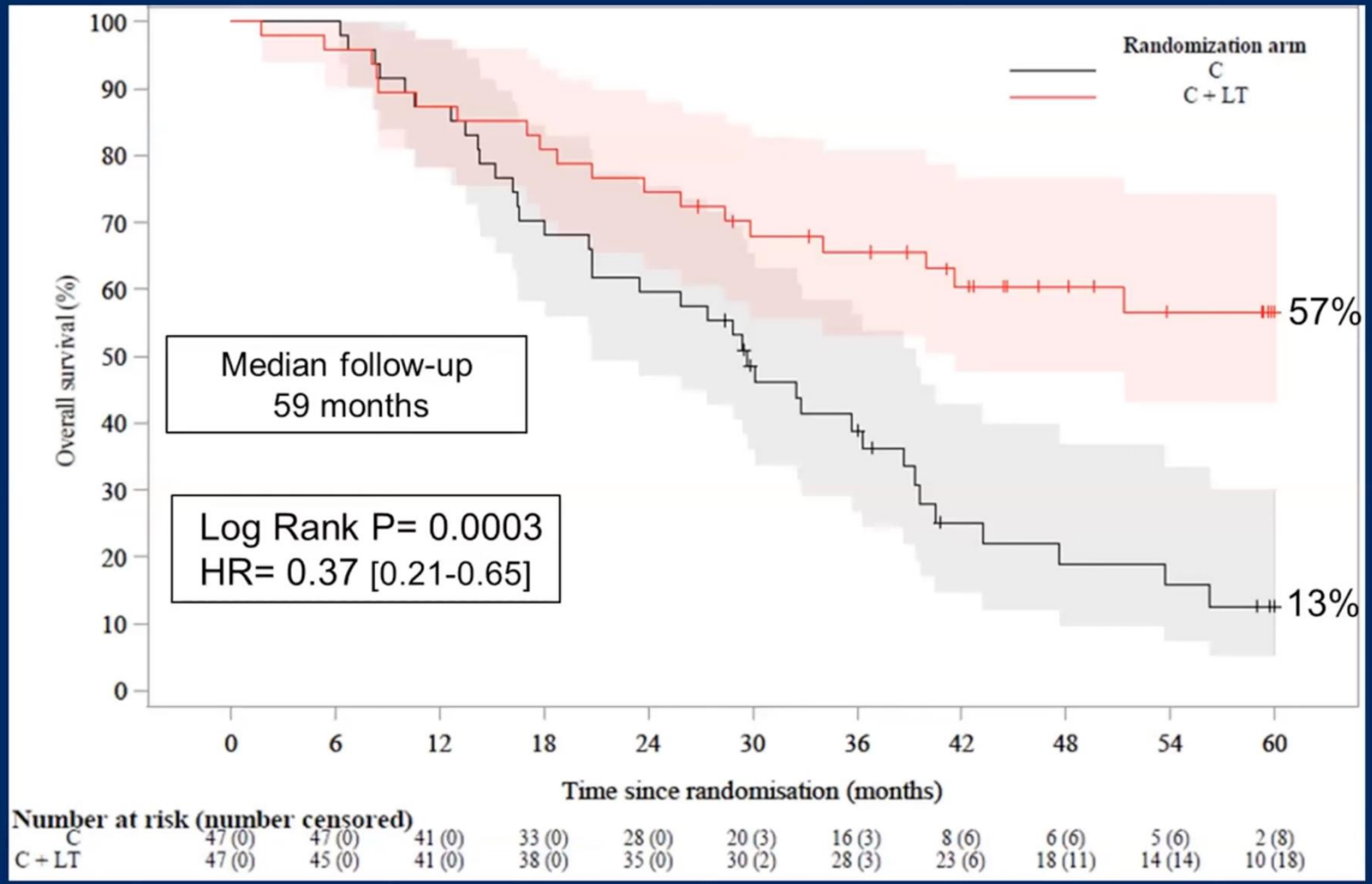
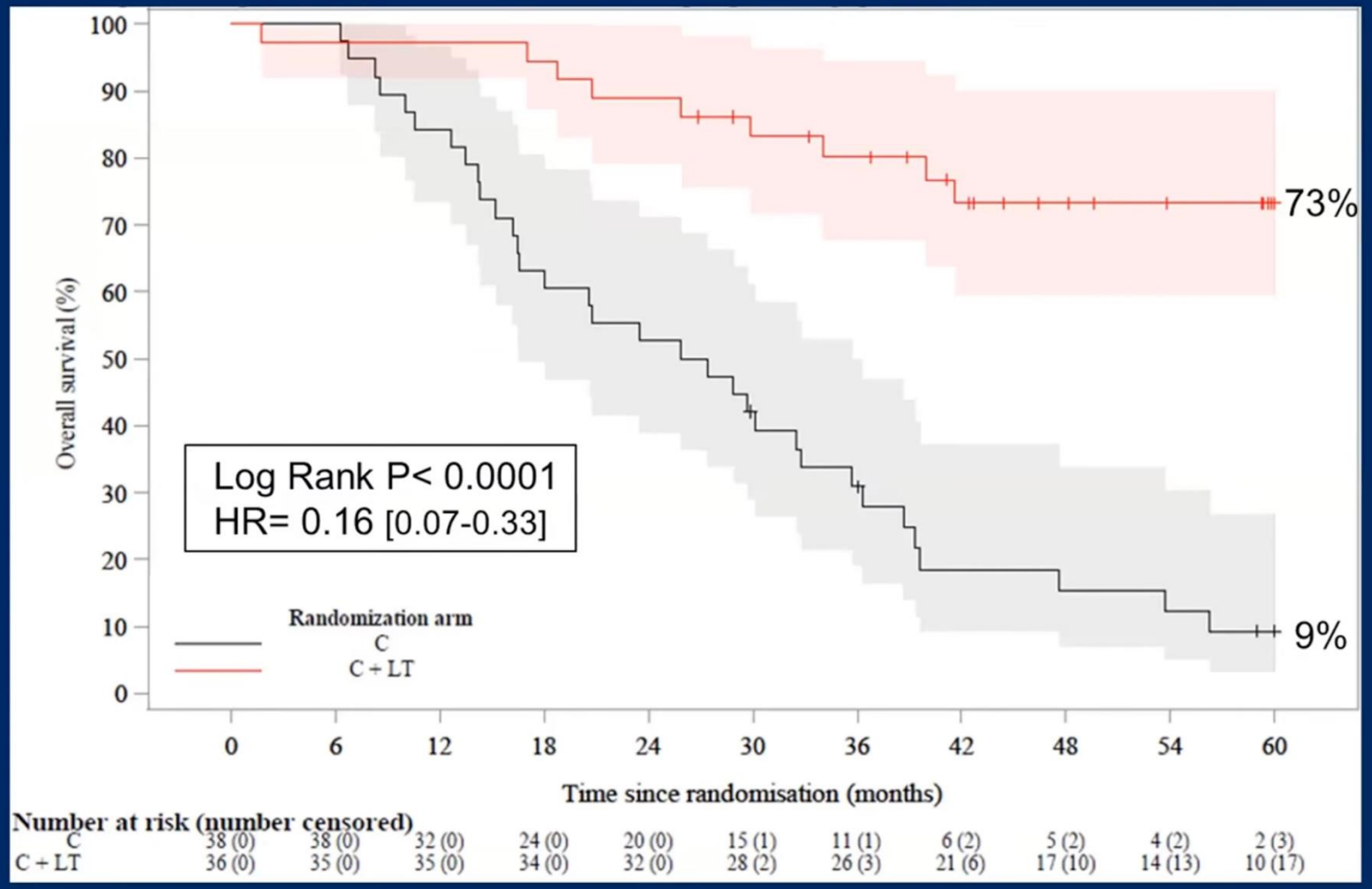
TransMet Trial : Primary Endpoint 5-Yr OS (ITT)



PRESENTED BY: Prof René Adam

TransMet Trial : Primary Endpoint 5-Yr OS (Per Protocol)



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PRESENTED BY: Prof René Adam

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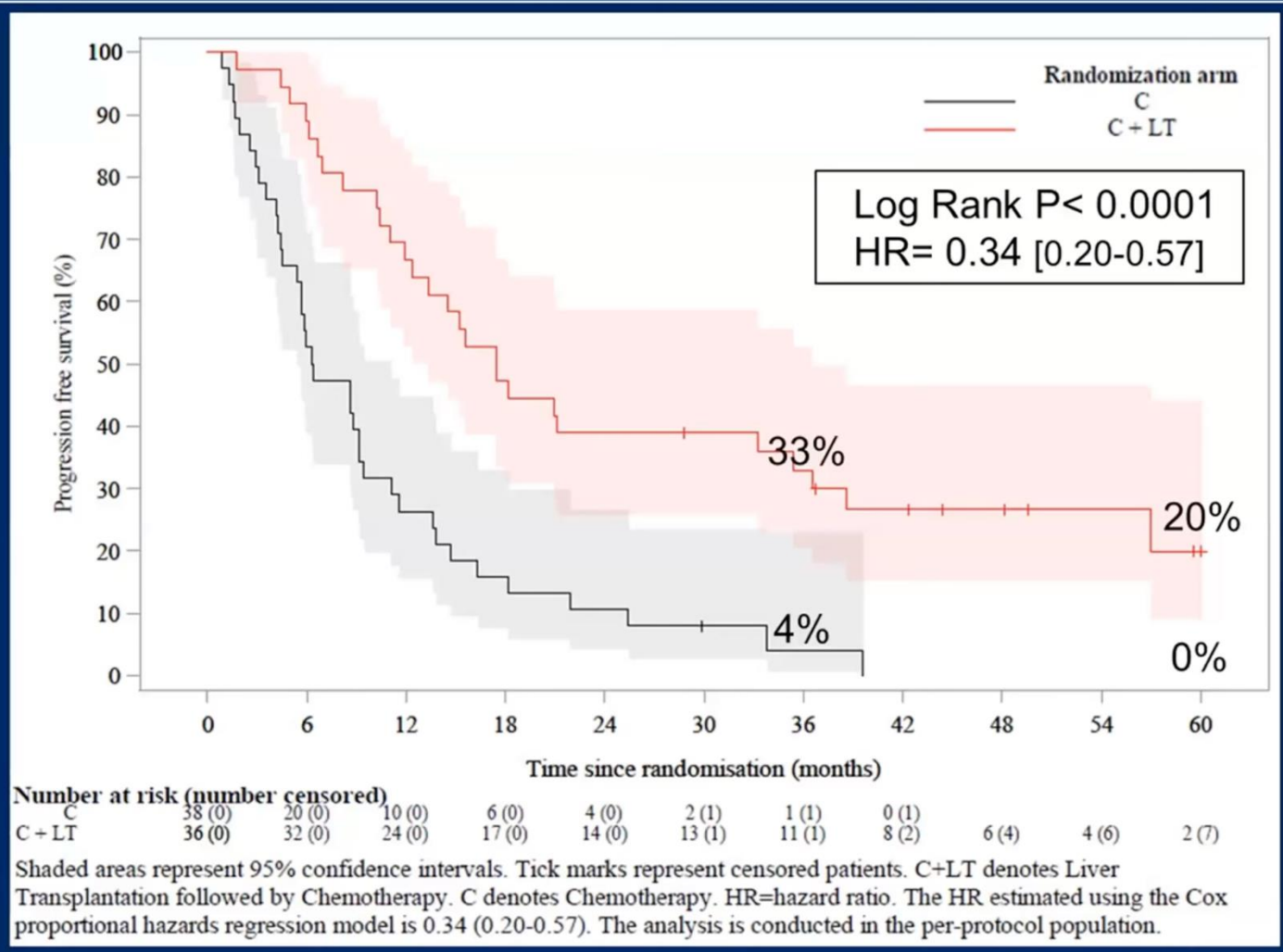
TransMet Trial : Secondary Endpoint 3–5–Yr PFS (Per Protocol)



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

Take Home messages from the TransMet trial

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

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

BARCELONA 2024 ESMO congress

Total Neoadjuvant Treatment (TNT) including Non-Operative Management (NOM) for Proficient Mismatch Repair Locally Advanced Rectal Cancer (pMMR LARC): First Results of NO-CUT Trial

Amatu A.[1], Zampino M. G.[2], Bergamo F.[3], Mosconi S.[4], Sibio D.[1], Gerardi M. A.[2], Prete A. A.[3], Filippone F. R.[4], Ferrari G.[1], Borin S.[2], Galuppo S.[3], Mariano S.[1], Tosi F.[1], Bonazzina E.[1], Patelli G.[1,5,6], Ghezzi S.[1], Lazzari L.[6], Bencardino K.[1], Sartore-Bianchi A.[1,5], and Siena S.[1,5]
on behalf of the NO-CUT Trial Cooperative Group

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[5] Università degli Studi di Milano, Milan, Italy
[6] IFOM ETS The AIRC Institute of Molecular Oncology

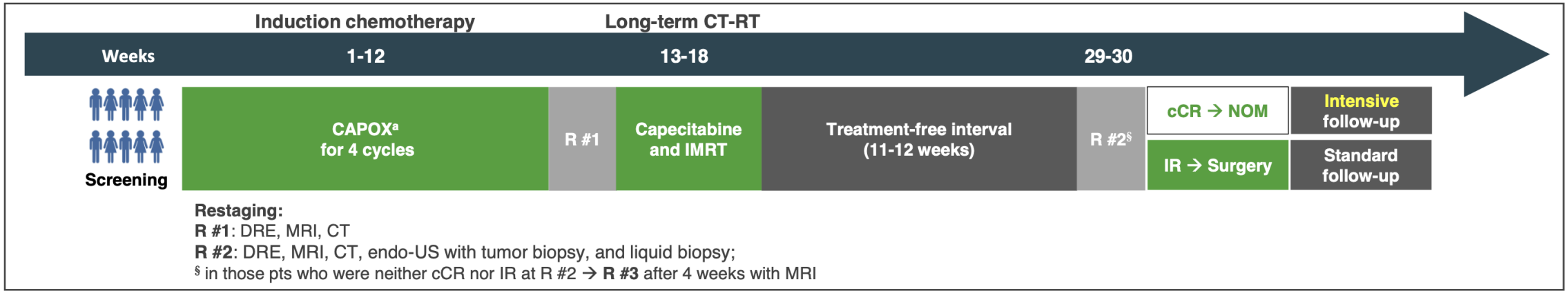
NO-CUT Trial
EudraCT 2017-3671-60

presented by Alessio Amatu, MD

ESMO 2024 Congress, Presidential Symposium Eyes to the Future, September 16, 2024

NO-CUT TRIAL design

180 patients with mid/low cT3-4 and/or cN1-2, cM0, pMMR/MSS, rectal adenocarcinoma; ECOG PS 0-1, fit for surgery



- **Primary endpoint**: % of patients alive and distant relapse free at 30 months ($DRFS_{30}$, H_0: 75% and H_1: 82%); at least 44 NOM patients were needed, with an α = 10% and β = 20% to reject H_0
- **Secondary endpoints**: cCR rate, organ preservation rate in NOM patients

Abbreviations: **cCR** = clinical complete response; **CT**: computed tomography scan with contrast medium of chest, abdomen, and pelvis; **CT-RT**: chemo-radiotherapy; **DRE**: digital rectal examination; **endo-US**: endoscopic Ultrasound; **IMRT**: intensive modulated radiation therapy; **IR**: incomplete response; **pMMR**: proficient mismatch repair; **MRI**: magnetic resonance imaging with contrast medium of pelvis; **NOM:** non-operative management; **R**: restaging. [a] FOLFOX 6 cycles if not eligible to CAPOX.

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NO-CUT Trial
EudraCT 2017-3671-60

Clinical tumor response to TNT

		cCR (%)	IR (%)	p-value
Number of patients		46 (26)	134 (74)	-
Tumor location	Low	26 (36)	47 (64)	0.017
	Medium	20 (19)	87 (81)	
Clinical T stage	T1	2 (100)	0 (0)	0.004
	T2	5 (39)	8 (61)	
	T3	37 (28)	96 (72)	
	T4	2 (6)	30 (94)	
Clinical TNM stage	II	9 (45)	11 (55)	0.065
	III	37 (23)	123 (77)	

- 180 patients, 59% mid-rectum
- 92% T3/T4
- 89% Stage 3

- 26% patients achieved cCR and proceeded with NOM
- 90% patients who had IR underwent surgery
- T stage was confirmed as a clinical predictor of cCR
- Tumor location (low) was associated with response

Abbreviations: **cCR** = clinical complete response; **IR**: incomplete response; **NOM:** non-operative management.

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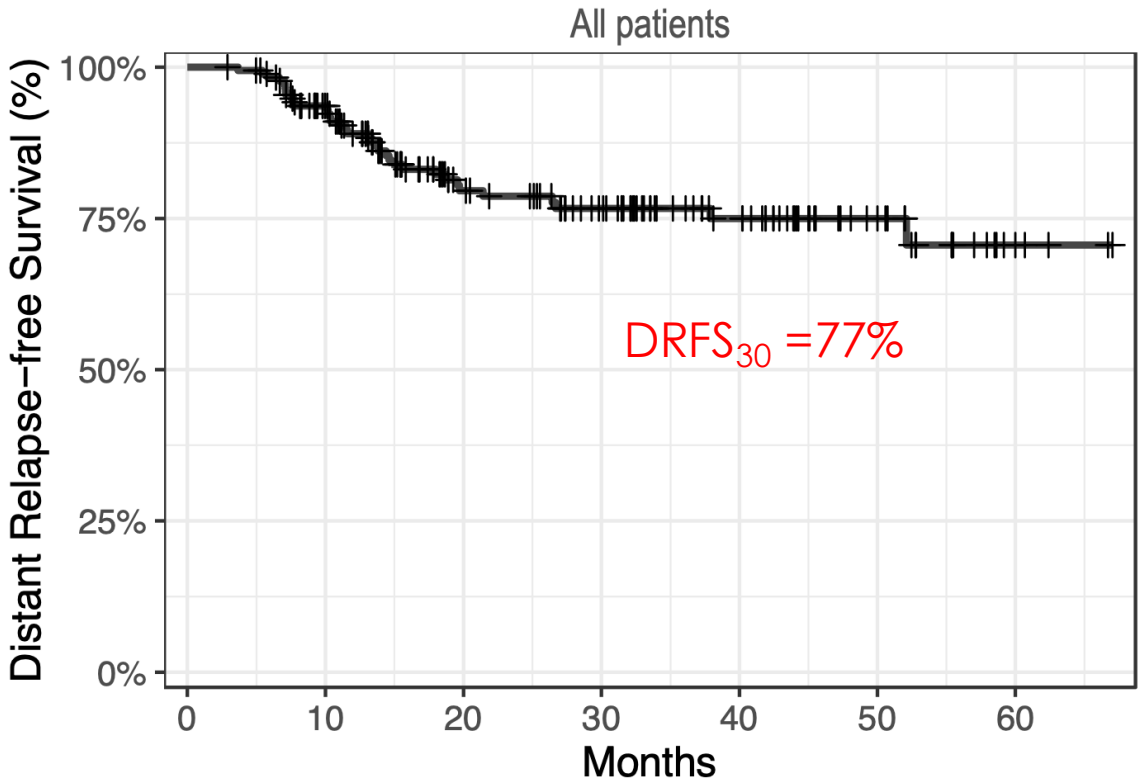
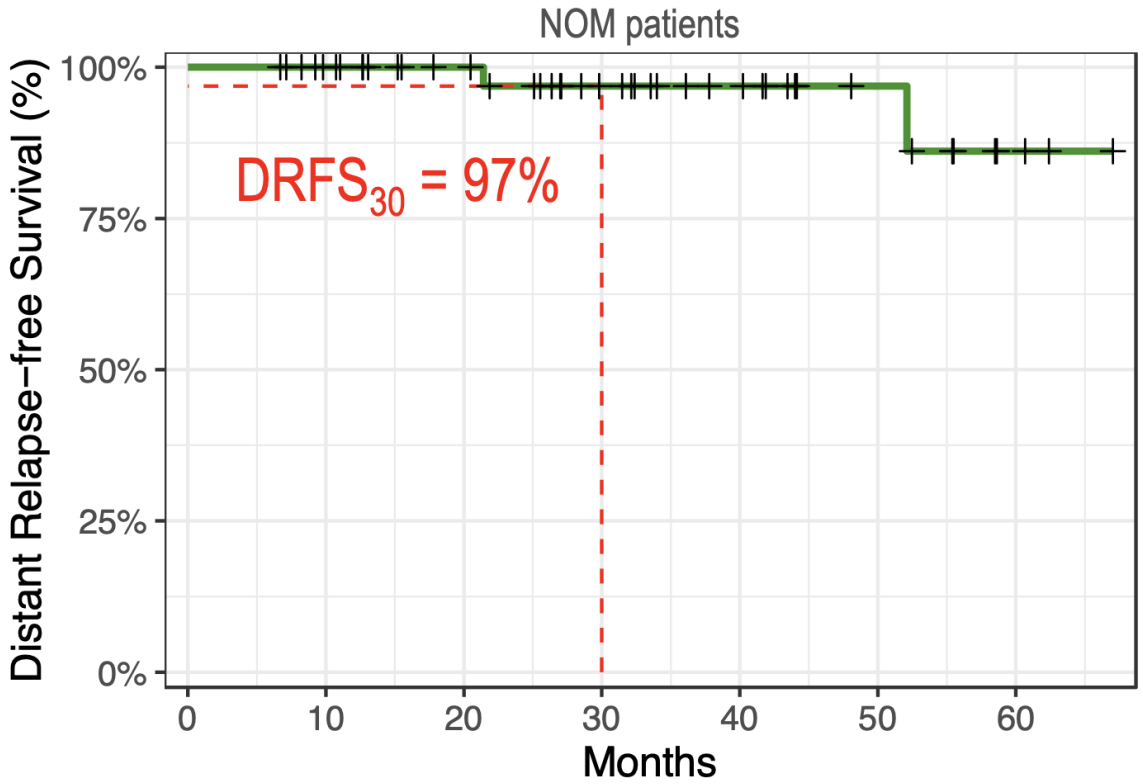
Primary Objective: Distant Relapse-Free Survival in NOM patients





Primary endpoint (Distant Relapse-Free Survival at 30 months, $DRFS_{30}$) was met:

- **In NOM pts (n = 46) $DRFS_{30}$ 96.9% (95%CI 91.0-100.0)**
- In **all pts** (n = 180) $DRFS_{30}$ 76.7% (95%CI 69.8-84.2)

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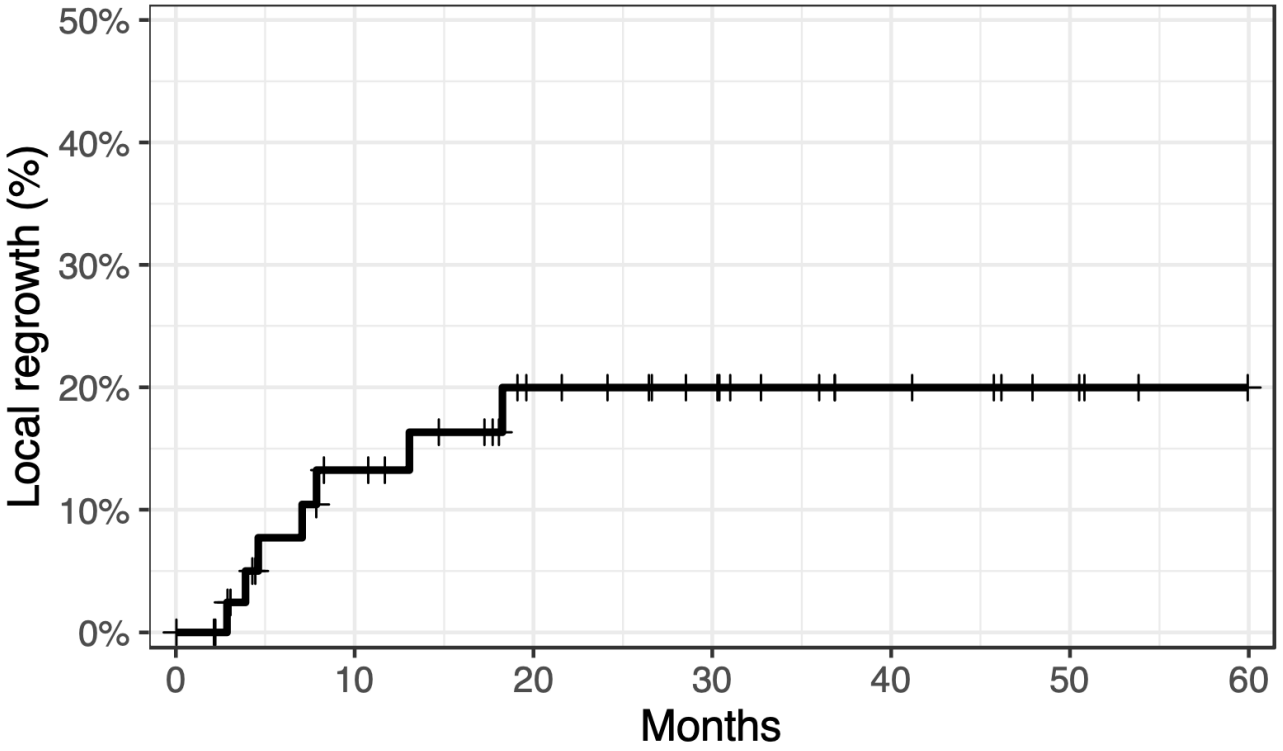
Secondary objective: Organ Preservation Rate in NOM patients



- **Organ preservation rate was 85% (39/46)**
- All patients with Local Regrowth (LR) underwent rescue surgery, 42% (3/7) sphincter sparing
- All LR occurred between 4 and 18 months

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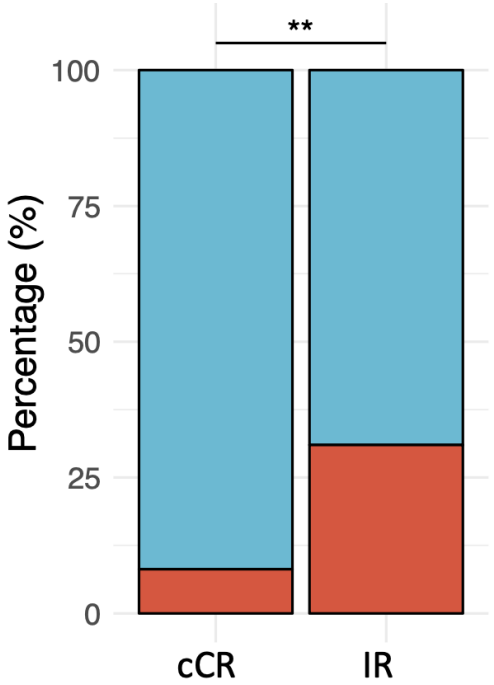
ctDNA status after TNT predicts clinical response and DRFS

ctDNA status according to clinical response (cCR vs IR)

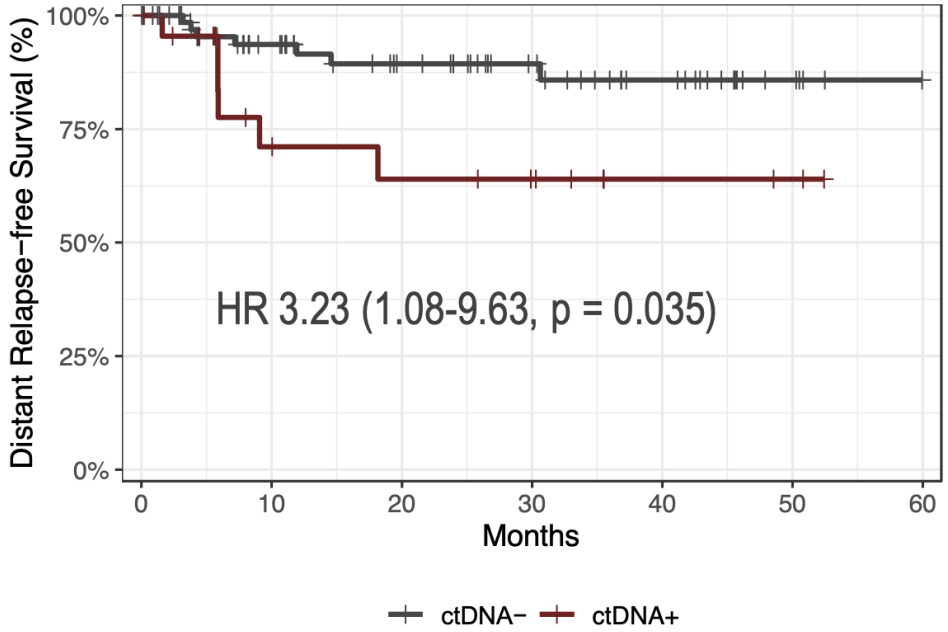


	cCR	IR
ctDNA- (%)	34 (92)	49 (69)
ctDNA+ (%)	3 (8)	22 (31)

**p = 0.008

- In 108 evaluable patients, absence of ctDNA was signficantly associated with tumor response

DRFS in overall population according to ctDNA status



- Patients with ctDNA+ had an increased risk for distant-relapse, regardless of surgery

DRFS	ctDNA-	ctDNA+
2-year	89.4% (81.6-97.9)	64% (44.3-92.5)
3-year	85.8% (76.0-96.9)	64% (44.3-92.5)

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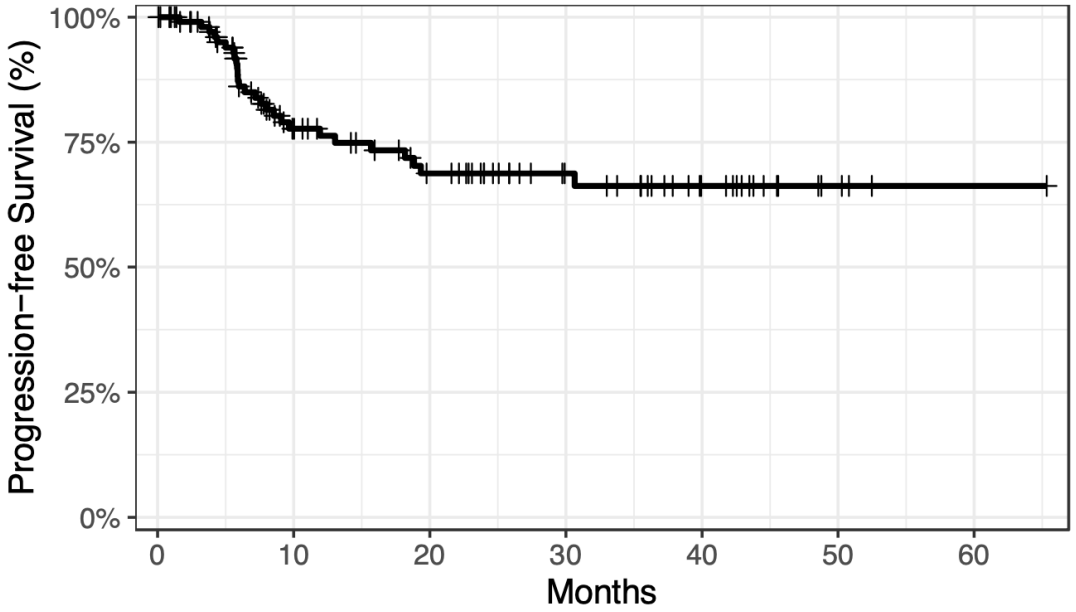
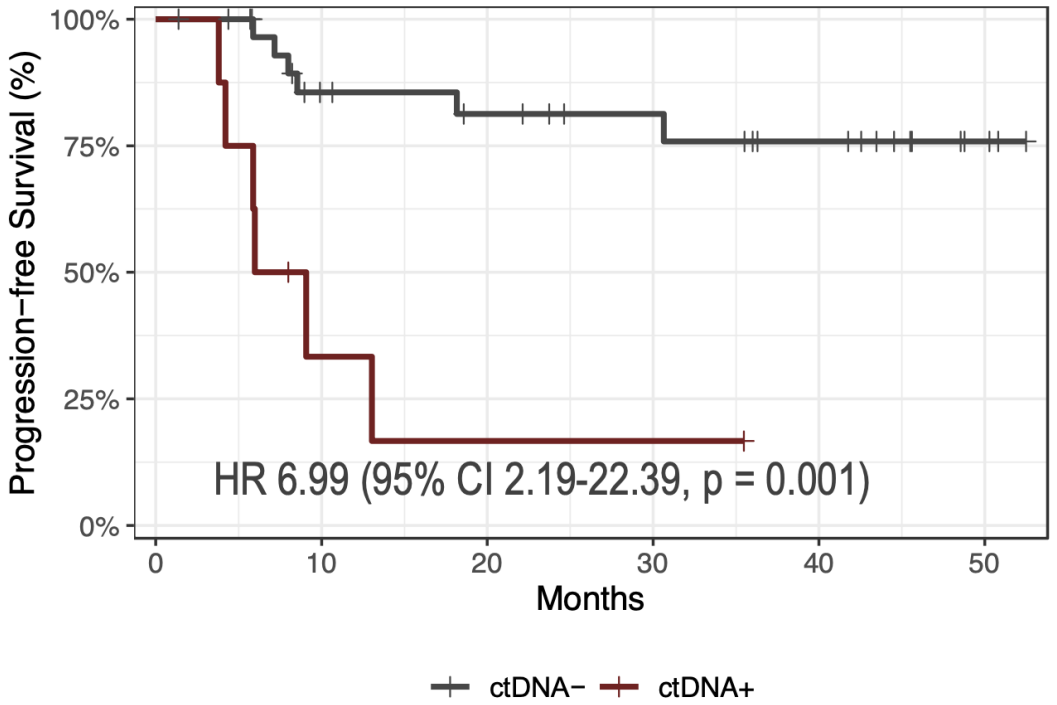
ctDNA status after surgery in IR patients predicts PFS

PFS after surgery (n=121)



PFS according to ctDNA status after surgery (n=43)



- In the 121 patients who undergo rectal surgery, 2y- and 3y-PFS rate was 68.7% (95% CI 59.2-69.8) and 66.2% (95% CI 56.1-78.2)
- Patients with ctDNA+ after surgery had a significant increased risk for progression

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Neoadjuvant immunotherapy in locally advanced MMR-deficient colon cancer

3-year disease-free survival from NICHE-2

M. Chalabi[1], L. van den Dungen, Y. Verschoor, S. Balduzzi, P. de Gooyer, N. Kok, E. Kerver, C. Grootscholten, E. Voest, J. Burger, E. Hendriks, T. de Wijkerslooth, A. Tin, T. Aukema, S. Oosterling, A. Aalbers, J. van den Berg, M. Van Leerdam, T. Schumacher, J. Haanen

[1]Netherlands Cancer Institute, Amsterdam

NICHE-2 study design

Key eligibility criteria

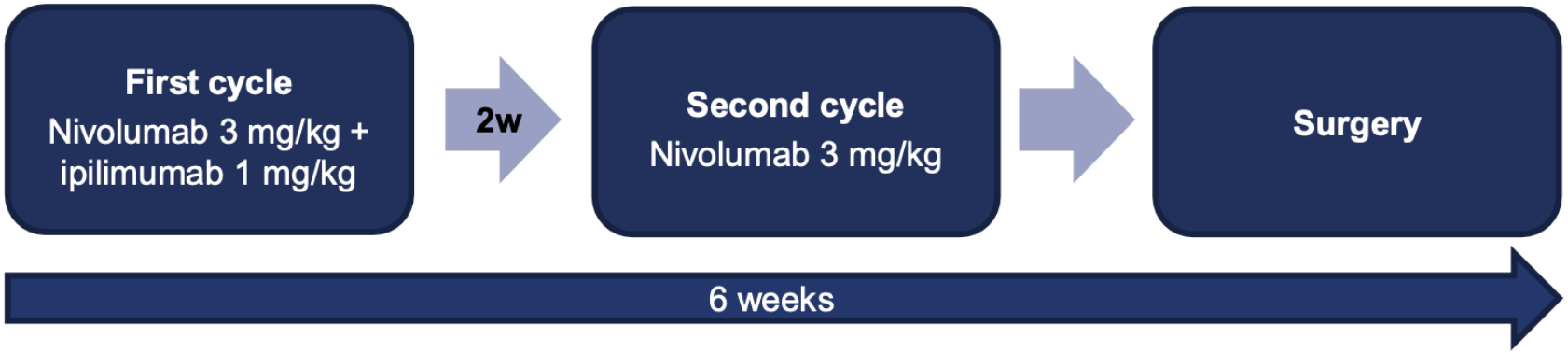
- Non-metastatic dMMR colon cancer, previously untreated
- cT3 and/or N+ based on radiographic staging
- No clinical or radiologic signs of obstruction or perforation

Investigat Basis of Trial

10-15% of non-metastatic colon cancers are dMMR

3yr RR for LACCa remains 20-40% despite SOC

Pathologic response 7% (FOxTROT)



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Endpoints and statistical design

- Two primary endpoints
  - Safety
  - **3-year disease free survival (DFS)**
- Secondary endpoints
  - Pathologic response rate
  - Translational research
  - **Circulating tumor DNA dynamics**

A 3-year DFS of 93% would be deemed successful, at a power of 80% and a two-sided alpha of 0.025 using a one-sample log rank test assuming a historical 82% DFS[1]

[1]Historical 82% DFS was calculated with the assumption of 60% stage III and 40% stage II tumors. The historical 3-year DFS used for these calculations was 75% for stage III tumors and 90% for stage II disease.

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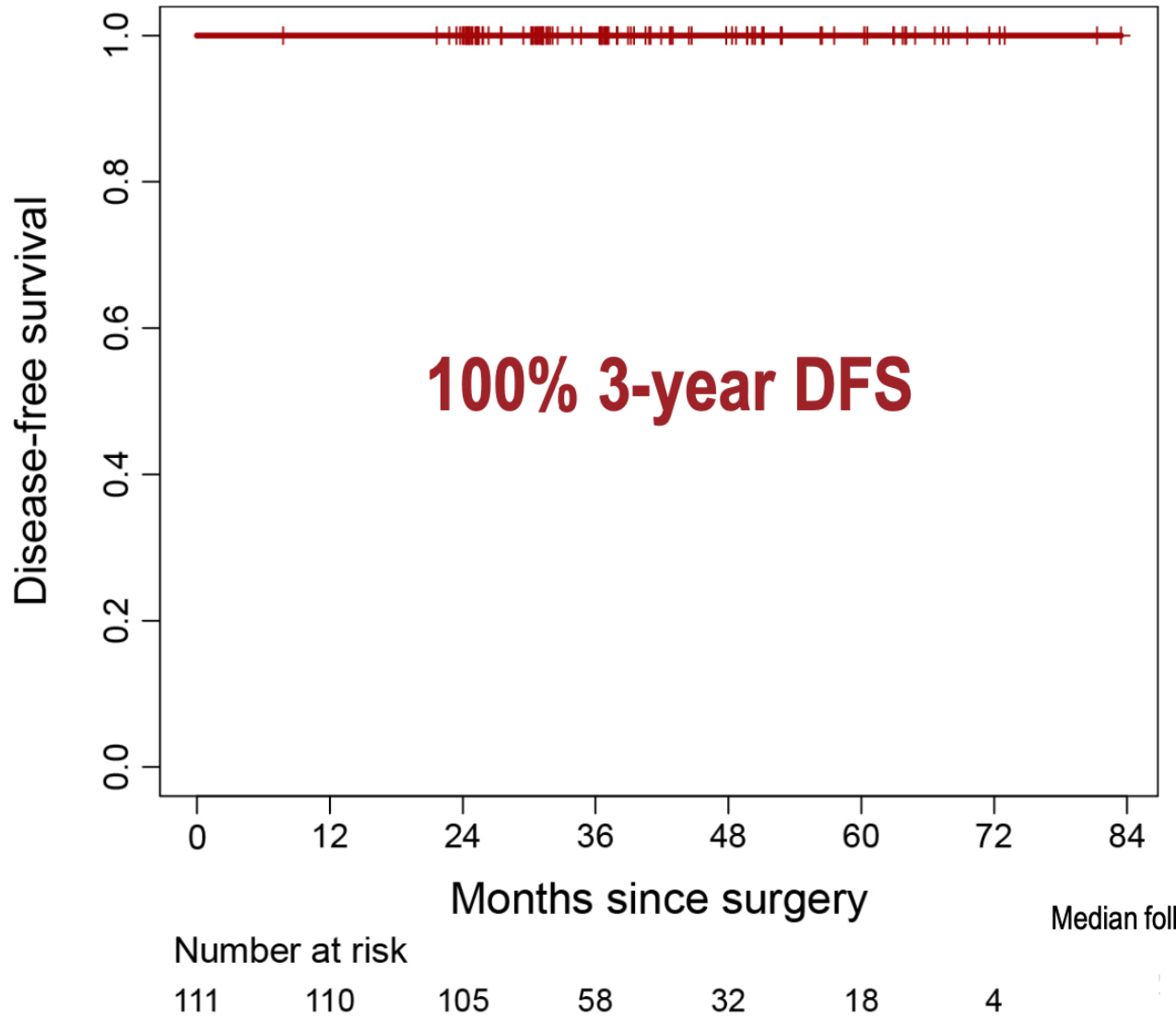
Results – 3-year disease-free survival 100%

Median F/U of 36 months

(7.8 to 83.4 range)

No Recurrences

105/111 with 2 yrs f/u



Median follow-up after surgery: 36.6 months (7.8 - 83.4)

Pathologic Response

- 98% of 111 pts
- 95% Major PR (<10% residual viable tumor)
- 68% Pathologic CR

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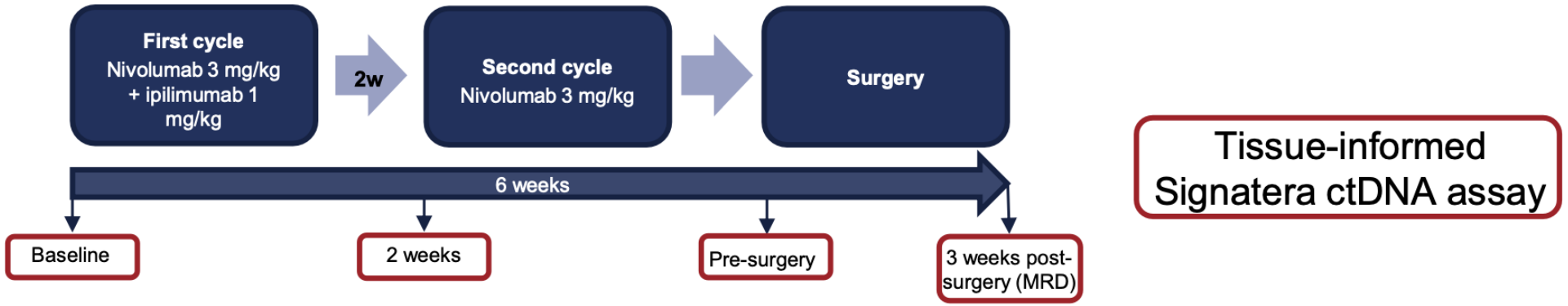
Data cut-off: 11 September 2024

Circulating tumor DNA in NICHE-2

1. Assess ctDNA at minimal residual disease (MRD) timepoint

2. Can ctDNA accurately predict pCR?
   - In NICHE-2: despite high pCR and MPR rates, inability to predict pathologic response with radiographic imaging



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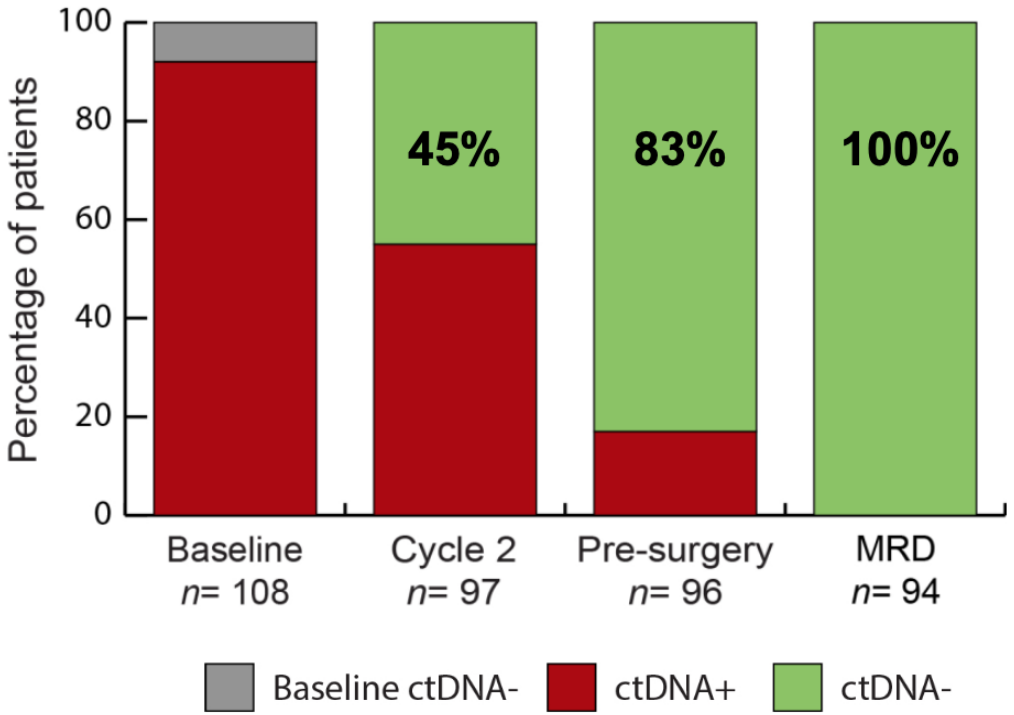
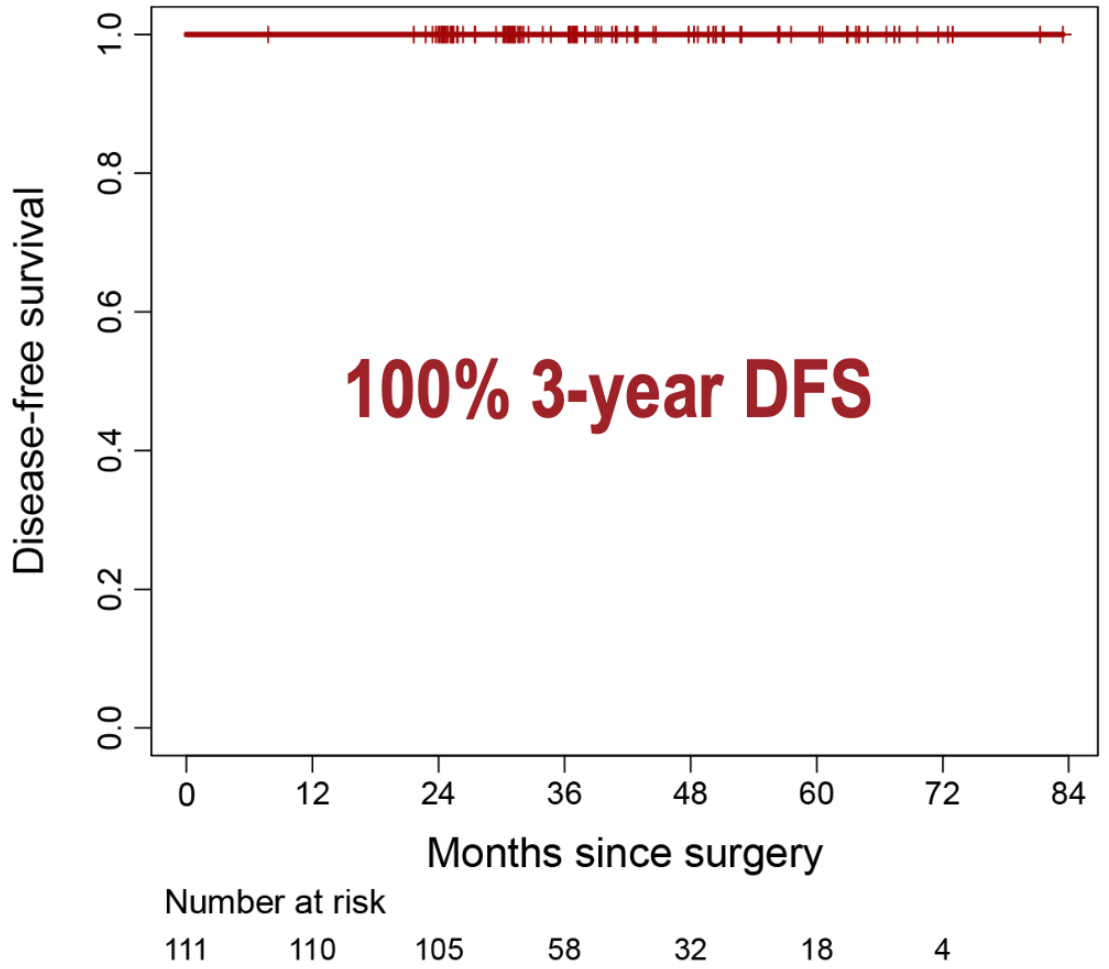
Chalabi et al. NEJM 2024; Hofste et al. Eur J Surg Oncol. 2023; Alden et al. Oncologist 2024; Kasi et al. ASCO GI 2024;

Minimal residual disease

All patients were ctDNA negative at the MRD time point (3 weeks after surgery)





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Thank You!

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