Carcinoma del colon retto – Biopsia liquida

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Circulating tumor DNA dynamics predict pathological response and guide therapy personalization in the neoadjuvant setting

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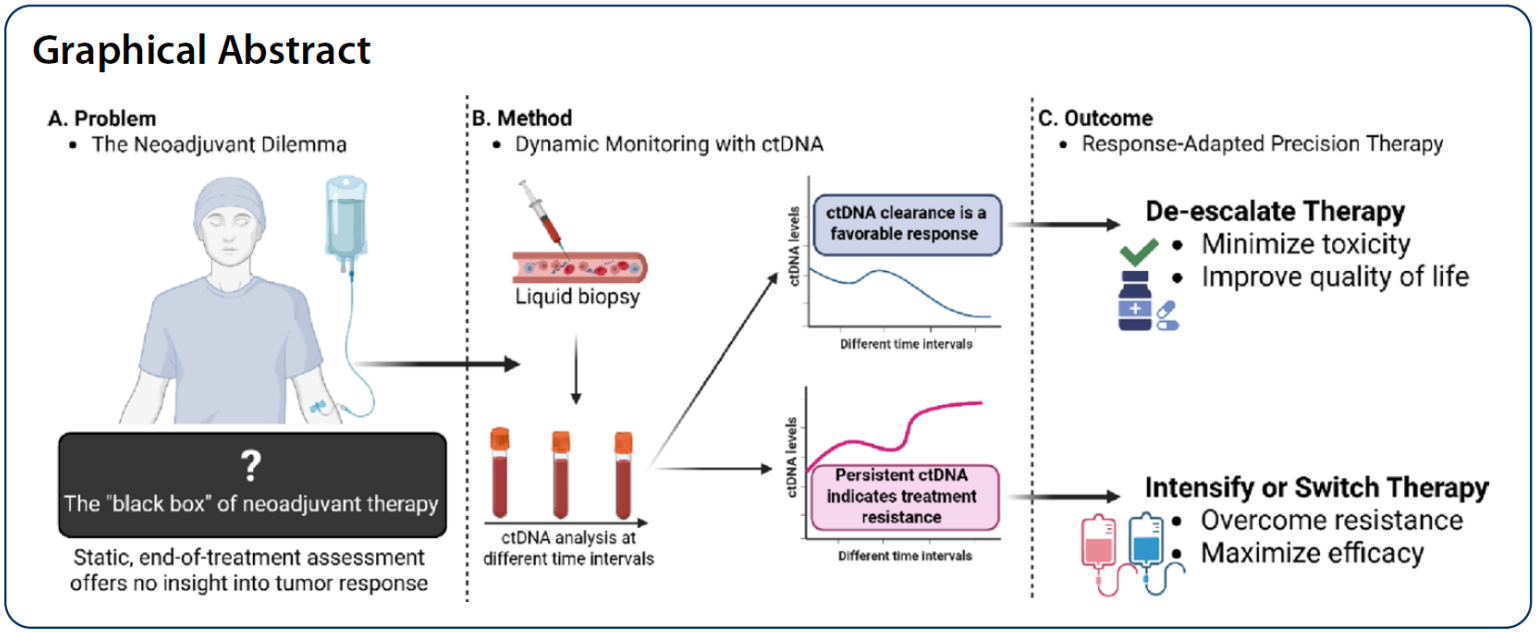
Ahmed *et al. Discover Oncology* (2026) 17:365
https://doi.org/10.1007/s12672-026-04495-2

Graphical Abstract



REVIEW Open Access

Circulating tumor DNA dynamics predict pathological response and guide therapy personalization in the neoadjuvant setting

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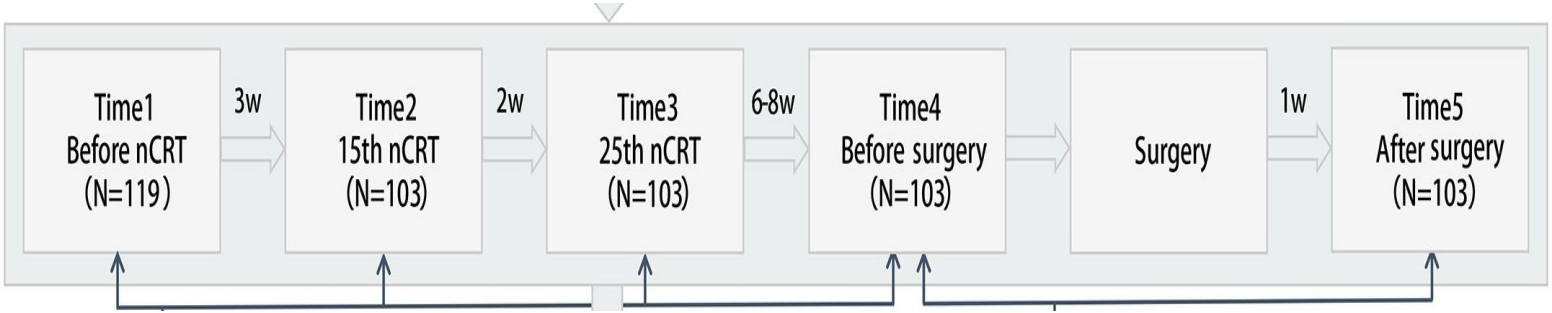
The dynamic properties of ctDNA, especially its **short half-life**, provide a unique opportunity to evaluate tumor burden in near real-time and guide therapeutic approaches:

1) the reduction of therapy for patients demonstrating a promising response

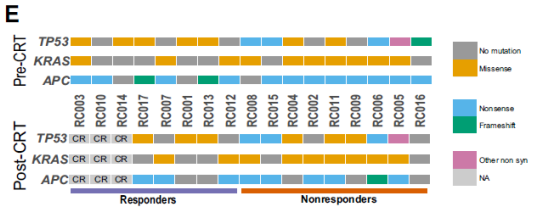
2) the intensification of therapy for those exhibiting signs of chronic or recurrent disease to improve oncological outcomes

Neoadiuvante

Adiuvante

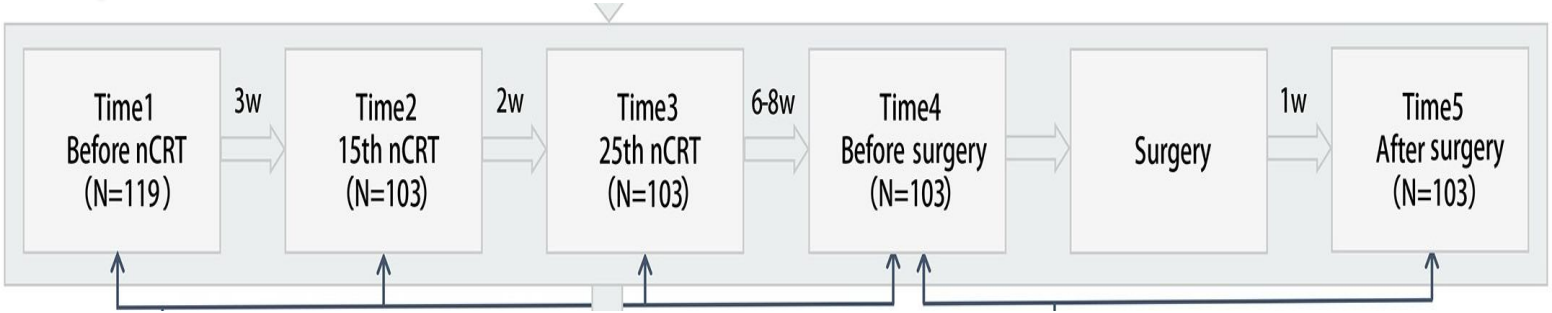


Chirurgia



Neoadiuvante

Adiuvante



Chirurgia

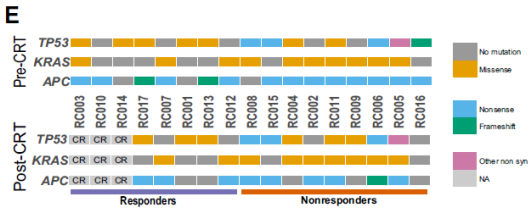


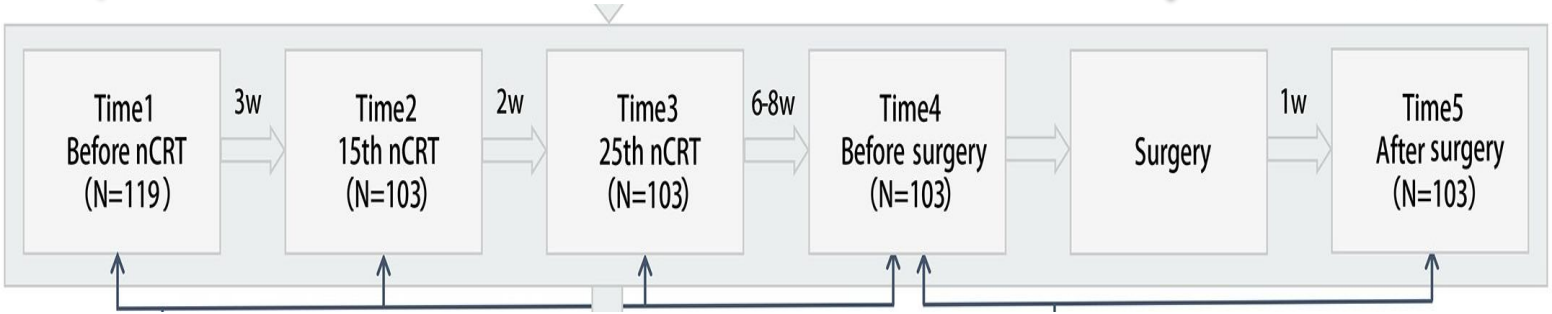
Table 6.03 Overview of the most commonly used systems for assessing tumour regression grade (TRG) [2036,1786]

Grade	Mandard	AJCC 2010	Rödel	MSKCC
TRG 0	–	No residual tumour cells	No regression	–
TRG 1	Absence of residual cancer, with fibrosis extending through the various layers of the oesophageal wall (complete regression)	Single cells or small groups	Fibrosis < 25% of tumour mass	100% response
TRG 2	Rare residual cancer cells scattered through the fibrosis	Residual cancer with desmoplastic response	Fibrosis 25–50% of tumour mass	86–99% response
TRG 3	An increase in the number of residual cancer cells, but fibrosis still predominates	Minimal evidence of tumour response	Fibrosis > 50% of tumour mass	< 86% response
TRG 4	Residual cancer outgrowing fibrosis	–	Complete regression	–
TRG 5	Absence of regressive changes	–	–	–

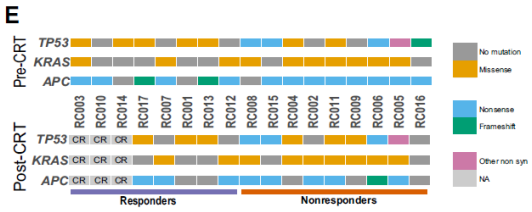
AJCC, American Joint Committee on Cancer; MSKCC, Memorial Sloan Kettering Cancer Center.

Neoadiuvante

Adiuvante



Chirurgia



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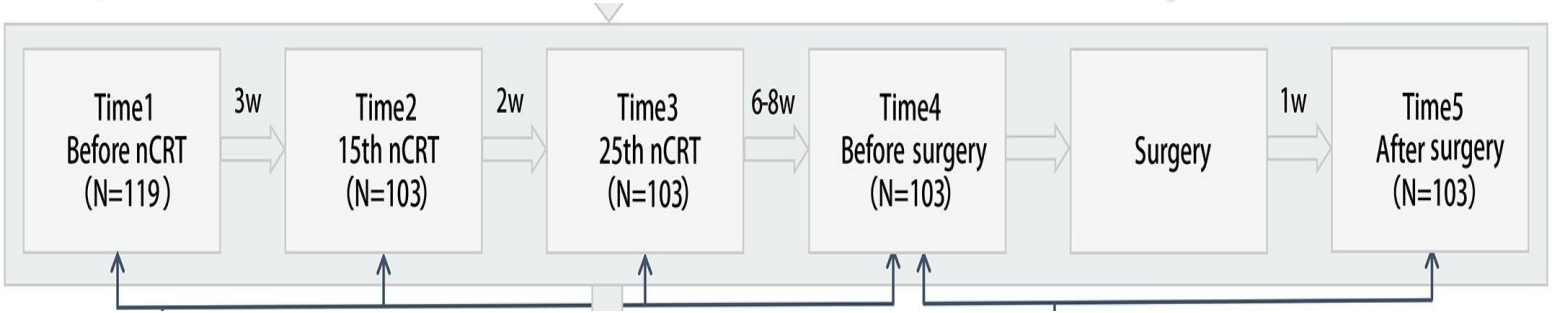
Neoadiuvante

Adiuvante



Original Reports | Gastrointestinal Cancer

Prospective Correlation of Magnetic Resonance Tumor Regression Grade With Pathologic Outcomes in Total Neoadjuvant Therapy for Rectal Adenocarcinoma

William A. Hall, MD[1]; Jiahe Li, MS[2]; Y. Nancy You, MD[3]; Marc J. Gollub, MD[4]; Joseph R. Grajo, MD[5,6]; Mark Rosen, MD[7]; Greg dePrisco, MD[8]; Greg Yothers, PhD[2]; Jennifer A. Dorth, MD[9]; Osama E. Rahma, MD[10]; Marcia M. Russell, MD[11]; Howard M. Gross, MD[12]; Samuel A. Jacobs, MD[13]; Bryan A. Faller, MD[14]; Sagila George, MD[15]; Tareq Al baghdadi, MD[16]; Michael G. Haddock, MD[17]; Richard Valicenti[18]; Theodore S. Hong, MD[19]; and Thomas J. George, MD[5,6]

Chirurgia

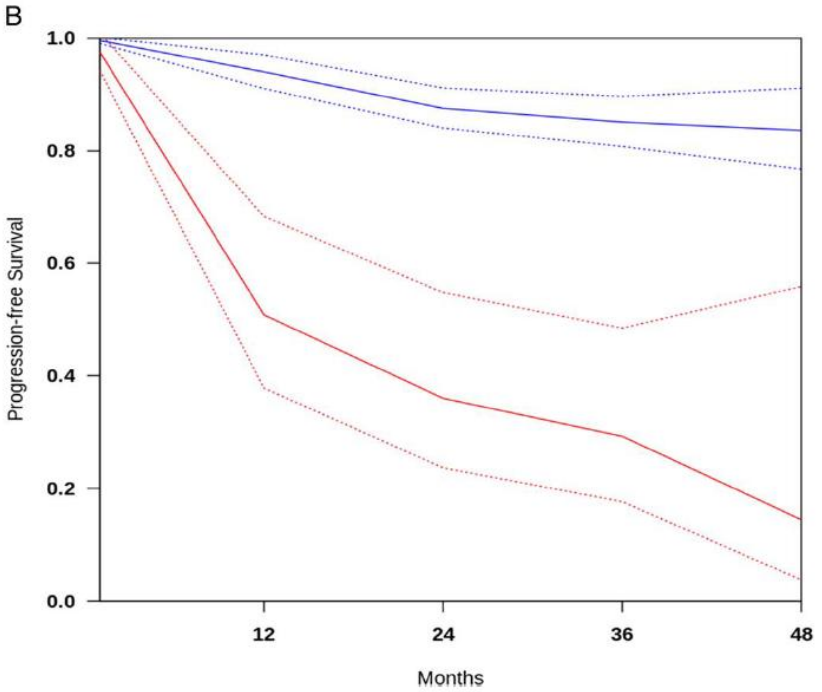
Circulating DNA in Rectal Cancer to Unravel the Prognostic Potential for Radiation Oncologist

A Meta-analysis

Francesco Fiorica, MD, PhD,† Maria Mandarà, MD,† Jacopo Giuliani, MD,† Umberto Tebano, MD,* Antonella Franceschetto, MD,* Milena Gabbani, MD,* Elvira Rampello, MD,† Giorgia Condarelli, MSc,* Giuseppe Napoli, MD,* Nicoletta Luca, MD,* Daniela Mangiola, MD,† Marco Muraro, MD,* Navdeep Singh, MD,* Andrea Remo, MD,‡ Carlotta Giorgi, PhD,§ and Paolo Pinton, PhD§*

(*Am J Clin Oncol* 2025;48:83–91)

Baseline	22%
After nCRT	81%
After surgery	86%



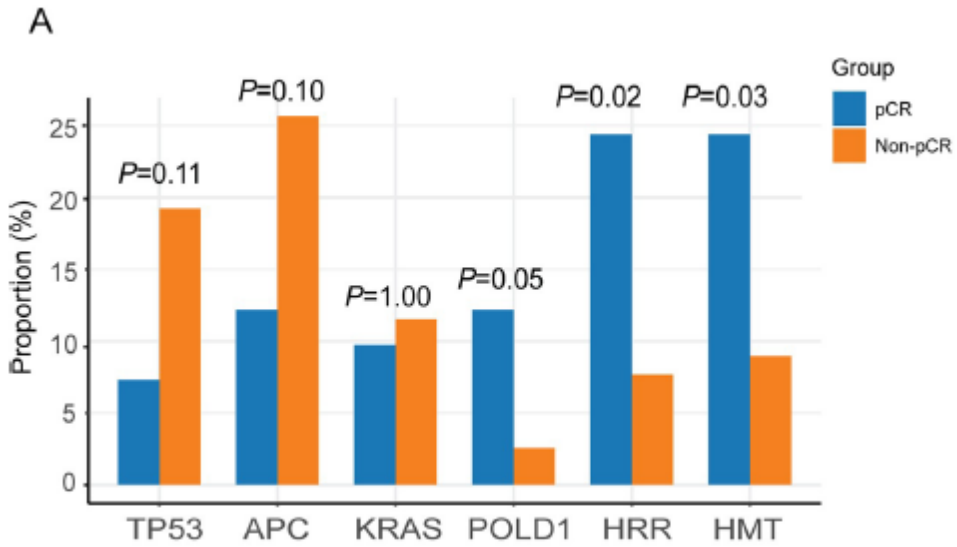
Baseline ctDNA status was not significantly associated with recurrence risk. Instead, there is evidence that the postsurgery presence of ctDNA in the bloodstream is a predictive biomarker for identifying patients at a higher risk of tumor recurrence.

RESEARCH ARTICLE

Utility of ctDNA in predicting response to neoadjuvant chemoradiotherapy and prognosis assessment in locally advanced rectal cancer: A prospective cohort study

Yaqi Wang[1,2,3☯], Lifeng Yang[1,2,3☯†], Hua Bao[4☯], Xiaojun Fan[4], Fan Xia[1,2,3], Juefeng Wan[1,2,3], Lijun Shen[1,2,3], Yun Guan[2,5], Hairong Bao[6], Xue Wu[4], Yang Xu[4], Yang Shao[6,7], Yiqun Sun[2,8], Tong Tong[2,8], Xinxiang Li[2,9], Ye Xu[2,9], Sanjun Cai[2,9], Ji Zhu[10,11,12,1,2,3‡*], Zhen Zhang[1,2,3‡*]

PLOS Medicine | https://doi.org/10.1371/journal.pmed.1003741 August 31, 2021



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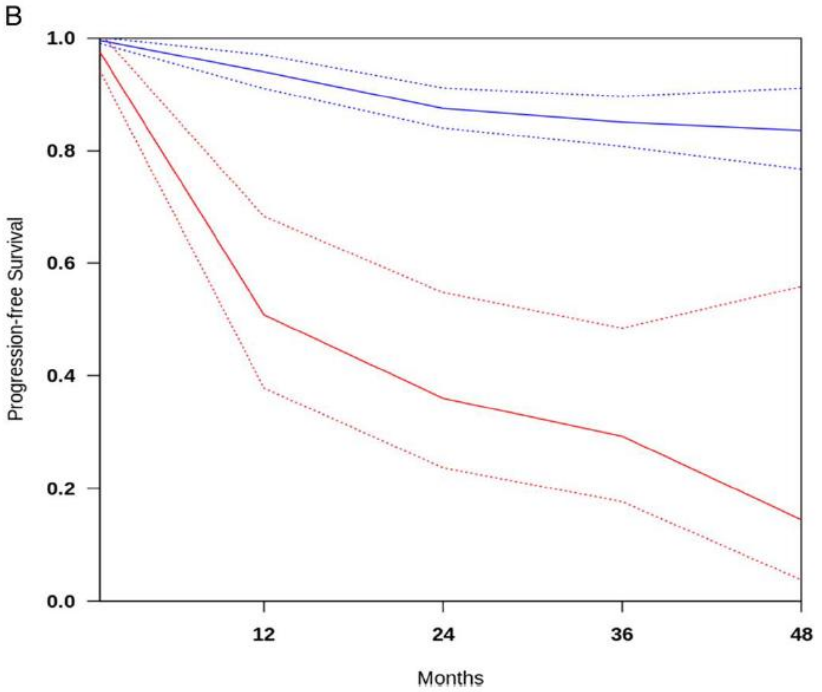
(*Am J Clin Oncol* 2025;48:83–91)

Baseline	22%
After nCRT	81%
After surgery	86%

13% - 41%

LOW-SHEDDING



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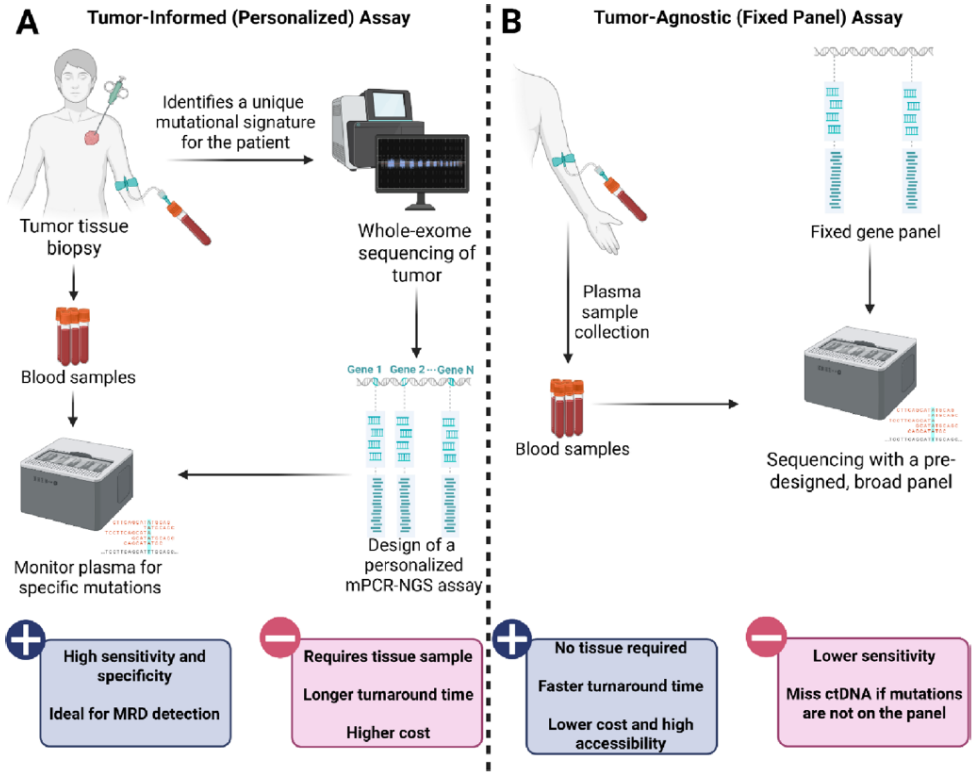

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(*Am J Clin Oncol* 2025;48:83–91)

- ctDNA-negative pCR =22% with a moderate heterogeneity
- ctDNA-positive pCR=10%

Jia-yi Li†, Xuan-zhang Huang†, Peng Gao, Yong-xi Song, Xiao-wan Chen, Xing-er Lv, Yv Fu, Qiong Xiao, Shi-yv Ye and Zhen-ning Wang*

Li *et al. BMC Cancer* (2021) 21:1214
https://doi.org/10.1186/s12885-021-08922-1

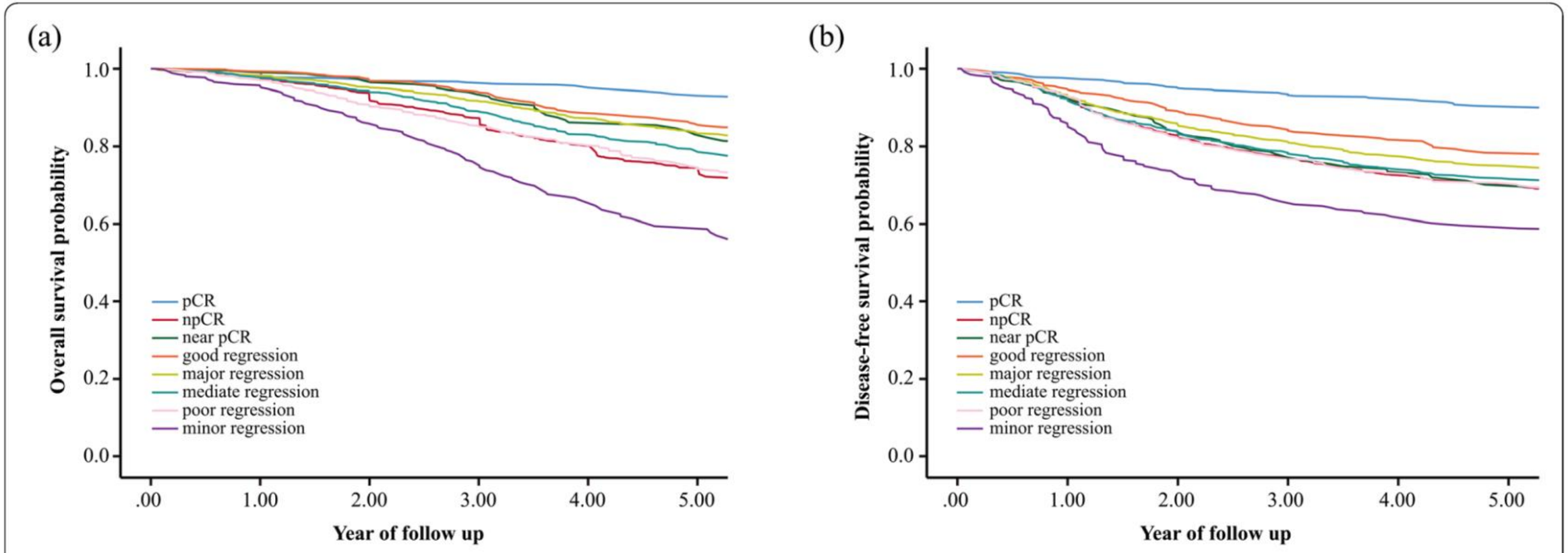

Fig. 2 The pooled Kaplan–Meier curves for 5-year survival outcomes (**a**) Overall survival; (**b**) Disease-free survival

JAMA Network Open

JAMA Network Open. 2025;8(7):e2521197. doi:10.1001/jamanetworkopen.2025.21197

Original Investigation | Oncology

Pathologic Complete Response and Survival in Rectal Cancer

A Systematic Review and Meta-Analysis

Kavin Sugumar, MD; Jessica Jin Lie, MD, MPH; Chee-Chee Stucky, MD; Yu-Hui Chang, PhD, MS; Justin Brady, MD; Nabil Wasif, MD, MPH; ohamad Bassam Sonbol, MD; David Etzioni, MD; Harvey Mamon, MD, PhD; Tanios Bekaii-Saab, MD; Zhi Ven Fong, MD, MPH, DrPH

Our trial-level analysis did not reveal a correlation between pCR and DFS or OS in rectal cancer RCTs with a high level of evidence. Our study's findings suggest a recommendation against using pCR as a SEP for neoadjuvant therapies in rectal cancer until conclusive trial-level evidence of its association with long-term outcomes is firmly established.

RESEARCH ARTICLE

Utility of ctDNA in predicting response to neoadjuvant chemoradiotherapy and prognosis assessment in locally advanced rectal cancer: A prospective cohort study

Yaqi Wang[1,2,3☯], Lifeng Yang[1,2,3☯†], Hua Bao[4☯], Xiaojun Fan[4], Fan Xia[1,2,3], Juefeng Wan[1,2,3], Lijun Shen[1,2,3], Yun Guan[2,5], Hairong Bao[6], Xue Wu[4], Yang Xu[4], Yang Shao[6,7], Yiqun Sun[2,8], Tong Tong[2,8], Xinxiang Li[2,9], Ye Xu[2,9], Sanjun Cai[2,9], Ji Zhu[10,11,12,1,2,3‡*], Zhen Zhang[1,2,3‡*]

PLOS Medicine | https://doi.org/10.1371/journal.pmed.1003741 August 31, 2021

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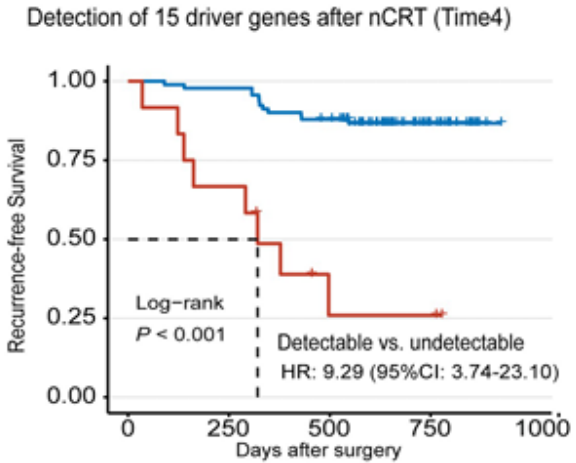

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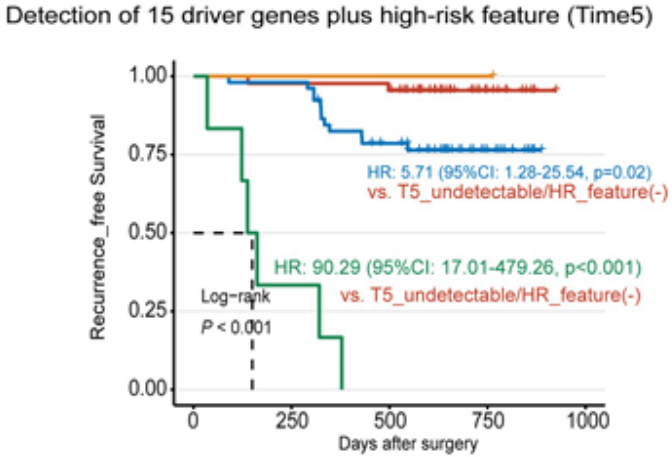

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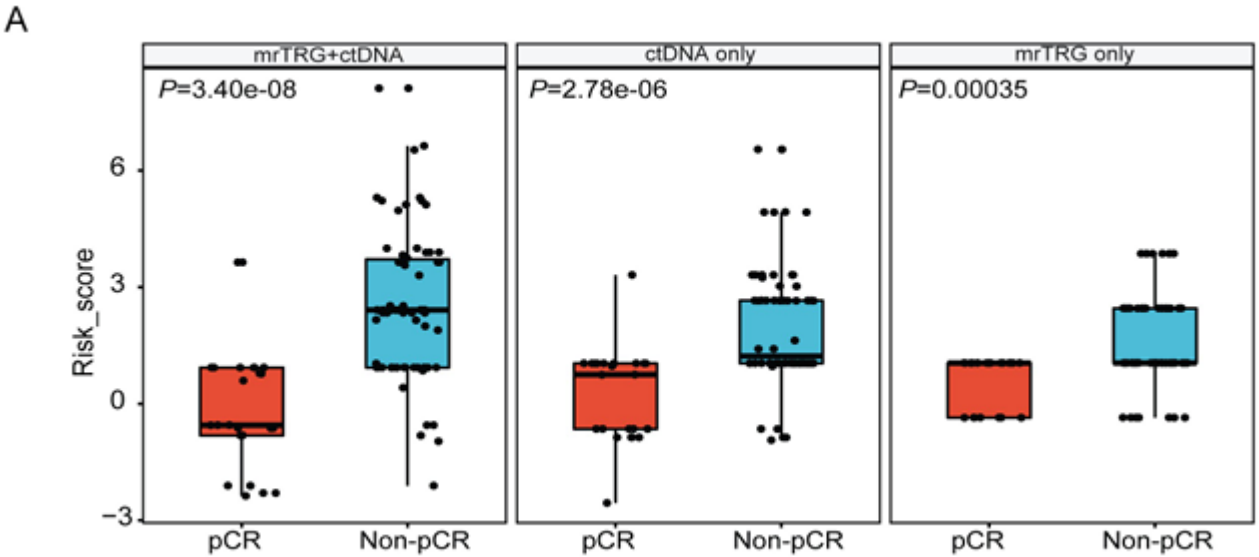


Clonal hematopoiesis of indeterminate potential (CHIP)

Notizie Cliniche
Paziente con neoplasie multiple
Finalità del test: diagnostico

Test Eseguito

Pannello NGS Custom TE-ERGI_v2 (80 geni) limitato ai geni:
VHL, BRK1cnv, MET, FH, FLCN, PTEN, BAP1, SDHA, SDHAF2, SDHB, SDHC, SDHD, TSC1, TSC2, PBRM1, TMEM127

Risultato

Non sono state rilevate alterazioni molecolari clinicamente significative correlate al quesito clinico.

Risultati incidentali: Si segnala la presenza nel gene TP53 della variante NM_000546.6:c.413C>T p.(Ala138Val) con una frequenza allelica di circa il 17% classificata verosimilmente patogenetica (classe 4) e confermata in un campione indipendente di DNA mediante sequenziamento Sanger.

L'analisi in silico (aGVGD e BayesDel) per questa variante suggerisce un potenziale impatto di questo cambiamento e tale dato è supportato da studi funzionali in vitro (PMID: 12826609, 39774325, 30224644, 29979965). Inoltre, una diversa sostituzione missenso al codone 138 (p.(Ala138Pro)) è stata riportata in letteratura in associazione a sindrome di Li-Fraumeni, suggerendo che questo residuo aminoacidico sia importante per la funzione della proteina p53.
Tale variante è stata descritta in letteratura in almeno due famiglie con sindrome di Li-Fraumeni (PMID: 22507745, 37562436) ed è stata identificata a bassa frequenza allelica in almeno un individuo con tumori non correlati alla sindrome (PMID: 37159554).
Sulla base delle evidenze attualmente disponibili e secondo i criteri dell'American College of Medical Genetics and Genomics applicati per il gene TP53 come specificato dal ClinGen TP53 Expert Panel (v2.4.0), la variante TP53 c.413C>T p.(Ala138Val) è stata classificata verosimilmente patogenetica (classe 4).
Tale dato potrebbe essere attribuibile o ad un mosaicismo germinale o al fenomeno dell'ematopoiesi clonale a potenziale indeterminato (Clonal Hematopoiesis of Indeterminate Potential, CHIP) che determina l'insorgenza di mutazioni somatiche nelle cellule staminali ematopoietiche, con conseguente espansione clonale.
Si rimanda al medico di riferimento la correlazione della variante TP53 a bassa frequenza allelica identificata con la storia clinica del paziente.

RESEARCH ARTICLE

Utility of ctDNA in predicting response to neoadjuvant chemoradiotherapy and prognosis assessment in locally advanced rectal cancer: A prospective cohort study

Yaqi Wang[1,2,3☯], Lifeng Yang[1,2,3☯†], Hua Bao[4☯], Xiaojun Fan[4], Fan Xia[1,2,3], Juefeng Wan[1,2,3], Lijun Shen[1,2,3], Yun Guan[2,5], Hairong Bao[6], Xue Wu[4], Yang Xu[4], Yang Shao[6,7], Yiqun Sun[2,8], Tong Tong[2,8], Xinxiang Li[2,9], Ye Xu[2,9], Sanjun Cai[2,9], Ji Zhu[10,11,12,1,2,3‡*], Zhen Zhang[1,2,3‡*]

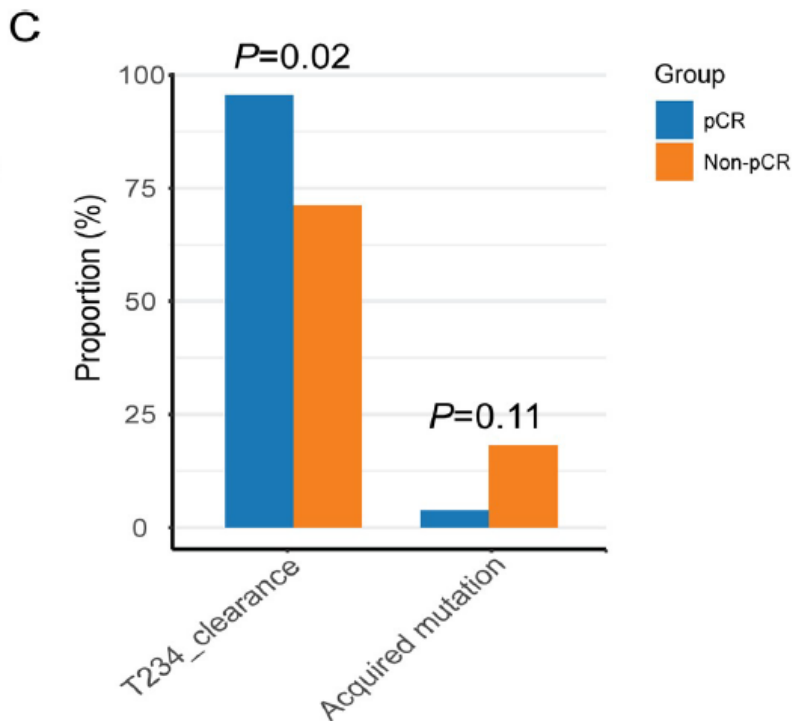
PLOS Medicine | https://doi.org/10.1371/journal.pmed.1003741 August 31, 2021

Integrative Molecular Characterization of Resistance to Neoadjuvant Chemoradiation in Rectal Cancer

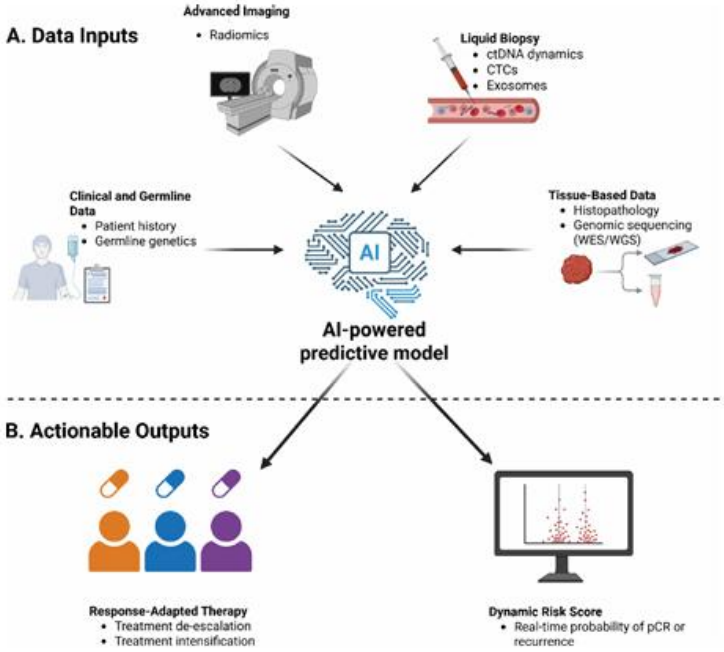
Sophia C. Kamran[1,2], Jochen K. Lennerz[3], Claire A. Margolis[2,4], David Liu[2,4], Brendan Reardon[2,4], Stephanie A. Wankowicz[2,4], Emily E. Van Seventer[5], Adam Tracy[2], Jennifer Y. Wo[1], Scott L. Carter[2,6], Henning Willers[1], Ryan B. Corcoran[5], Theodore S. Hong[1], and Eliezer M. Van Allen[2,4]

Am J Clin Oncol • Volume 48, Number 2, February 2025

Acquired mutations post-neoadiuvant



	pCR (n=26)	non-pCR (n=77)	Total (n=103)
Acquired mutation	1 (3.8%)	14 (18.2%)	15 (14.6%)


A. Data Inputs
Advanced Imaging
• Radiomics
Liquid Biopsy
• ctDNA dynamics
• CTCs
• Exosomes
Clinical and Germline Data
• Patient history
• Germline genetics
AI
Tissue-Based Data
• Histopathology
• Genomic sequencing (WES/WGS)
AI-powered predictive model
B. Actionable Outputs
Response-Adapted Therapy
• Treatment de-escalation
• Treatment intensification
Dynamic Risk Score
• Real-time probability of pCR or recurrence

ARTICLE OPEN

Detection of (pre)cancerous colorectal lesions in Lynch syndrome patients by microsatellite instability liquid biopsy

Mattia Boeri[1], Stefano Signoroni[2✉], Chiara Maura Ciniselli[3], Manuela Gariboldi[4], Susanna Zanutto[4], Emanuele Rausa[2], Miriam Segale[1], Anna Zanghi[1], Maria Teresa Ricci[2], Paolo Verderio[3], Gabriella Sozzi[1] and Marco Vitellaro[2,5]

Cancer Gene Therapy (2024) 31:842 – 850

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