



# Tumor informed ctDNA analysis to predict adjuvant chemotherapy benefit and improve long term survival in resectable CRC



A continuation of the data published Jan 2023 in Nature Medicine analyzing >2,240 patients with stage II-IV CRC patients from GALAXY



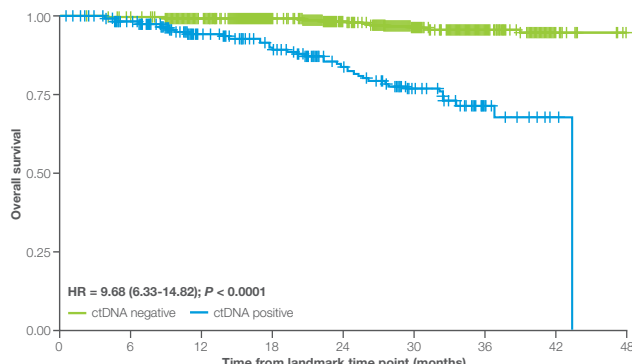
Includes 36M-DFS and 24M-OS data demonstrating the importance of post-surgical ctDNA analysis and its association with long term survival using Signatera™ MRD assay

## Key findings

- **Signatera™ MRD status is predictive of overall survival:** Signatera™-positivity in the post-op MRD window was found to be significantly associated with worse OS compared to Signatera™-negative patients
- **Signatera™ MRD status is predictive of an overall survival benefit from adjuvant chemotherapy:** High-risk stage II and stage III-IV patients who were Signatera™-positive after surgery and received ACT demonstrated superior OS
- **Signatera™ status remains the most significant predictor of recurrence:** Signatera™-positivity after surgery was the single most significant prognostic factor associated with inferior DFS
- **Sustained Signatera™ clearance after ACT is associated with improved survival:** Patients who clear their ctDNA and remain Signatera™-negative have superior DFS and OS, compared to those with transient clearance and those with no ctDNA clearance

## Signatera™-positivity at the MRD time point and during surveillance was predictive of inferior OS

All stages MRD window

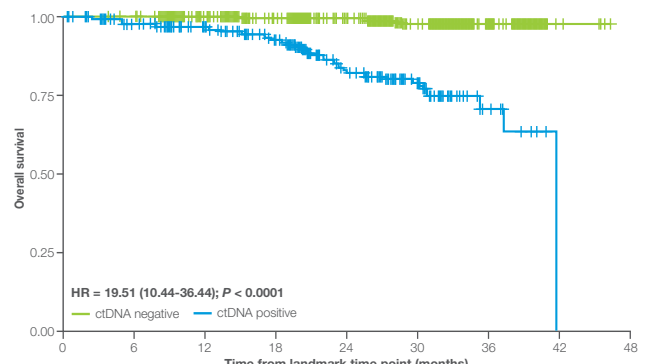


No. at risk	0	6	12	18	24	30	36	42	48
ctDNA negative	1,773	1,765	1,511	1,252	825	497	185	19	1
ctDNA positive	336	309	228	189	119	73	24	4	0

ctDNA status	ctDNA negative	ctDNA positive
24M-OS %*	98.5 (97.7-99.1)	83.65 (77.84-88.06)
36M-OS %*	96 (94.3-97.2)	71.8 (63.4-78.6)

\*MRD window: 2-10 weeks post surgery, prior to start of any adjuvant therapy – Landmark from MRD timepoint date

All stages surveillance



No. at risk	0	6	12	18	24	30	36	42	48
ctDNA negative	1,481	1,478	1,275	1,063	686	384	123	6	0
ctDNA positive	313	287	222	175	102	60	14	0	0

ctDNA status	ctDNA negative	ctDNA positive
24M-OS %*	99.3 (98.4-99.7)	83.2 (76.5-88.1)
36M-OS %*	97.9 (96.3-98.9)	70.5 (57.7-80.1)

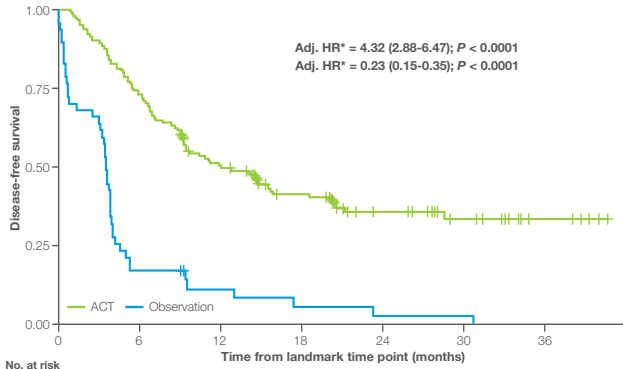
\*Surveillance window: from 4 weeks post-ACT or at the end of MRD window if patient had no ACT, until the last follow up or relapse/death.



Signatera™ negative patients experienced a 10x advantage in overall survival

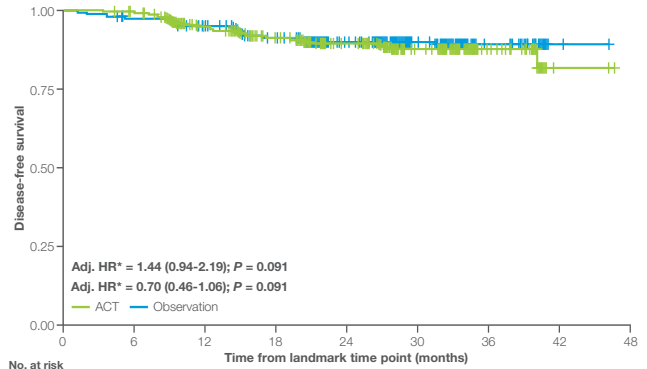
## Signatera™-positive patients who received ACT experienced superior OS

### MRD-positive – High risk Stage II/III



Treatment	ACT	Observation
Events %	60.68 (88/145)	95.74 (45/47)
24M-DFS % (95% CI)	35.83 (27.41–44.32)	2.84 (0.23–12.35)
mDFS (mo)	12.06 (9.30–18.57)	3.55 (3.16–3.95)

### MRD-negative – High risk Stage II/III



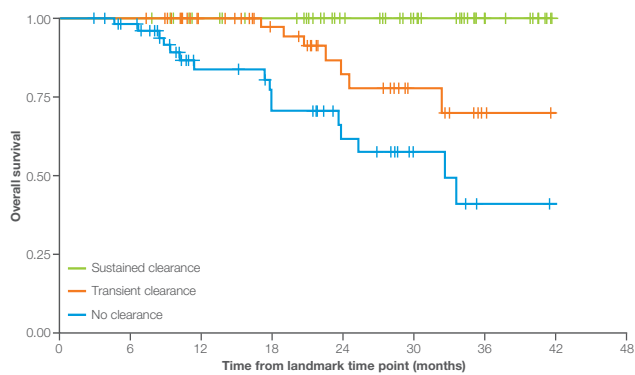
Treatment	ACT	Observation
Events %	9.63 (55/571)	8.53 (50/586)
24M-DFS % (95% CI)	89.11 (85.81–91.68)	89.9 (86.80–92.30)
mDFS (mo)	NR	NR



- High-risk stage II and stage III-IV patients who were Signatera™-positive after surgery and received ACT demonstrated superior DFS
- Signatera™ can predict patients most likely to benefit from adjuvant chemotherapy (ACT) and aid in de-escalation strategies for those that are more likely to have been cured by surgery alone

### OS according to ctDNA clearance in patients who were ctDNA positive in the MRD window

Landmark from MRD timepoint date



- When monitored with Signatera™ after ACT, the OS for patients with sustained ctDNA clearance was superior compared to patients with transient or no clearance
- Findings show how Signatera™ can predict post-treatment outcomes more precisely, enabling personalized surveillance strategies that may enable earlier detection of local recurrent disease in CRC

ctDNA status	Sustained clearance	Transient clearance	No clearance
24M-OS %*	100	82.3 (61.5–92.5)	61.7 (41.9–76.5)
HR	Reference	25.51	75.62
95% CI	Not applicable	3.1–3314.73	10.22–9650.93
P	Not applicable	0.0007	<0.0001



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#### References:

1. Kotani D. et al., Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer, Nature Medicine v29 Issue 1 Jan 2023
2. Nakamura, Y., Watanabe, J., Akazawa, N. et al., ctDNA-based molecular residual disease and survival in resectable colorectal cancer. Nat Med (2024)

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