A tumor-uninformed ctDNA assay detecting MRD in patients with resected stage II or III colorectal cancer predicts recurrence: Subset analysis from the GALAXY study in CIRCULATE-Japan

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Abstract No: 21

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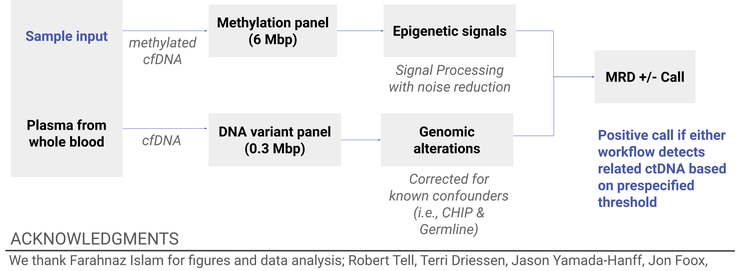
INTRODUCTION

The presence of circulating tumor DNA (ctDNA) after curative-intent surgery can identify patients with minimal residual disease (MRD) who are at risk of recurrence and aid with postsurgical risk stratification. ~80% of stage II and only 50% of stage III colorectal cancer (CRC) patients are cured by surgery alone. A tumor-naive plasma-only approach for MRD assessment accelerates the turnaround time, enabling rapid adjuvant chemotherapy (ACT) treatment decision making, optimizing the impact on patient outcomes.

METHODS

- We randomly selected 80 early stage CRC patients meeting pre-specified eligibility criteria from GALAXY, an observational arm of the CIRCULATE-Japan study (UMIN000039205)
  - Patients were selected with enrichment for recurrence to 50% while maintaining the stage II:III recurrent (R)/nonrecurrent (NR) ratio observed in GALAXY
  - Landmark time point (LMT) was 4 weeks after curative surgery in pathological stage II or III CRC patients.
- We used Tempus xM (xM), a tumor-naive ctDNA MRD assay to analyze residual plasma samples at LMT
  - xM integrates methylation and genomic variant classifiers to deliver a binary MRD call
  - All calls were blinded to clinical outcomes.

Figure 1. xM methyl and variant workflows



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SIGNIFICANCE

- Our tumor-naive xM MRD assay detects clinical recurrence of stage II/III CRC with high specificity (93.8%) and sensitivity (52.6%) at the LMT
- Our tumor naive xM has a 74% chance to observe true recurrences in our MRD+ detected patient population
- Liver site of recurrence had the highest true positive (TP) rate of 66.7% versus 20% for ovary, peritoneum and lung combined (p =0.011; Fisher's exact test)
- The clinically meaningful adjusted median DFS time by landmark 1-month post-surgery for xM MRD+ is 39.3 versus >72 weeks MRD- (Adj. HR 5.09)

RESULTS

Figure 2. Cohort selection from GALAXY-Japan

Figure 2. Pipeline for selecting patients from the GALAXY-Japan study.

Table 1. Patient cohort characteristics

Table 1.	Overall, n=70	xM (Methylation & Variant)	
		MRD+, n=22	MRD-, n=48
Age at enrollment			
Mean (SD)	69.27 (11.06)	71.50 (8.58)	68.25 (11.97)
Median	71	72	70
IQR	62.50 - 75.75	65.25 - 75.50	59.00 - 75.25
Min / Max	41 / 89	56 / 89	41 / 89
Sex			
Female	24 (34.3%)	5 (22.7%)	19 (39.6%)
Male	46 (65.7%)	17 (77.3%)	29 (60.4%)
Cancer Stage			
Stage 2	29 (41.4%)	11 (50.0%)	18 (37.5%)
Stage 3	41 (58.6%)	11 (50.0%)	30 (62.5%)
MSI-High status			
Positive	7 (10.0%)	1 (4.5%)	6 (12.5%)
Negative	63 (90.0%)	21 (95.5%)	42 (87.5%)
RAS status			
Positive	33 (47.1%)	13 (59.1%)	20 (41.7%)
Negative	37 (52.9%)	9 (40.9%)	28 (58.3%)
BRAF mutation status			
Positive	7 (10.0%)	1 (4.5%)	6 (12.5%)
Negative	63 (90.0%)	21 (95.5%)	42 (87.5%)
Histology			
Adenocarcinoma	69 (98.6%)	22 (100.0%)	47 (97.9%)
Adenosquamous carcinoma	1 (1.4%)	0 (0%)	1 (2.1%)
Adjuvant chemotherapy			
Yes	26 (37.1%)	5 (22.7%)	21 (43.8%)
No	44 (62.9%)	17 (77.3%)	27 (56.2%)

Table 1. Characteristics of patient cohort selected from GALAXY-Japan

Figure 3. xM clinical performance

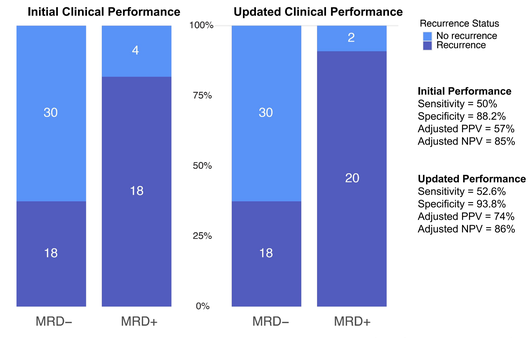

Figure 3. xM clinical performance before (left) and after (right) identifying 2 false positive (FP) patients who received ACT, cleared their ctDNA and thus were reclassified to true positive (TP). Adjusted PPV and Adjusted NPV are the PPV and NPV estimates adjusted by the anticipated true recurrence rate of 24%.

Figure 4. Clinical follow-up

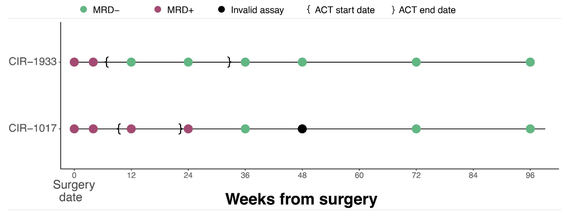

Figure 4. xM MRD assay results, recurrence status, and timing of adjuvant chemotherapy for the two false-positive patients. A swimmer plot with the full longitudinal follow-up can be found online in our supplementary slides.

Figure 5. Site of clinical recurrence

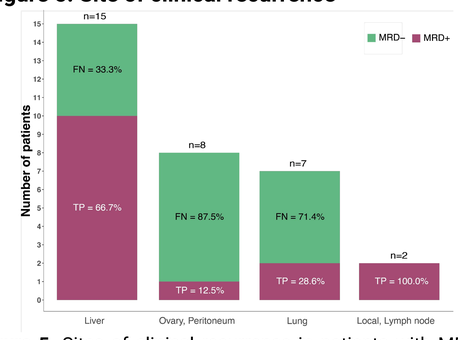

Figure 5. Sites of clinical recurrence in patients with MRD- and MRD+ xM values. Liver is the most common site of recurrence. There is a statistically significant difference in the TP rate of Liver v. combined Ovary/Peritoneum and Lung (p=0.011; Fisher's exact test). FN = false negative; TP = true positive

Figure 6. Disease-free survival

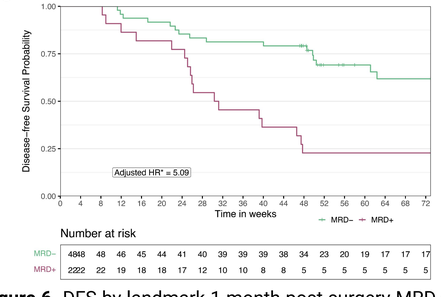

Figure 6. DFS by landmark 1-month post-surgery MRD status for patients with >1 year follow-up. The KM estimates are obtained based on the enriched sample (50% recurrence rate) and Adjusted HR* is the hazard ratio adjusted by the anticipated true recurrence rate of 24%. The adjusted median DFS time for MRD+ is 39.3 weeks and for MRD- is >72 weeks.