



# CIRCULATE-Japan Interim Analysis from 2022 ASCO Gastrointestinal Cancers Symposium

The largest prospective MRD study to date evaluates the clinical utility of ctDNA analysis in colorectal cancer (CRC)

## Study Overview: GALAXY portion of CIRCULATE-Japan

- An outcomes analysis of 1,040 patients with Stage II-IV CRC, enrolled into the observational GALAXY portion of CIRCULATE-Japan, with median clinical followup of 11.4 months.
- Some patients received adjuvant chemotherapy (ACT), and some did not.
- Results were analyzed to determine 6-month and 12-month disease-free survival (DFS), by MRD status, and by treatment status.<sup>1</sup>

### Prognostic results

#### Circulate Japan ASCO GI 22

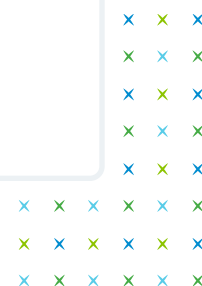
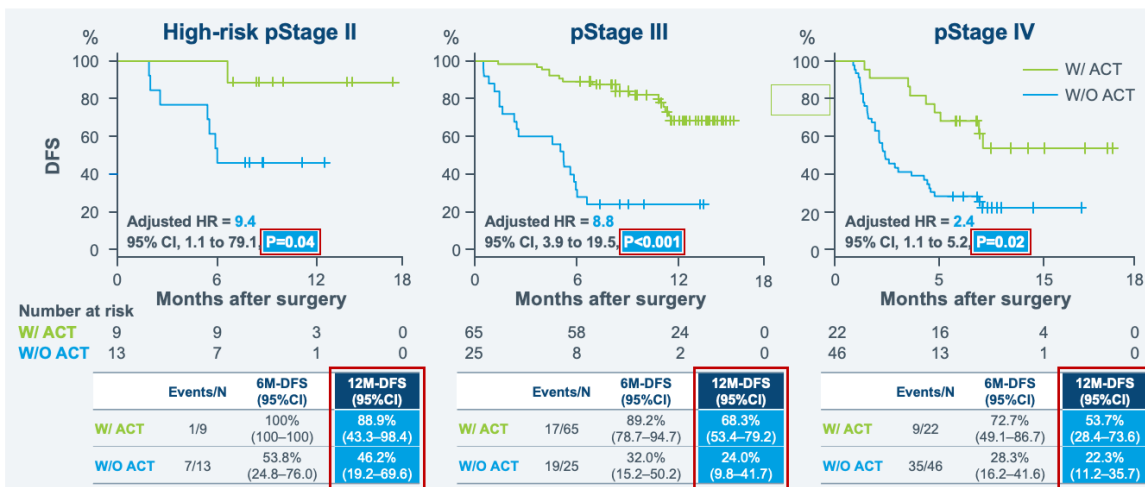
12M-DFS for MRD-positives	55.5%
12M-DFS for MRD-negatives	95.2%
Hazard Ratio (HR) for MRD-positive vs. MRD-negative	13.3
Sensitivity at 4w post-op	75%

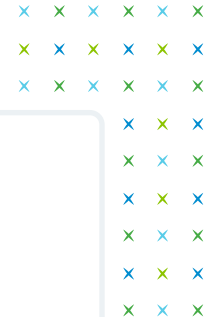
### Predictive results

- Signatera-positive post surgery: benefit significantly from adjuvant chemo (HR 8.8-9.4 in high-risk Stage II or III)
- Signatera-negative post surgery: no significant benefit from adjuvant chemo (Absolute risk reduction of only 1.5% at 12 months DFS)
- Signatera ctDNA clearance: predictive of treatment efficacy (HR 15.8 clearance vs. no clearance)

## MRD-positive patients benefit significantly from adjuvant chemotherapy, regardless of stage

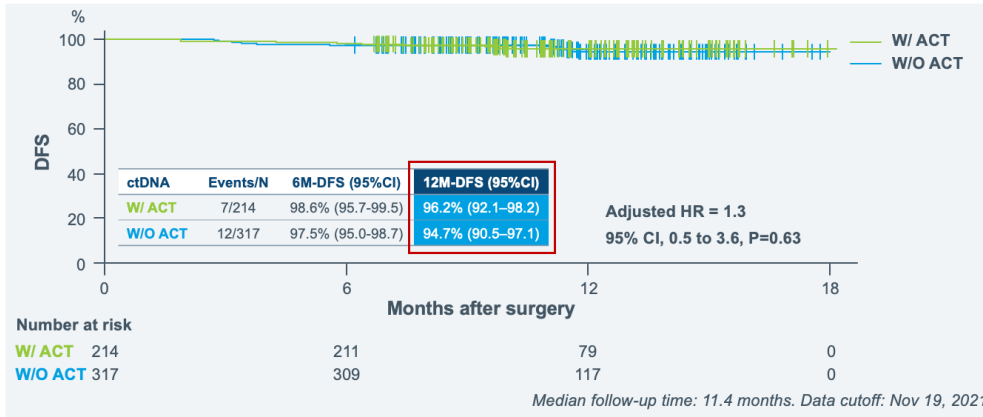
### DFS in post-op-4w MRD-positive population<sup>1</sup>





## No significant treatment benefit for MRD-negative patients

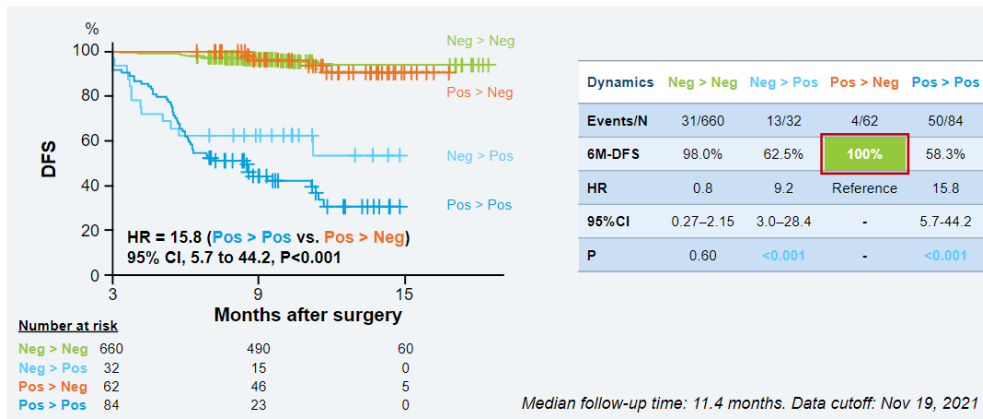
DFS in post-op-4w MRD-negative population (High risk stage II-III)



Patients that were MRD-negative post surgery received no significant benefit from ACT (Absolute risk reduction of only 1.5% at 12 months DFS)

## ctDNA clearance may serve as a new surrogate end point to predict treatment benefit

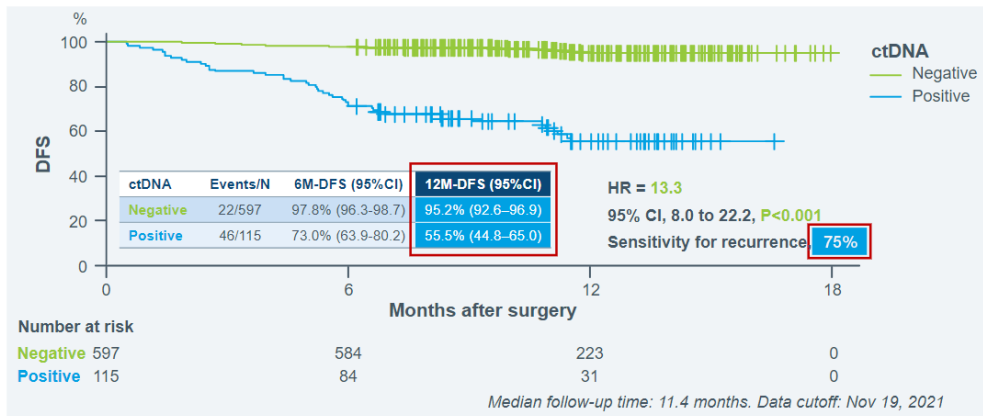
DFS by ctDNA dynamics from post-op-4w to 12w



68% of ACT-treated patients cumulatively cleared their ctDNA by week 24 and had significantly better outcomes compared to patients who remained ctDNA-positive (HR 15.8)

As previously demonstrated, ctDNA remains a strong prognostic factor and has been reproduced in the largest prospective cohort to date.

Disease free survival (DFS) based on ctDNA status at 4 weeks post-surgery (pStage II-III)



With a single test at 4w post-op, overall 12M-DFS of 56% in the MRD-positive group and 95% in the MRD-negative group, including all treated and non-treated patients

### References

1. Kotaka et al. Association of circulating tumor DNA dynamics with clinical outcomes in the adjuvant setting for patients with colorectal cancer from an observational GALAXY study in CIRCULATE-Japan. ASCO GI 2022.