Impact of NGS Testing Timing on Real-World Treatment Patterns and Clinical Outcomes in Colorectal Cancer: A Retrospective Observational Study

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Poster/Abstract
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OBJECTIVES

This study evaluates the impact of the timing of next-generation sequencing (NGS) on real-world overall survival (rwOS) in colorectal cancer (CRC) patients and aims to understand its importance in driving treatment decisions.

METHODS

This retrospective analysis of the Tempus real-world multimodal database included patients ≥18 years, diagnosed with CRC until 2024 (median year: 2019; sequencing date range: 2018-2024). For rwOS analysis, index date was defined as first-line (1L) treatment initiation and patients were censored at death, last known follow up, or 3 years post-index date.

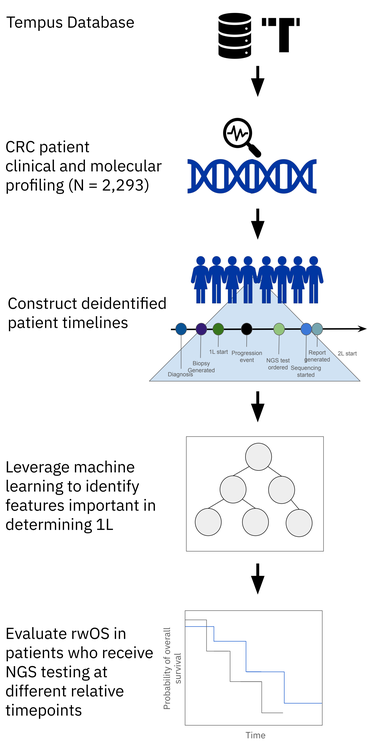


Figure 1 illustrates the study's design. Data from 2,293 de-identified patients in the Tempus database were analyzed. For each patient, the time between initial diagnosis and biopsy, biopsy and NGS ordering, NGS order and sequencing, and sequencing and report generation was measured and recorded on a timeline. These time intervals, combined with patient clinical characteristics, were used as input variables for a random forest algorithm. The algorithm was designed to predict first-line treatment (1L tx) choice. Subsequently, real-world overall survival (rwOS) was examined by grouping patients according to the NGS timing features identified as most influential by the predictive model.

KEY TAKEAWAYS

- ~90% of mCRC patients receive chemotherapy at 1L, despite approvals for 1L targeted treatment in mCRC
- The time taken to receive NGS results after diagnosis is a key factor influencing 1L treatment choice, with significant delays in ordering the NGS test
- Earlier NGS testing is associated with improved real-world overall survival, particularly in patients with stage 4 CRC disease

RESULTS

Treatment landscape of CRC patients with NGS testing results delivered before 1L therapy

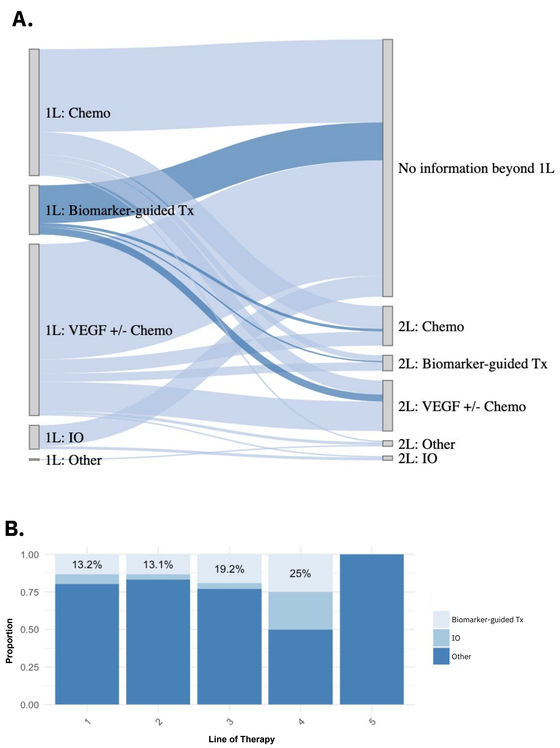
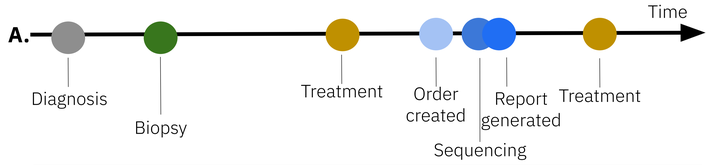
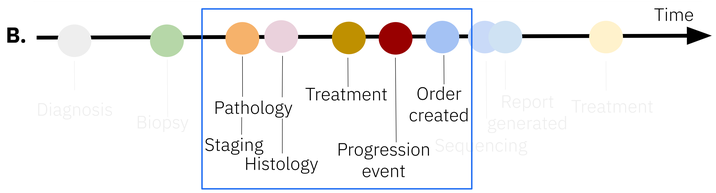


Figure 2. A. Sankey diagram of treatment landscape for patients with NGS testing results delivered prior to 1L start (N = 268 patients). Biomarker-guided Tx includes all treatment options where genomic status is needed for tx eligibility. An example is anti-EGFR tx where a KRAS WT status is confirmed prior to tx start. **B.** Bar graph showing the proportion of patients in the same cohort as above for each therapy class across lines of therapy 1-5. Numbers on the bars denote percentage of patients on biomarker-guided x.

Quantifying NGS time-based features in a patient's journey



NGS timing event	All Patients	Subpopulations		
	N = 2,293	BRAF V600E N = 138	HER2 amp N = 56	KRAS/NRAS N = 1,208
Diagnosis to Biopsy	28 (0, 569)	8 (0, 354)	60 (0, 980)	25 (0, 508)
Biopsy to NGS Order	51 (14, 286)	36 (13, 165)	44 (13, 132)	57 (14, 290)
NGS order to Sequencing	11 (9, 16)	12 (9, 16)	11 (9, 16)	11 (9, 16)
Sequencing to Result Report	3 (2, 5)	4 (3, 5)	4 (3, 7)	3 (2, 5)



Time from Biopsy to NGS results	Time between progression event and NGS order (days)	
	Median (IQR Q3-Q1)	Mean (SD)
0-3 mo	-99.9 (175.25)	-99.9 (235.1)
3-6mo	9.0 (132.5)	14.9 (259.5)
6-12 mo	17.0 (81.50)	36.6 (79.5)

Figure 3. A. Timeline of key events from diagnosis to treatment, highlighting the events related to NGS testing. The table below presents the median (IQR) time in days for each interval across the entire cohort and specific molecularly defined subpopulations. **B.** Similar timeline to **A**, with a focus on events relative to patient progression. Patient population filtered to include only stage 4 patient with biopsies within 30d of diagnosis (N = 197). The table shows the median (IQR) and mean (SD) time between biopsy and NGS results, categorized by the time of NGS order relative to first-line treatment (0-3 months, 3-6 months, and 6-12 months prior). Negative values indicate NGS order before a progression event.

Random forest feature importance in predicting biomarker-guided 1L treatment for stage 4 CRC

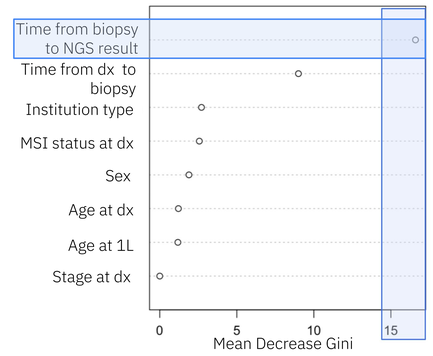
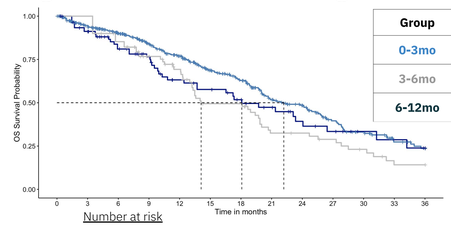


Figure 4. This plot displays the feature importance as determined by a random forest classifier trained to predict whether a stage 4 CRC patient who has NGS results available prior to 1L start receives a biomarker-guided tx at 1L. The time from biopsy to NGS result was identified as the most important feature in determining model accuracy. This timing metric, combined with two other top features, achieved high predictive accuracy (AUC = 0.92), highlighting the critical impact of NGS timing on treatment decisions.

Real-world overall survival stratified by time between diagnosis and NGS results in stage 4 mCRC



Group	Median OS
0-3mo	22.2 (20.02-25.8)
3-6mo	18.1 (10.82-26.4)
6-12mo	14.1 (2.48-20.0)

Figure 5. Kaplan-Meier survival analysis showing risk-set adjusted rwOS in stage 4 mCRC patients based on the time interval between biopsy collection and receipt of NGS results. Patients receiving NGS results within 3 months demonstrated significantly improved overall survival compared to those receiving results between 6 and 12 months ($p < 0.02$). Patient cohort was stratified based on those who received their biopsy within 30 days of diagnosis. Median OS (95% CI) shown in table.

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