FPN 61P

Correlation between Survival Outcomes and Duration of Sequential Treatment with Regorafenib and Trifluridine/Tipiracil for Refractory Metastatic Colorectal Cancer: Results from the Multicenter Retrospective ReTrITA Study

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ESMO GASTROINTESTINAL CANCERS Annual Congress
BARCELONA SPAIN 2-5 JULY 2025

The Author Presenter declares no competing interests in relation to this study.

BACKGROUND

In the setting of refractory metastatic colorectal cancer (mCRC), therapeutic options become increasingly limited, and further lines of treatment are seldom pursued. However, two key agents have emerged as viable options in this context: trifluridine/tipiracil (T), with or without the addition of bevacizumab, and regorafenib (R).

The ReTrITA study was designed to evaluate the real-world effectiveness of these two agents used alone or in sequence. In this analysis, we focused on a subgroup of patients who received both agents in sequence and were stratified by treatment duration. Our objective was to assess the impact of sequencing and exposure time on overall survival (OS) and progression-free survival (PFS), with the goal of identifying clinically relevant patterns that could support therapeutic decision-making in routine practice.

OBJECTIVES

To assess the relationship between survival outcomes and the duration of sequential treatment with R and T. Duration categories: < 6 months; 6 to < 12 months; ≥ 12 months

STATISTICAL ANALYSIS

Descriptive statistics were employed to summarize key information about the study.

Pearson's Chi-Square and Fisher's Exact tests were applied to assess potential associations. Progression-Free Survival (PFS) and Overall Survival (OS) were estimated using the Kaplan-Meier method. Differences between subgroups were evaluated with the log-rank test. Statistical significance was set at $p < 0.05$. All analyses were conducted using MedCalc for Windows, version 19.4.

KEY ELIGIBILITY CRITERIA

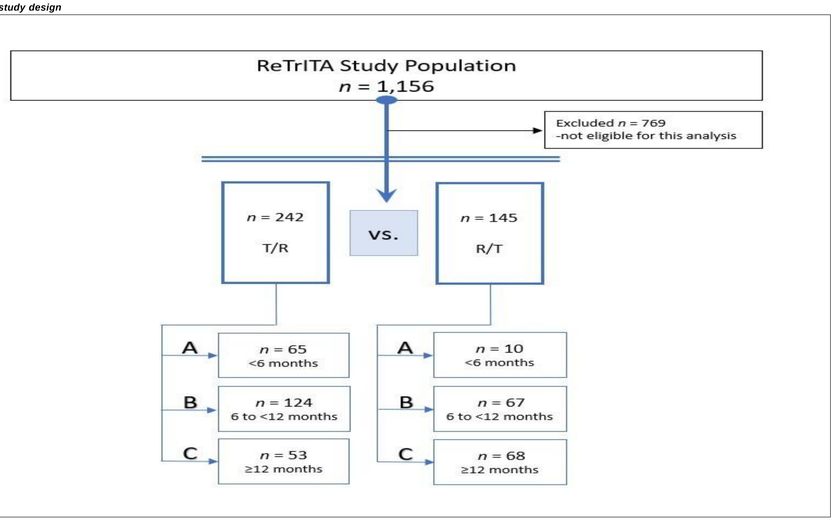
Patients included in the study had histologically confirmed mCRC and had previously received at least two standard chemotherapy regimens incorporating anti-VEGF and/or anti-EGFR agents.

All patients were treated with late-line therapies using either R or T and had an ECOG PS ranging from 0 to 2.

DESIGN AND METHODS

2012 - 2023: patients with mCRC treated with R or T, were retrospectively recruited at 17 Italian cancer centers (ReTrITA Study). This subgroup analysis includes patients receiving T/R or R/T sequence.

Fig.1 Substudy design



RESULTS

Fig.2. Kaplan-Meier curves of Overall Survival in Group A

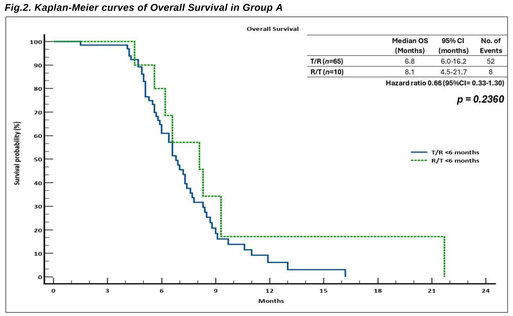


Fig.3. Kaplan-Meier curves of Overall Survival in Group B

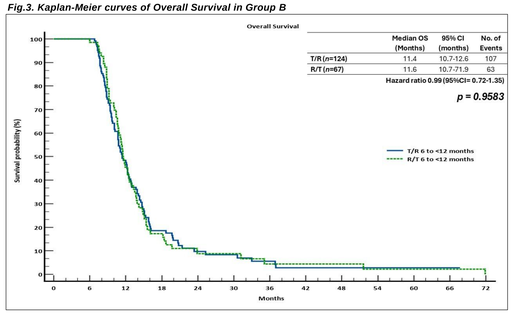
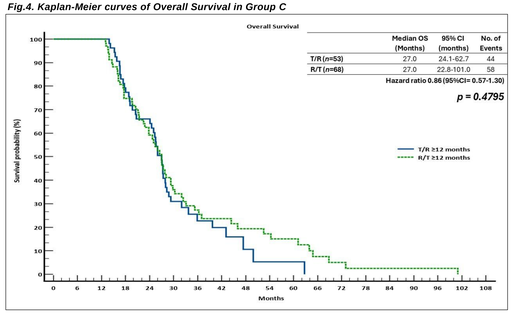


Fig.4. Kaplan-Meier curves of Overall Survival in Group C



This analysis is part of the larger retrospective ReTrITA study, which enrolled a total of 1,156 patients.

Among them, 261 (22.5%) received the T/R sequence, 155 (13.4%) received the reverse R/T sequence, 427 (37.0%) were treated with T alone, and 313 (27.1%) with R alone.

The current analysis focused on a subset of 387 patients, stratified by the duration of treatment sequences.

In Group A, 65 patients (16.8%) received T/R and 10 (2.5%) R/T for less than 6 months; in Group B, 124 patients (32.0%) were treated with T/R and 67 (17.4%) with R/T for 6 to <12 months; in Group C, 53 patients (13.7%) received T/R and 68 (17.6%) R/T for ≥12 months.

Median overall survival (OS) was 8.1 months for R/T and 6.8 months for T/R in Group A (p = 0.2360) (Fig. 2), remained comparable in Group B (11.6 vs. 11.4 months for R/T and T/R, respectively; p = 0.9583) (Fig.3). In Group C, both sequences achieved a median OS of 27.0 months (p = 0.4795) (Fig.4), with a significant interaction observed across groups (interaction p < 0.0001).

No significant differences in median progression-free survival (PFS) were identified: in Group A, 5.6 vs. 5.1 months in favor of T/R (p = 0.0723) (Fig. 5); in Group B, 9.0 vs. 8.7 months for R/T and T/R, respectively (p = 0.0800) (Fig.6); and in Group C, 19.1 vs. 18.6 months for T/R and R/T (p = 0.3768) (Fig.7). A statistically significant interaction effect was again observed (interaction p < 0.0001).

Fig.5. Kaplan-Meier curves of Progression-free Survival in Group A

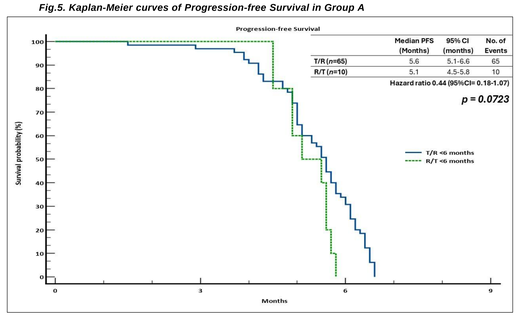


Fig.6. Kaplan-Meier curves of Progression-free Survival in Group B

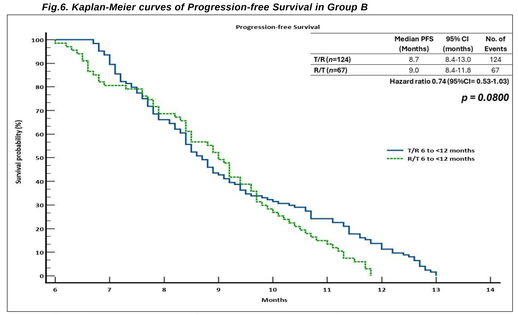
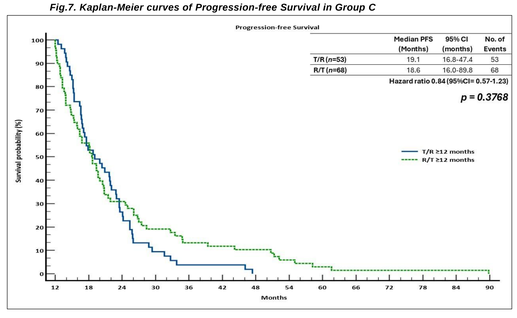


Fig.7. Kaplan-Meier curves of Progression-free Survival in Group C



CONCLUSIONS

In this real-world analysis of patients with refractory metastatic colorectal cancer (mCRC), sequencing regorafenib (R) before or after trifluridine/tipiracil (T), stratified by treatment duration, did not reveal significant differences in survival outcomes. These findings highlight the complexity of treatment decisions in this setting and underscore the need for informed, individualized therapeutic strategies when considering sequence options in refractory mCRC.

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