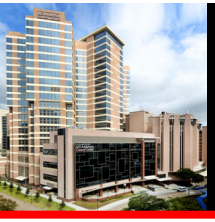

Impact of *KRAS* codon-specific mutations on survival of patients with metastatic CRC (mCRC) treated with trifluridine-tipiracil (TAS) plus bevacizumab (Bev): a real-world analysis

Giulia Maddalena[1,2], Ymke van der Pol[3], Zachary Rivers[3], Arvind Dasari[1], Jane E. Rogers[1], Justin Guinney[3], Scott Kopetz[1], Kanwal Pratap Singh Raghav[1]

[1]Department of Gastrointestinal Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Department of Surgery, Oncology and Gastroenterology, University of Padua, Padova, Italy [3]Tempus Labs, Inc., Chicago, IL

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Abstract Nr: 201

INTRODUCTION

- Clinical benefit and survival data utilizing later lines of therapy with TAS in metastatic CRC is limited, highlighting the need for better patient selection[1].
- Recently, codon-specific *KRAS* mutations have been implicated as biomarkers for TAS treatment. *KRAS* G12 was associated with a lack of benefit and G13 displayed improved benefit[2].
- However, it is unknown whether this differential prognostic impact occurs on TAS + Bev which has now supplanted TAS as the standard of care[3].

METHODS

- We retrospectively investigated outcomes in a cohort of 100 mCRC patients treated with TAS + Bev for ≥1 month between January 2020 and March 2023 at MD Anderson (cohort A) using institutional databases.
- For validation, a cohort of 98 mCRC patients from the Tempus database was used (cohort B). Mutation status was determined from tissue biopsy using clinical NGS[4].
- The primary endpoint was overall survival (OS), determined by Kaplan Meier estimators and risk set adjustment methods and compared using the log-rank test.

ACKNOWLEDGEMENTS

- To every patients and caregivers.
- To thank Fight CRC for their support of the research in collaboration with Tempus
- To whom believe in education and mentorship.

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SIGNIFICANCE

- In this two cohorts of mCRC treated with **TAS-Bev, codon-specific *KRAS* mutations did not appear to predict survival benefit**, unlike previously reported for TAS treated patients.
- Further investigations into *KRAS* codon-specific impact are required prior to incorporating this for patient selection for treatment, especially in a late line setting where options are limited for mCRC pts.

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RESULTS

Table 1. Demographic characteristics of cohort MDA and Tempus.

Baseline population	Cohort A n= 100	Cohort B n= 98
Sex		
Male	53 (53.0%)	56 (57.0%)
Female	47 (47.0%)	42 (43.0%)
Etnicity		
White or caucasian	62 (62.0%)	49 (75.0%)
Black or African American	16 (16.0%)	6 (9.2%)
Asian	8 (8.0%)	2 (3.1%)
Other	12 (12.0%)	8 (12%)
Unknown	2	33
Age – years	56 (47 – 61)	52 (47 – 60)

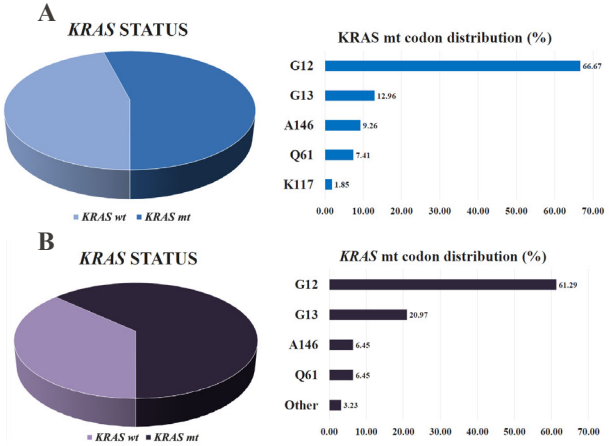

Figure 1. Pie chart for *KRAS* status (mutated or wild type) and bar plot for *KRAS* mutation codon distribution for MDA (A) and Tempus (B) cohorts.

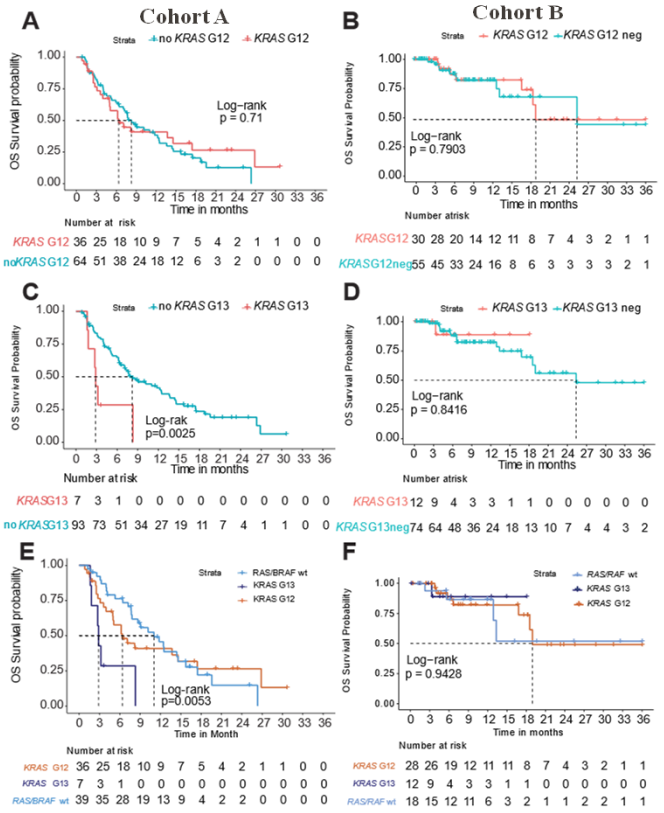

Figure 2. Overall survival depending on *KRAS* G12 status for cohorts A (A) and B (B), *KRAS* G13 status for cohorts A (C) and B (D), and *KRAS* G12 and G13 status versus RAS/BRAF wt for cohorts A (E) and B (F).

- Baseline characteristics of patients are listed in **Table 1**; of note, they are similar in the two cohorts with a higher prevalence of male sex and an overlapping age interval.
- Prevalence of *KRAS* G12 mt, G13 mt and *RAS/BRAF* wt is 36%, 7% and 39% respectively, in Cohort A and 40%, 13%, 21% in Cohort B. These data are comparable and consistent with previous literature (**Figure 1**).
- *KRAS* G12 mt does not seem associated to a worst prognosis in pts treated with Tas-bevacizumab. HR 0.91 (95CI: 0.56 – 1.49) in Cohort A, HR=1.17 (95%CI: 0.44 – 3.13) in cohort B (**Figure 2 A-B**).
- There is no conclusion on a possible predictive value of *KRAS* G13 mts, given also the limited numbers of pts carrying alteration in this specific codon (7 pts in cohort A, 13 pts in cohort B) (**Figure 2C-F**).

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Presenter: gmaddalena@mdanderson.org