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Utilisation and predictors of genomic testing prior to first-line (1L) therapy in patients (pts) with metastatic colorectal cancer (mCRC)

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Summary

Results from this analysis of mCRC molecular testing patterns from the US Flatiron Health EHR-derived de-identified database suggest changes in molecular testing frequencies between 2013 and 2020. While there were varying increases in the testing uptake for *RAS*, *BRAF* and MSI, rates in mCRC remain low compared with other cancer types.

ePoster

https://bit.ly/3jSZSmd

Supplement

https://bit.ly/3i8f0v8

Introduction

- While molecular profiling in mCRC has become integral to treatment decision making within the last 10 years (Supplementary Figure 1),[1–4] testing rates are low[4] and up-to-date data are lacking.
- We aimed to describe utilisation and predictors of *RAS*, *BRAF* and MSI testing prior to 1L therapy initiation in an mCRC population between 2013 and 2020.

Methods

- This study used data from the US, nationwide Flatiron Health EHR-derived, de-identified database (~280 cancer clinics from ~800 sites of care). This is a longitudinal database, comprising pt-level structured and unstructured data, curated via technology-enabled abstraction.[5,6]
- The majority of pts originated from community oncology settings (Supplementary Table 1); relative community/academic proportions may vary depending on study cohort.
- Detailed methodology for this analysis is shown in Supplementary Figure 2.
- Briefly, eligible pts had stage IV or recurrent mCRC and had initiated 1L systemic therapy for mCRC (1 Jan 2013–31 Dec 2020).
- Documented testing for *RAS*, *BRAF* and MSI that was performed between initial diagnosis and 1L therapy initiation were considered (including NGS and non-NGS testing).
- Test availability was determined by the observed specimen received date or biomarker test result date at or before 1L therapy initiation.
- Temporal trends were assessed based on the proportion of tested pts by year of 1L therapy initiation.
- Logistic regression was used to assess predictors for being tested.
- Institutional Review Board approval of the study protocol was obtained prior to study conduct, and included a waiver of informed consent.[6]

Results

- The study included 18,679 pts with stage IV or recurrent mCRC and most were male (55.7%; Supplementary Table 1).
- The proportion of *RAS*, *BRAF* and MSI alterations was consistent with published data (Supplementary Table 1).[7]
- Testing patterns differed depending on the year that 1L therapy was initiated (Figure 1).
  - There was a moderate increase in *RAS* testing between 2013 (40.6%) and 2020 (55.3%).
  - While *BRAF* testing was low in 2013 (11.0%), it increased with time and was comparable to *RAS* testing by the end of 2020 (51.7%).
  - MSI testing had the greatest increase in uptake over the course of the study (2013: 19.7%; 2020: 76.0%).
- NGS testing utilisation increased across all biomarkers (Figure 2).
- Supplementary Figure 3 graphically summarises the major 1L treatment classes initiated according to biomarker testing result.
- Various factors correlated with *RAS*, *BRAF* and MSI testing (NGS and non-NGS) included younger age at diagnosis, a more recent diagnosis, non-*de novo* metastatic status, colon vs rectal cancer and white ethnicity (Table 1).
  - The odds for being tested decreased with higher age at diagnosis (e.g. OR for MSI: 0.4 [95% CI 0.4–0.5] for pts ≥75 years old).

Figure 1. Biomarker testing proportions by 1L therapy initiation year

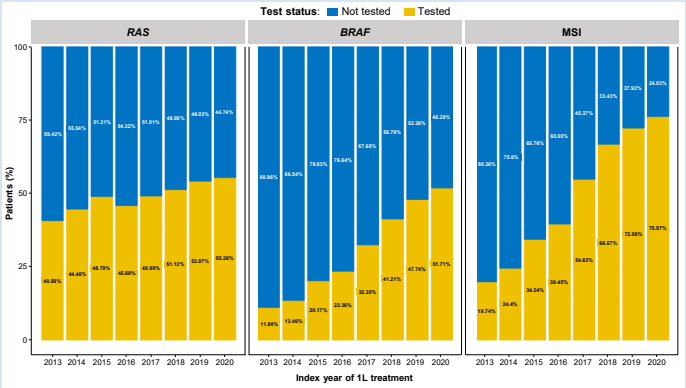

Figure 2. Biomarker testing proportions by 1L therapy initiation year (test type granularity)

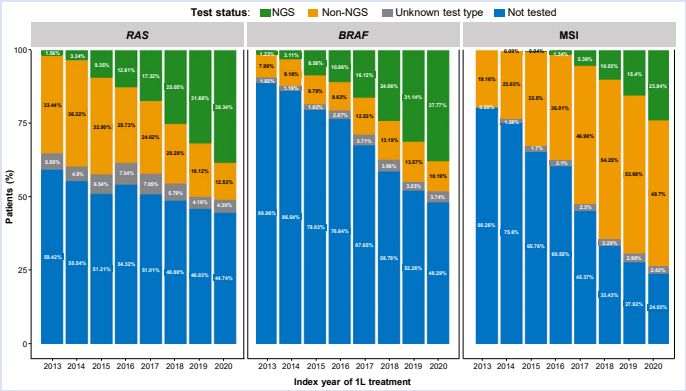

Table 1. Predictors for being biomarker tested

Characteristic	*RAS* testing OR	*RAS* testing 95% CI	*RAS* testing P-value	*BRAF* testing OR	*BRAF* testing 95% CI	*BRAF* testing P-value	MSI testing OR	MSI testing 95% CI	MSI testing P-value
Sex									
Female	–	–	–	–	–	–	–	–	–
Male	1.03	0.97–1.09	0.3	1.05	0.98–1.12	0.2	0.97	0.92–1.04	0.4
Age group at initial diagnosis, years									
<50	–	–	–	–	–	–	–	–	–
50–64	0.94	0.86–1.03	0.2	0.87	0.79–0.95	0.003	0.68	0.62–0.75	<0.001
65–74	0.87	0.79–0.95	0.002	0.82	0.75–0.91	<0.001	0.55	0.50–0.61	<0.001
≥75	0.67	0.61–0.74	<0.001	0.64	0.57–0.72	<0.001	0.44	0.40–0.49	<0.001
Year of initial diagnosis									
<2013	–	–	–	–	–	–	–	–	–
2013–2016	1.11	1.00–1.24	0.045	1.74	1.54–1.98	<0.001	3.20	2.85–3.60	<0.001
≥2017	1.36	1.22–1.52	<0.001	4.82	4.23–5.50	<0.001	13.0	11.4–14.8	<0.001
***De novo* metastasis**									
Progressed	–	–	–	–	–	–	–	–	–
De novo	0.64	0.60–0.69	<0.001	0.53	0.49–0.57	<0.001	0.36	0.34–0.39	<0.001
Unknown	0.61	0.51–0.72	<0.001	0.75	0.61–0.92	0.007	0.48	0.39–0.59	<0.001
CRC site									
Rectum	–	–	–	–	–	–	–	–	–
Colon	1.31	1.23–1.41	<0.001	1.28	1.18–1.38	<0.001	1.37	1.27–1.47	<0.001
Colorectal NOS	1.12	0.98–1.49	0.083	1.15	0.90–1.45	0.3	1.03	0.82–1.29	0.8
Practice type									
Community	–	–	–	–	–	–	–	–	–
Academic	0.81	0.64–1.04	0.093	1.29	0.97–1.73	0.086	1.23	0.95–1.60	0.12
Race/ethnicity									
Non-Hispanic White	–	–	–	–	–	–	–	–	–
Hispanic or Latino	0.82	0.73–0.92	0.001	0.82	0.72–0.94	0.004	0.78	0.69–0.89	<0.001
Non-Hispanic Asian	0.97	0.81–1.15	0.7	0.85	0.70–1.04	0.11	1.03	0.85–1.24	0.8
Non-Hispanic Black	0.98	0.89–1.08	0.7	0.80	0.71–0.89	<0.001	0.93	0.84–1.04	0.2
Other	0.86	0.79–0.94	<0.001	0.87	0.79–0.95	0.002	0.87	0.79–0.95	0.002
ECOG									
0/1	–	–	–	–	–	–	–	–	–
≥2	0.67	0.44–1.01	0.057	0.71	0.45–1.10	0.13	0.75	0.49–1.15	0.2
Unknown	1.21	1.06–1.38	0.006	0.97	0.84–1.12	0.6	1.27	1.10–1.46	0.001
US region									
Midwest	–	–	–	–	–	–	–	–	–
North-east	1.02	0.91–1.13	0.8	1.16	1.03–1.30	0.013	1.04	0.93–1.17	0.5
Null	0.90	0.73–1.10	0.3	0.74	0.58–0.94	0.015	0.95	0.76–1.18	0.6
South	0.93	0.85–1.02	0.15	1.16	1.04–1.28	0.005	0.94	0.86–1.04	0.3
West	0.86	0.77–0.95	0.004	0.93	0.83–1.05	0.2	1.07	0.95–1.20	0.3
Unknown	0.84	0.67–1.05	0.13	0.86	0.65–1.12	0.3	0.86	0.68–1.10	0.2

Conclusions

- Overall, although we observed moderate increases in *RAS* testing, stronger uptake of *BRAF* and MSI testing was observed from 2013–2020; the uptake in MSI testing may be due to increased availability of approved cancer immunotherapies.
- Study limitations included missing information on tumour sidedness, which may impact patient outcome and presence of biomarkers,[8,9] and other relevant clinical/therapeutic data.
- Despite increasing trends, testing rates in mCRC were relatively low vs other cancer types, e.g. ~90% of patients received at least one biomarker test for aNSCLC.[10,11]
- Based on the increased availability of molecularly guided therapies in mCRC, the identification of molecular subtypes is key; an increase in molecular testing rates is therefore of paramount importance.

Abbreviations
1L, first-line; aNSCLC, advanced non-small cell lung cancer; CI, confidence interval; CRC, colorectal cancer; ECOG, Eastern Cooperative Oncology Group; EHR, electronic health record; mCRC, metastatic colorectal cancer; MSI, microsatellite instability; NGS, next-generation sequencing; NOS, not otherwise specified; OR, odds ratio; pts, patients.

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Conflicts of interest
H-JL reports financial interests from BMS, Merck, Bayer, F. Hoffmann-La Roche Ltd, Oncocyte, Fulgent for advisory boards and research (medical writing support) from F. Hoffmann-La Roche Ltd. Please refer to the Supplementary for all author conflicts of interest. This study was sponsored by F. Hoffmann-La Roche Ltd.