Retrospective analysis of metastatic colorectal cancer based on clinical cancer registry data. Tumor biology, treatment, and outcome.

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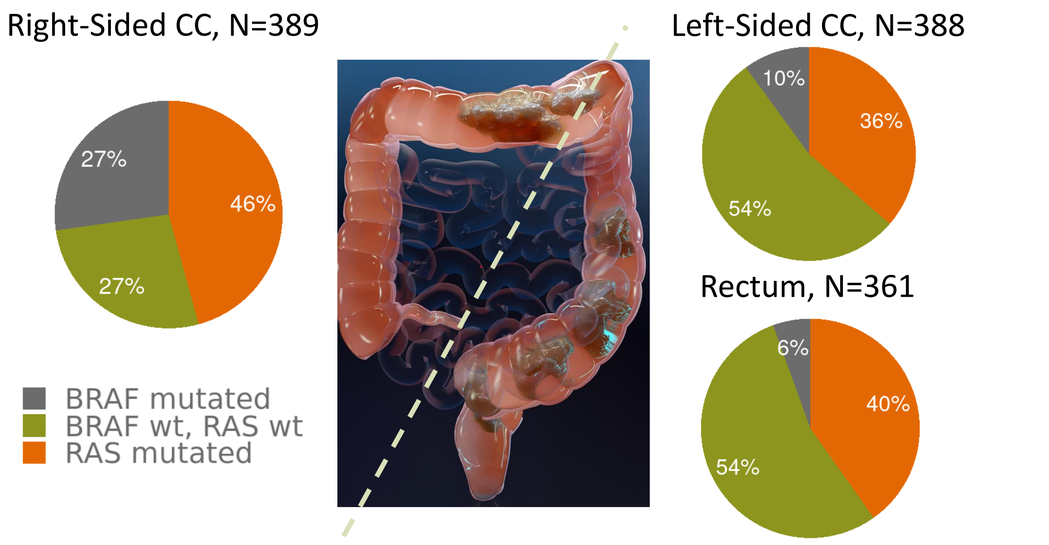
Background and Objectives

- Metastatic colorectal cancer (mCRC) is one of the most common causes of cancer-related death with median overall survival (OS) between 26-36 months [1]. Important prognostic factors are the localization and tumor biology [2]. Systemic chemotherapy has been the main treatment approach for non resectable mCRC [3].
- The aim of the present study is to explore clinical and biological profile of mCRC as well as the disease treatment and patient outcome based on the data collected in the cancer registry of Baden-Württemberg state, Germany.

Methods

- Records for patients with mCRC diagnosed in 2016-2022 were selected.
- Overall survival were assessed using Kaplan-Meier statistics and multivariable Cox proportional hazard models.
- The following parameters were considered: age, gender, tumor localization, BRAF and RAS mutations, MSI status and systemic treatment.

BRAF and RAS Mutations vs Localisation



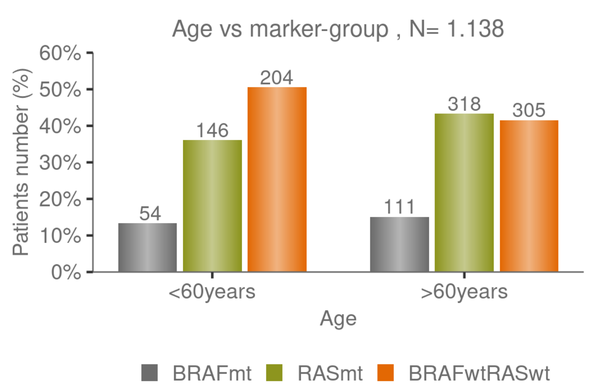
- Both BRAF- and RAS-mutations are mostly associated with right-sided-cancer

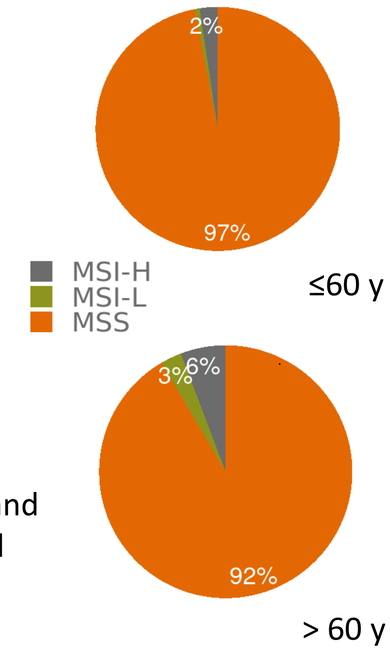
Patient demographics and clinical information

- Patients in the cohort are predominantly males and elderlies
- Tumors are mostly well- or intermediately differentiated
- BRAF- and RAS mutations are found more frequently in right sided cancer
- Most carcinomas are classified as MSS/MMRp.
- MSI-H/MMRd is reported in 4.4% of cases and more often found in right sided cancer

	All patients	Right	Left	Rectum
Number (%)	1138(100)	389(34)	388(34)	361(32)
Age,median (SD)	66(12,1)	69(12)	65(11,8)	65(12,5)
Patient sex				
- **Male (%)**	699(61)	206(53)	246(63)	340(67)
BRAF				
- **wt (%)**	973(86)	283(63)	349(90)	341(94)
- **mt (%)**	165(14)	106(27)	39(10)	20(6)
RAS				
- **wt(%)**	632(57)	181(50)	240(63)	211(59)
- **mt(%)**	470(43)	181(50)	142(37)	147(41)
- **Missing**	36	27	6	3
MSI				
- **MSI-H(%)**	19(4,4)	14(10)	4(3)	1(1)
- **MSI-L(%)**	8(1,9)	4(3)	1(1)	3(2)
- **MSS(%)**	400(94)	117(87)	112(96)	171(98)
- **Missing**	711	254	271	186
Tumor grade				
- **1 or 2 (%)**	754(72)	215(61)	280(78)	259(72)
- **3 or 4 (%)**	289(28)	137(39)	79(22)	73(22)
- **Missing**	95	37	29	29

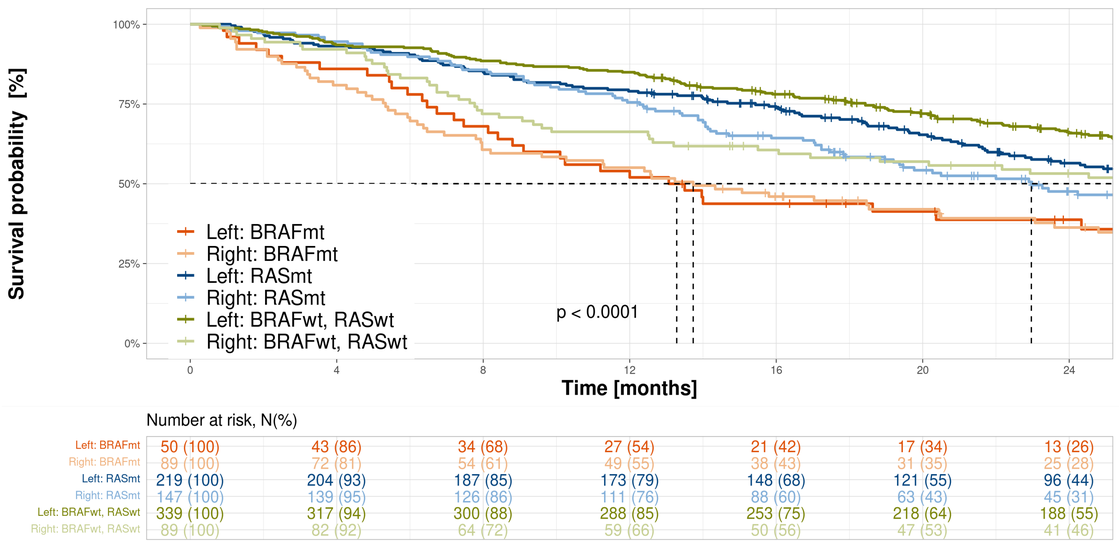
Mutation and Microsatellite Status vs age



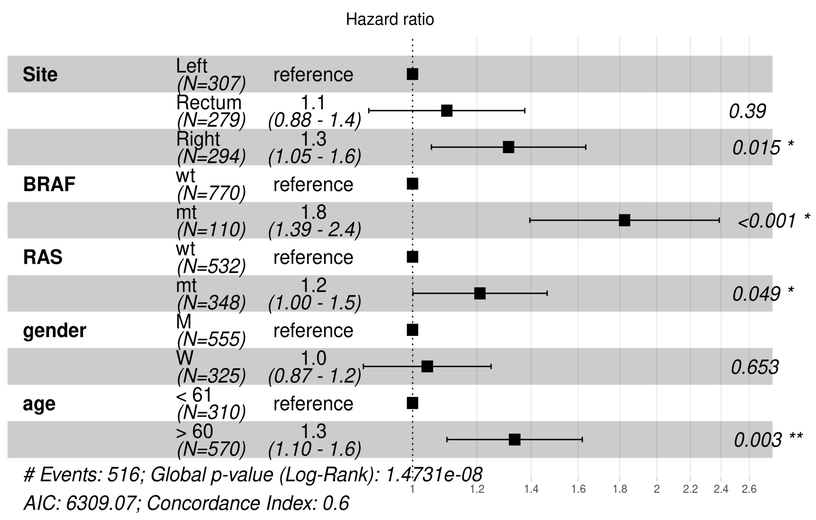


- our data show that the frequency of BRAF- and RAS-Mutations increases with age (statistical significance, p=0.018)

Overall survival



- BRAF mutation is the most significant prognostic factor with HR 1.8 (95% CI 1.39-2.4).
- BRAF wildtype: the OS of patients with right-sided carcinomas is significantly worse compared to those with left-sided carcinomas.

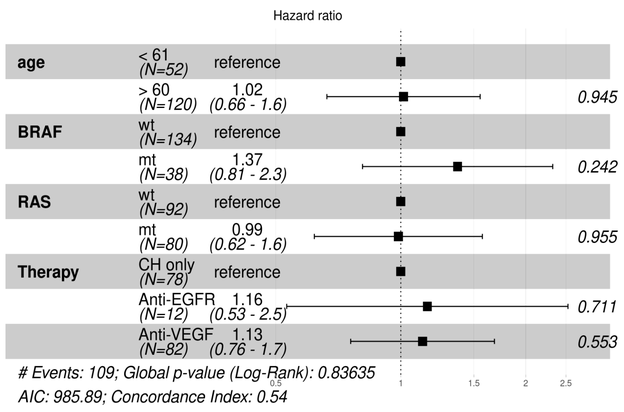


Therapy landscape

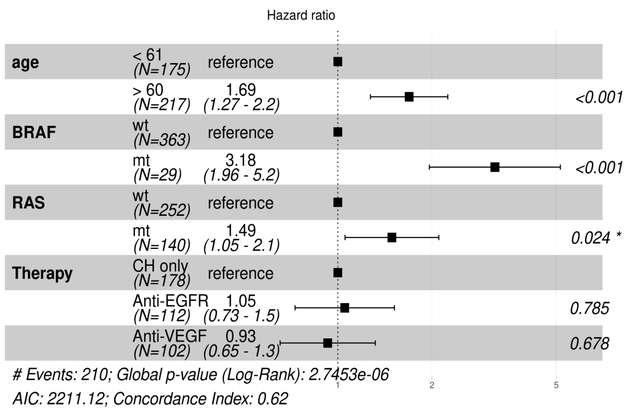
	CH only	CH + anti-EGFR	CH + anti-VEGF
Right-sided	**100**	**14**	**104**
- BRAF mt	35	1	20
- RAS mt	42	0	56
- BRAF, RAS wt	23	13	28
Left-sided	**104**	**79**	**75**
- BRAF mt	10	3	9
- RAS mt	40	3	51
- BRAF, RAS wt	54	73	15
Rectum	**107**	**59**	**65**
- BRAF mt	8	1	4
- RAS mt	40	0	50
- BRAF, RAS wt	59	58	11

- All patients received chemotherapy (mostly doublet).
- Right-sided carcinomas were treated with chemotherapy (CH) +/- anti-VEGF. EGFR directed therapy is rarely reported.
- Left-sided carcinomas wt/wt were treated with CH only, CH plus anti-EGFR or with CH plus anti-VEGF

Right-Sided CC



Left-Sided CC + Rectum



Discussion and Conclusion

- In the present study tumor biology, therapy modalities, and treatment outcomes were analyzed for mCRC cases.
- Real world data from the clinical cancer registry of Baden-Württemberg were employed.
- BRAF status was confirmed as the most important prognostic factor.
- BRAF and RAS mutations as well as MSI status were associated with right-sided colon cancer.
- Right-sided tumors were also associated with greater risk of death compared to left-sided ones and to rectal cancer.
- For left-sided tumors, BRAF, RAS wt tumors anti-EGFR treatment in addition to chemotherapy was reported for about half of the patients. No significant difference in OS was observed for patients who underwent different therapies.
- For right-sided tumors, no significant difference in OS was observed for the patients treated with CH only vs. those treated with CH plus anti-VEGF.
- Data of clinical cancer registries can be used to build an external control arm for clinical trials.

References

[1] Oliveira et al. *Frontiers in Oncology* (2019), 9, 396
[2] Ruiz-Bañobre J. et al, *JCO Precision Oncology* (2019), 3, 1-17
[3] Atreya et al., *American Society of Clinical Oncology Educational Book* 37 (2018) 246-256.

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