

# HER2 status in RAS and BRAF wild-type metastatic colorectal cancer – Portuguese study

M.J. de Sousa<sup>1</sup>, T. Fraga<sup>1</sup>, J. Correia Magalhães<sup>1</sup>, R. Basto<sup>1</sup>, C. Caramujo<sup>1</sup>, J. Paulo<sup>1</sup>, P. Jacinto<sup>1</sup>, N. Bonito<sup>1</sup>, J.P. Magalhães<sup>2</sup>, P. Figueiredo<sup>2</sup>, G. Sousa<sup>1</sup>;

<sup>1</sup>Oncology Department, Instituto Português de Oncologia de Coimbra Francisco Gentil E.P.E. (IPO Coimbra), Coimbra, Portugal; <sup>2</sup>Pathology Department, IPO Coimbra, Coimbra, Portugal

e-Poster: 69P

## BACKGROUND

Colorectal cancer (CRC) is the second most deadly cancer worldwide but currently, there are few precision treatments available. Amplification/overexpression of HER2 (HER2+) is a well-established therapeutic target in breast and gastric cancer. HER2+ is present in approximately 5% of CRC and has been implicated in resistance to therapy with anti-epidermal growth factor receptor antibodies. The aim of our study was to evaluate HER2 status in RAS and BRAF wild-type metastatic CRC (mCRC) and its correlation with clinicopathological characteristics and survival outcomes.

## METHODS

Single-centre retrospective analysis of RAS and BRAF wild-type mCRC patients undergoing systemic treatment from July 2014 to September 2020. Tissue HER2 status was determined by performing immunohistochemistry (IHC) and/or fluorescence in situ hybridization (FISH) and/or chromogenic in situ hybridization (CISH). HER2+ was defined as either IHC 3+ or IHC 2+ through FISH or CISH +.

## RESULTS

HER2- Population: 55 patients	
Age	years
Median	64
Range	33-82
Gender	n (%)
Male	26 (47.3)
Female	29 (52.7)
ECOG Performance Status	n (%)
0	42 (76.4)
1	13 (23.6)
Tumor Location	n (%)
Right-sided	8 (14.5)
Left-sided	47 (85.5)
Metastatic Sites	n (%)
Liver	32 (58.2)
Lung	21 (38.2)
Peritoneal Carcinomatosis	10 (18.2)
Other Location	13 (23.6)

Table 1: HER2 negative (HER2-) population characteristics

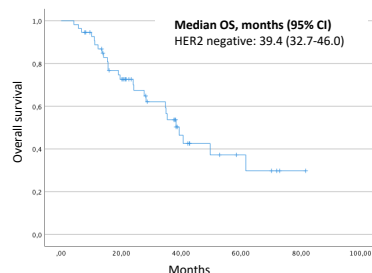


Figure 1. Kaplan-Meier Estimates of Overall Survival (OS) in the HER2 negative population

## RESULTS continued

HER2+ Population: 4 patients	
Age	years
Median	65
Range	54-72
Gender	n (%)
Male	3 (75.0)
Female	1 (25.0)
ECOG Performance Status	n (%)
0	3 (75.0)
1	1 (25.0)
Tumor location	n (%)
Right-sided	1 (25.0)
Left-sided	3 (75.0)
Metastatic Sites	n (%)
Liver	4 (100)
Lung	3 (75)
Peritoneal Carcinomatosis	2 (50)
Other Location	4 (100)

Table 2: HER2+ population characteristics

Overall Survival HER2+ Patients	months
Patient 1	18.4
Patient 2	20.4
Patient 3	29.6
Patient 4	30.2

Table 3: Overall Survival in the HER2+ Population

## CONCLUSIONS

To our knowledge, this is the first study reporting HER2+ in mCRC patients in a Portuguese population and the HER2+ rate was consistent with previous studies. Our study suggests that HER2+ may potentially be a marker that is able to predict poor prognosis in RAS and BRAF wild-type mCRC. There is potential that with the continued evolution of data in this area, HER2 may become a validated therapeutic target.

## REFERENCES

Alkayam, T., Sudo, C., Ogawara, H., Toyoshima, K., & Yamamoto, T. (1986). The product of the human c-erbB-2 gene: a 185-kilodalton glycoprotein with tyrosine kinase activity. *Science*, 232(4758), 1544-1546.

Yagawa, M., Sawada, K., Nakamura, T., Fujii, S., Nakai, S., Komatsu, T., ... & Taniguchi, H. (2020). Prognostic Value and Molecular Landscape of HER2 Low-expressing Metastatic Colorectal Cancer. *Clinical Colorectal Cancer*.

Yan, M., Schwedde, M., Argente, D., Mills, S. Z., Gatalica, Z., & Kuznetsov, R. (2015). HER2 expression status in diverse cancers: review of results from 37 892 patients. *Cancer and Metastasis Reviews*, 34(3), 157-164.

Sartore-Bianchi, A., Trusolino, L., Martino, C., Benedicchio, K., Lonardi, S., Bergamo, F., ... & Triani, T. (2016). Dual targeted therapy with trastuzumab and lapatinib in treatment-refractory, BRAF codon 12/13 wild-type, HER2 positive metastatic colorectal cancer (HERACLES): a proof-of-concept, multicentre, open-label, phase 2 trial. *The Lancet Oncology*, 17(6), 738-746.

Nakamura, Y., Okamoto, W., Kato, T., Hasegawa, H., Kato, K., Iwano, S., ... & Nomura, S. (2019). 526PD TRIUMPH: Primary efficacy of a phase II trial of trastuzumab T7 and pertuzumab PPI in patients (pts) with metastatic colorectal cancer (mCRC) with HER2 (ERBB2) amplification (amp) in tumor tissue or circulating tumour DNA (ctDNA): A GDGA sub-study. *Annals of Oncology*, 30(supplement\_5), m0246-004.

Stricker, J. H., Zema, T., Cho, F. S., Corcoran, A., Wu, C., Sanchez, F. A., ... & Nandorvics, D. (2019). Trastuzumab and lapatinib for the treatment of HER2 amplified metastatic colorectal cancer (mCRC): initial results from the MOUNTAINEER trial. *Annals of Oncology*, 30, v200.

Sartore-Bianchi, A., Lonardi, S., Martino, C., Fenciochio, E., Toi, F., Ghersi, S., ... & Arfanzoni, A. (2020). Pertuzumab and trastuzumab emtansine in patients with HER2-amplified metastatic colorectal cancer: the phase II HERACLES II trial. *ESMO open*, 5(5), e000911.

Meric-Bernstam, F., Hurwitz, H., Raghu, K. P. S., McWilliams, R. R., Fakih, M., VanderWalde, A., ... & Bose, R. (2019). Pertuzumab plus trastuzumab for HER2-amplified metastatic colorectal cancer (MyPathway): an updated report from a multicentre, open-label, phase 2a, multiple-bolus study. *The Lancet Oncology*, 20(4), 518-530.

Siena, S., Sartore-Bianchi, A., Marsoni, S., Hurwitz, H. I., Miccali, S. J., Penash-Gloria, F., ... & Trusolino, L. (2018). Targeting the human epidermal growth factor receptor 2 (HER2) oncogene in colorectal cancer. *Annals of Oncology*, 29(5), 1108-1119.

Bertotti, A., Papp, E., Jones, S., Adelf, V., Anagnostou, V., Lupu, B., ... & Niknafs, N. (2015). The genomic landscape of response to EGFR blockade in colorectal cancer. *Nature*, 521(7572), 263-267.

Bertotti, A., Magliardi, G., Galimi, F., Sansi, F., Torti, D., Iella, C., ... & Ribero, D. (2011). A molecularly annotated platform of patient-derived xenografts ("xenopatients") identifies HER2 as an effective therapeutic target in cetuximab-resistant colorectal cancer. *Cancer discovery*, 1(6), 508-523.

Leto, S. M., Sassi, F., Catalano, I., Torti, V., Migliardi, G., Zanella, E. R., ... & Trusolino, L. (2015). Sustained inhibition of HER3 and EGFR is necessary to induce regression of HER2-amplified gastrointestinal carcinomas. *Clinical Cancer Research*, 21(24), 5519-5531.

## FUNDING AND DISCLOSURE

This study was not sponsored.  
The authors have nothing to declare.

Correspondence should be sent to mariasousa2@campus.ul.pt