439P

Characteristics and Treatment Patterns Among Patients With HER2-Amplified Advanced/Metastatic Colorectal Cancer (mCRC): A Clinical-Genomic Database Study

John H Strickler[1], Ling-I Hsu[2], Kendra DeBusk[2], Phoebe Wright[2], Michael Stecher[2], Muriel Siadak[2], M Corinna Palanca-Wessels[2], Junhua Yu[3], Nicole Zhang[3], Carin R Espenschied[3], Kathryn Lang[3], Tanios S Bekaii-Saab[4]

[1]Division of Medical Oncology, Duke University Medical Center, Durham, NC, USA; [2]Seagen Inc., Bothell, WA, USA; [3]Guardant Health, Inc., Redwood City, CA, USA; [4]Division of Hematology/Oncology, Mayo Clinic, Phoenix, AZ, USA

Background

- Human epidermal growth factor receptor 2 (HER2) gene (*ERBB2*) amplification (HER2+) is present in ~3% of patients with metastatic colorectal cancer (mCRC), and is even higher in patients with *RAS/BRAF* wild-type tumours (~5–14%).[1]
- Awareness of HER2 as an important target in mCRC has increased following key publications from the HERACLES trial of trastuzumab plus lapatinib (2016)[2] and the MyPathway basket-trial subset analysis of trastuzumab plus pertuzumab (2019)[3] in patients with HER2-amplified mCRC, along with the subsequent inclusion of these HER2-directed therapies in National Comprehensive Cancer Network (NCCN) treatment guidelines in 2019.[4]
  - Current NCCN guidelines include 3 regimens (trastuzumab in combination with either pertuzumab or lapatinib and fam-trastuzumab deruxtecan-nxki monotherapy) as therapy options in patients with tumours that are *RAS* and *BRAF* wild-type and have HER2 overexpression.[1]
- Testing of tumour gene status for *KRAS/NRAS* and *BRAF* mutations, HER2 amplifications and microsatellite instability (MSI) high/mismatch repair are recommended for patients with mCRC to guide treatment decisions.[1]
- Despite increased awareness of HER2 in mCRC, there are currently no therapies approved by the US Food and Drug Administration for patients with HER2+ mCRC, and limited data are available on the evolution of real-world treatment of patients with HER2+ mCRC since the reporting of clinical trials of HER2-directed therapies in this population.

Objective

- This study examined the real-world treatment patterns of patients with HER2+ mCRC in the United States with confirmation of HER2+ status pre- and post-2018.

Methods

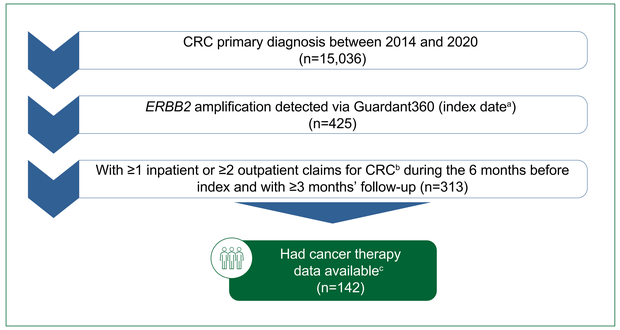
- Patients were identified from the Guardant INFORM™ clinical-genomic database from January 2014 to September 2020.
  - The Guardant INFORM™ database includes aggregated US commercial payer claims with de-identified records of over 137,000 subjects with Guardant360® (G360) genomic testing results.
  - G360 covers genes recommended for testing by the NCCN, including *ERBB2*.
- Key inclusion criteria were age ≥18 years, *ERBB2* amplification, ≥1 inpatient or ≥2 outpatient claims with a colorectal cancer diagnosis code at baseline, ≥3 months' follow-up from index, and provider-confirmed mCRC.
  - Index was the date of the first G360 report with *ERBB2* amplification, or start of a HER2-directed regimen (including trastuzumab, lapatinib, pertuzumab), whichever was earlier.
    - If patients initiated HER2-directed therapy before the G360 result date, it was assumed that they were aware of their HER2+ status before test confirmation.
- Treatment patterns, including the first treatment received post-index and real-world time to next treatment (rwTTNT), were assessed for patients receiving an approved systemic cancer therapy post-index.
  - Data on first post-index treatment were stratified by an index date pre- and post-2018 based on the timing of increased awareness of HER2 in mCRC.
  - rwTTNT was defined as the time between first therapy initiation and the start of the subsequent line of therapy (LOT), or known date of death, whichever occurred first.
    - Changes that defined a LOT were a gap in therapy of >180 days or switch/addition to a regimen after a 15- or 60-day gap in therapy (depending on the treatment/regimen).[5,6]

Results

Patient characteristics

- The study population included 142 patients (**Figure 1**); the mean age was 59.3 years, 52.8% were male, and 12.2% received prior anti-epidermal growth factor receptor (EGFR) therapy (**Table 1**).
- 19.7% of patients had *KRAS* mutations and 0% had *BRAF* mutations. The median *ERBB2* plasma copy number was 2.9.
  - Only 27% of patients had MSI data available (added to G360 in September 2018); none of them were MSI-high.

Figure 1. Patient attrition



[a]Index date is defined as the first Guardant360 report date with *ERBB2* amplification. If a patient initiated HER2-directed therapy before the Guardant360 result date, the index date was adjusted to be the start of the HER2-directed treatment initiation with the assumption that the patient knew their HER2+ status before test confirmation.
[b]Advanced or metastatic disease at time of index was indicated via the Guardant360 patient requisition form.
[c]Patients with no cancer therapy post-index did not receive an approved systemic cancer therapy but may have received hospice or supportive care. The low proportion receiving systemic therapy may be due to multiple factors (eg, shorter follow-up time, timing of testing, and differences in disease trajectory among untreated patients).
CRC, colorectal cancer; HER2, human epidermal growth factor receptor 2.

Table 1. Baseline demographic and clinical characteristics of patients who received systemic cancer therapy post-index

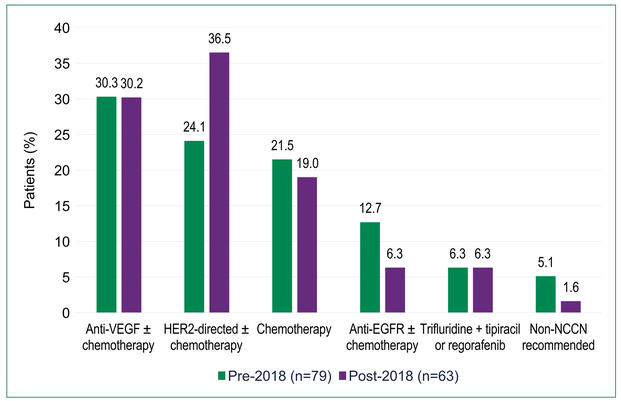
Parameter	Study cohort (n=142)
Age, years, mean (SD)	59.3 (13)
Age group, years, n (%)	
<50	39 (27.5)
50 to 64	57 (40.1)
65 or older	46 (32.4)
Male, n (%)	75 (52.8)
Insurance type, n (%)[a]	
Commercial	118 (83.1)
Medicare	64 (45.1)
Medicaid	26 (18.3)
Other	34 (23.9)
Charlson Comorbidity Index[b], mean (SD)	2.8 (1.4)
Prior treatment with anti-EGFR regimen(s)[c], n (%)	14 (12.2)

[a]Not mutually exclusive.
[b]The Charlson Comorbidity Index[7] is a weighted summary score of the number and severity of comorbid conditions in an individual.
[c]Only includes patients with a known metastatic diagnosis date identified by ICD secondary malignancy code (n=115).
EGFR, epidermal growth factor receptor; ICD, International Classification of Diseases; SD, standard deviation.

Treatment patterns

- Treatment received after confirming HER2 status was heterogeneous (**Figure 2**).
- In the overall cohort (n=142), anti-vascular endothelial growth factor (VEGF) ± chemotherapy (30.3%) and HER2-directed therapy ± chemotherapy (29.5%) were the most commonly received regimens.
  - For patients with an index date pre-2018 (n=79), anti-VEGF ± chemotherapy was the most common regimen (30.3%).
  - For patients with index post-2018 (n=63), HER2-directed regimens were the most common (36.5%).
  - Use of anti-EGFR ± chemotherapy declined from 12.7% pre-2018 to 6.3% post-2018.

Figure 2. First treatment regimen following HER2+ status confirmation, by time period



Non-NCCN treatments included trastuzumab emtansine (T-DM1), paclitaxel, carboplatin, cisplatin, gemcitabine, doxorubicin and crizotinib; anti-VEGF treatments included bevacizumab, aflibercept and ramucirumab; HER2-directed treatments included lapatinib, trastuzumab, pertuzumab and fam-trastuzumab deruxtecan-nxki; anti-EGFR treatments included cetuximab and panitumumab.
EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; NCCN, National Comprehensive Cancer Network; VEGF, vascular endothelial growth factor.

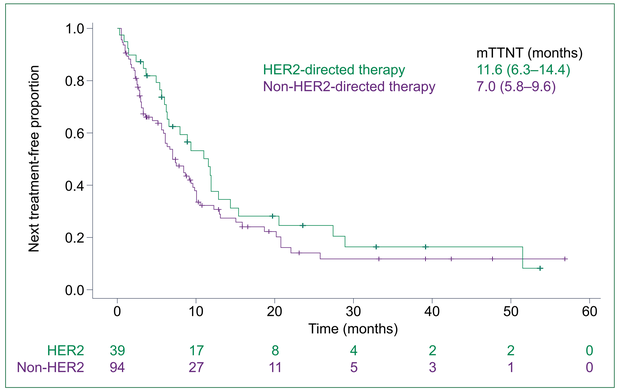
Real-world time to next treatment

- In the overall cohort, the median rwTTNT was 8.4 months (95% confidence interval [CI]: 6.5–10.0).
- Patients treated with HER2-directed therapy had numerically longer median rwTTNT compared with those treated with non-HER2-directed therapies (11.6 [95% CI: 6.3–14.4] vs 7.0 months [95% CI: 5.8–9.6]; **Figure 3**), indicating a potentially improved outcome with HER2-directed vs non-HER2-directed therapies in this population.

Limitations

- We used a heterogeneous definition for patients' index date because we did not have insight into prior biomarker test results on HER2 status.
- There are inherent limitations in analyses of real-world data, including the extent of missing clinical information, which is not routinely reported in administrative claims data.
- Focal and aneuploidy amplifications were included in the G360 test before September 2018; however, only focal amplifications were reported after that time point, resulting in higher specificity but lower sensitivity for detecting HER2-positivity.

Figure 3. Time to next treatment among patients treated with HER2-directed (n=39) vs non-HER2-directed (n=94) therapies



+ = censored.
HER2, human epidermal growth factor receptor 2; mTTNT, median time to next treatment.

Conclusions

- Using a unique clinical-genomic dataset, this study highlights the significant unmet need among patients with HER2+ mCRC.
  - We observed heterogeneous treatment patterns among patients, suggesting a lack of current standard of care.
  - Despite the increased awareness of HER2-directed therapies post-2018, utilisation of these therapies was still low.
  - ~10% of patients received anti-EGFR-based regimens despite potential resistance to anti-EGFR therapy in HER2+ patients.[8]
- Effective therapies and enhanced awareness of the unmet need in this patient population will facilitate improved, targeted treatment strategies.

References

1. Benson AB, et al. J Natl Compr Canc Netw. 2021;19:329-59.
2. Sartore-Bianchi A, et al. Lancet Oncol. 2016;17:738-46.
3. Meric-Bernstam F, et al. Lancet Oncol. 2019;20:518-30.
4. National Comprehensive Cancer Network; 2019. Accessed 6 August 2021. URL: https://www.nccn.org/guidelines/guidelines-process/transparency-process-and-recommendations/GetFileFromFileManager?fileManagerId=4936.
5. Bikov KA, et al. Med Care. 2015;53:e58-e64.
6. Yezefski TA, et al. JCO Oncol Pract. 2020;16:e425-e432.
7. Charlson ME, et al. J Chronic Dis. 1987;40:373-83.
8. Sartore-Bianchi A, et al. Oncologist. 2019;24:1395-1402.

DISCLOSURES: This study is sponsored by Seagen Inc., Bothell, WA, USA in collaboration with Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA. John Strickler reports advisory board membership/consulting fees/honoraria for AbbVie, Amgen, AstraZenca, Bayer, Mereo, Natera, Pfizer, SeaGen and Viatris; institutional local/coordinating principal investigator (no financial interest) for AbbVie, Amgen, AStar D3, AstraZeneca, Curegenix, Daiichi Sankyo, Exelixis, Leap Therapeutics, Nektar, Roche Genentech, Sanofi and SeaGen.

ACKNOWLEDGMENTS: Medical writing support was provided by Ann Cameron and Elizabeth Harvey of Curo, a division of Envision Pharma Group, and funded by Seagen Inc.

Corresponding author: John H Strickler (john.strickler@duke.edu).

Please scan this Quick Response (QR) code with your smartphone app to view an electronic version of this poster. If you don't have a smartphone, access the poster via the internet at: https://bit.ly/3yDOdMO

Poster presented at the European Society for Medical Oncology (ESMO) Virtual Congress 2021, 16–21 September 2021

Seagen | MSD