Observations in therapy interventions for stage III and stage IV colorectal cancer from 2010 to 2019

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Objectives

- The primary objective of this study was to evaluate treatment options for patients diagnosed with colorectal cancer (CC).
- Through evaluating changes in cancer treatment from 2010 to 2019, new and emerging therapeutics can be closely analyzed for benefits and risks.
- Surgery, chemotherapy (CH) and immunotherapy are possible therapeutics for CC depending on the clinical condition of the patient.

Introduction

- CC treatment options range from surgery, radiation therapy, systemic CH, targeted immunotherapy, or a combination of these depending on cancer staging.
- Stage III colorectal cancer includes tumor involving the submucosa, muscularis propia, outer layers of the colon as well as the peritoneum. In addition, there is also metastasis to regional lymph nodes or fat surrounding the lymph nodes. This stage has an overall survival of 44.9-65.4% (1).
- Stage IV colorectal cancer presents with metastasis to distant organs or distant lymph nodes. The overall survival for stage IV is at 0-8.3% (1).
- Surgical resection is the standard of care for cases with curative intent. CH is recommended in all cases of stage III cancer after surgery (2).
- Combination CH and immunotherapy have been FDA approved for use in recent years. With the advent of immunotherapy and the major breakthroughs in its curative ability, we intended to assess the shift in treatment of stage III and stage IV CC (2).

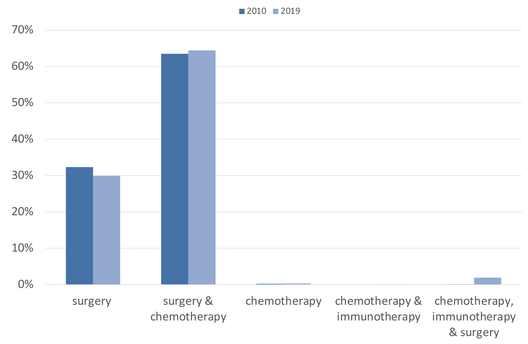
Methods and Materials

- The 2022 National Cancer Database Public Benchmark reports from the American College of Surgeons was utilized to extract data from 1391 hospitals.
- IRB approval was not required as the public database contains de-identified information.
- This study analyzed CC cases from 2010-2019 with first line course of treatment for AJCC stage III-IV.
- 15,897 patients in 2010 and 20,060 in 2019 with stage IV cancer were evaluated, respectively. For stage III CC, 20,036 and 21,954 were evaluated in 2010 and 2019, respectively.
- A two-sample proportion z-test was utilized for significance.

Table 1. Colorectal cancer treatment distribution for stage III and stage IV.

Stage III					
	surgery	surgery & chemotherapy	chemotherapy	chemotherapy & immunotherapy	chemotherapy, immunotherapy, & surgery
2010	32.3%	63.5%	0.2%	0.0%	0.1%
2019	29.9%	64.4%	0.3%	0.1%	1.9%
Stage IV					
	surgery	surgery & chemotherapy	chemotherapy	chemotherapy & immunotherapy	chemotherapy, immunotherapy, & surgery
2010	18.8%	38.9%	18.6%	0.2%	0.2%
2019	13.0%	19.3%	15.1%	12.7%	14.4%

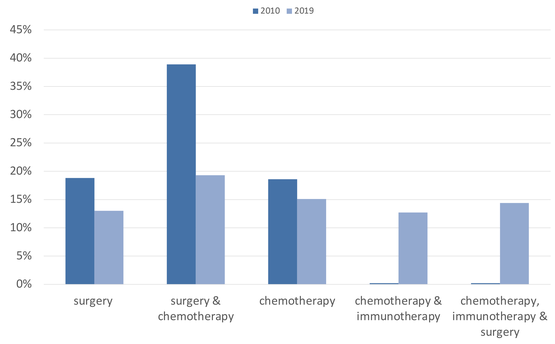
Figure 1. Stage III colorectal cancer treatment distribution.



Results

- Changes in trends were examined with stage III CC comparing the years 2010 and 2019 [Figure 1b]. Surgery in patients decreased (32.3% vs 29.9%, p<0.001). Surgery in combination with CH did not change significantly (63.5% vs 64.4%, p= 0.006).
- CH only also did not change significantly (0.2% vs 0.3%, p= 0.039). Immunotherapy combined with CH was limited (0% vs 0.1%).
- However, combination immunotherapy, surgery and CH increased use of immunotherapy (0.1% vs 1.9%, p< 0.001), and decreased treatment with surgery or CH alone.
- CH alone was used in 18.6% of cases in 2010 compared to 15.1% in 2019 for stage IV CC (p< 0.001) [Figure 1b]. Surgical treatment decreased over the years from 18.8% to 13% (p< 0.001). Surgery and CH combination also decreased (38.9% vs 19.3%, p< 0.001).
- In contrast, treatment with immunotherapy and CH increased (0.2% vs. 12.7%, p< 0.001). Immunotherapy in combination with surgery and CH also increased significantly in stage IV CC (0.2% vs 14.4%, p< 0.001).

Figure 2. Stage IV colorectal cancer treatment distribution.



Discussion

- In stage IV CC, the decreased use of CH treatments can be attributed to the rise of immunotherapy. With an extensive list of side effects, alternatives to chemotherapy should be studied and considered (3).
- More recently, immunotherapy has been FDA approved for other malignancies such as melanoma. Pembrolizumab, ipilimumab, and nivolumab are an immune checkpoint inhibitors that have been FDA approved for select unresectable or metastatic CC (3).
- Studies exploring the use of immunotherapy in earlier stages even in resectable CC should be further developed. In metastatic CC, the progression free survival was 8.2 months for CH compared to 16.5 months for pembrolizumab, showing the benefit of checkpoint inhibitors (4).
- In operable or earlier stages of CC, the rate of high-risk features such as microsatellite instability-high and mismatch repair deficient is greater at a rate of 25% compared to 6-8% in metastatic cancer. These features are also associated with improved response to immunotherapy (4).
- Adverse effects of immunotherapy should also be considered in management of CC. Common side effects include colitis, hypothyroidism, pancreatitis, rash and diarrhea (5).

Conclusions

- Treatment options between 2010 and 2019 were compared for stage III and stage IV CC. Stage IV CC treatment regimens have changed with increased use of immunotherapy and decreased sole use surgery and CH.
- However, stage III CC treatment regimens have largely been unchanged comparing 2010 to 2019.
- With the major successes of immunotherapy in treatment CC, there should be additional work and studies to support use in other stages.

Contact

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