



# A Review of 126 High Grade Neuro-endocrine Carcinomas of the Colon and Rectum

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## Background

High grade neuroendocrine carcinoma's (NEC) of the colon and rectum are rare tumors, constituting less than 1% of colorectal cancers. The purpose of this review is to identify the natural history and oncologic outcomes of this disease, the role of surgery and to determine the clinical and pathological factors associated with outcomes.

|                                      |            |
|--------------------------------------|------------|
| <b>Number</b>                        | <b>126</b> |
| Gender: M                            | 62 (48%)   |
| F                                    | 64 (52%)   |
| Median age (range)                   | 56 (30-91) |
| Histology: SCC                       | 49 (39%)   |
| LCC                                  | 23 (18%)   |
| Collision tumor (HGNEC with adenoca) | 18 (14%)   |
| Site: Anal                           | 5 (4%)     |
| Rectal                               | 53 (42%)   |
| Sigmoid                              | 9 (7%)     |
| Colon                                | 38 (30%)   |
| Caecum                               | 23 (18%)   |
| LVI: Y                               | 48 (84%)   |
| N                                    | 9 (16%)    |
| PNI: Y                               | 18 (50%)   |
| N                                    | 18 (50%)   |
| Median tumor size (range)            | 4 (0.1-11) |
| AJCC stage: 1                        | 0          |
| 2                                    | 15 (12%)   |
| 3                                    | 26 (21%)   |
| 4                                    | 85 (67%)   |
| Resection of primary tumor: Y        | 73 (58%)   |
| N                                    | 53 (42%)   |
| Treatment of M0 disease: Surgery     | 29 (71%)   |
| No Surgery                           | 12 (29%)   |
| IBD                                  | 8 (6%)     |
| Synchronous adenocarcinoma           | 4 (4%)     |
| Met disease: Liver                   | 64 (51%)   |
| Lung                                 | 11 (8%)    |
| Bone                                 | 10 (7%)    |
| RPLN                                 | 8 (6%)     |
| Peritoneal                           | 7 (5%)     |
| Inguinal LN                          | 5 (4%)     |
| Brain                                | 2 (2%)     |

**Table 1:** Patient demographics

SCC – small cell carcinoma, LCC – large cell carcinoma, LVI – lymphovascular invasion, PNI – perineural invasion, AJCC – American joint commission on cancer, IBD – inflammatory bowel disease, RPLN – retroperitoneal lymph nodes

## Methods

Following IRB approval patients with high grade NEC were identified from our institutional database. Patient charts and pathology reports were analyzed retrospectively for clinical and pathological factors.

## A

| Treatment (N=41) | Anorectal (61%) | Colonic (39%) |
|------------------|-----------------|---------------|
| Chemo only       | 9%              | 0%            |
| CRT only         | 38%             | 0%            |
| Surgery only     | 0%              | 19%           |
| CRT & Surgery    | 24%             | 0%            |
| Surgery & Chemo  | 19%             | 81%           |
| Surgery & CRT    | 10%             | 0%            |

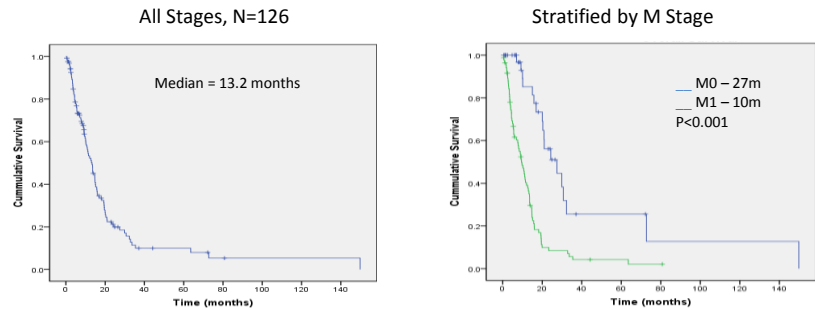
## B

| Treatment (N=85) | Anorectal (38%) | Colonic (62%) |
|------------------|-----------------|---------------|
| Chemo only       | 60%             | 32%           |
| CRT & Chemo      | 27%             | 0%            |
| Chemo & Surgery  | 0%              | 9%            |
| CRT & Surgery    | 3%              | 0%            |
| Surgery & Chemo  | 10%             | 60%           |

**Table 2:** Treatment of patients with (A) localized colorectal HGNEC and (B) metastatic colorectal HGNEC. CRT - chemoradiotherapy

## Results

126 patients with a median follow up of 9 months were identified. The median survival was 13.2 months. 85 (67%) of patients had metastatic disease at diagnosis. The 3 year overall survival (OS) was 5% and 18% for patients with and without metastatic disease respectively. Factors associated with improved OS on multivariable analysis were absence of metastatic disease and presence of an adenocarcinoma component within the tumor. For metastatic disease alone, response to chemotherapy was the only factor associated with survival. For localized disease, presence of an adenocarcinoma component within the tumor was the only factor associated with survival. Resection of the tumor was not statistically associated with survival in localized tumors or metastatic disease.



**Figure 1:** Kaplan Meir curves demonstrating overall survival and overall survival stratified for the presence of metastatic disease at presentation

## Conclusion

High grade colorectal NEC are extremely aggressive tumors with a poor prognosis. Patients appear to have a marginally better prognosis if they present without metastatic disease, have a component of adenocarcinoma within their tumor or respond to chemotherapy. Surgery, particularly in the presence of metastatic disease, may not offer a survival benefit for the majority of patients with this disease.

| Factor                           | Hazard Ratio | 95% Confidence Intervals | P value |
|----------------------------------|--------------|--------------------------|---------|
| Gender                           | 0.663        | 0.42 – 1.02              | 0.64    |
| Age                              | 1.002        | 0.99 – 1.02              | 0.83    |
| Site of tumor (colon vs. rectum) | 0.811        | 0.49 – 1.31              | 0.39    |
| Metastases                       | 0.365        | 0.20 – 0.67              | 0.001*  |
| Adenocarcinoma component         | 1.903        | 1.02 – 3.53              | 0.04*   |
| Resection of primary tumor       | 1.205        | 0.71 – 2.05              | 0.49    |
| Inflammatory bowel disease       | 2.536        | 0.59 – 10.98             | 0.21    |

**Table 3:** Multivariable analysis of factors influencing overall survival in patients colorectal HGNEC. IBD – inflammatory bowel disease, \*denotes statistical significance

| Factor                           | Hazard Ratios | 95% Confidence Intervals | P value |
|----------------------------------|---------------|--------------------------|---------|
| Site of tumor (colon vs. rectum) | 1.305         | 0.59 – 2.87              | 0.508   |
| Response to Chemotherapy         | 0.25          | 0.12 – 0.49              | <0.001* |
| Adenocarcinoma component         | 1.36          | 0.49 – 3.76              | 0.27    |
| Resection of primary tumor       | 0.62          | 0.26 – 1.45              | 0.27    |

**Table 4:** Multivariable analysis of factors influencing overall survival in patients with metastatic colorectal HGNEC. \*denotes statistical significance