First-Line Cisplatin plus Etoposide in High-Grade Metastatic Neuroendocrine Tumors of the Colon and Rectum

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Background

The combination of cisplatin and etoposide is effective in the treatment of small cell lung cancers and other high grade neuroendocrine tumors (NET) s.
This combination has been considered as a default treatment for patients with high grade NET of the colon and rectum (CRC).
Yet no formal series describe the activity of this regimen in this patient population.
We report a single institute experience on treating 8 patients with metastatic colorectal NET with cisplatin and etoposide.

Patient selection and methods

Using pharmacy and tumor registry records , we searched for metastatic CRC NET patients treated with cisplatin and etoposide during the period 2003-2010.
CT scans at baseline and on treatment were reviewed and responses were categorized using RECIST 1.1 guidelines.
Kaplan –Meier methods were used for estimation of survival distributions.

Results

We identified 8 patients with colon or rectal metastatic NET who were treated with cisplatin and etoposide between May of 2003 and August of 2010.
All patients had high grade/poorly differentiated NET.
Cisplatin was administered at 80 mg/m2 on Day 1 and etoposide at 80 mg/m2/day on Days 1-3, every 3 weeks.

Patient Characteristics

Patient characteristics were: median age of 64 yrs (31-83yrs), a male to female ratio of 5/3, and a rectal primary site in 5 patients. All patients had evidence of metastatic disease to the liver at presentation. One patient had concurrent lung metastases, and one patient had concurrent lung, bone, and distant lymph node involvement (Table 1).

Objective Responses

Radiographic response consisted of complete response (CR) in 1 patient, partial response (PR) in 4 patients, and stable disease (SD) in 2 patients. (Table 2)

CAT scan images of one the patient with complete remission is shown.
(Fig. 1 & 2)

Table 1: Patient demographics

Characteristics	No. of patients (n=8)
Gender: Male Female	 5 3
Median age (yrs) (range)	64 (31-83)
ECOG: 0 1 2	 3 4 1
Site of primary: Rectal Colon	 5 3
Site of metastasis: Liver Lung Lymph nodes	 8 3 5

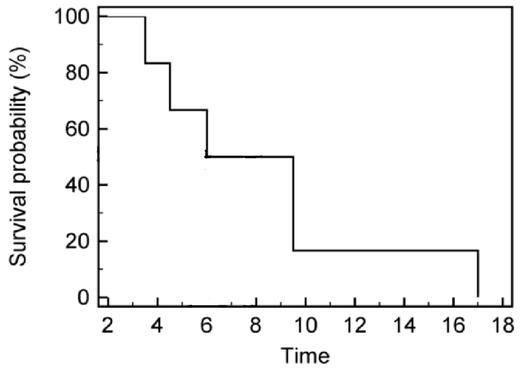
Table 3: Treatment summary

Pt.	#cycles	TTP (Months)	OS (Months)
1	5	3	6
2	6	5	9.5
3	3	2	3.5
4	2	3+	3+
5	6	4.5	9.5
6	3	4.5	4.5
7	6	9	17
8	2	5.5+	5.5+

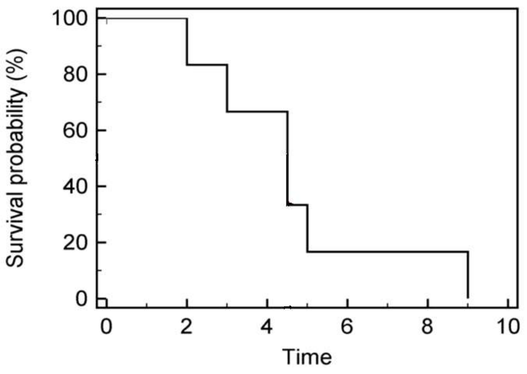
Table 2:Best radiographic response

Characteristic	No. of patients	%(n=8)
Complete response	1	12.5%
Partial response	4	50%
Stable disease	1	12.5%
Progressive disease	2	25%

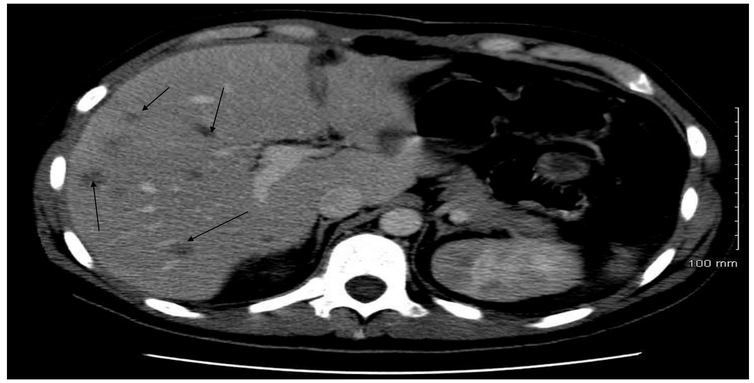
Median overall survival curve (graph 1)



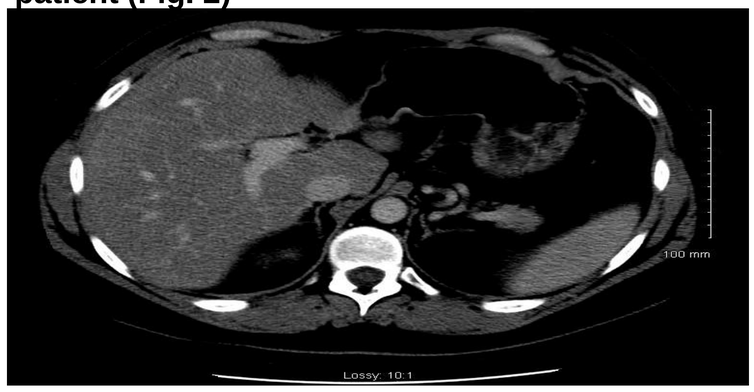
Median time to progression curve (graph 2)



CAT scan at baseline of patient 7 (Fig. 1)



CAT scan at complete remission of theabove patient (Fig. 2)



The median time to progression was 4.5 months (2 – 9 months) and the median overall survival was 7.75 months (3.5 – 17 months). Two patients received second-line treatment consisting of cisplatin plus irinotecan, both with progressive disease (curves seen in graphs 1 and 2).Treatment summary as seen above (Table 3).

Conclusion

Patients with high grade CRC NET have a high response rate to cisplatin and etoposide. The response is short-lived and most patients die within 1 year from diagnosis.