

Patterns of long-term remission or apparent cure in a cohort of patients with grade 3 neuroendocrine neoplasms (NENs).

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Introduction

Grade 3 disease is considered difficult or impossible to eradicate in most patients with neuroendocrine neoplasms (NENs). We sought to describe the pathways to long term treatment-free survival or apparent cure in a cohort of tertiary care patients.

Methods

A registry analysis identified NEN patients in our institution with 1) no imaging evidence of disease or 2) long-term nonprogressive disease without treatment seen over the previous 23 years. Criteria included Ki-67 >20% or high-grade histology and no evidence of disease on no treatment for >5 years (stage I-III) or no evidence of disease progression or activity for at least 2 years off treatment (for stage IV disease).

Results

A total of 51 patients (60.8% male, 39.2% female) were eligible for analysis. Whites consisted of 88.2% and African Americans were 11.8%. Most tumors were first time diagnoses and originated in the head and neck area (31.6%) followed by GI (29.8%) and GU (22.8%). Pathology was poorly differentiated in 54.9% and mixed in 25.5% of the cases. Patient staging on initial presentation was 1 (27.5%), 2 (21.6%), 3 (19.6%) and 4 (31.4%).

Most common general treatments strategies included a combination of approaches (62.8%). Commonly used patterns were surgery and chemotherapy (32%) followed by chemotherapy and radiation (20%) and surgery as single treatment (14%). Most common first line treatments were curative surgery (62.7%) followed by localized radiation (21.6%), with only 7.8% of patients stopping treatment because of intolerance. Most second line treatments consisted of chemotherapy with platinum and etoposide (31.4%) with localized radiation (11.8%). Some patients with metastatic disease on diagnosis were treated with immunotherapy. Most patients underwent surgery followed by platinum chemotherapy. Only 5.9% of patients received a 4th and only 2% received a 6th treatment. Only 3.92% of patients were enrolled in a clinical trial.

The highest survival or long-term remission noted in our study overall was noted in the Head/Neck group with a median survival of over 7 years. A high percentage of the patients in the GI group were able to achieve cure/remission with surgery and adjuvant chemotherapy or chemoradiation, mirroring patterns of treatment of more common histologies.

Conclusions

Based on our study , the primary population with G3 NENs who were able to achieve cure or long-term remission benefited mainly from surgery with platinum-based chemotherapy or chemoradiation in the perioperative setting. For upfront metastatic, resistant disease, a pathway to cure or long-term remission included immunotherapy.

Sex	Stage	Primary	Tx1	Tx2	Tx3	Tx4	Tx5	Tx6	DFFU	Status
GI										
Female	2	Ampula of Vater	Surgery	Cis/Etop					7	Alive
Male	2	Pancreas	Carbo/Etop						13	Alive
Male	4	Pancreas	Platinum/Etop						22	Alive
Male	3	Pancreas	RT	Cis/Etop	Carbo/Etop				4	Alive
Female	2	Pancreas	Surgery	Cap/Tem					4	Alive
Male	2	Rectum	Capecitabine/RT	Surgery					15	Alive
Female	3	Rectum	Surgery	Cis/5FU/RT					8	Alive
Male	4	Esophagus	RT	Pembrolizumab					5	Alive
Male	2	Esophagus	Surgery	5FU/Oxaliplatin					11	Alive
Female	4	Anus	Carbo/Etop/RT						12	Alive
Male	3	Anus	Surgery	Cis/Etop					7	Dead
Male	2	Stomach	Surgery						3	Alive
Male	3	Large intestine	Surgery	5FU/Oxaliplatin					8	Alive
Male	3	Large intestine	Surgery						13	Alive
Male	1	Large intestine	Surgery						17	Alive
Male	3	Large intestine	Surgery	5FU/Oxaliplatin					8	Alive
Female	2	Large intestine	Surgery	Carbo/Etop					6	Alive
Merkel										
Male	1	H/N(Merkel)	VAC	Cis/Etop/RT					13	Dead
Female	1	H/N(Merkel)	Surgery						8	Dead
Male	1	Skin(Merkel)	Surgery						17	Alive
Male	1	Skin(Merkel)	Surgery	Cis/Etop					24	Alive
Head and neck										
Male	4	Oropharynx	Cis/RT						7	Alive
Male	4	Oropharynx	Surgery						9	Dead
Male	4	Oropharynx	Cis/Etop/RT						9	Alive
Male	1	Oropharynx	Surgery	Cis/Etop					15	Alive
Male	3	Oropharynx	Surgery	Cis/Etop					5	Alive
Male	4	Oropharynx	Cis/Etop/RT						7	Alive
Male	1	Oropharynx	Surgery	RT	VAC				7	Dead
Male	2	H/N	Surgery						15	Alive
Male	2	H/N	Cis+Irinotecan	RT					5	Dead
Male	1	H/N	Surgery	Cis/Etop	RT				10	Dead
Female	4	H/N	Surgery	Cis/Etop	RT				8	Alive
Female	4	H/N	Surgery	Cis/5FU/Docetaxel	Cis/RT				8	Dead
Male	4	H/N	Surgery	RT					2	Alive
Female	4	Thyroid	Carbo/Etop/RT						6	Dead
Male	3	Thyroid	Cis/Etop/RT	Observation	RT				7	Alive
Urogenital										
Male	4	Prostate	Surgery	Cis/Etop	Leuprolide				9	Alive
Male	N/A	Prostate	RT	Leuprolide					5	Alive
Male	4	Prostate	Surgery	Leuprolide	Observation	RT	Octreotide	Leuprolide	4	Alive
Male	2	Bladder	Cis/Etop	Surgery					19	Alive
Female gynecological										
Female	4	Endometrium	Surgery	Cis/Etop					6	Dead
Female	3	Endometrium	Surgery	Cis/Etop					8	Alive
Female	4	Ovary/Endometrium	Carbo/Etop	Pembrolizumab					3	Alive
Female	1	Cervix	Surgery	Cis/Etop					23	Alive
Female	1	Cervix	Surgery	Cis/Etop					6	Alive
Female	1	Cervix	Surgery						20	Alive
Female	4	Cervix	Surgery	Carbo/Etop					11	Dead
Female	1	Cervix	Cis/RT						8	Alive
Other										
Female	1	Breast	Surgery	Letrozole					6	Alive
Female	4	Unknown	Carbo/Etop	Carbo/Paclitaxel	Ipi/Nivo (on trial)	Surgery			4	Alive
Female	3	Unknown	Surgery	Doxo/Cyclo/Paclitaxel	RT	Letrozole, tamoxifen, anastrozole			3	Alive

Table 1. Patient / treatment characteristics, Tx: Treatment, RT: Radiation therapy, VAC: Vincristine, adriamycin and cyclophosphamide, Carbo: Carboplatin, Etop: Etoposide, DFFU: Disease Free Follow-up (in years)