Above-Label Doses of Octreotide-LAR in Patients with Metastatic Small Intestinal Carcinoid Tumors

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Introduction

• Metastatic NET of the distal small intestine and cecum (embryonic midgut) commonly produce serotonin and other vasoactive products. Secretion into the systemic circulation produces flushing, diarrhea, and cardiac valvular fibrosis (malignant carcinoid syndrome).

• Octreotide is a potent inhibitor of serotonin release and prolongs time to tumor progression in metastatic midgut NETs

• The FDA label recommends a starting dose of 20 mg with titration to 30 mg in patients with sub-optimally controlled symptoms.

•Above-label doses of octreotide are commonly administered. However there is little literature supporting this practice.

• We performed a review of an institutional database to determine the frequency of 'above-label' octreotide dosing and assess outcomes.

Methods

• A database consisting of all histologically proven cases of midgut NETs seen at the Moffitt Cancer Center between 1995 and 2011 was created

• Data included:
  - Severity of baseline carcinoid syndrome (flushing and diarrhea)
  - Baseline levels of urine 5-HIAA and serum CgA
  - Starting dose and frequency of octreotide
  - Reason for initiation of octreotide (carcinoid syndrome, radiographic progression, anti-proliferative effect, other)
  - Response to treatment

• Definition of 'above-label dose': octreotide LAR given at any dose/schedule which exceeded 30mg every 4 weeks (includes: 30 mg every 3 wks)

• Quantitative measurements of changes in flushing and diarrhea were not typically available, therefore any documentation of symptomatic improvement was considered a "clinical response."

Results

• 458 patients with metastatic NETs were identified, among whom 338 had sufficient longitudinal follow up for abstraction **(Table 1)**

• 100 patients were found to have 'above-label dose' of octreotide LAR **(Table 2)**

• 10 patients received an 'above-label dose' and subsequent decrease to a recommended dose.

• After 1st 'above-label dose' escalation 60% and 53% reported improvement in diarrhea and flushing respectively **(Figure 1)**

• After 2nd 'above-label dose' escalation 70% and 54% reported improvement in diarrhea and flushing respectively.

Results

Table 1: Demographic and Tumor Characteristics of 338 Patients with Metastatic NETs

Characteristic	No.	%
Age (Years)		
Median	60	
Range	21-83	
Sex		
Male	166	49
Female	172	51
Race		
White	300	89
African American	18	5
Other*	20	6
Carcinoid Syndrome		
Present at baseline	100	32
Present subsequently	133	43
Absent	77	25
Tumor Grade		
Low	246	73
Intermediate	41	12
High	1	0
Unspecified	50	15
Presenting Symptoms		
Abdominal pain	149	44
Diarrhea	153	45
Flushing	138	41
Bowel obstruction	69	20
GI Bleeding	20	6
Nausea and/or Vomiting	13	4
Wheezing	7	2
Incidental Diagnosis		
Yes	56	17
No (symptomatic)	281	83
Elevated 5-HIAA		
Yes	269	83
No	54	17
Carcinoid Heart Disease		
Present at baseline	20	6
Present subsequently	13	5
Location of Metastases at Baseline		
Liver	297	88
Mesentery	179	53
Peritoneum	78	23
Retroperitoneum	43	13
Ovaries	25	7
Bone	10	3
Lung	8	2
Breast	6	2
Primary Reason for Initiation of Octreotide		
Carcinoid Syndrome	220	65
Anti-Proliferative	103	30
Radiographic Progression	14	4
Unknown	1	1

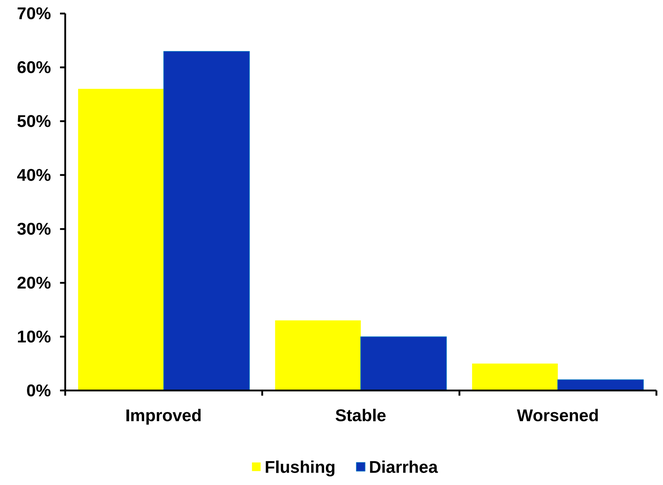
* Hispanic, Asian/Pacific Islander, or Native American

Results (Con't)

Table 2: Octreotide-LAR Doses Stratified by Number of Dose Escalations

One Dose Escalation		Two Dose Escalations		Three Dose Escalations	
Mg q Week	N	Mg q Week	N	Mg q Week	N
30 q 3	18	30 q 3		30 q 3	
30 q 2		30 q 2	2	30 q 2	
40 q 4	36	40 q 4	1	40 q 4	
40 q 3		40 q 3		40 q 3	
50 q 4	2	50 q 4		50 q 4	
50 q 3		50 q 3	1	50 q 3	
60 q 4	16	60 q 4	18	60 q 4	
60 q 3	1	60 q 3		60 q 3	2
70 q 4	1	70 q 4		70 q 4	
90 q 4		90 q 4	1	90 q 4	
90 q 3		90 q 3		90 q 3	1

Figure 1: Symptomatic Responses to Initial Above-Label Dose Escalation among Patients with Refractory Carcinoid Syndrome



Conclusions

• "Above-label Dose" Octreotide LAR is commonly prescribed

  -primarily for patients with suboptimal control of their carcinoid syndrome.

• The majority of patients appear to derive symptomatic benefit from this strategy.

• Prospective studies are required to validate this strategy