

## DRUG NAME: Octreotide

**SYNONYM(S):** Octreotide acetate, SMS 201-995, synthetic octapeptide analogue of somatostatin, SMS-LAR

**COMMON TRADE NAME(S):** SANDOSTATIN®, SANDOSTATIN® LAR®

**CLASSIFICATION:** Endocrine hormone

*Special pediatric considerations are noted when applicable, otherwise adult provisions apply.*

### MECHANISM OF ACTION:

Octreotide acetate is a synthetic somatostatin analogue with similar pharmacologic effects to naturally occurring somatostatin, but with a prolonged duration of action. It inhibits pathologically increased secretion of growth hormone, thyroid stimulating hormone, and serotonin, insulin, glucagon, and other peptides produced within the gastro-entero-pancreatic endocrine system.<sup>1</sup> Somatostatin is cell cycle phase-specific, mediating arrest at the G<sub>1</sub>-phase.<sup>2</sup> Long acting somatostatin analogues have been shown to inhibit tumour growth.<sup>2,3</sup>

### PHARMACOKINETICS:

The pharmacokinetic profile of octreotide **long acting** depot injection reflects the slow release of octreotide from its polymer matrix (microspheres) and its subsequent biodegradation. Once released into the systemic circulation, octreotide is distributed according to its known pharmacokinetic properties (see table). After intramuscular injection, there is an initial peak within 1 hour of the injection, and then a progressive decrease to an undetectable level over 24 hours. The level remains subtherapeutic for 7 days before gradually increasing to reach plateau concentrations around day 14 where the levels remain relatively constant for 3 to 4 weeks. Following a single IM injection, the octreotide concentration will decrease slowly after about day 42 and reflects the terminal degradation phase of the polymer matrix dosage form.<sup>1</sup>

Absorption	SC: rapidly and completely absorbed; peak plasma concentrations within 30 min IM ( <b>long acting</b> injection): steady state achieved at 3 months following injections at 4-weekly intervals	
Distribution	crosses human placenta to fetus <sup>4</sup> ; in animal studies, highest concentrations found mainly in liver, kidneys, skin, and lungs	
	cross blood brain barrier?	no information found
	volume of distribution	0.4 L/kg
	plasma protein binding	65%
Metabolism	30-40% extraction in the liver <sup>5</sup> ; possibly into smaller peptides	
	active metabolite(s)	no information found
	inactive metabolite(s)	no information found
Excretion	renally excreted <sup>5</sup>	
	urine	32% as unchanged drug <sup>5</sup>
	feces	no information found
	terminal half life	SC: 100 min; IV: biphasic (alpha half life = 10 min; beta half life = 90 min)
	clearance	160 mL/min

Adapted from reference<sup>1</sup> unless specified otherwise.

**USES:**

**Primary uses:**

- \*Acromegaly
- \*Carcinoid tumour
- \*VIPomas

\*Health Canada approved indication

No pediatric malignant indications.

**Other uses:**

- Pituitary tumour<sup>5-7</sup>
- Neuroendocrine tumour<sup>2,3,8</sup>
- Chemotherapy-induced diarrhea<sup>9,10</sup>

**SPECIAL PRECAUTIONS:**

**Caution:**

- **bradycardia, arrhythmias, and conduction abnormalities** (including QT prolongation) have been observed during treatment with octreotide; dose adjustment may be necessary for beta-blockers, calcium channel blockers, and drugs used for correction of fluid and electrolyte balance<sup>1</sup>
- mild transient **hypo- or hyperglycemia** is occasionally associated with octreotide and may result in overt diabetes; monitor serum glucose at start of therapy and at each dosage change<sup>1</sup>
- progressive impairment of **thyroid function** is sometimes reported following chronic therapy with octreotide; assess thyroid function at baseline and monitor periodically for duration of treatment<sup>1</sup>

**Carcinogenicity:** Not carcinogenic in animal studies.<sup>11</sup>

**Mutagenicity:** Not mutagenic in Ames test or in animal studies.<sup>11</sup>

**Fertility:** In animal studies, subcutaneous octreotide did not impair fertility in the test subjects. However, in female patients with acromegaly, the therapeutic benefit of the reduction in growth hormone levels and normalization of insulin-like growth factor concentration in humans is that it may **restore fertility**.<sup>1</sup>

**Pregnancy:** In animal studies, no direct or indirect harmful effects were reported with respect to pregnancy, embryonal/fetal development, parturition, or postnatal development. Some transient physiological growth delays were reported but those were considered a consequence of the drug's main pharmacological action (i.e., growth hormone inhibition).<sup>1</sup>

**Breastfeeding** is not recommended due to the potential secretion into breast milk. In animal studies, octreotide has been detected in the breast milk of lactating animals.<sup>1</sup>

**SIDE EFFECTS:**

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <b>bold, italics</b>	
allergy/immunology	anaphylactic and hypersensitivity reactions (rare)
auditory/hearing	otitis and tinnitus (0-2%)
cardiovascular (arrhythmia)	arrhythmia <sup>12</sup> (3-9%) <sup>13</sup>
	conduction abnormalities <sup>12</sup> (9-10%) <sup>13</sup>
	sinus bradycardia <sup>12</sup> (19-25%) <sup>13</sup>

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <b><i>bold, italics</i></b>	
cardiovascular (general)	edema (1-3%)
	hypertension <sup>12,13</sup> (≤13%)
constitutional symptoms	fatigue (1-10%, severe 0.5%*)
	fever (0-2%)
	weight gain (0-2%)
dermatology/skin	<b><i>extravasation hazard: none</i></b>
	acne (0-4%)
	alopecia (1-4%)
	bruise (0.5-4%)
	flushing (0.5-2%)
	<b><i>injection site: hematoma (0-10%), pain (8-10%); see paragraph following Side Effects table</i></b>
	pruritus (0-4%)
endocrine	diabetes mellitus (rare)
	hot flashes (0-2%)
	hypoadrenalism (0-3%)
	hypogonadism (0-2%)
	hypothyroidism (0-2%)
gastrointestinal	<b><i>emetogenic potential: nonemetogenic</i></b>
	abdominal: discomfort (4-44%), distention (0 <sup>+</sup> -8 <sup>+</sup> %)
	anorexia (0-2%)
	belching (0-2%)
	<b><i>biliary tract abnormalities</i></b> (including gallstones) (52-62%); see paragraph following <b>Side Effects</b> table
	cholecystitis (0-2%)
	constipation (1-9%)
	diarrhea (7-58%)
	dry mouth (0.5-2%)
	flatulence (0.5-13%)
	gallstones (24-22%)
	hemorrhoids (0-2%)
	nausea (9-30%)
	pancreatitis, acute (rare)
	pancreatitis, chronic (rare)
	rectal gas (0-4%)
	stools: abnormal (0.5-6%), loose (3-36%)
stools, fatty (0-4%)	
vomiting (3-4%)	
hemorrhage	epistaxis (0-2%)
hepatic	acute hepatitis (rare)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <b><i>bold, italics</i></b>	
	hyperbilirubinemia (rare)
infection	urinary tract infection (0-6%)
	vagina infection (0-3%)
metabolic/laboratory	<b><i>hyperglycemia</i></b> (15%) <sup>14</sup> ; see paragraph following <b>Side Effects</b> table
	hyperkalemia (rare) <sup>15</sup>
	hypoglycemia (0-2%)
	decreased serum zinc levels (rare)
	decreased vitamin B <sub>12</sub> levels (rare)
musculoskeletal	arm/leg: heavy or tired (0-3%)
	arthritis (0-3%)
	osteoarthritis (0-2%)
	twitching (0-2%)
	vertebral disk disorder (0-2%)
	weakness (1-0%)
neurology	dizziness (2-15%)
	irritability (0-2%)
	mood: anxiety (0.5-3%), depression (0.5-3%), moody (0-3%)
	numbness (0-2%)
	sleepiness/insomnia (0.5-2%)
ocular/visual	visual disturbances (0.5-3%)
pain	back pain (0.5-4%)
	cramps (0-3%)
	foot pain (0-2%)
	headache (2-18%)
	joint pain (0-4%)
	kidney pain (0-2%)
	leg: cramps (0-4%), pain (0-3%)
	throat pain (0.5-3%)
pulmonary	dyspnea (0-2%)
	nasal congestion (0-2%)
	sinusitis (0-4%)
renal/genitourinary	breast lump (0-2%)
	dysuria (0-2%)
	polyuria (0-2%)
	prostatitis (0-2%)
	urinary frequency (0-4%)
	vagina itch (0-2%)
secondary malignancy	breast tumour (0-2%)
syndromes	flu-like symptoms (0-6%)

Adapted from reference<sup>11</sup> unless otherwise specified.

**Biliary tract abnormalities** such as gallstones, sludge without stones and biliary duct dilatation, may occur after more than 12 months of therapy. Only 1% of patients becomes symptomatic and requires intervention. Patients on long-term octreotide should be assessed with ultrasound of the gallbladder and bile ducts every 6-12 months.<sup>11</sup> Gallstones usually respond to chenodeoxycholic acid or ursodeoxycholic acid. Interruption or discontinuation of octreotide may be considered based on the risk-benefit ratio of the patient.<sup>14</sup>

**Gastrointestinal (GI)** side effects may be reduced by giving SC injections between meals or at bedtime.<sup>11</sup> GI side effects with the octreotide **long acting IM injection** are mild to moderate, often disappear within 1-4 days of injection, and decrease with long term treatment.<sup>14</sup> Note that diarrhea in patients with carcinoid syndrome may be due to excessive hormone secretion or other causes and should be treated according to etiology.<sup>2</sup>

**Hyperglycemia** is usually transient and mild.<sup>14,16</sup> Reduced glucose tolerance may be due to imbalance between insulin, glucagon and growth hormone. Post prandial blood sugar may be increased in nondiabetics and type II diabetics. Patients should be observed more closely when starting octreotide or changing doses.<sup>11</sup>

**Injection site reactions** after SC injection include pain, stinging, tingling or burning, and rarely, redness, swelling or rash. Reactions usually last less than 15 minutes for SC injections or 60 minutes for **long acting IM injections**. Local discomfort may be reduced by allowing the solution to reach room temperature before injection and by injecting slowly.<sup>11</sup>

**Malabsorption** of dietary fats and vitamin B12 has been seen. There is no evidence that long-term treatment with SC octreotide has led to nutritional deficiency due to malabsorption. It is suggested that periodic quantitative 72-hour fecal fat and serum carotene determinations be performed to aid in the assessment of possible drug-induced aggravation of fat malabsorption. Depressed vitamin B12 levels and abnormal Schilling's tests have been observed, and monitoring of vitamin B12 levels is recommended during therapy with octreotide **long acting IM injection**.<sup>11</sup>

Sudden **loss of symptomatic control (escape)** may occur infrequently and results in rapid recurrence of severe symptoms. Escape from control can occur at varying intervals. Various mechanisms are suggested including tachyphylaxis, appearance of antibodies, mutations in the tumour cell, or decreasing octreotide bioavailability. Dosage adjustment may be required. The use of short acting somatostatin analogues may be necessary to control symptoms as they appear to have greater efficacy in managing the symptoms of escape than long acting formulations.<sup>1,6</sup>

#### INTERACTIONS:

AGENT	EFFECT	MECHANISM	MANAGEMENT
bromocriptine <sup>1</sup>	increased bromocriptine bioavailability	unknown	adjust bromocriptine dose as needed
cimetidine <sup>1</sup>	possible reduced efficacy of cimetidine	delayed intestinal absorption of cimetidine	monitor for loss of effect and adjust cimetidine dose as needed
cyclosporine <sup>1</sup>	decreased serum cyclosporine levels; possible contribution to transplant rejection	delayed intestinal absorption of cyclosporine	monitor serum cyclosporine levels; adjust cyclosporine dose as needed

Somatostatin analogues may decrease the clearance of compounds metabolized by CYP 3A4 through the suppression of growth hormone. Concurrent use of octreotide with substrates of CYP 3A4 should be done cautiously, particularly if the substrate drug has a low therapeutic index<sup>1</sup>; monitor for increased toxicity of the substrate drug.

## SUPPLY AND STORAGE:

### *Injection:*

#### **Short acting formulations:**

Novartis Pharmaceuticals Canada Inc. supplies octreotide for subcutaneous and intravenous injection as a buffered solution in a 1 mL ampoule in concentrations of 50 mcg/mL, 100 mcg/mL, and 500 mcg/mL, as well as 1000 mcg multi-dose vials in a concentration of 200 mcg/mL. Refrigerate. Protect from light.<sup>1</sup>

Omega Laboratories Ltd supplies octreotide for subcutaneous and intravenous injection as a buffered solution in 2 mL single-use vials in a concentration of 50 mcg/mL, 100 mcg/mL, and 500 mcg/mL, as well as 1000 mcg multi-dose vials in a concentration of 200 mcg/mL. Refrigerate. Protect from light.<sup>17</sup>

#### **Long acting formulations:**

Novartis Pharmaceuticals Canada Inc. supplies octreotide (SANDOSTATIN® LAR®) for intramuscular depot injection as a powder for suspension in 10 mg, 20 mg, and 30 mg vials. Octreotide is formulated in biodegradable microspheres for slow release. Vials are supplied in a kit containing a prefilled syringe of diluent. Refrigerate. Protect from light.<sup>1</sup>

Teva Canada Limited supplies octreotide for intramuscular depot injection as a powder for suspension in 10 mg, 20 mg, and 30 mg vials. Octreotide is formulated in biodegradable microspheres for slow release. Vials are supplied in a kit containing a prefilled syringe of diluent. Refrigerate. Protect from light.<sup>18</sup>

### **Additional information:**

- **Room temperature storage:** Octreotide solution (when supplied by Novartis or Omega as ampoules, single-use vials, or multi-dose vials) may be stored at room temperature for day-to-day use up to 2 weeks, if protected from light.<sup>1,17</sup> **Vials of octreotide powder for suspension (when supplied by Novartis or Teva) can be kept at room temperature only on the day of injection and should be prepared for administration immediately prior to IM injection.**<sup>1,18</sup>

**For basic information on the current brand used at BC Cancer, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.**

## SOLUTION PREPARATION AND COMPATIBILITY:

**For basic information on the current brand used at BC Cancer, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.**

**Compatibility:** consult detailed reference

## PARENTERAL ADMINISTRATION:

BC Cancer administration guideline noted in ***bold, italics***

<p>Subcutaneous<sup>1</sup> (<i>Octreotide long acting formulations must never be given SC</i>)</p>	<p>use the smallest volume that will deliver the prescribed dose</p> <ul style="list-style-type: none"> <li>• avoid multiple injections in the same site</li> <li>• local discomfort may be reduced by allowing the solution to reach room temperature before injection and by injecting slowly</li> </ul>
<p><b><i>Intramuscular<sup>1</sup></i></b> (<b><i>for octreotide long acting formulations only</i></b>)</p>	<p><b><i>by deep intragluteal injection;</i></b> avoid deltoid injections due to significant discomfort at the injection site</p> <ul style="list-style-type: none"> <li>• alternate between left and right gluteal muscles to avoid irritation</li> <li>• quadriceps may be used for self-administration<sup>19-21</sup></li> </ul>

BC Cancer administration guideline noted in **bold, italics**

Direct intravenous ( <i>Octreotide long acting formulations must never be given IV</i> )	over 3 minutes <sup>22</sup> ; used under emergency conditions <sup>1</sup>
Intermittent infusion ( <i>Octreotide long acting formulations must never be given IV</i> )	over 15-30 minutes (when diluted to 50-200 mL with NS or D5W) <sup>22</sup>
Continuous infusion ( <i>Octreotide long acting formulations must never be given IV</i> )	infuse at 25 mcg/h <sup>1</sup> ; rates of 50-150 mcg/h have been used <sup>23</sup>
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

## DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy.

### Adults:

BC Cancer usual dose noted in **bold, italics**

	Cycle Length:	
<i>Intramuscular:</i> ( <i>Octreotide long acting only</i> )	<b>4 weeks</b> <sup>1,19-21</sup> :	<b><i>octreotide long acting: 20-30 mg</i></b> (range 10-40 mg) <b><i>IM for one dose on day 1</i></b> <ul style="list-style-type: none"> <li>• <i>octreotide long acting</i> has been used without a prior or overlapping trial of octreotide SC<sup>3,24,25</sup>; or it may be started the day after the last dose of octreotide SC<sup>26</sup></li> <li>• if overlapping with octreotide SC: <ul style="list-style-type: none"> <li>○ continue octreotide SC for at least two weeks in the same dose as before the switch; some patients may require 3-4 weeks</li> </ul> </li> <li>• 10 mg starting doses are not recommended as therapeutic levels are reached more rapidly with 20 mg dose</li> <li>• for exacerbation of symptoms during maintenance treatment with octreotide <i>long acting</i>, octreotide SC may be given for a few days (at same dose prior to switch to octreotide <i>long acting</i>); discontinue octreotide SC when symptoms are controlled</li> </ul>
<i>Subcutaneous</i> <sup>1</sup> : ( <i>Octreotide long acting must never be given SC</i> )	n/a:	start at 50 mcg SC given once or twice daily; titrate dosage and number of injections based on tolerability and clinical response (range 100-900 mcg per day given in two to four divided doses) Maximum = 1500 mcg per day

	PRN:	100 mcg SC for 2 doses, 15 min and 6 h after chemotherapy <sup>27</sup>
<i>Intravenous</i> <sup>23,28</sup> : (Octreotide <i>long acting</i> must never be given IV)	Stat:	50 mcg IV, may repeat dose once in 15 seconds (range 25-500 mcg) or as an IV infusion at a rate of 50-150 mcg/h
<i>Dosage in myelosuppression:</i>		no adjustment required
<i>Dosage in renal failure:</i>		half life may be increased in patients with severe renal failure requiring dialysis; dose adjustment of the maintenance dose may be required <sup>1</sup>
<i>Dosage in hepatic failure:</i>		half life may be increased in patients with liver cirrhosis; dose adjustment of the maintenance dose may be required <sup>1</sup>
<i>Dosage in dialysis:</i>		half life may be increased in patients with severe renal failure requiring dialysis; dose adjustment may be required <sup>1</sup>
<b><u>Children:</u></b>		no information found

## REFERENCES:

1. Novartis Pharmaceuticals Canada Inc. SANDOSTATIN® and SANDOSTATIN® LAR® product monograph. Dorval, Quebec; 22 January 2020
2. Arnold R, Simon B, Wied M. Treatment of neuroendocrine GEP tumours with somatostatin analogues: a review. *Digestion* 2000;62(Suppl 1):84-marburg.de
3. Rinke A, Muller HH, Schade-Brittinger C, et al. Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR® in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the PROMID Study Group. *J Clin Oncol* 2009;27(28):4656-4663
4. Briggs Drugs in Pregnancy and Lactation® - Lexicomp Online (database on the Internet). Octreotide. Wolters Kluwer Clinical Drug Information Inc., 2017. Available at: <http://online.lexi.com>. Accessed 25 June, 2020
5. Yang LPH, Keating GM. Octreotide long-acting release (LAR): a review of its use in the management of acromegaly. *Drugs* 2010;70(13):1745-1769
6. Klibanski A, Melmed S, Clemmons DR, et al. The endocrine tumor summit 2008: appraising therapeutic approaches for acromegaly and carcinoid syndrome. *Pituitary* 2010;13(3):266-286
7. Melmed S, Colao A, Barkan A, et al. Guidelines for acromegaly management: an update. *J Clin Endocrinol Metab* 2009;94(5):1509-1517
8. Singh S, Dey C, Kennecke H, et al. Consensus recommendations for the diagnosis and management of pancreatic neuroendocrine tumours: guidelines from a Canadian national expert group. *Ann Surg Oncol* 2015;22(8):2685-2699
9. Wasserman E, Hidalgo M, Hornedo J, et al. Octreotide (SMS 201-995) for hematopoietic support-dependent high-dose chemotherapy (HSD-HDC)-related diarrhoea: dose finding study and evaluation of efficacy. *Bone Marrow Transplantation* 1997;20(9):711-4; Division of Medical Oncology, Hospital Universitario 12 de Octubre, Madrid, Spain.
10. Wadler S, Benson AB, 3rd, Engelking C, et al. Recommended guidelines for the treatment of chemotherapy-induced diarrhea. *Journal of Clinical Oncology* 1998;16(9):3169-78; Montefiore Medical Center, Bronx, NY 10467, USA. [wadler@jimmy.harvard.edu](mailto:wadler@jimmy.harvard.edu)
11. Novartis Pharmaceuticals Canada Inc. SANDOSTATIN® Product Monograph. Dorval, Quebec; January 9 2001
12. Novartis Pharmaceuticals Canada Inc. SANDOSTATIN® product monograph. Dorval, Quebec; September 3 2009
13. Basow DS editor. Octreotide. UpToDate 19.2 ed. Waltham, Massachusetts: UpToDate®; accessed 11 August 2011
14. Gillis JC, Noble S, Goa KL. Octreotide long-acting release (LAR). A review of its pharmacological properties and therapeutic use in the management of acromegaly. *Drugs* 1997;53(4):681-99; Adis International Limited, Auckland, New Zealand.
15. Sargent AI, Overton CC, Kuwik RJ, et al. Octreotide-induced hyperkalemia [see comments]. *Pharmacotherapy* 1994;14(4):497-501; Department of Pharmacy, Mercy Hospital of Pittsburgh, PA 15219.
16. Lamberts SW, van der Lely, A. J., de Herder WW, et al. Octreotide. *New England Journal of Medicine* 1996;334(4):246-54; Department of Medicine, Erasmus University, Rotterdam, The Netherlands.
17. Omega Laboratories Ltd. Octreotide acetate injection product monograph. Montreal, Quebec; 23 July 2010
18. Teva Canada Limited. OCTREOTIDE for injectable suspension Product Monograph. Toronto, Ontario; Aug 30, 2021



19. BC Cancer Gastrointestinal Tumour Group. (UGINFOCLAR) BC Cancer Protocol Summary for Management of Non-Functional Neuroendocrine Tumours of the GI Tract Using Octreotide (SANDOSTATIN LAR®). Vancouver, British Columbia: BC Cancer; 1 May 2020
20. BC Cancer Gastrointestinal Tumour Group. (UGIOCTLAR) BC Cancer Protocol Summary for Symptomatic Management of Functional Carcinoid and Neuroendocrine Tumours of the GI Tract Using Octreotide (SANDOSTATIN LAR®). Vancouver, British Columbia: BC Cancer; 1 February 2019
21. BC Cancer Neuro-Oncology Tumour Group. (CNOCTLAR) BC Cancer Protocol Summary for Treatment of Growth Hormone Secreting Pituitary Adenoma Using Octreotide (SANDOSTATIN LAR®). Vancouver, British Columbia: BC Cancer; 1 September 2019
22. Trissel LA. Octreotide acetate. Handbook on Injectable Drugs: 13th ed. Bethesda, Maryland: American Society of Health-System Pharmacists, Inc; 2005. p. 1131-1132
23. Seymour N, Sawh SC. Mega-dose intravenous octreotide for the treatment of carcinoid crisis: a systematic review. *Can J Anesth* 2013;60(5):492-499
24. Narayanan S, Kunz PL. Role of somatostatin analogues in the treatment of neuroendocrine tumors. *J Natl Compr Canc Netw* 2015;13(1):109-117
25. Marissa Dion-Meihuizen. Novartis Pharmaceuticals Medical Information Centre. Personal communication. 27 April 2015
26. Novartis Pharmaceuticals Canada Inc. SANDOSTATIN® and SANDOSTATIN® LAR® product monograph. Dorval, Quebec; 11 August 2014
27. Cascinu S, Fedeli A, Fedeli SL, et al. Control of chemotherapy-induced diarrhea with octreotide. A randomized trial with placebo in patients receiving cisplatin. *Oncology* 1994;51(1):70-3; Servizio di Oncologia, Ospedali Riuniti, Pesaro, Italy.
28. Kvols LK, Martin JK, Marsh HM, et al. Rapid reversal of carcinoid crisis with a somatostatin analogue [letter]. *New England Journal of Medicine* 1985;313(19):1229-30