Use of Somatostatin Analog Therapy in Patients with Advanced Pheochromocytoma or Paraganglioma and Somatostatin-Receptor Avid Disease

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Background

- Somatostatin receptor (SSR) expression may be assessed by SSR scintigraphy or somatostatin-analog (SSA) radiolabeled PET imaging.
- SSR imaging is commonly used in the management of many neuroendocrine tumors (NET) for disease staging and as a predictive test for the use of SSA agents.
- SSAs are used in the standard management of enteropancreatic NETs. SSAs may induce symptomatic and biochemical responses, and have additionally demonstrated anti-tumor benefit in prospective randomized trials.
- Pheochromocytoma and Paraganglioma (PPGL) may express SSRs at levels comparable to other NETs. Moreover, SSR imaging may be used as a complementary imaging test for detecting metastatic lesions in advanced PPGL.
- However, the potential clinical benefit of SSAs in PPGL remains largely unknown, with an existing literature largely limited to individual case reports.
- Our objective was to preliminarily assess the prevalence of SSR-avid disease and the clinical benefit of SSA therapy in patients with advanced PPGL.

Methods

- **Purpose:** To assess the prevalence of SSR-avid disease and to compare the clinical courses of a series of advanced PPGL patients with SSR avid disease treated with or without a SSA
- **Study Population:** Single-institution database of advanced PPGL patients (N = 76), including clinical, radiologic, and genomic data.
- **Data Collection:** Baseline SSR imaging and major clinical events of interest from time of baseline SSR imaging was retrospectively collected. Major clinical events of interest included the Initiation of additional systemic therapy, radiation therapy, radiopharmaceutical therapy, surgical debulking, symptomatic deterioration, or death.
- **Analysis:** The Kaplan-Meier method was used to estimate clinical progression-free survival (cPFS), defined as the time from SSR imaging to the first major clinical event following the initial treatment.

Results

- 20 patients underwent SSR imaging
  - N = 14 SSR-avid
  - N = 6 SSR-negative

TABLE 1: Baseline Patient Characteristics (N = 14)

Variable	Received SSA (N=8)	Did Not Receive SSA (N=6)
Age (years)		
Median (range)	53 (33 – 77)	37 (21 – 62)
Male	6	2
Primary Tumor Location		
Adrenal	3	1
Extra-adrenal	5	2
Head/Neck	0	3
Site of Metastases		
Lung	2	2
Liver	2	1
Bone	6	4
Lymph Node	7	5
Genetic Alteration		
SDHB	6	3
SDHA	0	1
None	1	1
Other (MSH2, NF1)	1	1
Treatment Prior to SSR Imaging		
Surgery	6	5
CVD	2	0
MIBG	2	1
Radiation	3	1
SSR Imaging Modality		
Octreoscan	6	5
Gallium-68 DOTATATE	2	1
Follow-up Time since SSR Imaging (months)		
Median (range)	13 (2 – 51)	18 (5 – 63)

TABLE 2: Treatment Characteristics (N = 14)

Variable	Received SSA (N=8)	Did Not Receive SSA (N=6)
Type of SSA		
Octreotide	7	
Lanreotide	1	
Initial Treatment after SSR Imaging		
SSA alone	4	
SSA + Cap/Tem	2	
SSA + Everolimus	1	
SSA + CVD	1	
Surgery/Radiation Therapy		1
CVD		2
MIBG		2
Observation		1
Clinical Progression	4	3
Median Time to Clinical Progression (months)		
Median (IQR)	24.7 (7.1 – 24.7)	20.8 (15.5 – NR)
Subsequent Therapy after Clinical Progression		
Surgery	1	0
Radiation Therapy	0	1
CVD	1	0
Cap/Tem	1	0
Clinical Trial	0	2
None	5	3

4 patients received SSA monotherapy

4 patients received SSA therapy in combination with alternative systemic therapies

Median cPFS 24.7 months vs. 20.8 months (log-rank p = 0.69)

Results

TABLE 3: Individual Patient Characteristics, Treated with SSA)

Patient	Primary Tumor	Site of Metastases	Genetic Alteration	Prior Therapies	Concomitant Therapies	SSR Imaging	123-I MIBG	Clinical Progression	Time until Clinical Progression (mos)	Subsequent Therapies	Vital Status	Notes
1	Adrenal	Liver, Bone, LN	SDHB	CVD	CVD	Unk	Avid	No (12 mos follow-up)			Alive	Planned for debulking surgery
2	Extra-adrenal	Bone	SDHB	Surgery, CVD	Everolimus	Mild uptake	Non-avid	Yes (surgery)	25	Sunitinib, CapTem, Liver-directed therapy, Surgery, RT	Alive	
3	Extra-adrenal	Bone, LN	SDHB	Surgery, RT, MIBG	CapTem	Avid	Avid	Yes (CVD)	7	CVD	Dead	
4	Adrenal	Bone, LN	None	Surgery	CapTem	Avid	Non-avid	No (12 mos follow-up)			Alive	
5	Extra-adrenal	Lung, LN	SDHB	Surgery	None	Avid	Non-avid	No (18 mos follow-up)			Alive	
6	Extra-adrenal	Liver, Bone, LN	SDHB	MIBG, RT	None	Avid	Avid	No (1 mos follow-up)			Alive	
7	Extra-adrenal	Bone, LN	SDHB	Surgery, RT	None	Avid	Non-avid	Yes (symptoms)	9		Dead	
8	Adrenal	Lung, LN	MSH2	Surgery	None	Avid	Non-avid	Yes (CapTem)	3	CapTem	Alive	Considering PRRT

Limitations

- This was a small retrospective, single-institution series of advanced PPGL patients. However, given the rarity of this disease and a prior literature limited to individual case reports, this represents one of the largest clinical series of advanced PPGL patients undergoing SSR imaging and SSA therapy.
- The study population represents a heterogeneous group with variable use of concomitant systemic therapies in conjunction with SSA therapy. Therefore, the clinical benefit of SSA therapy cannot be clearly defined. SSA therapy should be tested in prospective clinical trials of advanced PPGL patients.

Conclusions

- **A significant proportion of advanced PPGL patients demonstrate SSR-avid disease by conventional imaging**
- **Such patients may be treated with SSA therapy, either alone or in combination with other common systemic therapies.**
- **SSA therapy may provide a delay in clinical progression. This should be evaluated in randomized clinical studies.**

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