

# Prolonged Radiographic Stabilization of a Metastatic Octreotide Scan-Positive Poorly Differentiated Neuroendocrine Tumor Using Octreotide Acetate Therapy Alone\*

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## ABSTRACT

Pancreatic poorly differentiated neuroendocrine tumors (PDNETs) are a subtype of neuroendocrine Tumors (NETs) clinically distinguished by their much more rapid growth and immunohistochemically diagnosed by having a higher Ki-67 cancer cell staining percentage compared to their well or intermediately differentiated NET counterparts. While standard first line treatment for metastatic well or intermediately differentiated pancreatic NETs typically involves octreotide acetate therapy, here I report, to my knowledge, the first case of a patient with a pancreatic PDNET with radiographic stabilization of his disease with octreotide acetate use alone. Octreotide acetate was chosen after first establishing that, based on his octreotide scan, receptors might be targeted using the octreotide analog.

**Keywords:** PDNET; Octreotide Acetate; Pancreatic Cancer; mTOR Overexpression

## 1. Introduction

JF is a 56-year-old male who underwent a Whipple procedure in early 2011 and pathology showed a four cm pancreatic tumor with 3/27 lymph nodes involved (T3N1 Mx) that was a “poorly differentiated neuroendocrine tumor” (PDNET) of the pancreas (Ki-67 = 37%). Staging with a CT scan of his chest/abdomen/pelvis in July 2011 showed no evidence of metastatic disease and he declined adjuvant therapy.

However, a repeat CT scan only a few months later showed new liver lesions and an abdominal MRI confirmed that these multiple hepatic enhancing lesions were consistent with metastatic disease. On 10-26-2011 chemotherapy with carboplatin d1 (AUC = 4.5) and etoposide d 1, 2, 3 (120 mg/m<sup>2</sup>) every 21 days was initiated. He received 6 cycles. While a 12-5-2011 MRI suggested stabilization, by 3-13-2012 the MRI showed progression of the liver lesions (e.g. one lesion had increased in size from 10 to 14 mm and another from 4 to 7 mm). He was then treated on a Phase 1 study with the tyrosine kinase Inhibitor dovitinib, but again an MRI confirmed progres-

sion of his liver metastases occurring in just a few months while on therapy.

On 8-21-2012 a Somatostatin-Receptor Scintigraphy Study (Octreotide scan) showed multiple penitetrotide avid lesions “representing metastatic disease”, confirming somatostatin receptors on the liver metastases. A baseline abdominal MRI was done on 9-7-2012 and Octreotide acetate (Sandostatin LAR depot) was initiated at 20mg IM every month. Repeat abdominal MRIs in October 2012, December 2012, February 2013 and May 20, 2013 confirmed stable metastatic disease, and there has been no clinical evidence of progression of his PDNET.

## 2. Discussion

Pancreatic PDNETs are a type of neuroendocrine tumors (NETs) characterized clinically by rapid growth, initial responsiveness to platinum-based therapy and a very poor prognosis. The NCCN Guidelines for PDNETs suggest these patients be treated as small cell lung cancer (SCLC) is treated, as was the initial approach with our patient [1]. The guidelines suggest that octreotide acetate might be considered as well, although no references are found in the literature to support a benefit of octreotide

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acetate in treating patients with PDNETs. In searching the literature one study reported a lack of inhibition of SCLC cell lines using octreotide [2].

Well and Intermediately differentiated NETs are treated in a different manner. These tumors are typically far more indolent. Octreotide acetate is a standard therapy based largely on a significant prolongation in progression free survival (PFS) of roughly eight months compared to placebo use although no overall survival benefit has been demonstrated [3]. With progression of well or intermediately differentiated NETs, mTOR inhibitors and other targeted therapy have shown a significant PFS benefit compared to placebo and have FDA approval for use in this setting [4].

Per WHO criteria, intermediate NETs are defined immunohistochemically as having Ki-67 cancer cell staining of 2% - 20%, while PDNETs have Ki-67 staining of >20% [5]. We reasoned that between this somewhat arbitrary distinction and the positive octreotide scan, perhaps there might be a similar benefit to treating this PDNET with the "targeted" agent octreotide acetate. Given that his tumor had rapidly progressed on carboplatin/etoposide and later the TKI experimental therapy, but has for now been radiographically stable for eight months while he has been receiving octreotide acetate, it would appear that this patient's tumor is more closely related other NETs, rather than SCLC. It is possible that other PDNETs might similarly benefit; patients with these tumors have been excluded from studies of NETs. While it is also possible that a well or intermediate component of the cancer is the reason for the benefit from the octreotide acetate treatment, the rapid development of liver metastases after his surgery and during the other therapies described argues in favor of the tumor component being inhibited by octreotide acetate being a PDNET component. One prior case of a PDNET did respond to octreotide acetate therapy, but that therapy involved concurrent cisplatin and etoposide use [6].

### 3. Conclusion

In summary, this appears to be the first case of a patient with a PDNET showing growth inhibition with octreotide acetate use alone. A recent report suggests that, like other NETs, PDNETs similarly overexpress mTOR, underscor the possibility that patients with PDNETs should be in-

cluded in trials involving targeted agent therapies for other NETs [7]. These therapies may be found to have a role in treating PDNETs as well.

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