

Introduction

The *RET* proto-oncogene encodes a transmembrane receptor tyrosine kinase that is constitutively activated through two distinct mechanisms: mutations involving the cysteine-rich or kinase domains, and structural rearrangements leading to the fusion of *RET* to a 5' upstream partner. Collectively, these alterations result in ligand-independent signaling and oncogenesis.

Selpercatinib (Retevmo), a highly selective RET kinase inhibitor, was FDA approved in 2024 to treat RET-driven cancers and is primarily used for medullary thyroid cancer and metastatic pheochromocytomas. These diseases are primarily associated with Multiple Endocrine Neoplasia (MEN) divided into subgroups of a and b.

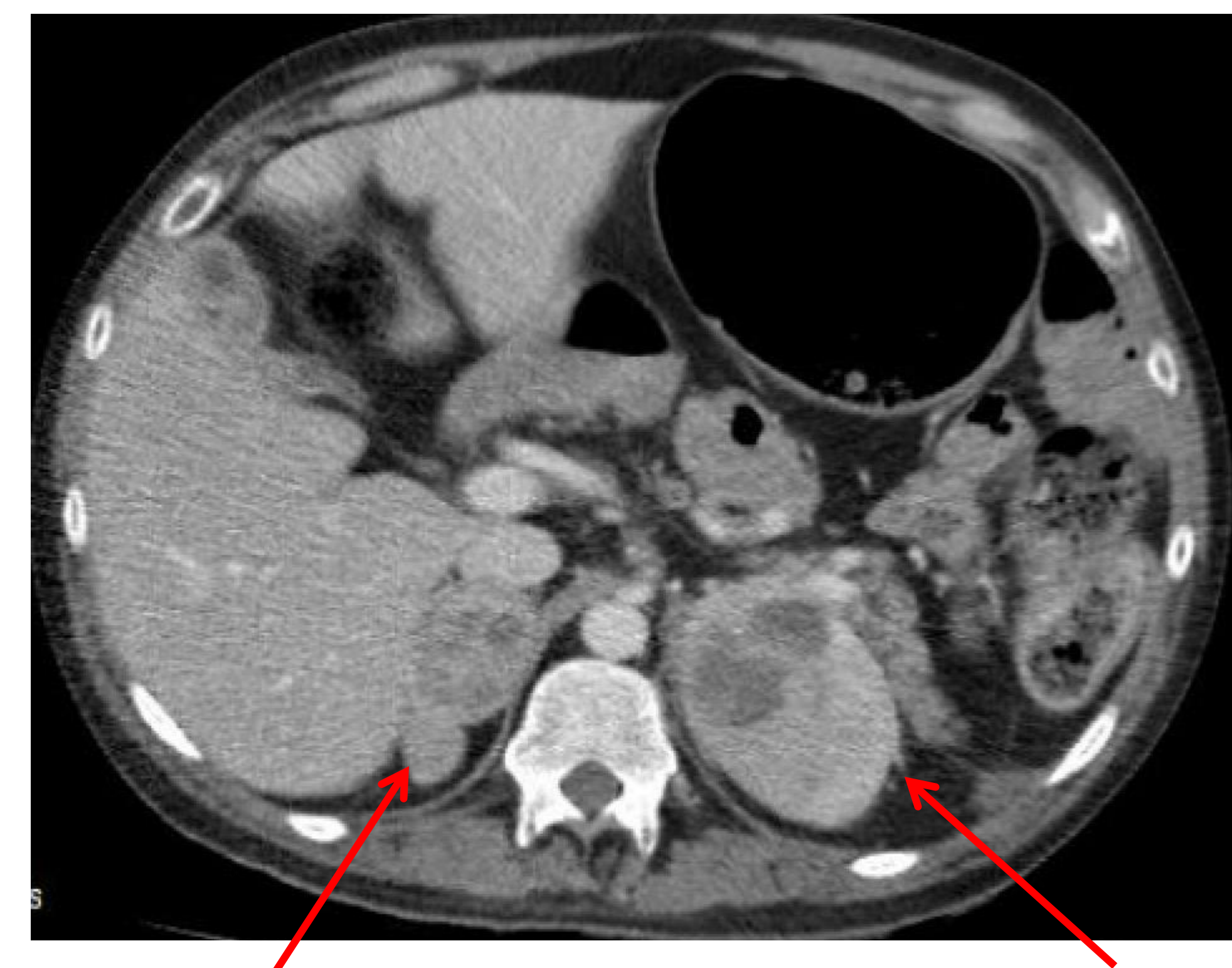
MEN2b characterized by genetic alterations in the RET proto-oncogene and phenotypically by pheochromocytomas, medullary thyroid cancer and marfanoid body habitus.

We present the case of a 36-year-old male with MEN2b treated preoperatively with selpercatinib to allow for minimally invasive bilateral adrenalectomy instead of a highly morbid open operation.

Methods and Procedures

While undergoing a spinal surgery in November 2024, this patient underwent a catecholamine-fueled hypertensive crisis, prolonged intubation, and consideration of ECMO, resulting in profound deconditioning. He was diagnosed clinically with bilateral pheochromocytomas, medullary thyroid cancer, facial mucosal neuromas, and marfanoid habitus. His clinical MEN2b was confirmed with genetic testing for a mutation in p.Met918Thr. Given his deconditioned state and uncontrolled blood pressure, he was deemed unsuitable for upfront surgical management. Treatment with Selpercatinib at 160 mg bid was initiated along with standard alpha blockade.

November 2024



March 2025

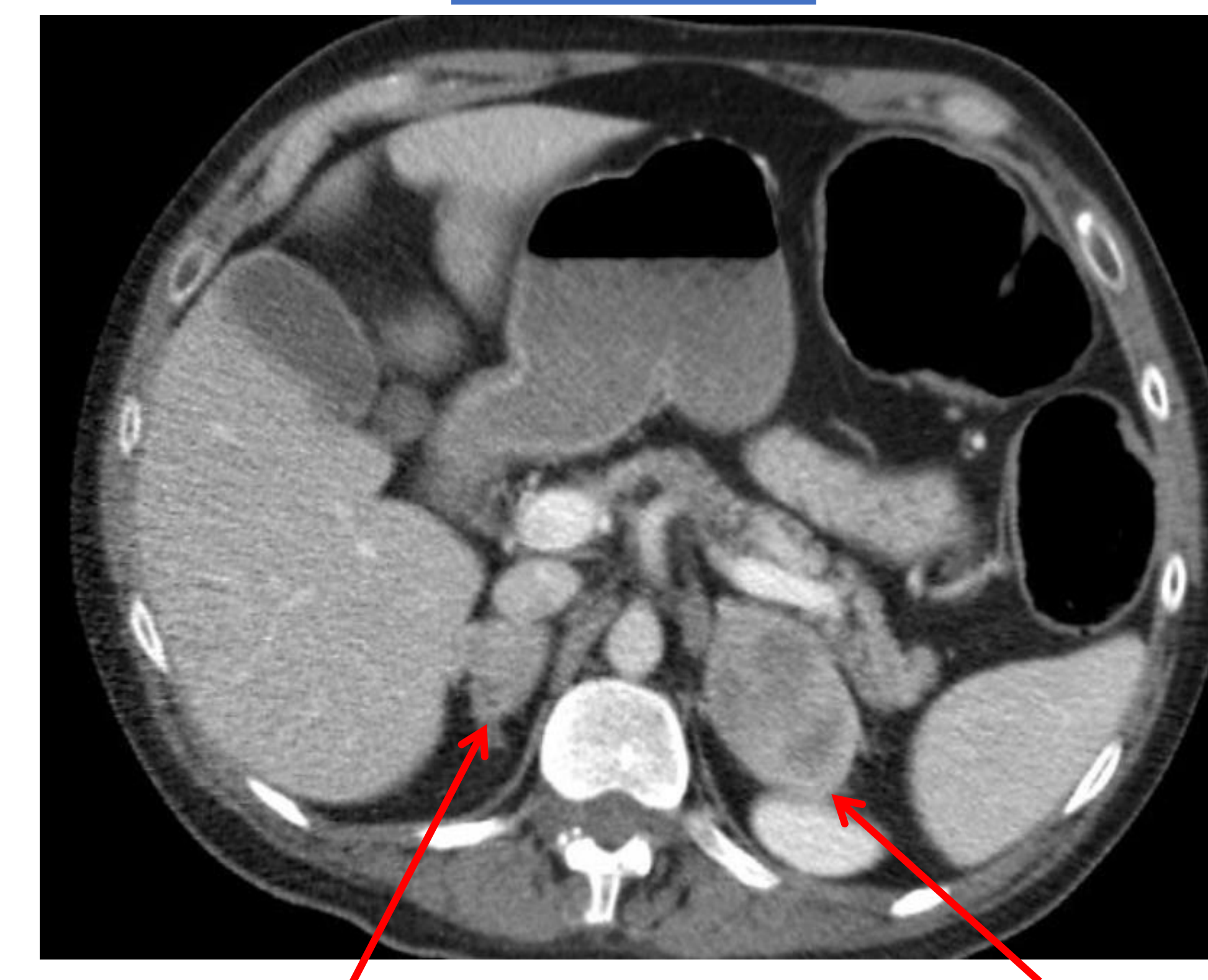


Figure 2 and 3: Representative CT slices showing significant decrease in both the left and right adrenal glands. Figure 3 is after approximately 5 months of therapy. Red arrows mark the left and right adrenal glands.

	Baseline	Pre-operative after 5 months of Selpercatinib	Post- Operative	Normal Value
Normetanephrine (nmol/L)	25.78	13.16	1.18	<0.9
Metanephrine (nmol/L)	31.33	6.79	<0.05	<0.5

Figure 1: Normetanephrine and Metanephrine levels during the course of treatment with selpercatinib

Results

An interval CT scan after 5 months of Selpercatinib therapy resulted in a volumetric decrease of the left adrenal gland by approximately 49% and the right adrenal gland by 70%. This facilitated the transition from the initial plan of an open bilateral adrenalectomy to our preferred method of a minimally invasive laparoscopic retroperitoneal approach. The patient was discharged home on post-operative day two. On his post-operative laboratory results, his metanephrines have returned to normal. This was followed by an uncomplicated total thyroidectomy five weeks later to address his medullary thyroid cancer.

Conclusion

Upfront Selpercatinib therapy may present an exciting new treatment option for those with RET-driven pheochromocytomas. To our knowledge, this is the first mention of the utilization of Selpercatinib for preoperative optimization, permitting transition from a large, potentially morbid open procedure to a minimally invasive approach.