The molecular genetics of G3 NET and NEC also differ. In NETs, MEN1 tumor suppressor gene is somatically mutated in 45% cases. Alterations in chromatin remodeling proteins ATRX and DAXX are also seen in upto 45% cases. Additionally, 15% of NETs have alterations in mTOR pathway genes such as PTEN, PIK3CA and TSC2. In contrast genetic alterations in NEC's involve cell cycle genes such as P53, RB, P16(CDKN2A) and lack alterations seen in NET.

Immunohistochemistry also plays a pivotal role in the diagnosis of these entities. In addition to neuroendocrine markers and Ki67 proliferation index (summarized in the table below) that help in grading of NEN, other hormonal markers such as Somatostatin, pancreatic polypeptide and glucagon help in further characterization of these tumors. Like for the genetic alterations, NETs can show DAXX imunolabelling with loss of ATRX expression and no significant P53 immunostaining in upto 45% cases[2]. On the other hand NECs may show overexpression of P53 with intact DAXX and ATRX expression as in Case B. IHC for somatostatin receptor expression especially SSTR2A can be used to identify patients who will benefit from treatment with Somatostatin analogues[3]