BT13

Molecular Profiling of Advanced Stage Neuro Endocrine Tumors (NETs): The Fox Chase Cancer Center (FCCC) Experience

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Background: NETs are rare making clinical trial accrual challenging. Given fewer approved therapies, a better understanding of underlying biology can help development of and assignment of patients to clinical trials.

Methods: Patients with advanced stage NETs (excluding small/large cell lung cancer) of all grades at FCCC were enrolled onto a prospective IRB approved protocol that utilizes an NGS platform to detect somatic mutations in targeted regions of 50 cancer-related genes (Cancer Code™). Archived tissue from primary or metastatic site was analyzed for mutations in *ABL1, AKT1, ALK, APC, ATM, BRAF, CDH1, CDKN2A, CSF1R, CTNNB1, EGFR, ERBB2,ERBB4, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, FLT3, GNA11, GNAQ, GNAS, HNF1A,HRAS, IDH1, IDH2, JAK2, JAK3, KDR, KIT, KRAS, MET, MLH1, MPL, NOTCH1,NPM1, NRAS, PDGFRA, PIK3CA, PTEN, PTPN11, RB1, RET, SMAD4, SMARCB1, SMO,SRC, STK11, TP53* and *VHL* genes. Central review of pathology specimens for grade/Ki -67% was done.

Results: Thirty-eight patients (median age 59 y, M: F ratio 0.9:1) were enrolled from October 2013 to May 2014. Ki-67 scoring was reviewed for 18/32 tumors. 4 (12%) patients had high grade tumors (Ki-67 > 20%) and 14 (43%) had low grade tumors (Ki-67 $\leq$20%). Gene profiling results are available on thirty-two patients. Twelve patients (38%) were found to have tumor specific mutations and twenty (62%) did not. 4 (12%) patients harbored >1 mutation [*KRAS/RB1*, *BRAF/PIK3CA*, *TP53/KRAS* (2)]. 30% (4/14) patients with low-grade NETs were mutation positive while all (4/4) of the high-grade NETs had tumor specific mutation(s) (*BRAF/TP53/PIK3CA, BRAF, TP53, KRAS/TP53*).

Mutations According to Primary Site

Primary site	n (total)	n (mutation positive)	Type of mutation
Small/large bowel	14	4	*BRAF, PIK3CA, TP53, KRAS*
Pancreas	12	5	*KRAS (2), RB1, ATM, TP53*
Other sites	8	3	*TP53 (2), CTNNB1*

Conclusion: Tumor specific mutations are seen in a minority of low grade NETs but are common in high grade tumors. Many of these may guide future therapies and participation in clinical trials. Enrollment continues and collaborations between centers may help to identify trends in a larger population.