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DAXX Mutation is Associated with Shorter Hepatic Progression Free Survival After Hepatic Artery Embolization of Neuroendocrine Liver Metastases

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BACKGROUND: We sought to establish the relationship between gene mutation status and hepatic progression after hepatic artery embolization (HAE) of neuroendocrine liver metastases (NLM).

METHODS: This is an Institutional Review Board approved single-institution study in which 35 patients (19 men, 16 women; median age, 57 years; range, 30-75 years) with NLM underwent HAE and had biopsy specimens obtained either at time of embolization or within 6 months of the embolization. Biopsy specimens underwent genetic analysis using an institutional multi-gene assay. Mutations with the highest frequency were identified and correlated with response to HAE. Procedure data, tumor volume, extrahepatic disease, tumor grade were also recorded in order to identify confounders. There were 17 patients with NLM from pancreaticobiliary origin (16 pancreatic, 1 gall bladder). There were 11 (31%) grade 1 tumors, 14 (40%) grade 2 tumors, and 10 (29%) grade 3 tumors. Hepatic progression free survival (HPFS) was the endpoint and cox proportional hazards model was used to identify significant predictors.

RESULTS: Table 1 summarizes most frequently mutated genes and their association with HPFS. The most frequently mutated genes were MEN1 (n=11, 31%), DAXX (n=9, 26%), and TP53 and TSC2 (n=6, 17%). DAXX was the only gene associated with shorter HPFS (HR=7.19, p=0.00038, 95% CI=2.42-21.33). Higher tumor grade was also associated with shorter HPFS (HR=3.26, p=0.00028,

CI=1.73-6.17). On multivariate analysis, DAXX mutation remained a significant predictor of HPFS (HR=3.50, p =0.038, CI=1.07-11.40), independent of grade.

Conclusion: DAXX mutation is associated with shorter HPFS in patients with NLM undergoing HAE.

Table 1:

Hepatic progression free survival (HPFS) for top 4 most commonly mutated genes using cox proportional hazards model to estimate hazard ratio (HR) and confidence interval (CI)

Gene	HR	p-value	95% CI
MEN1	1.99	0.085	0.91-4.35
DAXX	7.19	0.00038	2.42-21.33
TP53	2.81	0.058	0.97-8.15
TSC2	2.47	0.063	0.95-6.40