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Overexpression of MAML3 Increases Tumorigenicity and Invasion in Neuroendocrine Tumor Cells

Arun Kumar Arumugam Raajasekar*[1]*; *Aman Chauhan*[1]*; Kurt Hodges*[1]*; Lowell Anthony*[1]

[1]*University of Kentucky*

BACKGROUND: Delta-like protein 3 (DLL3) is a member of the Notch receptor ligand family that appears to inhibit Notch receptor activation. An agent that targets DLL3 protein is being studied in advanced solid tumors (NCT02709889). We hypothesized that DLL3 expression is a biomarker of platinum sensitivity in high grade neuroendocrine carcinoma.

METHODS: Patients with neuroendocrine carcinoma who were participating in the NCT02709889 trial underwent testing for DLL3 expression as part of the trial. We retrospectively analyzed patient_=99s response to platinum based chemotherapy and assessed any differences in radiological responses based on DLL3 expression.

RESULTS: Eleven patients with advanced high- grade neuroendocrine carcinoma were assessed for DLL3 expression. Seven patients (median age 67 years) were DLL3 positive. All seven patients treated with platinum based chemotherapy had response to treatment with a median progression free survival of 9 months (range 8-12months). Four out of eleven patients tested negative for DLL3 (median age 64 years). Only one of the four patients responded to platinum based chemotherapy in the DLL3 negative cohort. The median progression free survival for the DLL3 negative patients was 2.5 months (range 2-8 months) (Table 1).

CONCLUSION: In this small cohort of patients with high grade neuroendocrine carcinoma the expression of DLL3 protein is predictive of response to platinum based chemotherapy. This correlation has not been previously reported in the literature.

Table 1:

	DLL3+	**DLL3-**
N	7	4
Median Age	67y	64y
Median PFS	9m	2.5m