B-15

Survivin Expression in Neuroendocrine Tumors (NETs) is Associated with Poor Outcomes

Ahmad Hanif[1]; Ankush Chander[1,2]; Kristopher Attwood[1]; Robert Fenstermaker[1]; Jingxin Qiu[1]; Renuka Iyer[1]

[1]Roswell Park Comprehensive Cancer Center; [2] Roswell Park Cancer Institute

BACKGROUND: Survivin is an inhibitor-of-apoptosis protein (IAP) that is expressed in many human cancers and is undetectable in most adult tissues. We explored survivin expression in NETs to test its potential as a therapeutic target using survivin peptide mimic vaccine (SurVaxM).

METHODS: In tissue microarrays of 132 surgically resected NETs, survivin expression was determined by immunohistochemistry (present/ absent) using a rabbit monoclonal survivin antibody clone EP119 and correlated with clinical variables. Comparisons were made using the Mann-Whitney U and Fisher's exact tests at $\alpha = 0.05$. Patients were also classified according to Ki67 index as low (<3%) or high (≥3%). The correlation between survivin and Ki67 was evaluated using the Spearman correlation coefficient. Survival outcomes were analyzed using standard Kaplan-Meier methods and the log-rank test.

RESULTS: Significant associations were seen between survivin expression and age, smoking status, primary site, grade and tumor size. Patients with survivin-positive tumors were more likely to be younger with larger, high grade tumors, and have tobacco exposure. (Table)

Survivin positivity was associated with poor median overall survival (5.8y vs 18.3y, p<0.001) HR 2.89 (95% CI: 1.68-4.95). Due to variability in first therapy, association with freedom from progression in survivin-positive patients (5.6 vs 16 years, p=0.09) was not statistically significant. There was a moderate positive

correlation between survivin and Ki67 expression; survivin+ tumors tended to have high Ki67 (rs=0.54, p<0.001). On exploratory analysis of survivin with Ki67, patients with Ki67 Low/survivin- tumors had the best outcomes with median overall survival of 18.3 years followed by Ki67 Low/survivin+ with 9.1 years and Ki67 High/survivin+ tumors with 6.3 years (p<0.001).

CONCLUSION: Survivin expression in NETs is associated with aggressive biology and poor outcomes. There is a significant need to develop additional therapies for this population and survivin can be a potential target in these patients.

Table 1:

Significant patient characteristics in survivin-positive and negative tumors

Patients	Survivin Negative n=64 (%)	Survivin Positive n=68 (%)	P-value
Age <60/ ≥60	18(28)/ 46(72)	36(53)/ 32(47)	0.005
Males/ Females	21(33)/ 43(67)	26(38)/ 42(62)	0.59
Smoking History – pos/neg	32(50) /32(50)	57(84) /11(16)	<0.001
Grade I/ II/ III	36(61)/ 12(20)/ 11(19)	17(26)/ 10(15)/ 38(59)	<0.001
Primary Site – Lung/ GEP/ Other	22(34)/ 32(50)/ 10(16)	40(59)/ 16(23)/ 12(18)	0.003
Ki67 Low/ High*	59 (100)/ 0(0)	47(72)/ 18(28)	<0.001

***Not all samples were evaluable for Ki67, GEP=Gastroenteropancreatic**