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Identification of MEN1 Mutation via Next Generation Sequencing in the Cancer Treatment Centers of America (CTCA) Database.

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Background: MEN1 is a syndrome associated with increased risk of non-endocrine related malignancies, including breast cancer and lung cancer. We attempted to correlate the MEN1 gene alteration incidence and the allelic frequency (AF) the MEN1 mutations detected.

Methods: A retrospective review of 15 specimens (6 breast, 4 lung, 2 pancreas, 1 small intestine, 2 unknown primary cancers) with MEN1 gene alteration detected by Foundation OneTM (Foundation Medicine, Inc., MA). Next generation sequencing (NGS) test was performed. DNA was extracted from biopsy specimens and sequencing was performed per previously described methodology. AF is calculated as percent of reads at the position of a variant, which support the alternate allele. The reported value is not corrected for the specimen tumor content.

Results: N=2361, Breast Cancer N=414 (1.5%), Lung Cancer N= 369 (1.1%)

Mutation	Pathology	AF
MEN1 Q410*	Breast Neuroendocrine Carcinoma	41%
MEN1 R521fs*43	Small Intestine Adenocarcinoma	25%
MEN1 L278f2*	Breast Neuroendocrinc Carcinoma	63%
MEN1 loss	Pancreas neuroendocrine tumor pNet	0
MEN1 R521fs*15	Lung large cell neuroendocrine carcinoma	44%
MEN1 Q64*	Breast Invasive Ductal Carcinoma	13%
MEN1 P250fs*36	Lung atypical carcinoid	44%
MEN1 605fs*12 +	Lung Adenocarcinoma	11%
MEN1 R465*	Breast Invasive Ductal Carcinoma	52%
MEN1 E473fs*91	Unknown Primary undifferentiated neuroendocrine carcinoma	89%
MEN1 L175fs*21	Breast Carcinoma	38%
MEN1 Q458fs*77	Breast Carcinoma	15%
MEN1 N127fs*57	Pancreas neuroendocrine carcinoma	61%
MEN1 rearrangement (exons 1-5)	Lung adenocarcinoma	NA
MEN1 Q447*	Unknown Primary Melanoma	38%

Conclusions: MEN1 mutations are found in a variety of neoplasms with the majority in breast and lung carcinomas. Additional studies are underway to determine if MEN1 alterations may have a more substantial role in carcinogenesis than previously surmised.