O-6

Diagnostic Effectiveness of Chromogranin A and Multigene Liquid Biopsy (NETest) in Neuroendocrine Neoplasia: An assessment of Monoanalyte and Multianalyte Biomarker Efficacy

A. Malczewska[1], K. Oberg[2], B. Kos-Kudla[1]; [1]Department of Endocrinology and Neuroendocrine Tumors, ENETS Center of Excellence, Medical University of Silesia, Katowice/Poland, [2]Department of Endocrine Oncology, University Hospital, Uppsala/Sweden

BACKGROUND: A significant limitation in NEN management remains the absence of a reliable universal biomarker. CgA is still used despite reservations regarding accuracy and clinical utility. Different CgA assays are used at CLIA-certified laboratories (USA) and NET Centres of Excellence (CoE) and results are reported in several guidelines (ENETS/NANETS) and reimbursed by insurance companies. We evaluated the NEOLISA (EuroDiagnostica, IBL-America, CLIA-certified) and DD-ELISA (Demeditec Diagnostics, Germany; ENETS CoE) and compared results to the NETest, a CLIA-certified NET diagnostic.

METHODS: 258 NENs: pancreatic, n=67; small intestine, n=40; appendiceal, n=10; rectal, n=45; duodenal, n=9; gastric, n=44; lung, n=43.

Image-positive disease (IPD) (n=123; 25 RECIST-progressive, 98 radiologically stable), image/histology-negative (IND) (n=106), and image-negative/histology-positive (n=29).

NEOLISA, ULN: 108ng/mL, DD: ULN: 99ng/mL. Data mean±SEM.

NETest: PCR assay, ULN:20.

All samples de-identified and assessed blinded.

Statistics: Mann-Whitney U-test, Pearson correlation & McNemar-test.

RESULTS: Overall: CgA was positive in 53 (NEOLISA), 32 (DD).

NEOLISA levels significantly ($p<0.0001$) higher (98.6±11ng/mL) vs. the DD-assay (76±8ng/mL) (n=258). Assay concordance: Pearson $r=0.84$, $p<0.0001$). 12% (n=32) were discordant. NEOLISA detected more (n=23, 15%) true-positives than DD.

IPD (n=123): 41/123-CgA+ (33%, NEOLISA) vs. 23 (19%, DD). McNemar's $Chi^2=13.14$, $p=0.0003$.

NETest-positive in 122/123 (99%; McNemar's $Chi^2=79\text{-}97$, $p<0.0001$).

IND/histology-neg (n=106): 12/106-CgA+ (11%, NEOLISA) vs. 9 (8%, DD; p=NS).

NETest-positive in 35/106 (33%).

IND-histology+ (n=29): 9/29-CgA+ (7/9 GNETs, 2/20 RNETs NEOLISA) vs. 4/29 (4/9 GNETs DD).

NETest positive in 13 (9/9 GNETs, 4/20 RNETs)

Disease status (IPD):

No difference in CgA levels between progressive (PD: n=25) and stable disease (SD: n=98).

NETest significantly higher in PD (47±5) than SD (29±1), $p=0.0009$.

CONCLUSION: NETest, a multigenomic mRNA biomarker is ~99% accurate for detecting NEN disease compared to two standard CgA assays. These detected NET disease in 19-33%. NETest should be considered as the standard of care.

ABSTRACT ID: 153