Molecular comparison between peritoneal metastases (PM) and primary gastric (GC) and gastroesophageal junction (GEJ) cancer.

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PM from GC or GEJ portend a poor prognosis and molecular differences are ill defined.

METHODS
- We compared genomic profiles of primary (P) GC and GEJ with PM patients (pts) and other metastases (OM) sent to Caris Life Sciences.
- Testing included:
  - Next-generation sequencing (NGS) on genomic DNA of 592 cancer-related genes isolated from formalin-fixed, paraffin-embedded (FFPE) tumor samples utilizing NextSeq platform (Illumina Inc., San Diego, CA). The 592 genes were enriched with a custom-designed SureSelect XT assay (Agilent Technologies, Santa Clara, CA, USA). Variants were detected with >99% confidence based upon allele frequency and amplicon coverage, with an average sequencing depth of coverage >600X and an analytic sensitivity of 5% variant frequency.
  - Tumor mutational burden (TMB), reported in mutations per megabase (Mb), was determined by calculating the number of nonsynonymous somatic mutations identified by NGS after removing single nucleotide polymorphisms (SNP) identified in dbsNP (version 137) or in 1000 Genomes Project database (phase 3). 1.4 Mb were sequenced per tumor.
  - Immunohistochemistry (IHC) for expression rate of 27 proteins. Results were test-defined as positive or negative based on previously established thresholds. PD-L1 was assessed via combined positive score (CPS).
  - Copy Number Variation (CNV) analysis of 441 genes. Results were test-defined as amplified or non-amplified.
  - Microsatellite Instability (MSI) analysis using NGS panel. MSI-high was test-defined as >46 altered loci.
  - Statistical Analysis: Statistical analysis was completed with SPSS version 20.0. Chi-square testing with a two-tailed p-value of <0.05 was used.

RESULTS
- 1366 cases were identified (Table 1):
  - PM were increased in GC versus GEJ (9% v. 2%, p = 0.0001).
  - 91% of GC and 93% GEJ were adenocarcinoma (AD).
  - GC were more likely signet ring (SR) histology versus GEJ (11% v. 3%, p < 0.0001) and GC PM were more likely SR versus other OM or P (13% v. 12% v. 7%, p = 0.067).
- The mean age of PM pts (57 years) was younger than primary GC (63, p = 0.002) and OM (61; p = 0.044).
- More PM GC pts were female than P or OM (48% v. 35% v. 34%, p = 0.03).
- No molecular profiling differences were seen between GEJ and GC pts and they were combined for analysis; findings from 1246 AD pts are shown below in tabular and graphic forms.

CONCLUSIONS
- Compared to P and OM GC, PM pts were younger, more likely female and had a higher incidence of SR histology.
- Both PM and OM were more frequently MUTYH-mutated than P and PMs had more CDH1 mutations than P.
- PD-L1, HER2 IHC, and ERBB2 CNA were reduced in PM versus P, suggesting novel therapeutic targets are needed.

REFERENCES

Questions: Please contact
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Table 1. Characteristics of GC vs. GEJ samples.

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Table 2. Immunobiomarker Evaluation of PM or OM vs. P.

Table 3. Selected Molecular Features of PM or OM vs. P.