Comparison of metachronous epithelial ovarian carcinoma by next generation sequencing

Abstract #5545

Background

Epithelial ovarian carcinoma (EOC) is a relatively common malignancy which, by the time it becomes platinum-resistant, contains few good treatment options. Next-generation sequencing (NGS) is a promising technology with the potential to alter how this disease is managed. However, much remains unknown regarding its applicability in ovarian carcinomas. The purpose of this study is to compare metachronous epithelial ovarian carcinoma specimens arising from different sites in an attempt to better understand how to apply NGS in the management of this disease.

Methods

A retrospective analysis of sequencing results for 83 metachronous (defined as specimens collected greater than 28 days apart) EOC specimens was performed. In most instances, comparisons involved two different metastatic sites (n=50), while the rest involved a comparison of the primary and a subsequent metastatic specimen (n=33). All specimens had up to 47 genes analyzed using the Illumina MiSeq NGS platform. Tumors were sequenced to a depth of 1500x, on average.

Results

Out of the 83 specimens analyzed, 20(24.1%) showed complete agreement. The most common discordance was due to detection of mutations down to 10% variant frequency in 45 of the genes analyzed. For BRCA1 and BRCA2 mutations, detection of mutations was down to 20% variant frequency. Metachronous specimens collected from 43 to 2793 days apart (mean = 519) had disagreement in gene results and all of these disagreed expected given the large number of cells.

Conclusion

To the best of our knowledge, this is the first study where ovarian cancer paired specimens from a non-academic institution were analyzed. The overall low mutation rate is consistent with previous studies on EOC. A multiplex platform approach may identify additional potential targets in this lethal disease. Evaluating genetic mutations alone is not sufficient.

The high agreement rate between primary versus secondary specimens and metastatic versus metastatic sites suggests taking a baseline genetic reading may be sufficient in the majority of cases. Serial monitoring using DNA sequencing may not be necessary during late-stage disease. BRCA1 results did not change in the paired specimens analyzed. However, two pairs with BRCA2 mutations, classified as variant of unknown significance (VUS), were changed from VUS to mutation.

Future evaluations in our lab will expand on these initial findings by evaluating larger (i.e. 592-gene) panels.

References