A Big Advance In Personalized Medicine: Ovarian Cancer

By Chuck Dinerstein, MD, MBA — July 22, 2016

Personalized medicine is the rage everywhere, at least in blogs and marketing campaigns for health systems. But beyond the BRCA genes, estrogen receptor and the genomic promises of 23 and Me and its wannabes, actual personalized medicine has yet to realize much of its potential. That is why a study [1] that was recently reported in Scientific Review on "liquid biopsy" for ovarian cancer surveillance was such an excellent exposure to personalized medicine’s adjacent possibility.

Liquid biopsy detects cancer DNA, either within cells or circulating by itself in blood, obviating the need for more invasive tissue biopsy. The presence of cancer cell DNA has been strongly correlated with both progression and remission in breast and prostate cancer. Moreover, the short half-life of these DNA forms allows a better understanding of tumor dynamics and the real possibility that serial monitoring could enhance surveillance for recurrence.

Ovarian cancer represents only 30% of gynecologic cancers but is responsible for 50% of deaths, primarily because of its vague clinical presentation and absence of reliable screening methods. As a result, most women are diagnosed with advanced disease at presentation. And as you might expect, there is a high rate of recurrence, about 80%.

In a small proof of concept study [1] from Stanford, patient specific chromosomal rearrangements that were caused by ovarian cancer were detectable when cancer persisted and absent when ovarian cancer was not present. The study found that patient-specific chromosomal rearrangements of their ovarian tumors could be reliably detected using PCR techniques and could quantify tumor burden.

The American College of Obstetrics and Gynecology recommendations for surveillance for ovarian cancer consists primarily of asking the patient about symptoms, which we know are frequently vague; and a physical examination which may well miss early recurrent disease. CA 125 assays have been slightly more accurate than reliance solely on a patient's description of symptoms and physical examination and are considered optional in the absence of clinical suspicion of recurrent
disease. Similarly, imaging studies have no role in patients in surveillance that have no symptoms or signs of recurrent disease. In one retrospective study of 412 patients, examination identified 15% of recurrences, imaging 27% and CA 125 levels 23%. The combination of CA 125 and imaging resulted in detection of 35% of recurrences. Despite our best efforts, we still have no reliable means of detecting recurrent disease for the vast majority of women affected.

Physicians and patients face a dilemma regarding surveillance, use inconclusive examinations and symptoms or somewhat less ambiguous but more expensive testing. (CA 125 and CT scans would COST about $1200) That is why the Stanford study is so exciting and valuable. It may be quite sensitive, and the cost of PCR testing is a fraction of $1200.

Here is a part of their conclusion:

“The recent explosion of cell tumor DNA (ctDNA) studies and the rapid increase in sensitivity and specificity of methodologies for ctDNA detection allude to a coming clinical integration, and point to the possibility of routine measurement of ctDNA in cancer patients in the near future. OC patients appear particularly suited to benefit from this approach, as they shed relatively higher amounts of ctDNA than those with other cancers and are also at great risk of recurrence following initial chemotherapy.”

My physician’s heart is inspired by the possibilities; my MBA heart is equally gladdened at reducing healthcare costs in an effective, efficient way.

Citation: Faye R. Harris, Irina V. Kovtun, James Smadbeck, Francesco Multinu, Aminah Jatoi, Farhad Kosari, Kimberly R. Kalli, Stephen J. Murphy, Geoffrey C. Halling, Sarah H. Johnson, Minetta C. Liu, Andrea Mariani, George Vasmatzis, 'Quantification of Somatic Chromosomal Rearrangements in Circulating Cell-Free DNA from Ovarian Cancers', *Scientific Reports* 6, Article number: 29831 (2016) doi:10.1038/srep29831 [1]

NOTE:

(1)
(A) Blood is drawn before and after surgery. DNA from tumor is sequenced using the next-generation mate-pair sequencing (MPseq) protocol to identify chromosomal rearrangements. Several junctions are chosen to construct a personalized panel for each tumor. Percent of ctDNA out of total cfDNA is calculated at each time point of blood collection. (B) Number of junctions identified in cohort of 10 cases of serous stage 3 ovarian cancer. Count numbers are above the bars with the expected false negative count in parenthesis. cfDNA: cell-free DNA; ctDNA: circulating tumor DNA.

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