Consistent Testing Terminology Use Cases Workshop

March 11, 2021

Consistent Testing Terminology Working Group

Use Case – Ovarian Cancer

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Use Case: Ovarian Cancer
Presenter: Ovarian Cancer Research Alliance (OCRA)

DESCRIPTION OF DISEASE SETTING

- American Cancer Society estimates for ovarian cancer in the United States for 2021 are:
  - ≈ 21,410 women will receive a new diagnosis of ovarian cancer
  - ≈ 13,770 women will die from ovarian cancer
- Over the past 20 years, BRCA1/BRCA2-related discoveries have profoundly changed our understanding & management of HBOC (hereditary breast and ovarian cancer). **Patients with BRCA1/2 account for only approximately 15% of all women who have ovarian cancer**
- Guidelines by NCCN (National Comprehensive Cancer Network), SGO (Society of Gynecologic Oncology), and ACOG (American College of Obstetricians and Gynecologists) all agree that anyone with a personal history of ovarian cancer should receive genetic counseling and testing (regardless of family history, age, or other risk factor).
- According to NCCN (2021):
  - In addition to mutations in BRCA1/2 and the genes associated with Lynch Syndrome (e.g., MLH1, MSH2, MSH6, PMS2) germline mutations in a variety of other cancer genes have been associated with increased risk of ovarian cancer (e.g., ATM, BRIP1, NBN, PALB2, STK11, RAD51C, RAD51D).
  - Studies testing large panels of genes have found that 3%-8% of patients with ovarian cancer carry mutations in genes other than BRCA1 and BRCA2 known to be associated with ovarian cancer susceptibility.

Use Case: Ovarian Cancer

APPLICABILITY OF BIOMARKER TESTING

APPLICABILITY OF GENETIC TESTING FOR INHERITED MUTATIONS/INHERITED CANCER RISK

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2021
Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer

- **Tumor molecular analyses as clinically indicated:**
  - ◊ **Next-generation sequencing (NGS) for *BRCA1/2* mutations, other somatic mutations (eg, *NTRK* gene fusions), and tumor mutational burden [TMB]**
  - ◊ **Additional testing (particularly for endometrioid carcinomas)**
    - **– Immunohistochemistry (IHC) for DNA mismatch repair (MMR) proteins (MLH1, MSH2, MSH6, and PMS2)**
    - **– Microsatellite instability (MSI) testing**
  - ◊ **In addition to *BRCA1/2* testing, other methods for evaluating HR deficiency status (ie, genomic instability, loss of heterozygosity) can be considered.**
  - ◊ **Additional somatic tumor testing can be considered at the physician's discretion to identify genetic alterations for which FDA-approved tumor-specific or tumor-agnostic targeted therapy options exist.**

References

Continued

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

APPLICABILITY OF BIOMARKER TESTING

APPLICABILITY OF GENETIC TESTING FOR INHERITED MUTATIONS/INHERITED CANCER RISK

Use Case: Ovarian Cancer

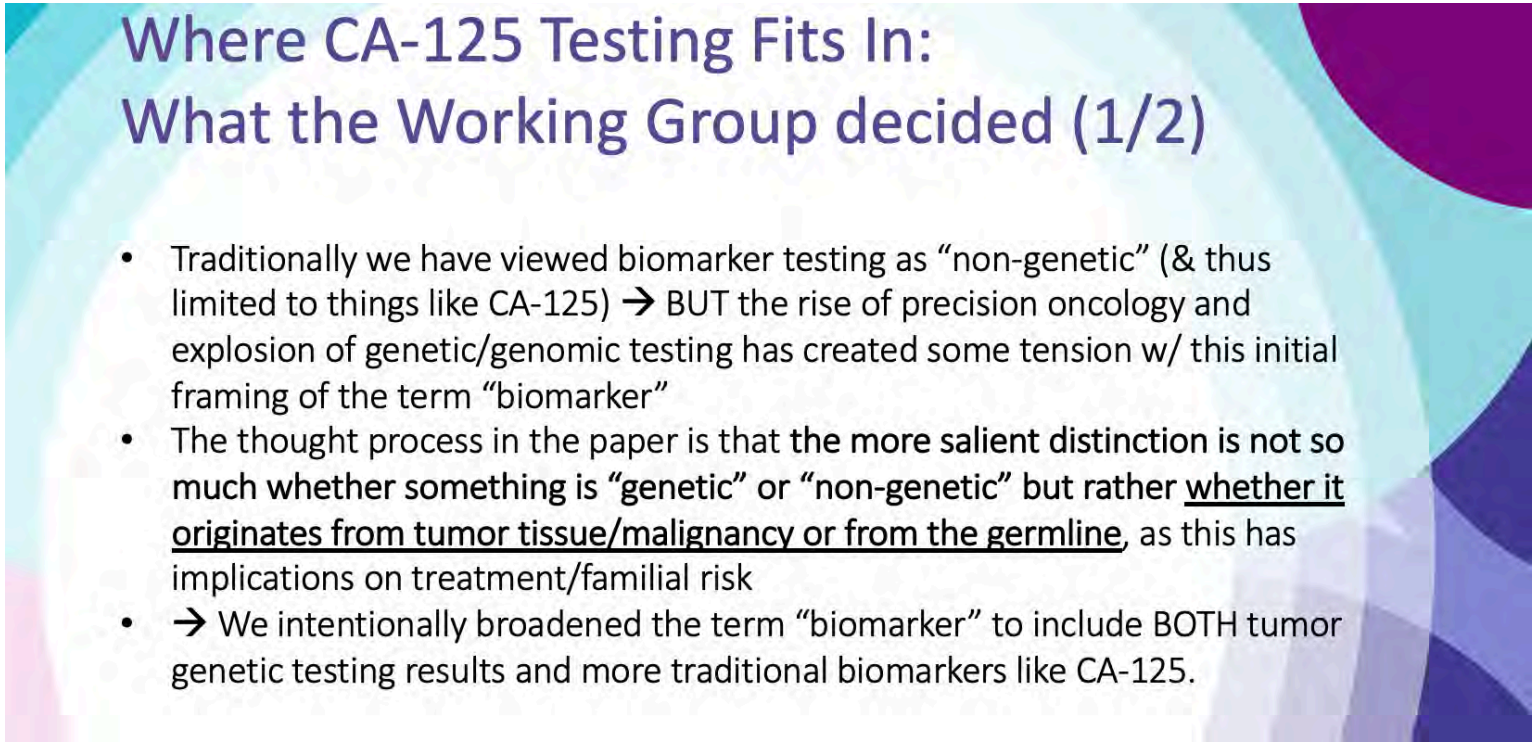
- Professional guidelines have been in place for 10+ years → **and yet, research shows alarmingly low rates of genetic testing among OC survivors**
- Last year, JCO (Journal of Clinical Oncology) published a baseline-setting study looking at genetic testing among rates among HBOC survivors → *first population study of hereditary cancer genetic testing the U.S. with laboratory-confirmed testing results*
- Study uses data from 83,000+ women from SEER cancer registries in California and Georgia and finds that, in 2013 and 2014:
  - → ≈ One-third of women with ovarian cancer underwent genetic testing for inherited BRCA1/2 mutations in compliance with guidelines
  - → Among patients who did receive genetic testing, 15% of ovarian cancer patients had “actionable” gene variants, meaning variants that might warrant changes in treatment, screening, and risk-reduction strategies

YOUR ORGANIZATION'S EXPERIENCE APPLYING TERMS

Use Case: Ovarian Cancer

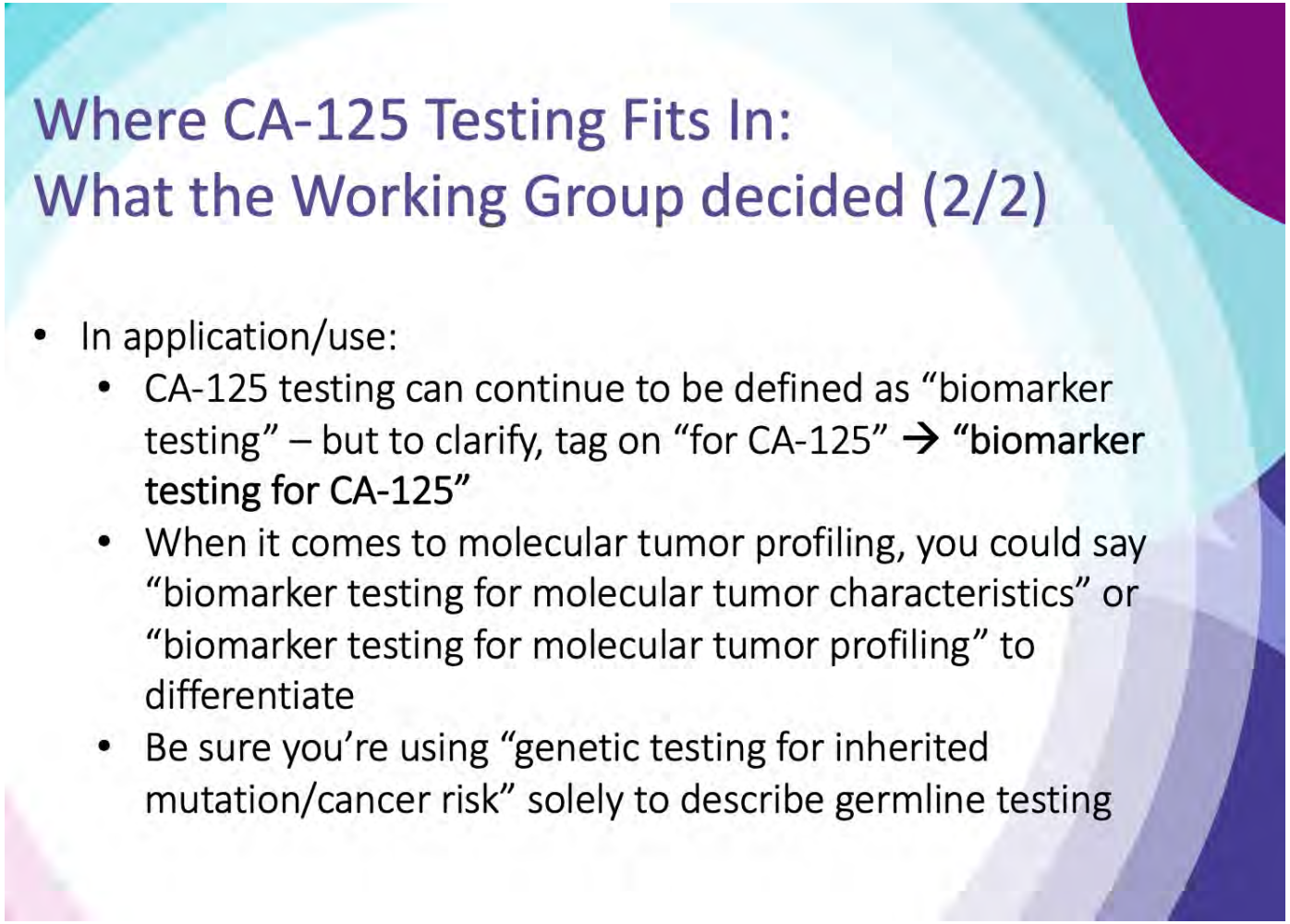
- Presented at OCRA's National Conference in September 2021 (300+ attendees)
- Heard a lot feedback about CTWG's position w/ respect to CA-125 testing

→ *Screenshots of pertinent slides*



YOUR ORGANIZATION'S EXPERIENCE APPLYING TERMS

Use Case: Ovarian Cancer



Session title:
"How to Talk about Genetic Testing and Precision Oncology (& Why It's So Confusing)"

Recommended session title:
"Understanding the Language of Cancer Testing: Biomarkers, Molecular Profiling, Genetic Testing."

CHALLENGES THAT AROSE

Use Case: Ovarian Cancer

<u>The sticky intersection between CA-125 testing & biomarker testing:</u>

- CA-125 is a glycoprotein (sugar associated protein) commonly referred to as a "biomarker" or "tumor marker". The CA-125 provides information via a blood sample.
- It can assist in diagnosing and following ovarian cancer (& has multiple other clinical applications.
- Limitations → CA-125 is only elevated in 50% of women w/ early-stage ovarian cancer and 85% of women w/ advanced cancer
  - The CA-125 can be elevated in someone who does not have cancer.
  - The number does not correlate with the extent of disease.
- How is the CA-125 used in ovarian cancer?
  - It is used s a tool to detect changes in CA-125 levels. If elevated in a woman with ovarian cancer, it can represent disease status.

CHALLENGES THAT AROSE

More on CA-125 in OC

- All women with ovarian cancer are given the CA125
- It is the most reliable and useful test for monitoring disease, however, for many women, it is not a good marker.
- Why do some gynecologic oncologists hate the CA-125? → Evidence suggests that using the CA125 to diagnose recurrent disease sooner does not result in overall improved survival.
- Following the CA-125 more closely caused physicians to administer more chemotherapy without improving outcomes.
- The CA-125 test causes incredible anxiety in women with the disease

LESSONS LEARNED
ONGOING NEEDS AND/OR GAPS

Use Case: Ovarian Cancer

- Make no mention of CA-125 tests in context of ”biomarker testing”
  - OC population is already familiar with CA-125 tests and its application & discussing as part of “biomarker testing” in context of precision seemed to serve no real purpose and caused confusion.

- Gaps in education and awareness are *considerable*
  - OC patients/survivors who are in the know when it comes to “biomarker testing” are highly sophisticated in their knowledge and understanding.
  - BUT overall awareness and understanding is alarmingly low. As the JCO study found, nearly two-thirds of OC survivors haven’t received basic biomarker tested for inherited cancer risk in BRCA1/2 genes (in compliance with guidelines).
  - Geographic disparities are a particularly significant barrier for OC patient population.