<table>
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<th>Guideline Page and Request</th>
<th>Panel Discussion/References</th>
<th>Institution Vote</th>
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<tr>
<td><strong>External request:</strong></td>
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<td>Submission from Guardant Health on 09/11/20 to:</td>
<td>Based on a review of the data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines due to insufficient data in ovarian cancer.</td>
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<td>• Consider listing liquid biopsy using a well validated circulating tumor (ctDNA) assay (such as Guardant360) to assure that all patients with advanced or recurrent ovarian cancer are completely profiled for all Guideline-recommended biomarkers, including germline and somatic BRCA1/2 mutations, microsatellite instability (MSI), and NTRK fusions. The goal is to give physicians greater autonomy in their choice of testing modality and provide patients with a non-invasive option. In patients whose diagnosis has already been histopathologically established, plasma-based testing may obviate the need for repeat invasive biopsy, as Guardant360 has been shown to identify targetable alterations at similar rates with similar matched-therapy outcomes as tissue-based profiling.</td>
<td>See Submission for references.</td>
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<td>• Since not all ctDNA tests are technically equivalent, you may wish to add specific language to suggest using a FDA-approved ctDNA assay that has not only published analytical and clinical validation, but has also achieved the gold standard for genomics tests: published outcomes studies based on ctDNA-identified germline and somatic BRCA1/2 mutations and MSI in ovarian cancer (e.g., Guardant360).</td>
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<tr>
<td><strong>OV-1</strong> External request:</td>
<td>Based on a review of the data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines due to insufficient available data.</td>
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<td>Submission from ASPIRA Women’s Health on 09/10/20 to consider the inclusion of the use of OVA1® (MIA) as part of the workup on an indeterminate adnexal mass after imaging diagnoses an adnexal mass but it is neither clearly benign nor malignant (on page OV-1 work flow chart at top, specifically “WORKUP” column section tied to footnote “c”).</td>
<td>See Submission for references.</td>
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**OV-1 and OV-2**

External request:

Submission from Astra Zeneca on 05/15/20 to consider multiple requests:

- Revise recommendation (following primary treatment) to, “Patients with...should receive genetic risk evaluation, germline and somatic **BRCA1/2 mutation** testing and/or **tumor homologous recombination deficiency (HRD) testing** (if not previously done)”
- Within footnote ‘e’, revise statement to “Germline and/or somatic **BRCA1/2** and/or **tumor HRD genomic instability status** informs maintenance therapy”
- Within PRIMARY TREATMENT section, revise recommendation to, “Neoadjuvant therapy...genetic risk evaluation, germline and somatic **BRCA1/2 mutation** testing and/or **tumor homologous recombination deficiency (HRD) testing** (if not previously done)”.

Based on a review of the data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines.

The panel consensus supported edits to footnotes f and g:

- f: Germline and/or somatic **BRCA1/2** status informs maintenance therapy.
- g: In the absence of a **BRCA1/2** mutation, homologous recombination (HR) **deficiency** (HRD) status may provide information on the magnitude of benefit of PARP inhibitor (PARPi) therapy (category 2B). *(See OV-B)*

See Submission for references.

**OV-1/OV-6/OV-B/OV-C**

External request:

Submission from Foundation Medicine on 09/18/20 to consider multiple requests:

- OV-1: Update footnote in algorithm for clinical presentation on pages OV-1, OV-2, and OV-3 to state “Germline and/or somatic **BRCA1/2** informs maintenance therapy. **Consider tumor molecular testing with validated, next-generation sequencing (NGS)-based assay to include at least: BRCA1/2, MSI, NTRK gene fusions, TP53, and tumor mutational burden. Tumor molecular testing can be performed as part of a single, NGS-based broad molecular profiling assay to inform patient treatment options, including clinical trials.”
- OV-6: Update footnote in algorithm for recurrent disease on pages OV-6, OV-7 to state “**Tumor molecular testing is recommended prior to initiation of therapy for recurrent or persistent disease with validated NGS-based assay** to include at least: BRCA1/2, MSI and/or DNA mismatch repair, **NTRK gene fusions**, **PARP inhibitor** (PARPi) therapy.”

Based on a review of the data and discussion, the panel did not use the language proposed in the submission. However, the panel supported revising the following language on OV-B (1 of 3):

- 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

See Submission for references.
TP53, and tumor mutational burden. Evaluation of homologous recombination deficiency can be considered. Tumor molecular testing can be performed as part of a single, NGS-based broad molecular profiling assay to inform patient treatment options, including clinical trials.”

- OV-B (1 of 3): Under Tumor Molecular Analyses indicate that MSI testing can be performed through a validated NGS panel, similar to the NCCN® Colon and Rectal Cancer Guidelines (COL-B page 4 of 8; REC-B page 5 of 8). Also, under Tumor Molecular Analysis (page OV-B 1 of 3), recommend tumor molecular testing via a single, validated NGS-based broad molecular profiling assay to include at least: BRCA1/2, MSI and/or DNA mismatch repair, NTRK gene fusions, TP53 and tumor mutational burden to inform patient treatment options, including clinical trials.

- In “Principles of Systemic Therapy,” (OV-C, 3 of 10) indicate that tumor molecular testing is recommended prior to initiation of therapy for recurrent or persistent disease with validated NGS-based assay to include at least: BRCA1/2, MSI and/or DNA mismatch repair, NTRK gene fusions, TP53, and tumor mutational burden. Evaluation of homologous recombination deficiency can be considered. Tumor molecular testing can be performed as part of a single, NGS-based broad molecular profiling assay to inform patient treatment options, including clinical trials.

OV-1 External request:

Submission from Myriad on 09/08/20 to consider multiple requests:

- Defining HRD consistently throughout the guidelines (Also pages OV-2,3,5): HRD defined by either: 1) deleterious or suspected deleterious BRCA mutation; or 2) genomic instability as defined by Myriad myChoice® CDx and progression >6 months after response to the last platinum-based chemotherapy.

Based on a review of the data and discussion, the panel did not support using the proposed language as a definition for HRD throughout the Guideline.

See Submission for references

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