myChoice CDx

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

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<th>Procedures addressed by this guideline</th>
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What is homologous recombination deficiency status

Definition

Homologous recombination repair (HRR) is the cellular mechanism for repairing double stranded DNA breaks. Impairment of this pathway leads to an increase in instability of genetic material and carcinogenesis. This impairment, called homologous recombination repair deficiency (HRD), can be caused by germline or somatic mutation of genes in the pathway, such as BRCA1 and BRCA2.

PARP

Poly (ADP-ribose) polymerase (PARP) is a family of proteins involved in a number of cellular processes including DNA repair and programmed cell death.

In the case of DNA repair, a PARP inhibitor blocks the PARP from performing its normal function of repairing damaged single-stranded DNA. If the damaged single-stranded DNA persists through cell replication and cell division, double stranded breaks in the DNA can occur.

Tumors manifesting HRD are especially sensitive to PARP inhibitors, as these agents increase the number of double stranded breaks, making cell death more likely in cells also manifesting HRD. Therefore, HRD and the presence of HRR gene mutations have become biomarkers for assessing PARP inhibitor sensitivity.

Test information

myChoice CDx is a next-generation sequencing based assay developed by Myriad that determines HRD status by the detection of “single nucleotide variants, insertions and deletions, and large rearrangement variants in protein coding regions and intron/exon boundaries of the BRCA1 and BRCA2 genes and the determination of Genomic Instability Score (GIS) which is an algorithmic measurement of Loss of Heterozygosity.
(LOH), Telomeric Allelic Imbalance (TAI), and Large-scale State Transitions (LST) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. "4,5

The results of the assay are used to identify individuals with ovarian cancer who may be eligible for treatment with niraparib (Zejula). 4,5

Guidelines and evidence

Food and Drug Administration (FDA)

The FDA approved niraparib (Zejula) in 2019 when prescribed based on results from an FDA-approved companion diagnostic

• “Zejula is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either:6
  o A deleterious or suspected deleterious BRCA mutation, or
  o Genomic instability and who have progressed more than six months after response to the last platinum-based chemotherapy.”

The FDA approved myChoice CDx as a companion diagnostic for niraparib in 2019.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN, 2019) guidelines include the following direction in regards to treatment section for ovarian cancer, fallopian tube cancer, and primary peritoneal cancer:

• Niraparib: “For patients treated with three or more prior chemotherapy regimens and whose cancer is associated with HRD-positive status defined by either: (1) a deleterious or suspected deleterious BRCA mutation; or (2) genomic instability and progression >6 months after response to the last platinum-based chemotherapy.” 7

Criteria

myChoice CDx testing may be considered in individuals who meet ALL of the following criteria:

• Member has a diagnosis of ovarian cancer, AND
• Member does not have a previously identified germline or somatic mutation in either BRCA1 or BRCA2, AND
• Member does not have a known BRCA mutation in the family,** AND
• Treatment with niraparib is being considered, AND
• Rendering laboratory is a qualified provider of service per the Health Plan policy

** Please see *BRCA Analysis* guideline for testing algorithm in cases where there is a known BRCA1/2 mutation in the family.

References


