COLLEGE of AMERICAN PATHOLOGISTS

Template for Reporting Results of DNA Mismatch Repair Testing in Patients Being Considered for Checkpoint Inhibitor Immunotherapy

Version: DNAMismatchRepair 1.0.0.1 **Protocol Posting Date: January 2018**

Pembrolizumab (Keytruda®) was approved by the FDA for adult and pediatric patients with metastatic or unresectable solid tumors that are either microsatellite instability-high (MSI-H) OR mismatch repair deficient (dMMR) that have progressed following prior treatment.

This biomarker template is NOT required for accreditation purposes but is provided to assist laboratories in reporting the results of testing done to identify patients who may be eligible for checkpoint inhibitor-based immunotherapy. This template is recommended for tumors other than colon and endometrium. For patients with colorectal or endometrial carcinoma, site-specific biomarker reporting templates are available and are recommended.

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Completion of the template is the responsibility of the laboratory performing the biomarker testing and/or providing the interpretation. When both testing and interpretation are performed elsewhere (eg, a reference laboratory), synoptic reporting of the results by the laboratory submitting the tissue for testing is also encouraged to ensure that all information is included in the patient's medical record and thus readily available to the treating clinical team. **This template is not required for accreditation purposes.**

Summary of Changes

Version 1.0.0.1
Modified MSI response from Indeterminate to Cannot be determined

DNA Mismatch Repair Testing for Checkpoint Inhibitor Immunotherapy

Template posting date: January 2018

+ Specimen site: _____

+ Testing performed on block number(s): _____

+ Immunohistochemistry (IHC) Results for Mismatch Repair (MMR) Proteins (select all that apply)
+ ___ MLH1
  + ___ Intact nuclear expression
  + ___ Loss of nuclear expression
  + ___ Cannot be determined (explain): _____
+ ___ MSH2
  + ___ Intact nuclear expression
  + ___ Loss of nuclear expression
  + ___ Cannot be determined (explain): _____
+ ___ MSH6
  + ___ Intact nuclear expression
  + ___ Loss of nuclear expression
  + ___ Cannot be determined (explain): _____
+ ___ PMS2
  + ___ Intact nuclear expression
  + ___ Loss of nuclear expression
  + ___ Cannot be determined (explain): _____

+___Background non-neoplastic tissue/internal control shows intact nuclear expression

+ Mismatch Repair (MMR) Interpretation
+ ___ No loss of nuclear expression of MMR proteins: No evidence of deficient mismatch repair (low probability of MSI-H)
+ ___ Loss of nuclear expression of one or more MMR proteins: deficient mismatch repair

+ Microsatellite Instability (MSI) Interpretation
+ ___ MSI–Stable (MSS)
+ ___ MSI–Low (MSI-L)
  + ___ 1%-29% of the markers exhibit instability
  + ___ 1 of the 5 NCI or mononucleotide markers exhibits instability
  + ___ Other (specify): _____
+ ___ MSI–High (MSI-H)
  + ___ ≥30% of the markers exhibit instability
  + ___ 2 or more of the 5 NCI or mononucleotide markers exhibit instability
  + ___ Other (specify): _____
+ ___ MSI–Cannot be determined (explain):_____

Note: The presence of MSI-H/deficient mismatch repair may also be an indication for additional testing for Lynch syndrome and genetic counselling.

Note: Heterogeneous expression of MLH1 and PMS2 has been infrequently encountered in endometrial carcinomas (up to 3% of cases). The incidence of heterogeneous expression in other cancer types and its impact on predicting sensitivity to checkpoint inhibition is not currently known.

+ COMMENT(S)

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_____

+ Data elements preceded by this symbol are not required.