Abnormal IHC result

- Loss of MLH1 with or without PMS2 loss
  - BRAF Mutation Analysis (CRC only)
    - V600E positive → *Lynch syndrome unlikely*
    - V600E negative
      - MLH1 and PMS2 sequencing and deletion/duplication, performed concurrently or sequentially
        - Mutation detected → *Lynch syndrome confirmed*
        - No mutation detected → *Lynch syndrome unlikely*

- Loss of MSH2 with or without MSH6 loss
  - *MSH2/EPCAM and MSH6 sequencing and deletion/duplication, performed concurrently or sequentially; if loss of MSH2 only, MSH6 genetic test may be omitted*

- Loss of MSH6 only
  - *MSH6 and MSH2 (including EPCAM) sequencing and deletion/duplication, performed concurrently or sequentially*

- Loss of PMS2 only
  - *PMS2 and MLH1 sequencing and deletion/duplication, performed concurrently or sequentially*

If BRAF V600E is positive, Lynch syndrome is unlikely; however, if the patient was diagnosed at a young age or has a significant family history, consider MLH1/PMS2 germline mutation testing. If germline testing is negative and there is a strong suspicion of hereditary cancer, consider testing for other CRC-related hereditary conditions. CRC, colorectal cancer.

This algorithm is intended as a guide for using Quest Diagnostics laboratory tests to diagnose Lynch syndrome. It is based on the National Comprehensive Cancer Network guidelines. The algorithm is provided for informational purposes only and is not intended as medical advice. A physician’s test selection and interpretation, diagnosis, and patient management decisions should be based on his/her education, clinical expertise, and assessment of the patient.