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MM23

Molecular Diagnostic Methods for Solid Tumors (Nonhematological Neoplasms)

This guideline covers the current state of molecular diagnostic techniques intended for the characterization of solid tumors, and covers a range of clinical applications including diagnosis, prognosis, therapeutic response prediction for available drugs and those still in clinical trials, as well as monitoring and presymptomatic and predisposition testing.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Molecular Diagnostic Methods for Solid Tumors (Nonhematological Neoplasms)

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Abstract

Clinical and Laboratory Standards Institute document MM23—*Molecular Diagnostic Methods for Solid Tumors (Nonhematological Neoplasms)* describes development and implementation of nucleic acid biomarker assays for accurate detection of somatic and germline alterations with applications to clinical decision making for cancer patients with solid tumors. It is intended for molecular diagnostic laboratory directors, industry laboratory professionals, and health care professionals, including anatomic and clinical pathologists. With the exception of cancer predisposition syndromes, the methods and recommendations discussed in this document focus primarily on detection of tumor-specific genetic abnormalities that are acquired during tumorigenesis and are distinct from normal variations in nonmalignant cells of the same tissue.

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Foreword

With the completion of the sequence of the human genome, researchers have identified opportunities for detecting and defining molecular alterations in the germline, as well as within malignant tumors. Identification of mutations that drive both neoplastic transformation of normal tissue, as well as progression to more advanced disease states, provides insight into the biology of neoplasia and therapies to arrest the disease. The discovery of many somatic alterations in the tumor cell genomes, new forms of regulatory nucleic acids, gene expression profiling, whole exome sequencing, and microRNA profiling are a few of the molecular tests used by the clinical laboratory to support the individualized use of therapies and improve the outcomes of cancer patients. Clinical oncology is moving from treatment selection that is based solely on the tissue of origin to one based on the molecular genetics of the particular cancer and mutation profiling to define optimal patient therapies. Genetic variations may be matched with available drugs that may not have been previously considered, or with drugs that are available through clinical trials. It is essential that these new tests be useful for medical decision-making purposes, and that their utility be evaluated as quickly and efficiently as possible.

The document development committee was formed to address the need for a guideline on the performance and interpretation of molecular assays used to characterize solid tumors. This guideline covers the current state of molecular diagnostic techniques intended for the characterization of solid tumors, as well as a range of clinical applications, including diagnosis, prognosis, monitoring tumor burden, presymptomatic and predisposition testing, and therapeutic response prediction for available drugs, as well as drugs still in clinical trials. This guideline does not include an extensive discussion of inherited cancer syndromes, which are covered in more depth in CLSI documents MM01[1] and MM19.[2] In addition, due to the rapidly changing nature of molecular diagnostics, this document may be incomplete due to the development of new techniques after its publication.

The methods and QC approaches described herein are not absolute or immutable. They represent expert consensus recommendations presented by the document development committee, and are intended for use by diagnostic laboratories. Such use is intended to facilitate both interlaboratory comparisons of results and diagnostic interpretations, as well as to ensure accuracy in diagnosis and tumor characterization.

Key Words

Cancer, carcinoma, companion diagnostic devices, genetics, genomics, genotyping, molecular methods, mutation detection, nonhematological, oncology, polymerase chain reaction, sequencing, solid tumor, somatic variants, targeted therapy

Molecular Diagnostic Methods for Solid Tumors (Nonhematological Neoplasms)

Chapter 1: Introduction

This chapter includes:

- Document scope and applicable exclusions
- Background information pertinent to the document content
- Standard precautions information
- "Note on Terminology" that highlights particular use and/or variation in use of terms and/or definitions
- Terms and definitions used in the document
- Abbreviations and acronyms used in the document

1.1 Scope

This guideline describes the development and implementation of nucleic acid biomarker assays for accurate detection of somatic and germline alterations with applications to clinical decision making in oncology. With the exception of cancer predisposition syndromes, the methods and recommendations discussed in this document focus primarily on detection of tumor-specific genetic abnormalities that are acquired during tumorigenesis and are distinct from normal variations in nonmalignant cells of the same tissue. Circulating tumor cells (CTCs) of solid tumor origin and circulating cell-free tumor nucleic acid assays are discussed. Distinguishing characteristics of familial cancer syndromes are presented briefly because many diagnostic testing criteria will be similar to those addressed in CLSI document MM01,[1] which describes inherited trait genetic testing. Genetic markers (acquired or inherited) that predict response to anticancer treatments, including targeted therapies, and the role of these markers in personalized medicine are discussed.

This guideline focuses on neoplasms that are neither leukemias nor lymphomas (hematological cancers) because these cancers have been addressed in great detail in CLSI document MM05.[3] This document focuses on the underlying nucleic acid tumor markers and variants, but does not examine cell-surface antigens, immunohistochemistry (IHC), or protein markers. Detailed guidance for the use of nucleic acid sequencing, microarrays, multiplex assays, and quantitative testing are covered in greater detail in CLSI documents MM01,[1] MM05,[3] MM07,[4] MM09,[5] MM12,[6] and MM17.[7]

This document is intended for molecular diagnostic laboratory directors, industry laboratory professionals, and health care professionals, including anatomic and clinical pathologists.