CLINICAL AND LABORATORY STANDARDS INSTITUTE®

1st Edition

CLSI C65™

Biochemical Tumor Marker Testing

CLSI C65 provides guidance and recommendations for optimal and effective serum tumor marker use.

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

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Biochemical Tumor Marker Testing

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Abstract

CLSI C65—*Biochemical Tumor Marker Testing* discusses preexamination, examination, and postexamination guidance as it relates to 10 commonly measured soluble biochemical tumor markers that circulate in blood and are usually measured in serum or plasma. Preexamination guidance is provided in relation to appropriate test selection for diagnosed cancer patients as well as those with suspected cancer, and also considers patient preparation, specimen collection and handling, and storage and transportation. CLSI C65 provides recommendations for method selection in the examination phase, implementation of internal and external QC (or proficiency testing) procedures, and identification of possible clinically relevant influences and other confounding factors that might affect results. Postexamination recommendations for tumor marker reporting are also presented. These include specifying the method used, cumulating serial results, and advising on clinical decision limits and clinically significant changes in tumor marker concentration.

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Contents

Foreword

Serum tumor marker measurements contribute significantly to the management of diagnosed cancer patients, have clinical utility in screening subjects who are asymptomatic, and aid in diagnosis and/or therapy prediction. Focusing on the serum tumor markers most often measured in routine practice, CLSI C65 provides preexamination guidance about when tumor markers should be measured, appropriate test selection for different cancers, and guidance relating to patient preparation and specimen handling.

Recommendations are also made for optimal performance in the examination phase, including internal and external QC and tumor marker standardization. Particular attention is paid to identifying examination errors and influences that are relevant to tumor marker measurements.

Postexamination recommendations are made regarding the content and format of reports, reference intervals and clinical decision limits, reference change values and tumor marker kinetics. The implementation of method changes and review of results and their interpretation are considered, along with detailed guidance related to investigating discordant results.

NOTE: The content of CLSI C65 is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

KEY WORDS

influence
interpretation
standardization
test selection
tumor marker

Chapter 1

Introduction

Biochemical Tumor Marker Testing

1 Introduction

1.1 Scope

CLSI C65 presents recommendations for optimal and effective service provision for several of the most widely used serum tumor markers: prostate-specific antigen (PSA) (total and free), carcinoembryonic antigen (CEA), cancer antigen (CA) 19-9, CA125, human epididymis protein 4 (HE4), α-fetoprotein (AFP), human chorionic gonadotropin (hCG), CA15-3 and CA27.29, thyroglobulin, and calcitonin. Serum tumor marker measurements contribute significantly to the management of diagnosed cancer patients and can also have clinical utility as aids for diagnosis and in screening of subjects who are asymptomatic.

Serum tumor marker measurements also might have clinical utility in screening of subjects who are asymptomatic, diagnosis, and/or therapy prediction, but their relatively low clinical sensitivities and specificities generally limit their use, particularly for diagnosis. A tumor marker result within the reference interval does not exclude malignancy. Tumor marker results should be interpreted together with other diagnostic and clinical information in accordance with standard clinical management guidelines. Typical clinical presentations that could prompt a tumor marker request are listed in Table 1. As erroneous tumor marker results can cause psychological distress for patients, it is important that tumor markers are requested appropriately, analyzed reliably, and reported informatively.

Table 1. Typical Clinical Presentations Which Could Prompt a Request For Serum Tumor Markers Considered in CLSI C65. Other cancers in which each marker is often elevated are also listed.

Tumor marker	Relevant Cancer	Typical Clinical Presentation	Other Cancers in Which Marker Might Be Elevated[a]
AFP	• Germ cell and testicular tumor • Hepatocellular carcinoma	• Ascites • Diffuse testicular swelling and hardness • Encephalopathy • Jaundice • Upper abdominal pain • Weight loss, early satiety in high-risk subjects (ie, hepatitis B- or C-related cirrhosis)	• Biliary • Gastric • Colorectal • Lung • Pancreatic
CA125	Ovarian cancer	• Pelvic mass • Persistent, continuous, or worsening unexplained abdominal or urinary symptoms • Bloating	• Cervical • Breast • Bladder • Endometrial • Hepatocellular • Lung • Pancreatic • Peritoneal • Non-Hodgkin lymphoma • Uterine

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