

CancerTYPE ID Clinical Evidence Overview

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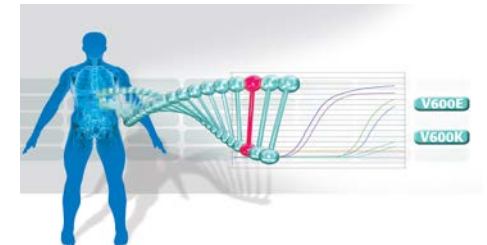
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Disclosure

- Dr. Schnabel is an employee of and owns stock options in bioTheranostics, Inc.

Molecular Approaches for Tumor Classification and Identification of Primary Site

- Personalized medicine is predicated on more accurate patient-specific information, and site of tumor origin is a fundamental building block of cancer care
 - Defines indications for use of therapies
 - Directs predictive biomarker testing as driver mutations vary specifically by tumor type
- The *unmet need* → Development of molecular approaches to better diagnose metastatic neoplasms for the significant number of patients with cancers of unknown or uncertain origin due to limitations of current standard of care
- Definitive diagnosis of tumor type will be increasingly important with availability of more site-specific and molecular-targeted therapies



Evidence-Based Diagnostics for Molecular Cancer Classification

Clinical Validity

- 7 published, blinded validation studies including 2883 patient cases¹⁻⁷
- 82%-89% accuracy across studies
- Collaborations with academic Centers of Excellence including:
 - Massachusetts General Hospital
 - Mayo Clinic
 - UCLA
 - Tufts University
 - University of Pennsylvania
 - The Methodist Hospital

Clinical Utility

- 2 published, blinded comparative effectiveness studies including a total of 279 patient cases demonstrating statistically significant improvements in accuracy of $\geq 10\%$ for molecular profiling for tumor classification vs IHC in poorly differentiated tumors⁸⁻⁹
- Prospective outcomes study of 289 CUP patients demonstrating favorable median overall survival following molecular classification-directed, site-specific therapy¹⁰

Health Outcomes/ Economics

- 3 published studies, including 232 patients, demonstrating the impact of molecular profiling for tumor classification on physician diagnostic and therapeutic decision-making¹¹⁻¹³
- Health economic study demonstrating cost effectiveness of molecular cancer classification¹⁴

- **The clinical evidence base includes >15 published studies and over 5900 patients**
- **Molecular cancer classification has been incorporated into published guidelines for the diagnostic workup of Cancers of Unknown Primary (CUP)^{15,16}**

CancerTYPE ID Overview

CancerTYPE ID is a 92-gene molecular classifier that can aid in the identification of a primary site in tumors with unknown, indeterminate or differential diagnosis, and is indicated for adjunctive use when traditional clinicopathologic evaluation does not lead to definitive diagnosis

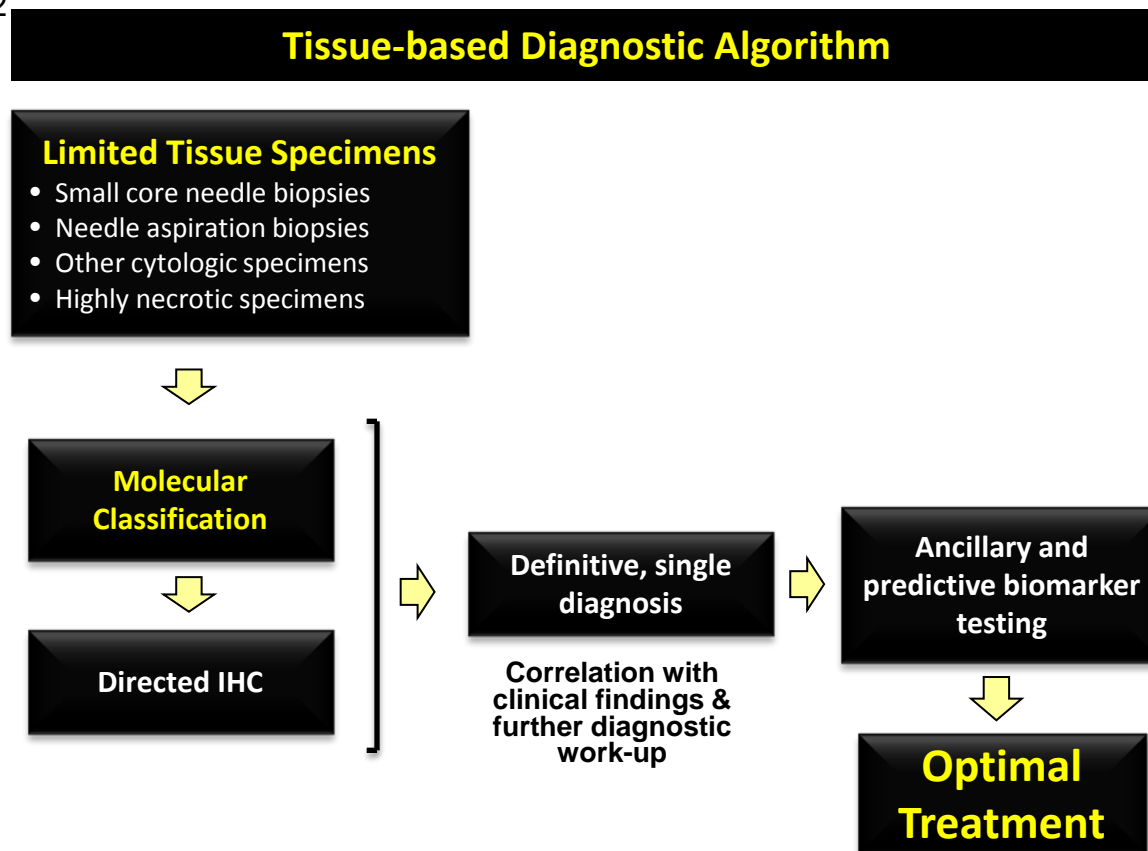
CLINICAL COMPATIBILITY & VALIDITY

- Biomarker panel is based on the RT-PCR expression profiling of 92 genes from a patient's formalin fixed paraffin embedded (FFPE) tumor tissue^{1,2}
- Biospecimen requirement is 300 tumor cells
- Assay sensitivity of 87% [95% CI: 0.84-0.89] was demonstrated in a prospectively-defined, blinded academic study (UCLA, Mayo, MGH) with adjudicated diagnoses³
- 95% accuracy for ruling out tumors of unlikely origin³
- CancerTYPE ID performance in clinical subsets³
 - Metastatic cases: 85%
 - High grade cases: 89%
 - Limited tissue and cytologic cases: 91%

CancerTYPE ID: Integration into Diagnostic Paradigm

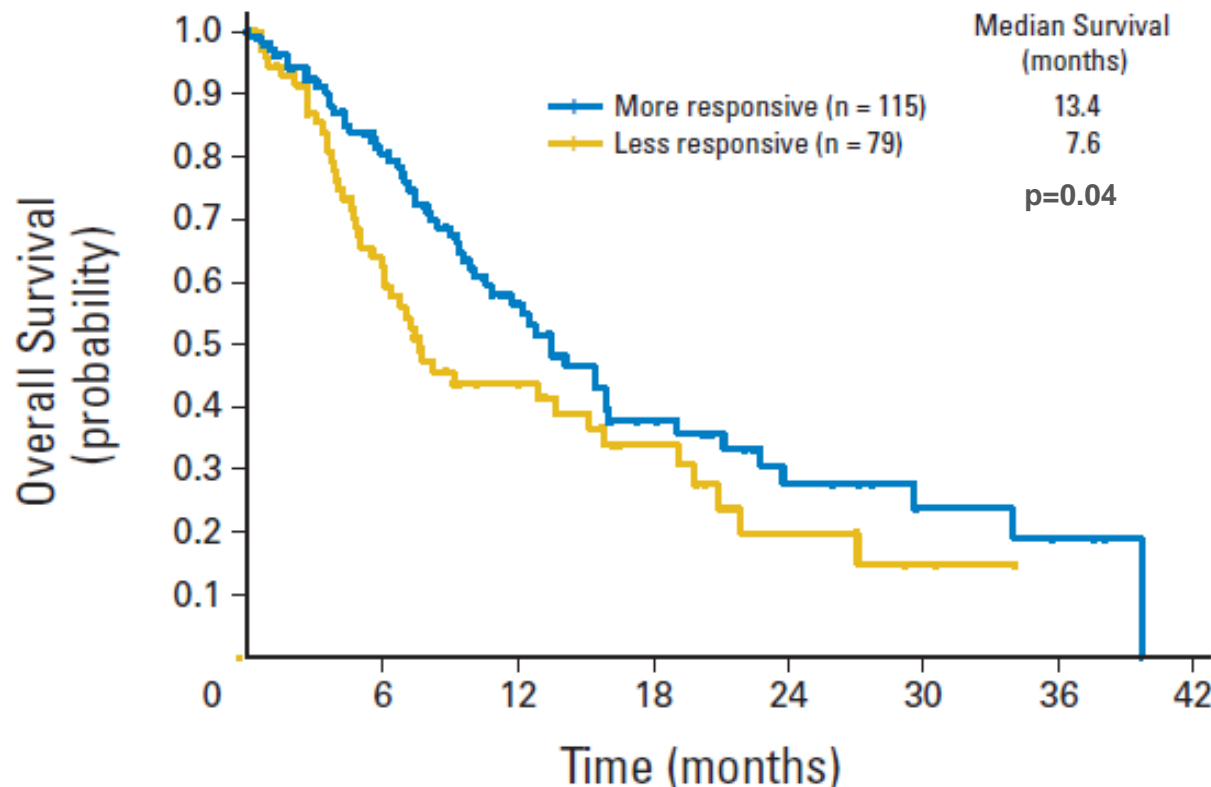
- Direct comparison to standard of care immunohistochemistry in metastatic, difficult to diagnose cases demonstrated an absolute improvement of 10% ($P=0.019$), and a relative improvement of 32% in diagnostic accuracy¹

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CancerTYPE ID: Impact on Overall Survival

- In a prospective study of patient outcomes, CancerTYPE ID-directed chemotherapy in clinical subsets showed a statistically significant improvement in overall survival¹



Less Responsive Tumors

- Biliary tract
- Pancreas
- Gastroesophageal
- Liver
- Sarcoma
- Cervix
- Carcinoid
- Endometrium
- Mesothelioma
- Melanoma
- Skin
- Thyroid
- Head and Neck
- Adrenal

Responsive Tumors

- Colorectal
- NSCLC
- Urothelium
- Breast
- Ovary
- Kidney
- Prostate
- Germ cell
- Lymphoma
- SCLC
- Neuroendocrine

¹Hainsworth, et al. J Clin Oncol. 2013;31:217-23

CancerTYPE ID: Clinical Decision-Making Study

- Medical oncologists who ordered CancerTYPE ID as part of clinical care were invited to participate in a survey-based retrospective study¹

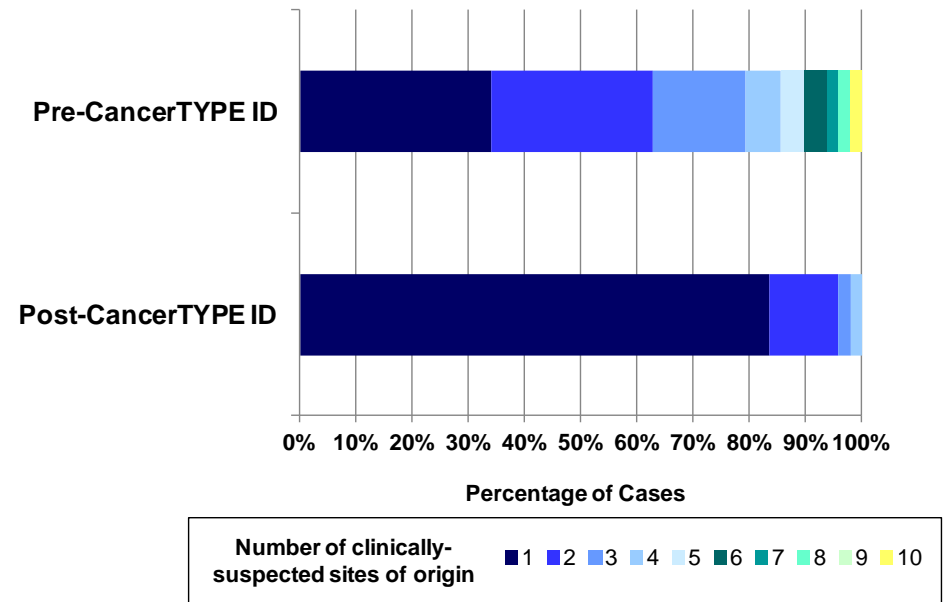
- **Diagnostic Decision-Making**

- CancerTYPE ID results reduced the number of suspected sites of origin
- CancerTYPE ID prediction was integrated into the final diagnosis in 84% of cases

- **Treatment Decision-Making**

- 81% of medical oncologists stated that CancerTYPE ID helped them determine the therapeutic treatment regimen

Number of clinically-suspected sites of origin, %



Concluding Remarks

- **Cancer care in the post-genomic era is undergoing a “Medical Renaissance”**
- **In the current practice of personalized medicine, individualized treatment requires knowledge of the molecular attributes of the tumor, and identification of responsive clinical subsets**
- **Over the last few years, there has been an increasing body of clinical evidence developed for molecular tests for identification of tumor type**
 - Clinical Validity
 - Multiple validation studies of high accuracy in indicated use population
 - Clinical Utility
 - Comparison to standard of care with significant improvement in accuracy in difficult to diagnose cases
 - Prospective study demonstrating favorable patient survival
 - Health Outcomes
 - Clinician integration into practice
- **Published clinical algorithms and consensus statements have recommended incorporation of molecular cancer classification for the diagnostic workup of Cancers of Unknown Primary (CUP)**