

Comparative Effectiveness of Gene Expression-Based Cancer Classification vs Standard of Care Immunohistochemistry

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Disclosure

- Dr Weiss is a Senior Consultative Pathologist with Clariant, Inc.
- He has a research stipend from Pathwork Diagnostics (>\$10,000).
- He has received honoraria and consulting fees (<\$10,000) from Pfizer and bioTheranostics.

Immunohistochemistry in Metastatic Cancer Diagnosis

- Standard of Care for pathologic diagnosis of tumor type in metastatic cancer (integrated with clinical parameters)



- IHC stains have varying sensitivities and specificities, occasionally with cross-reactivities that are potentially misleading (e.g., keratin in sarcoma, melanoma, glioma, or even lymphoma)
- IHC stains are not applied in an objective and standardized manner in routine clinical practice
- A meta-analysis reported that IHC had an accuracy of 66% in the characterization of metastatic tumors¹
- Given that optimal therapeutic approaches depend on a definitive diagnosis, this relative lack of diagnostic accuracy represents an important unmet clinical need

Comparative Effectiveness Study: Background and Study Objective

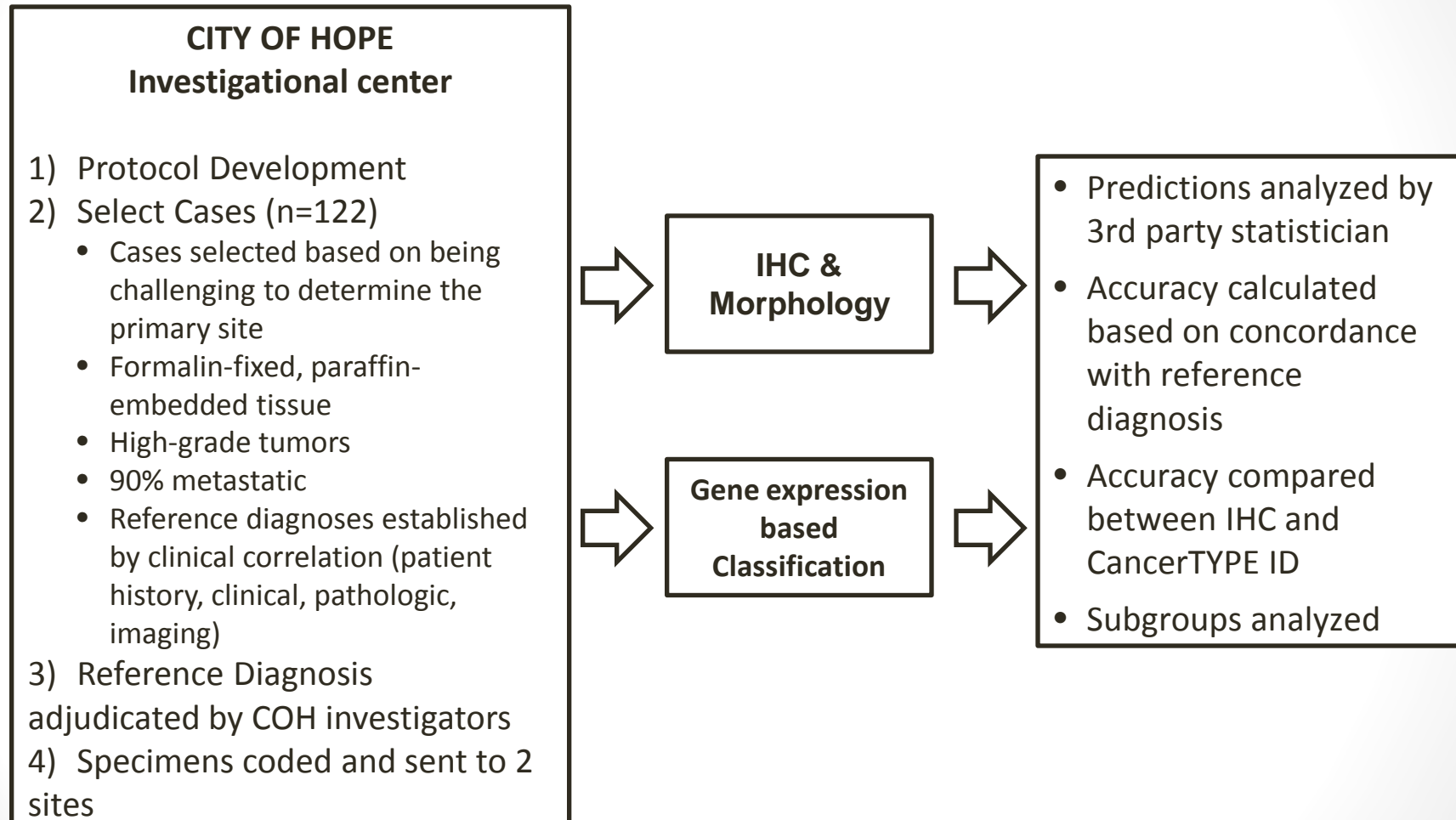
■ Objective

- To compare the accuracy of gene expression-based classification to that of standard of care (IHC) for tumor classification and subclassification in poorly- to undifferentiated, primarily metastatic neoplasms

■ Design

- Prospectively-defined, blinded comparator study in archival tumor specimens from City of Hope National Medical Center (COH)
- Cases and reference diagnoses were established with complete clinical information by 2 COH Pathologists
- Identical cases were submitted into 2 study arms:
 - IHC + Morphology consensus review by Pathologists at a national reference laboratory
 - Gene expression-based classification with the 92-gene assay (CancerTYPE ID)

Comparative Effectiveness Study: Study Design



Comparative Effectiveness Study: Results

- CancerTYPE ID demonstrated an increase in overall accuracy of 10% compared to IHC (79% vs 69%; $P = 0.019$)
- CancerTYPE ID accuracy was \geq IHC/Morphology in all tumor types examined

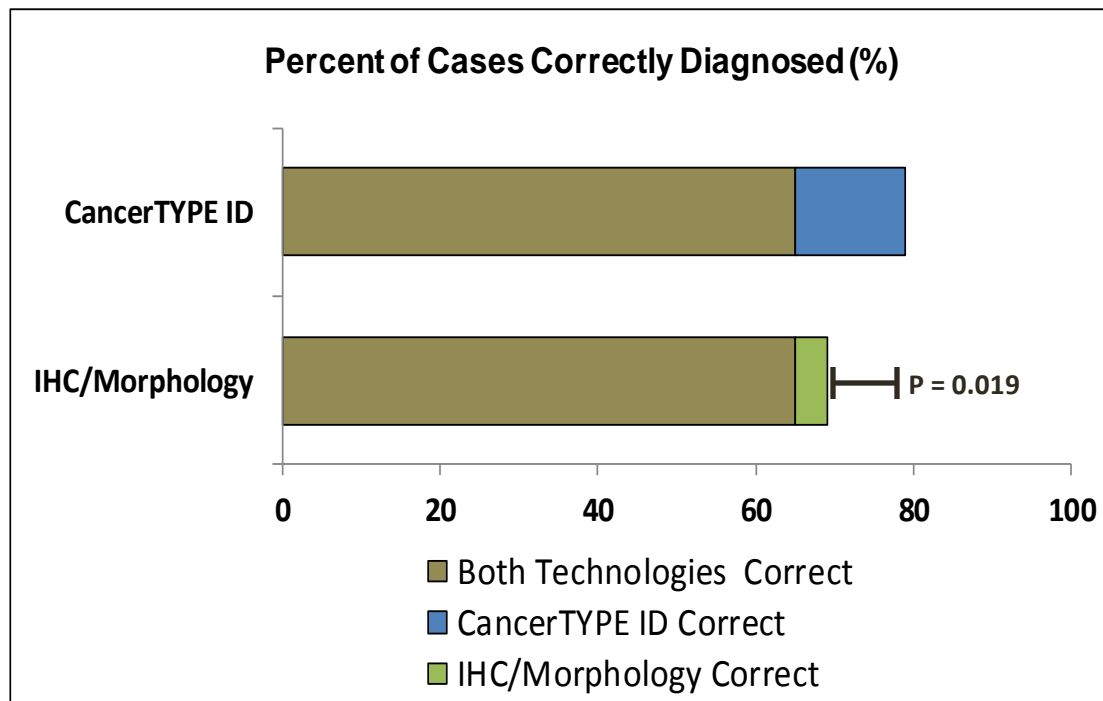
Tumor type	IHC/Morphology	CancerTYPE ID
GI (n=26)	92%	92%
Lung (n=24)	67%	75%
Kidney (n=13)	77%	77%
Bladder (n=11)	45%	82%
Breast (n=11)	55%	73%

Tumor types with >10 cases

Number of IHC stains performed: Mean 7.9, Median 8, Range 2-15

Comparative Effectiveness Study: Prediction Comparison

- Both technologies made correct predictions in 65% of the cases
 - CancerTYPE ID correctly identified the site of origin in which IHC/morphology was incorrect in 17 cases (14%)
 - IHC/morphology correctly identified the site of origin in which CancerTYPE ID was incorrect in 5 cases (4%)



Comparative Effectiveness Study: Study Summary

- Results from this blinded comparative effectiveness study demonstrated superior accuracy with gene expression-based classification in the diagnosis of high grade metastatic cancer
- These results suggest that gene expression-based classification may be better suited for diagnosis of primary site in high-grade metastatic tumors because:
 - The gene expression-based assay utilizes the collective expression of the 92-gene biomarker panel to classify tumors rather than relying on one or a few tumor markers, which may have atypical expression or loss of expression in a poorly-differentiated tumor
 - Poorly differentiated tumors may retain their RNA profile to a significantly greater extent than their morphologic and protein profile
- It is important to note that the cases selected for this study are not representative of daily practice in that they were specifically identified as difficult-to-diagnose tumors; thus, the study likely underestimates the overall accuracy of both methodologies

Study Implications:

Impact of CancerTYPE ID

- The results of this study suggest that a significant number of patients with high-grade metastatic cancers may be at risk of misdiagnosis
 - This represents an important clinical unmet need, as optimal therapeutic approaches that have been shown to improve patient outcomes rely on accurate tumor type identification
- Gene expression-based classification demonstrated its clinical value with improvement in diagnostic accuracy over standard of care