

## HIGH QUALITY TISSUE ESSENTIAL IN DEVELOPING PREDICTIVE BIOMARKER ASSAYS

### OVERVIEW

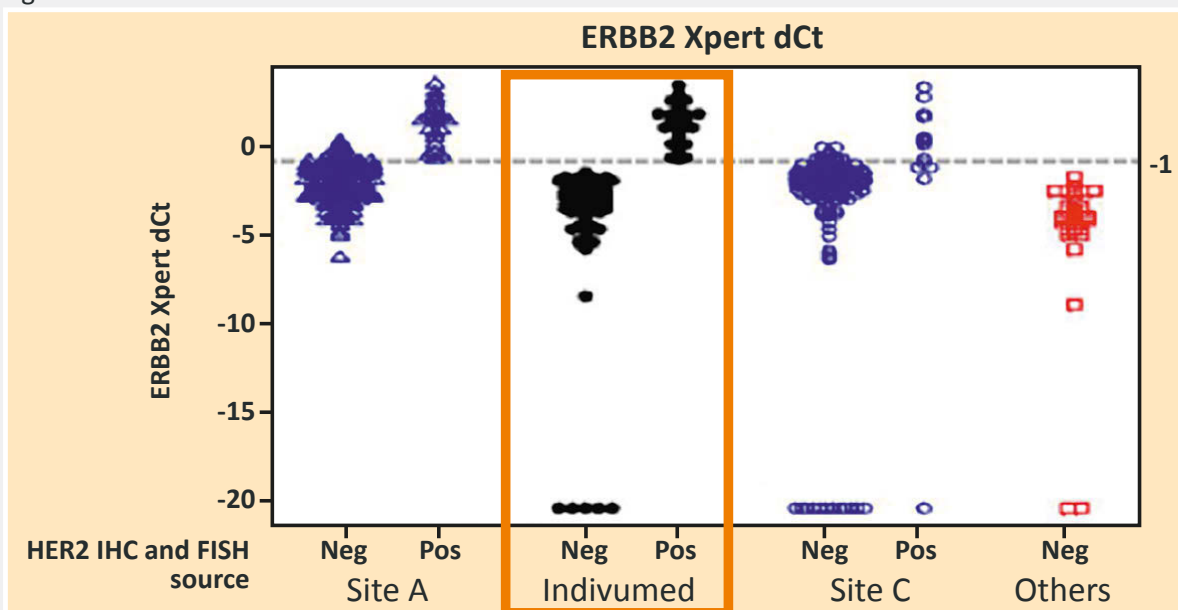
Results from any analytical assay are only as reliable as the quality of the analytes that are being evaluated. The tissue sample quality is the utmost important factor for accurately assessing genes and proteins as closely presented/expressed clinically in the patient's tumor. Here, breast cancer patient samples sourced from Indivumed as well as other biobanks were assessed for HER2 (ERBB2) gene amplification and protein overexpression using three different analytical methods. Indivumed's high quality tissues (low ischemic time and high standard tissue processing procedure) showed the highest concordance rate of HER2 status as determined by the new GeneXpert Breast Cancer Biomarker Assay (Xpert BC) and the two standard method of analyses immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH).

### STUDY SUMMARY

- › Xpert BC is a semi-quantitative real-time PCR test that utilizes cutoff values that were empirically derived from comparison analysis studies of PCR and corresponding FISH & IHC data for the ERBB2 gene and protein (Figure 1).
- › In order to validate the new Xpert BC assay, breast cancer tissues from Indivumed's biobank (117 samples) as well as other biobanks (384 total samples from different sources) were analyzed for (ERBB2) overexpression and gene amplification by the two standard companion diagnostic assays IHC (Herceptest) and FISH (PathVysion) respectively. The results obtained from the companion diagnostic assays were compared to those obtained from the Xpert BC assay.
- › The accuracy of the established Xpert BC assay was assessed by deriving positive (PPA) and negative (NPA) measured agreements as well as overall percent agreement (OPA) when compared to the standard assays (IHC and FISH).
- › Samples from Indivumed showed the highest concordance rate (100%) in all measured agreement including the OPA for high concordance in comparison to other tissue sources (Figure 2 A and 2 B).

**Figure 1: Cutoff value (delta cycle threshold (dCt)) as determined by Xpert BC and compared to IHC and FISH Results**

Figure 1



The delta cycle threshold (dCt) value is the normalized expression level of the mRNA compared to an endogenous control

**Figure 2: Comparison Study (IHC, FISH and Xpert BC). a) Individumed Samples b) Other Sites Sourced Samples**

Figure 2 A

ERBB2		IHC /FISH		Total
		POS	NEG	
Xpert	POS	35	0	35
	NEG	0	82	82
	Total	35	82	117

OPA: 100 % (95% CI: 96.9-100)

PPA: 100 % (95% CI: 90.0-100)

NPA: 100 % (95% CI: 95.6-100)

Figure 2 B

ERBB2		IHC /FISH		Total
		POS	NEG	
Xpert	POS	31	29	60
	NEG	5	317	322
	Total	36	346	382

OPA: 93 % (95%CI:87.8-93.8)

PPA: 86 % (95%CI:70.5-95.3)

NPA: 92 % (95%CI:88.2-94.3)

## INDIVUMED'S ADVANTAGE

- › The high concordance results observed for Individumed samples is due to the high quality of the tissues.
- › Tissue quality is affected by various factors including pre-analytical conditions such as ischemic time, sample processing/handling post-resection as well as the surgical procedure.
- › Individumed has established a distinctive infrastructure within the clinical networks in which Individumed's clinical teams are imbedded in the surgical OR. This unique arrangement allows the implementation of stringent tissue collection and processing protocols. Tissues are immediately fixed or frozen right after resection ensuring short ischemia time (on average 10 minutes)
- › In depth clinical data (over 250 points) per patient is also annotated for every collection
- › Quantity of the biological specimens and the data is guaranteed by a stringent validation process that is certified according to ISO 9001:2008

## IMPLICATIONS:

- › In cancer biomarker assay development, tissue quality used for validating the assay is paramount in ensuring proper determination of cutoff values
- › Whether an assay will be used as part of diagnostic, prognostic or predictive tool, a proper stratification of patients starts with accurately determined cutoff values acquired from highly validated assays with high quality tissues

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