

Discordance for Low and Intermediate Levels (1+ or 2+ by IHC) of HER2 Protein Expression in the Phase 3 PRESENT Trial

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Background

- ❖ Significant discordance exists between local and central laboratory testing for HER2 overexpression
 - HER2-targeted therapies may be withheld from patients who might benefit from their use
 - Discordance rates for tumors selected for HER2 0-2+ are not well described

PRESENT Study

- ❖ Design:
 - Phase 3
 - Multicenter
 - Prospective
 - Randomized
 - Double-blind
 - Controlled
- ❖ Objectives:
 - Assess efficacy/safety of the peptide vaccine NeuVax™, which targets cells expressing any level of HER2
- ❖ Eligible patients with breast cancer:
 - HLA-A2 and/or A3 positive
 - Early-stage
 - Node-positive
 - Expresses low/intermediate levels of the HER2 protein (1+ or 2+ by IHC)
- ❖ Screening for HER2 expression:
 - Step 1: Local HLA testing
 - Step 2: Central laboratory confirmation using DAKO HercepTest™

Results

Global Discordance Rates (N = 785)

Local Testing	Central Testing by IHC				Discordance Rate
	0 (n = 202)	1+ (n = 357)	2+ (n = 145)	3+ (n = 81)	
0 (n = 169)	80 (47%)	66 (39%)	20 (12%)	3 (2%)	53%
1+ (n = 380)	101 (27%)	208 (55%)	59 (16%)	12 (3%)	45%
2+ (n = 192)	17 (9%)	81 (42%)	62 (32%)	32 (17%)	68%
3+ (n = 44)	4 (9%)	2 (5%)	4 (9%)	34 (77%)	23%
Discordance Rate	60%	42%	57%	58%	

- ❖ 785 patient samples have undergone local and central IHC testing for HER2 expression
- ❖ 572/785 patients (73%) were eligible by local testing
 - 28% (162/572) were ineligible by central testing
 - 43% (92/213) of ineligible patients were eligible by central testing
 - 8% (44/572) of patients with HER2 1+ or 2+ results had 3+ results by central testing
 - 6% (47/741) of HER2 (-) patients were HER2 (+) by central testing
 - 23% (10/44) of HER2 (+) patients were HER2 (-) by central testing
 - Results varied most in patients with HER2 2+ expression by local testing (68% discordance)

Overall discordance rate 51% (401/785)

- ❖ Discordance rates varied by geographic location
 - North America = 47%
 - Eastern Europe, Israel, Russia, Ukraine = 52%

Conclusions

- ❖ Significant discordance exists between local and central laboratory test results for HER2 expression by IHC, even at lower levels of expression
- ❖ Current tests are defined by their ability to determine HER 2 3+ status
- ❖ To improve accuracy and specificity testing for HER 2 1+ and 2+ Status patients of testing and test a companion diagnostic for NeuVax, the Leica Bond™ Oracle™ HER2 IHC System is incorporated into HER2 IHC screening for the PRESENT study patients

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Disclosures:
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