

Clinical Concordance of Two Fully Automated HER2 IHC Assays

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Introduction

- The provision of an accurate HER2 test result is necessary to direct appropriate adjuvant therapy in breast cancer¹.
- Immunohistochemistry (IHC) is often selected as the frontline assay for HER2 testing.
- The introduction of Ready-To-Use kits for HER2 IHC has improved the standardization and reproducibility of HER2 testing over recent years.
- Kings College Hospital compare, over a large series of FFPE samples, the clinical concordance of two fully automated HER2 IHC assays: The Leica BOND Oracle HER2 IHC System performed on the Leica BOND-Max, and the Ventana Pathway HER2/neu 4B5 assay performed on the Ventana BenchMark XT.
- The final cohort will describe concordance data from 500 samples equally distributed across the protein expression range (125 x 0, 125 x 1+, 125 x 2+, 125 x 3+).
- This poster describes the concordance results from the dataset collected to date.

Results

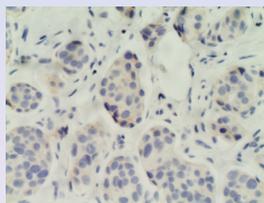
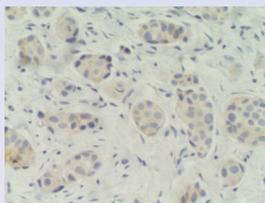
- 341 cases have been assessed to date. Comprising: 0 (n= 124), 1+ (n=84), 2+ (n= 77), 3+ (n= 56).
- Concordance analysis considers cases that are scored as equivocal (2+) with either assay (Leica Oracle or 4B5) to be concordant to positive or negative results with the alternative assay.
- Analysis shows a 99.7% agreement between the two assays (table 1) with only one case being discordant (Positive by 4B5, Negative by Oracle). Cohen's Kappa = 0.992.
- Of the 341 cases stained to date, 23% (n = 77) of cases were scored as equivocal (2+) with the 4B5 assay and 21% (n = 72) were scored as equivocal with the Oracle kit.

Table 1: 3X3 Concordance analysis

HER2 Status with Oracle	HER2 Status with 4B5			Grand Total
	Negative (0/1+)	Equivocal (2+)	Positive (3+)	
Negative (0/1+)	191	45	1	237
Equivocal (2+)	17	32	23	72
Positive (3+)	0	0	32	32
Grand Total	208	77	56	341

Oracle: IHC 1+

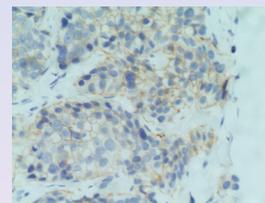
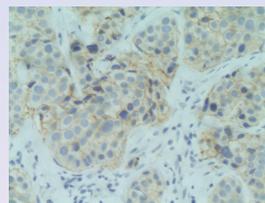
4B5: IHC 1+



Case No. 8

Oracle: IHC 2+

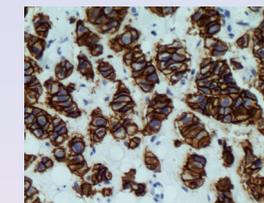
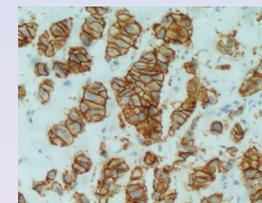
4B5: IHC 2+



Case No. 7

Oracle: IHC 3+

4B5: IHC 3+



Case No. 66

Materials and Methods

- Samples were selected for inclusion as they were received into the department for clinical HER2 testing.
- For each case two sequential sections were cut, one to be stained with Ventana's 4B5 assay and one with the Leica BOND Oracle HER2 IHC System.
- Each of the IHC assays were performed according to the manufacturer's instructions for use and the sections prepared as per laboratory standard operating procedures.
- Slides were scored as per the UK HER2 recommendations¹

Conclusion

- The two fully automated assays show a very high level of agreement (Concordance = 99.7%, Cohen's Kappa = 0.992) in assessing HER2 protein expression levels.
- The cohort will be increased in size to 500 cases and all equivocal and discordant cases will have their HER2 gene amplification status defined by FISH to more accurately define the concordance and the 'reflex to ISH confirmation rate' between the assays.

References

1: RA Walker et al. HER2 testing in the UK: further update to recommendations. *J Clin Pathol.* 2008; 61: 818-824

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