

# ASSESSMENT OF HER2 STATUS IN BREAST CANCER , ACCESS TO TRASTUZUMAB AND THEIR OVERALL SURVIVAL

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## Introduction

HER2 receptor expressing breast cancers are aggressive with poorer prognosis. They can be determined via immunohistochemistry(IHC) or in situ hybridisation(ISH). IHC score 2+ and 3+ need confirmatory test by ISH for HER2 gene amplification prior to starting trastuzumab therapy. Trastuzumab improves both disease free survival(DFS) and overall survival(OS). However this drug is expensive , limiting its access to many patients.

## Methodology

Analysis of female breast cancers with IHC score 2 and 3 (n=234 )were performed to determine the concordance with final ISH test for HER2 gene amplification. The HER2 positive tumors by ISH ( n=97) were analysed for access to trastuzumab. A Kaplan-Meier curve were produced to compare survival outcome between trastuzumab(n=20) and no-trastuzumab(n=77) group.

## Results

Our concordance rates between IHC score 2+ and 3+ and ISH were 20.2% and 89.6% respectively. Among HER2 amplified tumors, only 15.7% received trastuzumab and after a mean duration of 19 months from diagnosis. The 5-year overall survival was higher for trastuzumab group (76% vs 52%) (log rank test p = 0.05). The hazard ratio for trastuzumab group was 0.264 ( 95% CI 0.063 -1.115 ).

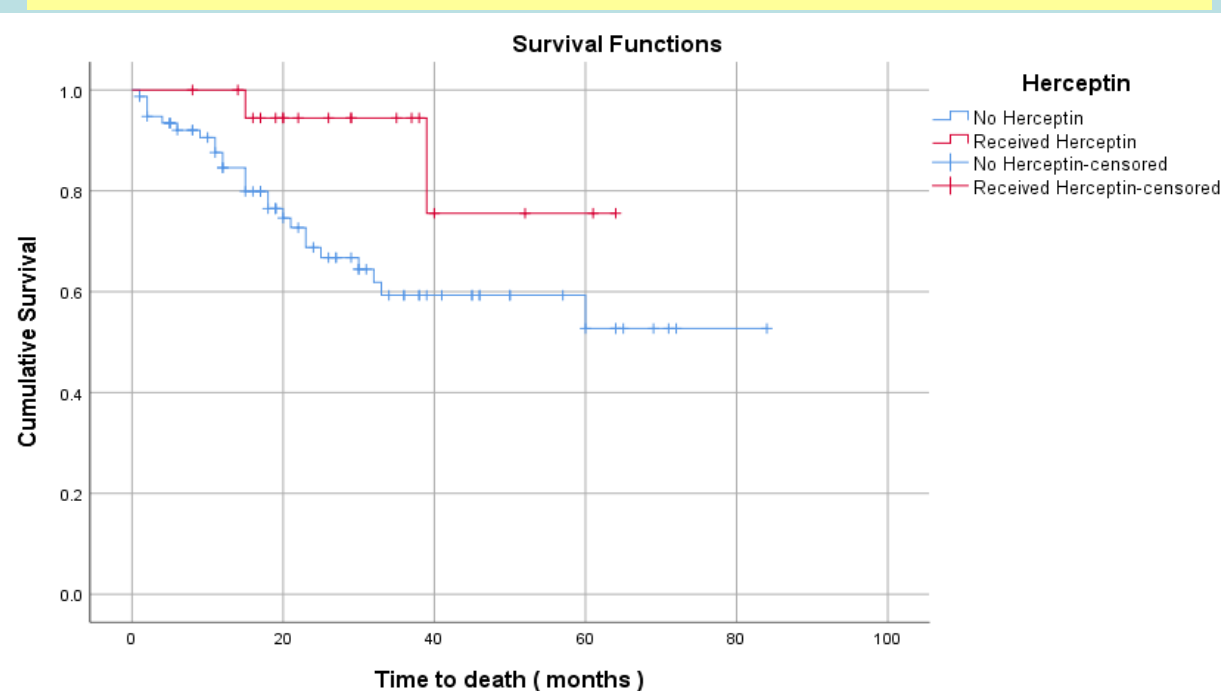
**Table 1 :** Concordance IHC score 2+ and 3+ with ISH

IHC score	n	HER2 not amplified	HER2 amplified
2+	119	95 ( 79.8% )	24 ( <b>20.2%</b> )
3+	115	12 ( 10.4% )	103 ( <b>89.6%</b> )

**Table 2 :** Preanalysis of survival outcome showing no difference between trastuzumab and no-trastuzumab groups except for stage

Characteristics	No trastuzumab [ n (%) ]	Trastuzumab [ n (%) ]	P-value
<b>Age group (n=127)</b>			0.580
<30	2 (1.8)	1 (5.0)	
30-39	14 (13.1)	3 (15.0)	
40-49	32 (29.9)	7 (35.0)	
50-59	37 (34.6)	8 (40.0)	
60-69	14 (13.1)	0 (0.0)	
>= 70	8 (7.5)	1 (5.0)	
<b>Stage (n=97)</b>			<b>0.031</b>
I	2 (2.6)	0 (0.0)	
II	16 (20.8)	10 (50.0)	
III	26 (33.8)	7 (35.0)	
IV	33 (42.8)	3 (15.0)	
<b>Estrogen receptor (n=97)</b>			0.345
Positive	45 (58.4)	14 (70.0)	
Negative	32 (41.6)	6 (30.0)	
<b>Progesterone receptor (n=97)</b>			0.161
Positive	29 (37.7)	11 (55.0)	
Negative	48 (62.3)	9 (45.0)	
<b>Molecular subtype (n=97)</b>			0.400
Luminal B with HER2 positive	46 (47.4)	14 (70.0)	
( ER+ or/and PR+ , HER2+)	31 (52.6)	6 (30.0)	

**Figure 1 :** Kaplan –Meier curve showing overall survival between trastuzumab and no-trastuzumab group



**Table 3 :** Comparison of access to trastuzumab at centres in high middle income countries

Centres	Number of patients	HER2+ breast cancer patients received trastuzumab
<b>HRPZ II , Kelantan</b> ( this study)	97	15.7 %
HKL, UMMC, 6 other private medical centres , <b>Malaysia</b> ( Lim et al )	209	19 %
UMMC, <b>Kuala Lumpur</b> ( Harissa et al )	170	19.4%
28 Medical Centres, <b>Brazil</b> (Liedke et al)	224	9% ( public hospitals) 53% ( private hospitals)
13 hospitals, Eastern <b>China</b> ( Jianbin et al )	1139	37.3% ( resource rich regions) 13.0% ( resource limited regions)

## Conclusion

- ❖ Our concordance rate for IHC score 2+ and 3+ were comparable with other centres, although IHC score 3+ concordance with ISH could be improved to achieve a target of more than 95%.
- ❖ Access to trastuzumab was still very limited in our centre with a delay in therapy commencement. Similar poor access to this expensive drug were seen at other centres in Malaysia and other high middle income countries.
- ❖ The 5-year overall survival rate was higher for those who received trastuzumab , although not statistically significant due to small sample size. The higher OS and DFS were already established , for patients receiving trastuzumab from many RCTs , meta analyses and systematic reviews.
- ❖ Access to trastuzumab needs to be addressed urgently in Malaysian public hospitals for these HER2+ poor prognosis breast cancers.