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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.

<u>Results</u>

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 : Co	Table 1 : Concordance IHC score 2+ and 3+ with ISH							
IHC score	n	HER2 not amplified	HER2 amplified					
2+	119	95(79.8%)	24 <u>(20.2%)</u>					
3+	115	12 (10.4%)	103 <u>(89.6%)</u>					

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

Table 2 : Preanalysis of survival outcome showing no difference between trastuzumab and no-trastuzumab groups except for stage **Characteristics** No trastuzumab Trastuzumab **P-value** [n (%)] [n (%)] Age group (n=127) 0.580 <30 2 (1.8) 1 (5.0) 14 (13.1) 30-39 3 (15.0)

Survival Functions					40-49	32 (29.9)	7 (35.0)	
	1.0		Hercepti	in	50-59	37 (34.6)	8 (40.0)	
		1	No Herceptin No Herceptin No Herceptin No Herceptin	ptin	60-69	14 (13.1)	0 (0.0)	
	0.8		Received Hercep	ptin-censored	>= 70	8 (7.5)	1 (5.0)	
val	Turner and the second s							
Survi	0.6				Stage (n=97)			0.031
ative			++++			2 (2.6)	0 (0.0)	
Inmr	0.4				Ш	16 (20.8)	10 (50.0)	
បី					111	26 (33.8)	7 (35.0)	
	0.2				IV	33 (42.8)	3 (15.0)	
						(-)	- ()	
	0.0				Estroaen receptor			0.345
				(n=97)				
		e to death (months)			(
					Docitivo		14 (70 0)	
					POSITIVE	4)()0.4)		
Tal	ble 3 : Comparison	of access to	trastuzumab at centres	in high	Negative	43 (38.4) 32 (41 6)	6 (30 0)	
Tal mic	ble 3 : Comparison ddle income countri	of access to ies	trastuzumab at centres	in high	Negative	43 (38.4) 32 (41.6)	6 (30.0)	
Tal mic Cer	ble 3 : Comparison ddle income countri ntres	of access to ies Number of	trastuzumab at centres HER2+ breast cancer pati	in high ients	Negative Progesterone	32 (41.6)	6 (30.0)	0.161
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Tal mic Cer <u>HRI</u> stuc HKI	ble 3 : Comparison ddle income countri ntres PZ II , Kelantan(this dy) _, UMMC, 6 other	of access to ies Number of patients 97 209	HER2+ breast cancer pati received trastuzumab 15.7 %	in high ients	Negative <i>Progesterone</i> <i>receptor (n=97)</i> Positive Negative	43 (38.4) 32 (41.6) 29 (37.7) 48 (62.3)	14 (70.0) 6 (30.0) 11 (55.0) 9 (45.0)	0.161
Tal mic Cer HRI stuc HKI	ble 3 : Comparison ddle income countri ntres PZ II , Kelantan(this dy) -, UMMC, 6 other vate medical centres	of access to ies Number of patients 97 209	HER2+ breast cancer pati received trastuzumab 15.7 %	in high ients	Negative <i>Progesterone</i> <i>receptor (n=97)</i> Positive Negative	 43 (38.4) 32 (41.6) 29 (37.7) 48 (62.3) 	14 (70.0) 6 (30.0) 11 (55.0) 9 (45.0)	0.161
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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.