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Blood serum HER2 as predictive marker for treatment effect assessment in patients with breast cancer undergoing neoadjuvant systemic treatment

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Background

About 20% breast carcinomas overexpress human epidermal growth factor receptor-2 (HER2) [1,2]. The extracellular domain of the HER2 protein can be detected in peripheral blood as serum HER2 (*sHER2*) [1,2]. A decrease in *sHER2* was associated with pathologic complete response, increased disease-free and overall survival [2]. Significant positive association between pCR and elevated *sHER2* levels, and a decrease of *sHER2* levels during neoadjuvant treatment (NAT) in HER2-positive, but not in HER2-negative breast cancer, was found [3,4]. Clinical relevance of *sHER2* is still unclear and being investigated [1].

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2. *Reix, N., Malina, C., Chenard, M.-P., Bellocq, J.-P., Delpous, S., Molière, S., … Mathelin, C. (2016). A prospective study to assess the clinical utility of serum HER2 extracellular domain in breast cancer with HER2 overexpression. Breast Cancer Research and Treatment, 160(2), 249–259. doi:10.1007/s10549-016-4000-z.*
3. *Witzel, I., Loibl, S., von Minckwitz, G., Mundhenke, C., Huober, J., Hanusch, C., … Müller, V. (2010). Monitoring serum HER2 levels during neoadjuvant trastuzumab treatment within the GeparQuattro trial. Breast Cancer Research and Treatment, 123(2), 437–445. doi:10.1007/s10549-010-1030-9.*
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Aim

1. measure *sHER2* levels in non-metastatic breast cancer patients before NAT and before surgery;
2. compare *sHER2* during NAT in HER2-positive and HER2-negative tumors;
3. evaluate association of pathologic response with *sHER2* changes.

Methods

1. This is a prospective observational single-centre cohort study.
2. Before each NAT cycle patient's specimen of blood was tested for *sHER2* with chemiluminescence method (@Siemens). The cut-off value for *sHER2* was 15 ng/mL.
3. Tumour biopsy specimen was analysed by immunohistochemistry (IHC) for HER2 expression.
4. After the surgical treatment pathologic response was evaluated. Data was analysed with IBM SPSS26 software.

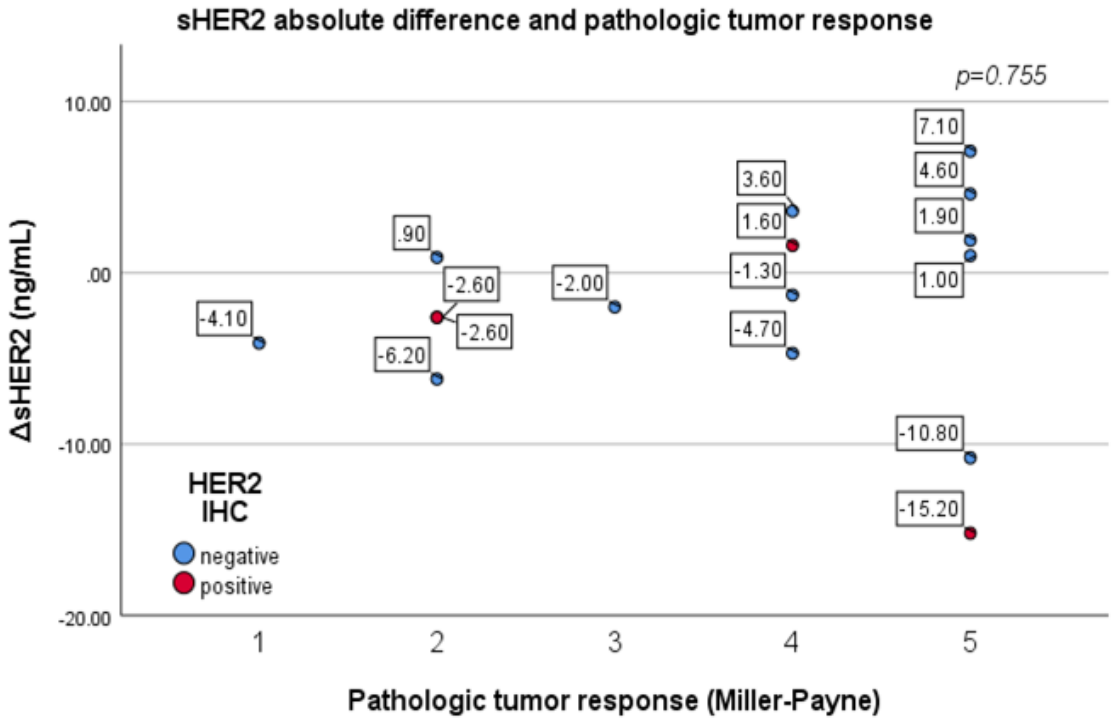
Results

Table 1: Characteristics of HER2-positive and HER2-negative breast cancer patients before NAC, prior and after surgery:

		HER2[a]		
		Positive	**Negative**	***p-value***
Patients N (%)		3 (23)	13 (77)	-
Age (years)	Median Range	41.0 40.0-63.0	46.0 32.0.-63.0	*0.704*
Stage N (%)	I II III	0 (0) 1 (33.3) 2 (66.7)	1 (7.7) 4 (30.8) 8 (61.5)	*0.410*
***sHER2* Median [CI 95%] (ng/mL)**	Baseline Before surgery	18.0 [18.0-32.3] 17.1 [17.1-18.9]	15.4 [19.4-20.8] 13.8 [20.4-24.2]	*0.146* *0.521*
***sHER2* positive N (%)**	Baseline	3 (100)	7 (54)	*0.214*
Δ*sHER2*[b] Median [CI 95%] (ng/mL)		-2.6 [-2.6-1.6]	-1.3 [3.6-7.1]	*0.439*
pCR[c] N (%)		1 (33)	5 (38)	*0.696*

[a] IHC from the core biopsy material; [b] difference between sHER2 before the first and the last courses of NAT; [c] pathologic complete response (Miller-Payne 5).

Graph 1: sHEr2 absolute difference between groups of pathologic response and HER2 IHC positivity



Conclusions

No significant association was found between *sHER2* dynamics and pathologic tumor response. However, positive tendency found in the only HER2-positive patient with pCR.

No significant difference in baseline *sHER2* and its dynamics found between HER2-positive and HER2-negative tumors.

This innovative test is studied for the first time in Latvia. Study population was small and represents only initial trends. Larger, better distributed groups of patients will show more precise data in the future.