INFLUENCE OF GENETIC POLYMORPHISMS ON THE RESPONSE AND TOXICITY OF CAPECITABINE THERAPY IN PATIENTS WITH BREAST CANCER

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Background

The response and the toxicity profile associated with **capecitabine** treatment shows great **interindividual variability**. The study of **genetic polymorphisms** of genes involved in the metabolism of capecitabine could help to predict the **response** and **toxicity** to breast cancer treatment.

Aim and objectives

The aim of the study was to evaluate both the **response** and **toxicity** of patients with breast cancer treated with capecitabine, as well as its relation to some **genetic polymorphisms** of genes involved in the **metabolism of capecitabine** (***UMPS***, ***TYMP*** y ***UPB1***).

Material and methods

Clinical and **demographic** characteristics were obtained by reviewing the clinical **history of the patients.**

Genetic markers were analyzed via OpenArray™ by **QuantStudio™** 12K Flex System using the **"TaqMan™ PGx Express"** array.

The **response** was evaluated according to the **RECIST 1.1** criteria and **toxicities** were categorized according to version 5.0 of the **CTCAE.**

The **relation** between demographic and clinical **variables** and **polymorphisms** with response and toxicityto treatment with capecitabine were studied using bivariate analysis with **R software** 4.1.1 version.

Results

A total of **63 patients** were treated with capecitabine in 2021.

- The **evaluation** of the **response** (n=38) resulted in: **Complete Response: 13.16%** (n=5), **Partial Response: 10.53%** (n=4), **Stable disease: 10.53%** (n=4) and **Progessive Disease: 65.79%** (n=25).
- An **association** was observed between the **nulliparity** (p=0.037) of the patients and the **response** to capecitabine (Table 1), as well as between **estrogen** (p=0.024) and **progesterone** (p=0.006) receptors with the appearance of **toxicity** after treatment (Table 2).
- **No association** was found between any of the studied polymorphisms with **response** (Table 3) or **toxicity** (Table 4) to capecitabine therapy, although most os the results matched those published by other studies.

Table 1. Association between demographic and clinical variables and responde to capecitabine therapy.

Variable	N	Response: No N (%)	Response: Yes N (%)	X^2	P*	Ref Cat.	OR	CI 95%
Nulliparity	34							
Yes		2 (40)	3 (60)	4.333	**0.037**	**No**	**7.2**	**0.96-67.19**
No		24 (82.8)	5 (17.2)					

Table 2. Association between demographic and clinical variables and toxicity to capecitabine therapy.

Variable	N	Toxicity: Mild (Grade 0-2) N (%)	Toxicity: Severe (Grade 3-4) N (%)	X^2	P*	Ref Cat.	OR	CI 95%
Estrogen receptors	60							
Positive (+)		37 (84.1)	7 (15.9)	5.084	**0.024**	**Negative**	**4.11**	**1.15-15.22**
Negative (-)		9 (56.2)	7 (43.8)					
Progesterone receptors	60							
Positive (+)		32 (88.9)	4 (11.1)	7.516	**0.006**	**Negative**	**5.71**	**1.62-23.84**
Negative (-)		14 (58.3)	10 (41.7)					

***p-value by Pearson's Chi-square test. OR: Probability of occurrence. CI: confidence interval.**

Table 3. Relation between genetic polymorphisms and response to capecitabine therapy.

Gen	SNPs	Response: Genotype	N	No N (%)	Yes N (%)	X^2	P*
UMPS	rs1801019	CC	1	1 (100)	0 (0)	2.187	0.335
		CG	10	9 (90)	1 (10)		
		GG	25	17 (68)	8 (32)		
		C	11	10 (90.9)	1 (9.1)	2.138	0.144
		G	35	26 (74.3)	9 (25.7)	0.343	0.558
TYMP	rs11479	AA	0	0 (0)	0 (0)	0.697	0.404
		AG	5	3 (60)	2 (40)		
		GG	31	24 (77.4)	7 (22.6)		
		A	5	3 (60)	2 (40)	0.697	0.404
UPB1	rs2070474	CC	7	7 (100)	0 (0)	3.294	0.193
		CG	17	11 (64.7)	6 (35.3)		
		GG	12	9 (75)	3 (25)		
		C	24	18 (75)	6 (25)	0	1
		G	29	20 (69)	9 (31)	2.897	0.089

Table 4. Relation between genetic polymorphisms and toxicity to capecitabine therapy.

Gen	SNPs	Toxicity: Genotype	N	Mild (Grade 0-2) N (%)	Severe (Grade 3-4) N (%)	X^2	P*
UMPS	rs4678145	CC	1	1 (100)	0 (0)	3.980	0.137
		CG	11	6 (54.5)	5 (45.5)		
		GG	44	36 (81.8)	8 (18.2)		
		C	12	7 (58.3)	5 (41.7)	2.917	0.088
		G	55	42 (76.4)	13 (23.6)	0.308	0.579
TYMP	rs11479	AA	0	0 (0)	0 (0)	0.601	0.438
		AG	8	7 (87.5)	1 (12.5)		
		GG	48	36 (75)	12 (25)		
		A	8	7 (87.5)	1 (12.5)	0.601	0.438
UPB1	rs2070474	CC	10	8 (80)	2 (20)	0.548	0.760
		CG	35	26 (78.8)	7 (21.2)		
		GG	13	9 (69.2)	4 (30.8)		
		C	43	34 (79.1)	9 (20.9)	0.542	0.462
		G	46	35 (76.1)	11 (23.9)	0.071	0.791

Conclusions

The results suggest that there is **no relevant relation** between the **genetic variants** analyzed with the **response and toxicity** to **capecitabine** therapy. However, these partly resemble that reflected by other studies. **Further research** with a bigger patient cohort is required in order to obtain **meaningful results**.

References

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