PHARMACOGENETIC STUDY OF THE INFLUENCE OF POLYMORPHISM IN TNFR1A AND FAS GENES ON THE RESPONSE TO RITUXIMAB AND CHEMOTHERAPY IN FOLLICULAR LYMPHOMA PATIENTS

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BACKGROUND

Interindividual variability in treatment response may be associated to the presence of gene polymorphisms. TNFR1A and FAS are receptors involved in the induction of apoptosis by the extrinsic pathway and polymorphisms in these genes may be implicated in the response to rituximab a monoclonal antibody targeting neoplastic B cell expressing CD20 antigen

PURPOSE

To assess the influence of the functional gene polymorphisms rs767455 TNFR1A and rs1800682 FAS on response to treatment with rituximab associated to chemotherapy type CHOP in follicular lymphoma (FL) patients

MATERIAL AND METHODS

Retrospective observational study including a cohort of FL patients treated with rituximab in combination with first line CHOP chemotherapy, recruited from two university hospitals. The clinical response was assessed after the fourth cycle and treatment completed, response criteria used were proposed by the International Working Group:

- **Complete Response** (CR)
- **Partial Response** (PR)
- **Stable Disease** (SD)
- **Relapsed Disease** (RD)

} **non-responders** (NR)

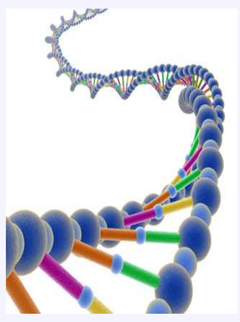
Gene polymorphisms were determined by fluorescent allelic discrimination. Statistical analysis was performed using statistical package SPSS 22.0.

RESULTS

PATIENTS: 78

MEN: 64%

AVERAGE AGE: 50.9±13.1 YEARS



MEDIAN NUMBER OF RITUXIMAB: 6.4±1.2

Pharmacogenetic study was performed to:
59 patients at the fourth cycle and to
76 (rs767455) and **75** (rs1800682) at the end of the treatment

Distribution for response/genotypes:

AFTER FOURTH CYCLE

	POLYMORPHISM rs767455			
	CC (%)	TC (%)	TT (%)	
NR	3 (100)	0 (0)	0 (0)	**P=0.271**
PR	3 (7.7)	18 (46.2)	18 (46.2)	
CR	3 (17.6)	9 (52.9)	5 (29.4)	

	POLYMORPHISM rs1800682			
	CC (%)	TC (%)	TT (%)	
NR	2 (66.7)	1 (33.3)	0 (0)	**P=0.204**
PR	12 (30.8)	17 (43.6)	10 (25.6)	
CR	3 (17.6)	12 (70.6)	2 (11.8)	

TREATMENT COMPLETED

	POLYMORPHISM rs767455			
	CC (%)	TC (%)	TT (%)	
NR	0 (0)	3 (100)	0 (0)	**P=0.171**
PR	3 (16.7)	6 (33.3)	9 (50.0)	
CR	4 (7.3)	32 (58.2)	19 (34.5)	

	POLYMORPHISM rs1800682			
	CC (%)	TC (%)	TT (%)	
NR	2 (66.7)	1 (33.3)	0 (0)	**P=0.604**
PR	4 (23.5)	9 (52.9)	4 (23.5)	
CR	15 (27.3)	26 (47.3)	14 (25.5)	

No statistically significant differences were found between genotypes and clinical response to rituximab after fourth cycle and treatment completed.

CONCLUSIONS

According to our results, gene polymorphisms rs767455 and rs1800682 do not appear to influence the response to treatment with rituximab associated to CHOP chemotherapy in FL.