



The 6<sup>th</sup> World Congress on  
CONTROVERSIES IN MULTIPLE  
MYELOMA (COMy)

# T-cells functional regeneration after autologous stem cells transplantation

Gartcheva L.<sup>1</sup>, Taskov H.<sup>4</sup>, Nikolova M.<sup>4</sup>, Mihova A.<sup>3</sup>, Dimitrova K.<sup>1</sup>, Terzieva V.<sup>2</sup>, Spassov B.<sup>1</sup>, Guenova M.<sup>1</sup>

<sup>1</sup> National Specialized Hospital for Active Treatment of Hematological Diseases – Clinical Immunology  
<sup>2</sup> Department of Clinical Immunology, University Hospital Lozenetz, Sofia University “St. Kliment Ohridski”  
<sup>3</sup> Lozenets Hospital, Lab Clinical Immunology  
<sup>4</sup> National Center of Infectious and Parasitic Diseases

## INTRODUCTION

Functional restoration of T-cell subpopulations and T-cell immune competence, which can be assessed by serum cytokine levels, may be among the most important consequences of transplant success.

The main objective of this study was to monitor and analyze the restoration of T-cell functional activity by flow cytometric evaluation of the Th1/Th2-cytokine profile in patients undergoing ASCT, before and at specific intervals after transplantation compared to healthy controls.

Samples from 34 patients (15 male and 19 female) with median age 25 years (14-50) were enrolled in the study. Serum Th1 and Th2-like cytokines as well as cytokine IL-10 starting levels in patients before ASCT and 2, 6, 9, 12, 18 and 24 months after transplantation were analyzed by flow cytometry using a Th1/Th2 CBA (Cytometric Bead Array) kit [BD Bioscience]. The obtained mean values of the individual indicators were compared with the data from a control group of 28 age-matched samples. Overall (OS) and progression free survival (PFS) were analyzed of the studied recovery parameters, depending on the levels achieved at the various indicators on day 100 after ASCT.

## RESULTS

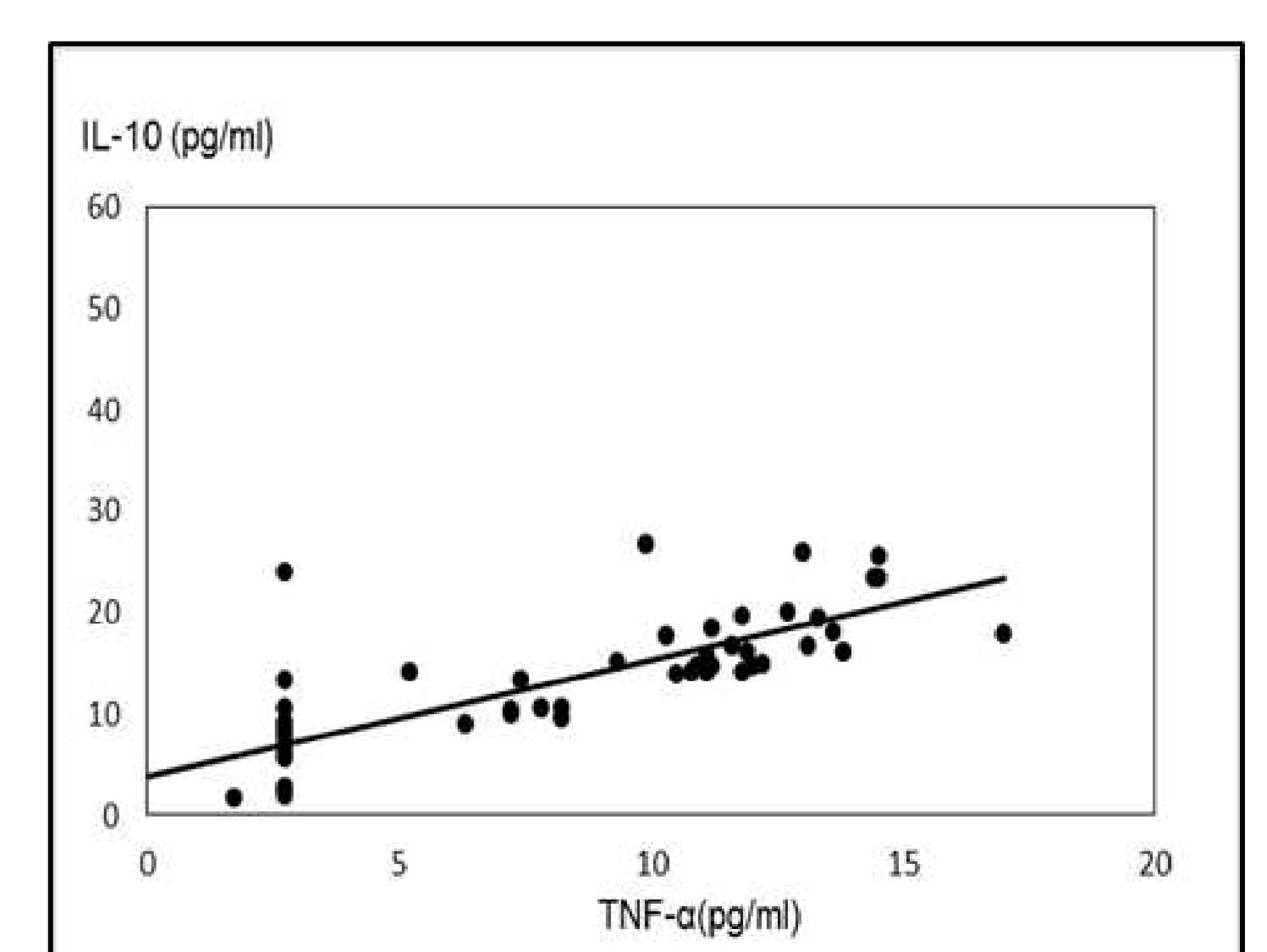
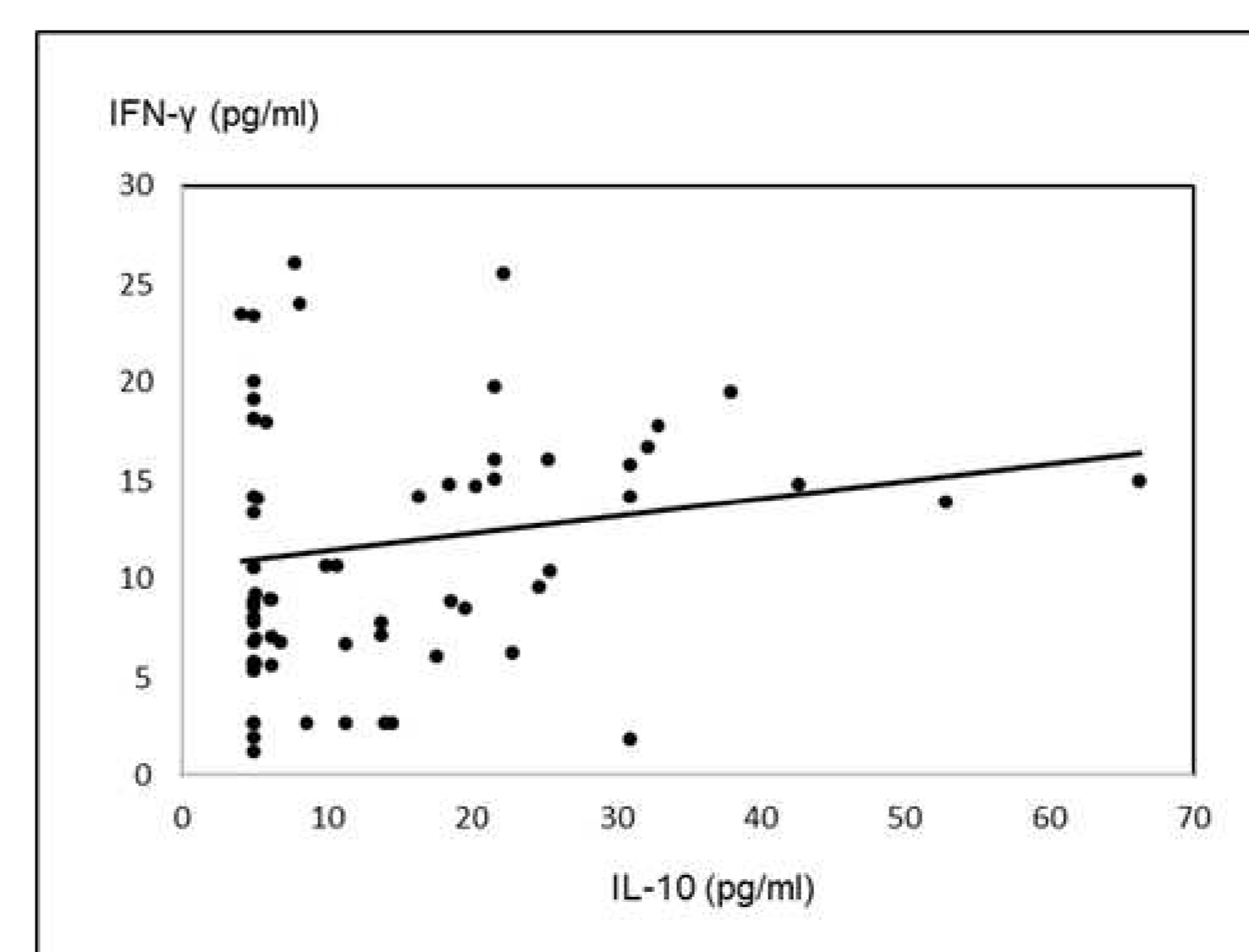
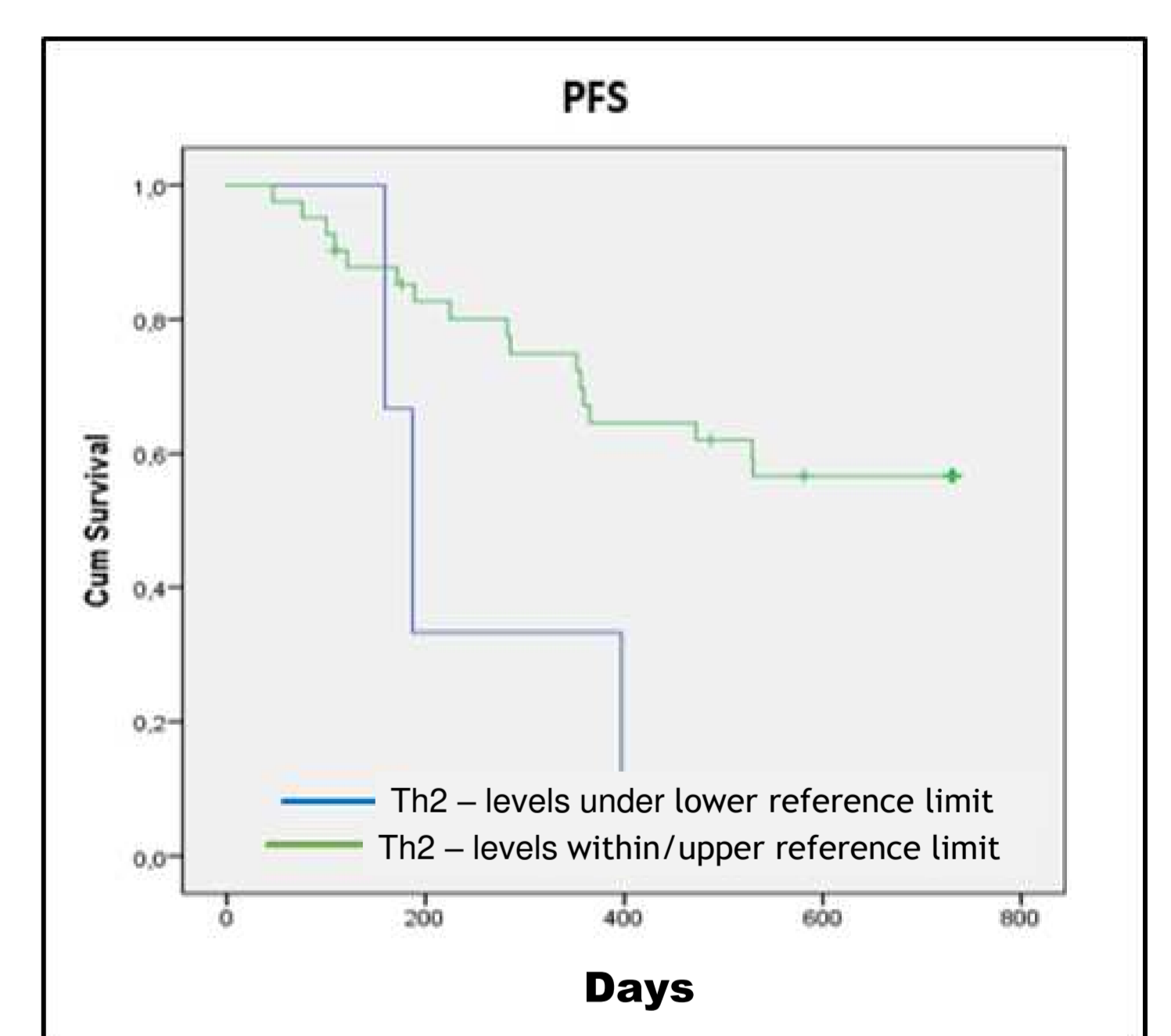
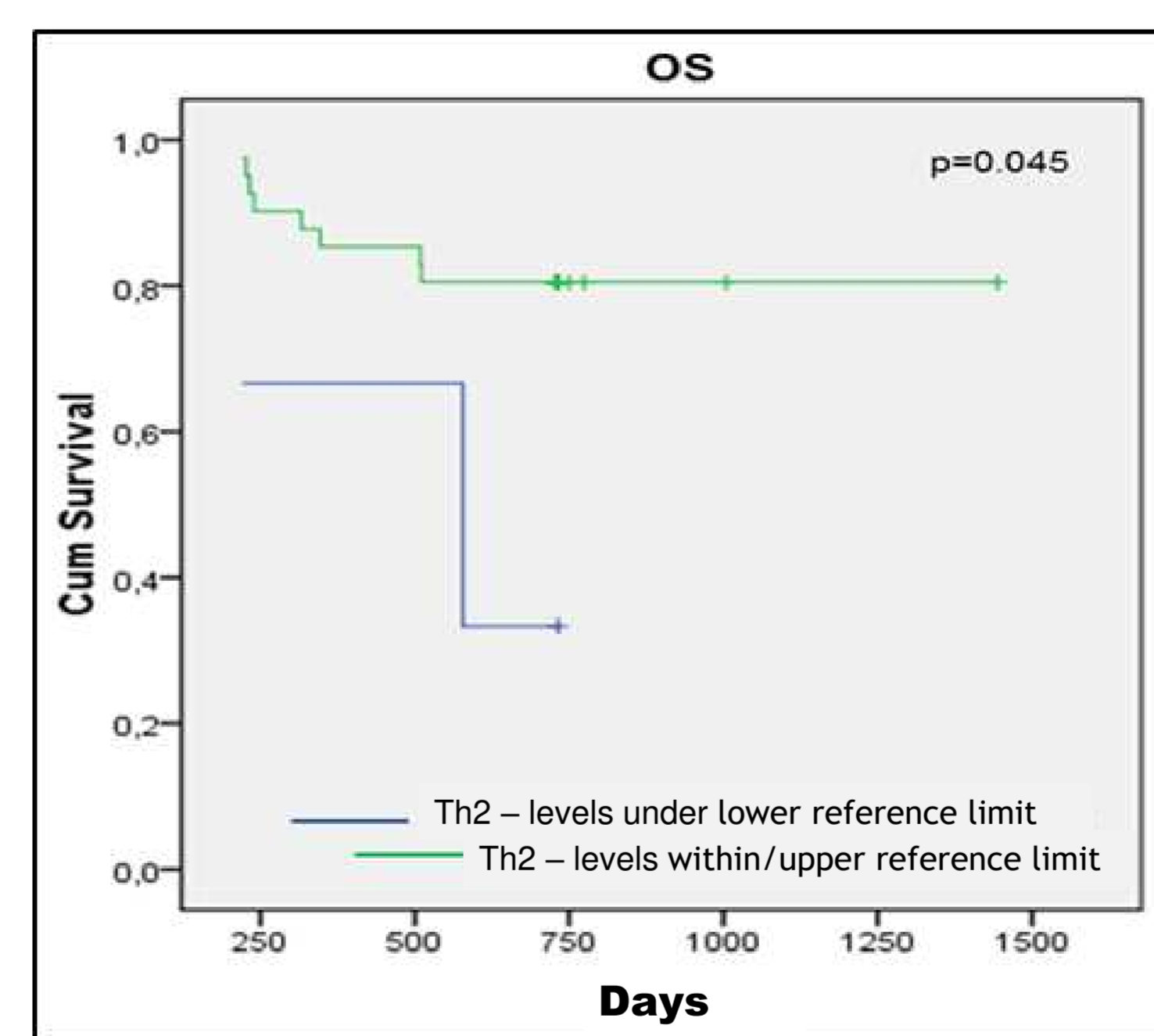
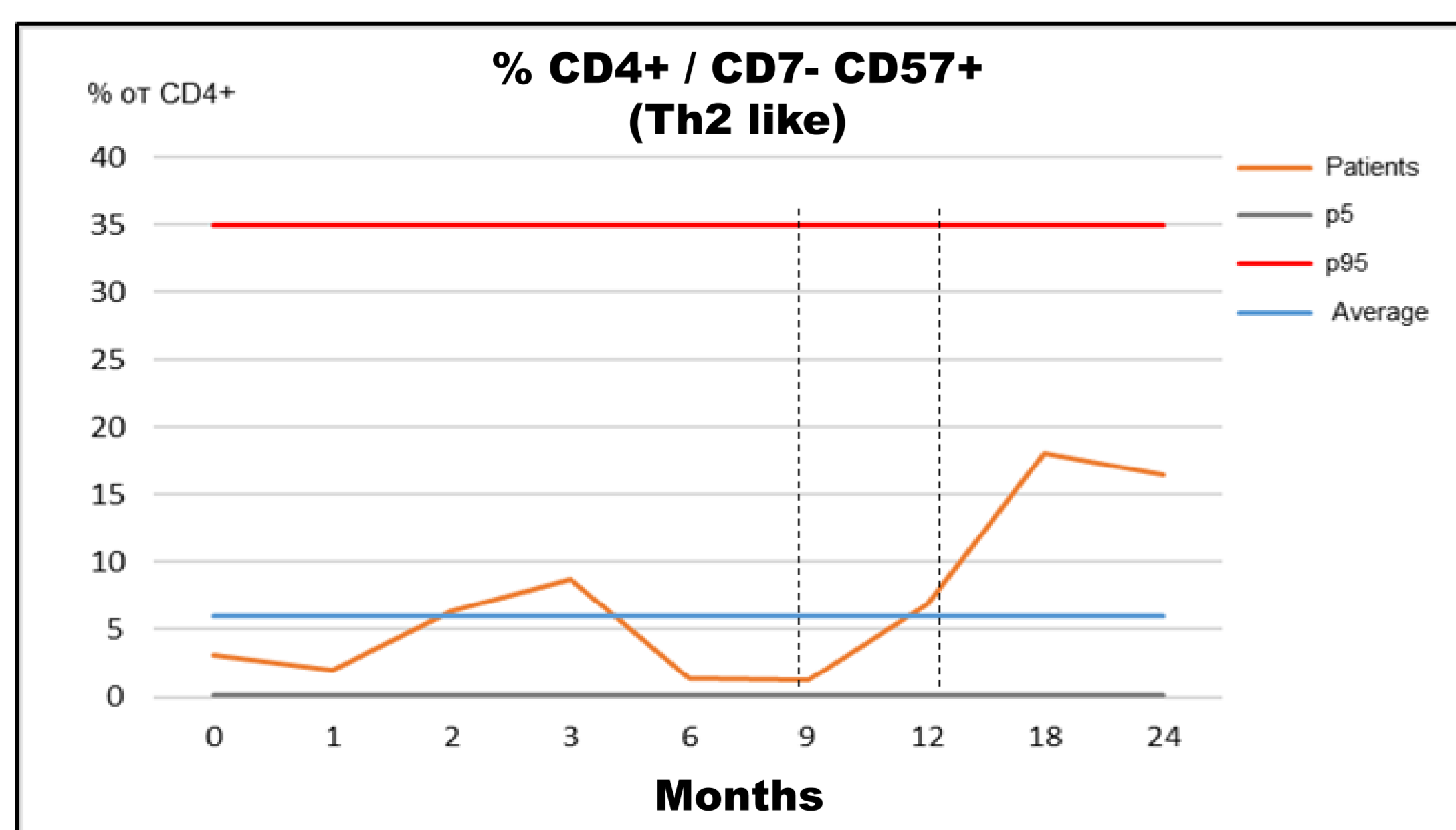
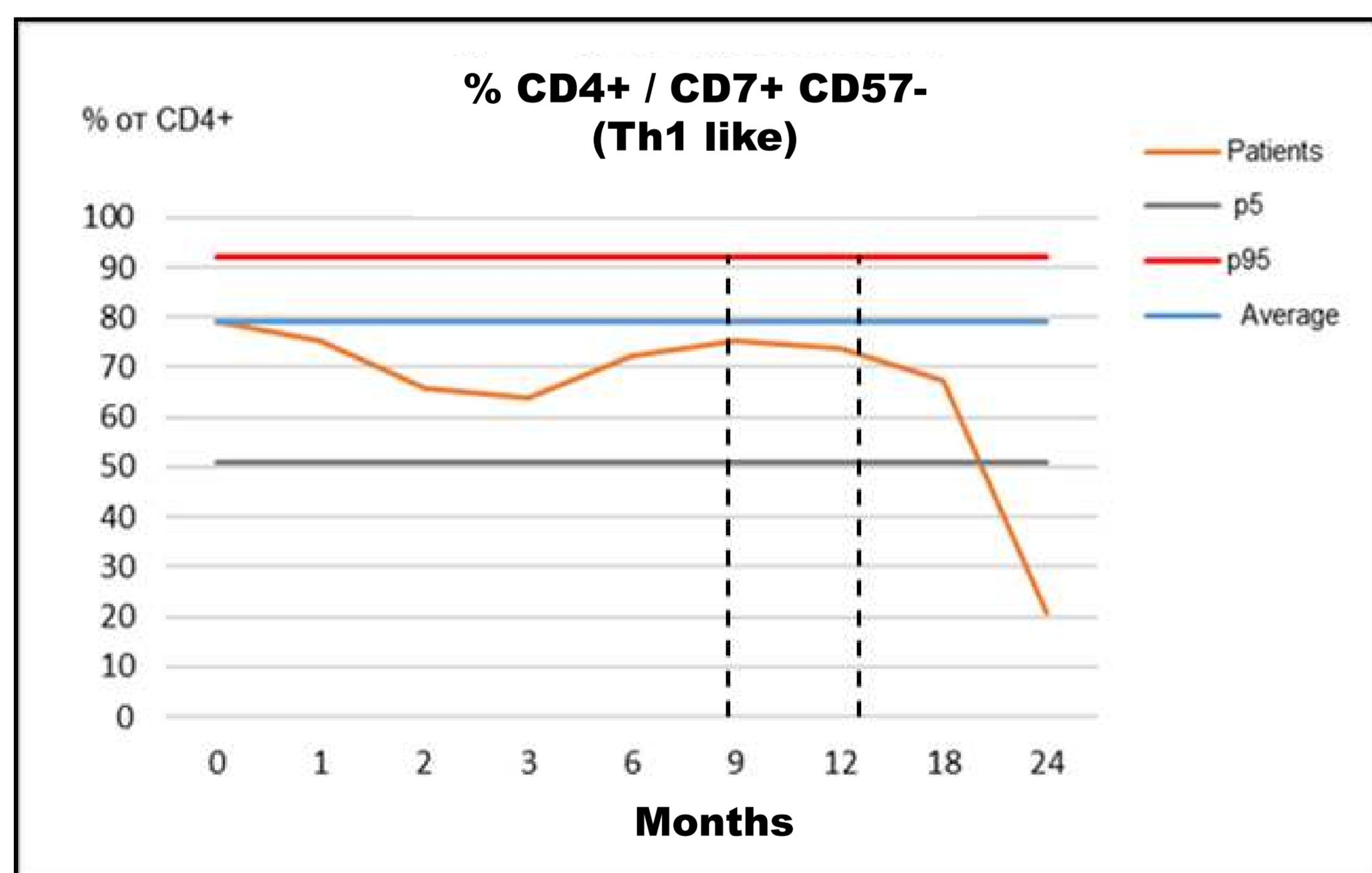
Serum cytokine (pg/ml)	Th1			Th2			
	IFN-gamma	TNF-alpha	IL-2	IL-4	IL-5	IL-10	
Control group	6.4-33.44	2.59-15.02	0.01-7.1	5.3-40.7	8-110	3.73-12.12	
Stages (months)	0	7.813	3.117	2.5	3.067	3.956	9.321
	3	9.63	2.7	3.043	3.571	4.667	9.933
	6	7.373	3.857	3.688	2.971	4.356	7.9
	9	68.453	11.507	12.727	12.26	8.427	16.673
	12	65.507	11.28	13.213	14.133	8.867	16.573
	18	7.662	2.877	4.523	3.554	4.785	5.3
	24	11.618	3.383	4.957	3.822	4.543	5.7

Th1 cytokines IFN- $\gamma$ , TNF- $\alpha$ , IL-2 as well as IL-10 had similar recovery dynamics. During the first 6 months, the values varied within the confidence interval. There was a subsequent significant increase over the 9-12 month period, which was the least pronounced in TNF- $\alpha$ .

Th2-like IL-4 and IL-5 levels were low in the first 6 months. Similar to Th1-like cytokines, an increase was observed during the 9-12 month period, and values reached the confidence limits. A significant decrease to values within the reference range was observed after the first year for all parameters.

At day +100	Overall survival (дни)		% Progression free survival		P=
	< lower reference limit	within/upper reference limit	< lower reference limit	within/upper reference limit	
<b>PFS</b>					
%CD19+	594	497	75.00%	54.50%	0.01
%CD3+	642	508	76.90%	55.40%	0.023
CD56+ AC	632	657	48.60%	75.00%	0.05
CD4+ effector	271	680	100%	48.70%	0.052
CD8+ memory	637	456	76.9%	45.20%	0.041
Th2	247	532	10%	58.50%	0.017
<b>OS</b>					
*Th2	510	681	33.30%	79.50%	0.055

Restoring levels of Th2-like cells within confidence limits at day 100 after ASCT correlated statistically with better OS - 79.5% and PFS - 58.5% compared to 33.3% and 10% respectively, in patients with low levels ( $p < 0.05$ ).



## CONCLUSION

The evaluation of Th1/Th2-cytokine profile is helpful for deeper understanding of T-cell functional activity recovery after ASCT and may provide additional prognostic information.