

Supplementary Material:

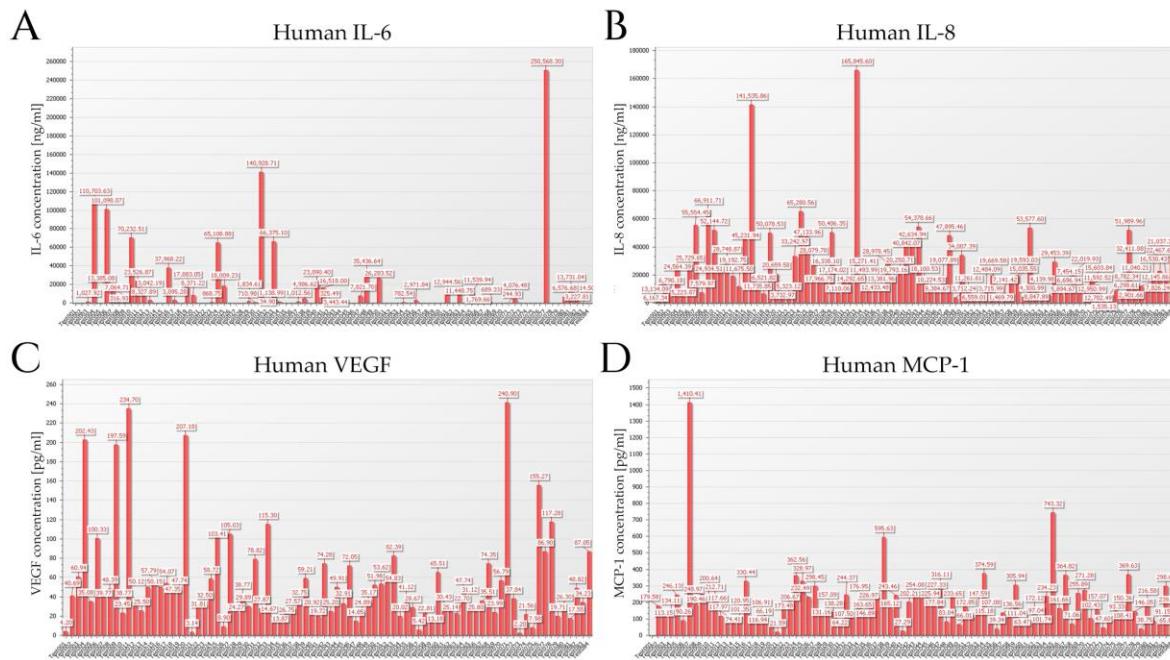


Figure S1. Concentrations of IL-6 (A), IL-8 (B), VEGF (C), and MCP-1 (D) using FCAP Array™ software (Becton Dickinson, New Jersey, USA). Abbreviations: IL-6—interleukin-6; IL-8—interleukin-8; VEGF—vascular endothelial growth factor; MCP-1—angiogenic chemokine monocyte chemoattractant protein-1.

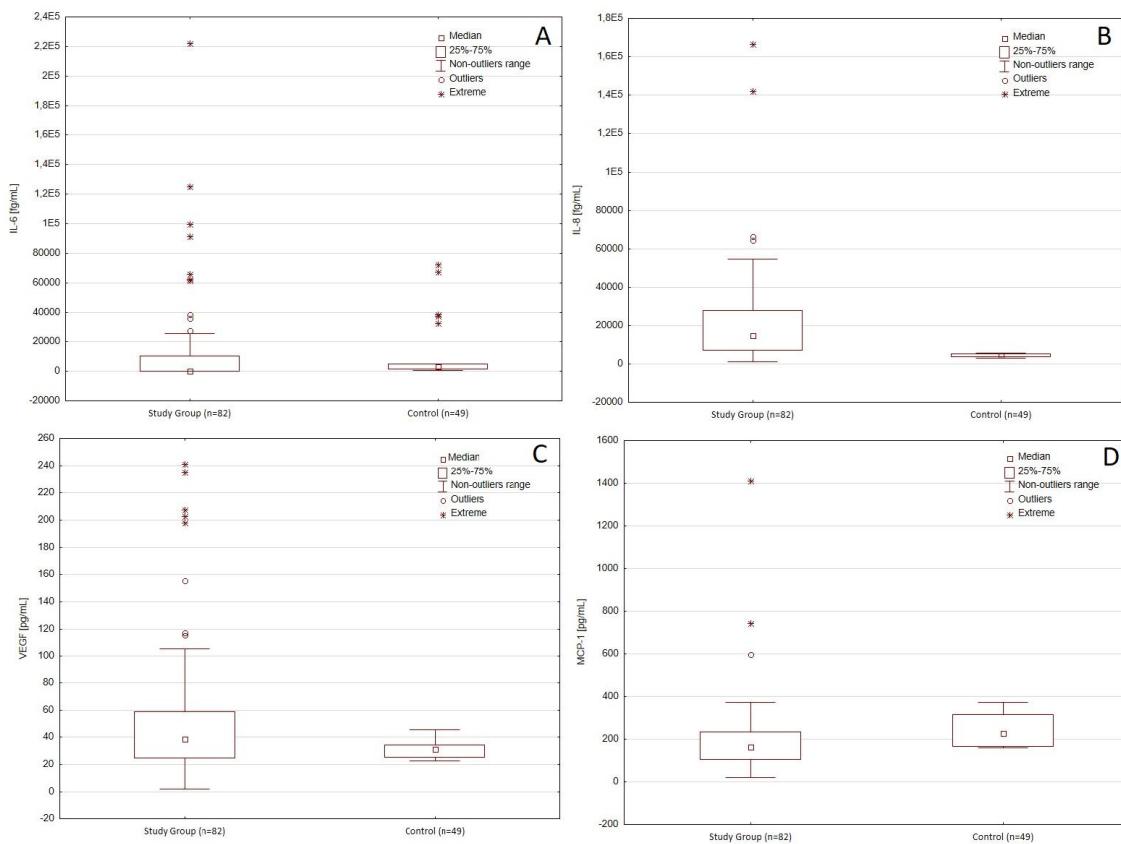


Figure S2. Box-and-whisker plot comparing the concentrations of IL-6 (A), IL-8 (B), VEGF (C), and MCP-1 (D) between the study and control groups. Abbreviations: IL-6—interleukin-6; IL-8—interleukin-8; VEGF—vascular endothelial growth factor; MCP-1—angiogenic chemokine monocyte chemoattractant protein-1.

Table S1. Relationship between demographic and clinical variables and progression-free survival or overall survival in the study group.

Variable	n	Progression-free survival				Overall survival			
		Univariate		Multivariate		Univariate		Multivariate	
		Median (months)	HR (95% CI) p	HR (95% CI) p	Median (months)	HR (95% CI) p	HR (95% CI) p	HR (95% CI) p	
Sex									
Men	40 (48.8%)	25	1.31 (0.80- 2.13)	0.99 (0.52-1.88)	38	2.17 (1.21- 3.88)	3.19 (1.17-8.69)		
Women	42 (51.2%)	25	0.268	0.002*	78	0.008*	0.002*		
Age >65 years									
Below the median	40 (48.8%)	27	0.61 (0.37- 1.01)	0.31 (0.73-2.65)	77	0.65 (0.36- 1.17)	1.36 (0.70-2.65)		
Above the median	42 (51.2%)	21	0.056	0.317	55	0.156	0.356		
Diagnosis									
Disease with monoclonal protein present	72 (87.8%)	25	0.67 (0.28- 1.58)	1.36 (0.52-3.52)	57	0.47 (0.15- 1.40)	2.57 (0.95-6.94)		
Light chain disease	10 (12.2%)	14.5	0.362	0.526	12	0.177	0.063		
A type of monoclonal protein	20 (27.4%)	18	1.08 (0.59- 1.99)	0.99 (0.39-2.47)	38	1.60 (0.77- 3.32)	0.64 (0.31-1.31)		
53 (72.6%)	25			0.990	77		0.227		

IgA		0.794		0.208		
IgG						
Light chains						
Kappa	48 (58.5%)	28	0.72 (0.43-1.21)	1.39 (0.75-2.59)	64	0.70 (0.38-1.28)
Lambda	34 (41.5%)	17	0.223	0.294	38	0.252
ISS Stage						
2 or 3	58 (71.6%)	17	2.92 (1.77-4.81)	2.38 (0.97-5.86)	48	2.99 (1.62-5.52)
1	23 (28.4%)	52	<0.001*	0.059*	-	0.004*
A/B renal function						
B	67 (81.7%)	15	2.12 (0.98-4.55)	2.29 (0.99-5.27)	18	2.78 (1.11-6.96)
A	15 (18.3%)	28	0.009*	0.051*	68	0.001*
Weight loss						
Yes	41 (50.6%)	18	1.41 (0.86-2.31)	1.03 (0.73-1.45)	33	2.11 (1.16-3.84)
No	40 (49.4%)	34	0.162	0.836	78	0.009*
ECOG scale						
0	8 (9.8%)	24	0.58 (0.26-1.28)	0.54 (0.15-1.95)	124	0.45 (0.18-1.10)
1. 2. 3	74 (90.2%)	25	0.184	0.352	55	0.082
17p deletion						
Yes	9 (16.7%)	11	2.72 (0.95-7.78)	2.44 (1.03-5.76)	28	2.83 (0.76-10.42)
No	45 (83.3%)	37	0.004*	0.042*	80	0.018*
Translocation (4;14)						
Yes	6 (11.1%)	21	1.05 (0.40-2.78)	1.24 (0.48-3.21)	49	2.38 (0.59-10.00)
No	48 (88.9%)	27	0.924	0.655	80	0.227
Translocation (14;16)						
Yes	3 (5.6%)	66	0.61 (0.19-1.92)	0.74 (0.09-5.89)	-	0.71 (0.13-3.92)
No	51 (94.4%)	27	0.487	0.779	77	0.730
Auto-HSCT						
No	45 (59.2%)	13	2.61 (1.56-4.38)	0.66 (0.31-1.42)	30	2.79 (1.53-5.08)
Yes	31 (40.8%)	39	<0.001*	0.297	-	<0.001*
Anemia before treatment						
(WHO)						
No	21 (25.6%)	34	0.56 (0.33-0.95)	1.34 (0.63-2.81)	57	0.79 [0.42-1.47]
Yes	61 (74.4%)	18	0.033	0.438	55	0.457
IL-6 (M 0.1)						
High	40 (49.4%)	17	1.89 [1.15-3.11]	1.19 (0.60-2.35)	28	2.62 [1.45-4.70]
Low	41 (50.6%)	35	0.008*	0.605	78	<0.001*
IL-8 (M 14823.57)						
High	40 (49.4%)	17	1.65 [1.01-2.71]	0.84 (0.41-1.70)	38	1.70 [0.94-3.07]
Low	41 (50.6%)	28	0.037*	0.631	68	0.062

VEGF (M 38.77)							
	39 (48.1%)	23	1.57 [0.95- 2.58]	0.80 (0.41-1.57)	51	1.34 [0.74- 2.41]	1.38 (0.76-2.50)
High	42 (51.9%)	27	0.060	0.531	57	0.305	0.291
Low							
MCP-1 (M 161.66)							
	40 (49.4%)	25	0.79 [0.48- 1.28]	1.26 (0.61-2.56)	57	0.80 [0.45- 1.43]	0.76 (0.41-1.40)
High	41 (50.6%)	25	0.337	0.526	55	0.448	0.393
Low							

* Statistically significant result.

Table S2. Evaluation of the usefulness of IL-6, IL-8, and VEGF concentrations in differentiating between various clinical conditions.

IL-6						
Variable		AUC [95% CI]	Sensitivity %	Specificity %	Cut-off point	p
ISS stage						
I	23 (28.4%)	0.64				
II or III	58 (71.6%)	[0.53-0.75]	50.00	81.82	>1165.53	0.011*
Weight loss before treatment						
No	41 (50.6%)	0.70				
Yes	40 (49.4%)	[0.59-0.80]	67.50	77.50	>756.68	<0.001*
IL-8						
Variable		AUC [95% CI]	Sensitivity %	Specificity %	Cut-off point	p
ISS stage						
I or II	23 (28.4%)	0.65				
III	58 (71.6%)	[0.54-0.75]	55.17	72.73	>15546.65	0.022*
A/B renal function						
A	67 (81.7%)	0.84				
B	15 (18.3%)	[0.74-0.91]	80.00	77.27	>20191	<0.001*
ECOG scale						
0	8 (9.8%)	0.75				
1, 2, or 3	74 (90.2%)	[0.65-0.84]	75.68	85.71	>8738.92	0.010*
Supportive treatment						
No	21 (25.6%)	0.77				
Yes	61 (74.4%)	[0.66-0.85]	65.57	80.00	≤16370.78	<0.001*
Auto-HSCT						
No	45 (59.2%)	0.68				
Yes	31 (40.8%)	[0.56-0.78]	64.52	65.91	≤14264.49	0.003*
Anemia before treatment						
No	21 (25.6%)	0.79				
Yes	61 (74.4%)	[0.68-0.87]	76.67	80.95	>11039.5	<0.001*
VEGF						
Variable		AUC [95% CI]	Sensitivity %	Specificity %	Cut-off point	p
A/B renal function						
A	67 (81.7%)	0.73				
B	15 (18.3%)	[0.62-0.82]	93.33	59.09	>37.84	<0.001*

* Statistically significant result.

Table S3. Comparison of the baseline concentrations of tested cytokines depending on the response to CTH after four, six, and eight cycles.

Variable	Study group (n=82)	IL-6 [fg/mL]		IL-8 [fg/mL]		VEGF [pg/mL]		MCP-1 [pg/mL]	
		Median [interquartile range]	p						
Response to								193.09	
CTH after		14632.96		21212.48		59.35		[145.72-291.17]	
four cycles	4 (6.2%)	[-]		[11595.20-37613.07]		[28.65-160.80]		157.07	
No	60	0.10		12397.80		35.08		[101.91-	
Yes	(93.7%)	[0.10-4200.37]	0.085	[6546.33-19715.46]	0.310	[24.48-58.11]	0.382	231.20]	0.310
Response to								259.99	
CTH after		110868.48		29660.28		47.44		[-]	
six cycles	2 (3.4%)	[-]		[-]		[-]		161.66	
No	56	0.10		13534.43		35.08		[103.59-	
Yes	(96.6%)	[0.10-4200.37]	0.463	[6546.33-20097.42]	0.487	[25.30-58.11]	0.828	234.08]	0.340
Response to								183.47	
CTH after	4	0.10		9562.55		38.10		[112.38-221.26]	
eight cycles	(16.7%)	[0.10-4155.35]		[7692.04-14127.92]		[17.14-50.01]		159.36	
No	20	0.10		11843.35		29.28		[107.74-	0.938
Yes	(83.3%)	[0.10-4653.81]	0.583	[6340.05-18897]	0.877	[14.36-36.67]	0.757	271.50]	

* Statistically significant result.