Results

This study included 40 patients with approved diagnosis of ALL who presented to the Medical Oncology Department, NCI, Cairo University in the period between 1999-2004.

Data obtained from study group:

Patients characteristics: (table 8, figures 7,8)

- **Age:**

Ranged from 16 to 60 years with a median of 27 years, 10% of patients were older than 50 years while 90% of patients were younger than 50 years.

- **Sex:**

Out of 40 patients, 27 patients were males (67.5%) and 13 patients were females (32.5%)

- **Lymph node involvement:**

Twenty eight patients (70%) showed lymph node involvement while 12 patients (30%) did not show any lymph node involvement.

- **Hepatomegaly:**

Thirty two patients (80%) showed hepatomegaly while 8 patients (20%) showed normal liver size.

- **Splenomegaly:**

Thirty one patients (77.5%) showed splenomegaly while 9 patients (22.5%) had normal spleen size.

- **Cerebrospinal fluid examination:**

Thirty four patients (85%) were negative for CNS involvement, 6 patients (15%) were positive for CNS involvement .

Laboratory evaluation: (table 9)

TLC:

Ranged from 600-223.000/µl with a median of 30.000/ µl

Blast cell % in peripheral blood:

Ranged for 20% to 98% with a median of 74.5%.

Platelets:

Ranged from 400 to 350.000/ µl with a median of 24.500/ µl.

HB concentration:

Ranged from 3.4g/dl to 12g/dl with a median of 7.35/dl

Bone marrow blast cell %:

Ranged from 20% to 99% with a median of 90%.

Time to complete remission (Table 10) (Fig. 9):

Out of 25 patients who showed complete remission, 22 patients (88%) showed CR in less than 4 weeks and 3 patients (12%) had complete remission in more than 4 weeks.

Immunophenotype (Table 11) (Fig. 10):

Out of 40 patients, 17 patients (42.5%) were C-ALL, 14 patients (35%) were pre-B, 2 patients (5%) were pro-B and 7 patients (17.5%) were T-ALL.

BCR-ABL fusion gene (Table 12) (Fig. 11):

Out of 40 patients, 29 patients (72.5%) were negative, while 11 patients (27.5%) were positive. Out of 11 patients positive BCR-ABL fusion gene, 8 (72.7%) were positive P_{190} and 3 patients (27.3%) were positive P_{210}.

Initial response to treatment (Table 13) (Fig. 12):

Out of 40 patients, 25 patients (62.5%) of patients showed complete remission while 8 patients (20%) of patients showed partial remission and 7 patients (17.5%) of our patients died before evaluations for complete remission.

Overall risk (Table 14) (Fig. 13):

Out of 40 patients, 18 (45%) were high risk, 11 (27.5%) were standard and 11 (27.5%) were very high risk.

Overall survival (Fig. 14):

At 15 months overall survival was 40%.

Disease free survival (Fig. 15):

At 15 months, disease survival was 61%.

Relapse rate (Table 15) (Fig. 16):

Out of 25 patients who showed complete remission 8 patients (32%) showed relapse while 17 patients (68%) showed no relapse. Out of 8 relapsed patients, 4 patients (50%) were very high risk, 3 patients (37.5%)were high risk and 1 patient (12.5%) was standard risk.

Correlations of prognostic factors to initial response to treatment (table 16, figure 17):

The correlation between initial response to treatment and sex:

Out of 25 patients showing complete remission, 17 patients were males (68%), 8 were females (32%), out of 8 patients who showed incomplete remission, 5 patients (625%) were males, 3 patients (37.5%) were females and out of 7 patients who showed early death,5

patients(71.4%) were males, 2 patients (28.6%) were females. There is no statistical significance difference, p value = 0.93.

The correlation between initial response to treatment and age:

Out of 25 patients showing complete remission, 23 patients (92%) were younger than 50 years, 2 patients (8%) were older than 50 years. Out of 8 patients who showed incomplete remission, 6 patients (75%) were younger than 50 years, 2 patients (25%) were older than 50 years while 7 patients (100%) who died early, were younger than 50 years. There is no significant statistical difference, p value = 0.24.

The correlation between initial response to treatment and BCR-ABL fusion gene:

Out of 25 patients showing complete remission, 19 patients (76%) were negative, 6 patients (24%) were positive. Out of 8 patients who showed incomplete remission, 5 patients (62.5%%) were negative, 3 patients (37.5%) were positive and out of 7 patients (100%) who died early, 5 patients were negative, 2 patients (28.6%) were positive. There is no significant statistical difference, p value = 0.76.

The correlation between initial response to treatment and cerebrospinal fluid examination:

Out of 25 patients showing complete remission, 19 patients (76%) were negative for malignant cells, 6 patients (24%) were positive, 8 patients (100%) having incomplete remission, were negative and the 7 patients who died early were negative. There is no significant statistical difference, p value = 0.12.

The correlation between initial response to treatment and total leucocystic count at the time of the presentation:

Out of 25 patients showing complete remission, 20 patients (80%) had TLC < 30.000/µl, 5 patients (20%) had TLC > 30.000/µl. Out of 8 patients who showed incomplete remission, 2 patients (25%), had TLC < 30.000/µl, 6 patients (75%), had TLC > 30.000/µl and out of 7 patients who died early, 4 patients (57.1%) had TLC < 30.000/µl were, 3 patients(42.9%) had TLC > 30.000/µl.. There is no significant statistical difference, p value = 0.29.

The correlation between initial response to treatment and immunophenotyping:

Out of 25 patients showing complete remission, 20 patients (80%) were C-ALL + Pre-B, 5 patients (20%) were T-ALL. Out of 8 patients showed incomplete remission, 6 patients (75%) were C-ALL + Pre-B, 1 patient (12.5%) was Pro-B and 1 patient (12.5%) was T-ALL and out of 7 patients who died early, 5 patients (71.4%) were C-ALL + Pre-B, 1 patients (14.3.%) was T-ALL,1 patient (14.3%) was pro-B. There is no significant statistical difference, p value = 0.85.

The correlation between initial response to treatment and overall risk:

Out of 25 patients showing complete remission, 8 patients (32%) were standard risk, 17 patients (68%) were high and very high risk. Out of 8 patients who showed incomplete remission, one patient (12.5%%) was standard risk, 7 patients (87.5%) were high and very high risk while out of 7 patients who died early, 2 patients (28.6%) were standard risk and 5 patients (71.4%)were high and very high risk. There is no statistical significance difference, p value = 0.56

Correlations to BCR-ABL fusion gene: (table 17, figure 18)

BCR-ABL fusion gene was correlated to different prognostic factors. Out of 40 patients, 11 patients were positive for BCR-ABL gene and 29 patients were negative for BCR-ABL gene.

The correlation between BCR-ABL fusion gene and sex:

Out of 11 patients positive for fusion gene, 9 patients (81.8%) were males, 2 patients (18.2%) were females, while out of the negative 29 patients, 18 patients (61.1%) were males, 11 patients (37.9%) were females. There is no significant statistical difference, p value 0.23.

The correlation between BCR-ABL fusion gene and age:

Out of 11 BCR-ABL positive cases, 10 patients (90.9%) were younger than 50 years, 1 patients (9.1%) were older than 50 years, while out of 29 BCR-ABL negative patients, 26 patients (89.7%) were younger than 50 years, 3 patients (10.3%) were older than 50 years. There is no significant statistical difference, p value = 1.00.

The correlation between BCR-ABL fusion gene and total leucocytic count at the time of presentation:

Out of 11 patients positive for BCR-ABL fusion gene, 5 patients (45.5%) had TLC less than 30.000/µl, 6 patients (54.5%) had TLC greater than 30.000/µl, while out of negative 29 patients, 15 patients (51.7%) had TLC less than 30.000/µl, 14 patients (48.3%) had TLC greater than 30.000/µl. There is no significant statistical difference, p value = 1.00.

The correlation between BCR-ABL fusion gene and cerebrospinal fluid examination:

Out of 11 patients positive for BCR-ABL fusion gene, the CSF of 10 patients (90.9%) was negative for malignant cells, the CSF of 1 patient

(9.1%) was positive while out of 29 positive BCR-ABL patients, the CSF of 24 patients (82.8%) was negative for malignant cells, the CSF of 5 patients (17.2%) was positive for malignant cells. There is no significant statistical difference, p value = 1.

The correlation between BCR-ABL fusion gene and immunophenotyping:

The 11 patients (100%) positive for BCR-ABL fusion gene, were C-ALL + Pre-B, while out of 29 negative BCR-ABL gene, 20 patients (69.0%), were C-ALL + Pre-B, 2 patients (6.9%) were pro-B and 7 patients (24.1%) were T-ALL. There is no significant statistical difference, p value = 0.11.

Correlations of disease free survival in relation to different prognostic factors:

Disease free survival in relation to sex (Fig. 19):

The mean disease free survival of males was 22.32 months (± SD 3.13 months) while the mean disease free survival of females was 12.13 months (± SD 4.1 months). There is no significant statistical difference p. value = 0.1.

Disease free survival in relation to age (fig. 20):

Mean disease free survival of patients aged less than 50 years was 21.24 months (± SD 2.83 months) while that of patients aged more than 50 years was 1.75 months (± SD 0.25 months). There is significant statistical difference, p value = 0.019.

Disease free survival in relation total leucocytic count at time of presentation (Fig. 21):

The mean disease free survival of patients who had TLC at time of presentation < 30.000/µl was 18.33 months (± SD 2.67 months), while those who had TLC at time of presentation > 30.000/µl was 20.68 months (± SD 4.47 months). There is no significant statistical difference p. value = 0.35.

Disease free survival in relation to CSF affection (Fig. 22):

The mean disease free survival of patients whose CSF was negative for malignant cells was 17.76 months (± SD 2.58 months), while mean disease free survival of those whose CSF was positive for malignant cells was 19.2 months (± SD 5.92 months). There is no statistical difference p. value = 0.8.

Disease free survival in relation to Immunophenotype (Fig. 23):

The mean disease free survival of patients whose immunophenotypes belonged to C-ALL + Pre-B was 18.54 months (± SD 3.14 months), while mean disease free survival of those immunophenotypes belonged to T-ALL was 17 months (± SD 3.58 months), while there was no survival for patients with pro-B phenotype. There is no significant statistical difference p. value = 0.55.

Disease free survival in relation to BCR-ABL Fusion gene (Fig. 24):

The mean disease free survival of patients who were negative for BCR-ABL fusion gene was 19.84 months (± SD 3.29 months) while the mean disease free survival of positive BCR-ABL fusion gene patients was

13.5 months (± SD 0.85 months). There is no statistical significance p. value = 0.95.

Disease free survival in relation to total overall risk (Fig. 25):

The mean disease free survival of patients with very high and high risk was 10 months (± SD 1.47 months), while the mean disease free survival of standard risk patients was 27.67 months (±SD 2.13 months). There is significant statistical difference p. value = 0.016.

Correlation of overall survival to different prognostic factors:

Overall survival was correlated to age, sex, TLC, CSF analysis and immunophenotype and BCR-ABL fusion gene.

Overall survival in relation to age groups (Fig. 26):

The mean survival of patients aged less than 50 years was 13.92 months while that of patients aged more than 50 years was 6.13 months. There is no significant statistical difference p. value = 0.32.

Overall survival in relation to immunophenotype (Fig. 27):

The median survival of those who were C-ALL + Pre-B was 11 months, while the median survival of those who were T-LL was 6 months. There is no significant statistical difference p. value = 0.69

Overall survival in relation to total overall risk (Fig. 28):

The mean survival of patients with very high and high risk was 9.7 months (± SD 2 months), while the mean disease free survival of standard risk patients was 19.17 months (±SD 4.19 months). There is no significant statistical difference p. value = 0.09.

Table (8): Clinical characters of patients.

Characters	Number	Percent
Age		
< 50 years	36	90%
> 50 years	4	10%
Sex		
Male	27	67.5%
Female	13	32.5%
LN involvement		
Positive	28	70%
Negative	12	30%
Hepatomegaly		
Positive	32	80%
Negative	8	20%
Spleen		
Positive	31	77.5%
Negative	9	22.5%
CFS involvement		
Positive	6	15%
Negative	34	85%

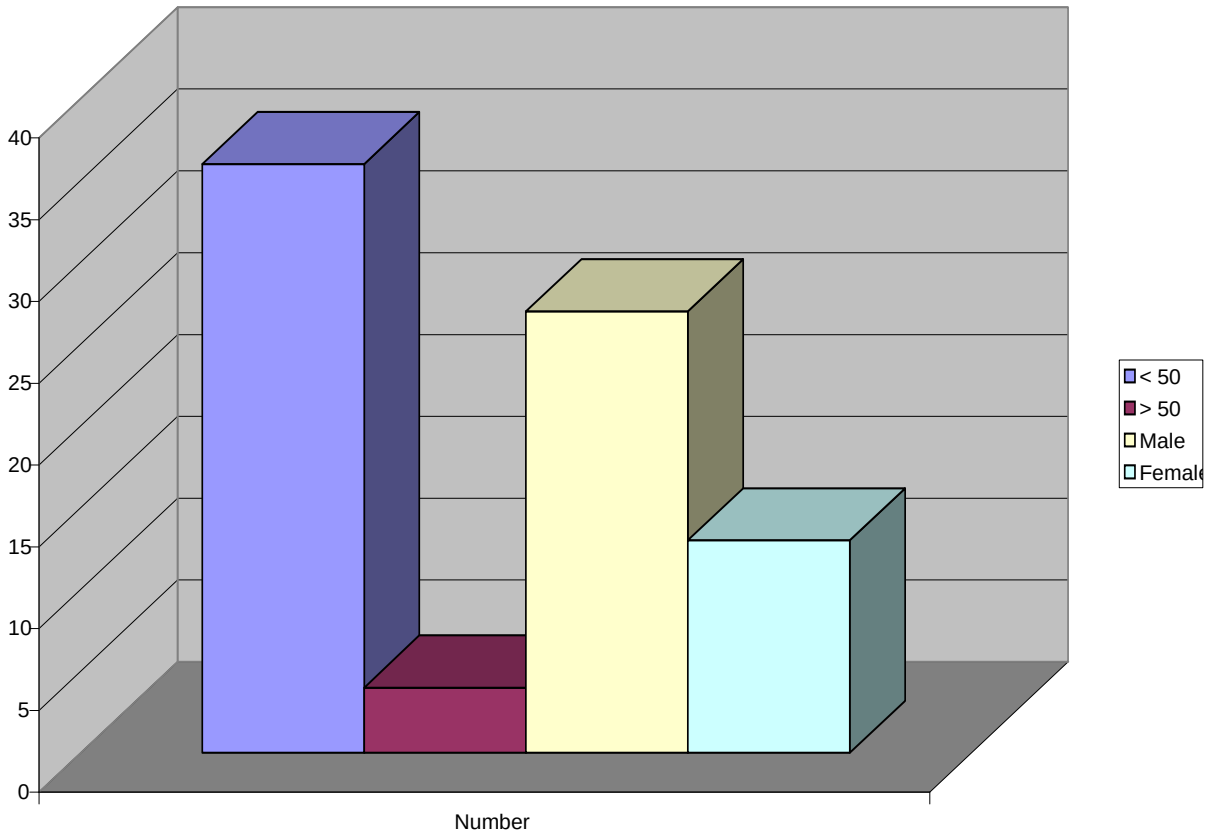

Figure (7): Clinical characters of patients

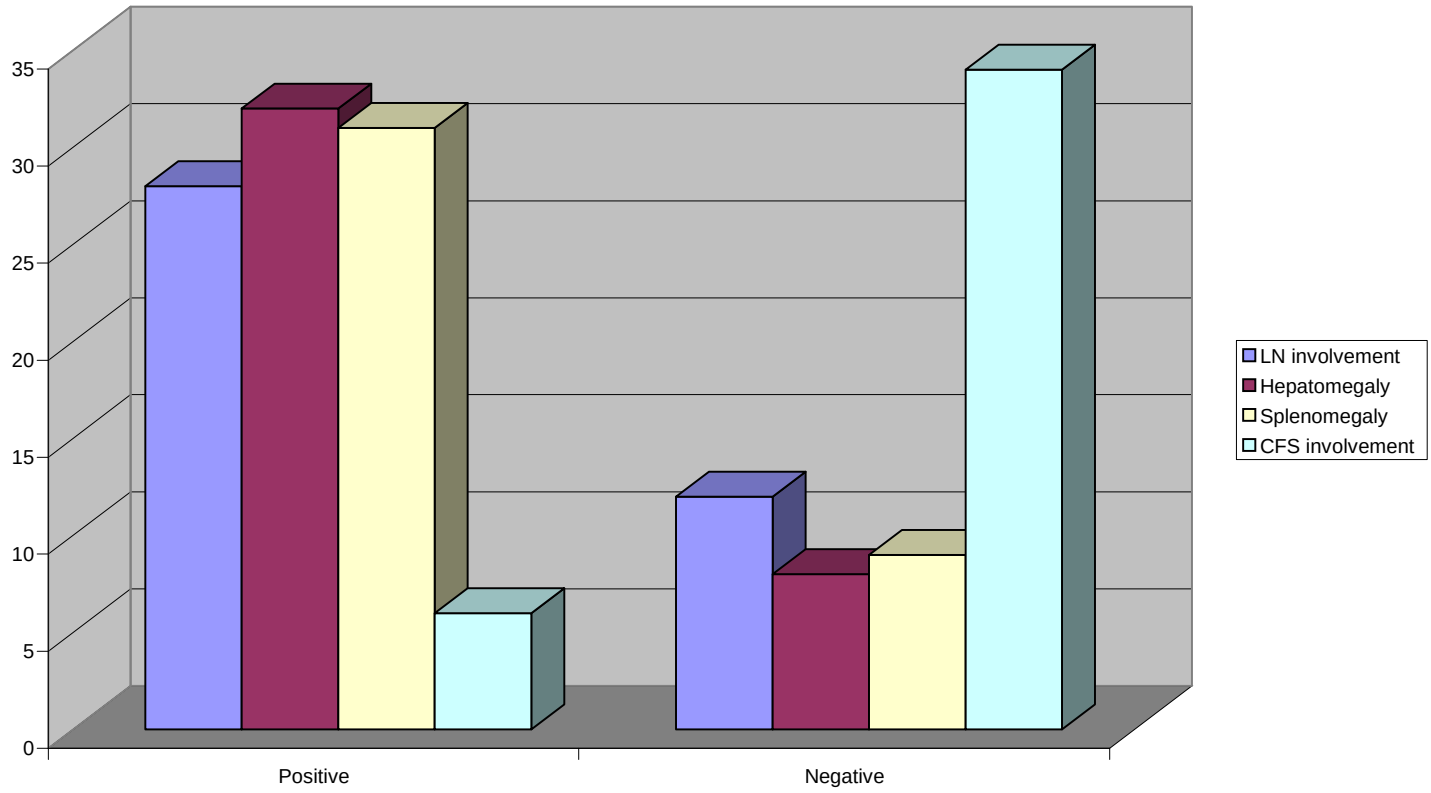

Figure (8): Clinical characters of patients.

Table (9): Laboratory evaluations of patients.

Characters	**Median**	**Range**
TLC x 1000/µl	300.000	600-423000
Peripheral blood blast cell %	74.50	20% - 98%
HB g/dl	7.35	3.4 – 12
Platelet x 1000/µl	24.500	400 – 350000
BM blast %	90	20% - 99%

Table (10): Time of CR.

	Time of CR	
	Count	**%**
< 4wks	22	88%
> 4wks	3	12%

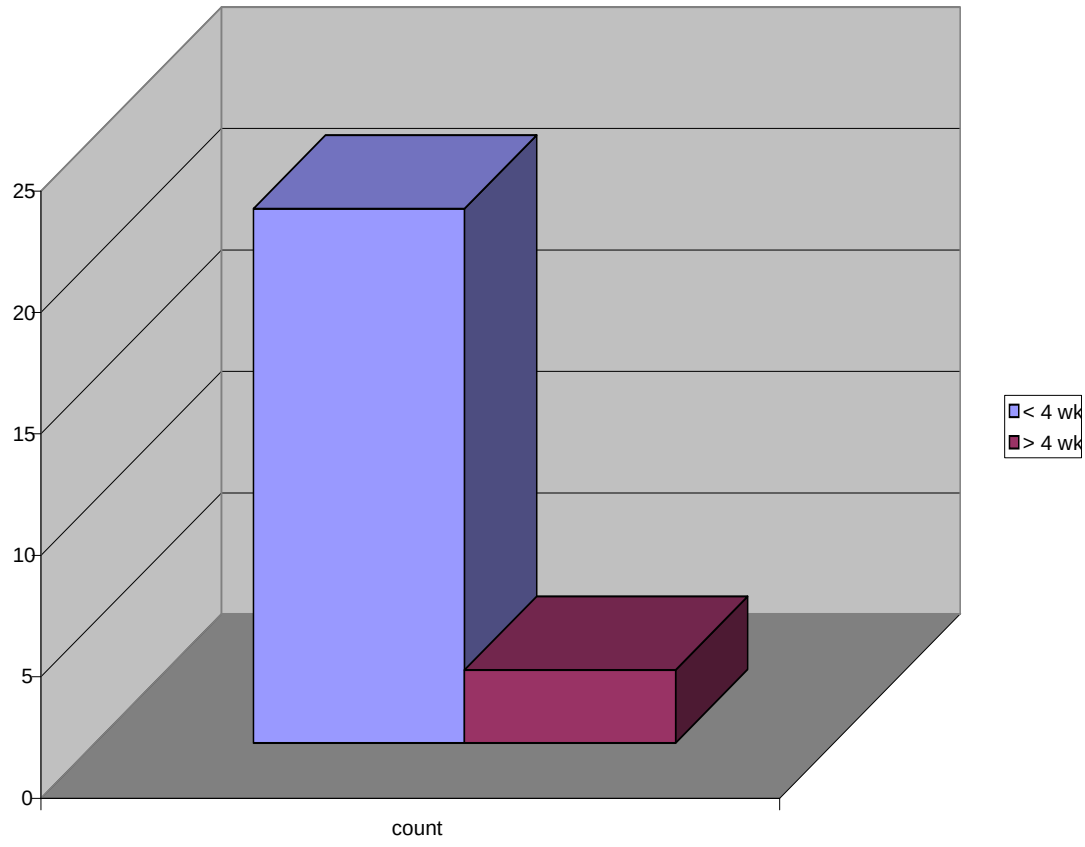

Figure (9): Time of CR

Table (11): Distribution of immunophenotype.

	Immunophenotype	
	Count	**%**
C-ALL + Pre	31	77.5%
Pro	2	5%
T-ALL	7	17.5%

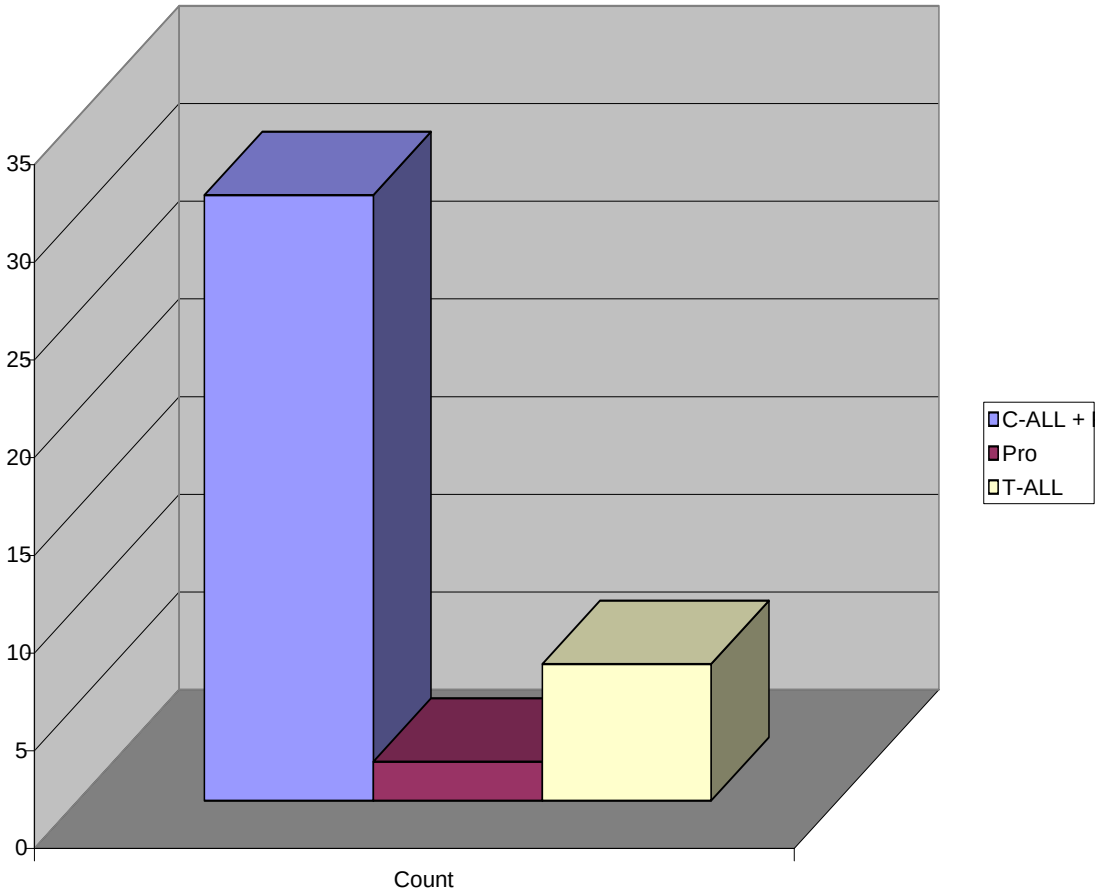

Figure (10): Distribution of immunophentype.

Table (12): Distribution of BCR-ABL fusion gene.

BCR-ABL	Number	Percent
Negative	29	72.5%
Positive	11	27.5%
P190	8	72.7%
P210	3	27.3%

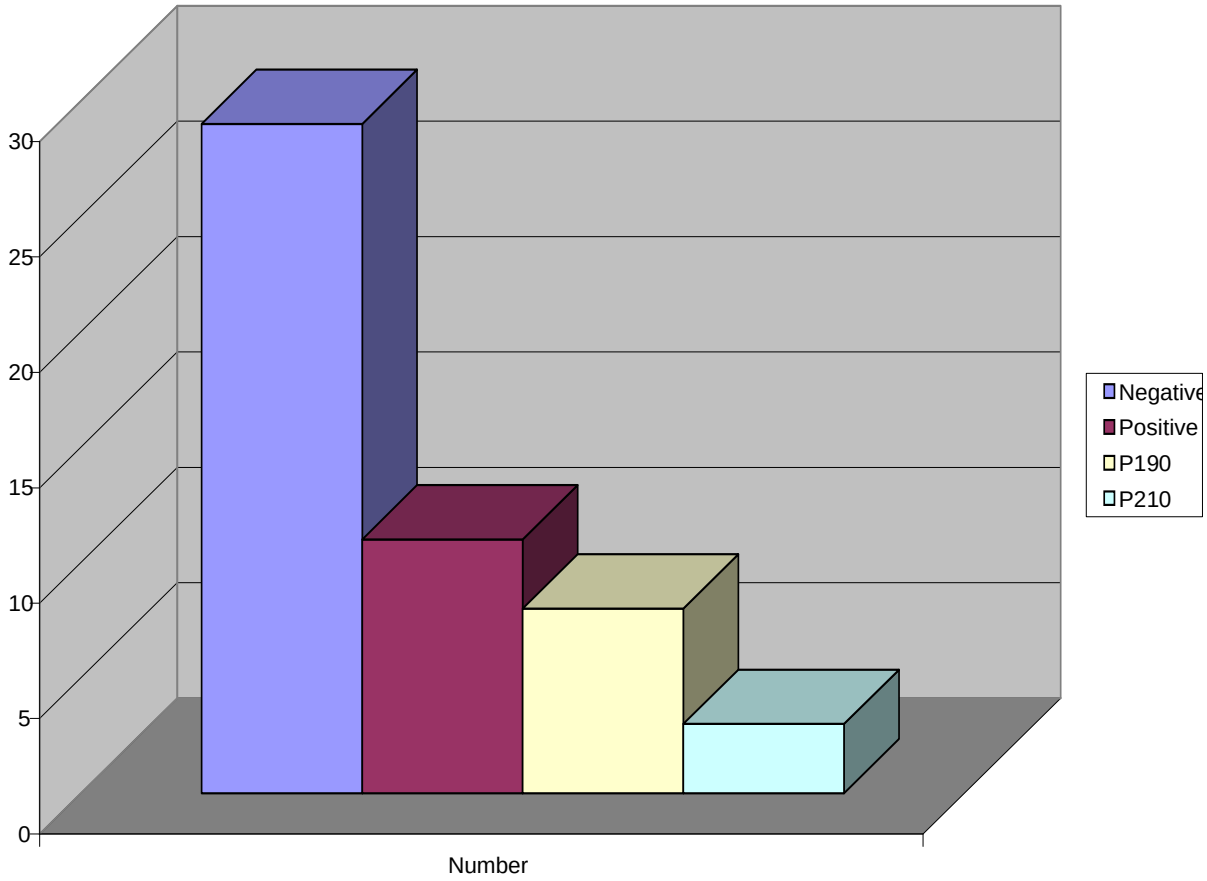

Figure (11): BCR-ABL fusion gene.

Table (13): Initial response to treatment.

	Initial response to treatment	
	Count	**%**
CR	25	62.5%
Not evaluated	7	17.5%
No CR	8	20%

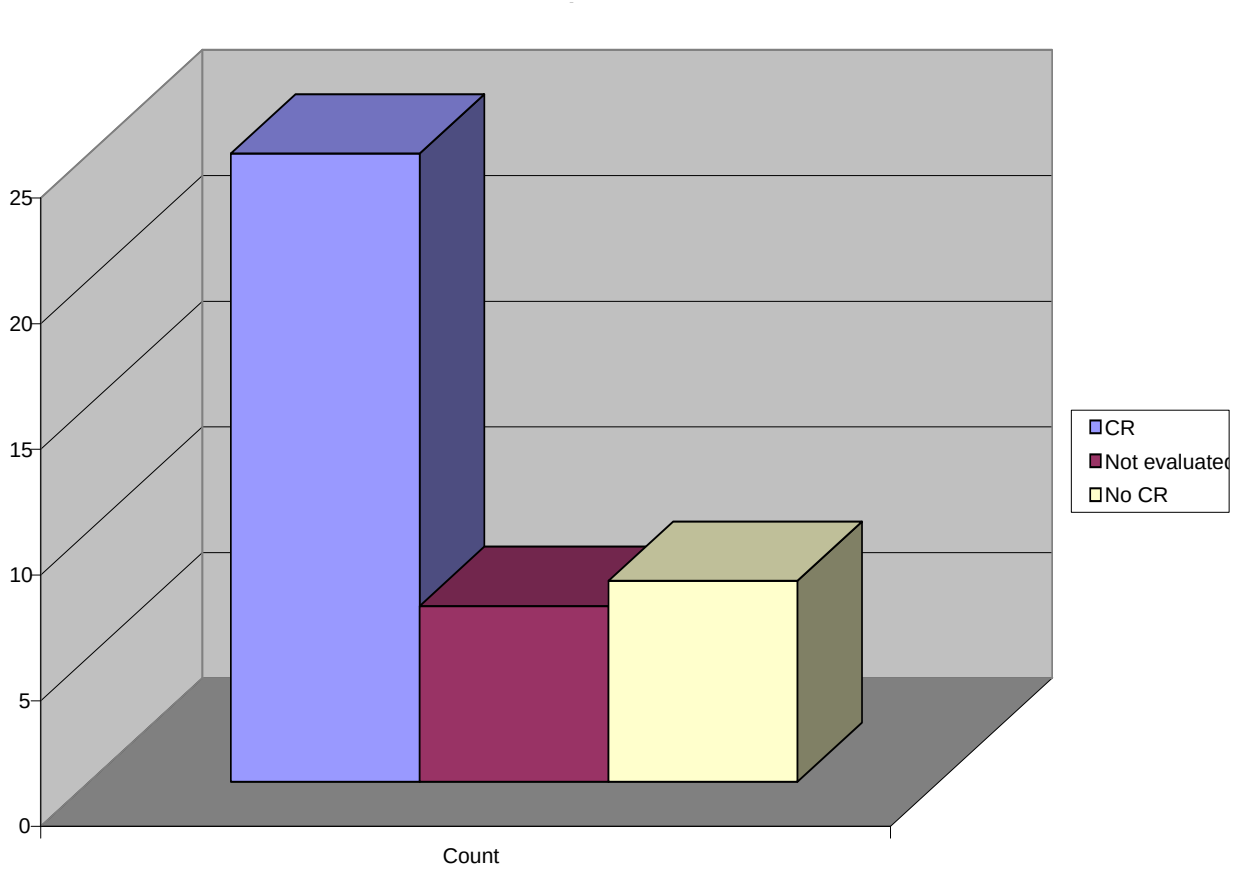

Figure (12): Initial response to treatment.

Table (14): Distribution of overall risk.

	Overall risk	
	Count	**%**
High	18	45%
Standard	11	27.5%
Very high	11	27.5%

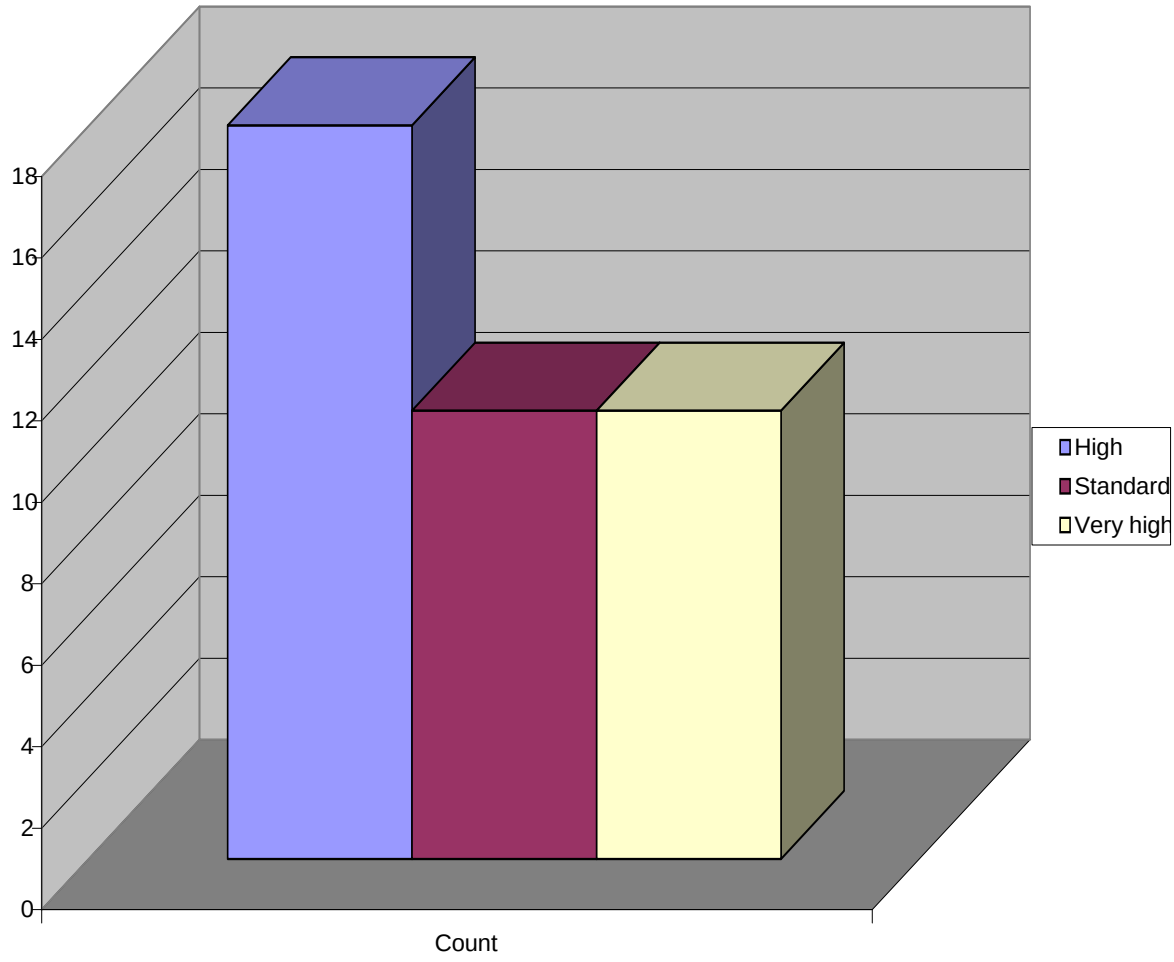

Figure (13): Overall risk.

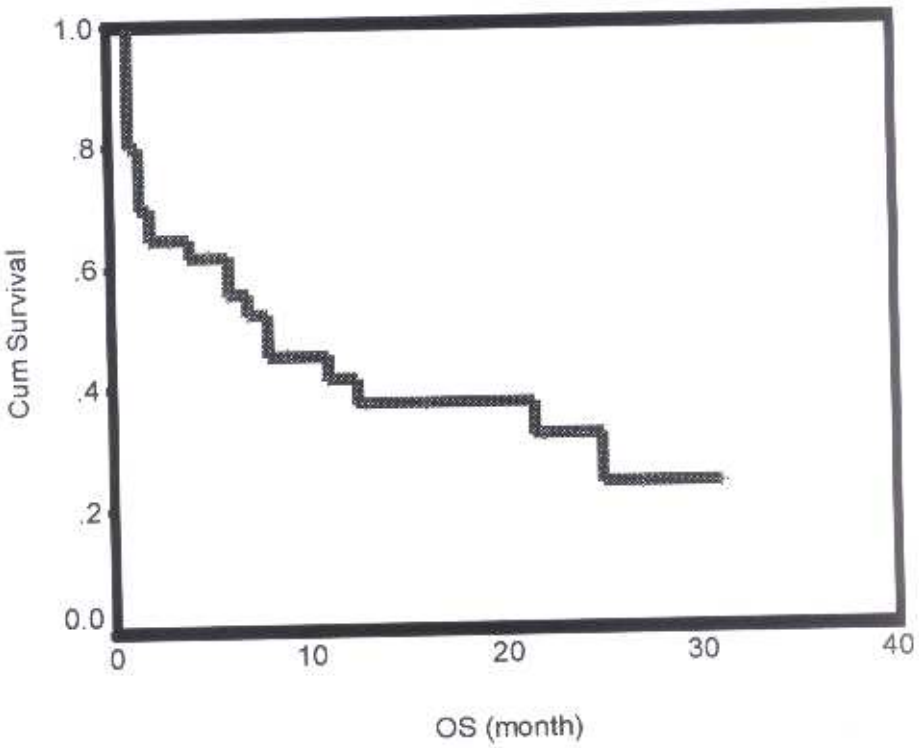

Figure (14): Overall Survival

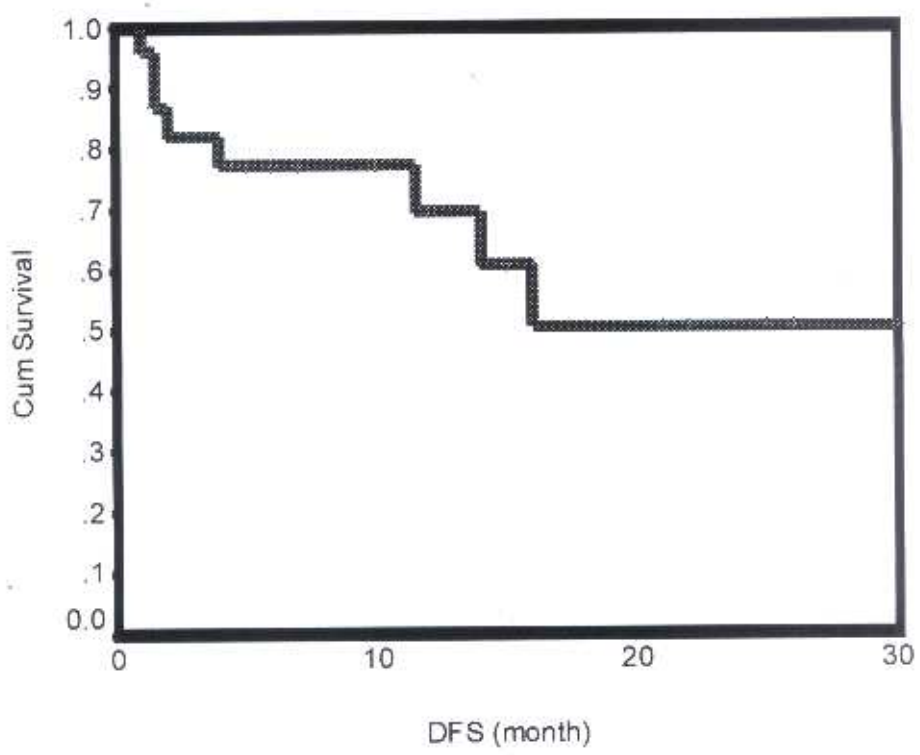

Figure (15): Disease free survival.

Table (15): Number and percentage of relapse rate.

	Relapse rate	
	Count	**%**
No	17	68%
Relapse	8	32%

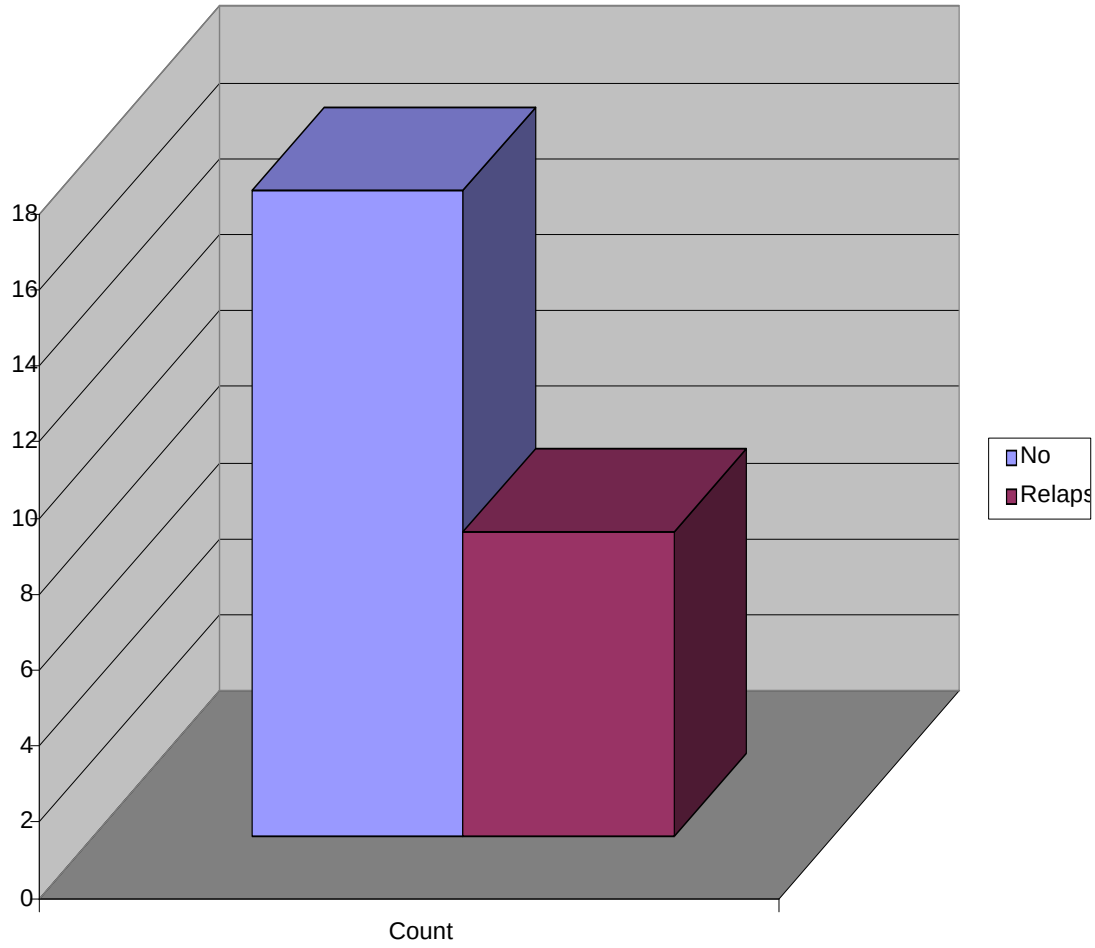

Figure (16): Number and percentage of relapse rate

Table (16): The correlations to initial response to treatment

Initial response to treatment							
Character	**CR**		**NE**		**No CR**		**P value**
	Count	**%**	**Count**	**%**	**Count**	**%**	
Age							
< 50 y	23	92%	7	100%	6	75%	0.24
> 50 y	2	8%			2	25%	
Sex							
Male	17	68%	5	71.4%	5	62.5%	0.93
Female	8	32%	2	28.6%	3	37.5%	
Overall risk							
High + Very high	17	68%	2	28.6%	1	12.5%	0.56
Standard	8	32%	5	71.4%	7	87.5%	
BCR-ABL							
Negative	19	76%	5	71.4%	5	62.5%	0.76
Positive	6	24%	2	28.6%	3	37.5%	
CSF examination							
Negative	19	76%	7	100%	8	100%	0.12
Positive	6	24%	-	-	-	-	
TLC							
< 30.000	14	56%	4	57.1%	2	25%	0.29
> 30.000	11	44%	3	42.9%	6	75%	
Immunophenotype							
C-ALL + Pre-B	20	80%	5	71.4%	6	75%	0.85
Pro-B	-	-	1	14.3%	1	12.5%	
T-ALL	5	20.%	1	14.3%	1	12.5%	

CR = complete remission No CR = no complete remission NE = not evaluated

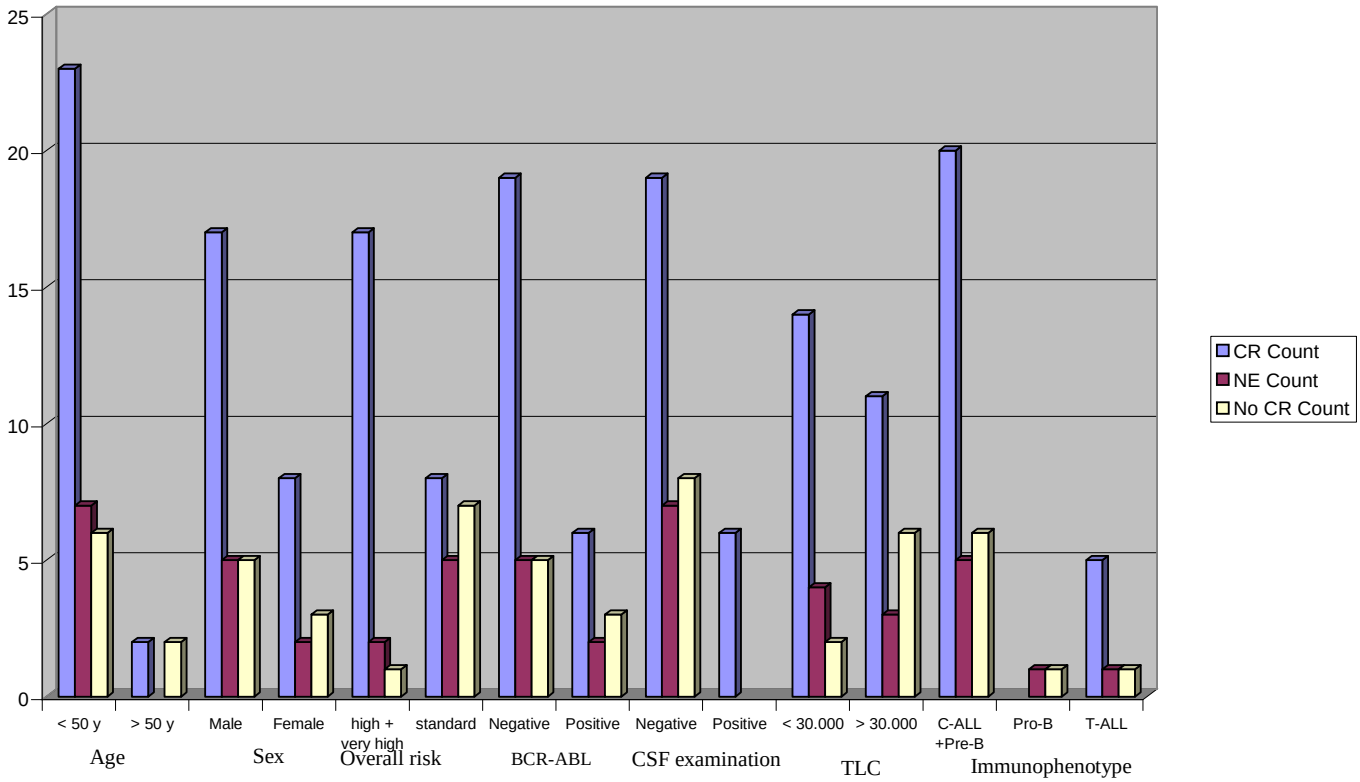

Figure (17): The correlations to initial response to treatment

Table (17): The correlations to BCR-ABL fusion gene

BCR-ABL fusion gene					
Character	**Negative**		**Positive**		**P value**
	Count	**%**	**Count**	**%**	
Age					
< 50y	26	89.7%	10	90.9%	1.00
> 50 y	3	10.3%	1	9.1%	
Sex					
Male	18	62.1%	9	81.8%	0.23
Female	11	37.9%	2	18.2%	
TLC					
< 30.000	15	51.7%	5	45.5%	1.00
> 30.000	14	48.3%	6	54.5%	
CSF examination					
Negative	24	82.8%	10	90.9%	1.00
Positive	5	17.2%	1	9.1%	
Immunophenotype					
C-ALL + Pre-B	20	69%	11	100%	0.21
Pro-B	2	6.9%	-	-	
T-ALL	7	24.1%	-	-	

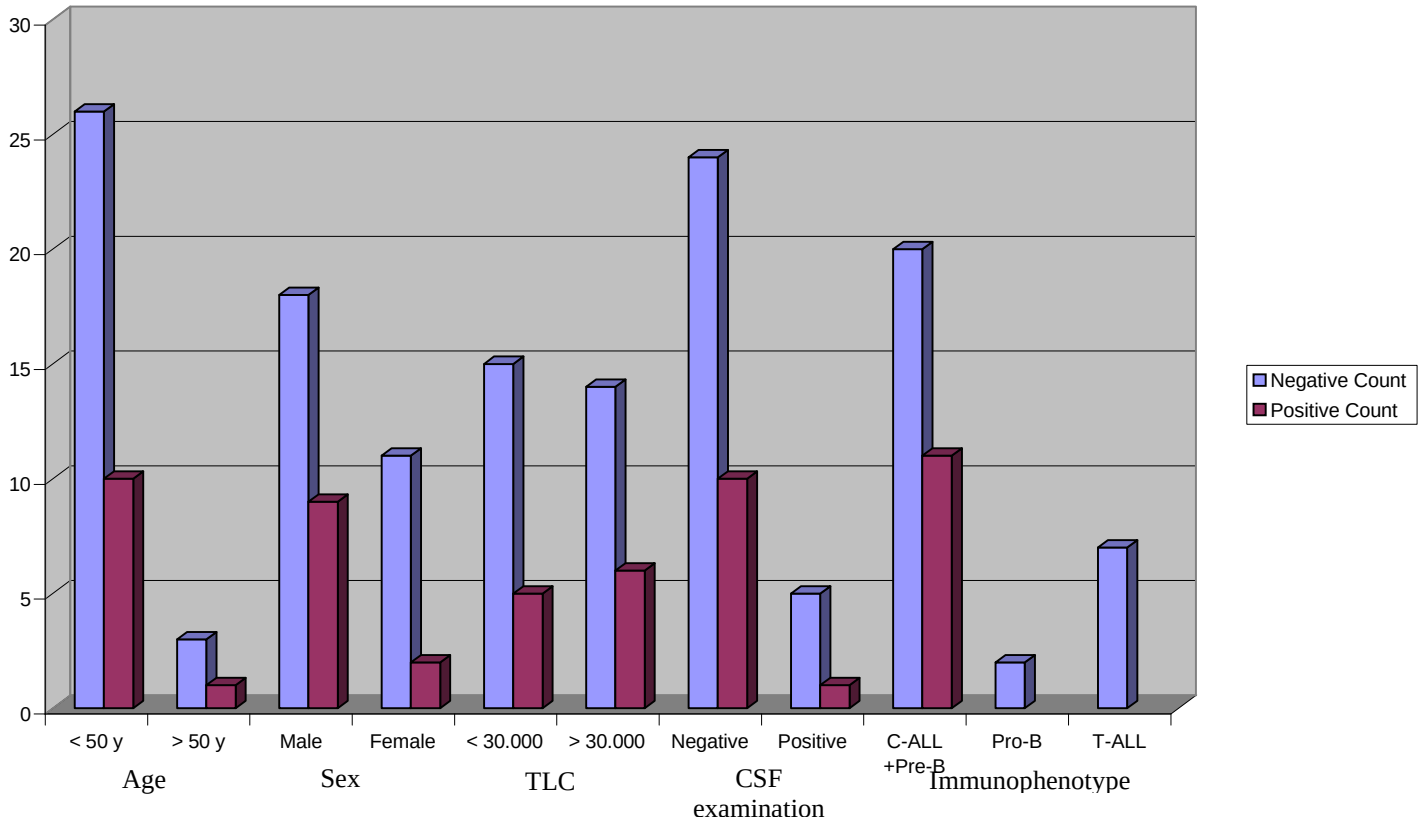

Figure (18): The correlations to BCR-ABL fusion gene.

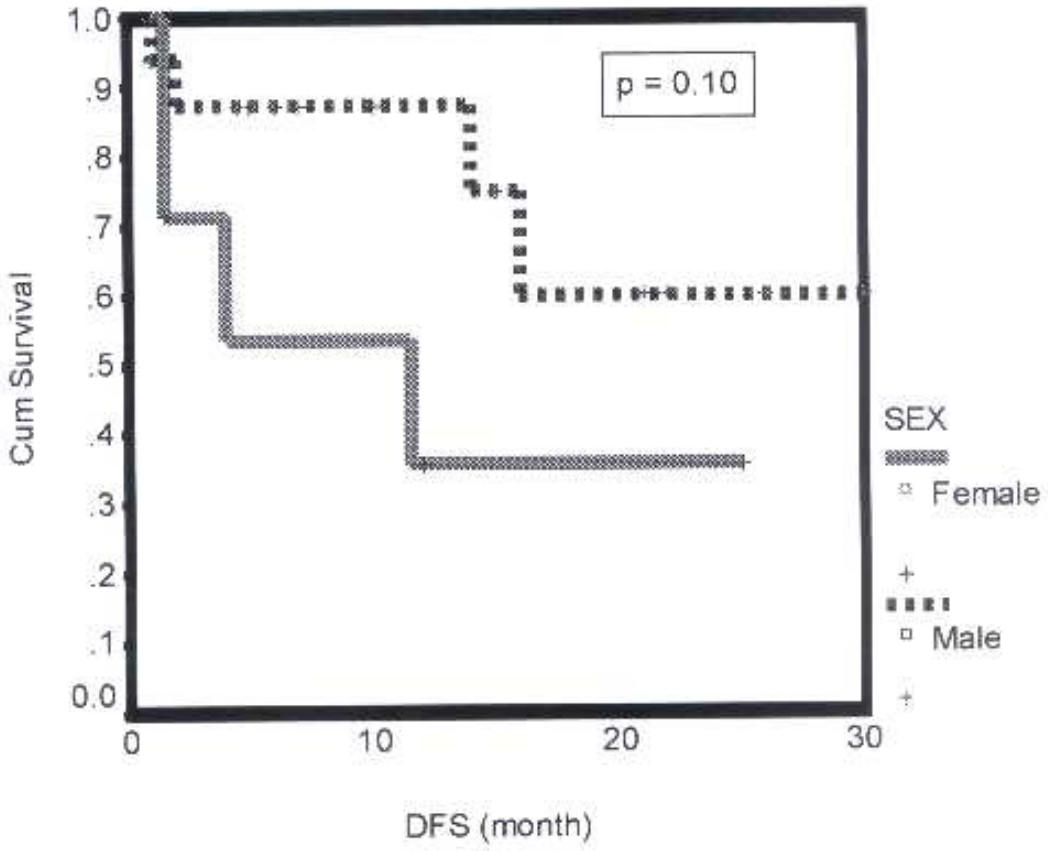

Figure (19): Disease free survival according to sex.

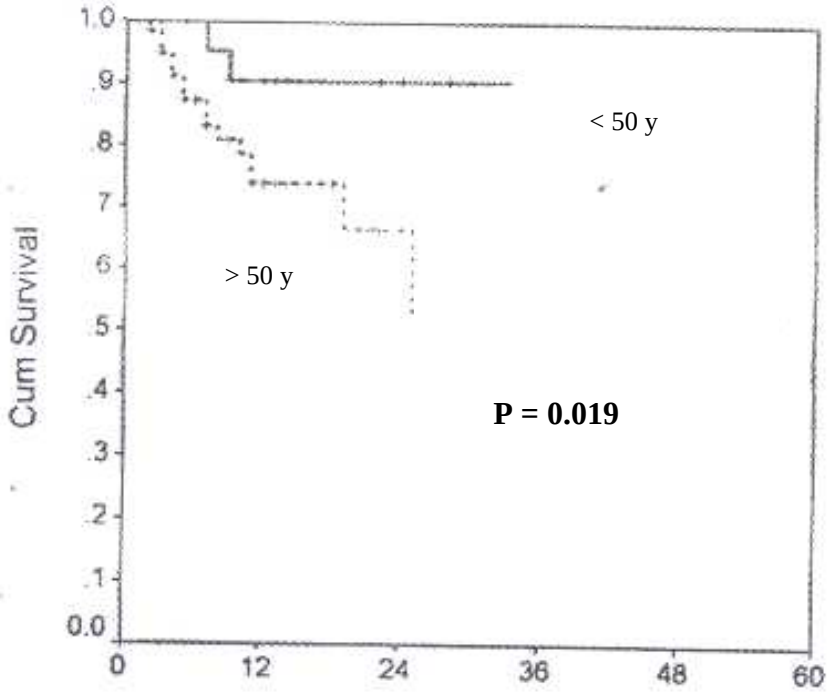

Figure (20): The correlation between disease free survival and age.

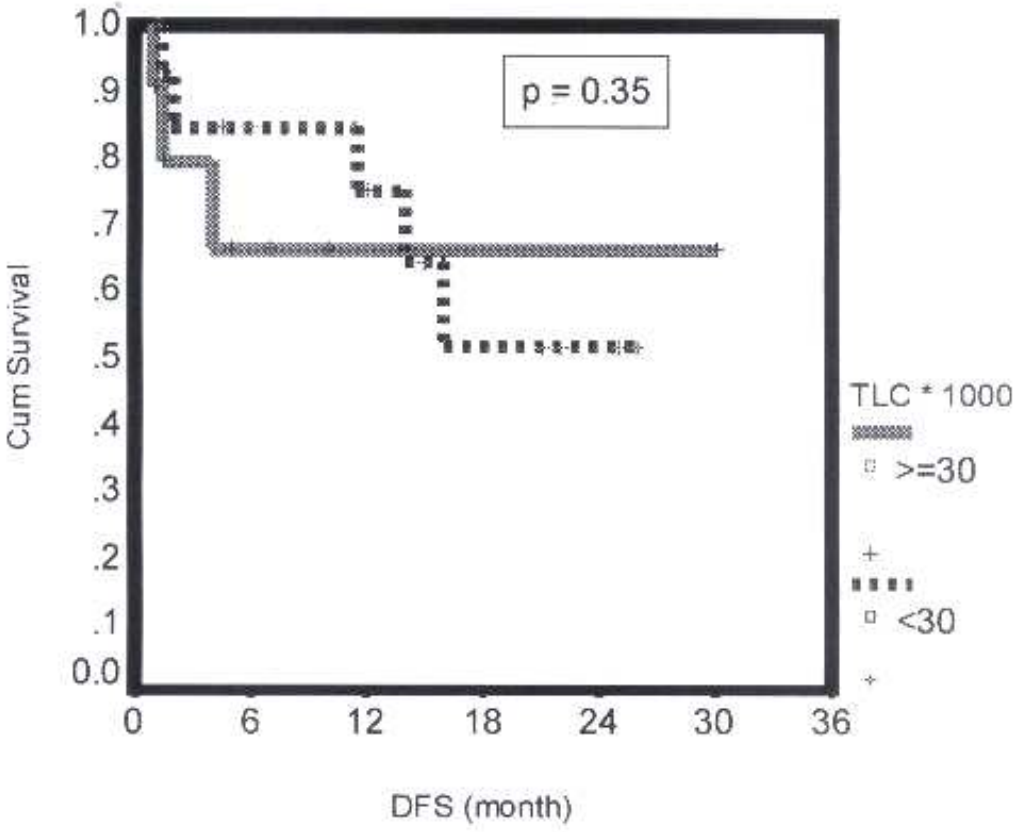

Figure (21): Disease free survival according to TLC.

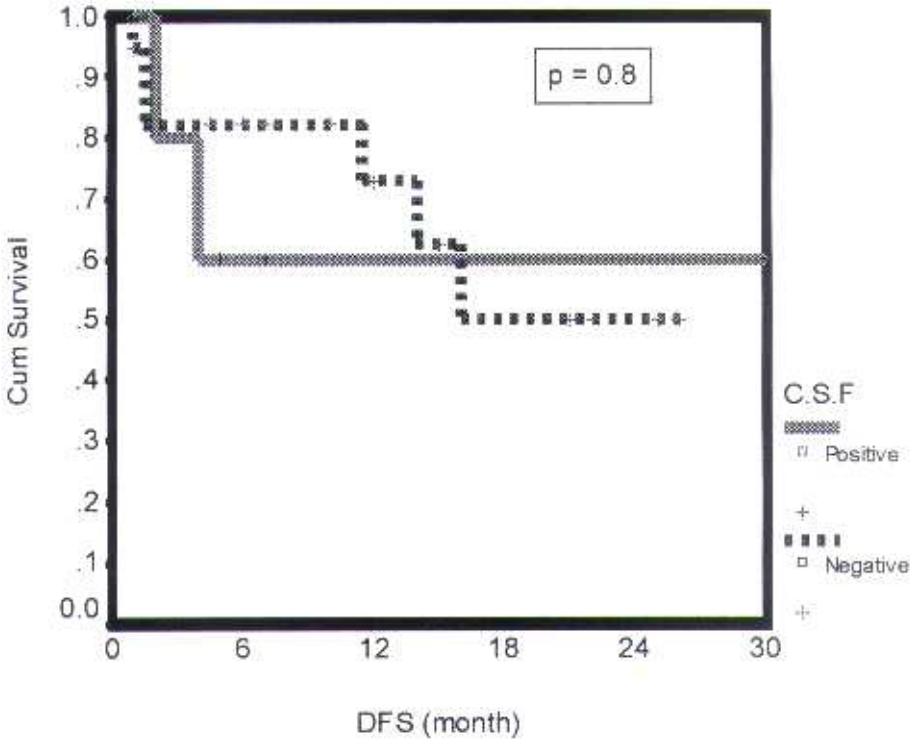

Figure (22): Disease free survival according to CSF.

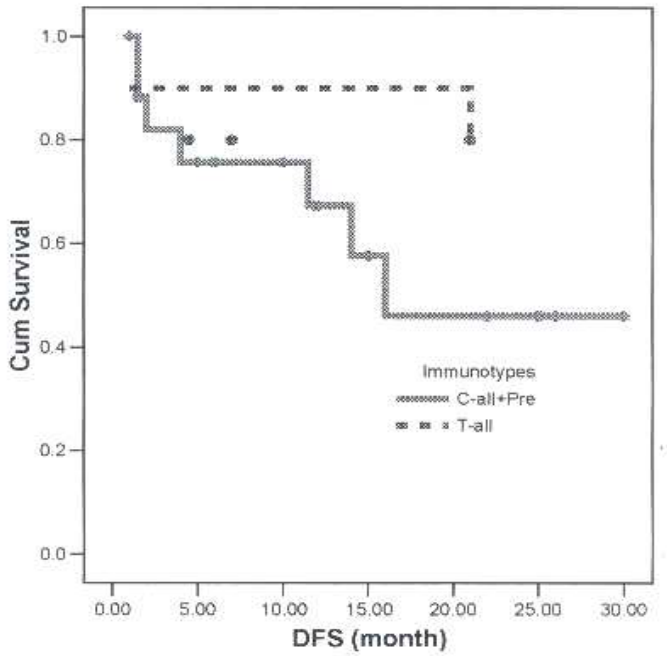

Figure (23): Disease free survival according to immunophenotype.

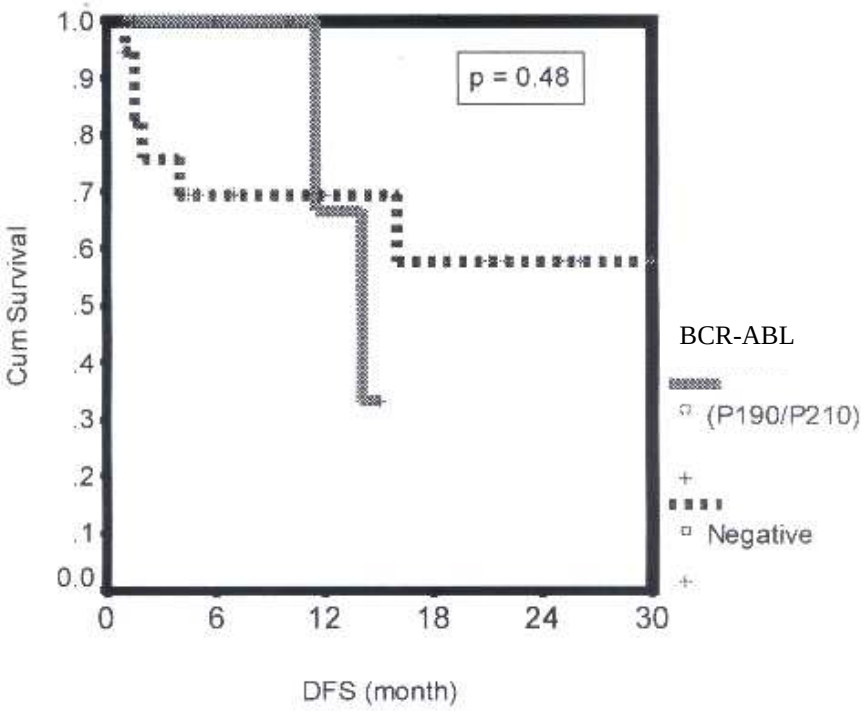

Figure (24): Disease free survival according to BCR-ABL result.

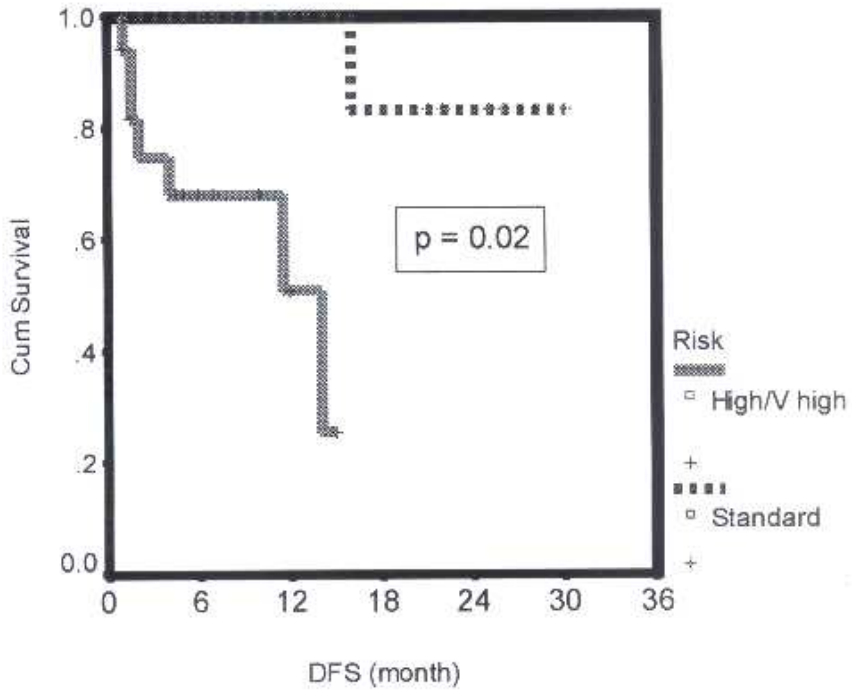

Figure (25): Disease free survival of standard risk group versus others

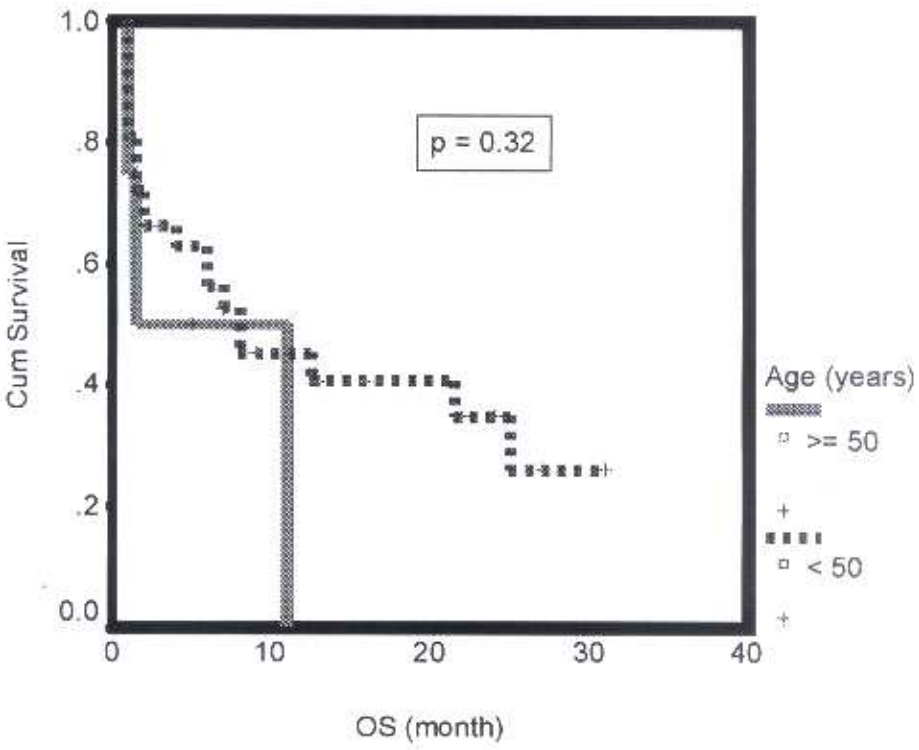

Figure (26): Overall survival according to age.

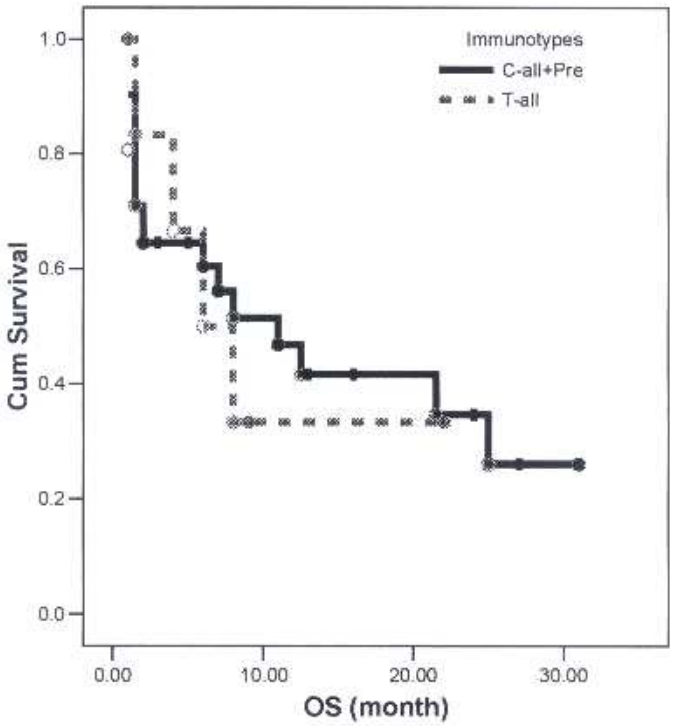

Figure (27): Overall survival according to immunophenotype.

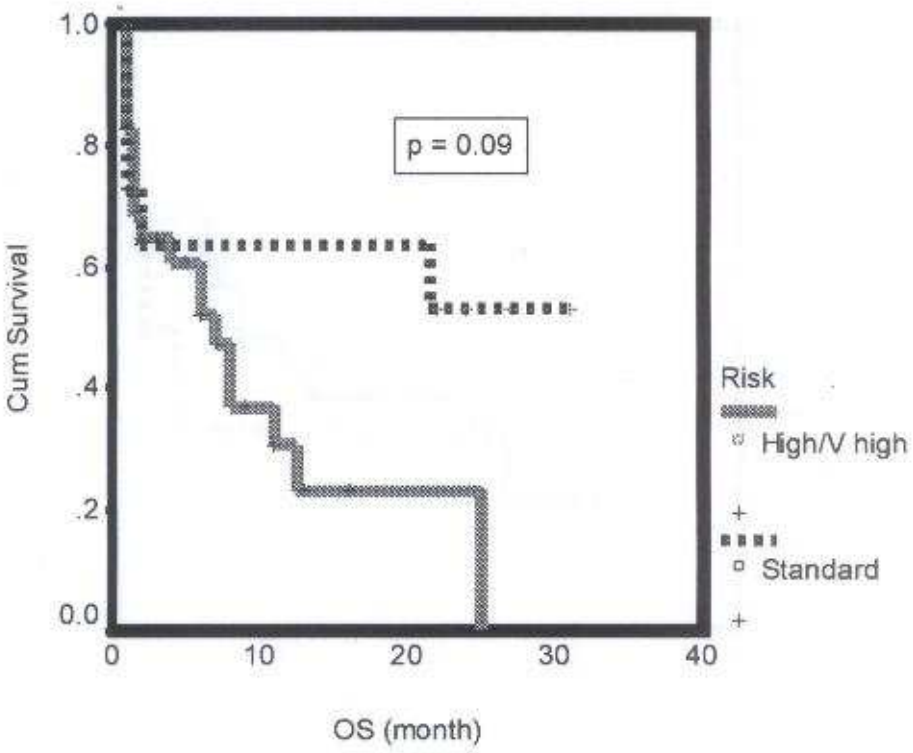

Figure (28): The correlation between overall survival and total overall risk