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ISRCTN12539707 **https://doi.org/10.1186/ISRCTN12539707**

The role of the P-53 gene and the P-53 protein in non-Hodgkin malignant lymphomas

Submission date

08/11/2022

Registration date

12/11/2022

Last edited

05/03/2023

Recruitment status

No longer recruiting

Overall trial status

Completed

Condition category

Cancer

✓ **Retrospectively registered**

✓ Study completed

Plain English Summary

Background and study aim

P-53 gene mutations are the most common genetic abnormalities of cancer. They have been extensively studied in various mature B-cell malignancies, including chronic lymphocytic leukemia (CLL). In recent years, more attention has been paid to the importance of the p53-expressed protein in CLL, and a combination with low survival and non-response to classical conventional chemotherapy, due to mutations in the p53 gene, with progression to Richter Syndrome. Identifying different p53 gene mutations is very important because these mutations have an impact on the patient's clinical course in CLL.

Who participated

Patients with CLL-B who were hospitalized in the Hematology departments of the Targu Mures Oncology Institute and Cluj-Napoca, Emergency County Hospital Targu Jiu, between November 2016 and September 2019-2020.

What does the study involve?

Participants undergo a complete physical examination and laboratory blood tests for p53 protein levels are measured at a single timepoint.

What are the possible benefits and risks of participating?

-P-53 Gene mutations are the most common genetic abnormalities of cancer. They have been extensively studied in various mature B cell malignancies, including Chronic Lymphocytic Leukemia, (CLL).

- In recent years, more attention has been paid to the importance of the p53-expressed protein in CLL, and a combination with low survival and non-response to classical conventional chemotherapy, due to mutations in the P-53 gene, with progression **to Richter Syndrome.**

-Identifying different P-53 gene mutations is very important because these mutations have an impact on the patient's clinical course in CLL with the p-53 protein mutant isoform.

Where is the study run from?

Titu Maiorescu University of Bucharest, Faculty of General Nursing, (AMG), Targu Jiu Branch, City Targu Jiu, Romania

When is the study starting and how long is it expected to run for?

October 2016 to March 2020

Who is funding the study?

Investigator initiated and funded

Who is the main contact?

Dr Aurelian Udristioiu, aurelianu2007@yahoo.com

Trial website; http://aurelianudristioiu.blogspot.com

Contact information

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Additional identifiers; None

EudraCT number; None

Nil known; None

IRAS number

ClinicalTrials.gov number: None

Nil known; None

Protocol/serial number:

Dr. AURELIAN UDRISTIOIU; Web of Science Researcher ID: I-3687-2019,

UEFISCDI ID (UEF-iD): U-1900-063Y4656

Study information: Scientific title; The role of the P-53 gene and the P-53 Protein in the oncogenesis of non-Hodgkin malignant lymphomas

Acronym

None

Study hypothesis

P-53 gene mutations are the most common genetic abnormalities of cancer. They have been extensively studied in various mature B-cell malignancies, including chronic lymphocytic leukemia (CLL). In recent years, more attention has been paid to the importance of the p53-expressed protein in CLL, and a combination with low survival and non-response to classical conventional chemotherapy, due to mutations in the p53 gene, with progression to Richter Syndrome. Identifying different p53 gene mutations is very important because these mutations have an impact on patients' clinical course in CLL with the p53 protein mutant isoform.

Ethics approval

Ethics approval statement, patient consent statement, and permission to reproduce material from other sources: are not applicable.

Study design

Scope

This paper aimed to highlight the stages of Chronic Lymphocytic Leukemia type B (CLL-B), which did not meet the standard treatment criteria for malignant haematological diseases due to mutations in the P-53 gene, with progression to Richter Syndrome.

Method

The frequency of p-53 protein expression in 85 patients diagnosed with CLL was analyzed by the Enzyme-Linked Immune-Absorbent Assay (ELISA) technique to investigate the relationship of this protein to the stage of the disease, as well as the impact on response to treatment and survival. Cell extracts $10^3 \times 10^3$/L in 100 µl lysis buffer were applied to ELISA plates coated with PAb 240 capture antibody.

Results

The frequency of increased positivity of the protein with the modified structure, the isoform, p-53 in type CLL-B, was 17% in the 85 cases initially included in the study. The percentage of p-53 protein isoforms, positive above normal value, with very high values, 50, 60, respectively 140 µg / dl was found in the percentage of 3.5% with the transformation of CLL into non-Hodgkin's malignant lymphomas, (NHL) type Diffuse Large Lymphoma, (DLL) or in Mantle Lymphoma, from Richter syndrome.

Conclusions

In the context of a heterogeneous condition such as LL-B, this cheap and safe method, ELISA seems to provide a useful prognostic tool capable of identifying patients who can be considered candidates for therapeutic, targeted, personalized strategies.

Observational cohort study

Primary study design

Observational; The cases were classified as CLL with> 5000 lymphocytes in absolute value, present at the cytological examination of the blood smear, from the peripheral blood or LLC with less than 10% prolymphocytes based on the peripheral blood smears May-Grunwald Giemsa, stained.

Secondary study design

Immunophenotyping The diagnosis of CLL was confirmed by immune phenotyping. All samples that entered the study were lymphocytes with positive $CD19^{+}$, $CD20^{+-}$, $CD5^{+}$ and $CD23^{+}$ cell receptors. The CD38 + receptor was considered positive if the distinct lymphocytes of the population showed a higher intensity of staining than the granulocytes in the sample and were associated with the presence of protein ZAP-70.

Cohort study: After analyzing the 85 LLC samples, in different stages of disease evolution, starting with stage zero (stay and watch) and up to stage IV, 20 patients were selected, eligible for this study, to be investigated for the detection of p-53 protein isoforms responsible for resistance to oncological treatments of the disease with Rituximab, Cyclophosphamide, Doxorubicin hydrochloride, Vincristine sulfate (Oncovin), and Prednisone, (R-CHOP), after 2 cycles of relapses, representing a group of 16 men and 4 women aged 39-85 years.

Trial setting;

The presence of protein isoforms in the studied group was calculated as a percentage of 17%, and the un-favourable evolution and transformation of Chronic Lymphocytic Leukemia in the stages studied in Diffuse Large Lymphoma was calculated to be in a percentage of 3.5% of the studied cases, as in the meta-analyzes from the specialized literature, Diffuse Large lymphoma is considered a rare disease.

Other Trial type

None

Diagnostic

Patient information sheet

Chronic lymphocytic leukaemia (CLL), the most common leukaemia in adults and the elderly, is characterized by clinical stages with unpredictable evolutions regardless of age or sex, men or women. In the last decade, through various methods of paraclinical investigations, several features have been identified that can predict the evolution of the disease or the survival of patients with CLL. An increasing amount of evidence suggests that anticancer drugs exert their action, at least in part, by triggering apoptosis. Among the factors that control and regulate the process of apoptosis, the p-53 protein is considered to be of major importance.

In relapsed CLL, p-53 protein function is inactivated by P-53 gene mutations that lead to the production of an isoform p53 protein with modified structure by amino acid substitution, in poly-morpho-variant forms, with increased stability in type B lymphocytes,

Condition

Genomic analysis showed that in most patients, Richter syndrome is derived from the initial predominant CLL clone through a linear path of genetic evolution involving the development of additional genetic lesions in extra poetic tissues by migration of bone marrow stem cells including bone marrow events. activation of the MYC oncogene and disruption of the functionality of the P-53 gene. Finally, Richter Syndrome has been described in some patients who received the BCL2 venetoclax or Ibrutinib inhibitor although the exact prevalence and characteristics of this transformation remain to be determined

Non-Hodgkin malignant lymphomas

Intervention

The antibody is suitable for the techniques: ICC / IF and ELISA. Research antibody PAb 1620 has been reported to be specific for the conformation of the normal p-53 protein, (Cook and Milner 1990) and PAb 240 antibodies bind specifically to denatured p-53 protein, i.x. p53 in the "mutant" conformation

Complete physical examination: In patients diagnosed with CLL-B, symptoms such as frequent cough, night sweats, and retrosternal pain were evaluated. Clinical examination and ultrasound revealed lymphadenopathy and/or splenomegaly, with an enlarged spleen.

Laboratory examinations: Hemoleukogram with 5 Diff and cytological examination of the blood smear on the peripheral blood in the May Grunwald-Geimsa staining, and bone marrow puncture, BM with medullary forcing. The cases were classified as CLL with >5000 lymphocytes in absolute value, present at the cytological examination of the blood smear, from the peripheral blood or LLC with less than 10% prolymphocytes based on the peripheral blood smears May-Grunwald Giemsa, stained.

Immunophenotyping: The diagnosis of CLL was confirmed by immune phenotyping. All samples that entered the study were lymphocytes with positive $CD19^{+}$, $CD20^{+-}$, $CD5^{+}$ and $CD23^{+}$ cell receptors. The CD38+ receptor was considered positive if the distinct lymphocytes of the population showed a higher intensity of staining than the granulocytes in the sample and was associated with the presence of protein ZAP-70.

A sandwich ELISA colorimetric quantitative method was used for direct detection of the p53 isoform protein, the product of gene p53: Specificity: human p53 protein (aa20-25); Format: Purified product: Monoclonal antibody clone: Isotype DO-1: IgG2a. The antibody is suitable for the techniques: ICC / IF and ELISA. The research antibody PAb 1620 has been reported to be specific for the conformation of the normal p-53 protein, and PAb 240 antibodies bind specifically to denatured p-53 protein. Compatible sample types: cell culture supernatants, plasma, serum; solid support: 96-well microplate; firm: Ray Biotech Life, Inc.

Plasma is collected from patient samples using vacutainers with EDTA or heparin as an anticoagulant by centrifuging the samples for 15 minutes at 4500 rpm (280 G). After the blood

sample has been centrifuged and its plasma has been separated from red blood cells, the plasma is fractionated into four distinct fractions placed on a layer of white blood cells (lymphocytes).

With a pipette, a quantity of 100 µl is extracted from the lymphocyte ring. The extracted lymphocytes are introduced into 25 ml cuvettes with a 3 ml wash buffer medium for washing the lymphocytes. Washing is done three times, once after 10 minutes at 1500 revolutions/minute and twice for 10 minutes at 1000 revolutions/minute. Lysis of washed lymphocytes is done with a Mini Wave Smart Laboratory microwave. In the case of small-volume samples, a preliminary step dilution, such as 1: 5 or 1:10, can be performed using PBS buffer (0.02 mol / L pH 7.0-7.2) as the diluent. The final dilution should always be done using the same buffer used to dilute the Standards.

This analysis is based on the sandwich ELISA principle. Each well of the microtiter plate was pre-coated with a specific target capture antibody. Standards or samples are added to the wells and the target antigen, in this case, the p53 protein, binds to the capture antibody.

Summary of test procedure:

1. Prepare all reagents, samples and standards: add 100 µl of sample, standard or blank to each well and incubate for 2.5 hours at room temperature or overnight at 4 °C

2. Aspirate the volume of liquid initially added and wash three times

3. Add 100 µl of biotinylated detection antibody (biotin detection antibody) and incubate for 1 hour at room temperature

4. Vacuum and wash three times

5. Add 100 µl of HRP-streptavidin conjugate and incubate for 45 minutes at room temperature

6. Add 100 µl of TMB substrate and incubate for 30 minutes at 37 °C

7. Add 50 µl of stop solution

8. Read immediately at 450 nm wavelength

A series of dilutions of the positive control standard must be performed in duplicate or triplicate, the last well in each series being the negative control sign. The tests should also be performed in duplicate or in triplicate. Unknown samples should function as dilution series to identify the optimal dilution that produces an OD value in the OD range of the standard control dilution series.

Data analysis: Prepare a standard curve from the serial dilution data with concentration on the x-axis (logarithmic scale) from the absorption on the Y-axis (linear). Peroxidase (HRP) and alkaline phosphatase (ALP) are the two most widely used enzymes for detection in ELISA tests. Measure the yellow color of nitrophenol at 405 nm after 15-30 minutes of incubation at room temperature and stop the reaction by adding an equal volume of 0.75 M NaOH.

Intervention type

Genetic Phase

The antibody is suitable for the techniques: ICC / IF and ELISA. Research antibody PAb 1620 has been reported to be specific for the conformation of the normal p-53 protein, (Cook and Milner 1990) and PAb 240 antibodies bind specifically to denatured p-53 protein, i.x. p53 in the "mutant" conformation

Drug names; Not applicable

Primary outcome measure

Results obtained by the ELISA method

After analyzing the 85 LLC samples, in different stages of disease evolution, starting with stage zero (stay and watch) and up to stage IV, 20 patients were selected, eligible for this study, to be investigated for the detection of p-53 protein isoforms responsible for resistance to oncological treatments of the disease with Rituximab, Cyclophosphamide, Doxorubicin hydrochloride, Vincristine sulfate (Oncovin), and Prednisone, (R-CHOP), after 2 cycles of relapses, representing a group of 16 men and 4 women aged 39-85 years.

Male results: Protein concentration in p-53 / µg / dL: 20, 15, 18, **40**, 10, 12, 14, **60,** 30, 10, 13, 15, 5, 10, 15, 12.

Women's results; Protein concentration p-53 / µg / dL: **140**, 30, 13, 10.

Normal values of normal cell lines on equipment: ELISA = 0.25-0.5 µg / dL, or 2.5- 5ng/mL, [7].

Statistical Interpretations: Concentration of the p-53 isoform protein representing the P-53 mutant gene in 17 cases, after excluding the 3 out-line cases present in the study, were calculated at the mean value of 14.8 µg / dL, with Standard Deviation, STDEV = 6.46, CV = 0.4% and the probability index (NORMDIST), "P" was calculated in the value of p = 0.079. Multivariate (MA) analyzes were performed for OS on any significant variables at the level of P <0.20 at univariate analysis, with the gradual elimination of insignificant variables.

The presence of protein isoforms in the studied group was calculated as a percentage of 17%, and the unfavourable evolution and transformation of Chronic Lymphocytic Leukemia in the stages studied in Diffuse Large Lymphoma was calculated to be in a percentage of 3.5% of the studied cases, as in the meta-analyzes from the specialized literature, Diffuse Large lymphoma is considered a rare disease.

The comparison between the categorical variables and the numerical variables was performed using the exact Fisher test.

Fisher test

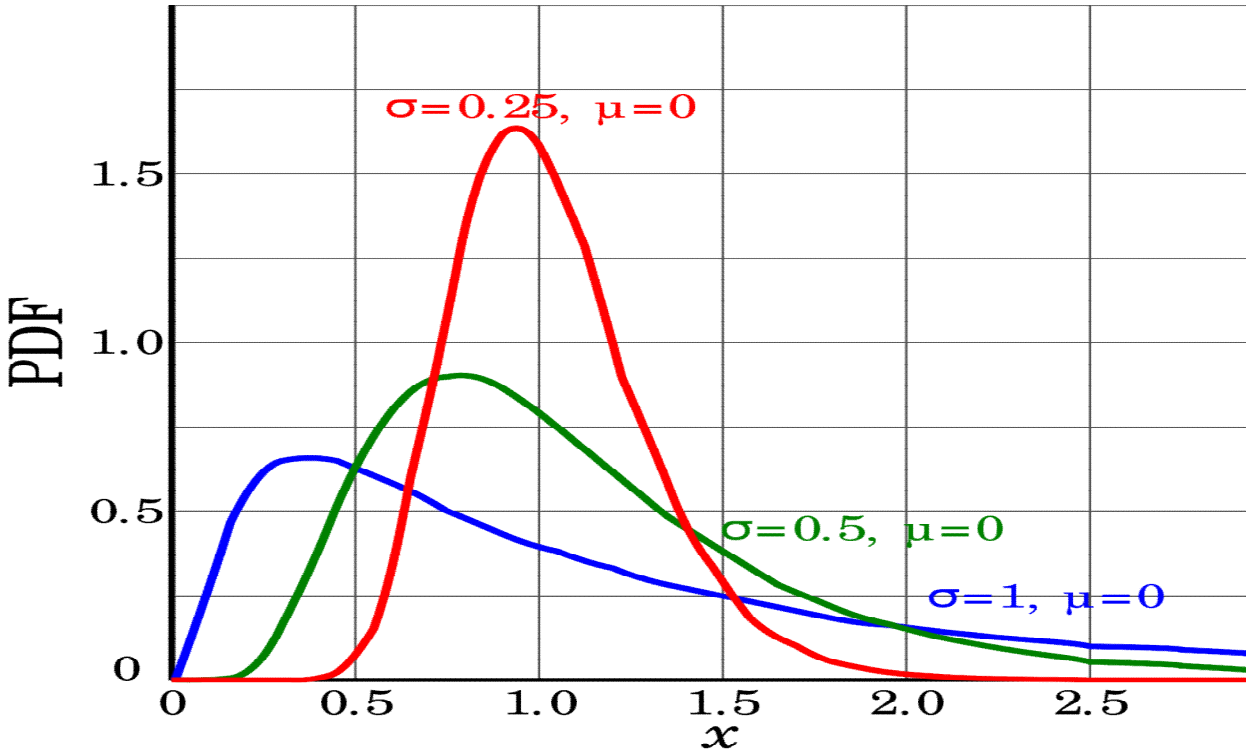
Number of patients in the study group = 85

Eligible 20 a + b = 3 + 17

Ineligible 65. c + d = 5 + 60

Total a + c b + d a + b + c + d (= n) = 85

p = {a + b} \ {a} x {c + d} \ {c}: [{n} \ {a + c}] = 20 / 3x65 / 5 / 8,125 = 10.2 = 1.1 log in base 10, result that we indicate that all statements are true. {\ frac {(a + b)! (c + d)! (a + c)! (b + d)!} {a! b! c! d! n!}, in the calculations made by the statistical software where (n / k), is the binomial coefficient and the symbol "!" show that factorial**, {Graphic 1}.**



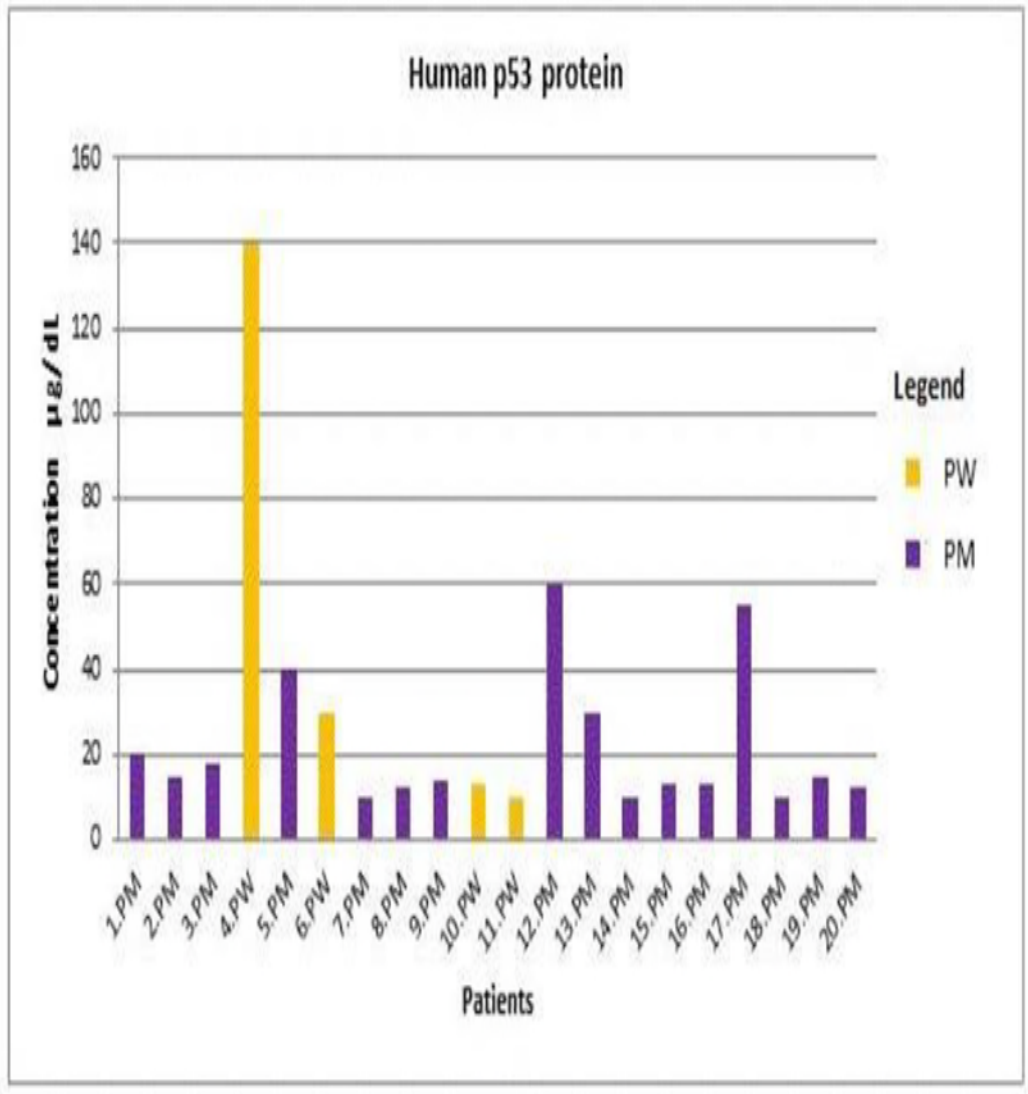
Graphic 1. All expressions under the sign of the logarithm are indicated as positive which is under the sign of the logarithm and as a basis, the remaining expression below the logarithm is positive, in value 1.1 and indicates a linear relationship between the 2 variables.

ANOVA test, concentration frequency, [Table 1].

The interval of concentration **(i)**	**The middle classes (m)**	**Frequency of concentration (f)**
30-32	31	1
27-29	28	0
24-26	25	0
21-23	22	0
18-20	19	2
15-17	16	2
12-14	13	8
9-11	10	4
6-8	7	0
3-5	4	1 17%

Concentrations of p-53 / μg / dL isoform protein in peripheral blood in CLL with deletions and mutations in chromosomes 13-14q, 11-22q, 17p and 6-7q:0, 15, 18, 40, 10, 12, 14, 60, 30, 10, 13, 13, 5, 10, 15, 12, 140, 30, 13, 10. Very high pathological values in the 3 cases of p-53 were calculated in 2 men with the value of

60 µg / dL, respectively at 40 µg / dL, and in the case of females it was calculated in the amount of 140 µg / dL the frequency of chronic lymphocytic leukaemia with transformation into Diffuse Large Lymphoma, (DLL), **[Graphic 2].**



P1	M
P2	M
P3	M
P4	F
P5	M
P6	F
P7	M
P8	M
P9	M
P10	F
P11	F
P12	M
P13	F
P14	M
P15	M
P16	M
P17	M
P18	M
P19	F
P20	M

Graphic 2. Very high pathological values in the 3 cases of p-53 were calculated in 2 men with the value of 60 µg / dl, respectively at 40 µg / dl, and in the case of females it was calculated in the amount of 140 µg / dl, the frequency of chronic lymphocytic leukaemia with transformation into Diffuse Large Lymphoma, (DLL).

CLL – Age patients	CLL stage I/II, (n=17 patients) P-53 protein concentration in reactive lymphocytes B	CLL stage III/IV (n = 3 patients] Percentage of p53 isoform proteins	p-value
The age of patients with CLL ranges from 39 to 85 years.	*The average p-53 protein concentration in CLL, 16.76 µg / dL*	*P-5 isoform proteins with elevated values were present in 15% (3 of 20 cases 2 Men = 50µg / dL and 60µg / dL, respectively 1 Female = 140µg / dL*	*p-value 0.034*
Haematological parameters in peripheral blood	***Mean values of haemogram:*** *No. Leukocytes = 35-50 x 10³/µL Hb = 11.8g / dL; Platelet = 140 x 10³/µL Lymphocytes = 65-80%*	*No. Leucocytes = 250-500 x 10³/µL Hb = 8.6g / dL Thrombocytosis = 45x10³/µL Lymphocytes = 85-90%*	*p-value 0.05*

Table 2. Expression of hemogram parameters and p-53 protein concentration in different stages of CLL-B

In some international studies, the immunological characteristics of patients with CLL having p-53 protein positive, were measured by immunohistochemistry, (IHC). In the second part of the study CLL on the stage I/II, (n=47 patients), the P-53 protein isoform concentration in reactive Lymphocyte B, the average p-53 protein concentration in CLL was on average 47 U/m with 16.7% of samples studied, (7 out of 42 cases), Hematological parameters in peripheral blood, Leucocyte number = 35x10³/µL, Hb = 12,2g /dL,

Thrombocyte = 140 x10³/µL, Lymphocytes in peripheral blood = 75-80%. The average p-53 protein concentration in CLL was on average 47 U/m, in CLL the stage III/IV (n = 140 patients] and the percentage of p53 isoform varied from 7-32%.; Hematological parameters in peripheral blood were changed as Leukocytes number = 350 x10³/µL, Hb = 10,8g / dL, Thrombocytes = 80 x 10³/µL, Lymphocytes in peripheral blood = 80-90%; Percent p-53 positive was in percent of 15% [10] **[Table 3].**

CLL – Age patients	**CLL stage I/II, n=47 patients) P-53 protein concentration in reactive Lymphocyte B**	**CLL stage III/IV (n = 140 patients] Percentage of p53 isoform proteins**	***p-value***
The age of patients with LLC, ranges from 52 to 84 years, with an average of 62 years.	*In the samples studied at CLL, it was 16.7% (7 out of 42 cases).*	*The percentage of positive p53 cells varied from 7-32%.*	*0.398*
Haematological parameters in peripheral blood	*No. Leucocyte = 35x x 10³/µL Hb = 12,2g / dL Thrombocyte = 140 x 10³/µL Lymphocytes = 75-80%*	*No. Leukocytes = 350 x10³/µL Hb = 10,8g / dL Thrombocytes = 80 x 10³/µL Lymphocytes = 80-90%*	*0.398*
p53 (+ve) n=7/42	*4/30*	*3/12*	*0.398*
The mean p-53 protein concentration: 27.9 U / ml in healthy people	*The average p-53 protein concentration in CLL was on average 47 U/m*	*Percent p-53 positive = 15%.*	*0.398*

Table 3 Immunological characteristics of patients with CLL having p-53 protein positive measured by IHC

In another international study, 103 LLC cases were investigated for the impact of p53 protein expression with its β and γ isoforms. Interestingly, the relative levels of expression between the p53 protein full length and its β and γ isoforms were significantly altered in LLC even without 17-β13 deletion compared to normal B cells (p = 0.005.) **[Table 4].**

LLC - Patients	**CLL stage I / II, n = 47 patients) P-53 protein concentration in reactive B LymphocyteS**	***CLL stadiul III/IV (n = 140 de pacienți] Procent de proteine izoforme p53***	***p value***
The age of CLL patients ranged from 52 to 84 years, with a mean age of 62 years.	*In the samples studied at CLL, it was 16.7% (7 out of 42 cases).*	*The percentage of p53-positive cells ranged from 7-32%.*	*0.398*
Haematological parameters in peripheral blood	*No. Leukocyte = 35x10³ / dl Hb = 12.2g / dL Thrombocytes = 140 x 10³/µL Lymphocytes = 75-80%*	*Nr. Leukocytes = 350 x10³/µL Hb = 10.8g / dL Thrombocytes = 80 x 10³/µL Lymphocytes = 80-90%*	*0.398*
P53 proteins form, (positive) n = 7/42	*15%*	*25%*	*0.398*

Table 4. Differential expression of p53 isoforms could disrupt p53 response and may contribute to pathogenesis LLC. Differential expression of p53 isoforms could disrupt p53 response and may contribute to LLC pathogenesis, [8].

Between the two methods, ELISA, ICC, the CC, Pearson (r) Correlation Coefficient was calculated according to the following formula:

$$r = \frac{\sum (x - M_x)(y - M_y)}{n * Sx * Sy}$$

where: x, y is the sum of the products between the two variables = 567 and 1313.3, My and My are the averages of the two variables, 38,35 and 27,94, n = the number of subjects in the sample = 20 + 47 = 67, Sx and Sy are the standard deviations of the two variables, 8.25 and 17.35.

CC = (567-16.7) x (1313.3-27.9) / 67 x 8.25 x 17.35.

CC = 550.3 x 12854 / 9.590.2125 = 7.073.556.2 / 9.590.2125 = 0.74

It was observed that “r”, CC obtained (0.74), is also significant at a level of significance higher than p <0.001, respectively 0.034. The (r) Pearson index can be significant, with “r” values being compared between 0.74 and 0.80, (> 0.50).

When the percentage of p-53 positivity was correlated with the clinical stage of the disease, the proportion of positive p53 cases increased significantly from stage A Binet, (7.4%) stage B (24.4%) and stage C, (29.2%) (p = .002). The results of this study indicated that in CLL, p53 protein expression analyzed by an the immunocytochemical method is strongly associated with p-53 gene mutations and a variant morphological analysis of p-53, [9].

Discussions

The diagnosis of non-Hodgkin's lymphoma may be suspected in the presence of a single growing lymph node or several lymph nodes in an area that has appeared consecutively (in turn), or the presence of a tumour in any organ or other tissue. However, the diagnosis of non-Hodgkin's lymphoma is necessarily morphologically confirmed by puncture and biopsy of the lymph node or tumour formation.

The diagnosis of CLL was initially established because of peripheral smears and bone marrow, lymphocytosis and lymphocytic infiltration of the bone marrow were evident. Lymph node biopsy is especially important in patients under 40 years of age when CLL is uncommon. It is suspected that a large proportion of patients under this age, diagnosed as having CLL, would have follicular lymphoma if a lymph node biopsy was performed.

P-53 isoform protein concentration measured using sandwich ELISA colorimetric quantitative method at a single timepoint

Secondary outcome measures

There are no secondary outcome measures

Overall trial start date

15/10/2016

Overall trial end date

15/03/2020

Reason abandoned (if study stopped)

Not applicable

Eligibility

Participant inclusion criteria

1. Patients diagnosed with CLL-B who were hospitalized in the Hematology departments of the Targu Mures Oncology Institute Cluj-Napoca and Emergency County Hospital Targu Jiu, between November 2016-September 2019 and March 2020.

2. CLL with> 5000 lymphocytes in absolute value, present at the cytological examination of the blood smear, from the peripheral blood or LLC with less than 10% prolymphocytes based on the peripheral blood smears May-Grunwald Giemsa, stained

Participant type

Patient

After analyzing the 85 LLC samples, in different stages of disease evolution, starting with stage zero (stay and watch) and up to stage IV, 20 patients were selected, eligible for this study, to be investigated for the detection of p-53 protein isoforms responsible for resistance to oncological treatments

Age group; Senior**,** Gender**,** Both

Target number of participants 85

Total final enrolment; 20

Participant exclusion criteria

Does not meet inclusion criteria the patients starting with stage zero (stay and watch) in CLL.

Recruitment start date

01/11/2016

Recruitment end date

03/03/2020

Locations

Countries of recruitment; Romania

Trial participating centre; Titu Maiorescu University of Bucharest**,** Faculty of Medicine

Damboviciului Street, NoL 22, Bucharest, 040051, Romania

Sponsor information

Organisation; Titu Maiorescu University

Sponsor details; Faculty of Medicine, Dambovicіului Street, No: 22, Bucharest, 040051

Romania, +40 (0)723326663; manole.cojocaru@yahoo.com

Sponsor type

University/education

Website; http://www.brainmap.ro

GRID; grid.445737.6

Funders

Funder type other

Funder name; Not applicable

Investigator initiated and funded; Alternative name(s); Funding Body Type; Funding Body Subtype; Location

Not applicable

Results and Publications

Publication and dissemination plan;

American Journal of Surgery and Clinical Case Reports. Energetic and Genetic Mechanisms of Transformation of Normal Cells into Malignant Cells. Citation: Udristioiu A. Energetic and Genetic Mechanisms of Transformation of Normal Cells into Malignant Cells . Ame J Surg Clin Case Rep. 2023; 6(5): 1-11

Planned publication in a high-impact peer-reviewed journal

Journal " Scientific Report" Nature Journal BMC, Part of Springer Nature.

Intention to publish date

11/07/2022

Individual participant data (IPD) sharing statement

The datasets generated and/or analysed during the current study will be published as as supplement to the results publication

Participant level data

11/07/2022

Published as a supplement to the results publication

Trial outputs

Output type Details Date created Date added Peer reviewed? Patient-facing?

Additional files, Editorial Notes; Not applicable

14/11/2022: Internal review. 11/11/2022: Trial's existence confirmed by Universitatea "Titu Maiorescu" of Bucharest