*Med. J. Cairo Univ., Vol. 85, No. 5, September: 1975-1980, 2017*
www.medicaljournalofcairouniversity.net

# Philadelphia-Positive B-Acute Lymphoblastic Leukemia: Does it Differ from Philadelphia-Negative One?

FATMA G. ABD EL-NASSER, M.Sc.*; RAAFAT ABD EL-MALEK, M.D.**;
SOMAYA EL-DEEB, Ph.D.*** and NEEMAT M. KASSEM, M.D.**

*The Department of Clinical Oncology, Cairo Oncology Center, Giza*, The Department of Clinical Oncology & Nuclear Medicine, Kasr Al-Ainy Centre, Faculty of Medicine, Cairo University** and The Department of Zoology, Faculty of Science, Cairo University***, Egypt*

## Abstract

*Background:* Approximately one-fourth of adult Acute Lymphoblastic Leukemia (ALL) expresses the oncogenic protein BCR-ABL1 that results from the *t* (9;22) chromosome translocation known as the Philadelphia (Ph) chromosome. Formerly seen as a poorly tractable therapeutic problem; Ph-positive (Ph+) ALL is associated with at least a 10% lower chance of Complete Remission (CR) than Ph-negative (Ph–) disease and with an extremely poor prognosis overall. However, multiple clinical trials of BCR-ABL-specific Tyrosine Kinase Inhibitors (TKIs) have conclusively demonstrated significantly superior initial responses resulting in higher CR rates without additional toxicity.

*Purpose:* Little evidence exists regarding the prevalence, clinical outcomes and molecular response of adult patients with Ph+ versus Ph– B-ALL in our country. The aim of our study was to explore the presence of minor BCR-ABL (P190) gene in Egyptian B-ALL patients and correlate it with treatment outcome.

*Patients and Methods:* Quantitative assessment of minor BCR-ABL gene expression was performed by quantitative Real-Time Polymerase Chain Reaction (qRT-PCR) in 48 Egyptian B-ALL patients. All patients received classic ALL treatment in addition to TKI (Imatinib) in the minor BCR-ABL +ve patients.

*Results:* Only Ten patients (21%) were positive for minor BCR-ABL. Concerning molecular response, minor BCR-ABL fusion gene was expressed in mRNA of patient leukocytes (Mean ± SD=0.006±0.006), with a 3 log reduction from baseline ratio after receiving treatment. Disease Free Survival (DFS) was significantly higher among Ph+ve patients than Ph-ve patients ($p$=0.049).

*Conclusion:* In conclusion, the TKIs have significantly improved outcomes for adult patients with Ph-positive ALL, with the use of imatinib in combination with intensive chemotherapy early in the treatment course. Over the coming years, the treatment of adult ALL will certainly change from disease-type to molecular-target type and from risk-stratified treatment schedules to more personalised therapies. More specific therapies and new immunotherapy-based approaches are the most promising advances for improving prognosis and reducing treatment-related morbidity.

***Key Words:*** *B-ALL – Minor BCR-ABL – qRT-PCR – TKIs.*

***Correspondence to:*** Dr. Fatma G. Abd El-Nasser,
The Department of Clinical Oncology, Cairo Oncology Center, Giza, Egypt

## Introduction

**THE** genetics of ALL are becoming well understood and the incidence of individual chromosomal abnormalities varies considerably with age [1]. ALL has a bimodal age distribution, being most commonly seen in children with a subsequent decline in incidence in middle age and a subsequent increase in older individuals [2]. In Egypt, the annual incidence is approximately four cases per 100 000 children per year in the National Cancer Institute (NCI) Cairo University.

ALL constitute 30% of all pediatric malignancies and 70% of pediatric leukemias. Cases show a male to female ratio of 2.3:1. The 2-10 years age group constitutes 68.5% [3]. In the last decade, microarray and sequencing analysis of large ALL cohorts has revolutionized our understanding of the genetic basis of this disease. These studies have identified new ALL subtypes, each characterized by constellations of structural and sequence alterations that perturb key cellular pathways, including lymphoid development, cell-cycle regulation, and

tumor suppression; cytokine receptor, kinase, and Ras signaling; and chromatin modifications. Several of these pathways, particularly kinase-activating lesions and epigenetic alterations, are logical targets for new precision medicine therapies [4]. The Ph chromosome reflects a balanced reciprocal translocation between the long arms of chromosome 9 and 22 [*t* (9;22) (q34;q11)] involving the BCR and ABL genes. At present, detection of BCR/ABL gene rearrangement is mandatory in B-ALL patients at diagnosis for prognostic stratification and treatment decision [5]. Significant advances in treatment of Ph-positive ALL have been made since the discovery of Imatinib which is a selective ABL tyrosine kinase inhibitor. Whereas the outcome with standard chemotherapy was previously poor, incorporation of Imatinib into treatment protocol has improved survival [6]. Recently, Ph-like ALL cases have been identified which lack BCR-ABL, exhibit a gene expression profile similar to BCR-ABL positive ALL, harbor alterations of B-lymphoid transcription factor genes, and have poor outcome [7,8]. The prevalence of Ph-like ALL increases with age and varies according to ethnicity, in part because CRLF2 (cYtokine Receptor Like Factor 2) alterations are associated with Hispanic ethnicity and native American genetic ancestry [9]. Ph-like ALL is associated with high-risk clinical features, a poor response to induction chemotherapy, elevated Minimal Residual Disease (MRD) levels, and/or poor survival. Several observations indicate that Tyrosine Kinase Inhibitors (TKIs) may be effective in Ph-like ALL [10,11].

As, little evidence exists regarding the prevalence, clinical outcomes and molecular response of adult patients with Ph+ versus Ph-B-ALL in our country. The current study aimed to investigate the prognostic significance of minor BCR-ABL (P190) gene expression and correlate it with treatment outcome.

## Material and Methods

After informed patient consent and approval by the Institutional Review Board (IRB), 48 newly diagnosed B-ALL patients referred to Kasr Al-Ainy Centre of Clinical Oncology and Nuclear Medicine in the period from January 2013 to December 2015 were enrolled in our study. Twenty age and sex matched healthy controls were also enrolled. All patients were diagnosed and treated at Clinical Oncology Department, Kasr Al-Ainy, Cairo University.

*Treatment regimen and response to therapy:*

All patients were treated using standard induction regimen: Phase I (weeks 1-4), consisted of doxorubicin 25 mg/m$^2$ administered intravenously on days 1, 8, 15, and 22; vincristine 1.4mg/m$^2$ administered intravenously on days 1, 8, 15, and 22; L-asparaginase 10000IU administered intramuscularly on days 17 to 28 and prednisone 60mg/m$^2$ administered orally in divided doses on days 1 to 28; and methotrexate 12.5mg administered intrathecally on day 15.

Patients with Ph+ ALL received Imatinib 400mg daily all through the induction. Bone marrow assessment at end of induction is done and patient is considered in complete remission if his marrow blasts <5%. Patients went on to phase II of induction regardless of whether residual leukemia was in their marrow at the end of phase I. Phase II therapy (weeks 5-8) consisted of cyclophosphamide 650mg/m$^2$ intravenously on days 1, 15, and 29 and cytarabine 75mg/m$^2$ intravenously on days 1 to 4, 8 to 11, 15 to 18, and 22 to 25. 6-Mercaptopurine (60mg/m$^2$) was administered orally on days 1 to 28, and methotrexate 12.5mg was administered intrathecally on days 1, 8, 15, and 22. Patients were evaluated for response at the end of each of the 2 phases of induction using bone marrow aspiration and BCR-ABL assessment by qRT-PCR for those with Ph+ ALL. The patient is considered in complete remission if his marrow blasts <5%. Those who achieved CR went on to the intensification/CNS prophylaxis phase using 3 cycles of high-dose methotrexate, 3g/m$^2$ intravenously given on days 1, 8, and 22, followed by L-asparaginase 10 000IU on days 2, 9, and 23 and standard leucovorin rescue. This is followed by 4 cycles of consolidation phase: Cycle 1 consisted of cytarabine 75mg/m$^2$ intravenously on days 1 to 5; etoposide 100mg/m$^2$ intravenously on days 1 to 5; vincristine 1.4mg/m$^2$ intravenously on days 1, 8, 15, and 22; and dexamethasone 10mg/m$^2$ orally on days 1 to 28. Cycle 2 was started 4 weeks after cycle 1 and consisted of cytarabine 75mg/m$^2$ intravenously on days 1 to 5 and etoposide 100mg/m$^2$ intravenously on days 1 to 5. Cycle 3 was started 4 weeks after cycle 2.

It consisted of doxorubicin 25mg/m$^2$ intravenously on days 1, 8, 15, and 22, cyclophosphamide 650mg/m$^2$ intravenously on day 29, cytarabine 75 mg/m$^2$ intravenously on days 31 to 34 and 38 to 41, and 6-Mercaptopurine 75mg/m$^2$ orally on days 29 to 42. Cycle 4 of consolidation therapy was identical to cycle 2 and was to begin 8 weeks after the end of cycle 3.

Maintenance therapy consisted of monthly treatment of vincristine 1.4mg/m 2 intravenously, prednisone 60mg/m2 orally for 5 days, 6-mercaptopurine 75mg/m2 orally daily, and methotrexate 20mg/m2 orally once a week. Maintenance therapy was to continue for a total of 2.5 years from the start of intensification therapy.

*Endpoints:*

The Overall Survival (OS) rate was defined from the date of the first visit till the last follow-up or death, while the Disease Free Survival (DFS) rate was defined from the date of CR achievement till the date the patient relapsed.

*Quantitative assessment of minor BCR-ABL gene expression:*

Total RNA was extracted from peripheral blood or bone marrow blast cells using commercially available extraction kits (Qiagen, Germany). The amount of RNA was measured spectrophotometrically. The RNA integrity was tested on the Nanodrop. All samples had an OD 260/280nm ratio >1.8, indicating high purity. For the generation of first strand cDNA, 10 ll of total RNA was reversed transcribed in a final volume of 20 ll with the high capacity cDNA Archive Kit (Applied Biosystems, Netherlands). cDNA specific mbcr-abl Taqman primers and probe sets were used. Minor BCR-ABL was detected by complete Kit (ipsogen BCR-ABL P190 mbcr e1a2 transcripts-ref no. 670023, lot no. 9480942), according to manufacture protocol.

All PCR reactions were performed on the Step one Sequence Detection System (Applied Biosystems) using the fluorescent Taqman methodology. The PCR cycle at which the fluorescence arises above the background signal is called the Cycle threshold (Ct) and it is inversely proportional to the log of the initial copy number. In total 10 ll of the reverse transcription volume (cDNA) was used for each PCR reaction in a total volume of 25 ll. A real time PCR reaction was carried out. One primer pair amplified the target gene and the other amplified the endogenous reference gene. Primer and probe concentrations for the target gene were optimized according to the manufacturer's procedure. The thermal cycling conditions comprised 10min at 95ºC, 120s at 50ºC (40 cycles of 15s denaturation at 95ºC) and 60s annealing at 60ºC.

*Data analysis:*

All data were tabulated and statistically studied by descriptive analysis as well as survival analysis in relation to BCR-ABL expression. Comparison between the two groups was done using Student t test for continuous data and Chi square ($\xi 2$) test for categorical data. Survival analysis was done according to Kaplan-Meier method and compared by log-rank test for significance. Univariate analysis using Cox regression module was performed to test the power of relation between the independent variables and survival differences were considered significant if $p$-value was less than 0.05. All statistical calculations, data management and analysis were performed using computer programs Microsoft Excel Version 7 (Microsoft Corporation, NY, USA) and SPSS Version 20 (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA).

## Results

Forty eight patients with diagnosis of acute lymphoblastic leukemia were included, 29 (60.4%) were males and 19 (39.6%) were females with a male to female ratio 1.5: 1 . The median age 29 years (range: 18-57). The most common primary clinical presentations in our study group were: Fever in 27 patients (65.3%), easy fatigability in 22 patients (48.5%), bleeding tendency in 13 patients (27.1%), hepatomegaly in 10 patients (20.8%), splenomegaly in 15 patients (31 .3%) and lymphadenopathy in 18 patients (37.5%). Philadelphia chromosome was present in 10 patients (21%). By comparing patients with positive and negative minor BCR-ABL expression, there was no statistical significant difference between both groups in relation to age and gender ($p$=0. 169 and 0.164) respectively. Regarding the clinical data, also there was no statistical significant difference between both groups. Hematological response in Ph+ve patients achieved within 12 months showed significant difference ($p\Delta$0.005). In respect of response to treatment and survival, complete remission was achieved in 71% of Ph-ve cases compared to 100% in Ph+ve. Disease free survival Fig. (1) was significantly higher among Ph+ve patients than Ph-ve patients ($p$=0.049). Before treatment, minor BCR-ABL fusion gene was expressed in mRNA of Ph+ve patients leukocyte at ratio of (0.05 t0 1.45), while after receiving chemotherapy accompanied with Imatinib, there was a Major Molecular Response (MMR), where minor BCR-ABL fusion gene was expressed with 3 log reduction at a ratio of (0.02 to 0.0003) after 12 months.

Table (1): Clinicopathological parameters according to Ph status.

| Parameter | Ph positive | Ph negative | *p*- |
|---|---|---|---|
| Number | 10 patients | 38 patients | value |
| *Age:* | | | |
| Median | 42.5 | 26 | 0.169 |
| Range | | | |
| Mean | 37.9 | 31.2 | |
| SD | 12 | 13.5 | |
| *Gender:* | | | |
| Male | 4 | 25 | 0.164 |
| Female | 6 | 13 | |
| *Presentation:* | | | |
| Fever | 7 (70%) | 20 (30%) | 0.478 |
| Easy fatigability | 7 (70%) | 15 (39.5%) | 0.152 |
| Bleeding tendency | 4 (40%) | 9 (23.7%) | 0.425 |
| Hepatomegaly | 1 (10%) | 9 (23.7%) | 0.664 |
| Splenomegaly | 1 (10%) | 14 (36.8%) | 0.140 |
| Lymphadenopathy | 3 (30%) | 15 (39.5%) | 0.722 |
| *Laboratory parameters (Mean ± SD):* | | | |
| WBCs ($X10^3/mm^3$) | 58.8±72.8 | 1.0±52.5 | 0.203 |
| Hb (g/dl) | 7.9± 1.8 | 8.5±2.1 | 0.458 |
| Platelets ($X10^3/mm^3$) | 55.2±27.3 | 58.0±47.6 | 0.611 |
| P.B blasts (%) | 62.1 ±22.8 | 64.1±26.6 | 0.816 |
| B.M blasts (%) | 94.7±3.7 | 82.8±23.5 | 0.483 |
| CD 10 | 54.0±33.1 | 60.6±29.6 | 0.594 |
| CD 19 | 83.6± 17.7 | 80.3± 15.6 | 0.341 |
| CD22 | 67.5± 15.8 | 61.8±20.8 | 0.509 |
| CD97a | 71.6±27.1 | 60.6±29.6 | 0.594 |

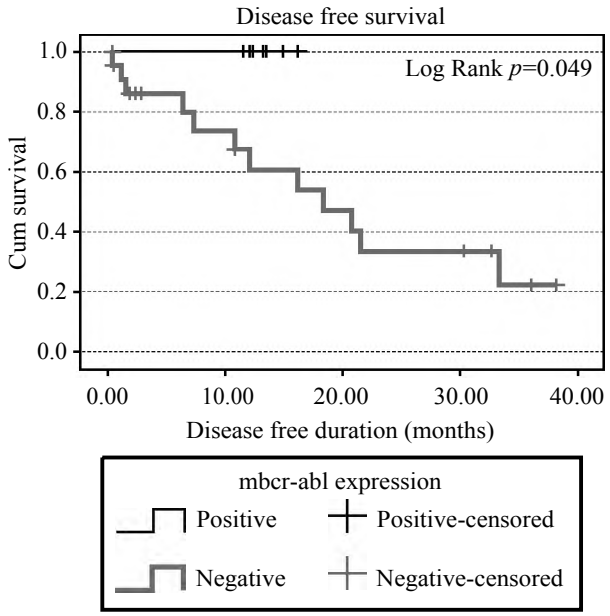


Fig. (1): Disease free survival according to Ph chromosome status.

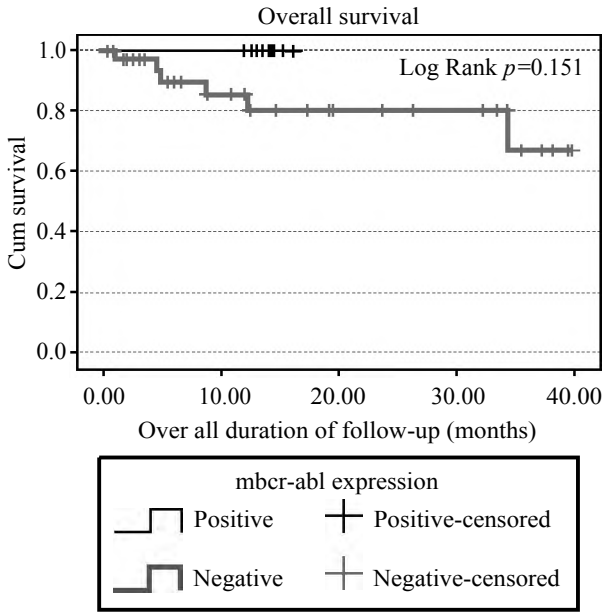


Fig. (2): Overall survival according to Ph chromosome status.

## Discussion

Among 48 patients of newly diagnosed B-acute lymphoblastic leukemia, 21% of all patients possess Ph chromosome. Patients presenting with Ph+ve ALL differed from those with Ph-ve ALL at some aspects, firstly regarding the clinical data, the present study showed that median age is slightly higher; also the most presenting symptoms in Ph+ve patients were easy fatigability and fever while bleeding, hepatomegaly and seplenomegaly were only 10%. These findings were different from Ph-ve patients although the difference was sometimes not significant. Our data compared to study

from Pakistan and Singapore showed similarity regarding incidence, age and presentation **[12,13]**. Regarding laboratory data, many studies including ours showed that Ph+ve is associated with higher initial leukocyte counts and more blasts in the peripheral blood and bone marrow **[12,13]**. In respect of immunophenotyping, similar to western data **[14]**, the present study showed that CD 19, CD22 and CD79a % were higher in the Ph+ve, while data from Asian study reported that CD 10 expression had significant difference **[15]**. In the matter of treatment outcome, in the present study, the disease free survival was significantly higher among Ph+ve patients than Ph-ve patients ($p$=0.049). This finding compared to older studies prior to use of Imatinib in Ph+ ALL showed that Ph+ patients had poorer outcome **[15-17]**. Concerning Molecular Response (MR), in the present study after receiving chemotherapy accompanied with Imatinib, minor BCR-ABL fusion gene was expressed in mRNA of patient leukocyte (mean ± SD = 0.006±0.006), with a 3 log reduction from baseline ratio. This is in accordance with the results previously reported that when Imatinib is added to induction therapy, minor BCR-ABL, mRNA was reduced at least 1 log from baseline after the first induction therapy. In conclusion the TKIs have significantly improved outcomes for adult patients with Ph-positive ALL, with the use of imatinib in combination with intensive chemotherapy early in the treatment course, and continuing through consolidation and maintenance considered as the current standard of care. The second-generation TKIs, such as dasatinib, are likely to yield better results and ongoing trials are evaluating them in combination with chemotherapy.

Monotherapy with TKIs should be reserved for the elderly and those unable to tolerate intensive chemotherapy. Monitoring MRD should be part of standard care of all patients with Ph-positive leukemias. Although high initial response rates are seen with the incorporation of TKIs, disease relapse remains a major cause of mortality. There is further need for incorporating newer agents, like ponatinib, which overcomes resistance related to the T3 15I mutation, a frequent cause of Ph positive ALL resistance, to potentially achieve more durable responses. Over the coming years, the treatment of adult ALL will certainly change from disease-type to molecular-target type and from risk-stratified treatment schedules to more personalised therapies. More specific therapies and new immunotherapy-based approaches are the most promising advances for improving prognosis and reducing treatment-related morbidity.

*Conflicts of interest:*

The authors declare that they have no conflicts of interest.

*Acknowledgements:*

We would like to thank Nashwa Medhat, M.Sc., Bassant Nagdy, M.Sc. and Mustafa Tarek; Kasr Al-Ainy Molecular Lab.-Oncology Department; for their technical efforts, sincere help and interest in our work.

## References

1- CHRISTINE J. HARRISON: Targeting signaling pathways in acute lymphoblastic leukemia: New insights. ASH, 118-25, 2013.

2- CARIO G., RHEIN P., MITLOHNER R., ZIMMERMANN M., BANDAPALLI O.R., ROMEY R., MOERICKE A., LUDWIG W.D., RATEI R., MUCKENTHALER M.U., KULOZIK A.E., SCHRAPPE M., STANULLA M. and KARAWAJEW L.: High CD45 surface expression determines relapse risk in children with precursor B-cell and T-cell acute lymphoblastic leukemia treated according to the ALL-BFM 2000 protocol. Haematologica, 99 (1): 103-10, 2014.

3- SHALABY R.H., ASHAAT N.A., EL-WAHAB N.A., EL-HAMID M.A. and El-WAKEEL S.H.: Bcl-2 expression and chromosomal abnormalities in childhood acute lymphoblastic leukemia. Academic Journal of Cancer Research, 3 (2): 34-43, 2010.

4- STEPHEN P. HUNGER and CHARLES G. MULLIGHAN: Redefining ALL classification: Toward detecting high-risk ALL and implementing precision medicine. Blood, 125 (26): 3977-87, 2015.

5- YENAN LI, DEHUI ZOU, YAOZHONG ZHAO, YINGCHANG MI, JIANXIANG WANG, and LUGUI QIU: Clinical characteristics and outcomes of adults with Philadelphia chromosome positive and/or bcr-abl positive acute lymphoblastic leukemia: A single center study from China. Leukemia & Lymphoma, 51 (3): 488-96, 2010.

6- THOMAS D.A.: Philadelphia Chromosome-Positive Acute Lymphocytic Leukemia: A New Era of Challenges. Hematology Am. Soc. Hematol. Educ. Program, 435-43, 2007.

7- MULLIGHAN C.G., SU X., ZHANG J., et al.: Children's Oncology Group. Deletion of IKZF1 and prognosis in acute lymphoblastic leukemia. N. Engl. J. Med., 360 (5): 470-80, 2009.

8- DEN BOER M.L., VAN SLEGTENHORST M., De MENEZES R.X., et al.: A subtype of childhood acute lymphoblastic leukaemia with poor treatment outcome: A genome-wide classification study. Lancet Oncol., 10 (2): 125-34, 2009.

9- HARVEY R.C., MULLIGHAN C.G., CHEN I.M., et al.: Rearrangement of CRLF2 is associated with mutation of JAK kinases, alteration of IKZF1, Hispanic/Latino ethnicity, and a poor outcome in pediatric B-progenitor acute lymphoblastic leukemia. Blood., 115 (26): 5312-21, 2010.

10- VAN DER VEER A., WAANDERS E., PIETERS R., et al.: Independent prognostic value of BCR-ABL1-like

signature and IKZF1 deletion, but not high CRLF2 expression, in children with B-cell precursor ALL. Blood, 122 (15): 2622-9, 2013.

11- ROBERTS K.G., PEI D., CAMPANA D., et al.: Outcomes of children with BCR-ABL1-like acute lymphoblastic leukemia treated with risk-directed therapy based on the levels of minimal residual disease. J. Clin. Oncol., 32 (27): 3012-20, 2014.

12- QAISER HASNAIN, IFTIKHAR ABIDI and MICHAEL IFTIKHAR: Comparison between philadelphia positive and philadelphia negative adult acute leukemias. Biomedica, 24: 31-6, 2008.

13- VELLUPILLAI M., TAN L.T., LAU L.C., FOOK-CHONG S.M. and LIM L.C.: Haematological characteristics, molecular analysis and three year follow-up-a single institution study. Ann. Acad. Med. Singapore., 29 (2): 159-63, 2000.

14- PRETI H.A.1., O'BRIEN S., GIRALT S., BERAN M., PIERCE S. and KANTARJIAN H.M.: Philadelphia-chromosome-positive adult acute lymphocytic leukemia: Characteristics, treatment results, and prognosis in 41 patients. Am. J. Med., 97 (1): 60-5, 1994.

15- UDOMSAKDI-AUEWARAKUL C., PROMSUWICHA O., TOCHAROENTANAPHOL C., MUNHKETVIT C., PATTANAPANYASAT K. and ISSARAGRISIL S.: Immunophenotypes and Outcome of Philadelphia Chromosome-Positive and-Negative Thai Adult Acute Lymphoblastic Leukemia. Int. J. Hematol., 78 (4): 337-43, 2003.

16- JESSE JASO, DEBORAH A. THOMAS, KRISTA CUNNINGHAM, JEFFREY L. JORGENSEN, HAGOP M. KANTARJIAN, L. JEFFREY MEDEIROS, and SA A.WANG: Prognostic Significance of Immunophenotypic and Karyotypic Features of Philadelphia Positive B-Lymphoblastic Leukemia in the Era of Tyrosine Kinase Inhibitors. Cancer, 117 (17): 4009-17, 2011.

17- WANG J., SHEN Z.X., SAGLIO G., JIN J., HUANG H., HU Y., et al.: Phase 3 study of nilotinib vs imatinib in Chinese patients with newly diagnosed chronic myeloid leukemia in chronic phase: ENESTchina. Blood, 125 (18): 2771-8, 2015.

# كروموسوم فيلادلفيا الإيجابى فى سرطان الدم الليمفاوى-ب الحاد فى المرضى المصريين

مقدمة: توجد آدلة قليلة فيما يتعلق بمدى الإنتشار والإستجابة السريرية والجزيئية فى المرضى البالغين الذين يعانون من سرطان الدم الليمفاوى–ب الحاد الإيجابى لكروموسوم فيلادلفيا مقابل السلبى له فى بلدنا. الهدف من دراستنا هو إستكشاف وجود الجين mbcr-ab1 بإستخدام تفاعل البوليميراز المتسلسل اللحظى فى حالات مرضى سرطان الدم الليمفاوى–ب المصريين، ومقارنتها مع الحالات السلبية لهذا الجين، ومدى إرتباط هذه النتائج بنتيجة العلاج.

\المرضى ومنهج \العمل: تم تسجيل مرضى سرطان الدم الليمفاوى–ب الحاد الذين تم تقديمهم إلى قسم الآورام فى جامعة القاهرة فى الدراسة خلال الفترة من يناير ٢٠١٣ حتى ديسمبر ٢٠١٥. خضع جميع المرضى للتقييم السريرى والفحوصات الآساسية بما فى ذلك القياس الكمى للواصمات السطحية للخلايا بإستخدام تقنية القياس الخلوى بالجريان بالإضافة إلى التقييم الكمى للجين mbcr-ab1 بإستخدام تفاعل البوليميراز المتسلسل اللحظى. كما جمعت بيانات العلاج والنجاة. تلقى جميع المرضى العلاج الكلاسيكى لمرض سرطان الدم الليمفاوى ب–الحاد بالإضافة إلى العلاج lmatinib فى الحالات الإيجابية لكروموسوم فيلادلفيا.

\النتائج: شملت دراستنا ٤٨ مريضا وكانت نسبة الذكور إلى الإناث ١:١.٥. تم العثور على عشرة (٢١٪) من الحالات الإيجابية لكروموسوم فيلادلفيا. وكان متوسط عمر المرضى الإيجابيين لكروموسوم فيلادلفيا ٤٢.٥ سنة مقارنة ب ٢٦ عاما للمرضى الغير إيجابيين. وفيما يتعلق بالبيانات السريرية، لم يكن هناك فرق إحصائى بين المجموعتين: آظهرت الإستجابة الخاصة بكرات الدم الحمراء لدى الحالات الإيجابية لكروموسوم فلادلفيا بعد ١٢ شهرا فروق إحصائية. آيضا كان معدل البقاء مع الخلو من المرض آعلى بكثير بين المرضى الإيجابيين.

\الخلاصة: الكشف عن جين m-bcr له آهمية فى التكهن بالشفاء والعلاج. عندما آضيف ال lmatinib جنبا إلى جنب مع العلاج الكيميائى فى الحالات الإيجابية لكروموسوم فيلادلفيا كان معدل البقاء مع الخلو من المرض آعلى بكثير من الحالات الغير إيجابية.