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(ELN recommendations, ESMO guidelines,
ERIC guidelines, Lugano criteria for response etc.)

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European LeukemiaNet Recommendations for the Management of Chronic Myeloid Leukemia (CML)

Response definitions for any TKI first line, and 2nd line in case of intolerance, all patients (CP, AP, and BC)

Time	Optimal response	Warning	Failure
Baseline		High risk Major route CCA/Ph+	
3 mos.	BCR-ABL ^{IS} ≤10%* Ph+ ≤35% (PCyR)	BCR-ABL ^{IS} >10%* Ph+ 36-95%	No CHR* Ph+ >95%
6 mos.	BCR-ABL ^{IS} <1%* Ph+ 0% (CCyR)	BCR-ABL ^{IS} 1-10%* Ph+ 1-35%	BCR-ABL ^{IS} >10%* Ph+ >35%
12 mos.	BCR-ABL ^{IS} ≤0.1%* (MMR)	BCR-ABL ^{IS} 0.1-1%*	BCR-ABL ^{IS} >1%* Ph+ >0%
Then, and at any time	MMR or better	CCA/Ph- (-7, or 7q-)	Loss of CHR Loss of CCyR Loss of MMR, confirmed** Mutations CCA/Ph+

*and/or **in 2 consecutive tests, of which one ≥1% IS: BCR-ABL on International Scale

Treatment recommendations

Line	Event	TKI, standard dosage ¹					Transplantation				
Chronic phase											
		Imatinib 400 mg/qd	Nilotinib 300 mg/bid	Dasatinib 100 mg/qd	Bosutinib 500 mg/qd	Ponatinib 45 mg/qd	Search for		alloSCT		
							HLA type + sibs	unrelated donor	consider	recommended	
1 st	Baseline	X	X	X			X ²				
2 nd	Intolerance to 1 st TKI	Any other TKI approved 1 st line									
	Failure 1 st line of	imatinib	X ³	X	X	X	X		X	X	
		dasatinib	X ³		X	X	X	X	X	X	
3 rd	Intolerance to/failure of two TKI	Any remaining TKI								X	
Any	T315I mutation					X	X	X	X		
Accelerated or blast phase											
In newly diagnosed, TKI naive patients	start with	X ³	X ³				X	X			
	no optimal response, BP								X ³	X ³	
TKI pre-treated patients		Any other TKI				X ³			X ³	X ³	

¹choice of the TKI consider tolerability and safety, and patient characteristics (age, comorbidities). ²only in case of baseline warnings (high risk, major route CCA/Ph+). ³400 mg/bid, ⁴70 mg/bid or 140 mg/qd, ⁵may be required before SCT to control disease and to make patients eligible to alloSCT. ⁶in case of T315I mutation, ⁷only patients who are eligible for alloSCT, not in case of uncontrolled, resistant BP. ⁸400 mg bid in failure setting

References: 1. Baccarani M, Deininger M, Rossi G, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia. *Blood* 122:872-884, 2013. 2. Baccarani M, Cortes J, Pane F, et al. Chronic myeloid leukemia. An update of concepts and management Recommendations of the European LeukemiaNet. *J Clin Oncol* 27:6041-51, 2009. 3. Baccarani M, Saglio G, Goldman J, et al. Evolving concepts in the management of chronic myeloid leukemia: recommendations from an expert panel on behalf of the European LeukemiaNet. *Blood* 108:1809-1820, 2006.

Other definitions

CCA	Clonal chromosome abnormalities
CCA/Ph+	CCA in Ph+ cells which define failure if newly arisen
CHR	Complete hematologic response: Platelet count < 150 x 10 ⁹ /L; WBC count < 10 x 10 ⁹ /L; Differential: no immature granulocytes, basophils <5%; no palpable spleen
High risk	Evaluated by Sokal-Score (>1.7), Funt-Score (>1.480) or PLTOS-Score (>87)
Major route CCA/Ph+	Major route CCA/Ph+ are trisomy 8, 2 nd Ph+ [-der(22)t(9;22)(q34;q11)], isochromosome 17 [i(17)(q10)], trisomy 19, and ider(22)(q10)t(9;22)(q34;q11)
Mutations	BCR-ABL kinase domain point mutations (not to be confused with ABL1 polymorphisms), Mutational analysis by conventional Sanger sequencing is recommended in case of progression, failure and warning.

Timing of Cytogenetic and Molecular Monitoring

At diagnosis	CBA, FISH in case of Ph (for cryptic or variant translocations), qualitative PCR (transcript type)
During treatment	RQ-PCR every 3 months until MMR has been achieved, then every 3 to 6 months and/or CBA at 3, 6, and 12 months until CCyR has been achieved, then every 12 months. Once CCyR is achieved, FISH on blood cells can be used.
Failure, progression	RQ-PCR, mutational analysis, and CBA. Immunophenotyping in blast phase.
Warning	Molecular and cytogenetic tests more frequently. CBA in case of myelodysplasia or CCA/Ph-

CBA: Chromosome banding analysis of marrow cell metaphases at least 20 metaphases analysed

Response definitions to 2nd line therapy in case of failure of imatinib (can be used provisionally, NOT for the response to 3rd line treatment).

Time	Optimal response	Warnings	Failure
Baseline		No CHR Loss of CHR on imatinib Lack of CyR to 1 st line TKI High risk	
3 mos.	BCR-ABL ^{IS} ≤10%* Ph+ <65%	BCR-ABL ^{IS} >10%* Ph+ 65-95%	No CHR, or Ph+ >95%, or New mutations
6 mos.	BCR-ABL ^{IS} <10%* Ph+ <35% (PCyR)	BCR-ABL ^{IS} <10%* Ph+ 35-65%	BCR-ABL ^{IS} >10%* Ph+ >65%* New mutations
12 mos.	BCR-ABL ^{IS} <1%* Ph+ 0 (CCyR)	BCR-ABL ^{IS} 1-10%* Ph+ 1-35%	BCR-ABL ^{IS} >10%* Ph+ >35%* New mutations
Then, and at any time	MMR or better	CCA/Ph- (-7 or 7q-) or BCR-ABL ^{IS} >0.1%	Loss of CHR, or Loss of CCyR or PCyR New mutations Loss of MMR** CCA/Ph+

*and/or **in 2 consecutive tests, of which one ≥1% IS: BCR-ABL on International Scale

Definition of response

Optimal response	Best long-term outcome No indication for a change of treatment.
Failure	Patient should receive a different treatment to limit the risk of progression and death
Warning	Characteristics of disease and response to treatment require more frequent monitoring to permit timely changes in therapy, in case of treatment failure.

4. Tests/procedures for a patient with acute myeloid leukemia

Tests to establish the diagnosis

Complete blood count and differential count

Bone marrow aspirate

Bone marrow trephine biopsy^a

Immunophenotyping

Molecular genetic analyses

Cytogenetics^b

Screening for gene mutations including^c

NPM1, *CEBPA*, *RUNX1*, *FLT3*, *TP53*, *ASXL1*

Screening for gene rearrangements^d

PML-RARA, *CBFB-MYH11*, *RUNX1-RUNX1T1*, *BCR-ABL1*, other fusion genes (if available)

Additional tests/procedures at diagnosis

Physical examination and medical history^e

Family history^f

History of bleeding history^g

Performance status (Eastern Cooperative Oncology Group/World Health Organization score)

Assessment of comorbidities

Chemistry, coagulation tests, urine analysis^h

Pregnancy testⁱ

Information on oocyte and sperm cryopreservation^j

Risk assessment for allogeneic HCT (incl. HLA-typing)^k

Hepatitis A, B, C; HIV-1 testing

Chest x-ray, 12-lead electrocardiogram, echocardiography or MUGA (on indication)

Lumbar puncture^l

Banking^m

Post-treatment assessment of response by quantitative real-time PCR (RT-qPCR) or multi-color flow cytometry (MFC)ⁿ

RT-qPCR^{o,p} for *NPM1* mutation, *CBFB-MYH11*, *RUNX1-RUNX1T1*, *BCR-ABL1*, other fusion

genes (if available)

Multi-color flow cytometry (MFC)^{n,q}

^a In patients with a dry tap (*punctio sicca*).

^b Results from cytogenetics should be obtained preferably within 5 to 7 days. At least 20 bone marrow metaphases are needed to define a normal karyotype, and recommended to describe an abnormal karyotype. Abnormal karyotypes may be diagnosed from blood specimens.

^c Results from *NPM1* and *FLT3* mutational screening should be available within 48 to 72 hours (at least in patients eligible for intensive chemotherapy), and results from additional molecular genetics within the first treatment cycle. Screening for gene mutations is an evolving field of research; screening for single genes may be replaced by gene panel diagnostics.

^d Screening for gene rearrangements should be performed if rapid information is needed for recommendation of suitable therapy, if chromosome morphology is of poor quality, or if there is typical morphology but the suspected cytogenetic abnormality is not present.

^e Including race or ethnicity, prior exposure to toxic agents, prior malignancy, therapy for prior malignancy, information on smoking.

^f Thorough family history needed to identify potential myeloid neoplasms with germline predisposition.

^g History of bleeding episodes may inform cases of myeloid neoplasms with germline predisposition and pre-existing platelet disorders.

^h *Biochemistry*: glucose, sodium, potassium, calcium, creatinine, aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase, lactate dehydrogenase, bilirubin, urea, total protein, uric acid, total cholesterol, total triglycerides, creatinine phosphokinase (CPK)

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Coagulation tests: prothrombin time (PTT), international normalized ratio (INR) where indicated, activated partial thromboplastin time (aPTT)

Urine analysis: pH, glucose, erythrocytes, leukocytes, protein, nitrite.

ⁱ In women with childbearing potential.

^j Cryopreservation to be done in accordance with the wish of the patient.

^k HLA typing and CMV testing should be performed in those patients eligible for allogeneic hematopoietic-cell transplantation (HCT).

^l Required in patients with clinical symptoms suspicious of central nervous system involvement; patient should be evaluated by imaging study for intracranial bleeding, leptomeningeal disease, and mass lesion; lumbar puncture considered optional in other settings (e.g., high white blood cell count).

^m Pretreatment leukemic bone marrow and blood sample; for further optional storing see section 5.5

ⁿ Sensitive assessment of response can be performed at early timepoints, e.g., following induction and consolidation courses to assess remission status and determine kinetics of disease response, and sequentially beyond consolidation to detect impending morphologic relapse. No generally applicable timepoints can be defined, since kinetics of minimal residual disease (MRD) response differs by treatment given, marker analyzed and method used.

^o Monitoring of response by RT-qPCR recommended in clinical trials and clinical practice.

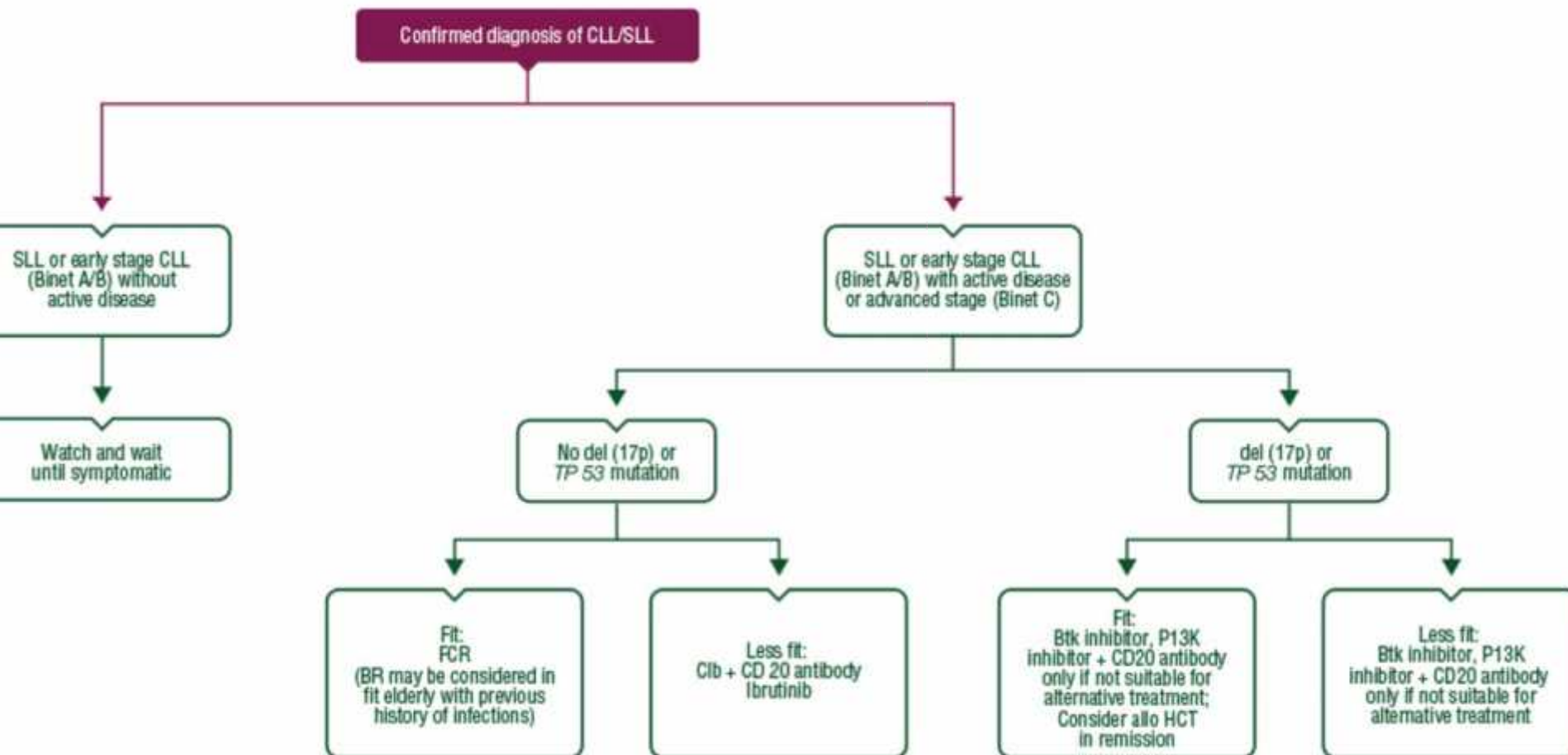
^p Sensitivity of response assessment varies by method used, and by marker tested; test used and sensitivity of the assay should always be reported; analyses should be done in experienced laboratories (centralized diagnostics).

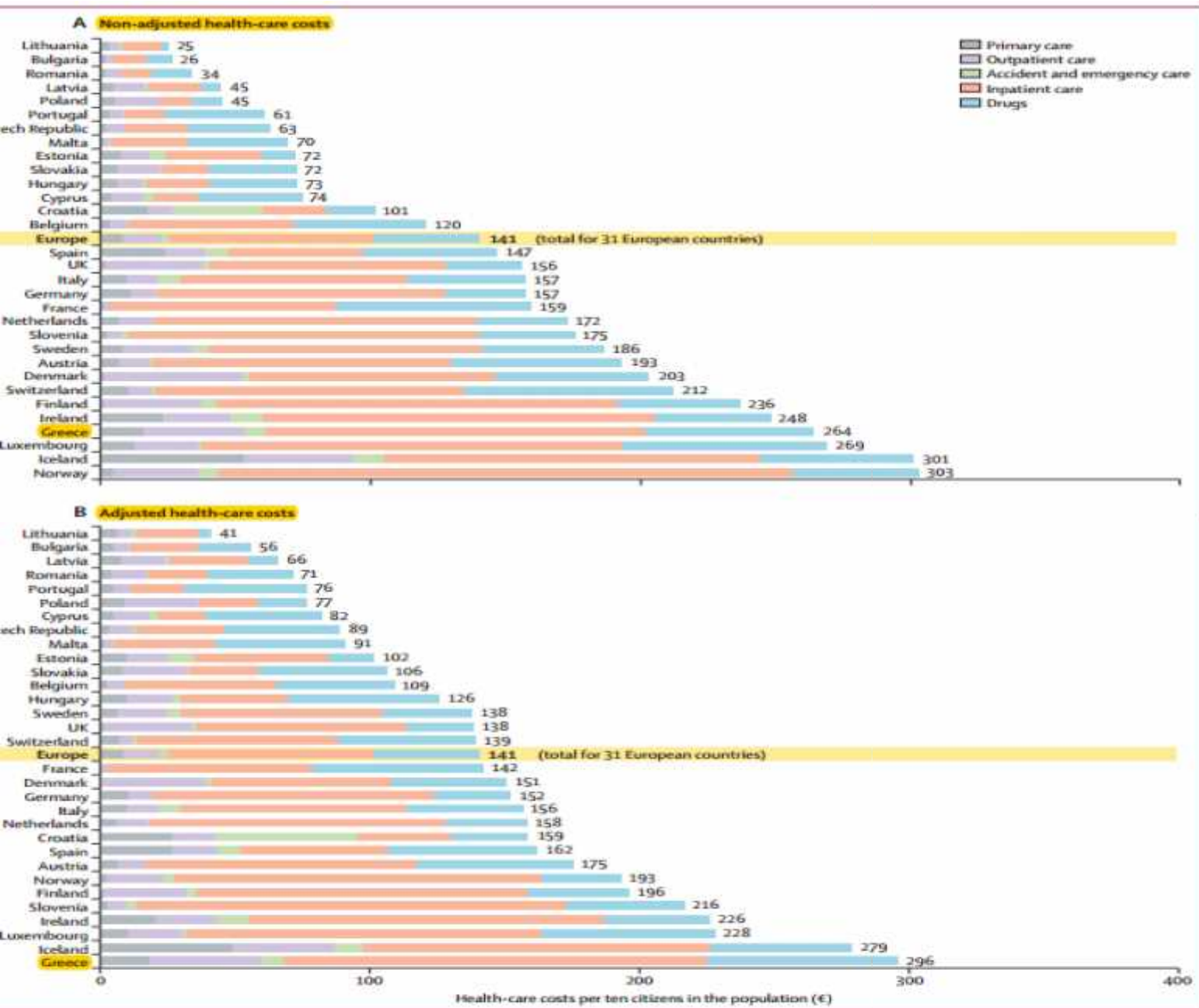
^q Increasing evidence that response assessment by MFC qualitatively provides a better remission status than morphologic assessment and is of high prognostic impact.

Update – Chronic Lymphocytic Leukaemia Treatment Recommendations

Published: 21 September 2016. Authors: B. Eichhorst¹, T. Robak², E. Montserrat³, P. Ghia⁴, P. Hillmen⁵, M. Jakschik⁶ & C. Buske⁷, on behalf of **the ESMO Guidelines Committee**

Algorithm for Frontline Treatment





Κακοήθη αιματολογικά νοσήματα
Κόστη ιατρικής περίθαλψης ανά άτομο σε 31 ευρωπαϊκές χώρες

Lancet Haematol 2016; 3: e362–70

Ενώ ο διάμεσος χρόνος ενδονοσοκομειακής παραμονής στην Ευρώπη ήταν 14 ημέρες, **στην Ελλάδα ήταν 48 ημέρες.**

Figure 1: Health-care costs of malignant blood disorders per ten citizens in 31 European countries in 2012, by health-care service category. Cost data not adjusted for price differentials. (B) Cost data adjusted for price differentials.

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Η ΕΑΕ οργανώνει τη συλλογή κλινικοεργαστηριακών δεδομένων, ανά νόσο, από όσο το δυνατόν περισσότερους Έλληνες ασθενείς.

Τα δεδομένα αναλαμβάνει να συλλέξει μία ομάδα Αιματολόγων (σχεδιασμός βάσης δεδομένων, επαφή με διάφορα κέντρα σε όλη τη χώρα, στατιστική επεξεργασία των πληροφοριών κτλ.)

Τα δεδομένα συλλέγονται για επιστημονικούς σκοπούς και για τη δημιουργία μίας βάσης, προκειμένου να σχεδιαστούν μελλοντικές κλινικές μελέτες ή να επιλεγούν ασθενείς κατάλληλοι για υπάρχουσες.



• December 6, 2014, Blood, 124 (23), 5557

Greek Registry of Myelofibrosis: Baseline Characteristics and Therapeutic Strategy

Damianos Sotiropoulos, **Argiris S. Symeonidis**¹, **Vassilios K Papadopoulos**^{*2}, **Panagiotis Tsirigotis**^{*1}, **Theodoros Iliakis**^{*1}, **Konstantinos Gkirkas**^{*1}, **Aggeliki Vourtsi**^{*2}, **Anastasia Marvaki**^{*1}, **Emmanouil Papadakis**^{*1}, **Dimitrios Kokkinidis**^{*1}, **Maria Kotsopoulou**^{*1}, **Maria Dimou**^{*3}, **Panagiotis Zikos**^{*1}, **Evangelia Tzouvara**^{*1}, **Alexandra Kouraklis**, **Efthymia Vlachaki**^{#, 2}, **Nikolaos Anagnostopoulos**¹, **Achilles Anagnostopoulos**², **Maria Pagoni**^{#2}, **Nora Athina Viniou**¹, **Theodoros Marinakis**^{*2}, **Panayiotis Panayiotidis**¹, **Constantinos Tsatalas**¹

Abstract

The Greek Registry of Myelofibrosis (MF) is held under the auspices of the Acute Leukemias and Myeloproliferative Neoplasms Study Group of the Hellenic Society of Hematology. The preliminary results after two years of retrospective data collection are presented. The total number of patients included is 226, from 10 Greek sites; the initial diagnosis was made between 1975 and 2013.



ANALYSIS OF THE DEMOGRAPHIC, CLINICAL, LABORATORY AND TREATMENT-RELATED DATA OF ITP PATIENTS IN GREECE BASED ON THE NATIONAL ITP REGISTRY OF THE HELLENIC SOCIETY OF HAEMATOLOGY

Author(s): Emily Stavroulaki, Vassilis Tzikoulis, Maria Kaparou, Peggy Kanellou, Panayiotis Panayiotidis, Panayiotis Tsaftaridis, Nora Viniou, Ekaterini Bitsani, Vassiliki Bartzi, Theodoros Iliakis, Athanasios Galanopoulos, George Kanavos, Spyros Hondropoulos, Eyridiki Michalis, Nikolaos Anagnostopoulos, Argiris Symeonidis, Alexandra Kourakli, Polyxeni Lampropoulou, Aikaterini Megalakaki, Aikaterini Palla, Maria Papaioannou, Georgia Kaiafa, Dimitra Liapi, Efthymia Vlachaki, Stavroula Giannouli, Ioannis Kotsianidis, Despoina Kyriakou, Maria Protopappa, Eleftheria Hatzimichael, Panayiotis Zikos, Charalampos Pontikoglou, George Chalkiadakis, Helen Papadaki

(Abstract release date: May 18, 2017) EHA Learning Center. Stavroulaki E. May 18, 2017; 182821

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(European Registries)

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Publications

Swart et al. 2015.

[Labile Plasma Iron \(LPI\) Is a Clinical Indicator of Overt Iron Overload in Patients with Lower-Risk Myelodysplastic Syndromes \(MDS\) from the European Leukemianet MDS Registry](#)

Louise De Swart, Chloé Reiniers, Tim Bagguley, David Bowen, Jaroslav Cermak, Eva Hellström-Lindberg, Aurelia Tatic, Argiris Symeonidis, Gerwin Huls, Panagiotis Panagiotidis, Hege Garelius, Dominic Culligan, Marta Krejci, Corine van Marrewijk, Jackie Droste, Alexandra Smith, Dorine W. Swinkels, Theo de Witte.

de Swart et al. 2015.

[Transfusions and presence of ringsideroblasts influence hepcidin and ntbi levels in patients with lower-risk myelodysplastic syndromes \(mds\) - a report from the european leukemianet mds registry](#)

L. de Swart, C. Reiniers, T. Bagguley, C. Van Marrewijk, D. Bowen, J. Cermak, E. Hellström-Lindberg, A. Tatic, A. Symeonidis, G. Huls, P. Panagiotidis, H. Garelius, D. Culligan, M. Krejci, J. Droste, A. Smith, D. Swinkels, T. de Witte.

Leukemia



Original Article

Leukemia (18 March 2015) | doi:10.1038/leu.2015.73

The EUTOS population-based registry: incidence and clinical characteristics of 2904 CML patients in 20 European Countries

V B Heffmann, M Baccarini, J Hasford, D Lindtner, S Burgstaller, D Seric, P Costeaș, J Mayer, K Indrak, H Everaus, P Kocskanvesa, J Guilhot, G Schubert-Fritschle, F Castagnetti, F Di Raimondo, S Lejniec, I Griskevicius, M Thielens, T Sarha, A Hellmann, A G Turkina, A Zartskey, A Bogdanovic, Z Brinska, I Zupan, J-L Steegmann, B Simonsson, R E Clark, A Covelli, G Guddi and R Hehlmann


This population-based registry was designed to provide robust and updated information on the characteristics and the epidemiology of chronic myeloid leukemia (CML). All cases of newly diagnosed Philadelphia positive, BCR-ABL1+ CML that occurred in a sample of 92.5 million adults living in 20 European countries, were registered over a median period of 39 months. 94.3% of the 2904 CML patients were diagnosed in chronic phase (CP). Median age was 56 years. 55.5% of patients had comorbidities, mainly cardiovascular (41.9%). High-risk patients were 24.7% by Sokal, 10.8% by HIRI, and 11.8% by EUTOS risk scores. The raw incidence increased with age from 0.39/100,000/year in people 20–29 years old to 1.52 in those >70 years old, and showed a maximum of 1.09 in Italy and a minimum of 0.69 in Poland (all countries together: 0.99). The proportion of Sokal and Euro score high-risk patients seen in many countries indicates that trial patients were not a positive selection. Thus from a clinical point of view the results of most trials can be generalized to most countries. The incidences observed among European countries did not differ substantially. The estimated number of new CML cases per year in Europe is about 6370.

Μητρώο Χρόνιας Μυελογενούς Λευχαιμίας

Πρόσβαση στην εφαρμογή

 <http://www.onregistry.gr/>

Εγκύρια λειτουργίας του Μητρώου

 Ανακοίνωση Έγκυρης -Οδηγίας για ιατρούς

Οδηγίες

 Οδηγίες για Φαρμακεία ΕΘΠΥ

 Οδηγίες χρήσης της εφαρμογής του Μητρώου για ιατρούς

Ευχαριστώ πολύ