

An Update From the European Research Initiative on CLL (ERIC)

Paolo Ghia

ERIC President

Conflict of interest disclosure

Research Support/P.I.	AbbVie, Gilead, Janssen, Sunesis, Novartis
Employee	
Consultant	
Major Stockholder	
Speakers Bureau	
Honoraria	AbbVie, ArQule, AstraZeneca/Acerta, Adaptive, BeiGene, Celgene/Juno, Dynamo, Gilead, Janssen, Sunesis
Scientific Advisory Board	AbbVie, ArQule, AstraZeneca/Acerta, Adaptive, BeiGene, Celgene/Juno, Dynamo, Gilead, Janssen, Sunesis

From which region are you from?

1. Europe
2. North and South America
3. Middle and Far East
4. Africa, Australia

Are you a member of the ERIC?

1. YES
2. NO, I did not know it
3. No, but I will become soon
4. No, but someone at my institution is

ERIC: a scientific community for scientists with a passion for CLL research

ERIC Information



- **Non-profit organization** according to German law
Klinik I für Innere Medizin, Universitätsklinikum Köln
Kerpener Straße 62, 50937, Köln
- Established on 31st January 2006
- **Executive office:**
Hematology Department, Hospital Sant Pau
C/Sant Antoni M. Claret, 167 Pabellón 18, Despacho 38
08025, **Barcelona**, Spain
- **PIC** Number: 930535939
- ☐ **WP7 - European Leukemia Net**
- ☐ **Scientific WG - EHA**

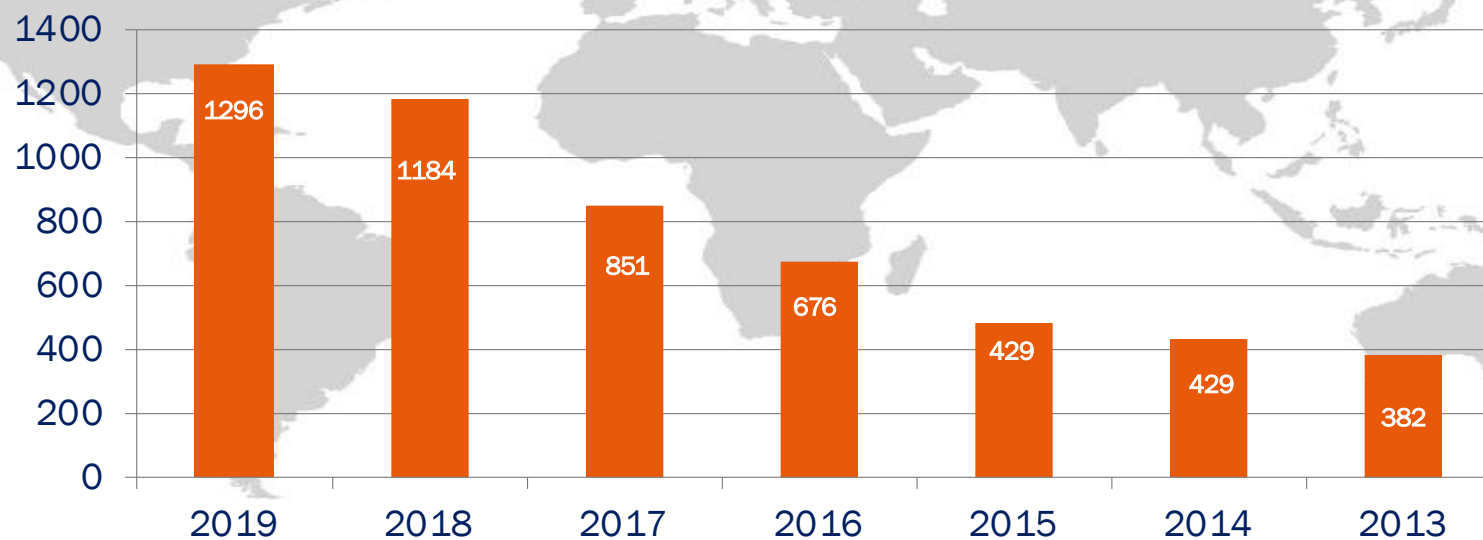


ERIC Membership

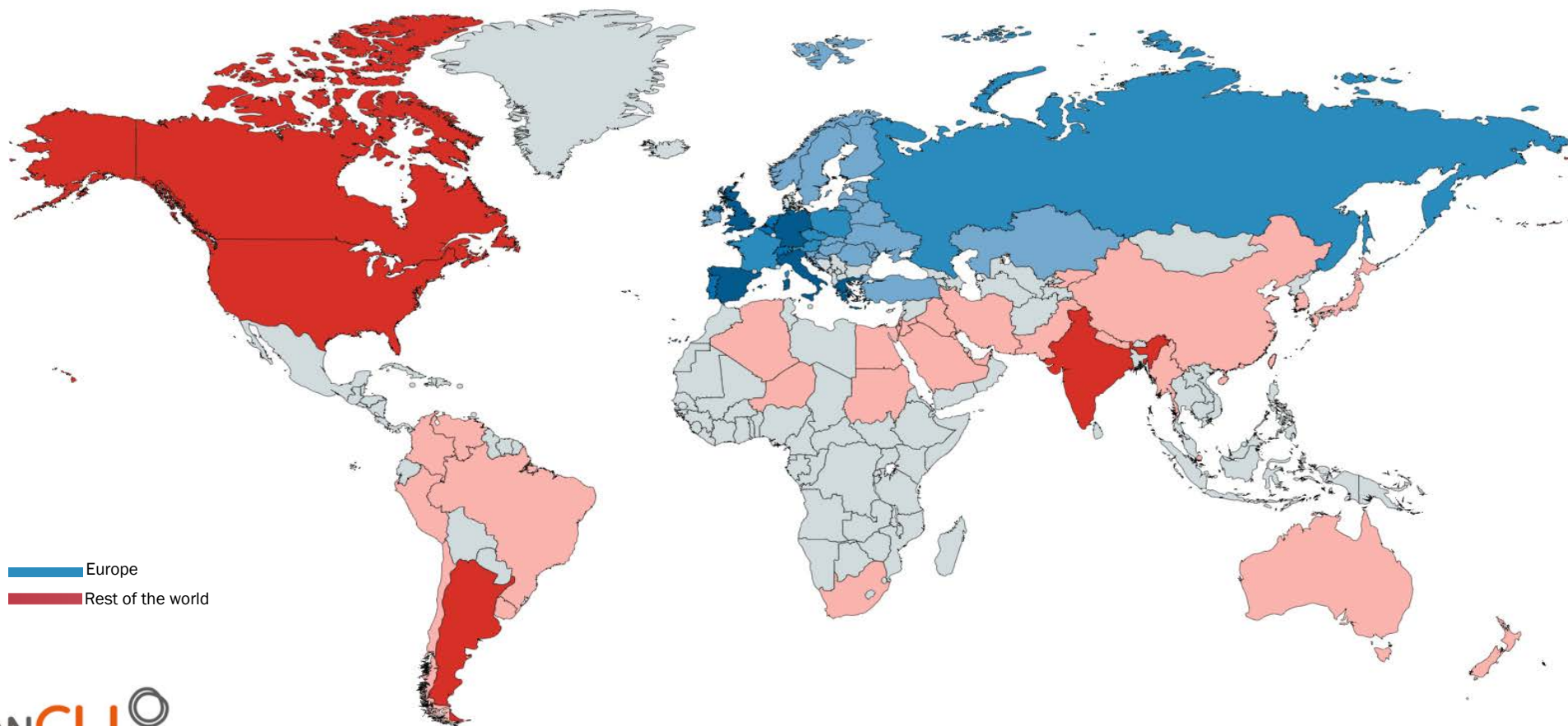
➤ 1296 Members

➤ Distributed amongst 79 countries / 680 different institutions

Number of ERIC members (per year)



ERIC Membership



ERIC Mission & Activities

To improve the outcome of patients with chronic lymphocytic leukemia (CLL) and related diseases through basic, translational and clinical research

through collaborative effort at European level

- Research Projects/Activities
- Publications
- Harmonization/Recommendations
- Meetings/Educational events

ERIC Mission & Activities

To improve the outcome of patients with chronic lymphocytic leukemia (CLL) and related diseases through basic, translational and clinical research

through collaborative effort at International level

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ERIC Mission & Activities

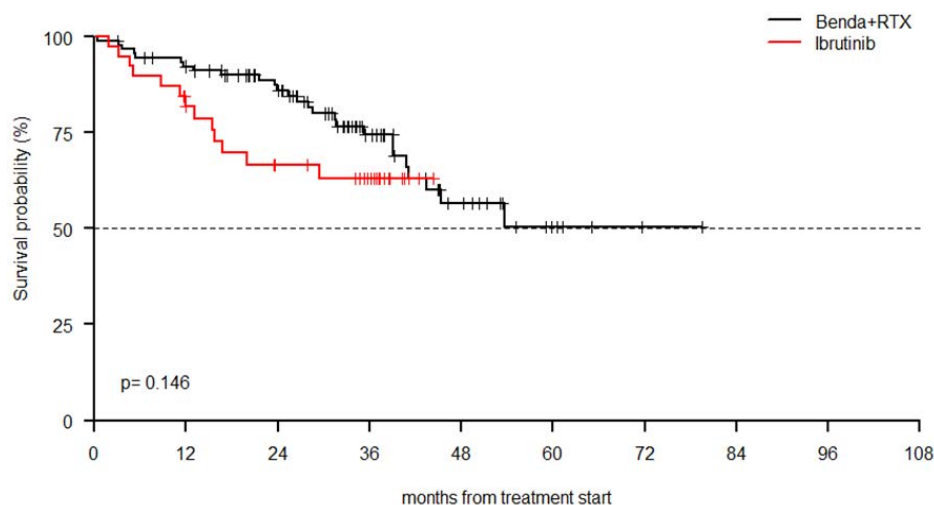
To improve the outcome of patients with chronic lymphocytic leukemia (CLL) and related diseases through basic, translational and clinical research

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Efficacy and safety of BR outside clinical trials in previously untreated older patients with CLL: an indirect comparison with ibrutinib

1. Efficacy and safety of BR in previously untreated CLL (35 GIMEMA and ERIC centres)



Variable	frequency (%)		p
	Benda + R n=237	Ibrutinib n=95	
Age [median (range)]	70.4 [39.4-87.8]	69.3 [27.5-85.3]	0.344
Age years ≤65/>65	69 (29.1)/168 (70.9)	32 (34.0)/62 (66.0)	0.427
Gender M/F	168 (70.9)/69 (29.1)	60 (63.2)/35 (36.8)	0.215
ECOG PS (%) 0-1/≥2	198 (90.0)/22 (10.0)	75 (83.3)/15 (16.7)	0.147
Stage Rai III/IV or Binet C no/yes	165 (78.6)/45 (21.4)		
Bulky lymph nodes (>5cm) no/yes	20 (8.9)/204 (91.1)		
Comorbidities 0-1/≥2	98 (41.7)/137 (58.3)		
Creatinine clearance (ml/min) ≤70/>70	100 (46.9)/113 (53.1)		
CD38 (>20%) neg/pos	52 (47.3)/58 (52.7)		
17p- yes/no	23 (12.6)/ 160 (87.4)	33 (39.8)/ 50 (60.2)	<0.001
FISH 13q-/ +12/11q-/17p-/no aberrations	45 (24.6)/32 (17.5)/38 (20.8)/23 (12.6)/45 (24.6)		
IGHV Mutated/Unmutated	40 (27.4)/106 (72.6)	14 (38.9)/22 (61.1)	0.251
Months between 1 st and 2 nd treatment <36/≥ 36	124 (52.3)/113 (47.7)	54 (75.0)/18 (25.0)	0.001
Previous treatment			
ORR rate to 1 st line treatment (%)	195 (82.3)/42 (17.7)	56 (78.9)/15 (21.1)	0.636
yes/no	174 (90.6)/18 (9.4)		
Refractory No/yes	95 (41.0)/137 (59.0)	22 (23.7)/71 (76.3)	0.005
CIT No/yes	39 (41.1)/42 (44.2)/14 (14.7)		
Chemo Ch/FL-based/Bendamustine	19 (13.9)/77 (56.2)/41 (29.9)		
CIT Ch/F-based/Bendamustine			
<6 cycles and/or dose reductions	140 (59.6)/95 (40.4)	-	-
Yes/no			

A Retrospective Study to Examine the Efficacy and Safety of Obinutuzumab + Chlorambucil and Obinutuzumab Monotherapy in the Frontline Treatment of CLL Patients-Outside Clinical Trials



Total patients: 460
(Excluded: 28)

Medical centers: 51
in 40 cities,
in 13 different countries:

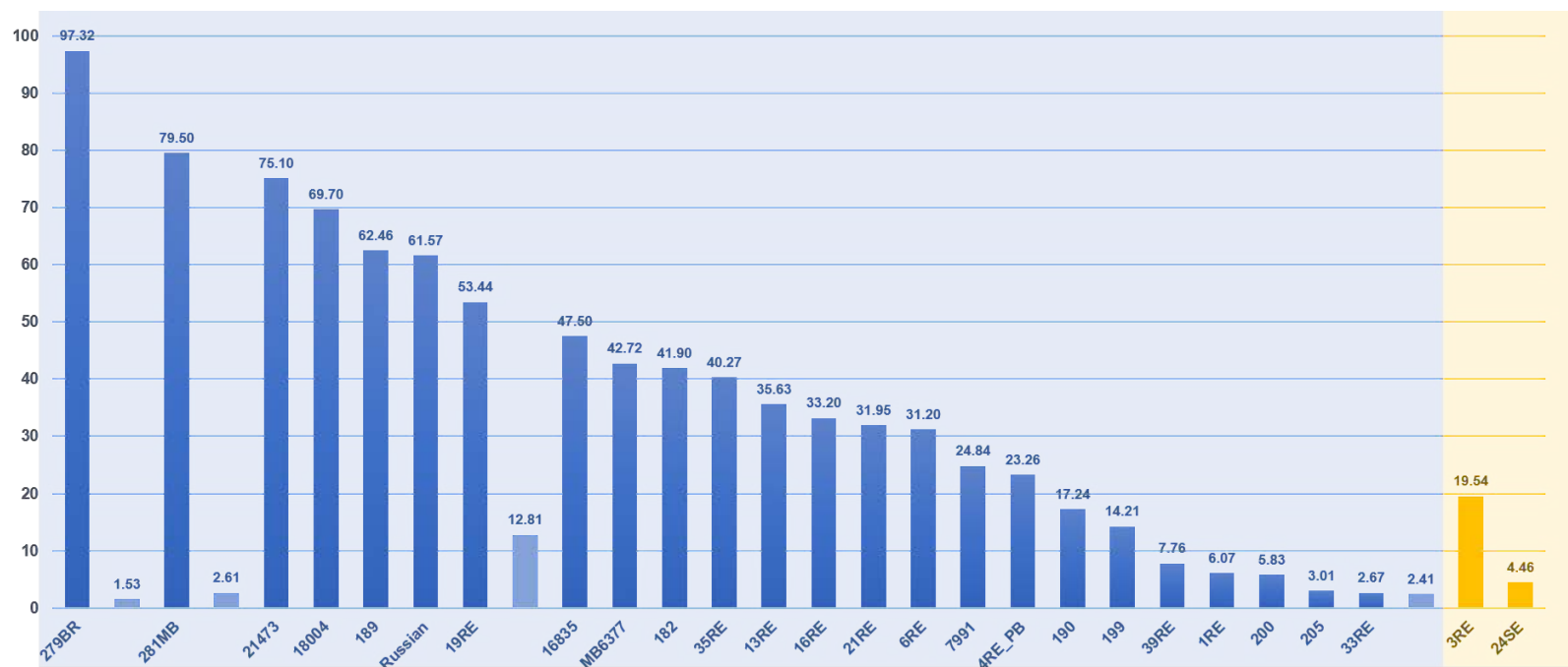
- Belgium (6 patients)
- Canada (3)
- Croatia (57)
- Czech Republic (36)
- Greece (9)
- Hungary (8)
- Israel (198)
- Italy (41)
- The Netherlands (1)
- Poland (30)
- Romania (35)
- Spain (30)
- Switzerland (3)



HALF OF CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS RELAPSING UNDER IBRUTINIB CARRY BTK AND PLCG2 MUTATIONS: A EUROPEAN RESEARCH INITIATIVE ON CLL (ERIC) REAL-WORLD STUDY



- 24/49 relapsed CLL cases with at least 1 BTKC481 mutation (49.5%)
- 2/50 responder CLL cases with 1 BTK mutation (4%)



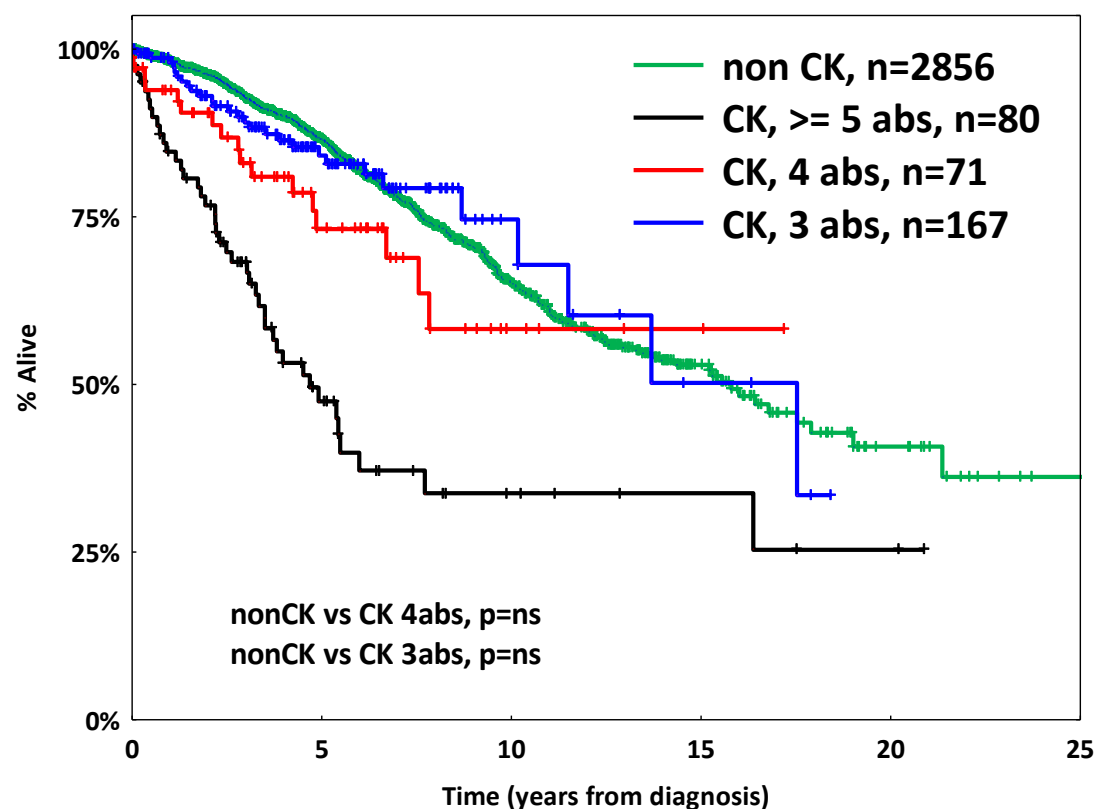
Total patients: ~100
(50 responders
50 resistant)

Medical centers: 20
Countries: 10

CYTOGENETIC COMPLEXITY IN CHRONIC LYMPHOCYTIC LEUKEMIA: DEFINITIONS, ASSOCIATIONS WITH OTHER BIOMARKERS AND CLINICAL IMPACT

Total patients: 5479
(93% CLL, 7% MBL)
189 (3%) excluded

Medical centers: 17
chromosome banding analyses
available



Big Data To Enable Better And Faster Treatments For Patients With Hematological Malignancies

Harnessing big data to predict prognosis in Chronic Lymphocytic Leukemia

To evaluate **11 of the most frequently mutated genes in CLL** and assess their prognostic and clinical relevance.

27 institutions
12 countries

Dataset
4999
CLL/MBL/SLL
cases

ATM
BIRC3
MYD88
NOTCH1
SF3B1
TP53
EGR2
POT1
NFKBIE
XPO1



★
India

ERIC CLL patient empowerment program (ERICdb)



Total patients:
~5386

Medical centers: 11
Countries: 6

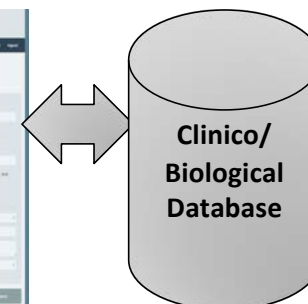
Retrospective data collection

- A template Excel will be available at ERIC site
- Files with anonymized retrospective data will be collected, reviewed and integrated into the common repository

Prospective data collection

- A web interface will be used for real time prospective data collection
- New cases and updates will be stored in a common repository in anonymized way

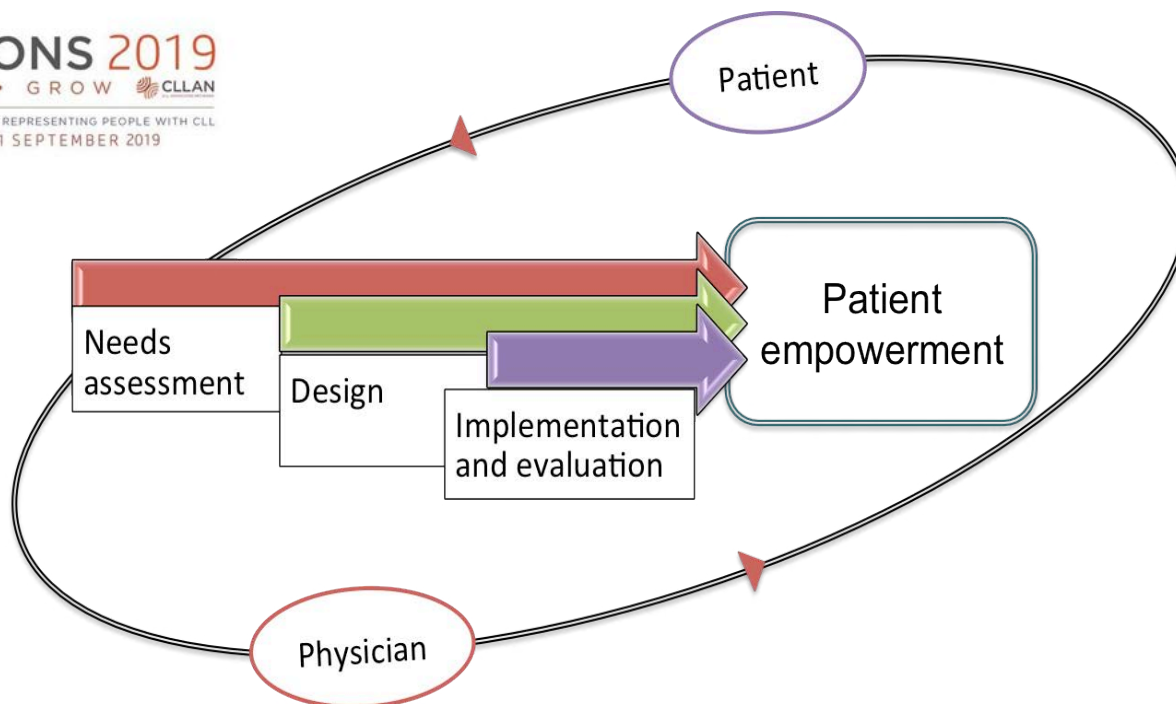
web forms



online upload & import tool

ERICdb will be connected to the other real world data projects of ERIC

ERIC CLL patient empowerment program



“CLL members know the disease but CLL patients know the illness”

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Recent ERIC Publications

CYTOGENETIC COMPLEXITY IN CHRONIC LYMPHOCYTIC LEUKEMIA: DEFINITIONS, ASSOCIATIONS AND CLINICAL IMPACT

P. Baliakas, S. Jeromin, M. Iskas, A. Puiggros, K. Plevova, F. NguyenKhac, Z. Davis, G.M. Rigolin, A. Visentin, A. Xochelli, J. Delgado, F. Baran-Marszak, E. Stalika, P. Abrisqueta, K. Durechova, G. Papaioannou, V. Eclache, M. Dimou, T. Iliakis, R. Collado, M. Doubek, M. J. Calasanz, N. Ruiz-Xiville, C. Moreno, M. Jarosova, A.C. Leeksma, P. Panayiotidis, H. Podgornik, F. Cymbalista, A. Anagnostopoulos, L. Trentin, N. Stavroyianni, F. Davi, P. Ghia, A. P. Kater, A. Cuneo, S. Pospisilova, B. Espinet, A. Athanasiadou, D. Oscier, C. Haferlach and K. Stamatopoulos *Blood*. **2019 Mar 14;133(11):1205-1216.**

IMMUNOGLOBULIN GENE ANALYSIS IN CHRONIC LYMPHOCYTIC LEUKEMIA.

Agathangelidis A, Rosenquist R, Davi F, Ghia P, Belessi C, Hadzidimitriou A, Stamatopoulos K. *Methods Mol Biol*. **2019;1881:51-62**

TAILORED APPROACHES GROUNDED ON IMMUNOGENETIC FEATURES FOR REFINED PROGNOSTICATION IN CHRONIC LYMPHOCYTIC LEUKEMIA.

Baliakas P, Moysiadis T, Hadzidimitriou A, Xochelli A, Jeromin S, Agathangelidis A, Mattsson M, Sutton LA, Minga E, Scarfò L, Rossi D, Davis Z, Villamor N, Parker H, Kotaskova J, Stalika E, Plevova K, Mansouri L, Cortese D, Navarro A, Delgado J, Larrayoz M, Young E, Anagnostopoulos A, Smedby KE, Juliusson G, Sheehy O, Catherwood M, Strefford JC, Stavroyianni N, Belessi C, Pospisilova S, Oscier D, Gaidano G, Campo E, Haferlach C, Ghia P, Rosenquist R, Stamatopoulos K; European Research Initiative on CLL (ERIC). *Haematologica*. **2019 Feb;104(2):360-369.**

HIGH-RISK CHRONIC LYMPHOCYTIC LEUKEMIA IN THE ERA OF PATHWAY INHIBITORS: INTEGRATING MOLECULAR AND CELLULAR THERAPIES.

Dreger P, Ghia P, Schetelig J, van Gelder M, Kimby E, Michallet M, Moreno C, Robak T, Stilgenbauer S, Montserrat E; European Research Initiative on CLL (ERIC) and the European Society for Blood and Marrow Transplantation (EBMT). *Blood*. **2018 Aug 30;132(9):892-902.**

EFFICACY OF BENDAMUSTINE AND RITUXIMAB AS FIRST SALVAGE TREATMENT IN CHRONIC LYMPHOCYTIC LEUKEMIA AND INDIRECT COMPARISON WITH IBRUTINIB: A GIMEMA, ERIC AND UNK CLL FORUM STUDY

Cuneo A, Follows G, Rigolin G M, Piciocchi A, Tedeschi A, Trentin L, Medina Perez A, Coscia M, Laurenti L, Musuraca G, Farina L, Rivas Delgado A, Orlandi E A, Galieni P, Romana Mauro F, Visco C, Amendola A, Billio A, Marasca R, Chiarenza A, Meneghini V, Ilariucci F, Marchetti M, Molica S, Re F, Gaidano G, Gonzalez M, Forconi F, Ciolli S, Cortelezzi A, Montillo M, Smolej L, Schuh A, A Eyre T, Kennedy B, Bowles K M, Vignetti M, de la Serna J, Moreno C, Foà R, Ghia P. *Haematologica* **2018 April 19**

ERIC RECOMMENDATIONS FOR TP53 MUTATION ANALYSIS IN CHRONIC LYMPHOCYTIC LEUKEMIA - UPDATE ON METHODOLOGICAL APPROACHES AND RESULTS INTERPRETATION

Malcikova J, Tausch E, Rossi D, Sutton LA, Soussi T, Zenz T, Kater A, Utoft Niemann C, Gonzalez D, Davi F, Gonzalez Diaz M, Moreno C, Gaidano G, Stamatopoulos K, Rosenquist R, Stilgenbauer S, Ghia P, Pospisilova S & on behalf of the European Research Initiative on Chronic Lymphocytic Leukemia (ERIC) – TP53 network *Leukemia* (2018) doi:10.1038/s41375-017-0007-7

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Harmonization

- ☐ **ZAP70**
Letestu et al, Cytometry part B (2006)
- ☐ **MRD**
Rawstron et al, Leukemia (2007)
Rawstron et al, Leukemia (2014)
Rawstron et al, Leukemia (2017)
- ☐ **IGHV genes**
Ghia et al, Leukemia (2007)
Langerak et al, Leukemia (2011)
Rosenquist et al, Leukemia (2017)
- ☐ **TP53 aberrations**
Zenz et al, Leukemia (2010)
Pospisilova et al, Leukemia (2012)
Benner et al, Haematologica (2014)
Te Raa et al, Br J Haematol (2014)
Malcikova et al, Leukemia (2018)
- ☐ **Novel gene mutations**
Baliakas et al, Leukemia (2015)
- ☐ **Cytogenetic complexity**
Baliakas et al, Blood (2019)
Leeksma et al, submitted 2019

TP53 Network

- ERIC promotes and supports, through education, the:
 - Importance of testing for **TP53** aberrations all cases needing therapy, before first and later lines of treatment
 - Adoption of appropriate diagnostic techniques to ensure reliable and comparable results
→ **Certification of laboratories**
- The countries in green have at least 1 certified centre
- Besides Europe, ERIC also has certified centres in Australia, Brazil, Canada and India



167
Certified
Centres from
32 countries



11
Reference
Centres



3
Certifying
Centres



8
TP53 Certification
Rounds completed



IGHV Network

- ERIC promotes and supports, through education, the:
 - Importance of **immunogenetic analysis** across the medical community before using CIT
 - Adoption of appropriate diagnostic techniques to ensure reliable and comparable results
→ **Certification of laboratories**
- The countries in blue have at least 1 certified centre
- Besides Europe, ERIC also has certified centres in Argentina, Australia, Taiwan and USA



92
Certified
Centres from
30 countries



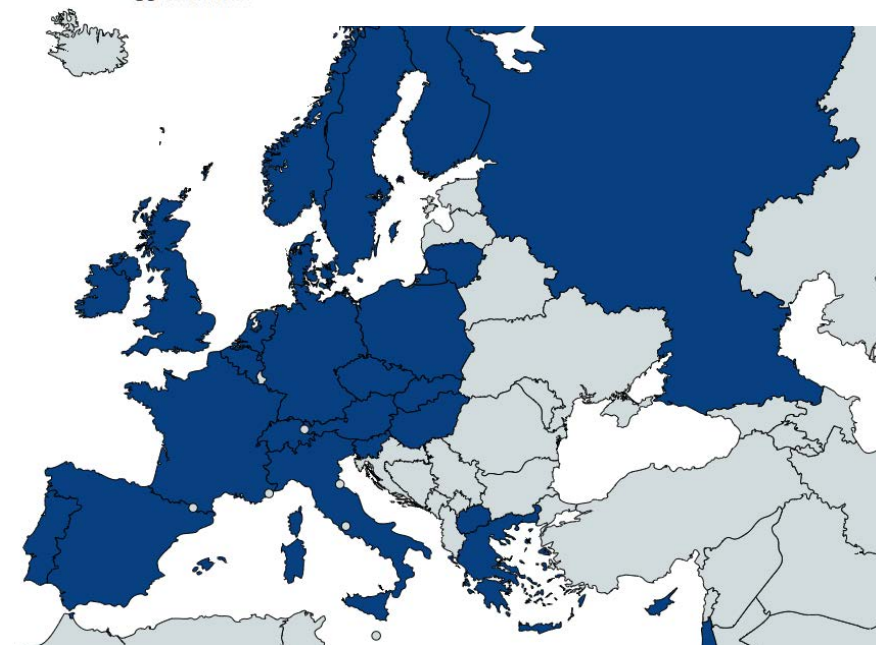
7
Reference
Centres



2
Certifying
Centres



4
IGHV Certification
Rounds completed



New External Quality Assessment(EQA/PT) for TP53 variant detection and IGHV mutation status testing in CLL



UK NEQAS

Leucocyte Immunophenotyping



- ERIC to continue to certify laboratories for *TP53* sequencing and IGHV mutation status testing
- **GenQA and UK NEQAS LI to jointly provide re-certification** in the form of an ongoing External Quality Assessment (EQA) programme
- Participation in EQA requires prior ERIC Certification
- Small pilot study of 15 participants to be performed in Autumn 2019 to validate EQA samples, reporting and marking processes



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Past Educational Workshops

- **HANDS-ON WORKSHOP ON IGHV GENE ANALYSIS IN CLL**
 - 1st 14-15 JUNE 2007, UPPSALA (SWEDEN)
 - 2nd 9-11 OCTOBER 2008, PARIS (FRANCE)
 - 3rd 24-25 SEPTEMBER 2009, THESSALONIKI (GREECE)
 - 4th 6 - 7 APRIL 2011, STRESA (ITALY)
 - 5th 26-27 SEPTEMBER 2013, BRNO (CZECH REPUBLIC)
 - 6th 22-23 SEPTEMBER 2016, UPPSALA (SWEDEN)
- **ERIC WORKSHOP ON IGHV ANALYSIS IN CLL**
 - 23 MAY 2017, TEL AVIV (ISRAEL)
 - 04 JULY 2018, TEL AVIV, ISRAEL
 - 10 APRIL 2019, TEL AVIV (ISRAEL)
 - 02 JULY 2019, TEL AVIV (ISRAEL)
 - 03 JULY 2019, NABLUS (PALESTINE)
- **NIH-ERIC WORKSHOP ON IGHV GENE ANALYSIS IN CLL**
 - 28-29 MARCH 2019, BETHESDA (MARYLAND, USA)
- **ERIC WORKSHOP ON TP53 ANALYSIS IN CLL**
 - 1st 1-3 OCTOBER 2015, MASARYK UNIVERSITY CAMPUS, BRNO (CZECH REPUBLIC)
 - 2nd 7-8 NOVEMBER 2017, HOTEL LA PALMA, STRESA (ITALY)
- **IMMUNOGENETICS IN CLL IN THE NGS ERA (ONE DAY WORKSHOP)**
 - 24 NOVEMBER 2017, ROTTERDAM, (THE NETHERLANDS)
- **INTERNATIONAL WORKSHOP ON BIOMARKER-GUIDED MANAGEMENT OF CLL**
 - 13 APRIL 2018, MOSCOW (RUSSIA)
 - 16-17 MARCH 2018, BELGRADE (SERBIA)
- **ERIC WORKSHOP ON MRD ANALYSIS IN CLL**
 - 1st 15-16 MARCH 2019, HOTEL LA PALMA, STRESA (ITALY)

Online Access to ERIC Workshops

ERIC WORKSHOP ON MRD ANALYSIS IN CHRONIC LYMPHOCYTIC LEUKEMIA

- 15-16 MARCH, 2019 (STRESA, ITALY)

EDUCATIONAL WORKSHOP ON IMMUNOGLOBULIN GENE ANALYSIS ON CLL

- 28-29 MARCH, 2019 (BETHESDA, US)

The screenshot shows the VuMedi website interface. At the top, there is a navigation bar with links: ABOUT US, OUR STORY, TEAM, CAREERS, NEWS, PARTNER WITH US. To the right of these links are input fields for 'Email...' and 'Password...', a 'SIGN IN' button, and a 'Forgot password?' link. Below the navigation bar, the main content area features a large teal background. On the left, there is a portrait of Dr. Kenneth Rosenfield, a man in a white lab coat. To his right, a quote reads: "VuMedi is a pressure-free environment where you can access medical education and make decisions on your own terms". Below the quote, his name and title are listed: Kenneth Rosenfield, MD, MASSACHUSETTS GENERAL HOSPITAL, Section Head, Vascular Medicine and Intervention, Cardiology Department. A 'LEARN MORE' button is positioned to the right of his name. On the right side of the main content area, there is a white box containing the VuMedi logo and the text 'Join over 250,000 Clinicians'. Below this text are several input fields: 'Select specialty' (a dropdown menu), 'First name' and 'Last name' (two separate text boxes), 'Email' (a text box), 'Choose Password' (a text box), and 'Confirm Password' (a text box). Below these fields is a line of text: 'By registering you agree to VuMedi Terms'. At the bottom of the white box is a 'CREATE ACCOUNT' button. Below the main content area, there is a section titled 'HOSPITAL PARTNERS' which displays logos for several medical institutions: Stanford MEDICINE, COLUMBIA UNIVERSITY MEDICAL CENTER, UPMC LIFE CHANGING MEDICINE, JOHNS HOPKINS MEDICINE, and Tufts Medical Center.

2020 ERIC Workshops

ERIC WORKSHOP ON TP53 AND IG GENES ANALYSIS IN CHRONIC LYMPHOCYTIC LEUKEMIA

- 26-27 FEBRUARY, 2020 (CHANDIGARH, INDIA)

WP7 MEETING/ERIC ASSEMBLY

- 31 MARCH, 2020 (MANNHEIM, GERMANY)

ERIC WORKSHOP ON MRD ANALYSIS IN CHRONIC LYMPHOCYTIC LEUKEMIA

- JULY, 2020 (JAPAN)

2nd EDUCATIONAL WORKSHOP ON IMMUNOGLOBULIN GENE ANALYSIS ON CLL – NORTH AMERICA

- NOVEMBER, 2020, Mayo Clinic, (SCOTTSDALE, AZ, US)

ERIC International Meeting 2018

- TOTAL 365 ATTENDEES

❖ Delegates	210
❖ Students/Trainees	47
❖ Pharma/Industry	53
❖ Faculty	42

- FROM 32 COUNTRIES

❖ Argentina	❖ Latvia
❖ Australia	❖ Lithuania
❖ Austria	❖ Netherlands
❖ Belgium	❖ Norway
❖ Canada	❖ Poland
❖ Colombia	❖ Portugal
❖ Czech Republic	❖ Romania
❖ Denmark	❖ Russia
❖ Estonia	❖ Serbia
❖ France	❖ Spain
❖ Germany	❖ Sweden
❖ Greece	❖ Switzerland
❖ Hong Kong	❖ Turkey
❖ Hungary	❖ Ukraine
❖ Israel	❖ United Kingdom
❖ Italy	❖ United States



ERIC International Meeting 2020

SAVE THE DATE



SAVE THE DATE

ERIC International Meeting
New frontiers in CLL Research

1-3 October 2020
Barcelona

- For registration: www.ericll2020.org

ERIC People



ERIC EXECUTIVE BOARD



PAOLO GHIA

Università Vita-Salute San Raffaele
Milan, Italy
President 2015-2018



ARNON KATER

The University of Amsterdam
Amsterdam, The Netherlands
Coordinator for education & Co-responsible for patient empowerment



CAROL MORENO

Hospital Sant Pau - Barcelona, Spain
Treasurer & Responsible for Clinical Studies



SARKA POSPISILOVA

The University Hospital Brno - Brno,
Czech Republic
Coordinator of TP53 Network



KOSTAS STAMATOPOULOS

INAB/CERTH - Thessaloniki, Greece
Responsible for Fundraising & Co-responsible for patient empowerment

OTHER WORKING GROUPS



ANASTASIA HADZIDIMITRIOU

INAB/CERTH - Thessaloniki, Greece
EU Infrastructures and frameworks & Database coordination



ANDY RAWSTRON

HMDS - Leeds, United Kingdom
Responsible for diagnosis and monitoring



RICHARD ROSENQUIST

Karolinska Institutet - Stockholm, Sweden
Responsible of Translational Genomics



LESLEY-ANN SUTTON

Karolinska Institutet - Stockholm, Sweden
Coordinator of NGS studies

ERIC MANAGEMENT



ESTHER LÓPEZ

ERIC Executive Office Barcelona, Spain
Office Manager

Are you a member of the ERIC?

1. YES
2. NO, I did not know it
3. No, but I will become soon
4. No, but someone at my institution is

Become an ERIC Member!

Joining ERIC could not be easier:
It is quick, simple and free to join!

[JOIN HERE](#)

[OUR MEMBERS](#)

- ✓ Receive updates on ERIC activities
- ✓ Participate in ERIC projects
- ✓ Network with other CLL experts
- ✓ it's free
- ✓ Join by going to our webpage:

www.ericll.org

**THANK YOU VERY MUCH
FOR YOUR ATTENTION**

www.ericll.org