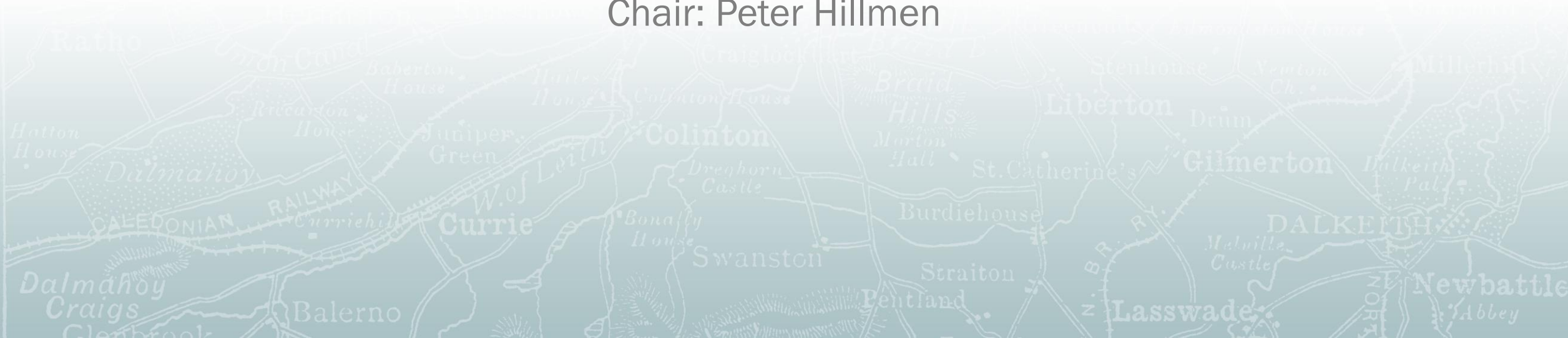




International Workshop on CLL  
20-23 SEPTEMBER 2019 EDINBURGH

# Session 11: iwCCLL UPDATES

Chair: Peter Hillmen



# 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

**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 31<sup>st</sup> 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**

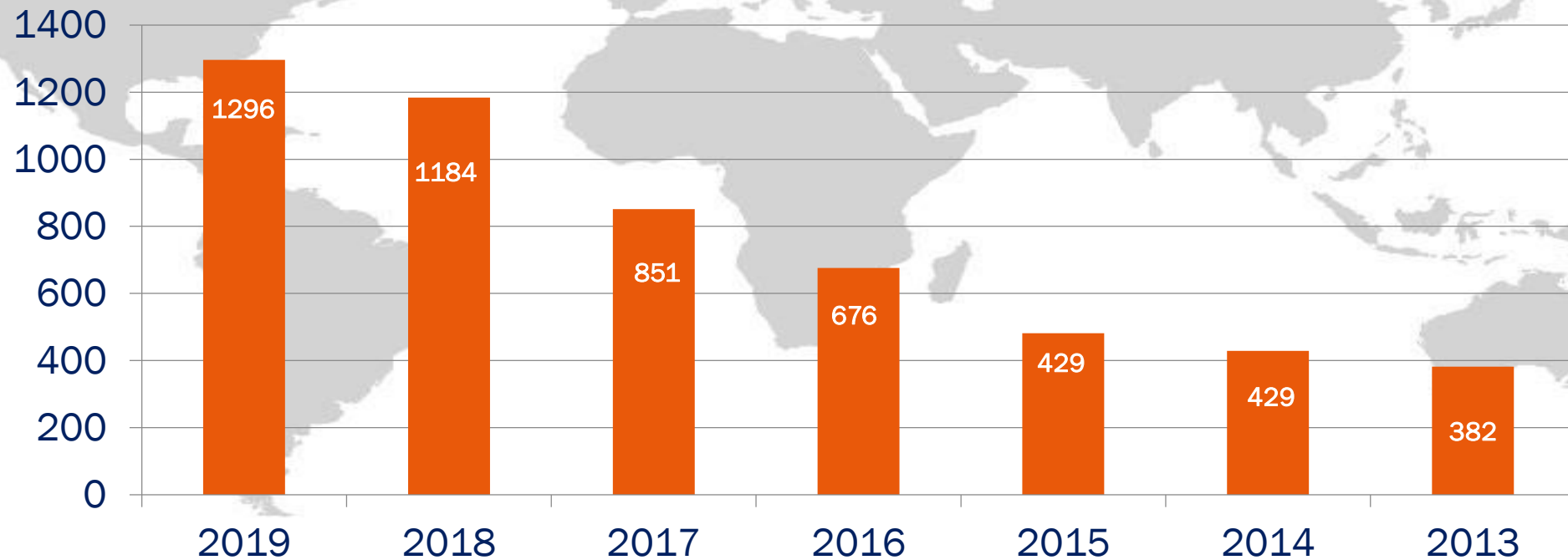


# ERIC Membership

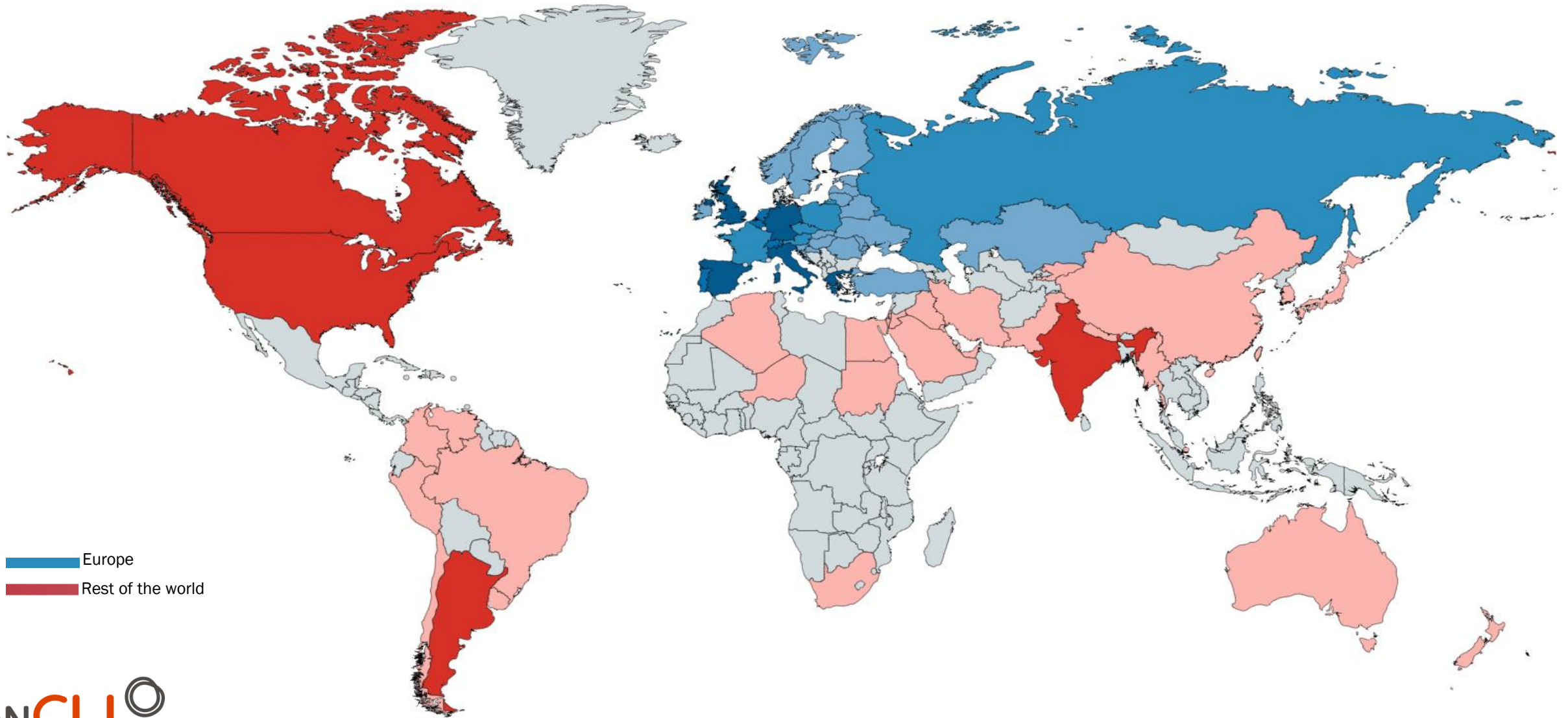
➤ **1296 Members**

➤ **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**

- **Research Projects/Activities**
- **Publications**
- **Harmonization/Recommendations**
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# ERIC Mission & Activities

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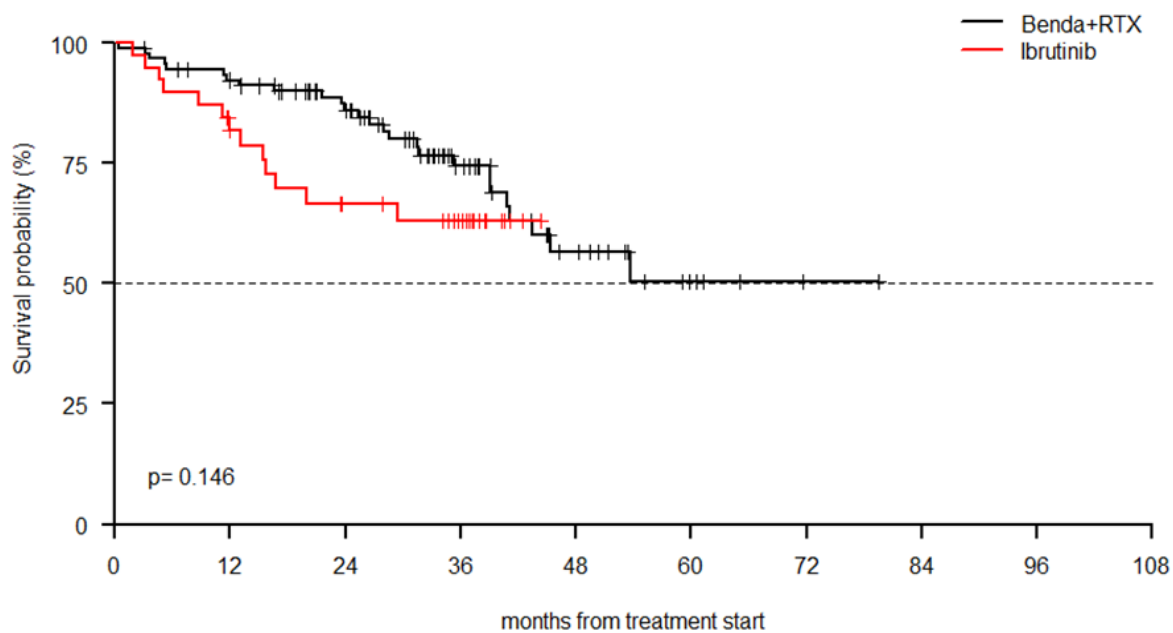
To improve the outcome of patients with chronic lymphocytic leukemia (CLL) and related diseases through basic, translational and clinical research

**through collaborative effort at International level**

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

# 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 <sup>st</sup> and 2 <sup>nd</sup> treatment <36/≥36	124 (52.3)/113 (47.7)	54 (75.0)/18 (25.0)	0.001
Previous treatment	-	-	-
ORR rate to 1 <sup>st</sup> line treatment (%) yes/no	195 (82.3)/42 (17.7) 174 (90.6)/18 (9.4)	56 (78.9)/15 (21.1)	0.636
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 Chl/FL-based/Bendamustine	19 (13.9)/77 (56.2)/41 (29.9)	-	-
CIT Chl/F-based/Bendamustine	-	-	-
<6 cycles and/or dose reductions Yes/no	140 (59.6)/95 (40.4)	-	-

# 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 (GIMEMA and ERIC centres)
2. Comparison with ibrutinib in patients with CLL treated in the front-line setting at 20 community and academic cancer centers in the U.S.

# 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)

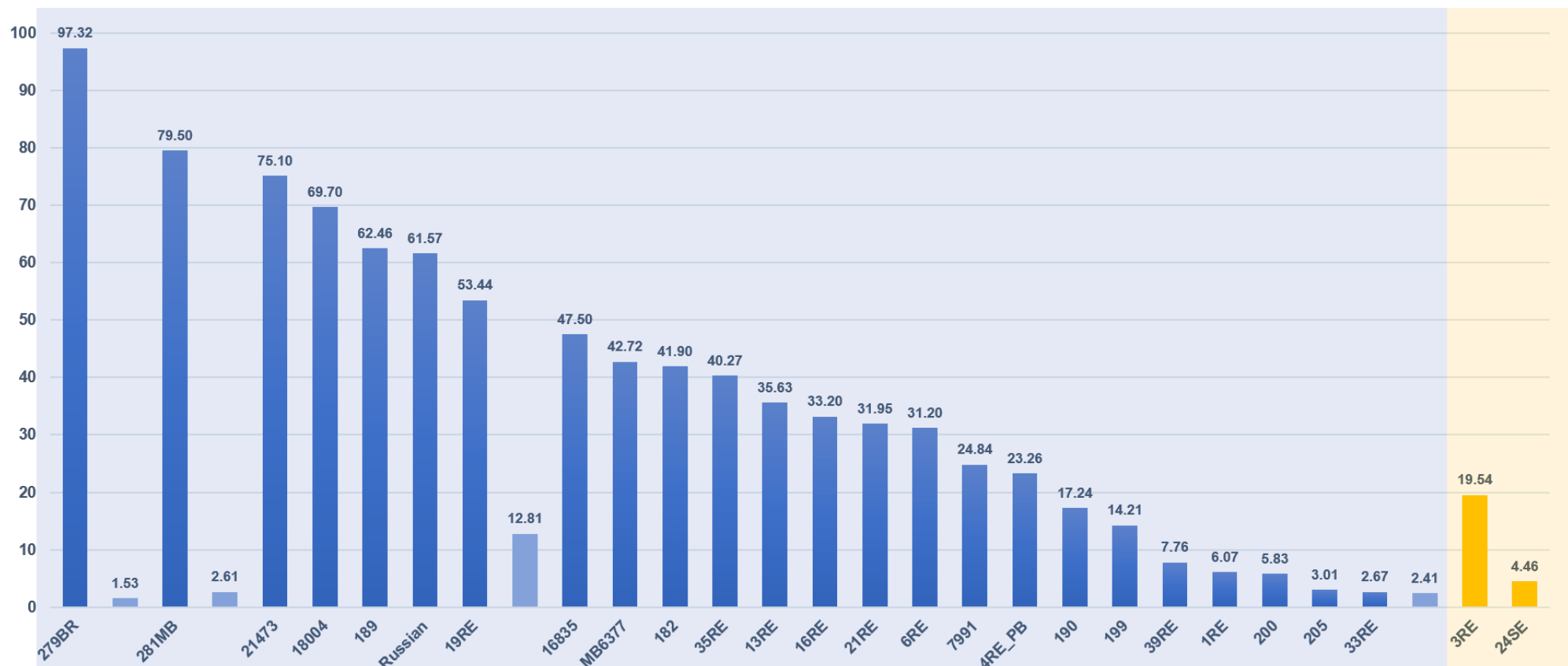


# HALF OF CHRONIC LYMPHOCYtic LEUKEMIA PATIENTS RELAPsing UNDER IBRUTINIB CARRY BTK AND PLCG2 MUTATIONS: A EUROPEAN RESEARCH INITIATIVE ON CLL (ERIC) REAL-WORLD STUDY

- 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)

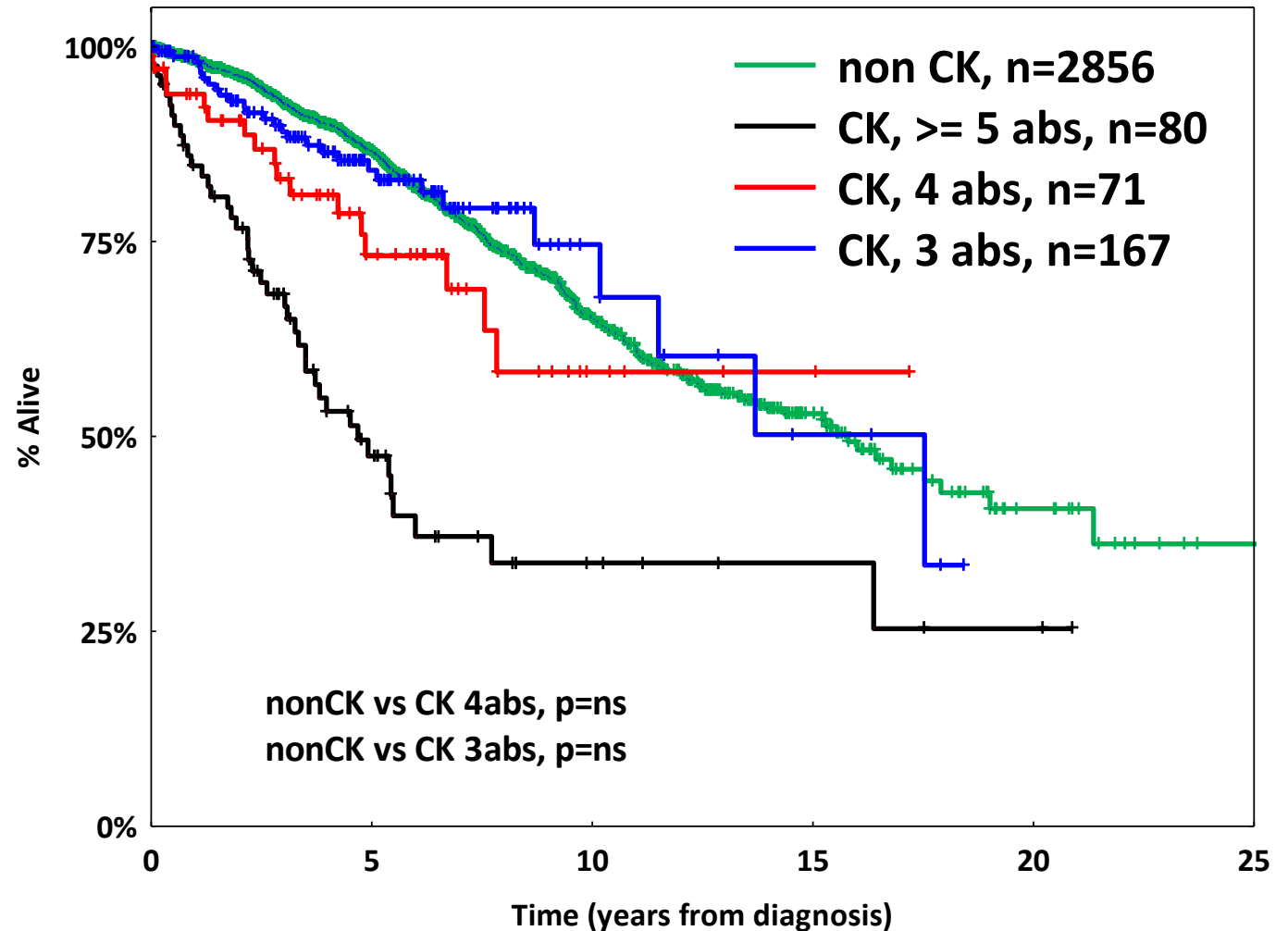
Medical centers: 20  
Countries: 10



# 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 International database (ERICdb)

Total patients:  
~5386

Medical centers: 11  
Countries: 6

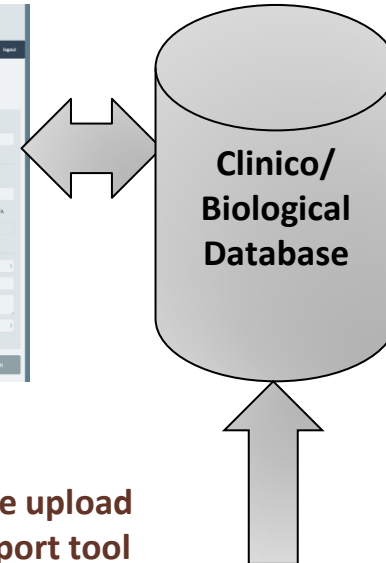
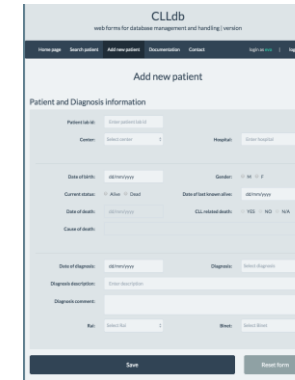
## *Retrospective data collection*

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

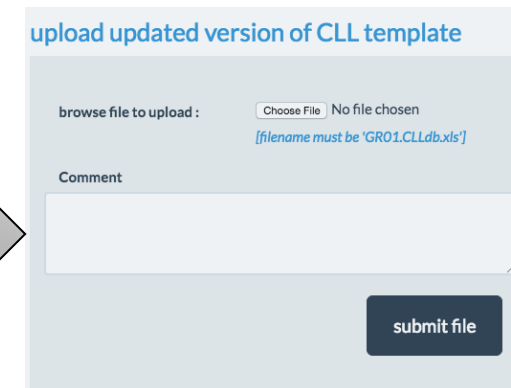
## *Prospective data collection*

- 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

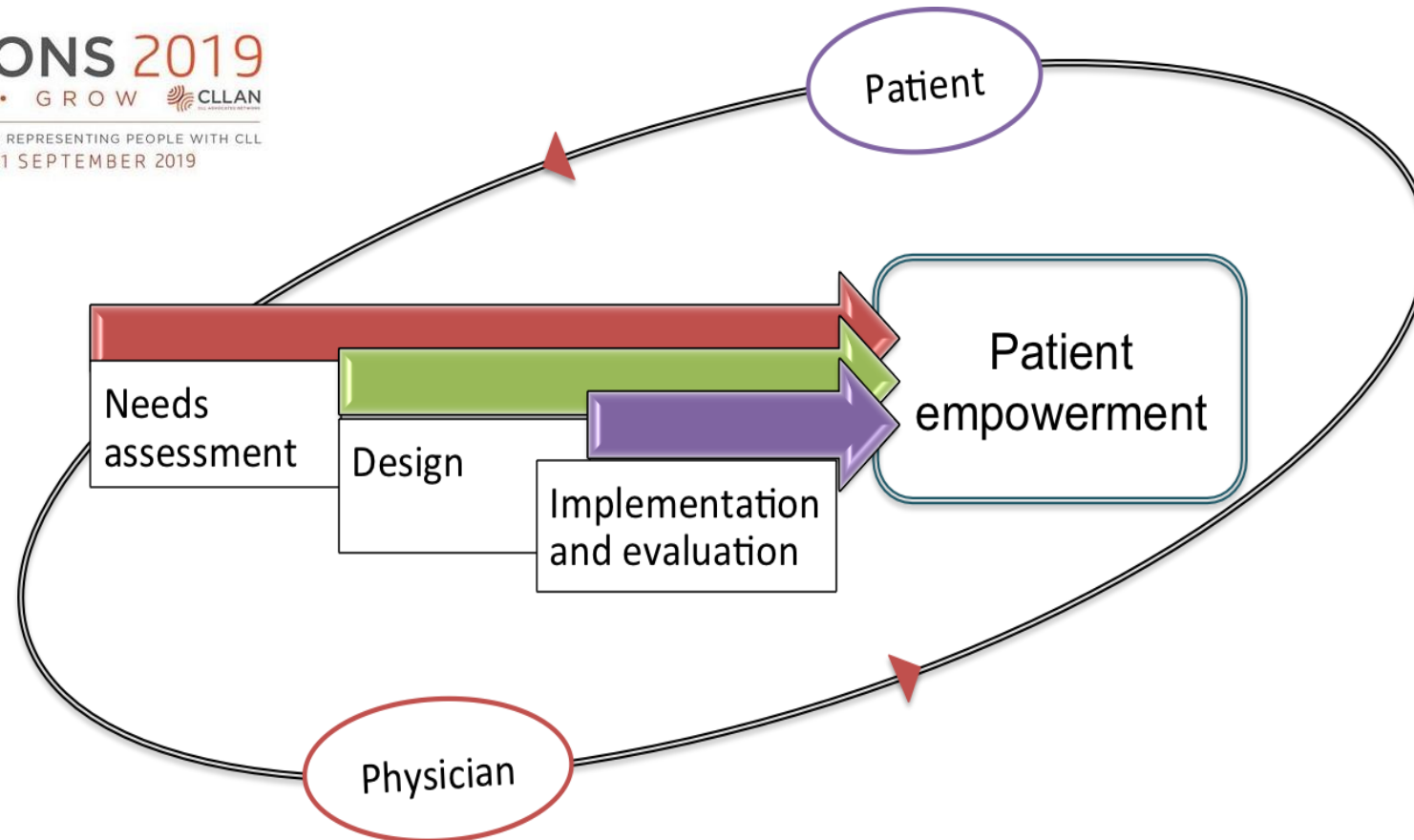
### web forms



### online upload & import tool



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



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

# ERIC Mission & Activities

---

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**through collaborative effort at an International level**

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

# 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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- Meetings/Educational events

# 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)  
Leeksa 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



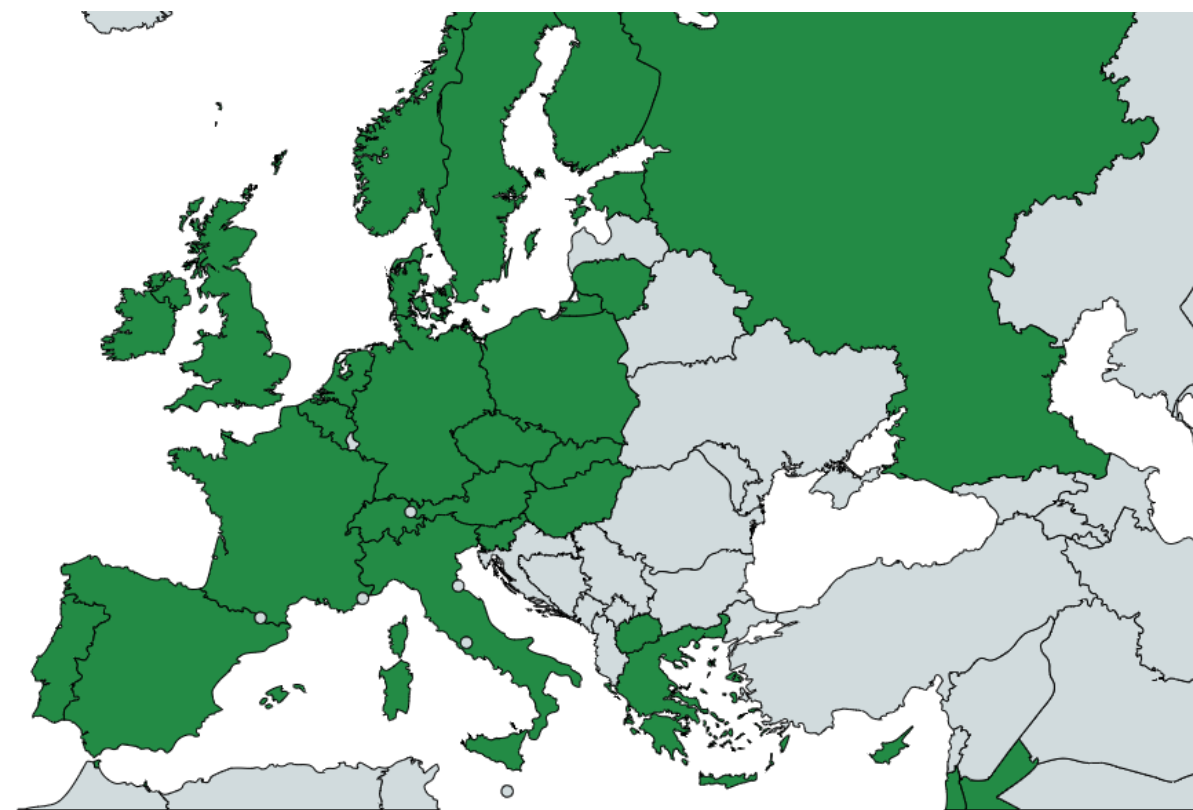
11  
Reference  
Centres



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



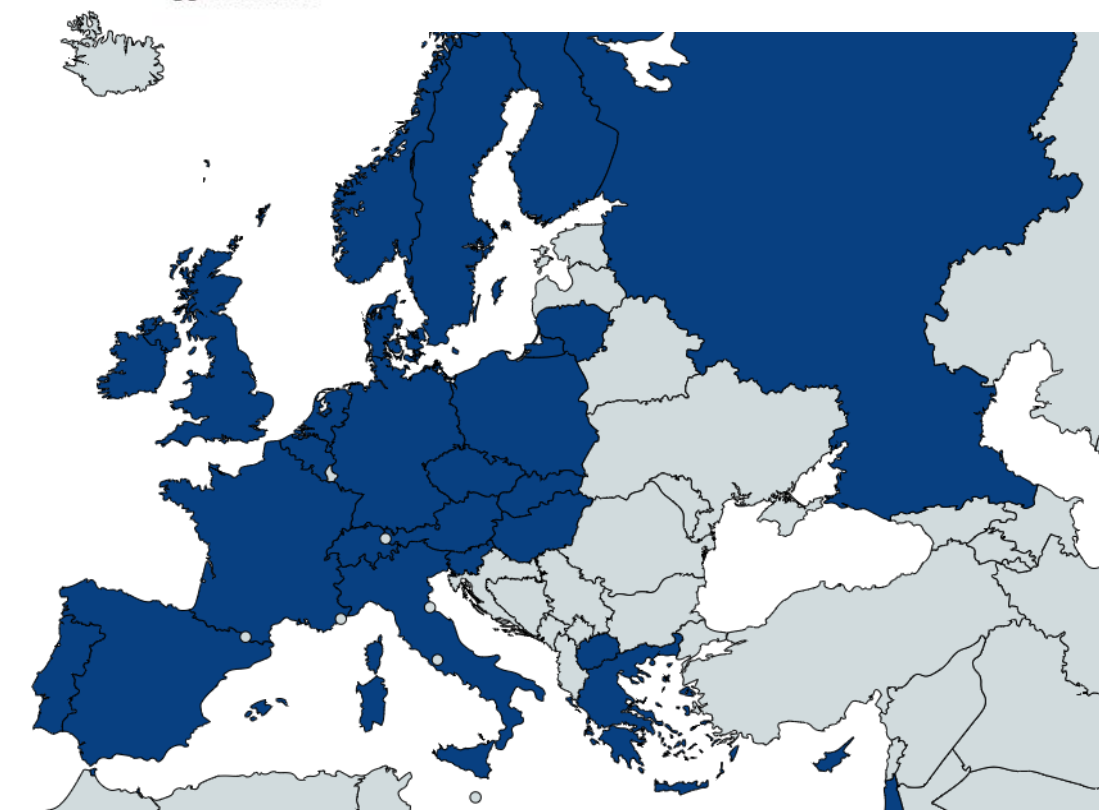
7  
Reference  
Centres



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

- 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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---

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- **Meetings/Educational events**

# 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)

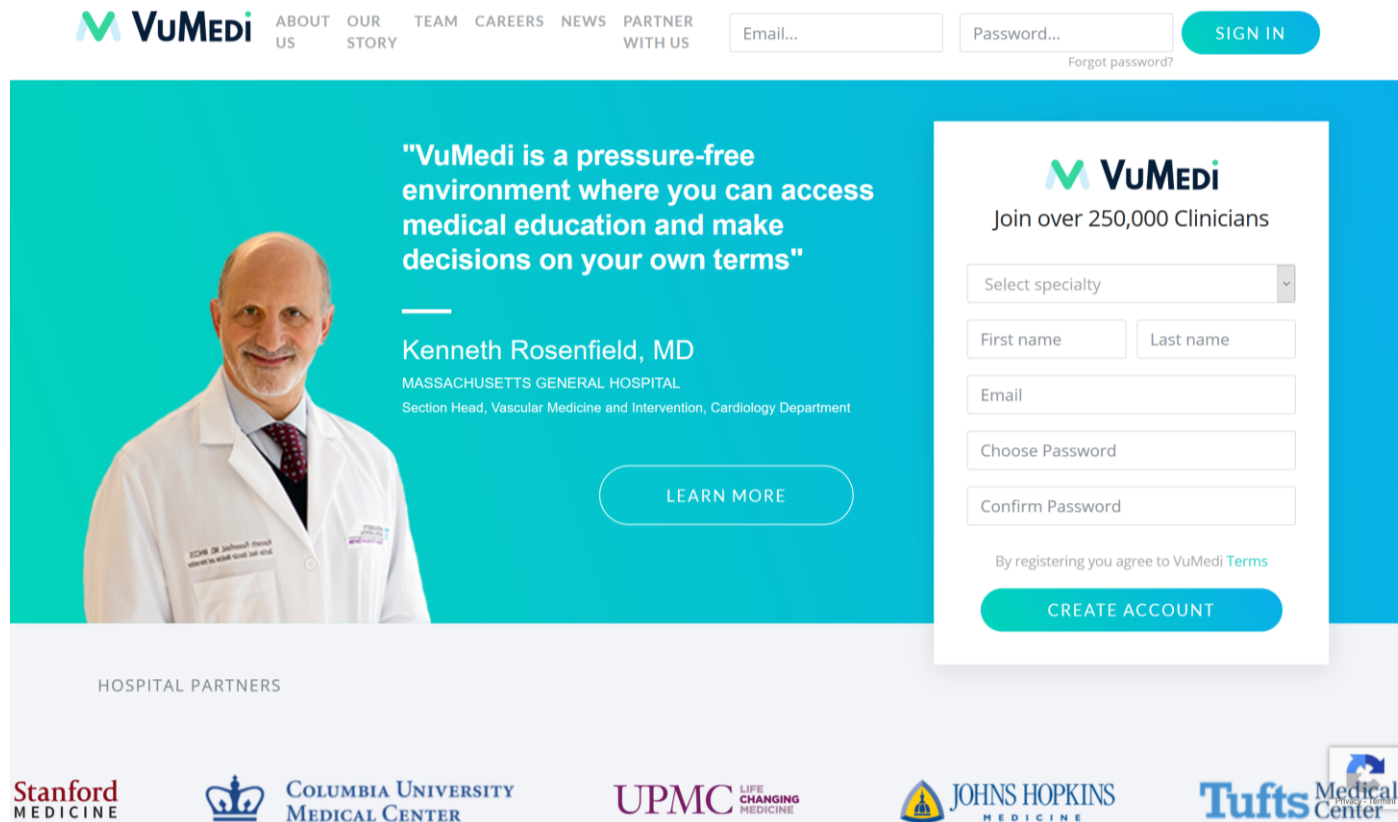
# Online Access to ERIC Workshops

## 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)



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# 2020 ERIC Workshops

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## 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 International Meeting 2018

- TOTAL 365 ATTENDEES

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

- FROM 32 COUNTRIES

- ❖ Argentina
- ❖ Australia
- ❖ Austria
- ❖ Belgium
- ❖ Canada
- ❖ Colombia
- ❖ Czech Republic
- ❖ Denmark
- ❖ Estonia
- ❖ France
- ❖ Germany
- ❖ Greece
- ❖ Hong Kong
- ❖ Hungary
- ❖ Israel
- ❖ Italy
- ❖ Latvia
- ❖ Lithuania
- ❖ Netherlands
- ❖ Norway
- ❖ Poland
- ❖ Portugal
- ❖ Romania
- ❖ Russia
- ❖ Serbia
- ❖ Spain
- ❖ Sweden
- ❖ Switzerland
- ❖ Turkey
- ❖ Ukraine
- ❖ United Kingdom
- ❖ 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](http://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 POSPISOLOVA**

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*



# 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](http://www.ericll.org)

**THANK YOU VERY MUCH  
FOR YOUR ATTENTION**

**[www.ericll.org](http://www.ericll.org)**