Newsletter

iCMLf International Chronic Myeloid Leukemia Foundation

November 2014
Edition 10

About the iCMLf

The International CML Foundation (iCMLf) is a Foundation established by a group of leading hematologists with a strong interest in CML. The mission of the iCMLf is to improve the outcomes for patients with CML globally. The Foundation is registered as a charitable organisation in England and Wales but its charter is global. Its aims are to foster and coordinate global clinical and research collaborations and to improve clinical practice and disease monitoring in CML, especially in emerging economic regions. Scientific advisors and national representatives spanning over 30 countries provide guidance and advice to further the aims of the iCMLf.

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Please support the iCMLf! Your donations and unrestricted grants enable us to support the opportunity for all CML patients to have the best possible outcome no matter where they live.

Dear Colleagues,

"Education is the most powerful weapon which you can use to change the world." Nelson Mandela

We see and hear this time after time as people take part in the iCMLf's educational activities. Increasing access to high quality CML education, along with ongoing discussions is at the core of the iCMLf's mission to improve outcomes for CML patients globally. From the one to one preceptorships, group meetings such as the John Goldman International CML Meeting and the iCMLf Forum for Physicians from Emerging Regions, or our online educational program, we continuously hear how these activities change clinical practice and make a real, practical difference to how CML patients are managed.

100 Clinical Preceptorships

We are so proud to have reached the target of 100 preceptorships for physicians treating CML in emerging regions.

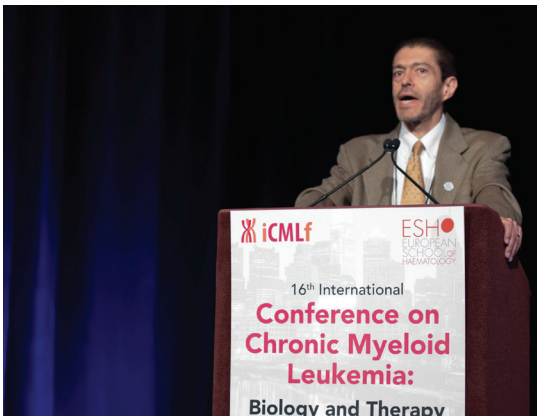
"It is true that not everything will be feasible in countries classified as emerging and in other words poor. But this experience helped to have a new vision for the treatment of disease. For our patients, they will be supported much better because I had more information on the disease and its treatment, and a discussion of issues with outside doctors." Dr Harivony from Madagascar who visited Bologna as the first iCMLf Preceptor in 2010

Launched in December 2009 the iCMLf Clinical Preceptorship Program is a unique opportunity for clinicians from developing countries who treat CML to undertake an intensive educational program to develop and expand their management skills.

The Preceptorship Program has been such a rewarding first project for the iCMLf to implement and 5 years on, we continue to learn how to meet the individual needs of hematologists as they travel from such diverse countries with varying facilities. From 5 host sites of clinical excellence we have expanded to 13 and now offer programs in 6 languages. The 2015 program is now open for applications. To apply email *melissa@cml-foundation.org.*

New virtual education on the iCMLf website

As you know, clinical data for CML is rapidly evolving, posing a challenge for many clinicians who are trying to keep up with developments, especially those who can't easily travel to one



Jorge Cortes opening the 2014 John Goldman CML Conference

of the major hematology meetings. The iCMLf website provides a portal to access the latest CML publications, meeting highlights, case discussions and clinical trials. If you are looking for something 'CML related' you will find it, or at least a link to it at *www.cml-foundation.org.* New this month are the latest updates on treating frontline CML as presented by Tim Hughes, Junia Melo and Susan Branford.

Understanding Scientific and Clinical Progress

The annual international CML meeting co-sponsored by the iCMLf and the European School of Haematology is well established as the premier CML meeting of the year. In 2014, in honour of Professor Goldman it was renamed the John Goldman International CML Conference: Biology and Therapy. You can read an overview of the meeting and reviews of the keynote presentations from the 2014 iCMLf Prize winners, Dr Owen Witte and Dr Rudiger Hehlmann, on pages 2-8 of this newsletter.

This edition of the iCMLf newsletter is dedicated to the education that the iCMLf can offer and the change that is possible because of it. We hope you can also make use of this 'weapon.'

Remember, become a member of the iCMLf, join our community and together we will continue to work towards improving outcomes for CML patients worldwide.

Your iCMLf team

16th Annual Conference on CML: Insights into biology and treatment of CML

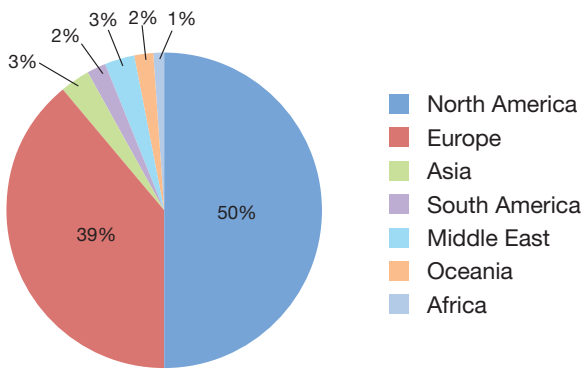
The Annual Conference on CML co-sponsored by the iCMLf and the European School of Haematology is *the* premier CML meeting presenting the latest updates on CML biology, clinical research and therapies. This year the meeting was held for the 16th time and renamed to the 'John Goldman Conference on CML: Biology and Therapy' in remembrance of the late Professor John Goldman who chaired and left his mark on the meeting for many years.

"I am honoured to now chair, together with Professor Tim Hughes and Professor Tessa Holyoake, this important scientific meeting. We continue working with the outstanding group of co-organizers John had put together to ensure the ongoing success of the meeting", said Jorge Cortes. Professor Cortes is deputy chair and Professor of Medicine at the Department of Leukemia at the University of Texas where he directs the CML program.

Chairs of the meeting: Professor Jorge Cortes (USA), Professor Timothy Hughes (Australia) and Professor Tessa Holyoake (UK)

"I enjoyed the total focus on CML, the format of the program and the presence of so many worldwide experts" (Attendee at the 16th John Goldman CML Meeting)

Delegates at the 16th John Goldman CML Meeting by Region



From September 4-7, 2014 over 520 clinicians and researchers from 45 different countries gathered in Philadelphia to discuss progress in the biology and therapy of CML. The conference again presented latest research findings from both a biological and a scientific perspective: *"It is amazing to see what we can achieve if clinicians and scientists with a strong CML focus bring together their expertise and jointly discuss their recent research results."* said Professor Jorge Cortes.

Meeting highlights

The distinguished scientific program was reviewed from clinical and scientific perspectives. The program included:

1) Nine scientific sessions that highlighted the latest findings in CML. Topics included; the leukemic stem cell, microenvironments and epigenetics, molecular biology, early new targets/agents for CML, mechanisms of resistance, monitoring, standardization and mutation assessment as well
as the safety of TKI therapy
2) Two workshops for non-clinical scientists:
   a. Generation and application of induced pluripotent stem cells (IPSC)
   b. How can epigenetics improve our understanding of haematological malignancies?
3) Two satellite symposia:
   a. Similarities and differences in chronic myeloproliferative neoplasms
   b. Practical aspects of monitoring in CML. (This session was so popular there was standing room only!)
4) Mentored clinical and biology poster walks.

Professor Deb White (Adelaide) leading a poster walk

John Goldman Fun Run

On Sunday morning it was an early start to the day for some attendees who ran with colleagues and friends at the inaugural 'John Goldman 5k Fun Run'. A special thank you to those who donated to the iCMLf and received a JMG Run T-Shirt (whether you ran or not!). We raised over $1,500 and this goes directly to iCMLf programs increasing access to education, diagnostics and treatment in emerging economic regions.

"It was a really great experience seeing the participants running through downtown Philadelphia and the sense of community uniting in a good cause!" Nicola Evans - iCMLf

2014 iCMLf Prizes – Recognising excellence in CML understanding and management

The **iCMLf Rowley Prize** recognises outstanding lifetime contributions to our understanding of the biology of CML. Following nominations from the CML community, the award is decided each year by a panel of past Rowley Prize winners and the iCMLf chair. Previous winners are; Brian Druker, Moshe Talpaz, John Goldman, George Daley and Connie Eaves.

The **iCMLf Goldman Prize** complements the Rowley Prize as a clinical equivalent by recognising lifetime contributions to the management of patients with CML. The new award has been created in memory of the late iCMLf chair Professor Goldman. Following nominations from the CML community the award is decided by a panel of past prize winners and the iCMLf Directors.

You can nominate colleagues and mentors for the **2015** iCMLf Rowley and Goldman Prizes by emailing *nicola.evans@cml-foundation.org*

Goldman Prize 2014
Recipient: Professor Rüdiger Hehlmann

The iCMLf Director's decision to award Rüdiger Hehlmann the first Goldman prize was due to the incredibly important contributions he made that have improved the outcomes for CML patients globally. As one of the leading CML scientists in Europe he was strongly committed to the creation of international CML study groups and networks to foster international research cooperation. Professor Hehlmann was founder of the German CML Study Group and involved in the creation of the European LeukemiaNet (ELN) that established common standards and guidelines for the treatment of leukemia across Europe. He was also President of the International Association for Comparative Research and Leukemia and Related Diseases (IACRLRD).

Jorge Cortes awarding the iCMLf Goldman medal to Dr Hehlmann

"This decision was made due to the incredible important contributions he made that have improved the outcomes for CML patients globally"

Rowley Prize 2014
Recipient Professor Owen Witte

This iCMLf award recognises Dr Witte's outstanding contributions to the understanding of the biologic fundamentals of leukemia and the development of therapeutic strategies for Ph+ positive leukemia. Owen Witte is a Distinguished Professor of Microbiology, Immunology and Molecular genetics. He is Director of the Eli and Edythe Broad Centre of Regenerative Medicine and Stem Cell Research at the University of California Los Angeles (UCLA) and a Howard Hughes Medical Institute Investigator. He currently holds the UCLA Presidential Chair in Developmental Immunology, Microbiology, Immunology and Molecular Genetics. His research focused on the interrelated problems of cell growth regulation and differentiation, and in understanding the function of cancer-causing genes found in human leukemia and epithelial cancers. This fundamental research became the foundation for the later development of imatinib as the first targeted therapy for CML.

The iCMLf was very pleased to award these Prizes during the Annual John Goldman Conference on CML. Over the coming pages you can read summaries by Professor's Witte and Hehlmann of their key note presentations.

Connecting Tyrosine Kinases to Cell Growth Control and Cancer Therapy

Owen N. Witte, M.D.
Broad Stem Cell Research Center at UCLA

In the 1970s the NCI supported many laboratories to investigate viral models of cancer. Joining the laboratory of David Baltimore at MIT as post-doctoral fellow in 1976, I was introduced to the Abelson murine leukemia virus by Naomi Rosenberg who had perfected methods to in vitro transform B lymphoid progenitors. In a highly collaborative effort including Steve Goff, Tony Shields, and others we deciphered the genome structure, protein expression and transformation behavior of this small defective retrovirus. During a recombination event the replication competent parental Moloney virus strain had captured a portion of the cellular Abl gene and produced a fusion protein with a portion of the viral group antigen gene (Gag) at its amino terminus. All of the transforming activity of the Abelson virus for fibroblasts, and hematopoietic cells was carried in this single fusion protein.

The first hint as to the mechanism of action for the Gag-Abl fusion came from work on a the Avian sarcoma virus protein Src by Mark Collett and Ray Ericson who demonstrated a kinase activity in immunoprecipitates incubated with 32P-ATP and divalent cation. We tried this assay and demonstrated that Gag-Abl proteins could autophosphorylate themselves and most interestingly that mutant versions that were transformation defective were also kinase deficient. In multiple attempts to define the end product of this autophosphorylation as either the expected serine or threonine residue I repeatedly generated only free phosphate following the 110 degrees C and 6N HCL hydrolysis procedure. Alternative phosphorylation linkages were considered including phosphotyrosine because other work in the Baltimore lab on the replication of poliovirus showed that a small protein was linked to the 5' end of the genome via a tyrosine phosphate bond. A sample of phosphotyrosine was obtained from the lab of James Wong at Harvard who was studying the enzyme to DNA linkage of one form of the topoisomerase enzyme family, which was also via a tyrosine residue. Armed with this standard and great help from Asim Dasgupta we shortened the time course and captured phosphotyrosine as an intermediate in the hydrolysis procedure. Independent work by Tony Hunter and colleagues on polyoma middle T and src immunoprecipitates defined phosphotyrosine using an alkaline hydrolysis method.

Timothy Hughes presenting the 2014 Rowley medal to Owen Witte

"Dr Witte discovered the tyrosine kinase activity for the ABL gene and the demonstration of the BCR-ABL oncoproteins in leukemia. He demonstrated that this kinase is critical for the leukemic phenotype of CML and related types of leukemia."

Connecting Tyrosine Kinases to Cell Growth Control and Cancer Therapy (continued)

Although we recognized the uniqueness of the tyrosine kinase activity we could not have imagined at the time the impact of this finding for subsequent understanding of normal and neoplastic growth control and cancer therapeutics.

Moving to my own laboratory at UCLA in 1980, my group continued to study the Abelson viral and normal cellular forms of the protein. The classic studies of Peter Nowell defining the Philadelphia chromosome, the critical observations of Janet Rowley defining the reciprocal translocation of chromosomes 9 and 22, and the cytogenetic mapping of Abl to the region of chromosome 9 near the translocation border all came together in the early 1980s with the definition of the Bcr-Abl genomic structure, chimeric RNA and fusion protein. By a different mechanism a new fusion protein with the Abl tyrosine kinase had been created which was similar to the viral form in being strongly activated for phosphotyrosine kinase activity. When cloned and expressed from a retroviral vector, the Bcr-Abl gene could transform immature lymphoid cells, other hematopoietic elements and even hematopoietic stem cells to create a useful model of CML. These collected studies defined that Bcr-Abl was the key pathogenic driver of a human leukemia and that inhibition of this activity would be potentially therapeutic and strongly influenced the drug discovery pathway for Imatinib and other Abl inhibitors now in clinical practice. This stands as the first and most dramatic example of inhibiting a key driver mutation in cancer with considerable therapeutic efficacy.

Parallel work in my lab continued into the 1990s on growth regulation via paracrine mechanisms and cytokines of immature B lymphocytes in a murine in vitro bilayer culture system (often called Whitlock-Witte cultures). The cell types expanding in such cultures included pre-B cells undergoing active immunoglobulin gene rearrangement and were known to be efficient targets for Abelson virus and the Bcr-Abl oncogene fusion. We searched for new kinases that might be responsible for the active growth of such immature lymphocytes and discovered a cytoplasmic tyrosine kinase, which is now named Bruton's tyrosine kinase. Unique structural features including protein interaction domains SH2 and SH3 were found along with a new lipid interaction domain called the plextrin homology or PH domain. This kinase was critically involved in the development of B lymphocytes and proliferation of these cells in response to signaling via the B cell immunoglobulin receptor. When Btk is mutated it results in selective B cell immunodeficiencies in mouse and man. Several critical receptor systems including immunoglobulin, Fc receptors, and some cytokine receptors depend on Brk for efficient signal transduction and utilize a kinase relay of Src family kinases to activate Btk in these developmental and growth control processes predicting a role for Btk in selected lymphomas and leukemias. These findings eventually lead to Btk inhibitors like Ibrutinib becoming effective therapies for activated B cell lymphomas and CLL in blast crisis.

Recent work has shifted to the study of epithelial cancers and in particular prostate cancer. We have used mass spectrometry to define activated kinases and pathways in the castration resistant stage of this disease to hopefully define new targets for therapy when androgen receptor blockade becomes ineffective. Time will tell.

Optimizing treatment of chronic myeloid leukemia (CML)

Rüdiger Hehlmann
Heidelberg University

Improvement of treatment and outcome of a disease can be achieved by new drugs, new techniques, or optimization of available treatments. In CML, treatment has been improved by interferon, transplantation and most recently by tyrosine kinase inhibitors. The German CML-Study group has a history of optimizing available treatments by randomized controlled trials.

Currently, three tyrosine kinase inhibitors (TKI) are available and recommended for first-line treatment of CML: imatinib, dasatinib and nilotinib. Improvement of outcome is impressive, but each drug has some properties requiring special consideration.

Evidence for first-line use is based mostly on single randomized studies. Only for imatinib confirmatory and treatment optimization studies have been published. Table 1 gives an overview of outcomes with primary imatinib.

Key criteria for evaluating new drugs are efficacy and safety. Efficacy criteria include speed of achieving remission (cytogenetic, molecular), depth of remission (molecular), progression, and survival. The new longevity of CML makes survival a problematic endpoint, since survival of CML patients may well exceed life expectancy of the investigator. Therefore cytogenetic and molecular remissions and rate of progression to advanced phases have become the preferred criteria for evaluation.

1

Survival with imatinib in clinical trials

Study	IM-dose mg	n	5yr survival %	8–10yr survival %	Median observation Years
CML-IV[2]	400 – 800	1536	90	84 (10yr)	7.1 (max. 11.7)
IRIS[1]	400	553	89	85 (8yr)	8
GIMEMA[3]	400 – 800	559	90		5
Hammersmith[4]	400	204	83		3.2
PETHEMA[5]	400	210	97.5		4.2
TOPS[6]	400 800	157 319	94 (4yr) 93.4 (4yr)		3.5 3.5
MDACC[7]	400 800	70 201		80 (10yr) 84 (10yr)	8 (min.) 8 (min.)
ILTE[8] (CCR only)	NR	832	98 (6yr)	95 (8yr)	5.8
Median			90%	84%	

NR = not reported; yr = year; min. = minimum

[1] Deininger M, et al. ASH 2009. Poster I-148; [2] Hehlmann R, et al. J Clin Oncol. 2014 Feb 10;32(5):415-23.;
[3] Baccarani M et al. EHA 2009. Haematologica 2009; 94[suppl.2]:254 abs. 0626;
[4] de Lavallade H et al. JCO. 2008 Jul 10;26(20):3358-63.; [5] Cervantes F et al. Haematologica. 2010 Aug;95(8):1317-24.;
[6] Baccarani M et al. Int J Hematol. 2014 May;99(5):616-24.; [7] Sasaki K, et al. ASCO 2014. Abstract 7024.;
[8] Gambacorti-Passerini C, et al. J Natl Cancer Inst. 2011 Apr 6;103(7):553-61.

Table 1

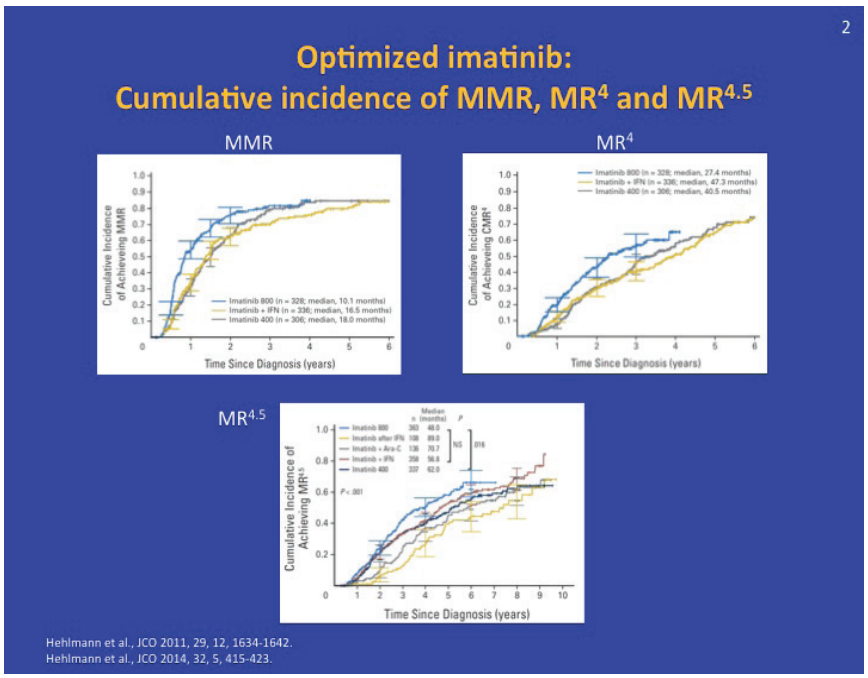
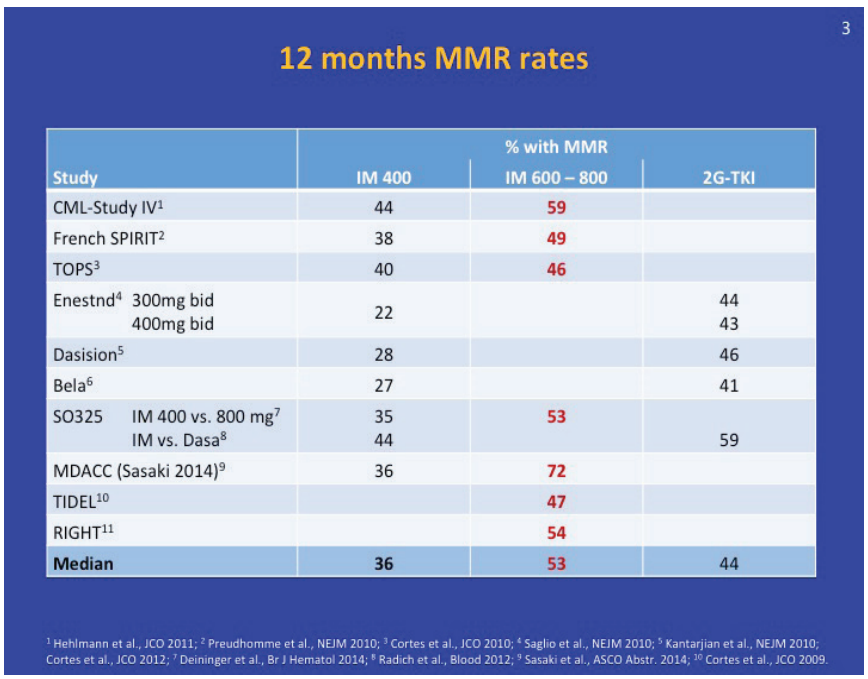


Fig. 1



Study	% with MMR IM 400	IM 600 – 800	2G-TKI
CML-Study IV[1]	44	59	
French SPIRIT[2]	38	49	
TOPS[3]	40	46	
Enestnd[4] 300mg bid	22		44
400mg bid			43
Dasision[5]	28		46
Bela[6]	27		41
SO325 IM 400 vs. 800 mg[7]	35	53	
IM vs. Dasa[8]	44		59
MDACC (Sasaki 2014)[9]	36	72	
TIDEL[10]		47	
RIGHT[11]		54	
Median	**36**	**53**	44

[1] Hehlmann et al., JCO 2011; [2] Preudhomme et al., NEJM 2010; [3] Cortes et al., JCO 2010; [4] Saglio et al., NEJM 2010; [5] Kantarjian et al., NEJM 2010; Cortes et al., JCO 2012; [7] Deininger et al., Br J Hematol 2014; [8] Radich et al., Blood 2012; [9] Sasaki et al., ASCO Abstr. 2014; [10] Cortes et al., JCO 2009.

Table 2

As a result, all studies evaluating efficacy of new TKI refer to comparative speed of cytogenetic and molecular remissions. In general 2nd generation TKI achieve remission faster than imatinib at the standard dose 400 mg. Also, fewer progressions to advanced phase are observed.

If higher initial doses of imatinib are given at 600 to 800 mg/day like in the current German CML-Study IV, rates of remission are similar to those achieved with 2nd generation TKI. Table 2 gives an overview on the 12 months MMR rates achieved in various randomized and observational studies on imatinib in standard or high dose and on 2nd generation TKI. Data from CML-Study IV (Fig. 1) show that MMR, MR4 and MR4.5 are reached significantly faster with dose optimized imatinib than with imatinib at standard dose.

The translation of ELN and NCCN recommendations for first-line treatment into routine practice require also consideration of safety criteria. After 15 years in clinical use imatinib can be considered a safe drug without serious adverse drug reactions (ADR) and no late toxicity. This is in contrast to the 2nd generation TKI nilotinib and dasatinib which are both associated with rare, but potentially life threatening ADR requiring careful assessment of vascular or pulmonary risk factors. This is not evidence against first-line use of 2nd generation TKI, but individual assessment of treatment is needed taking into account comorbidities and risk factors.

Evolving questions address a possible cure of CML (identification of candidates for a successful TKI discontinuation), early identification of patients likely to progress to advanced disease phases in order to deliver more intensive treatments, and the future of treatment optimization trials in the face of a legislation that values all studies analogous to registration trials and the given financial restrictions of academic research.

iCMLf Website – A new key interactive CML platform

The iCMLf's website is designed as an interactive resource that features information on the Foundation's programs and meetings, up-to-date scientific information on CML, e-learning lectures from key CML experts and a discussion forum providing expert advice on challenging CML cases. With an average of more than 130,000 page impressions and 24,000 visitors per month the iCMLf website is a well-received and well-used platform. The most frequently visited pages on the iCMLf website in 2014 are the:

- Clinical Case Discussion Forum
- Virtual Education Program
- iCMLf Board of Directors and Scientific Advisory Board

24,000 website visitors per month

How can the iCMLf website assist you?

If you would like to, or currently do any of the following then this CML website is for you…

- Find latest publications on CML in peer-reviewed journals on the **Scientific CML section** and submit interesting articles and publications to share with others
- Post and discuss interesting/challenging CML cases on the **Case Discussion Forum**
- View and share e-lectures from the iCMLf Virtual Education Program
- Catch up on the **iCMLf Programs** and download application forms
- Nominate online for one of the **iCMLf prizes**
- Check **Diary Dates** for important scientific meetings
- Subscribe to the **monthly iCMLf email newsletter**

If you have any ideas to enhance our website or would like to contribute please contact us at *info@cml-foundation.org.*

Tailor-made tools for physicians and emerging regions

The iCMLf website is accessed from 152 countries worldwide. A clear focus is from visitors from the emerging economic regions where access to information and resources are most limited.

The **Emerging Regions** section of the website is specifically customised to the needs of hematologists from emerging economic regions featuring:

- Information on the iCMLf's **Emerging Regions Support and Partnership (ERSAP) Programs**
- **French and Spanish speaking modules** of the Virtual Education Program
- Reports and webcasts from the annual **iCMLf Forum for Physicians from Emerging Regions**

Sharing up to date CML knowledge and education is such an important way for the iCMLf to facilitate best practice management of CML globally. So come and join the iCMLf community and visit *www.cml-foundation.org*. Watch out for new scientific publications, new educational modules and new features coming soon…

iCMLf Virtual Education Program – More than 140,000 e-lectures provided

The iCMLf Virtual Education Program is one of the key programs of the Foundation designed to address the need for equal access to up-to-date CML education and best practice CML management. The program, now in its 5th year, aims to share latest scientific findings on CML and to improve practical knowledge of CML treatment by providing online presentations from leading CML experts. Educational presentations include; pregnancy in CML, safely stopping therapy, molecular monitoring, transplantation in CML and new drugs in CML. Many topics consider the specific challenges that occur in the emerging economic regions.

Available on the iCMLf website, CML practitioners can access this up-to-date education in English, French and Spanish. The iCMLf Virtual Education Program has been very well received with more than 140,000 web streams of these educational lectures viewed by people from all over the world. Approximately 104,000 web streams were in English, 25,500 in French and 15,000 in Spanish. View the program at *www.cml-foundation.org/index.php/virtual-education-program.*

New series available

To provide wider access to the latest scientific findings on the biology and management of CML a new educational series has been added to the Virtual Program. We are pleased to make available presentations from the COLT Meeting 2014. COLT is an annual CML Opinion Leader Training that takes place in Adelaide (Australia). Each year international CML experts along with local delegates gather to discuss the latest information on CML management. In 2014, Professor Cortes joined the 10-year anniversary of the meeting which is supported by Novartis.

The first three modules cover frontline therapy for chronic phase CML.

1) **Addressing the Key Biological Questions in CML** – Prof. Junia Melo

- Pitfalls of tyrosine kinase inhibitor therapy
- The role of B-lymphoid kinase (Blk) in CML development
- Regulation of Blk and the role of Pax5 and cyclin-dependent kinase inhibitor p27
- Critical molecular pathways in LSCs
- Other key biological questions

2) **Risk Profiles, Molecular Targets and Pharmacokinetics** – Prof. Timothy Hughes

- Ways to optimize CML Therapy:
- Towards an accurate risk profile
- Early molecular response
- Kinase inhibition/ pharmacokinetics
- Study results from the ENESTxtnd sub-study of Australian patients and the OPTIM dasatinib trial

3) **The Importance of Deep Molecular Response for Patients with CML** – A/Prof. Susan Branford

- Importance of deep molecular response in CML
- Time duration to achieve deep molecular response
- Factors associated with deep molecular response
- Discontinuation trial criteria
- Patient cases and clinical studies with patients on imatinib based therapy

Go to *www.cml-foundation.org>>Science and Education>>Virtual Education* to view these e lectures.

Additional modules will be added over the coming months. Topics include; High risk CML and New developments in CML.

Other highlights from the 2014 iCMLf online education platform

1) Web streams from a special CML Colloquium at EHA 2014

To ensure key CML presentations are available to a broader audience, the iCMLf also provides web streams of important CML meetings. In 2014 the iCMLf website featured presentations on 'Milestones of the developing understanding of the molecular biology of CML over the past decades and the evolution of the treatments of CML'. These presentations were made during a special CML Colloquium in memory of Janet Rowley and John Goldman during the annual meeting of the European Hematology Association (EHA) in 2014. The meeting was co-organised by Alpine Oncology Foundation, EHA and the iCMLf.

Presentations still available for viewing are:

Christina Harrison

The Cytogentic Story: Is the Philadelphia chromosome really the initiating event for CML in CP?

Michael Deininger

The Molecular Biology Story: Unravelling the molecular biology of CML

Jorge Cortes

The Imatinib Story: The beginning of a successful treatment revolution for patients with CML?

Jane Apperley

The Stem Cell Transplantation Story: Optimizing to select suitable patients

Jerald Radich

The Monitoring Story: Evolution of the molecular tools for optimal diagnosis and monitoring

Guiseppe Saglio

The 2G- and 3G-TKIs Story: The challenge to improve outcomes and discontinue therapy effectively and safely

Go to *www.cml-foundation.org>>Science and Education>>Meetings* to see these Colloquium presentations.

2) Adherence in CML

A module on non-adherence of CML patients was added to the Virtual Education Program earlier in 2014 and is still available for viewing. Giora Sharf presents data from the global adherence survey of the CML Advocates Network.

Thank you to all our supporters!

We appreciate and thank all the 'Friends of the Foundation' who give both of their time, and financially to further the aims of the iCMLf.

We thank our corporate partners for their generous contributions that help us to improve the outcomes for patients with CML globally.

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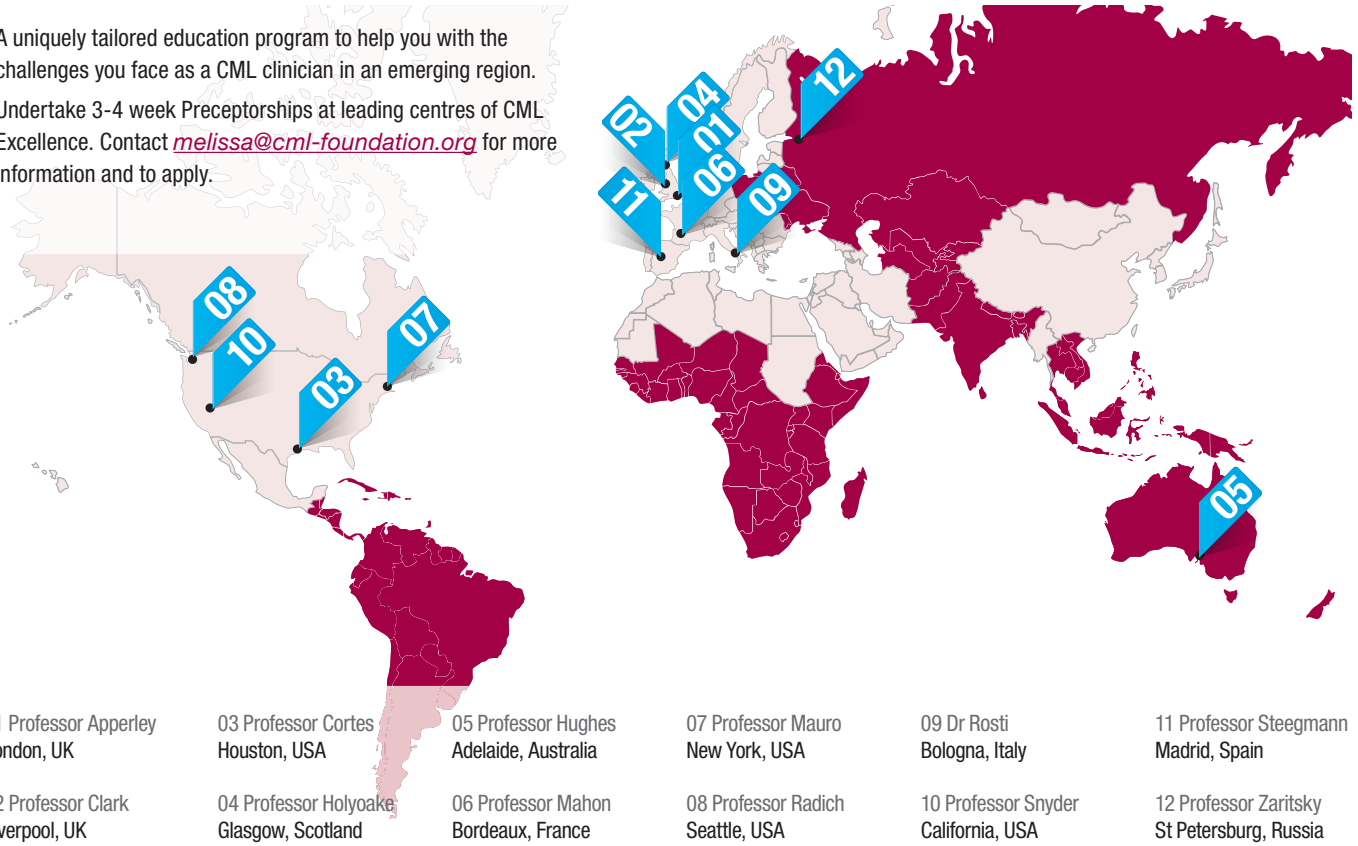
To donate to the work of the iCMLf go to *www.cml-foundation.org*

Apply now for the 2015 iCMLf preceptorship program

A uniquely tailored education program to help you with the challenges you face as a CML clinician in an emerging region.

Undertake 3-4 week Preceptorships at leading centres of CML Excellence. Contact melissa@cml-foundation.org for more information and to apply.



01 Professor Apperley
London, UK

02 Professor Clark
Liverpool, UK

03 Professor Cortes
Houston, USA

04 Professor Holyoake
Glasgow, Scotland

05 Professor Hughes
Adelaide, Australia

06 Professor Mahon
Bordeaux, France

06 Professor Nicolini
Lyon, France

07 Professor Mauro
New York, USA

08 Professor Radich
Seattle, USA

09 Dr Rosti
Bologna, Italy

10 Professor Snyder
California, USA

11 Professor Steegmann
Madrid, Spain

12 Professor Zaritsky
St Petersburg, Russia

Join us at these 2015 international meetings

17th Annual John Goldman Conference on

CHRONIC MYELOID LEUKAEMIA: BIOLOGY AND THERAPY

Estoril, Portugal October 1-4, 2015

Chairs: J. Cortes, T. Holyoake, T. P. Hughes
Organisers: M. Copland, M. Deininger, F.X. Mahon, D. Perrotti, J. Radich, R. Van Etten

To register and for further information: www.esh.org
Email: nicolas.jaillard@univ-paris-diderot.fr