



International
Chronic Myeloid Leukemia
Foundation

International CML Foundation **Annual Report**

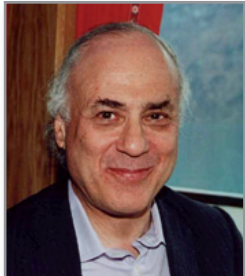
1st September 2011 to 31st August 2012



Contents

Chairman's welcome and Chief Executive's overview	3
iCMLf mission, aims, priorities and principles	4
Governance of the iCMLf	5
iCMLf Website	6
Emerging Regions Support and Partnership Preceptorship Program	7
iCMLf Forum	8
iCMLf Virtual Education Program	9
Emerging Regions Support and Partnership Diagnosis and Testing Program	10-14
iCMLf-ESH International CML Meeting	15
The iCMLf Rowley Prize 2011	16
International CML Awareness Day	17
iCMLf Expenditure	18

Chairman's welcome



John Goldman

In Athens in 2005 Tim Hughes, Jorge Cortes and I were discussing how other diseases had foundations that were able to do so much for patients and how CML seemed to have a big gap. The iCMLf germinated from this conversation. With an overall mission to improve outcomes for people with CML globally, the more specific aims of the iCMLf are to foster and coordinate global clinical and research collaborations and to improve CML clinical practice and disease monitoring worldwide. Now in its third year we can

clearly see the progress we have made towards these objectives.

The particular strengths of the iCMLf lie in our collective expertise in CML and in our global focus. We can build on these strengths to develop and implement the iCMLf programs that really impact on patient care.

With our two major educational programs, the Emerging Regions Support and Partnership (ERSAP) Preceptorship Program and the iCMLf Virtual Education Program we are able to provide access to information which until now has perhaps been limited. Through the iCMLf-ESH International CML Meeting and the iCMLf Forum for Physicians from Emerging Regions we are expanding CML education both globally and locally in emerging economic regions. These educational programs and meetings enhance the international

CML networks and can develop the strategies, research and future projects, which all impact directly on the management of individual patients with CML.

This year I am especially pleased to see the spread of CML diagnostic methods in emerging regions, through the iCMLf activities. The value of being able to provide for the first time molecular analysis of BCR-ABL1 in Ethiopia, Uzbekistan, and the Philippines cannot be overestimated.

Progress with diagnosis and monitoring will continue as a direct result of the GeneXpert BCR-ABL1 research project, where we will not only confirm definitely the clinical diagnosis of CML at the centres involved, but also gather useful, transferable data throughout the emerging regions.

With the support of all those we work with we have made significant progress. Through our multi-country, multifaceted programs we are influencing and enhancing the treatment of CML all over the world.

I believe that this Annual Report exemplifies the way in which other specialised medical practices can in the near future be made available very much more widely than they currently are – to the real benefit of literally millions of persons worldwide. I hope you enjoy reading it.

John M Goldman
Chairman of the Board



Nicola Evans

From little things, big things grow. From the germ of an idea from three leading hematologists the iCMLf has grown into a global Foundation changing the outcome of CML patient care around the world.

The aim for the iCMLf these last 12 months was to consolidate and build on the successful programs of last year, extend the influence of

the iCMLf through the members, partners and supporters of the Foundation and finally, increase the operational support of the iCMLf to enhance our capacity for future growth.

In 2011-2012 we have achieved and in many cases surpassed expectations. The iCMLf programs in emerging economic regions are the major focus for the Foundation. Through these projects 30 practicing hematologists (preceptors) attended educational programs at internationally renowned CML centres of excellence, we have provided in excess of 13,000 people access to up to date online education sessions from leading CML experts and developed specific projects to establish unprecedented access to CML diagnostics as part of the ERSAP Diagnosis and Testing Program.

These iCMLf programs are revolutionising the way CML is managed in the countries where access to treatment, monitoring and support is limited.

The goals and global reach of the iCMLf are strengthened through partnerships with other organisations with similar objectives. The iCMLf Forum and Virtual Education Program are both presented in conjunction with the Max Foundation and their success' are directly attributable to our effective partnership. As the iCMLf goes from strength to strength we have needed to expand accordingly, appointing a dedicated ERSAP Programs Coordinator. We also invited members into the iCMLf to build a strong network of people focused on furthering the progress towards best possible management of CML patients.

On behalf of the iCMLf Directors I sincerely thank all our members, partners and sponsors. Without your support, the iCMLf would not have achieved the progress of the last 12 months and continue to improve the treatment of CML patients globally. We have much still to do and many ideas, with your sustained support the iCMLf will continue to enhance patient care where assistance is needed most.

Nicola Evans
iCMLf Chief Executive

Chief executive's overview



The mission of the iCMLf is to improve the outcomes for patients with CML globally.

iCMLf aims and priorities

Registered as a charitable foundation in England and Wales, the iCMLf has a global charter. Formed by a leading group of hematologists, the aims of the iCMLf are to foster and coordinate global clinical and research collaborations and to improve clinical practice and disease monitoring in CML. There are numerous activities that could come within this broad charter but the initial focus is to meet the needs in CML that are not already being met by other groups, particularly those needs that are best met by a global organisation.

iCMLf guiding principles

- A focus on chronic myeloid leukemia and related disorders
- A truly independent not-for-profit foundation
- Collaboration with, but independence from, the pharmaceutical industry
- A global foundation with broad representation from all geographic regions
- Priorities and policies determined by hematologists and scientists involved in CML research and patient care
- Close consultation and cooperation with CML patient groups
- Active collaborations with key national and regional leukemia groups

Governance of the iCMLf

Board of Directors:



*John Goldman
(Chair) Imperial
College London, UK*



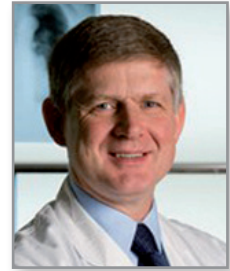
*Michele Baccarani
S. Orsola University
Hospital, Bologna,
Italy*



*Jorge Cortes
University of Texas
MD Anderson
Cancer Center, USA*



*Brian Druker
Knight Cancer
Institute, Oregon
Health & Science
University, USA*



*Andreas Hochhaus
University Medical
Center, Jena,
Germany*



*Timothy Hughes
Royal Adelaide
Hospital, Australia*



*Jerald Radich
Fred Hutchinson
Cancer Research
Center, USA*

Scientific Advisory Committee

There are eleven members of the iCMLf Scientific Advisory Committee. Members are respected hematologists, scientists and patient representatives who provide feedback and support for the activities of the Foundation.

Board of National Representatives

To ensure global influence and representation for the iCMLf, physicians from countries on all continents have agreed to become national representatives of the iCMLf.

The iCMLf National Representatives provide advice to the board and assist implementation of initiatives at a local level.

The 36 countries currently represented are:
Argentina, Australia, Austria, Belgium,
Brazil, Canada, China, Croatia, Cuba, Czech
Republic, England, Finland, France, Germany,
Hong Kong, India, Ireland, Israel, Italy,
Japan, Korea, Lithuania, Malaysia, Moldova,
Netherlands, New Zealand, Poland, Portugal,
Russia, Scotland, Serbia, South Africa, Spain,
Sweden, USA, Venezuela.

Operational Team



*Nicola Evans
Chief Executiver*



*Jan Geissler
Communications
Manager*



*Melissa Davis-Bishop
Emerging Regions
Support and
Partnership Programs
Coordinator*

The iCMLf website has become the educational social media platform for physicians treating patients with CML

Beyond providing all information about the Foundation, the iCMLf website (www.cml-foundation.org) has grown into a worldwide educational social media platform for health professionals treating CML patients. It not only features reports from iCMLf meetings and projects, but also provides “news and views” on CML issues from leading hematologists. Over the past three years, the website has become a vivid and interactive educational resource with up to date information for the CML community.

More than 13,000 visitors from more than 90 countries – each month

With an average of 85,000 page impressions and 13,000 unique visitors per month, the iCMLf website has become a frequently visited resource of hematologists. The website is accessed from more than 90 countries each month, with most common non-English language countries being China, Ukraine, Czech Republic, Russia, Poland, India, Sweden, France, Argentina, Japan and Germany, but the “long tail” also includes Mauritius, Burkina Faso, Ivory Coast, Kyrgyzstan, Nepal, Rwanda, El Salvador and many more ...

Write once, view many: iCMLf Discussion Forum shares insights on difficult CML cases

While information about the International CML Foundation is by itself the most popular piece accessed in the first place, the “Difficult CML Cases Discussion Forum” and the “ERSAP Program” are always following closely within the top five. The Difficult CML Cases Forum is a very good example of how information provided via Social Media multiplies in audience: While only 49 posts have been made in total, the most popular cases and their responses have been viewed a couple of hundred times – the “CML and Pregnancy” thread with almost 800 views, or the “Chronic phase CML but with granulocytic sarcoma” with around 270 views!

Current active cases on the iCMLf Difficult CML Cases Forum include:

- CML and pregnancy
- Multi-resistant, difficult to treat CML patient
- Chronic phase CML with granulocytic sarcoma
- Menorrhagia complicating imatinib therapy
- Imatinib and cardiomyopathy
- Pediatric CML
- Dilated cardiomyopathy and medications
- Pregnancy and 2nd generation TKIs



Almost 13,000 educational web lectures provided

The iCMLf Virtual Education Program (www.cml-foundation.org/vep) has become a valuable educational tool for clinicians from emerging regions, with leading hematologists provide e-learning tutorials about best practices for the management of patients with CML. More than 12,800 video streams providing educational lectures of leading CML experts. Clearly, the iCMLf website demonstrates the need for up-to-date eLearning resources in multiple languages. More detail about the iCMLf Virtual Education Program can be found on page 7.

“Brilliant presentation and very useful data regarding the importance of molecular monitoring”

Amisa Mukaj

Spreading the word

There are still many physicians treating CML patients that are not yet aware about the valuable educational resources provided on the iCMLf website. We continue to work to increase visibility of the iCMLf website, asking all members to link from their institution’s website to the iCMLf webpage. In this way we will continue to increase awareness of the iCMLf’s activities and overall support for the Foundation.

CML centres of excellence offer practical experience and one to one tuition



*Dr Kotlyarchuk (Uzbekistan) and
Dr Azevedo (Brazil) with Jane Apperley
at Hammersmith Hospital*

Now in its third year the Emerging Regions Support and Partnership (ERSAP) Preceptorship Program remains a critical project for the iCMLf. This program is a unique opportunity for physicians from emerging regions who treat CML to undertake an intensive education program to develop and expand their CML knowledge and skills.

Preceptorships take place at internationally renowned CML centres of excellence and participants conclude the program with practical understanding of the most up to date information influencing the care of patients with CML.

CML Centres of excellence

All the host centres donate their time and experience to ensure the success of the preceptorships and we thank all of the people involved for their time and dedication to the program and their visitors.

- **Hammersmith Hospital, London, UK** - Professor Jane Apperley
- **MD Anderson Cancer Center, Houston, USA** - Professor Jorge Cortes
- **OHSU Knight Cancer Institute, USA** - Professor Brian Druker and Associate Professor Michael Mauro
- **Royal Adelaide Hospital, Australia** - Professor Tim Hughes
- **S.Orsola-Malpighi University Hospital, Italy** - Professor Michele Baccarani
- **Centre Hospitalier Universitaire (CHU) de Bordeaux, France** - Professor Francois-Xavier Mahon
- **The Royal Liverpool University Hospital, UK** - Professor Richard Clark
- **Hospital Universitario de la Princesa, Madrid, Spain** - Professor Juan Luis Steegmann
- **City of Hope, California, USA** - Professor David Snyder
- **Fred Hutchinson Cancer Research Center, Seattle, USA** - Professor Jerry Radich

"This experience has reinforced to me the importance of timely monitoring of response to treatment and appropriate work-up and management of patients who have suboptimal response to treatment. In addition to these, I have also learned how the experts manage drug side effects. These additional knowledge and confidence in managing challenging cases of CML will improve the way I treat my CML patients"

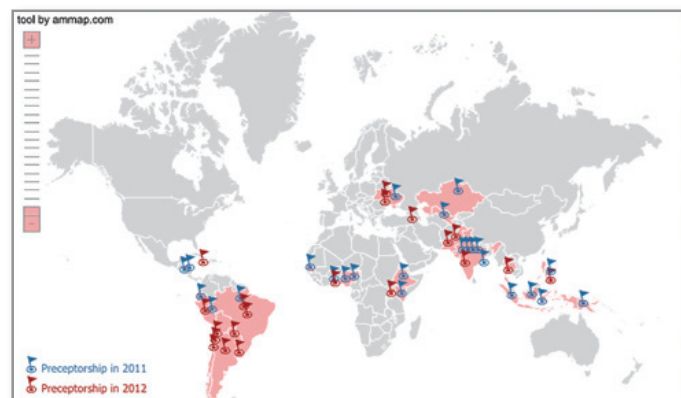
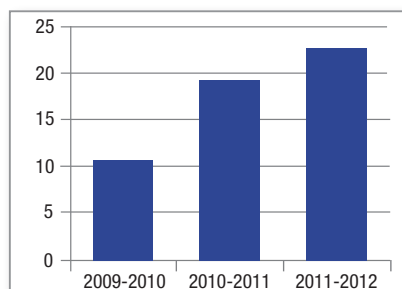
Dr Escasa, Phillipines, 2011

Global reach of the program

Since its initiation over 70 preceptors have participated in the ERSAP Preceptorship Program and each year we see a broader global representation of countries.

Over the three years we have seen the number of participants increase, host sites expand and the program has become more flexible to account for the differing needs and backgrounds of each preceptor. This has allowed us to broaden the skill set of those participating, increase preceptors speaking French and Spanish and enhance the benefit of the program for all involved.

Countries represented by ERSAP preceptors



"I finished this training with many ideas, and a wish is to transfer these benefits brought about by advances in treatment to my patients ..."

Dr Ndiaye, Senegal, 2011

Feedback from preceptors remains exceptionally positive and we continue to receive reports of the impact of the program for physicians and their patients alike.

Given the continued success of this program the iCMLf is very pleased to continue the ERSAP Preceptorship Program in 2013. Further details will be available in September 2012.

The ERSAP Preceptorship Program is part sponsored by Pfizer.

iCMLf Forum for Physicians from Emerging Regions – overcoming challenges treating CML



On the 9th December 2011, the iCMLf in partnership with The Max Foundation (MAX) held the second iCMLf Forum for Physicians from Emerging Regions. This event, held during the annual American Society of Hematology meeting, is a unique opportunity for clinicians and scientists from these regions to come together to discuss the challenges they face in the treatment of their CML

patients. Guided by an expert panel from the iCMLf, the conversation focused on the unique aspects of CML management in countries with limited resources and the potential solutions to address these.

Clinical cases presented

Three physicians from emerging economic countries presented clinical cases to outline their current practice and challenges.

- 1) Pediatric management of CML.
Dr Ximena Jordan Bruno, Bolivia
- 2) The road from symptoms to access to treatment.
Dr Peter Mwamba, Nairobi, Kenya
- 3) Managing CML – Decision making in a developing country.
Dr Neelam Varma, Chandigarh, India



Dr Peter Mwamba presents his case for discussion

Key outcomes

- Over 90 attendees from emerging economic countries
- Clinical case presentations by physicians from Bolivia, Kenya and India
- Open discussion sharing the challenges faced in the regions with advice from the expert panel and comment from the audience
- Increased awareness across the iCMLf executive and industry partners of the issues and needs in these regions
- Networking opportunity to establish potential collaborations and clinical support
- Increased awareness of the iCMLf and the educational programs offered for CML
- 100% of collected surveys rated the meeting 4, or 5 out of 5 for value.



The iCMLf panel moderated by Pat Garcia-Gonzalez (Executive Director of MAX)

"This iCMLf Forum is the ideal opportunity for the executive members of the Foundation to listen to the challenges faced by colleagues in emerging countries so we can adapt the activities of the iCMLf and provide assistance where possible"

Professor John Goldman, iCMLf Chairman

Survey results

The short survey completed by participants gave valuable feedback and useful suggestions for future meetings.

Question	Rating %				
	5	4	3	2	1
How valuable did you find the iCMLf Forum?	70	30	-	-	-
How relevant were the case study's to your practice?	30	60	10	-	-
How would you rate the format of the meeting?	45	50	5	-	-
How would you rate the length of the meeting?	58	37	5	-	-

5 = excellent, 1 = poor

Looking forward

There is a clear need and desire from both physicians from emerging countries and CML opinion leaders to continue the momentum started in the iCMLf Forums in 2010 and 2011. The discussions and networking opportunities in this unique setting are valuable for the CML community. We will continue to evaluate the forums and adapt over the years to get the maximum benefit from this annual meeting. The 2012 iCMLf Forum will focus on the solutions generated treating CML where resources are limited. Further opportunities for networking for the attendees will be built in to the agenda..

The iCMLf Forum is supported by an unrestricted grant from Novartis Pharmaceuticals.

Extending the reach of CML education – presentations now available in French and Spanish

The iCMLf Virtual Education Program (VEP) is a series of presentations on best practice management of CML. Following on from the success of the program in 2010, series one, the key initiative in 2011 was to extend the reach of the program to non-native English speakers. As part of the iCMLf VEP series two, in 2011 modules outlining current CML management were introduced in French and Spanish. Additional content on mutation analysis, molecular monitoring and transplant enhanced the VEP content available in English.

The iCMLf VEP series two was launched and made available to attendees at the iCMLf Forum held during ASH 2011. USB drives containing the iCMLf VEP have been distributed in emerging countries by The Max Foundation (MAX) and all modules are available on the iCMLf website.

Virtual Education Program - module viewing figures

VEP Series Two December 2011	Average views per module
English (3 modules)	454
French (4 modules)	540
Spanish (4 modules)	215
VEP Series One December 2010	
English (5 modules)	1264
TOTAL PROGRAM VIEWS	10,701

(data available May 2012)



"Thanks for the information about the Virtual Education Program 2011, the Spanish module is excellent and will be a big help for all our associates...Congratulations to all the team for this important support"

Key outcomes

- 11 new modules are available as series two of the VEP in 2011
- CML educational presentations now available in French (Professor François Mahon) and Spanish (Professor Jorge Cortes)
- Presentations on mutation analysis, molecular monitoring of CML patients (Associate Professor Susan Branford) and transplantation for CML in 2011 (Professor Jerry Radich), are included in the 2011 program
- The VEP is made available through the networks, website and newsletters of both the iCMLf and MAX
- 800 USB drives distributed, primarily in Latin America and French speaking Africa
- In the first month of VEP production iCMLf web traffic increased 50% to 7000 visitors with 4500 unique visitors
- 94% of people viewing the program rated it 4 or 5 out of 5
- 78% of people viewing the program are clinicians/clinically focused

Looking forward

As awareness of the iCMLf grows, the further we extend the global reach of the Virtual Education Program. Best practice in CML management is constantly changing and it is important for all CML practitioners to be able to access up to date education. The iCMLf Virtual Education Program is an ideal tool to allow this to occur, especially for those less able to travel to international meetings. The iCMLf would like to continue to expand the program with additional content and languages to continue to increase access to best practice management of CML around the world.



Presented in partnership with The Max Foundation, the iCMLf Virtual Education Program is supported by an unrestricted grant from Novartis Pharmaceuticals

The ERSAP Diagnosis and Testing Program – working towards equal access to CML monitoring around the world

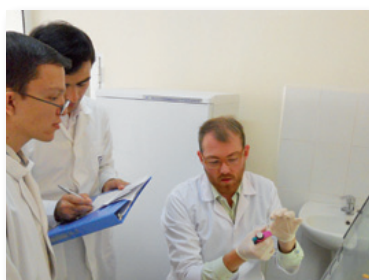
The lack of diagnostic capabilities for CML is a barrier to optimising clinical outcomes in many low and middle income countries. Only two countries in Sub-Saharan Africa can diagnose CML and monitor treatment and testing is limited, or not existent in most countries in Central America and Central Asia.

The iCMLf has established a specific program to address this. Through various projects the ERSAP Diagnosis and Testing Program will assist clinicians in emerging regions use objective testing to confirm CML diag-

nosis via FISH, cytogenetics, or Polymerase Chain Reaction (PCR) to detect the BCR-ABL1 gene, or transcripts. The long-term goal for this program is to provide equipment and training for clinical and laboratory staff at the local level.

Solutions will differ according to the local situation to allow centres to become self-sufficient to monitor their own CML patients and potentially patients from other local centres. In this way the iCMLf will develop a multifaceted approach to build sustainable local capacity for CML diagnosis and testing while ensuring adequate ongoing support from clinical and laboratory mentors.

There are five current projects as part of the ERSAP Diagnosis and Testing Program. These are outlined over the following pages...



Jordan Smith from the FHCRC training technicians in Uzbekistan

iCMLf funding to enhance local capacity for CML diagnostics

In 2011, the iCMLf launched the ERSAP Diagnosis and Testing Grants Program. The program offered small seeding grants to hematology institutions in emerging economic regions to facilitate the diagnosis and long term monitoring of CML patients. Grants provide funding of up to US \$10,000 as well as additional support from a partnering centre of excellence to ensure the successful implementation of the proposal and ongoing mentoring and support at a clinical and laboratory level.

The inaugural grant applications were reviewed by the iCMLf Directors and evaluated based on the following criteria:

- The primary focus for the iCMLf grant will improve or introduce facilities for CML diagnosis and monitoring in an existing area of need
- The iCMLf funding will underpin the development of on site facilities
- The project utilises both the partnership with the CML centre of excellence, and the iCMLf funding
- Clear plan of action with reporting of measurable outcomes

Centre awarded the iCMLf grant	Brief Overview of the Project	6 month prog
Birla Cancer Center, SMS Medical College Hospital, Jaipur, India	Free/subsidised testing for diagnosis and monitoring; Free/subsidised mutational testing; Internal training in advanced molecular techniques; External training in PCR and sequencing techniques. Aim to have investigations available at every medical college of the state of Rajasthan	Collection and arc 177; TRI Vials (st 70; BCR ABL tem Sequencing done:
Institute of Hematology and Blood Transfusion, Health Ministry of Uzbekistan, Tashkent, Uzbekistan	Phase I - Advanced training of two staff; Phase II - Seminars by a key opinion leader in the field of CML for physicians and patients; Phase III - Acquisition of reagents and test-systems	Diagnostic equipm monitoring of CML
Kenyatta National Hospital/University of Nairobi, Nairobi, Kenya	The iCMLf funding will assist bridging the diagnostic gap especially for the very poor	Initial first rests 14 test; Payments for
Korle Bu Teaching Hospital, Korle-Bu, Accra, Ghana	Establish in house diagnostics using quantitative PCR	Now one of the pri diagnosis and mo
Nizam's Institute of Medical Sciences, Hyderabad, India	Purchase consumables and reagents to set up a cheap quantitative RT-PCR assay system for quantification of BCR-ABL. Provide free T315I mutation analysis	BCR-ABL quantifi in 24 patients. Po with the time sche
Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria	Improve our existing laboratory by training technical staff at an expert reference centre. The iCMLf grant will be used to procure PCR consumables	Training will occur
Patan Hospital, Patan Academy of Health Sciences, Katmandu, Nepal	Hasten early diagnosis and treatment of CML. Encourage regular follow-up visits and counselling. Facilitate early detection of non-compliance, poor response and/or resistance	We are in testing database manage
Post-graduate Institute of Medical Education & Research, Chandigarh, India	Enhance testing facilities at neighboring institutes. Develop a low cost strategy for sending samples to a central reference laboratory. Implement a quality assurance program for accurate molecular monitoring	At present focus is diagnosis and est between August a
Sam Ratulangi Medical Faculty / Prof.Dr.RD. Kandou Hospital, North Sulawesi, Indonesia	Provide early detection and monitoring of treatment	19 samples sent t

"The partnering CML centre of excellence has been very supportive. I am able to discuss and seek advice on cases and issues. They are also with me every step of the way to help me achieve the aims and objectives of the project."

Dr Benneh, Ghana

Awarded Grants

Nine projects were awarded iCMLf grants in late 2011. The grants are being utilised in the following ways: laboratory staff training, set up of additional laboratory equipment, PCR analysis at a local centre, PCR shipment and analysis at a distant reference centre, and PCR standardisation projects along with mutational analysis and standardisation.

The progress of the projects has been reported and evaluated at 6 months, May 2012, and will be again at 12 months. A synopsis of the 6 month progress is outlined below:



Key outcomes

- The program has achieved its initial aim, providing seeding grants to initiate change in local capacity and practice of CML diagnostics. This will hopefully lead to long term benefits for CML patients with ongoing support from a CML centre of excellence
- For many of the centres awarded iCMLf grants the partnership with the centre of excellence has been instrumental in the successful implementation of the project
- The response to this program has been overwhelming and there is a clear need for ongoing support of funding and education in a similar manner to this structured iCMLf program

The iCMLf will extend this program and the grants available in late 2012. A key initiative will be to enhance the network of grant awardees inviting the sharing of experience and successes as part of the ERSAP Diagnosis and Testing Program.

Dr Varma from Chandigarh, India and Dr Branford from Adelaide, Australia, forming a partnership to standardise PCR testing as part of an iCMLf grant

Progress at May 2012	Comment
Shipping of new and follow-up CML patient samples: Total No. of samples collected: 173; RNA Isolated: 72; cDNA synthesized: 173; ABL PCR product and GEL CUT: 26; Successful sequencing: 28; BCR ABL quantification done: 30	We have now trained staff available to carry on the project work. We have made substantial progress in developing and starting testing for poor patients without charge. We have been able to start sequencing and are now testing for mutations
Equipment installed and staff trained; Completed further education in diagnostics and patients, introduction of FISH method and better interpretation of diagnostic results	Ongoing collaboration with Dr. Radich's laboratory, consulting on treatment of patients
Patients' samples collected and tested; 4 patients have had repeat 2nd staff: Phlebotomist, Messenger, Records person	We have had good progress so far with no difficulties enrolling patients. Difficulty has been to screen patients to ensure that only those who are extremely poor receive the free diagnostic tests
Many sites for CML Testing- GeneXpert Research Project. This will address the monitoring of patients in house using quantitative PCR	Future plan to develop in house mutational analysis. Funds will be used for the 7 patients that currently need mutational analysis
Sequencing performed for 108 patients. Repeat testing for 50 patients. T315I analysed sensitive in 2. Since the test is at no cost, almost every patient showed compliance with the schedule	At the end of a year's follow up for the first one hundred new patients, we would be able to analyse the data in terms of compliance to treatment and arrive at parameters that impact the remission
In September 2012. The reference site will donate a PCR machine	Step-down training for other laboratory staff members is expected to increase the number of people capable of running the laboratory
Phase of our cytogenetic lab and developing software for the appropriate management. 20 potential candidates to be evaluated for enrolment and reimbursement	The project has been impacted by lack of manpower with regard to appropriate management of the laboratory and clinic. This is expected to improve over time
To enhance facilities at neighbouring hospitals/ institutes to improve morphological and cytochemical diagnostic techniques for CML. Training will be imparted from October, 2012	Permission to send the patient samples to centre of excellence is awaited from Indian Council of Medical Research
Go to Jakarta for diagnostic test	Limitation in sample transport as only 5 samples received every air transport. Reference site is a referral centre for all regions in Indonesia

The Automated System – increasing access to CML diagnostic equipment in emerging economic regions



Dr Gebremedhin and his team waiting patiently for the first CML diagnostic result in Ethiopia

One option to give centres in emerging regions local capacity to assess levels of BCR-ABL1 transcripts is through the GeneXpert System manufactured by Cepheid. The GeneXpert System is a self-contained, automated platform combining on-board sample preparation with real-

time PCR amplification and detection functions for fully integrated and automated nucleic acid analysis. The systems consist of an instrument, computer, and preloaded software for running tests and viewing the results. The system requires the use of single-use, disposable GeneXpert cartridges that hold the reagents and host the PCR processes. The instrument can be used for molecular monitoring of CML using the specific Xpert BCR-ABL1 cartridge.

Introducing the assay with donated cartridges

1) The existence of the GeneXpert instruments in emerging countries (installed for tuberculosis diagnostics) has provided the opportunity to pilot the use of the Xpert BCR-ABL1 cartridges in this setting. Dr Amha Gebremedhin, from Tikur Anbessa Hospital, Addis Ababa, Ethiopia was trained on the use of the GeneXpert System at the Royal Adelaide Hospital, Australia as part of his educational preceptorship supported by the iCMLf.

240 assays have been donated to this site. As of 1st August 2012:

- 70 assays have been used to confirm diagnosis of CML
- 10 assays have been used to monitor CML patients

Due to the high cost of shipping samples overseas for analysis (>\$700), in the initial stages of this pilot, priority has been given to confirm the diagnosis of CML and commence TKI therapy where appropriate.

2) The Scientific & Research Institute of Hematology and Blood Transfusion in Uzbekistan also has access to a GeneXpert machine, and has used an iCMLf grant to facilitate the training of the laboratory staff on the system by staff from the Fred Hutchinson Cancer Research Center, who previously collaborated with Cepheid to develop the assay.

Dr Kazakbaeva and her team have conducted 40 tests using donated Xpert BCR-ABL1 cartridges:

- 8 Children and 29 adults
- BCR-ABL positive 27
- BCR-ABL negative 4
- Over 70% of positive tests led to a therapeutic change

A further 100 cartridges will be made available in late 2012.

Preferential pricing for emerging economic regions

At the request of MAX and the iCMLf, Cepheid has agreed to offer a preferential price for the GeneXpert IV System and Xpert BCR-ABL Monitor Assay for public sector end users in 68 high burden low and middle-income countries. This preferential pricing has been established through a collaboration agreement between MAX and Cepheid, and will apply to orders placed by MAX to Cepheid.

Public institutions treating CML in eligible countries can now purchase test cartridges and instrument costs under this agreement represent a 50 to 60% reduction relative to the market price.

	GeneXpert 4-module with desktop	GeneXpert 4-module with laptop	BCR-ABL Monitor Assay (10 cartridge kit)
Price**	US\$ 17,000	US\$ 17,500	US\$ 500 (US\$ 50 each)

**Other costs such as shipping and handling may apply.

"... This is the first CML-related molecular assay in Ethiopia ... We are extremely glad to know the molecular status of our patients. No more blind treatment of CML patients in Ethiopia"

Dr Amha Gebremedhin

We sincerely thank Cepheid, the Fred Hutchinson Cancer Research Center and The Max Foundation (MAX) for the donations of cartridges and resources that have made these pilots possible.

Preparing the first BCR-ABL GeneXpert test in Uzbekistan



Detail on the MAX-Cepheid collaborative agreement can be found at:

www.themaxfoundation.org

To request further information contact MAX: info@themaxfoundation.org

The GeneXpert research project

Assessing the GeneXpert System for reliability, and reproducibility when used to measure BCR-ABL1 transcript levels in patients with CML in emerging economic regions

The iCMLf, supported by Cepheid and MAX, are conducting a global 18 month study of six countries. 'The CML Testing – GeneXpert Research Project'. This project will assess the reliability, practical use and therapeutic impact of the GeneXpert System to measure the levels of BCR-ABL1 transcripts in patients with CML in emerging economic regions. Six primary sites will be provided with GeneXpert System and Xpert BCR-ABL1 cartridges for the period of the study. Each site will be partnered with a CML centre of excellence as a reference site. In conjunction with Cepheid, the reference site will provide the technical training and ongoing clinical support and advice throughout the study period. In this manner the primary sites will receive dedicated support for the study duration. 10% of all samples analysed at the primary site will be validated at the corresponding reference site. Duplicate samples will be collected, stored and shipped to the reference site. These will be analysed using the standardised local RQ-PCR test and the GeneXpert System located at the reference site. In addition to producing valuable data the project will enable physicians to monitor their CML patients with current technology in order to identify, in many instances for the first time, which patients are responding poorly and which patients are responding appropriately.



Primary sites

The primary study sites have been selected with the view to effectively conducting the study and analysing the data produced. These sites cover a wide range of emerging countries; Central America, Africa, Eastern Europe and Asia. This broadens the reach of the study and, as a result, the global significance of the data.

The expert reference sites are world renowned centres in the treatment of CML. Lead investigators at these sites are leaders in the field of CML and Directors of the iCMLf.

Primary and reference sites involved in Phase 1.

Country	Centre	CML patients	Reference site
Ethiopia	Tikur Anbessa Hospital, Addis Ababa	280	Royal Adelaide Hospital, Australia
Ghana	Korle-Bu Teaching Hospital, Accra	50	Fred Hutchinson Cancer Research Center, USA
Honduras	Instituto Ema Callejas, Tegucigalpa	125	Fred Hutchinson Cancer Research Center, USA

Primary outcomes measured

- To evaluate the use of the GeneXpert System in an oncology/hematology setting in emerging economic countries
- To validate the results of the GeneXpert System used in emerging regions with results achieved by standardised RQ-PCR testing (IS) at a central reference laboratory
- To validate the results of the GeneXpert System used in centres in emerging regions with results obtained from GeneXpert Systems used at a central reference laboratory

Study phasing

The project is divided into two phases. Phase I - an initial smallscale study with initiation and validation of three sites over a period of 6 months. After evaluating the preliminary data, the use of protocols and the reporting procedures, Phase II will incorporate three further sites and last for an additional 12 months. In this manner 18 months of data will be collated, evaluated and reported. Phase II validation will depend on the results of Phase I. If the results align closely there may be no need for further validation, or we may need more extensive analysis if there are significant discrepancies.

This research collaboration creates the opportunity to assess the portability and validate the use of the GeneXpert System to improve the management of CML at these centres. The study will provide useful data to move forward with future diagnostic projects in the emerging economic regions where the need for assistance and practical technology is greatest.

We sincerely thank Cepheid for participating in this research initiative.

Further information about the GeneXpert System can be found at: www.cepheid.com

First time testing for CML patients – Blood screening across the Pacific

For centres in emerging regions that do not have access to CML diagnostics sometimes the only option is to send patient samples overseas for analysis. This presents other challenges including, cost of the test and cost of shipment, with most of this burden falling on patients with very limited resources. Timing shipments to ensure sample viability is also critical.

Eight iCMLf Directors and Advisers have offered free PCR testing at their centres. In September 2011 we had the first opportunity to make use of this valuable and generous resource.

The Max Foundation approached the iCMLf to help a patient in the Philippines, a child who despite being on Gleevec for 5 years had never been monitored using PCR.

The closest iCMLf centre to the Philippines with free testing is Adelaide, Australia. To make optimal use of the shipment 30 patient samples were collected, shipped and analysed.

The first result was available in a month – Major Molecular Response – what a result!

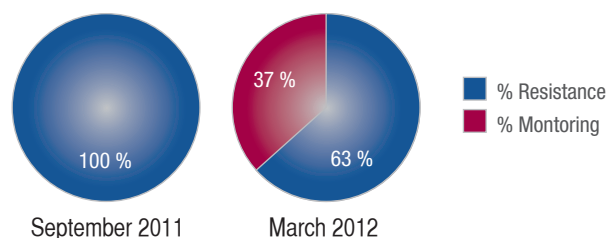
The results of the sample analysis were invaluable for the physicians and patients alike and we now have a cost effective system in place as a solution for on going evaluation for these patients. The iCMLf will continue to fund 6 monthly shipments for CML diagnostics while local capabilities are established.

The second of these shipments occurred in March 2012. A snapshot of all the results obtained are shown here:

BCR-ABL Level indicated	% Sept 2011*	% March 2012**
Undetectable BCR-ABL	3.6	6.9
Major Molecular Response	7.1	6.9
Major Cytogenetic Response	7.1	24.1
Complete Cytogenetic Response	3.6	17.3
Failure to respond to TKI therapy	78.6	44.8

* two failed samples **one failed sample, one sample of poor quality

Reasons for testing



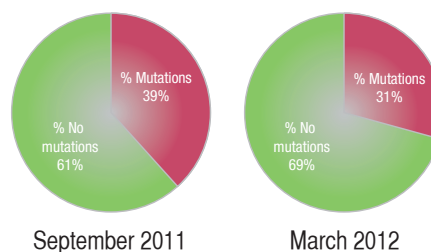
"We highly appreciate the efforts you are extending to us to improve the management of our CML patients."

Dr Escasa, Philippine General Hospital, June 2012



Patients and staff from the Philippines involved in the first sample shipment to Australia

Percentage of samples with mutations



Shipment	Mutations Detected
September 2011	D276G, E255K, E453K, F359V, F359C, G250E, M244V, T315I, Y253H
March 2012	E255K, F317L, F359V, F359C, L248V, T315I, Y253H

Shipment	Price per BCR-ABL result*
September 2011	\$43.44
March 2012	\$50.97

*each patient has duplicate samples shipped and analysed

Key outcomes:

- This initiative has established a long-term partnership between Adelaide and Philippines General Hospital (PGH)
- Patients from PGH will now receive regular CML monitoring to optimise their care
- This project is a cost effective way to monitor limited numbers of CML patients. However it is reliant on the donation of time and resource from a CML centre of excellence.
- Projects such as this should be viewed as interim measures while local solutions to introduce CML diagnostics are implemented

The individuals involved in the success of this project are too numerous to mention by name. We especially thank Dr Susan Branford, Jodie Prime, and Dr Tim Hughes from The Royal Adelaide Hospital, Australia, along with Nelia Medina from The Max Foundation, Philippines for their donated time and expertise.

Supporting international educational congress



Professor Cortes
opening the
13th International
CML Meeting

In September 2011 the 13th iCMLf-ESH International CML Meeting, held in Estoril, Portugal, welcomed a record number of participants. Over 460, physicians, scientists and researchers attended from around the globe. While the majority were Europeans, a record number of Americans attended this year. In total one in five attendees

crossed the Atlantic to discuss the latest developments in CML. A growing number of participants also came from Oceania, Asia, and South America. These increasing numbers indicate that this conference is becoming more internationally renowned.

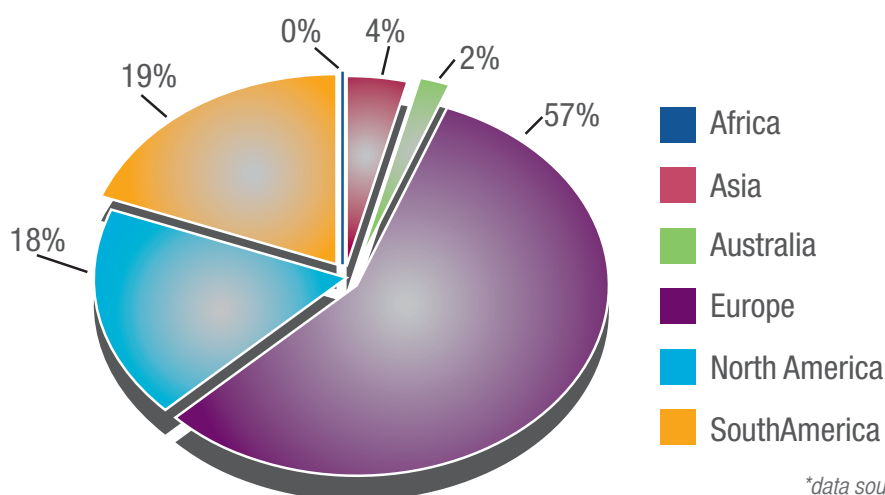
The International CML Meeting, co sponsored by the iCMLf and the European school of hematology (ESH), is one of the key scientific activities of the iCMLf each year. The program is configured under the guidance of three iCMLf Directors; John Goldman, Jorge Cortes and Tim Hughes.

The program in 2011 included a stronger clinical component, addressing current clinical issues such as; choice of TKIs, molecular monitoring, defining responses, recognition of resistance, place of stem cell transplantation, etc. with more time for discussion on each topic. Increased emphasis was placed on posters and the poster walks led by senior academics, were very successful. Small scientific workshops led by postdoctoral researchers were also a progressive addition to this year's meeting. Feedback from participants was positive and these new components will be repeated in 2012.

The iCMLf-ESH 14th International CML Meeting: Biology and Therapy will be held September 20-23, 2012 in Baltimore, USA.

"I was able to get updated on new basic research approaches and enjoyed the quality of speakers, the informal format, the location and the interaction with colleagues"

Attendees at the International CML Meeting in Estoril



*data sourced from www.esh.org (November 2011)

"Post-doc presentations gave an excellent hands-on focus to the meeting"

The conference was supported in part from educational grants from BMS (Diamond Conference Partner), Pfizer Oncology (Emerald Conference Partner), Ariad (Ruby Conference Partner) and Novartis Oncology (Ruby Conference Partner).



The iCMLf Rowley Prize – recognising outstanding contributions advancing CML management



The Rowley prize is awarded annually by the iCMLf to a person who has made a major contribution to our understanding of the biology of CML, or to the management of patients with CML. Nominations are received through the year, reviewed then ratified by the iCMLf Directors. The 2011 recipient was Professor John M. Goldman.

"I am so delighted to learn that John Goldman is the recipient of the 2011 Rowley Prize. He is a most worthy recipient for many reasons. ... In all his research, he has combined state of the art therapy with the most advanced technology to monitor response to the therapy and to develop rigorous tests of efficacy"

Professor Janet Rowley



The 2011 iCMLf Rowley Prize winner John Goldman presented by Dr Tim Hughes

Professor Goldman has a long standing interest in the biology and therapy of CML. Dr Goldman was the first to autograft patients with CML using peripheral blood stem cells and started allogeneic stem cell transplant for CML in 1980. He pioneered the use of unrelated donors for transplanting CML patients and developed PCR technology for monitoring residual disease. He confirmed the preclinical efficacy of the original tyrosine kinase inhibitor (STI571, now imatinib) in 1997 and first used it in the clinic in 1999. Thereafter he has been involved in development of second generation TKIs, notably dasatinib and nilotinib.

Currently Emeritus Professor of Haematology at Imperial College in London and Medical Director of the Anthony Nolan Trust, his former positions include Chair of the Department of Haematology at the Imperial College of Medicine at Hammersmith and Fogarty Scholar of Hematology at the National Institute of Health in Bethesda, Maryland.

This iCMLf award is named in honour of Professor Janet Rowley. The Rowley Prize was awarded for the first time in 2009 to Professor Brian Druker, followed by Professor Moshe Talpaz in 2010.

Professor Janet Rowley will present the 2012 iCMLf Rowley Prize during the 14th International CML Meeting in Baltimore.

"It is unusual for someone to have such a profound impact on a field as John has had on CML ... suffice it to say that John's trainees have become world leaders in this field and will remain so for decades to come"

Professor Brian Druker

The iCMLf supports International CML Awareness Day

On the 22nd September 2011 (22/9), patient advocacy groups and health professionals from all around the world celebrated the inaugural International CML Awareness Day. On this day the CML community jointly called upon all stakeholders to speak with a united voice, build upon the standards in treatment guidelines published by CML experts and work together to improve access to diagnosis, treatment and care.

The date (22/9) symbolizes the genetic change of chromosomes 9 and 22 which causes CML and 22 September 2011 is the first year where activities were coordinated on a worldwide level. These activities ranged from meetings of key experts and politicians, release of awareness videos, press conferences, as well as fundraising and awareness events. Dr Jorge Cortes opened the iCMLf-ESH congress in Estoril, Portugal with a keynote, marking the first International CML Awareness Day and honoring the close collaboration between patients and hematologists.

In recognition of the day the patient community, through the CML Advocates Network, received more than 2200 signatures from 62 countries to proclaim 22 September as International CML Awareness Day. 153 photographs of "Faces of CML" were collected, including that of a Canadian CML patient who has been living with CML for 34 years, possibly one of the longest living CML survivors worldwide.



The iCMLf advisors who met in Estoril

"It is so important for CML patients that groups are available to offer advice and support throughout the patient journey. The International CML Foundation welcomes the launch of the first ever International CML Awareness Day and calls on all members of the worldwide CML community to sign the proclamation."

Prof. John M Goldman, iCMLf Chairman

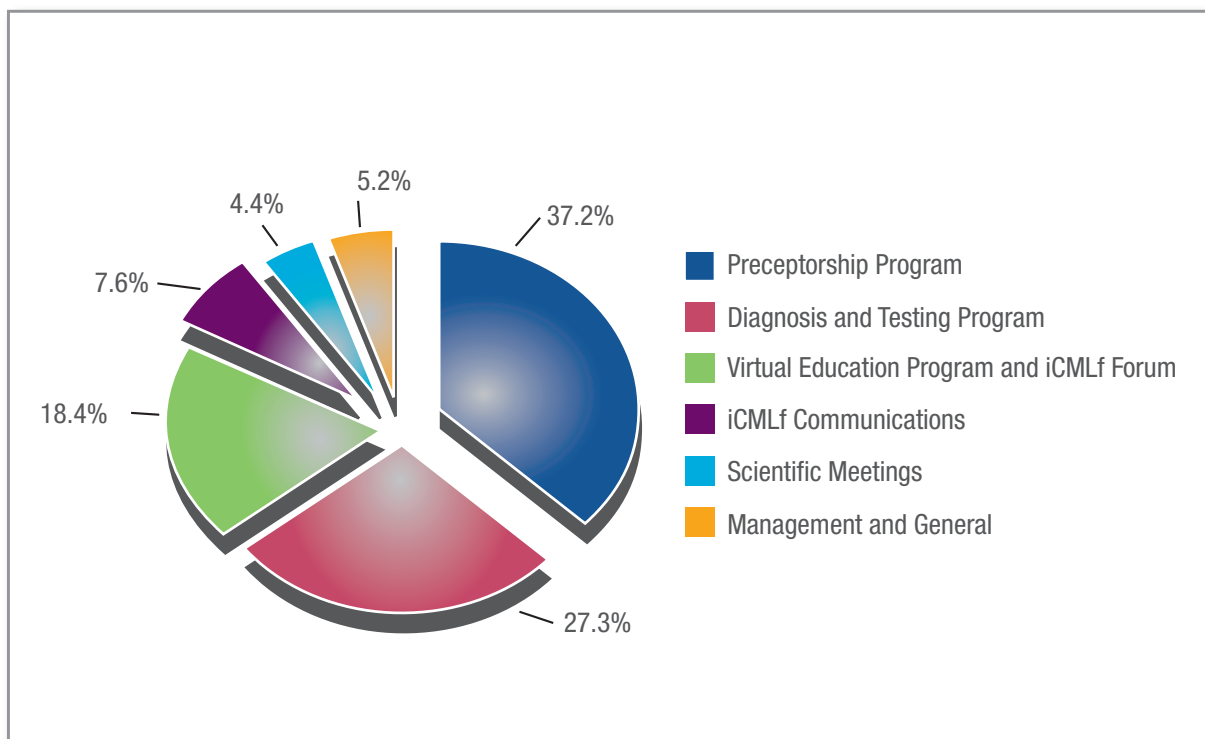


The faces of CML



iCMLf Expenditure

iCMLf Expenditure on Activities



- 83% of expenditure spent on the three major iCMLf programs
- 65% of iCMLf expenditure directed towards improving CML management and patient outcomes in emerging economic regions
- 27% of expenditure spent on new initiatives for the iCMLf in 2011-2012

"We have been encouraged by the progress we have made in improving CML diagnosis, monitoring and therapy in the emerging economic regions over the past 3 years. Our challenge in 2013 is to consolidate these programs as well as broadening our scope to increase our impact on the management of CML patients in the wider global community"

Professor Tim Hughes, cofounder of the iCMLf

Acknowledgement of support

Grants and donations

As a charitable Foundation the iCMLf relies on grants and donations to continue the programs and activities that positively influence the lives of patients with CML. The mission of the iCMLf is to improve the outcomes for patients with CML globally. We thank our corporate partners for their generous contributions that help us achieve this.

Friends of the Foundation

The iCMLf also receives individual donations. We appreciate and thank all those who give both of their time, and financially to further the aims of the Foundation.

Premium Supporters:



Major Supporters:



Other Supporters:



iCMLf Membership

For the first time in March 2012 the iCMLf invited applications for membership of the Foundation. We thank all the members who have joined with us to achieve our goals.

Members of the iCMLf:

- Become part of an international network focused on improving outcomes in CML
- Contribute to the global research and educational programs of the iCMLf
- Access a network of international contacts, including leading hematologists and scientists, with a common interest in CML
- Are invited to attend the iCMLf's regional meetings
- Can nominate candidates for the annual iCMLf Rowley prize
- Can nominate candidates for the iCMLf Scientific Advisory Committee and National Representative Board
- Have the opportunity to contribute as a reviewer to the scientific publications of the iCMLf
- Submit articles for the iCMLf twice yearly newsletter
- Receive regular updates on the programs and activities of the iCMLf
- Receive the iCMLf Newsletter and Annual Report

Membership of the iCMLf is US\$100 annually.

A lesser amount can be contributed if full payment is difficult (minimum \$10)

