

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 and friends in the CML community,

When the iCMLf was first conceived one of the major motivations for forming a global foundation was our concern that the remarkable progress seen over the past decade in CML management with the development and clinical application of imatinib, was largely confined to the more developed countries. Our mission to improve CML outcomes globally made the care of CML patients in the less developed nations our number one priority.

In 2011 we reported that increasing access to CML diagnosis and testing was the next major goal for the iCMLf. This is an enormous task and one where we have only just started to scratch the surface of what is needed. However, every journey begins with one step and reaching every goal begins by starting small projects. In this newsletter we give you an update on the ways we, along with our partners, have begun to address this problem and are working towards every person with CML having the same access to treatment and monitoring no matter where they live.

Since our last newsletter the iCMLf has held the second annual meeting of our advisors. One of the challenges for the iCMLf is to make use of the wealth of experienced and willing people wanting to assist the foundation. This annual meeting is a good opportunity to seek input from our global advisors and the key discussion topics of the meeting are outlined on page 5.



John Goldman opening the CML advisors meeting on International CML awareness day

We were fortunate that the first International CML Awareness day, 22nd September 2011, or 9/22 2011 was held on the exact day of our advisors meeting. An ideal opportunity to celebrate and recognise all the efforts of researchers, scientists, and physicians not only to treat CML, but continue to find better ways to manage and improve

quality of life over the years. The iCMLf is very fortunate to work closely with CML patient advocacy groups and though the work of these groups, 9/22 has moved from a national celebration to an international collaboration. We are proud to stand side by side with them to recognise 9/22 as International CML Awareness day.

The 2012 ERSAP Preceptorship Program is well underway and the first month long educational visits will begin in early April. We are delighted to welcome City of Hope, California and Fred Hutchinson Cancer Research Centre, Seattle, to the team of CML centres of excellence hosting preceptors. These centres donate their time and experience to make the preceptorships successful and we thank all of the people involved clinicians, scientists and administration staff for your commitment to the program. iCMLf newsletters usually include updates on the preceptorship program from the iCMLf's perspective. In this edition we turn it over to those it matters most to, Dr Digumarti shares his overview of his time in Portland and Prof Tim Hughes gives a host centres perspective on the preceptorships.

The 'iCMLf Forum for Physicians from Emerging Economic Regions' has become an annual event during ASH. Conducted with The Max Foundation, this event 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. Version 2 of the iCMLf Virtual Education Program was also launched during this event, an online CML educational program that now contains modules in French and Spanish. The Virtual Education Program is only one of our online tools and Jan Geissler, the iCMLf communications manager, outlines the other useful components of the iCMLf website on page 11.

Over the last 3 years the iCMLf has made a significant difference in the treatment of so many CML patients and you can see in this newsletter our activities are gaining impetus. In 2012 we would like to welcome the CML community to contribute to the workings of the iCMLf by becoming members of the Foundation. More information about iCMLf membership and how to join the iCMLf is on page 12. By joining the iCMLf as a member, you will ensure our momentum in maintained and help us continue to positively impact the standard of CML care around the globe.



Dr Mwamba from Kenya presenting at the iCMLf Forum at ASH 2011

*Nicola Evans, John Goldman
Tim Hughes, Jan Geissler*

Significant progress through multifaceted support to increase diagnosis and monitoring of CML in emerging economic regions



Jordan Smith from the FHCRC training technicians in Uzbekistan as part of an iCMLf grant

Many hospitals in developing countries do not have the capability to confirm the diagnosis of CML either by cytogenetics or by molecular tests, which results in patients not being able to access the medication available to enhance and extend their quality of life. Moreover once treatment has started, continued monitoring is essential to detect early evidence of drug resistance, or disease progression, that in many cases could be better managed with a change in therapy.

Through the ERSAP Diagnosis and Testing Program the iCMLf will help clinicians in emerging regions use objective testing to confirm CML diagnosis via FISH, cytogenetics, or PCR to detect the BCR-ABL1 gene, or transcripts. Partnerships will be established between CML doctors and centres in emerging regions and staff at international CML centres of excellence to develop diagnostic and monitoring services. No single model of how this will work optimally is assumed. It is likely that solutions will differ according to the local situation. The strategic placement of an automated instrument in a centre plus the provision of appropriate training and support may be an effective solution in one centre, whereas in another situation training of local technicians to establish and maintain an in-house assay may be the most cost-effective way to establish a local service. The long-term goal for this program is to provide equipment and training for

clinical and laboratory staff at the local level. This would allow specific centres in emerging regions to become self-sufficient to monitor their own CML patients and eventually patients at 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 on going support from clinical and laboratory mentors. With this in mind this program will go a long way towards meeting the objective of equal access to monitoring around the world.

"I am really happy that iCMLf has come up with an innovative program and I am very confident that this will help save a lot of lives around the whole world."

Dr Kayastha, Kathmandu, Nepal

The next 2 pages outline the current projects underway to achieve this in each there are three critical components:

1. Clinician training – it is vital that the clinicians involved in patient care and decision making have access to the most up date CML knowledge
2. Long term partnerships – each centre in emerging regions has a partner CML centre of excellence to ensure ongoing clinical and laboratory support and advice
3. Every centre taking part in the iCMLf programs establishes a tailored, flexible solution according to the local needs, making use of existing resources



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

iCMLf Grants - building local facilities for CML diagnostics

In June 2011, the iCMLf launched the ERSAP Diagnosis and Testing Grants Program. The program makes available small seeding grants to hematology institutions in emerging economic regions to facilitate the diagnosis and long term monitoring of CML patients.

The 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
- The project will impact an existing area of need
- An indication that the iCMLf funding could 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
- Clear budget outline
- Applicant's CV/biosketch

Nine grants were awarded in 2011

- Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria
- Birla Cancer Center, SMS Medical College Hospital, Jaipur, India.
- Nizam's Institute of Medical Sciences, Hyderabad, India
- Korle –Bu Teaching Hospital, Korle-bu, Accra, Ghana
- Patan Hospital, Patan Academy of Health Sciences Katmandu Nepal
- Institute of Hematology and Blood Transfusion, Health Ministry of Uzbekistan Tashkent, Uzbekistan
- Post-graduate Institute of Medical Education & Research, Chandigarh, India.
- Kenyatta National Hospital/University of Nairobi, Nairobi, Kenya
- Sam Ratulangi Medical Faculty / Prof.Dr.RD. Kandou Hospital, North Sulawesi, Indonesia

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The grants awarded are being utilized 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 awarded grants will be followed, evaluated and reported at 6 and 12 months. The response to this program has

been overwhelming and the iCMLf hopes to extend this program and make more grants available in 2012.

“On behalf of director of Hematology Institute, I would like to thank you for your support. This news is very exciting for us and a success in the support and treatment of patients with oncohematological diseases. Also, this award demonstrates the power and effective stated mission of the iCMLf.”

Dr. Kazakbaeva, Uzbekistan

The Automated System

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 nucleic acid analysis. This instrument can also be used with appropriate reagents for molecular monitoring of CML.

The existence of the GeneXpert instruments in emerging countries (installed for tuberculosis) has provided the opportunity to pilot the use of the Xpert BCR-ABL1 cartridges in this setting. 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 (FHCRC) who previously collaborated with Cepheid to develop the assay.

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

- 8 Children and 29 adults
- BCR-ABL positive 27
- BCR-ABL negative 4
- 70.4% of positive tests led to a therapeutic change



The GeneXpert System

To date the Tikur Anbessa Hospital has conducted four tests using the system. The physician at this centre was trained on the use of the GeneXpert at the Royal Adelaide Hospital, Australia as part of his educational preceptorship supported by the iCMLf. Below is an overview from Pat Garcia-Gonzalez, Executive Director of The Max Foundation on the progress in Ethiopia.

No More Blind Treatment of CML Patients in Ethiopia



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

On the 6th of October 2011, the first batch of BCR-ABL assays with the GeneXpert equipment was successfully carried out in Addis Ababa, Ethiopia. The handful of cartridges, which I had the privilege of hand delivering, were provided through The Max Foundation, with technical support from the Radich lab at FHCRC, and run using a GeneXpert instrument donated by FIND Diagnostics to the Ethiopian Nutrition and Health Research Institute (ENHRI). The tests were performed on 4 CML patients who had been on imatinib for periods ranging from 4-7 years.

The results varied from 0.0017 to 6.1%. In the words of Dr Amha Gebremedhin, Head of the Hematology Unit at Tikur Ambessa (Black Lion) Hospital, “We are extremely glad to know the molecular status of our patients. No more blind treatment of CML patients in Ethiopia.”

Dr Amha goes on to explain: “for reasons we are not clear yet, CML accounts for 40-50% of all adult leukemia cases in our hospital. Although we have more than 300 patients currently receiving imatinib, we did not know their cytogenetic or molecular response status. We followed them for their hematologic response only. The event of October 6th was of particular importance and unforgettable; this is the first CML-related molecular assay in Ethiopia.”

Lack of diagnostic and monitoring capabilities for CML is a barrier to optimizing clinical outcomes in many low and middle income countries. Only two countries in Sub-Saharan Africa can diagnose

and monitor treatment, and testing is limited or not existent in most countries in Central America and Central Asia.

On February 2011, The Max Foundation convened a coalition of expert partners to address this issue. Alongside our organization in this effort are the iCMLf, FIND Diagnostics, the International Network of Cancer Treatment and Research (INCTR), and others. Individual efforts of each partner organisation were strengthened by working together, and the events of October 6th in Ethiopia were a direct result of the relentless efforts of members of the coalition in the past few months.

The importance of this leap in the ability of doctors to successfully treat patients was felt like a shockwave throughout the health care community of the Ethiopia. The excitement of the veil of darkness being lifted was enhanced with the hopeful anticipation of a full monitoring program coming soon.

On behalf of The Max Foundation, the CML Foundation of Ethiopia, Dr Amha and Dr Abdulaziz at Black Lion Hospital, we would like to forward our sincere thanks to the iCMLf, FIND Diagnostics, the Cepheid Company, the Radich lab at the Fred Hutchinson Cancer Research Center, the South Australia Pathology: Center for Cancer Biology, the INCTR, the EHNRI, the Department of Internal Medicine in the School of Medicine, College of Health Sciences, Addis Ababa University, and others, without whose concerted effort and support, this extremely important molecular assay for CML patients would not have been possible.

Pat Garcia-Gonzalez

Making use of existing technology to enhance CML outcomes

In collaboration with the Fred Hutchinson Cancer Research Centre and The Max Foundation, the iCMLf is bringing wider access to CML diagnostics in Africa.

Initiated by Corey Casper MD, the Uganda Cancer Institute/Hutchinson Center Cancer Alliance seeks to develop effective prevention and treatment strategies for infection-associated cancers to benefit the millions of people in Uganda, the United States and worldwide who suffer from these malignancies.

Under the direction of Dr Casper, this research is being bolstered with the addition of The Uganda Cancer Institute/Fred Hutchinson Cancer Research Center Clinic and Training Institute. The new facility houses state-of-the-art infectious disease, cancer histopathology

and molecular diagnostics laboratories and will quickly expand patient access to diagnosis and treatment.

Through the work of Dr Jerry Radich the iCMLf will link with the UCI/Hutchinson Center Cancer Alliance utilising the existing experience and systems to establish validated PCR testing for CML, enabling local CML diagnosis and monitoring in Uganda for the first time. As a first step to expand this CML partnership Dr Nixon Niyonzima from UCI will attend the FHCRC as part of the ERSAP Preceptorship Program in April 2012.

This project has huge potential and over the next three years is planned to expand into Tanzania, Kenya, Zimbabwe, and Senegal.

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

“All roads led to the Philippine General Hospital on 8 September 2011 for the unprecedented event involving 30 patients and their caregivers. Office workers filed their absences from offices, kids will be late for classes, moms and dads and senior citizens had to change their schedules for the day, BUT NOBODY CARED! Everyone understood the importance and their fortunate luck to be part of this! Call time was at 8am. We were there at 730am. We lined –up at no. 14”

Rod Padua, Touched by Max

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

the doctors which 30 patients would have samples analysed, arranging the frozen sample courier pick up and making sure all 30 patients were at the hospital on the same day in the right place for sample extraction.

The 8th of September arrived and what took months in the making was over in three hours. The first result was available in a month – Major Molecular Response – what a result!

This initiative has established a long-term partnership between Adelaide and Philippines General Hospital and we are very pleased to announce that we have secured funding to continue these shipments every 6 months. These patients will now receive regular CML monitoring to optimise their care.

The people involved in this project are too numerous to mention, but without the support from the Philippines, Australia and USA it would not have been possible, so thank you.

Nicola Evans
Chief executive iCMLf



Collected in batches

In September 2010 eight of our advisors offered free PCR testing and in July 2011 we had the first opportunity to make use of this.

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

The closest reference centre to the Philippines with free testing was Adelaide so to make optimal use of the shipment 1 patient developed to 30. I personally will never forget doing a practice run, ‘squeezing’ test tubes into a bag to make sure we could fit as many as possible. Knowing that every tube we could ship and then analyse would give someone vital information about their condition.

After writing collection, freezing and storage protocols, sending PAXgene tubes to the Philippines, and establishing a reporting form, The Max Foundation in the Philippines took over coordinating with



Inside the freezer waiting for transport



Thanks from the Philippines

***iCMLf-ESH 13th International CML Meeting
– a record number of attendees.***



Professor Cortes opening the 13th International CML Meeting

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.

Speakers at this meeting present the newest and often unpublished data that relate to the biology of CML including the origin of BCR-ABL1, signal transduction, basis of disease progression, action of tyrosine kinase inhibitors (TKI) and mechanisms underlying resistance

to TKI, along with aspects of CML treatment including prediction and definition of responses, drugs used in combination, molecular monitoring, targeting residual stem cells and approaches to cure.

In 2011 the 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 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.



Tim Hughes, John Goldman and Jorge Cortes prepare for the poster walks

Annual meeting of the iCMLf advisors – a meeting of minds

The second annual meeting of the iCMLf advisors was held in Estoril during the iCMLf-ESH international CML meeting. The iCMLf currently has 38 national representatives from 34 countries. 11 of these are scientific advisors. In 2011 15 of our advisors met to discuss the activities and future directions of the Foundation.

Key discussion topics included:

1. Current and future iCMLf activities; participation of advisors, improvements and recommendations
2. Future training programs
3. iCMLf involvement to support clinical trials
4. Membership of the iCMLf

Thank you to all those who attended and we look forward to sharing the outcome of these discussions over the year to come.

If you are interested in becoming an iCMLf national representative, representing your country's CML experience and needs, please contact nicola.evans@cml-foundation.org.



The iCMLf Advisors who met in Estoril

The iCMLf Rowley Prize – recognising outstanding achievements in CML



Professor Goldman receiving the Rowley Prize from Professor Hughes during the International CML Meeting, Estoril, Portugal

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.

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 (ST1571, 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.

"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

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.

"There are few experts in this disease in the world who have not either worked with John personally or been guided by him in their work. His knowledge, enthusiasm and interest in this disease have been imparted to an entire generation of haematologists who have passed through his department."

Professor Jane Apperley

As well as being the founding president of the British Society for Blood and Marrow Transplantation, he is a former president of the International Society for Experimental Hematology. He has also served as president of several international haematology organisations including the European Group for Blood and Marrow Transplantation and the European Hematology Association. Professor Goldman is also a member of the ESH Scientific Committee and has chaired the International CML conference organised jointly with the iCMLf for over ten years

"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

John Goldman is editor of Bone Marrow Transplantation, a former editor of The Haematology Journal, and an associate editor of the European Journal of Haematology. He is also an editorial board member of numerous other journals and, during the course of his career, has published over 800 papers in peer-reviewed journals. His first paper was published in 1967 and first paper on CML in 1974.

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.



Chronic myeloid leukemia – a short history of treatment since the mid-20th century



Prof John M. Goldman

The treatment of CML over the last 50 years can be divided into three distinct eras, first cytotoxic drugs, then the choice of allogeneic stem cell transplantation or interferon-alfa (IFN) and most recently the era of tyrosine kinase inhibitors (TKI).

Even purely palliative radiotherapy was rather haphazard and only temporarily effective before the 1950s. In 1953 David Galton, a young clinical investigator working at the Royal Marsden Hospital in London, was given a new alkylating agent recently synthesized by Alexander

Haddow, a very talented chemist, who suggested that he test it in variety of malignant conditions. Galton quickly discovered that the drug, then called myleran and subsequently busulfan, was highly effective in reversing the splenomegaly and controlling the leukocyte counts in patients with newly diagnosed CML. In 1968 he published a paper reporting that busulfan-treated patients lived longer than those who received radiotherapy and thereafter busulfan became the standard treatment for CML in the UK. Hydroxyurea gained popularity in the United States. Both drugs were convenient to administer, lacked short-term toxicity, although busulfan regularly rendered women infertile and men azoospermic. In those days the median survival from diagnosis was about 5 years. Galton suspected that though busulphan was a valuable drug in the short term, it might actually be mitogenic and thus hasten the advent of blastic transformation, and this may well have been the case.

Two new approaches were introduced in the early 1980s. Investigators in Seattle had shown that CML patients transplanted with marrow cells collected from their identical twins could expect a number of years without evidence of leukemia detectable in their body. This led investigators on both sides of the Atlantic to explore the possibility that transplants performed with 'stem' cells from a patient's HLA-identical sibling might offer benefit for a CML patient who lacked an identical twin. This proved to be the case, though the morbidity and indeed mortality associated with allogeneic stem cell transplants remained a major problem. About this time Moshe

Talpaz in Houston pioneered the use of IFN to treat CML. Some of the patients who received this treatment achieved Philadelphia chromosome negativity and a small number of patients who achieved this status did not relapse when the IFN was discontinued. Interferon was associated with modest prolongation of life when compared with the use of hydroxyurea but still in the 1980s treatment for CML patients remained very imperfect.

In the 1990s Brian Druker in conjunction with scientists at Ciba Geigy in Basel started working on the notion that a small molecule that blocked the enzymatic action of the BCR-ABL protein might be clinical value. The culmination of their research was the development of a phenylaminopyrimidine molecule, then called CGP-57148B and now imatinib, that seemed to have selective action against CML cells in the laboratory. It was first used in the clinic in 1998 to treat patients with interferon-resistant CML in chronic phase. Soon thereafter it was used to treat previously untreated CML patient. By 2011 it is clear that 50-60% of patients treated with imatinib for five or more years can expect to have durable complete cytogenetic responses and to remain alive and well for at least 10 years - with the prospect of many more years or even decades without medical problems. The clinical picture has been further improved by the introduction of more powerful agents that act in a manner similar to imatinib, namely dasatinib, nilotinib and bosutinib, though the last drug is not yet approved for use outside the context of a clinical study.

Viewed over a period of 50 years, the treatment of CML must be regarded as a remarkable success. Many but not all patients diagnosed in chronic phase can today look forward to a normal expectation of life comparable to that of a person without CML. Perhaps of even greater importance has been the remarkable demonstration that understanding the molecular basis of malignancy can lead to logical or 'rational' development of very specific small inhibitory molecules that can lead to control or even in some cases cure various malignant diseases. This seminal observation has led to the revision of research strategies in leukemia and cancer and has unquestionably brought somewhat nearer the day when all malignant diseases can be treated and eradicated with comparative ease.

John Goldman
Imperial College London

HOLD THE DATE

The iCMLf-ESH 14th International Conference Chronic Myeloid Leukemia: Biology and Therapy will be held September 20-23, 2012 in Baltimore, USA.

We look forward to seeing you there.
For more information visit: www.ESH.org



The ERSAP Preceptorship Program – a view from both sides

Perspective from the Preceptor

The journey started with a thorough reading of material that the iCMLf provided on its website as well as on a pen-drive. The information was rich in content, authoritative and coherent. The management guidelines were not new, but something I could look forward to seeing being implemented at a world-class center. I carried the Emperor of Maladies (by Siddarth Mukherjee) to read along on the 28-hour journey. While it may not sound novel reading for oncologists, it gives a glimpse of the emotional isolation that patients face as well as the rigor of training a fellow in oncology training endures.



The OHSU Campus

my work schedule and the departmental program and a computer system with a personal log in.

Dr. Mauro soon met me and I plunged into clinical work on a busy Monday morning. A typical workweek consisted of 2 to 3 clinics, ward rounds, disease-specific tumour boards, a grand round and several presentations. It started at 7.30 am and ended by about 5.30 pm. I had access to a sprawling library and the numerous cafeterias that were strategically located.

The clinics and the ward rounds with Dr. Mauro very instructive, elaborate, unhurried and exhaustive. The Nurse-Clinician would give me her back-ground notes on all the patients scheduled for the day, with invaluable anecdotes about each patient – personal, social, interpersonal, occupational, financial and disease related information, as a printout. I would get an idea of the expectations of the family and care givers even before I met the patient. Dr. Mauro would first seek the permission of the patient and family before I went in. After formal introductions, I would participate in the discussion for the day as well as attend on any procedures that Dr. Mauro performed on the patients. Returning to the physicians' room, Dr. Mauro would then have an elaborate discussion on the status of each of the patients, answering all questions patients and instantaneously passing on to me any articles that could shed more light on the discussion! Each patient interaction lasted between 45 minutes to 2 hours.

Patients consulting the OHSU Center for Hematological Cancers came from not just the United States, but from across the world! There were patients from South America, India, Canada, Europe,

I started walking down the hill towards the OHSU – which, like my own university (NIMS), is a health sciences university. With a call to Mrs. Dean, and, with some 'correction of course' to an obvious stranger, I reached the department. In a matter of minutes, I got a spot to sit, a mug-shot identity card, some supply of stationery,

Central America and the Far East. They had translators in case they did not speak English. All consultations were more elaborate, checking to see whether the information given was understood as it was meant.

The clinics continued until the last patient was seen and Dr. Mauro entered the last patient's notes into the electronic case records. I would then meet Mrs. Dean for a briefing on the next day's program, with changes if any in writing!

I had an opportunity to see patients who were on the various clinical trials with new drugs for CML as well as for many of the other hematological malignancies. Indeed, I met the 1st patient on Interferon for CML, the first patient on imatinib, dasatinib, nilotinib and ponatinib in the world!

Ward rounds with Dr. Mauro were even more exciting. There was a bewildering array of patients with all the hematological diseases, including the rare Mast Cell Disorders group. There were patients with multiple malignancies, prostate being the commonest. There were treatment related cancers, transplants and indigent patients.

The ward team consisted of primary oncologists, attending oncologists, nurse clinicians (very knowledgeable), fellows from all branches of medicine rotating through hemato-oncology, pharmacists, psychologists, medical social workers, nutrition specialists and occupational therapists. I enjoyed their weekly joint sessions – all those listed above attended the meeting. It was informal, frank, candid and incisive. It gave a collective perception of what was wrong with the patient in non-medical terms as well as the game plan for those that were terminally ill, including a post-discharge care-giver plan. The emphasis was on the totality of care through teamwork.

Ward rounds taught me how to look up drug-drug, drug-food and drug-beverage interactions instantaneously. Nothing was left to chance. Every visit was preceded by a review of the chart, medication and labs. Hence, it was easy to answer every query of the patient or family thoroughly, honestly and truthfully. Indeed, every patient's room had internet and intranet access, with a possibility of real-time review of the case record and labs even by the patient!

My opinion on how I would manage a patient was always sought – both by the patient as well as by the team. Dr. Mauro would specifically point out the alternative plan in a low cost setting – how to make the treatment work in a low resource setting – sterilisable steel instead of disposable plastic, sterilisable cloth instead of paper, latex instead of vinyl.

The topic discussions and the lymphoma tumour boards had participation by the radiation oncologists, imageologists and the



Skyway to the Knight Cancer Center day unit

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pathologists. While fellows presented the patient details, the consultants discussed the nitty-gritty of the diagnosis and management. It was essentially a teaching session. Once again, my opinion was sought.

The entire department, including the administrative assistants, attended the Grand-Rounds on Fridays. It was an encapsulated version of a sitting round, briefing the progress until that morning and the plans ahead for each patient. This was of immense help to the weekend team to catch up on nuggets of information.

There were several highlights in the visit: a weekly lunch hour visit to the Farmer's Market on the lawns of the Medical School, a visit to the Molecular Diagnostic Labs of the OHSU in the downtown on the University Shuttle bus, rides down the cable-car with magnificent vistas of the river valley to the daycare unit of the Knight Cancer Center down the hill, the Molecular Pathology Department and to Molecular MD, a specialised lab for CML diagnosis and monitoring.

The most prized of the several interactions were informal discussions with Dr. Mauro and Prof Druker (the legend!) on strategies for Indian

CML patients, with Dr. Press on a plan for molecular monitoring of diseases, a teleconference with Dr. Jerald Radich at the Fred Hutchinson Cancer Center on a similar strategy, and a chance to participate in the 10th Anniversary Celebrations of the launch of Gleevec.



Dr Digumarti

I bring back a rich clinical experience, a plan to adapt some of the clinical practice in my clinic, act on building a molecular diagnostic lab, build a network of CML treating clinicians, a CML support group by patients, friends and families, a CML registry and finally a firm plan to collaborate in further exchange programs as well as basic research in CML.

Looking back at the several similar programs that I have been to, I think this has been the most valuable and insightful for me.

Raghunadharao Digumarti
MD DM

The clinical preceptorship program: experience from the receiving end.



Dr Amha Gebremedhin (Ethiopia) with the team in Adelaide at the end of his iCMLF preceptorship

When we first started to develop our priorities for the International CML Foundation we thought that education and training for clinicians from the emerging regions would be an area where we could make a substantial impact in a cost-effective manner. I think this has proved to be the case - the clinical preceptorship program has exceeded our expectations when we look at what has already been achieved. So far

over 40 haematologists and pathologists from 25 emerging countries have received a 3-4 week training session at one of 10 premier CML centres. In Adelaide we have had the pleasure of working with 9 haematologists from 6 countries over the first 2 years of the program. The feedback from the preceptors has been overwhelmingly positive as can be seen from first hand accounts in this newsletter and on the website. However what I wasn't expecting was the positive feedback I have received from my colleagues in Adelaide and at the other CML centres. I have been surprised by how rewarding this program has been for us as well. Working closely with haematologists who have successfully managed large cohorts of CML patients with limited resources and difficult conditions has been inspirational. Rather than the one-way transfer of information and skills that we envisaged when the program was set up, there has been an exchange of ideas and experiences that will be mutually beneficial. The opportunity to collaborate with key clinicians in the emerging regions has already led to partnerships being formed between preceptors and their host clinicians. These partnerships might be established initially to facilitate PCR standardisation or sample exchanges but can grow into clinical and research collaborations looking, for instance, at

resistance patterns in different regions or comparing drug adherence across different cultures. We saw further evidence of the partnerships that are developing when we reviewed the 30+ applications we received for our diagnosis and monitoring program. Over half of these applications included a commitment from an expert CML centre to support the project that could be traced back to a collaboration established through the preceptorship program.

On a personal level the preceptorship program has enabled me to develop friendships with a remarkable group of clinicians from around the world who battle local challenges and limited funding to provide the best possible care for their CML patients.

When developing the preceptorship program we debated the relative merits of selecting junior clinicians with limited experience and limited access to international meetings versus senior clinicians with large CML practices and significant local influence. The argument in favour of selecting junior candidates was the opportunity to give a clinician with limited experience an intensive course in CML management that would improve his/her local practice significantly with consequent long-term benefits to his community. The attraction of selecting senior clinicians is that the "pupil" can become the master when they return to their country so that one person well trained could lead to many clinicians then receiving excellent cost-effective training locally. Both strategies have merit and we have tended to select a mix of the two types of candidates.

Our enthusiasm for the clinical preceptorship program has led us to our next program – preceptorships for laboratory clinicians and scientists that will focus on developing the skills to enable molecular monitoring to be set up locally in ERSAP regions. I look forward to an equally satisfying experience developing partnerships and collaborations with these preceptors over the next few years.

Professor Tim Hughes
Head of Hematology SA Pathology, Royal Adelaide Hospital

iCMLf Forum 2011: Physicians spotlight challenges of managing CML in emerging countries



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

On the 9th December 2011, the iCMLf in partnership with The Max Foundation held the second 'iCMLf Forum for Physicians from Emerging Regions'. This event, held during ASH, 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 of iCMLf Directors including; John Goldman, Jorge Cortes, Jerry Radich, Michele Baccarani, Andreas Hochhaus

and Tim Hughes, the conversation focused on the unique aspects of CML management in countries with limited resources and potential solutions to address these.

Key highlights of this year's iCMLf Forum were the presentations from three emerging countries:

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

The iCMLf Forum in 2011 was a great success. Over 90 physicians attended the event from emerging regions and 100% of collected surveys rated the meeting 4 or 5 out of 5 for value.

"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

There is a clear need and desire from both physicians from developing 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 continue to evaluate the forums and adapt over the years to get the maximum benefit from this annual meeting. In 2012 we would propose a strong theme for the case presentations focusing on the solutions generated in these regions. More opportunity for networking for the attendees will be built in to the agenda.

We welcome any suggestions you may have to enhance the iCMLf Forum in 2012. Please contact us at info@cml-foundation.org



Extending the reaching of CML education – new presentations in French and Spanish

evidence of the need in eLearning tutorials by physicians treating CML patients all around the world. In addition, the tutorials were also provided on 800 USB flash drives to physicians that do not have broadband Internet access.

Feedback from viewers:

"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. I will write a small article on our web page and put in it the link. Congratulations to all the team for this important support."

Venezuela

"It's a very valuable information, with an excellent presentation"

Indonesia

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

Albania

During the iCMLf Forum at ASH 2011, the iCMLf launched the 2011 version of its web-based Virtual Education Program for clinicians from emerging regions. In this innovative format, leading hematologists including Jorge Cortes, Timothy Hughes, John Goldman, Michele Baccarani, Francois-Xavier Mahon, Susan Branford and Jerry Radich provide e-learning tutorials about best practices for the management of patients with CML, taking into consideration the specific challenges in these regions. Version 2 features more languages (French and Spanish) and additional modules on molecular monitoring, BCR-ABL kinase domain mutation analysis and stem cell transplantation. All modules are available on the iCMLf website, and USB flash drives are currently being provided to physicians in emerging regions.

This program has been well received by the global CML community: With more than 4800 web streams delivered to date, there is great

The iCMLf Virtual Education Program is provided in partnership with The Max Foundation and is supported by an unrestricted educational grant from Novartis.

On 22/9, iCMLf and patient groups celebrate “International CML Awareness Day”, calling for joint action to improve patients’ access to diagnosis, treatment and care



22 September 2011 is a very special date for patients affected by CML, a rare blood cancer that has played a key role in the path towards personalized medicine. On 22/9, patient advocacy groups and health professionals from all continents, including the CML Advocates Network, The Max Foundation, the International CML Foundation and Alianza Latina, celebrated “International CML Awareness

Day”. The CML community jointly called upon 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 cause CML. 22 Sept 2011 was the first day where activities were coordinated on a world-wide level. Activities ranged from meetings of key experts and politicians, release of awareness videos, press conferences, as well as fundraising and awareness events. On that special date, Dr Jorge Cortes opened the iCMLf-ESH congress in Estoril, Portugal with a keynote, honoring International CML Awareness Day and the close collaboration between patients and hematologists.

For 22/9/2011, the patient community received more than 2200 signatures from 62 countries to proclaim 22 September as

“International CML Awareness Day”. 153 photos of “Faces of CML” were collected. This also includes a photograph of a Canadian CML patient who has been living with CML for 34 years, possibly one of the longest living CML survivors world-wide.

“Everyone working to support patients around the world is extremely excited about International CML Awareness Day and all of the great work which is being undertaken to support patients worldwide,” says Giora Sharf who is a CML patient for 11 years and co-founder of the CML Advocates Network, a global network of 64 CML patient organizations in 51 countries. “There are many leukemia patient organisations around the world which do fantastic work to support survivors. For all of us to campaign with a ‘united voice’ today is a real achievement and big advance. It is a significant call to action to positively impact the well-being of people living with CML around the world”, adds Pat Garcia-Gonzalez, Executive Director of The Max Foundation.

Commenting on the patients’ initiatives on International CML Awareness Day, Prof. John M Goldman, chairman of the Board of the iCMLf, said: “It is so important for CML patients that groups are available to offer advice and support throughout the patient journey. The iCMLf 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.”

Jan Geissler
iCMLf Communications Manager

iCMLf online: fostering education and interaction for physicians treating patients with CML

Beyond providing all information about the iCMLf, the iCMLf website (www.cml-foundation.org) has grown into an interactive social media platform for health professionals treating CML patients all around the world. It not only features reports from the iCMLf’s meetings and projects, but also provides “news and views” on CML issues from leading hematologists. In 2011, the website has become a valuable and interactive web resource with up to date information for the CML community.

The iCMLf’s web-based Virtual Education Program is an authoritative educational tool for clinicians from emerging regions, with leading hematologists providing e-learning tutorials about best practices for the management of patients with CML. More than 4800 educational sessions have been delivered through the online iCMLf Virtual Education Program to date.

To support the sharing of best practice within the CML community even further, the iCMLf launched its Difficult CML Cases Discussion Forum in 2010. Since then, many interactive discussions on the cases, have emerged. Examples of cases include; pediatric CML,

aplastic anemia during CML treatment, pregnancy in CML, menorrhagia complications and cardiomyopathy during TKI treatment. Even though a relatively small number of forum contributions have been posted, those 43 forum posts have been viewed 28,838 times to date! This clearly demonstrates how an online discussion forum benefits a wider community by spreading expertise.

As clinical reality in CML is in constant change, the new section on news from CML clinical research provides updates about CML diagnostics, treatment and care that have been published in leading journals. It is interactive – all visitors of the website can suggest key articles that they find most interesting.

It is of key importance that physicians treating CML patients are able to find the valuable resources provided on the iCMLf website. You can contribute to increase visibility of the iCMLf in your community: **please provide a link from your institution’s website to the iCMLf webpage!** Please support the iCMLf!



Become a member of the iCMLf – help shape our future

The mission of the iCMLf is to improve outcomes for people with CML globally. Established in 2009 by a leading group of hematologists, the aims of the iCMLf are to foster and coordinate global clinical and research collaborations and to improve CML clinical practice and disease monitoring worldwide.

“The improved survival in CML directly attributable to the use of tyrosine kinase inhibitors is so dramatic that these new agents must be made available to the greatest possible number of eligible patients as rapidly as possible throughout the whole world”

John Goldman iCMLf Chairman

There are numerous activities that come within the iCMLf's broad charter but the initial focus of the Foundation is to address the needs in CML that are not already being met by other groups, particularly those needs that are best met by a global organisation. Even for this disease area with effective treatment, so much still needs to be tackled to make sure that all patients around the world receive the best possible therapy and care.

Now in its third year the iCMLf has already achieved a great deal:

- Over 40 practicing hematologists (preceptors) have attended educational programs at internationally renowned CML centres of excellence
- Through the iCMLf Virtual Education Program the iCMLf has provided in excess of 5500 people access to up to date CML education sessions from leading experts
- The ERSAP Diagnosis and Testing Program is providing unprecedented access to CML diagnostics allowing access to treatment along with enhanced monitoring ensuring optimal outcomes for people with CML. The impact of this program has

the potential to be dramatic for the people reached along with their community's.

These iCMLf programs are revolutionising the way CML is managed in the countries we are helping.

We invite you to join us!

Now is your opportunity to contribute to the work of the iCMLf by becoming a member. Members of the iCMLf will:

- 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
- Be invited to attend the iCMLf's regional meetings
- Nominate candidates for the annual iCMLf Rowley prize
- 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 restrictive at this time
(minimum \$10)

Through the work of the iCMLf your support will further the progress towards best possible management for CML patients where ever they reside.

For more information and to become a member of the iCMLf please go to www.cml-foundation.org/membership or contact info@cml-foundation.org

Sponsors of the iCMLf in 2012

As a charitable Foundation it is only through grants and donations that the iCMLf can positively influence the lives of patients with CML in regions where this assistance is most needed. The mission of the iCMLf is to improve the outcomes for patients with CML globally. The programs and activities implemented to achieve this would not be possible without the generous contributions from our corporate partners.



Premium Sponsors:

- Novartis Oncology
- Bristol-Myers Squibb

Major Sponsors:

- ARIAD Pharmaceuticals, Pfizer

Other Sponsors:

- World Courier Australia

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

For more information about sponsoring the activities of the iCMLf please contact info@cml-foundation.org

