Newsletter

iCMLf International Chronic Myeloid Leukemia Foundation

May 2011

Dear Colleagues and friends in the CML community,

In this edition of the iCMLf newsletter we are fortunate to have Prof. Carlo Gambacorti-Passerini review his recent publication on the Imatinib Long Term Effects (ILTE) study. At the beginning of his article Dr. Gambacorti says, *"The best outcome a physician can dream about for patients with advanced cancer is to give them a normal life expectancy."*

When reflecting on the mission of the iCMLf, the results demonstrated in the ILTE study is what the Foundation is striving to achieve in the real-life, global population, improving the outcomes of all people with CML. The iCMLf vision is that over time:

- every person with CML has the same access to treatment and testing,
- every physician has the same access to education, technology and equipment and
- every CML patient no matter where they live, has the opportunity of a normal life expectancy.

And so with each project and initiative of the iCMLf, this is what we work towards.

Improving CML Education

The major focus of the iCMLf is ensuring that access to CML education is available for those clinicians in emerging economic regions. The Emerging Regions Support and Partnership (ERSAP) Preceptorship Program has been very successful and the feedback from participants consistently talks about the benefits of the program and how much knowledge can be shared back at their home institution. More information on the ERSAP Preceptorship Program can be found on page 2.

Dr Damodar and Dr Rajendranath with ERSAP Program Director Nicola Evans during the preceptorships in Adelaide, Australia November 2010

For those that can't undertake preceptorships, the iCMLf developed the Virtual Education Program, a series of CML presentations by leaders in the field. These modules are available on the iCMLf website and distributed on USB drives for clinicians with low bandwidth Internet http://www.cml-foundation/vep.

Sharing Experience and Knowledge

The iCMLf is also extending online communication within the CML community. In the discussion forum clinicians submit interesting or difficult CML cases for review, advice and comment by other CML experts. The discussion has been lively – please join!

In February this year, the iCMLf joined forces with the CML Advocates Network to launch the pediatric section of the iCMLf website as the first part of an online Pediatric CML Community for physicians. The long term goal for this project is to support collaboration and sharing of experience of physicians as well as researchers involved in the treatment of children with this ultra-rare condition http://www.cml-foundation/pediatric.

Scientific Meetings

The iCMLf co-sponsors the annual International Conference 'CML - Biology and Therapy' with the European School of Haematology. This year's is the 13th annual conference and we hope to see you in Portugal on 22-25 September this year.

Partnerships

Sharing resources and experience is vital and the iCMLf works closely with The Max Foundation on many projects. At the American Society of Hematology meeting (ASH) in December 2010, The Max Foundation and iCMLf held a networking meeting specifically for physicians from countries in emerging regions. More than 150 people attended and discussed their local situations and ideas to improve CML management across these regions. This meeting will be repeated at ASH in 2011.

The iCMLf have recently joined with expert partners in a coalition to improve CML outcomes in Sub-Saharan Africa. We very much look forward to sharing the achievements of this coalition and transferring these to other areas of need.

Increased Access to CML Diagnosis and Monitoring

Improving access to diagnostics is one of the most challenging issues to address on a large scale. Through small grants and partnerships with CML centres of excellence the ERSAP Diagnosis and Testing Program plans to enable centres in emerging regions to increase their local capacity to conduct diagnostic and long term monitoring of their CML patients. We hope that, for the first time in many cases, physicians will be able to locally confirm the diagnosis of CML patients, leading to better treatment and long term care. This has the potential to dramatically alter the lives of the patients and their families, in some cases whole communities.

As Professor Tim Hughes writes in his article outlining the ERSAP Diagnosis and Testing Program on page 8, and to paraphrase Lao Tzu, ***"This tiny step takes us on a great journey"***.

As always we appreciate your comments and suggestions on the work of the iCMLf team. Please contact us at info@cml-foundation.org

Nicola Evans, John Goldman
Tim Hughes, Jan Geissler

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.

Registered Address:

International CML Foundation
33 Northumberland Place
London W2 5AS - UK

E-Mail: info@cml-foundation.org
Web: www.cml-foundation.org

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.

The Emerging Regions Support and Partnership (ERSAP) Preceptorship Program - improving CML education for clinicians across emerging economic regions

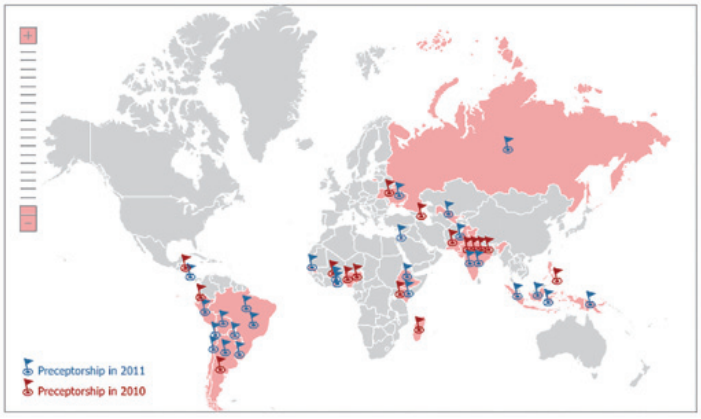
On behalf of myself, my institution, the Institute of Blood Pathology and Transfusion Medicine AMS of Ukraine, and on behalf of the whole hematology service of Ukraine I would like to thank very much once again the iCMLf, the Board of this foundation and its whole team for the possibility to attend this training and support during my participation in ERSAP project. I am sure that our joint work and efforts now and in future will improve significantly the level of CML management in my country.

LL Ukraine 2010

We couldn't ask for better feedback than that above for the inaugural project launched by the iCMLf. Physicians attending the ERSAP preceptorships at all centres have consistently reported positively enhancing their CML education and refining skills across many areas of CML management during their attendance.

The ERSAP Preceptorship Program is designed for clinicians from emerging economic regions with a specific interest in the treatment of CML and a significant CML patient load. The program enhances clinical knowledge and skills in the treatment of CML through preceptorships at internationally renowned CML centres.

Following on from a successful program in 2010 the 2011 ERSAP Preceptorship Program offers more host centres of excellence to a greater number of preceptors. The map below illustrates the originating countries of the preceptors in 2010 and 2011 demonstrating the wide reach of the program and the potential positive impact in regions where clinicians may face challenges accessing up-to-date knowledge regarding best practice management of patients with CML.



Originating countries of the ERSAP preceptors

30 physicians from emerging regions across the globe have been offered preceptorships in 2011. Dr Kazakbaeva from Uzbekistan was the first preceptor this year. In March she attended the S.Orsola-Malpighi University Hospital, Bologna, Italy with Professor Baccarani and his team. Dr Kazakbaeva had the following comments to make following her 4 week preceptorship:

Dr Kazakbaeva and the hematology team at S.Orsola-Malpighi University Hospital, Bologna during her ERSAP preceptorship in March 2011

"I have learned morphological method – Punction of bone marrow another approach, from Doctor Rosti. I my opinion this method is very beneficial for me. I have participated in the Bone marrow transplantation operation, about which I only have read in the scientific articles. I have learnt the step by step processing of molecular biology laboratory tests and analysing Philadelphia chromosome methods in cytogenetic laboratory. At the paediatric oncology centre, I have seen the psychological lessons with children diagnosed cancer.

The whole programme was for me beneficial and I will try to incorporate to our programmes. So it means our patients with CML will benefit from this. For example, the visit of patients at the outpatient clinic, preparation, the organization of queue system, registration database, waiting list, and consultation process are different to our system, but in my opinion quite effective, so I will suggest incorporating also.

KK Uzbekistan 2011

In the coming months a clinician from India will travel to Portland to spend 4 weeks with Dr Michael Mauro and the haematology team at OHSU, a clinician from the Philippines travels to the MD Anderson for 4 weeks and clinicians from Papua New Guinea and Kenya will travel to the Hammersmith Hospital in the UK for 3 week preceptorships.

The iCMLf are very grateful to the sponsors of the ERSAP Preceptorship Program and we are delighted to announce that the program will continue in 2012. Further details will be available later this year, but we can already reveal that Professor's Andreas Hochhaus and Jerry Radich have agreed that their departments will be added to the CML centres of excellence hosting the program.

We still have many countries to reach so please share the information about the ERSAP Preceptorship Program with colleagues who may benefit. This program is a unique opportunity for clinicians from developing countries who treat CML to undertake an intensive educational program to develop and expand their CML management skills.

"It was an honor and a pleasure to have participated in this training, despite the vast difference between these institutions and hospitals in developing countries. It is certain that all is not feasible to us but we can certainly learn to improve our management."

TH Madagascar 2010

Nicola Evans
ERSAP Program Director

Chronic Myeloid Leukemia in Nigeria

Dr. Anthony Oyekunle

Nigeria is an ethno-culturally diverse country of over 350 ethnic groups and indigenous languages with an estimated population of 140 million (2007 census); most of whom are illiterate. Quality public healthcare services are largely concentrated in the urban locations, and several of the private hospitals are unaffordable for the majority of the populace. A national health insurance scheme has only recently been started, with coverage limited to basic healthcare services such as malaria, uncomplicated deliveries and infections (which probably account for the bulk of hospital visits); but it is yet to cover ailments such as cancers. Even then, medical insurance coverage has yet to reach 50%.

In Nigeria, CML is one of the commonest leukemias, and before the advent of the GIPAP scheme, it used to be managed using conventional cytoreductive agents by all specialist haematologists. However, since the introduction of GIPAP through Dr. M. A. Durosinmi in 2003, and the consequent availability of free imatinib in Nigeria, CML patients have been referred to the OAU Teaching Hospitals, Ile-Ife, where the Ph chromosome and/or the BCR/ABL1 status are confirmed prior to enrolment. We currently (April 2011) have 343 patients registered on GIPAP. After commencing imatinib, we continue to follow-up these patients with conventional karyotyping and/or quantitative molecular testing for BCR/ABL1 (by RT-PCR or FISH). A few patients showing signs of suboptimal response or failed therapy have had to be screened for BCR/ABL1 kinase domain mutations. Unfortunately, Nigeria has never had a local facility for molecular tests, putting the cost of these tests beyond the reach of most of our patients.

Studies from our group and others have consistently shown that the median age at diagnosis of CML in Nigeria is 38 years (well within the reproductive age-range) as against 67 years in the West. This has raised the relative significance of several issues in the Nigerian setting, such as concerns about the impact of the disease and imatinib on fertility, pregnancy and lactation. We are beginning to accumulate data that may also suggest an impact of this relatively younger age on the perception of the disease and on poorer drug compliance. We have reason to believe that not all CML patients have come forward for therapy; probably due to inadequate awareness of the scheme, or a deep belief in the "traditional" and/or faith healers, or even poverty and the resultant inability to afford the transport fare to our hospital, which happens to be the only coordinating centre for GIPAP in Nigeria.

A number of recent developments have brought renewed hope for our CML patients; the first being the launching of a CML patients support group (MaxCare Nigeria) in March 2011, and the opening of an indigenous private laboratory that promises to carry out all relevant molecular tests for CML. However, some pertinent challenges remain to be surmounted including; the need for a CML registry, improved awareness, increased availability of standardized molecular testing sites and the need for more research. It is also becoming apparent that African countries need to come together to foster better collaboration in CML clinical research, so that locally relevant guidelines can be drawn-up to address some uniquely African challenges in the management of these patients.

Dr. Anthony Oyekunle
Obafemi Awolowo University Teaching Hospitals, Ile-Ife, Nigeria

Improving CML outcomes in Sub-Saharan Africa

Launch of the coalition in Geneva, Feb 2011: Viji Venkatesh, The Max Foundation; Dr Giorgio Roscigno, FIND Diagnostics; Pat Garcia-Gonzalez, The Max Foundation; Dr Martine Raphael, INCTR; Anne Reeler, Axios; Dr Baerbel Porstmann, FIND; and Jan Geissler, iCMLf and CML Advocates Network

For the past 10 years there has been unprecedented access to Glivec treatment for CML in many countries in Sub-Saharan Africa as well as in other low-to-middle-income countries. However, socio-economic barriers and lack of infrastructure have prevented the achievement of optimal clinical outcomes for patients diagnosed with CML in the region.

The Max Foundation has formed a coalition of expert partners to work towards rectifying this situation. Along with the iCMLf, FIND Diagnostics, the International Network of Cancer Treatment and Research (INCTR), Axios International and the CML Advocates Network are all participants. As organisations with overlapping interests in the area of cancer control in Sub-Saharan Africa our activities directly or indirectly benefit CML patients. Learning about each other's projects will help the coalition leverage our collective efforts for the benefit of patients. Further more, working in coordination will enable more efficient use of resources and tracking of results.

"As we launch into 2011 we feel there is great momentum to put all these organizations together and generate a joint project. Our goal is to form and launch a coalition to improve CML outcomes in Sub-Saharan Africa. We hope to start with a pilot project in Black Lion Hospital (Tikur Anbessa) in Ethiopia," said Pat Garcia-Gonzalez Executive Director of The Max Foundation and convener of this coalition.

This coalition compliments the work of the iCMLf through the Emerging Regions Support and Partnership Projects. The iCMLf will play a key role in providing training and support to physicians, perhaps also providing mentoring and guidance as diagnostics become available.

We look forward to updating you further as the year progresses.

A normal life expectancy is possible for CML patients treated with imatinib, a new study finds

Prof. Carlo Gambacorti-Passerini. ILTE Study Chairman

The best outcome a physician can dream about for patients with advanced cancer is to give them a normal life expectancy. This outcome is difficult to achieve because either the treatment is not effective, or its short or long-term toxic effects preclude such a result.

A recent publication (Gambacorti-Passerini C, Antolini L, Mahon FX, Guilhot F, Deininger M, Fava C, Nagler A, Della Casa CM, Morra E, Abruzzese E, D'Emilio A, Stagno F, le Coutre P, Monroy RH, Santini V, Martino B, Pane F, Piccin A, Giraldo P, Assouline S, Durosinmi MA, Leeksma O, Pogliani EM, Puttini M, Jang E, Reiffers J, Valsecchi MG, Kim DW. Multicenter Independent Assessment of Outcomes in Chronic Myeloid Leukemia Patients Treated With Imatinib. J Natl Cancer Inst. 2011 Mar 21; 103: 553-561) provides the first evidence that normal life expectancy can be achieved in the majority of Chronic Myelogenous Leukemia (CML) patients.

Imatinib was the first drug shown to produce complete and lasting cytogenetic responses in up to 70-80% of CML patients, and is now widely used as first-line treatment. However, most information on the long-term effects of the oral, targeted agent has come from industry-sponsored trials at selected centers. To learn about outcomes in patients taking imatinib under more normal circumstances, Carlo Gambacorti-Passerini, M.D. of the University of Milano Bicocca/ San Gerardo Hospital in Monza, Italy and colleagues collected data on patients from 27 centers in Europe, North and South America, Africa, the Middle East, and Asia. Patients taking imatinib (Glivec or Gleevec) for CML, and in remission after two years of treatment were eligible. Published data now show that they have a mortality rate similar to that of the general population according to a study published online March 22 in the Journal of the National Cancer Institute (JNCI).

The Imatinib Long Term Effects (ILTE) study enrolled 832 patients who were in complete cytogenetic response after two years of taking the drug. Of these, 478 received imatinib as second-line treatment, and 354 as first-line therapy. The study was designed to focus on long-term effects; for this reason the first two years of treatment, in which most acute problems can develop, were excluded from the analysis.

Another important characteristic of the ILTE study was its independent funding, which derived from the Italian Drug Safety Agency (AIFA), the Lombardy Regional Government, and the Italian Association for Cancer Research (AIRC).

The median duration of imatinib treatment was 6 years, corresponding to a total of 3247 person-years that were available for analysis at the time of the submission of the present report.

Twenty deaths occurred during the follow-up period, for a mortality rate of 4.8%, similar to what would be expected in a comparable group of people in the general population. Only six of these deaths were related to CML.

The rate of loss of cytogenetic responses seems to be stable over time at approximately 1% per year, in line with (although slightly higher than) previous publications, with no significant differences between first-line and second-line treated patients. Many patients in the ILTE study reported side effects, but survival rates remained high, at 95.2%, even after eight years of taking the drug. Serious adverse events, such as cardiovascular and digestive system problems, were reported in 139 patients, but were considered related to imatinib in only 27 cases. In fact less than 3% of patients discontinued imatinib for adverse events during the period of observation.

Other adverse events, less serious but judged by treating physicians to substantially affect quality of life, occurred in more than half of patients after 8 years of treatment, and were frequently linked to imatinib use. The most frequent ones were muscle cramps, asthenia (weakness), edema, skin fragility, diarrhea, conjunctival hemorrhages, osteoarticular pain and tendon or ligament lesions. Nineteen patients (or 2.3%) stopped taking imatinib because of side effects; at least half of these switched to one of the other targeted drugs for CML, dasatinib or nilotinib, which became available in 2006.

Therefore it can be concluded that patients on imatinib "frequently suffer from side effects that are non-serious but can nonetheless reduce their quality of life." These findings highlight the "importance of a good relationship between health care providers and patients, and of the availability of CML-dedicated clinics, where side effects are easily communicated and addressed to reduce/avoid non-compliance."

The term "operational cure" can be used in this case. Although the disease is not eradicated in the majority of patients, imatinib obtains such a good control over CML and with such limited toxicity, that the negative effect of the disease on the life expectancy of patients is abrogated. Before imatinib the usual survival after CML diagnosis was only 2-3 years.

These data will have important repercussions outside of the medical environment and inside the broader social milieu. Issues like adoption rights, mortgage approvals, solid organ transplantation waiting lists, life insurance and others will be affected. It will be essential that a discussion of these topics with the various patients associations be immediately started in order to address them and to fight discriminatory

next page ...

... continued from previous page

behaviors. The fact that the total number of CML patients is going to substantially increase in the future thanks to the availability imatinib, is making the discussion over these issues even more critical.

The ILTE study as it was published, leaves of course some open questions.

- Approximately one half of the ILTE patients did not receive imatinib as first line treatment; even if the two groups were shown to have similar outcomes, only 354 patients in the ILTE study received imatinib as first line therapy.
- Over 20% of the ILTE patients had consistently negative PCR results, and their management remains a matter of discussion in the scientific community. Several trials of programmed drug suspension are now close to being opened, with one of them (ISAV) stemming directly from the ILTE experience.

In an accompanying editorial, B. Douglas Smith, M.D., of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, writes that the study adds "real-life, long-term" data on the efficacy and side effects of imatinib. "Remarkably, survival rates and the incidence of secondary malignancies in this patient cohort did not differ statistically significantly from the general population, which speaks to the astounding effect imatinib has had on the clinical course of this disease," he writes.

Imatinib has survived both the test of time and that of an independent study, confirming its long-term efficacy and safety. Similar studies should now be undertaken for the so called "second generation" TKIs. These molecules are now approaching first-line use, but much less data on their long-term effects are available to treating physicians, compared to imatinib.

In 1998 this same journal accepted for publication one of the early preclinical studies that laid the ground for imatinib clinical trials. An accompanying editorial from the JNCI editor Edward Sausville concluded at that time: "With CGP57148B (i.e. imatinib), it is hoped that these (CML) patients will reap the first fruits of therapeutic efforts

Location of active Imatinib Long-Term (ILTE) centers

rationally designed and directed against these targets". The 2011 publication of the data coming from the ILTE study ideally concludes that path, initiated in the late 90's, by showing that imatinib not only leads to durable cytogenetic remissions, but also that there are no "hidden cost" from the treatment which can divert CML patients from remaining on the survival curve of the general population.

The ILTE investigators plan to present updated results at the next ASH meeting, when a median treatment duration of 8 years and more mature data regarding the development of second cancers will become available.

Dr. Carlo Gambacorti-Passerini
University of Milano Bicocca/San Gerardo Hospital in Monza, Italy

iCMLf/ESH Meeting 2011

Each year the iCMLf co-sponsors an international CML meeting with the European School of Haematology (ESH). This meeting is entirely focused on the biology and treatment of CML.

In 2011 the 13th International Conference **CHRONIC MYELOID LEUKEMIA - Biology and Therapy** will be held in Estoril Portugal from the 22 -25 September.

Speakers at this meeting will present the newest and often unpublished data that relate to the (1) Biology of CML including the origin of BCR-ABL1, signal transduction, basis of disease progression, action of tyrosine kinase inhibitors and mechanisms underlying resistance to TKI, and (2) Aspects of treatment including prediction and definition of responses, drugs used in combination, molecular monitoring, targeting residual stem cells and approaches to cure.

We look forward to seeing you there.

For further information visit **www.esh.org/agenda11.htm**

Extending communication through the global CML community

iCMLf Online Discussion Forum features lively conversations about challenging CML cases

To share and enhance best practice management of CML, the iCMLf has opened an online Discussion Forum, for clinicians to discuss difficult or interesting CML patient cases. Within the first four months, lively discussions have started, featuring 42 contributions and more than 3.200 views. Current cases include:

- Paediatric CML cases; feeding and nutrition in young children with CML
- Menorrhagia complicating Tyrosine Kinase Inhibitor (TKI) therapy
- Marrow aplasia during CML treatment
- CML and pregnancy
- A multi-resistant, difficult-to-treat CML patient
- TKI therapy and cardiomyopathy
- Chronic phase CML with granulocytic sarcoma

Joining existing discussions is easy: visit **http://www.cml-foundation.org/forum**, enter the specific discussion thread and contribute by clicking on "Reply topic".

Click on "New topic" to submit a new case for discussion: submit a brief history of the patient and the case for discussion (no more than 200 words). Details that are not critical to the discussion should be removed to preserve anonymity. The patient should consent to the case being shared. Each clinical case accepted will initially be sent to the iCMLf expert panel for a brief independent response. The case and the expert opinions will then be posted on the iCMLf Discussion Forum and further comments, questions and discussions are invited.

iCMLf Virtual Education Program for Physicians from Emerging Regions has been well received

In December 2010, the iCMLf, in partnership with The Max Foundation, launched the iCMLf Virtual Education Program for clinicians from emerging regions. In this innovative format, leading haematologists Prof John Goldman (London, UK), Prof Timothy Hughes (Adelaide, Australia), Prof Jorge Cortes (Houston, USA) and Prof Michele Baccarani (Bologna, Italy) provide e-learning tutorials about best practices for the management of patients with CML, taking into consideration the specific challenges in these regions.

The iCMLf Virtual Education Program has been made widely available in two ways: via video streams on the iCMLf website, and on USB flash drives for offline viewing. The USB flash drives were distributed to physicians via The Max Foundation to provide access to the Virtual Education Program when broadband internet access at the workplace is not available.

The online version of the Virtual Education Program is available at **http://cml-foundation.org/vep**. Each video has been viewed around 300 times since it was made available. The iCMLf intends to extend the program in the near future – if you have suggestions about future tutorials, please send them to **info@cml-foundation.org**.

Jan Geissler
iCMLf Communications Manager

CML in young patients: iCMLf and CML Advocates Network join forces

The iCMLf and the CML Advocates Network, the international platform of patient groups supporting patients and relatives suffering from CML, have joined forces to support physicians treating young patients affected by CML. As CML in children is very rare, collaborating across national borders is all the more important. The project was launched on International Childhood Cancer Day on 15 February 2011.

The newly launched web resource on paediatric CML is available on the iCMLf website and provides:

- a description of paediatric CML,
- a comprehensive overview of scientific publications and ongoing trials in paediatric CML,
- links to patient organisations supporting young CML patients.
- the iCMLf Discussion Forum features a number of discussions on young CML cases
- in the future, regular teleconferences will give paediatricians additional opportunities to share data and experiences.

Various persons with a special interest in paediatric CML give their views:

"As the coordinator of a number of clinical trials in paediatric CML, I know well how important it is to share best practice between those that treat young patients with CML. I am very supportive of this initiative and wish both organisations great success", says Prof. Meinolf Suttorp, Division of Paediatric Haematology and Oncology, Department of Paediatrics, University Hospital Carl Gustav Carus, Dresden, Germany.

Prof Meinolf Suttorp

"We perceive a need for communications between paediatricians treating children and adolescents with CML. At the same time, parents feel uncertainty how young CML patients can managed in the best way. Joining forces between the iCMLf, connecting physicians, and the CML Advocates Network, connecting patient advocates, is a perfect match", says Jan Geissler who is both a CML patient, a co-founder of the CML Advocates Network and the manager of the paediatric project at the iCMLf.

"Five years ago, my youngest son just turned 9 years old when he was diagnosed with CML", says Rod Padua, president of the patient organisation 'Touched By Max Philippines'. "We are grateful that the international community is now collaborating to improve care of this very rare childhood leukaemia", he adds.

CML is very rare in children and young adults, accounting for less than 3% of all childhood leukemias and less than 10% of all CML cases. Incidence increases with age, being exceptionally rare in infancy, rising to 0.7/million/year at ages 1 to 14 years and to 1.2/million/year in adolescents. As a consequence, most CML data are derived from adult studies. Specific issues in children and adolescents with CML include the uncertainty about long-term effects of TKI therapy, challenges of adherence to therapy, fertility and family planning issues as well as psycho-oncology.

For more information or to join the Pediatric CML Community: http://cml-foundation.org/pediatric

Diagnostic testing and monitoring for CML patients globally: The next challenge for the iCMLf

Prof Tim Hughes

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. One of the most cost-effective ways we could make an impact initially was through physician education and training. We have made good progress in our first program to facilitate preceptorships for physicians from emerging regions (see article page 2) and our e-education program (article on page 6) has also made a solid start. We now need to embark on a more complex and ambitious program that will require more resources and a thoughtful management. We would like to improve access to diagnostic tests and monitoring for CML patients in emerging economic regions.

Pat Garcia-Gonzalez from The Max Foundation has been working towards the same goal. She has recognised the importance of these services from her perspective running the Glivec International Patient Assistance Program (GIPAP) program to provide imatinib to CML patients with limited means who are from the emerging regions. She saw that a drug access program without adequate support from a diagnosis and monitoring program was not optimal.

next page ...

... continued from previous page

What is the need for diagnosis testing?

It could be argued that the diagnosis of CML can be made with a moderate level of confidence by clinical and morphological studies alone without the need to BCR-ABL mRNA testing or detection of the Philadelphia (Ph) chromosome in marrow metaphases. However this assumes a level of experience and training that will not always be available. Detection of BCR-ABL or the Ph chromosome provides a definite diagnosis in the right clinical context.

Many hospitals and clinics in developing countries do not have the capability to confirm the diagnosis of CML either by cytogenetics or by molecular tests. There are also hundreds of CML patients globally who can't access imatinib through the GIPAP program because they can't afford a diagnostic test. These factors result in too many patients not being able to access the medication available to enhance and extend their quality of life.

To increase access to these tests for patients in emerging regions the iCMLf, in partnership with The Max Foundation aims to set up facilities at a local level to either bring high quality testing to the patient, or to develop a low cost strategy for sending patient samples to a central laboratory for testing.

What is the need for monitoring?

Many patients who are able to access imatinib through GIPAP or other national programs do not have access to regular molecular or cytogenetic monitoring. This means that the first sign of poor drug adherence, drug resistance or disease progression is often frank haematological relapse or blast crisis. Salvage therapy in these settings is often ineffective so that the opportunity to intervene at an early stage when a switch in therapy or an allogeneic transplant may have been effective is lost.

Reliable, sensitive monitoring is important to evaluate the effect of treatment, provided that the tests are performed on a regular basis. It is also critical that the treating physician is able to interpret the result appropriately. It may not be realistic to aim for ongoing 3-6 monthly testing in all patients so our initial focus will be on achieving early molecular screening 6 and 12 months after therapy begins. We know that patients who are not below 10% BCR-ABL (IS) by these time points have a high risk of progression. Identifying these patients within the first year may provide the opportunity for an effective intervention such as an increased dose of imatinib, a switch to another TKI or consideration for allogeneic transplant.

Self sufficient sites

The long-term goal for this program is to provide equipment and training for clinical and laboratory staff at the local level. This will allow specific centres in emerging regions to become self-sufficient for diagnosis and monitoring of their CML patients.

How can we achieve our goals?

To quote Lao Tzu, *"The journey of a thousand miles begins with one step"*. As part of the Emerging Regions Support and Partnership (ERSAP) Diagnosis and Testing Program the iCMLf would like to form partnerships with CML doctors and centres in emerging regions to develop diagnostic and monitoring services. No single model of how this will work optimally is assumed. It is likely that solutions will be different in different countries. The strategic placement of an automated machine in a centre plus the provision of appropriate training and support may be an effective solution in one centre. 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. We will be the facilitators of this process but the emphasis will be on finding partners in emerging regions who want to work out a local solution and can leverage local support on top of the limited support we are able to offer at present from the iCMLf. The iCMLf will provide seed funding to assist in funding tests, reagents, sample transport and the logistics to conduct the program. To ensure high quality of care there is a need to establish strong links between local centres and CML centres of excellence, to provide the technical and clinical support necessary for result interpretation and clinical follow up.

iCMLf grants

To facilitate this, in 2011 the iCMLf will offer a limited number of grants to hematology centres in emerging regions. These grants will be awarded on evaluation of submitted proposals that clearly demonstrate how the funded activity will improve access to CML diagnosis and testing. The grants will provide funding of up to a maximum of US $10,000 per grant along with additional support from a partnering CML centre of excellence.

This model, with the iCMLf as facilitator of locally driven enterprises, rather than as a controller of the program will allow the local sites the flexibility to run the program according to their local situation with the support of a CML centre of excellence. After the first year the success of the different projects will be evaluated to refine and enhance the program to achieve maximum cost-effectiveness. For further information about the iCMLf funding and support to increase access to CML diagnosis and monitoring contact nicola.evans@cml-foundation.org.

Tim Hughes
iCMLf Director and Co-founder

Sponsors of the iCMLf in 2011

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 sponsors.

Premium Sponsors:
Novartis Oncology, Bristol-Myers Squibb

Major Sponsors:
ARIAD Pharmaceuticals

Other Sponsors:
- The 2011 iCMLf Virtual Education Program is supported by an unrestricted grant from The Max Foundation
- We are delighted to welcome World Courier Australia as a partner of the ERSAP Diagnosis and Testing Program.

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