Newsletter

iCMLf International Chronic Myeloid Leukemia Foundation

June 2022
Edition 19

Winners of the iCMLf Prizes 2009-2021

Dear Colleagues,

On the shoulders of giants we stand.

The strength of the iCMLf lies in the people who are its foundation. The idea of this newsletter is to give you a snap shot of the iCMLf over the last 6 months and it is clear that the giants in the community lead every aspect of our work. Our directors and advisors and all those who lead our programs give freely of their time to help, not just their own patients, but also the entire CML community.

Therefore, it was with a particularly heavy heart that we learnt of the death of one of the iCMLf's Founding Directors in December last year. Michele Bacarrani was a much-loved member and inspirational leader of the CML community. He combined a very sharp intellect with great wisdom to guide our thinking about CML. Michele has been a staunch supporter of the goals and the programs of iCMLf most particularly the clinical preceptorship program where he mentored 15 visitors from low and middle-income countries to improve the understanding and management of CML.

Professor Baccarani's legacy and work will live on through out the world CML community and a remembrance is planned during the John Goldman conference in 2022.

One of the ways the iCMLf celebrates CML 'giants' is through the prizes awarded each year. This year we celebrate Rowley Prize winner - Professor Oliver Hantschel, Goldman Prize winner – Professor Andreas Hochhaus and Giora Sharf and Jan Geissler who are awarded the iCMLf Prize in 2022 for their global patient advocacy work.

Also in this newsletter (pages 8-10) we showcase the work of previous prizewinners; Professor Jane Applerley, Professor Ravi Bhatia and Dr Sabira Kurtovic. Dr Kurtovic talks about her work during and after the war in Bosnia and Herzegovina and the challenges and effect of the subsequent lack of access to treatment, for people with CML. *"What does delayed treatment means in COVID times? - Unfortunately, we have the data"*

While we have not yet seen the full affect of the pandemic on CML management, the iCMLf CANDID study, a registry of cases of people with CML infected by SARS-CoV-2, has shown that age, specific comorbidities and country income have significant affect on mortality. An overview of this study is on page 4 and on page 5 we have a synopsis of the first sub analysis of the CANDID data looking at CML patients in treatment free remission. This work was only possible because of the time and commitment of over 200 physicians from 58 countries providing data and follow up for 1058 cases giving the CML community evidence on the affect of COVID-19 for those with CML.

On the shoulders of giants we stand.
Your iCMLf team

VALE MICHELE BACARRANI

"We share the sorrow of losing another giant in CML research, education and patient care. The CML community has lost one of its most influential leaders and I personally have lost a teacher and friend. His thoughtful discussions and scholar contributions influenced many in the scientific community and challenged us to always aim for better outcomes for our CML patients."

Professor Jorge Cortes, Director Georgia Cancer Centre, USA

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 low and middle-income countries. 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.

The iCMLf Global Alliances

For a year now the iCMLf has been working with the Harmony Alliance to harness the power of our international collaborators to drive research into CML.

The HARMONY Big Data platform facilitates data pooling and sharing for specific hematologic malignancies with a central repository of data. The iCMLf is leading the way in further bringing together research specifically for CML through the HARMONY Plus database.

HARMONY Plus is an extension to the HARMONY Big Data project, which expands the scope of data sharing to other hematologic malignancies, including CML. Both the iCMLf Genomics Alliance and the iCMLf Treatment Free Remission Alliance currently have projects underway with HARMONY Plus.

iCMLf Genomics Alliance - Investigating Clonal Hierarchy in CML

The iCMLf's Genomics Alliance has achieved key milestones since our last update.

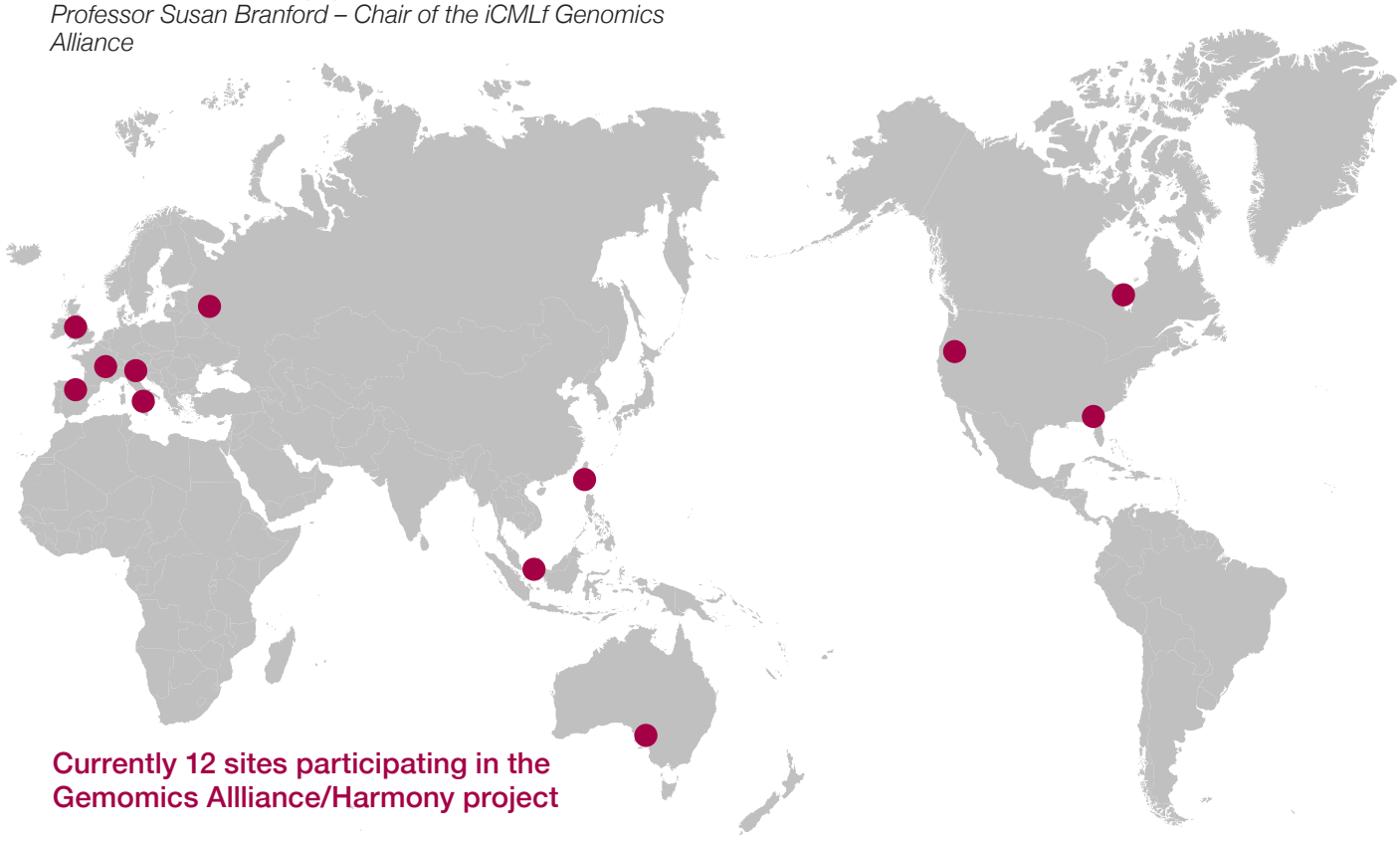
To obtain insights into the role of mutations other than BCR-ABL1 kinase domain mutations, a large database with clinical and genetic data from thousands of patients is required. Since 2021, the iCMLf has been working with the Harmony Alliance to establish a CML database to upload and analyse multicentre genomic data.

The iCMLf Genomics Alliance research project, Investigating Clonal Hierarchy in CML, is now underway.

Led by Professor Thomas Ernst (University Hospital Jena, Germany), this project aims to elucidate the hierarchy of genomic events that underlie the disease course in CML. Key research questions are to investigate if certain mutations might be associated with an increased risk in terms of TKI response and progression and how this knowledge could influence our therapeutic decision-making. The ultimate goal is to improve CML management and patient outcomes.

"A goal of the iCMLf Genomics Alliance is to pool mutatational data through a shared database. This will enhance statistical power in order to understand the impact of genomic variation on treatment response for patients with CML."

Professor Susan Branford – Chair of the iCMLf Genomics Alliance



Currently 12 sites participating in the Gemomics Allliance/Harmony project

Big Data leads to big opportunities

iCMLf TFR Alliance - Establishing an International TFR Registry

While the ultimate goal of the iCMLf is finding a cure for CML, optimising treatment free remission (TFR) as the treatment target for patients on TKI therapy is an important short term goal. With successful TFR attempts remaining at around 50%, only 20-25% of newly diagnosed CML patients will achieve a successful TFR a number that needs to be improved.

As a means to maximise the achievement of TFR and minimise failed TFR attempts and other negative outcomes, the iCMLf created the iCMLf TFR Alliance for a global initiative on TFR research.

iCMLf TREATMENT FREE REMISSION ALLIANCE

41 collaborators from **21** countries

Enhancing successful TFR attempts for people with CML

Big Data to Identify Optimal TFR

In 2021, led by Torsten Dahlén from the Swedish CML Registry Group, the TFR Alliance began the process to establish an International TFR Registry. This registry will be an optimal way to study clinically (and pharmaco-economically) important research questions on treatment-free remission on a global scale. In April, the research project proposal 'Use of big data to identify optimal treatment pathways leading to successful treatment-free remission in CML.' Was accepted by the Harmony Alliance into the Harmony Big-Data platform.

By utilising the Harmony Big-Data Platform, and collecting pooled data from multiple contributors within the iCMLf TFR Alliance, we plan to investigate key components and actions potentially influencing the outcome of TKI discontinuation focusing on the following aims:

1) Studying treatment pathways in terms of individual TKIs (1st and 2nd generation TKIs, sequential combinations), duration of treatment and duration and level of clinical response before TKI discontinuation to identify any association to molecular relapse (at e.g. 6, 12 and 24 months) post TKI discontinuation
2) Building and evaluating a prediction model, using available clinical input data, to explore the risk of molecular relapse after TKI discontinuation
3) If data availability allows, also further exploring patient outcome measures, such as the risk of the TKI withdrawal syndrome depending on pre-discontinuation factors (e.g. TKI dosing adjustments) and quality of life measures

By harnessing the power of pooled patient-level data we hope to identify the optimal treatment pathway leading to an increased likelihood of a successful, prolonged TFR. This would allow for a better guided clinical care, possibly even cure, as well as a more precise construction of future clinical trials.

Data requirements for the project are currently being finalised and site initiation will begin in July. We look forward to seeing how this alliance progresses throughout 2022 and into 2023.

Torsten Dahlén, (Karolinska Institutet, Stockholm) leads the iCMLf TFR Alliance/ Harmony Plus project

COVID-19 in Patients with Chronic Myeloid Leukemia -

The iCMLf CANDID study represents the largest global cohort study to date characterizing COVID-19 in CML. This real world data collection, from over 200 physicians in 58 countries, is essential to differentiate impact of patient, disease, and therapy specific factors on risk and outcomes, as the pandemic continues.

From March 2020 to November 2021, the iCMLf collected data, with contributions from physicians treating people with CML and partner organizations.

Poor outcomes for patients with comorbidities, older age, advanced phase disease, and those from low income countries: an update of the CANDID Study

In data presented at ASH 2021 by Katia Pagnano*, 642 cases of COVID-19 in patients with CML, were reported from 50 countries. COVID-19 was diagnosed by PCR and/or serology in 601 pts (94%) and clinically suspected in 41 pts (6%).

COVID-19 was asymptomatic in 53 cases (8%), mild in 363 cases (56%), moderate in 119 cases (18%), severe/ critical in 86 cases (13%) and of unknown severity in 21 cases (3%).

Patients characteristics (n=642)

Characteristics	All patients (n=642)	Recovered (n=558)	Deceased (n=48)
Male	380 (59%)	329 (59%)	31 (64%)
Median age, years (range)	53.01 (16-94)	52.73 (18-94)	57.02 (16-89)
Median duration of CML	8.34y (0-34y)	8.33y (0- 34y)	7.43y (0- 17.25y)
Active smoking	26 (4%)	24 (4%)	1 (2%)
Former smoking	47 (7%)	43 (7.7%)	3 (6%)
Significant comorbidities*	281 (44%)	245 (43%)	24 (50%)

*Cancer, smoking, obesity, heart conditions (HF/CAD/Cardiomyopathies/Hypertension); chronic kidney disease; chronic lung diseases (COPD, asthma, interstitial lung disease, cystic fibrosis, and pulmonary hypertension; immunocompromised state; stroke or cerebrovascular disease, solid organ or blood stem cell transplant; liver disease; pregnancy; sickle cell disease; dementia or other neurological conditions; down Syndrome; HIV infection

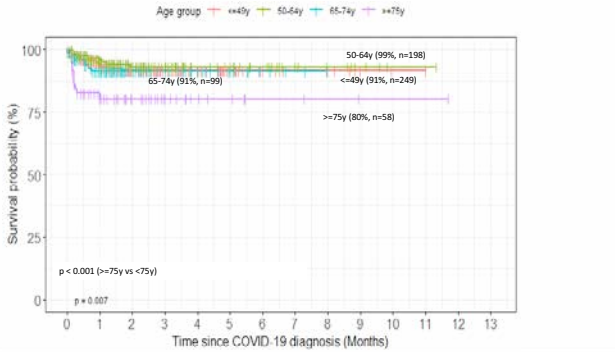
Results

At the data cut-off, from the 606 pts with known outcome, 48 pts died (8%) and 558 (92%) recovered.

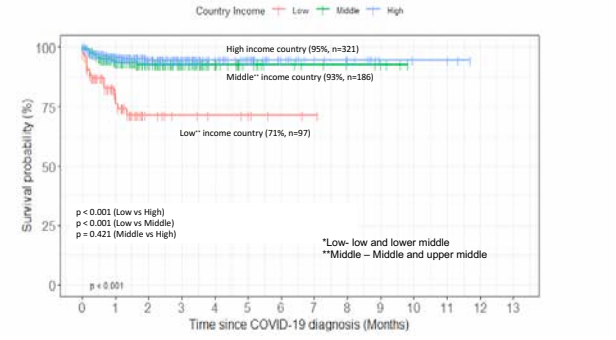
Conclusions

We confirmed a higher mortality for CML pts with COVID-19 in older pts (>75y), pts with cardiovascular or pulmonary comorbidities and from low and low-middle income countries, the latter probably related to limitations in supportive care. Additionally, more deaths occurred in pts in advanced phases and in pts not in MMR.

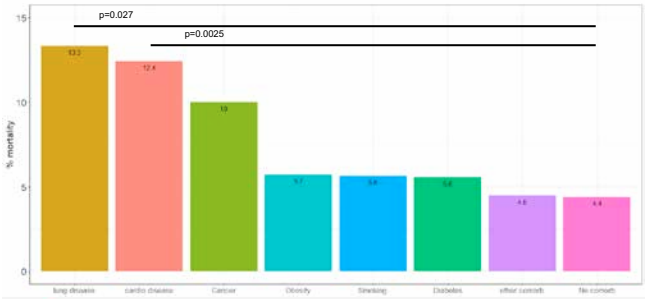
Overall survival according to age group



Overall survival according to country income



Mortality and comorbidities



*https://ash.confex.com/ash/2021/webprogram/Paper150026.html?fbclid=IwAR2819-bFTVfopwCBGzjlVxjgg1RXnlvzlakCn9yfUnxPPdLNnrv-3Tph8s

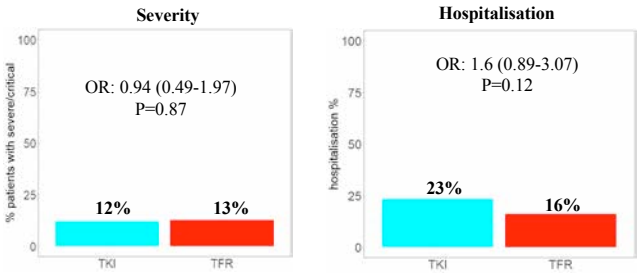
The iCMLf CANDID (Cml AND covID) Study

Following initial analysis the iCMLf undertook 3 sub-analysis of the data. The first, looking at people with CML in treatment free remission infected with SARS-CoV-2, will be presented at the European Heamatology Association meeting in Vienna.

COVID-19 In Patients With Chronic Myeloid Leukemia In Treatment-Free Remission: Disease Severity And Impact On TFR Status

Severe SARS-CoV-2 infections associated with high mortality rates are Our initial data showed that CML patients with uncontrolled disease have a higher mortality risk when infected with SARS-CoV-2. The impact of SARS-CoV-2 infection on CML patients in treatment-free remission (TFR) has not been studied so far. In particular, as immune control of residual disease may be important for TFR, the concern is that the infection could induce loss of TFR.

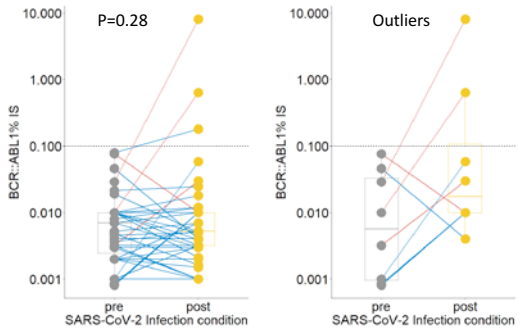
For this sub-analysis additional information were collected including; molecular remission status (BCR::ABL1 ratios) before, during and after SARS-CoV-2 infection



No statistical differences in hospitalisation rate and severity of COVID-19 symptoms in TFR vs TKI CML patients.

Results

By December 2021, of 1050 COVID-19 positive CML patients registered, 95 patients were in TFR at the time point of SARS-CoV-2 infection of which 89 (93.68%) recovered and 6 deceased (6.32%).

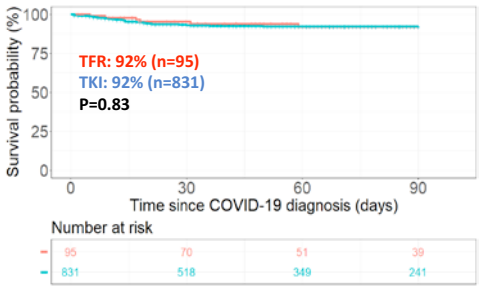


No significant difference in BCR::ABL1 level pre vs post SARS-CoV-2 infection covering at least 6 months.

Conclusions

- There was no statistically significant difference in PCR results before, during and after infection (p>0.2).
- Probability of TFR loss was higher in patients with a TFR duration < 6 months compared to patients with TFR duration >6 months

In this sub-analysis of the CANDID study, CML patients in TFR had similar severity and survival to CML patients who were on TKI therapy and there was no evidence of an increased risk of TFR loss after SARS-CoV-2 infection.



No overall survival differences for TFR and TKI treated CML patients after SARS-CoV-2 infection.

Acknowledgment

The iCMLf sincerely thank all physicians contributing data, the patients willing to help and our partners, the Max Foundation and the CML Advocate Network.

We also thank Arlene Harriss-Buchan for case collection and Chung Kok for statistical analysis.

Sincere thanks also to Novartis Oncology and Pfizer for study funding.

Congratulations to the 2022 iCMLf Prize Recipients

Since the first iCMLf Prize, the Rowley Prize, was awarded to Professor Brian Druker in 2009, the Foundation has honoured 33 individuals for their lifetime contributions to our understanding of CML and its management with the three iCMLf Prizes.

Over the years, this has become an impressive 'who's who' of CML. It is thanks to the amazing work, the passion and the tireless efforts of these people and their teams that the situation of people living with CML around the world has made such tremendous progress.

We are delighted to present the 2022 iCMLf prize winners, who were chosen from many nominations from the CML community, by a panel of past prize winners, iCMLf Directors and Advisors.

The 2022 medals will be presented during award ceremonies at the annual John Goldman Conference on CML in October.

iCMLf PRIZE

Giora Sharf (Israel)
Jan Geissler (Germany)

The 2022 iCMLf prize has been awarded to two powerful voices for patients with CML and co-founders of the CML Advocates Network: Giora Sharf (Israel) and Jan Geissler (Germany). Bwoth Jan and Giora have used the experience of their own diagnosis to help other people with CML and to integrate patient advocates as valuable partners in medical research. They represent the patient's perspective on CML on various industry advisory boards and are highly regarded speakers at scientific conferences. An important part of their work is gathering patient evidence from the global CML community.

This iCMLf Prize is awarded for outstanding contributions to the improvement of CML treatment under the challenging conditions of emerging economic countries with unequal access to monitoring and treatment.

> *'The iCMLf Prize for Giora Sharf and Jan Geissler is a natural and almost due recognition of their passionate work establishing a bridge between the worldwide community of CML patients and their doctors. They have built an open forum in which the voice of patients expressing their needs, their aspirations and also their fears, are clearly heard and understood by the treating clinicians. In this way, Giora and Jan have been able to transfer a more serene vision on their status to many CML patients and have also directly contributed to the great success achieved in CML therapy.'*
>
> Professor Beppe Saglio,
> University of Turin

On behalf of the entire CML community we congratulate all recipients on their prizes.

GOLDMAN PRIZE

Professor Andreas Hochhaus (Germany)

The iCMLf has awarded the 2022 Goldman Prize to Professor Andreas Hochhaus, Head of the Department of Hematology and Medical Oncology at Jena University Hospital, in recognition of his outstanding clinical leadership in CML and his lifelong contributions to the optimization of CML therapy – through his work on mechanisms of resistance and stem cell persistence, through leading clinical studies and through the development of clinical recommendations.

The iCMLf Goldman Prize is the clinical equivalent of the Rowley Prize recognising outstanding lifetime contributions to the management of patients with CML.

"Andreas Hochhaus is an international leader in the clinical management of CML and has been involved in the management of randomised trials by the German CML Study Group for more than 30 years. Professor Hochhaus's notable contributions include development and application of molecular monitoring for optimisation of treatment, understanding mechanisms of resistance and promoting access to clinical trials for all patients."

Professor Nick Cross,
University of Southampton

ROWLEY PRIZE

Professor Oliver Hantschel (Germany)

The 2022 Rowley Prize is awarded to Professor Oliver Hantschel, Director of the Institute for Physiological Chemistry, Chair of Biochemistry, Faculty of Medicine, Philipps University of Marburg, for his translational scientific research on structural biochemistry of tyrosine kinase oncoproteins that helped to describe novel targetable pathways in the pathophysiology of BCR-ABL and ultimately to find new therapeutic approaches.

The iCMLf Rowley Prize is designed to recognise persons who have made major contributions to the understanding of the biology of CML.

"Oliver devoted his entire scientific career to structural biochemistry of tyrosine kinase inhibitors, in particular ABL1 and first described the option to target the allosteric binding site of BCR::ABL1. He started this research as a PhD student and has collaborated with many laboratories worldwide."

Professor Andreas Hochhaus,
Jena University Hospital

Jane Apperley and 40-years in medicine

I was truly honoured to receive the iCMLf Goldman prize in 2020 and am indebted to those who nominated and voted for me. With such prizes come responsibilities – to engage, to entertain, to inform and to acknowledge others, and I cannot be the only recipient who struggled to get the balance right. It is not the forum to try to present new data, and should not focus entirely on one's own work, but it was an opportunity to talk very personally about my own journey in CML.

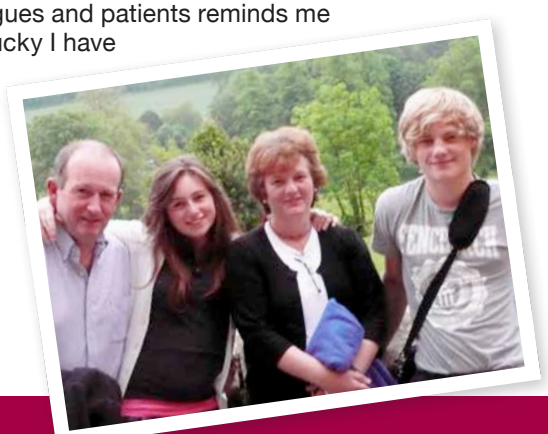
On reflecting on over 40 years in medicine, I am aware how much things have changed in society in general and hopefully also in medicine, particularly with respect to the acceptance of diversity and the opening of opportunities to all. I wanted to try and convey my experience, and although I hope young female doctors will not be exposed to the same degree of discrimination as I was, I suspect that in many places and on many occasions, conscious and unconscious bias are alive and well. On a more positive note, I wanted to convey the real enjoyment that I have experienced throughout my career, the amazing advances made in the management of CML, describe the highs and lows, and recognise the many friends that I have made on the way.

I didn't come from a medical family so had no role models. I came from a very small town in the north of England and lacked the self-confidence to apply to one of our more prestigious medical schools. In retrospect this was not such a bad thing because in attending one of our red-brick (somewhat patronising term used to describe the Victorian universities) institutions, I received a first-class clinical education, with exposure to so many patients and their diseases and a 'see-one, do-one, teach-one' apprentice style approach to learning. I lacked exposure to academic medicine, was unaware of medics doing higher degrees and did not appreciate the importance of mentorship. My ignorance of the 'right way' of doing things may have been an advantage because I just ploughed on, took any opportunity that came my way, and was usually blissfully unaware of any attempt to use my age, sex, class or educational background against me. Light usually dawned later! I mention all of this because I think if I can reach a senior faculty position in a leading university, then anyone can. I might have preferred to do this through design rather than serendipity but so be it!

I became involved with CML very early on because I found the intellectual challenge of stem cell transplant so stimulating. People often say that transplant doctors are at the 'surgical' end of the internal medicine speciality and that suited my personality. There is no doubt that arriving at the Hammersmith and meeting John Goldman in December 1983 was the turning point of my career, but there are many other people and places that influenced and shaped me. I had a great time during my post-doc in Boston and made some wonderful and life-long friends, and on return to Europe, found fantastic colleagues within the EBMT. But in December 1999, I was among the many that squashed into the meeting room at ASH to hear Brian Druker talk about the clinical results from STI571, and the world of CML changed almost overnight. Thereafter the privilege of being involved in bringing the TKIs into clinical practice cannot be underestimated, and this era brought me many more outstanding colleagues and collaborations.

> *"My real enjoyment that I have experienced throughout my career, and the amazing advances made in the management of CML. I have made many friends that I have made along the way."*

Managing a full-time clinical academic career is not always conducive to family life. Maybe my lack of awareness of the difficulties ahead stood me in good stead here also. But I do know that my family have been hugely important in my life and I cannot thank them enough for keeping me grounded and giving me so much happiness. The positive reinforcement that I receive from family, colleagues and patients reminds me every day of how lucky I have been in my career and personal life and apologies that there aren't photos of all.



Jane Apperley - *winner of the 2020 Goldman prize*

Ravi Bhatia, MD: The seed and the soil – the leukemia stem cell in its niche and the quest for cure

Dr. Janet Rowley's discovery of the 9;22 translocation opened a new understanding of the genetic bases of cancer. It is an honor to be in the company of the distinguished previous winners of this award, who have been recognized for their seminal discoveries leading to understanding of the molecular pathogenesis of CML, of the BCR-ABL gene and its activity, and the development of BCR-ABL tyrosine kinase inhibitors. They have also led investigations into the problem of the leukemia stem cell. Their studies have revolutionized treatment of CML and advanced knowledge and care of cancer in general.

My own journey started in India where I grew up and had my schooling and medical education. I moved to Minnesota in 1989 for by Hematology and Oncology training. My research career started in Minnesota in the lab of Phil McGlave and Catherine Verfaillie. It was under their wonderful mentorship that I started studying CML hematopoiesis and how leukemia stem and progenitors respond to and resist therapeutic exposures. As I established my independent career, it was the dawn of the tyrosine kinase inhibitor (TKI) era, and we were drawn to the question of how CML stem cells respond to TKI treatment. As we observed patients going into cytogenetic and molecular remission, we also observed that BCR-ABL+ stem cells continue to be detected in patients in deep remission. Work in Tessa Holyoake and our lab showed that TKI were quite effective in inhibiting the proliferation of CML stem cells, but that quiescent leukemia stem cells were resistant to TKI and were enriched after TKI treatment.

The significance of leukemia stem cells persistence is the risk of leukemia relapse after stopping TKI, potentially leading to a requirement for lifelong treatment. However, we also know that for many patients in deep remission after TKI treatment, it is possible to stop TKI and still maintain TFR. This is a very exciting and important finding- and TFR has become the new goal of CML treatment. However, many patients cannot achieve TFR and face the need for lifelong TKI treatment with risk of non-compliance and treatment failure, side effects and considerable financial costs. These limitations clearly indicate the need for further progress

The weight of evidence is that TKI treatment inhibits BCR-ABL kinase activity in CML stem cells. This suggests that other non-kinase dependent mechanisms are responsible for LSC persistence. What can these mechanisms be? An obvious choice are signals from microenvironmental niches. Stem cells in the bone marrow localize to specialized niches that regulate their maintenance and fate. Stem cells and niche interactions are bidirectional and reciprocal. We found that CML stem cells demonstrate enhanced growth in the leukemic microenvironment compared to normal stem cells. We have also shown that CML modifies the BM leading to altered levels of several chemokines and cytokines and alteration in mesenchymal stromal cell subpopulations that promote enhanced growth of CML compared to normal stem cells. Our recent results support a role for leukemia-elaborated inflammatory factors in stimulating CML stromal progenitors to express factors that enhance CML stem cells self-renewal and expansion. Other studies have identified mesenchymal stromal subsets that function as specific niches that maintain CML stem cells quiescence, and determine TKI sensitivity. Improved understanding of mechanisms by which the niche signals affect leukemia stem cells state and drug resistance is providing new opportunities for therapeutic targeting of residual leukemia stem cells.

In conclusion, the advent of BCR-ABL tyrosine kinase inhibitors has revolutionized treatment for CML. However, leukemia stem cells persist in patients in remission as a source of disease recurrence. We are gaining a better appreciation of the role of the niche in maintenance and drug resistance of LSC. Identification of key cellular components, important secreted factors, and niche-regulated alterations in LSC state is forming the basis for potential approaches to enhance opportunities for treatment-free remission in CML patients.

Ravi Bhatia - *winner of the iCMLf Rowley Prize 2020*

CML management in war and peace: lessons that shaped future approaches

Cancer patients in developing and low-income countries have limited access to target therapies. The availability of TKI therapy for CML patients started in 2005, in the aftermath of the war in Bosnia and Herzegovina.

Due to the limited availability of imatinib, only a few patients received the drug. Over the years, the availability of imatinib gradually increased, but never so that all CML patients were treated with TKIs. Nilotinib, the second generation TKI, was introduced as first line or second line therapy in March 2011. From 2005, CML patients were placed on the waiting list, where almost two thirds of these patients received imatinib within a 14 month waiting period time.

CML patients in the war

- Basic necessities were missing
- CML patients were not properly treated
- Patients in AP/BC tried to leave the country to get treated

At that time, from 2005 to 2013, our efforts were focused on two issues: one was to reduce the waiting time for imatinib and nilotinib and the other was to establish the laboratory for BCR-ABL1 testing. Regarding the first issue, after a continuous battle with administrative obstacles and search for funds, the waiting list was terminated in 2013 with the end outcome that all patients are now able to receive either imatinib or nilotinib upon the diagnosis with rate of success comparable to leading centres around the world. Regarding the second issue, there was no cytogenetic testing for CML patients in Bosnia and most were diagnosed based only on clinical and morphological parameters; in other words, we were administering imatinib without testing or proof of the presence of BCR-ABL1. When we thought of establishing the laboratory, we realized that there were no trained laboratory professionals who could conduct molecular and proper cytogenetic testing. It was an endeavour that had to encompass adjacent facilities and infrastructure. We initiated the formation of molecular and cytogenetic laboratory in 2007 that could conduct karyotype, FISH, and later in 2010 QF-PCR assays.

After a successful start in 2007, it took two years to reach a level where the laboratory was operating at an comparable level to other large centres. The laboratory at the Clinical Center of the University of Sarajevo now conducts a wide range of assays not just for CML, but also for other hematological patients including blood and tissue FISH panels for AML, ALL, CLL, multiple myeloma, lymphoma, qualitative and quantitative PCRs for other translocations, BCR-ABL1 mutations, FLT3, NPM1, CALR, MPL, thrombophilia, hemochromatosis, and many others.

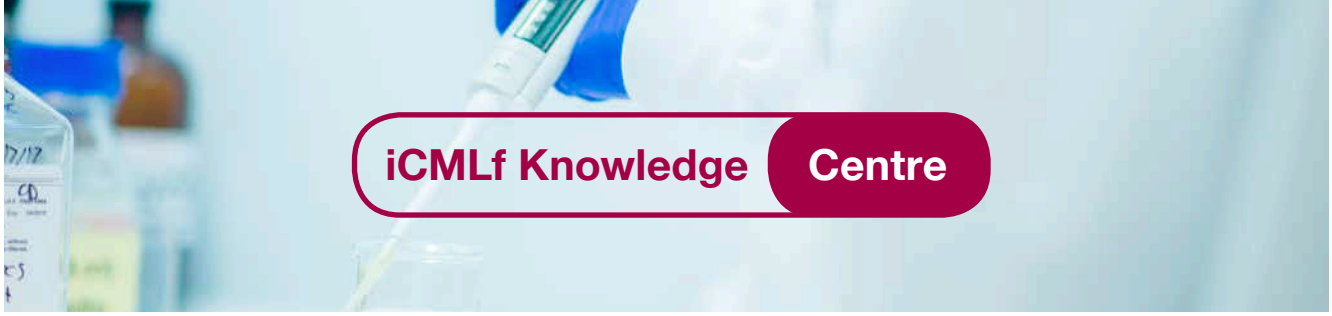
The availability of molecular and cytogenetic testing allowed us to create a database, monitor, and analyze the effect of delayed start of imatinib and nilotinib on CML patients in Bosnia and Herzegovina. We found that 16% of patients received immediate TKI treatment (< 3 months of diagnosis), while 66% of patients received therapy after a median 14-month wait period. In order to analyse the effect of delayed treatment on outcome, three patient groups were studied depending on the length between the diagnosis and the start of the TKI treatment (0–5 months, 6–12 months and > 13 months delay). At 12 months of therapy, CCyR and MMR rates on imatinib were significantly lower in patients who waited for more than 1 year: CCyR was achieved in 67% of CML patients in the immediate imatinib treatment group, 18% of patients in 6–12 months group and 15% of patients in > 13 months wait group. MMR rates at 12 months occurred in 10% of patients with immediate treatment, 6% of those in 6–12 months group and 0% of patients in > 13 months wait group. Our surprise came when we analyzed patients on first line nilotinib, where CCyR and MMR rates in patients on nilotinib were not associated with duration of treatment delay. We found that nilotinib was a superior option compared to imatinib in all subgroups of patients, regardless of whether patients received therapy immediately upon diagnosis or after several months or years. Thus, the deleterious effect of a delaying TKI therapy may be reduced by the more active TKI nilotinib.

> *"Extraordinary times require extraordinary measures. You adapt quickly and start using most resources that you have, sometimes in creative ways."*

Our study directly showed the effect that therapy delay has had on the success of CML treatment. Through our unfortunate circumstances, we highlighted the significance of the immediate start of treatment. Our results may also be useful in this pandemic, when many cancer patients, including CML patients, had to wait to start their treatment. If the wait is longer than 6 months, then options such as nilotinib may be worth considering as first line treatment.

Sabira Kurtovic - *winner of the 2020 iCMLf prize*

AT THIS TIME
our hearts go out to all those affected by the war in Ukraine.



"The Knowledge Centre is a perpetual congress for the CML community of physicians and scientists, a forum for sharing cutting edge, best practice CML management. This online program is presented by expert practitioners and importantly, is where we embrace the challenges of implementation and decision making in real life clinical practice, often in challenging or resource constrained context."

Professor Giuseppe Saglio - Knowledge Centre Chairman

The current modules were developed by an international panel of 27 CML experts from 16 countries.

MODULE 1

CML Therapy

(4 presentations)

Chaired by
Professor Jorge Cortes (USA)
Professor Qian Jiang (China)

Module 1 outlines the current therapies for CML, looks beyond the chronic phase and discusses the international guidelines supporting therapeutic decisions.

MODULE 2

Treatment-free remission

(5 presentations)

Chaired by
Professor Timothy Hughes (Australia)
Dr Katia Pagnano (Brazil)

Module 2 discusses treatment-free remission to help clinicians conducting TFR attempts and to manage patient appropriately during these attempts.

MODULE 3

From the Laboratory – Non Clinical

(5 presentations)

Chaired by
Professor Nick Cross (UK)
Dr Neelam Varma (India)

Module 3 focuses on laboratory aspects of testing for CML for non-clinical scientists looking at current best practice for diagnosis and testing of CML and challenges in applying these approaches in resource-constrained environments.

MODULE 4

From the Laboratory – for Clinicians

(6 presentations)

Chaired by
Professor Jerry Radich (USA)
Dr Carolina Pavlovsky (Argentina)

Module 4 discusses laboratory aspects of testing from the perspective of clinicians looking at CML monitoring from diagnosis to monitoring response and the role of genomic mutation screening in case of relapse or resistance.

MODULE 5

Management Practicalities – Part 1

(5 presentations)

Chaired by
Professor Giuseppe Saglio (Italy)
Professor Mohammed Yassin (Qatar)

Module 5 features various topics on the practical management of CML including managing intolerances and relevant comorbidities, TKI interactions and adverse events. More content will follow in the coming months, including pregnancy and fertility in CML and pediatric CML.

The iCMLf Knowledge Centre is supported by Novartis Oncology.

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24th Annual John Goldman Conference on
CHRONIC MYELOID LEUKEMIA: BIOLOGY AND THERAPY

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