13th International Conference on Chronic Myeloid Leukemia: Biology and Therapy
Estoril, Portugal
September 22 – 25, 2011

Chairs: J.M. Goldman, J. Cortes, T.P. Hughes

Co-Organizers: T. Holyoake, F-X Mahon, D. Perrotti, J. Radich


PROGRAMME SEPTEMBER 12th, 2011: STILL SUBJECT TO MINOR MODIFICATIONS

Thursday 22nd September

12.00-14.00 Registration, mounting and viewing of posters

14.00-14.05 Welcome
John Goldman (London)

14.05-14.40 Rowley Prize Presentation
Chairs: Tim Hughes (Adelaide), Jorge Cortes (Houston)

CML – Reminiscences and dreams
John Goldman (London)

SESSION 1:
LEUKEMIA HSC BIOLOGY AND NOVEL THERAPEUTIC APPROACHES FOR CML ERADICATION
Chair: Tessa Holyoake (Glasgow)

14.40-15.00 Keynote lecture:
Finding the soft spot: targeting CML stem cells
Mike Deininger (Salt Lake City)

15.00-15.15 Reconstructing CML stem cell niche using patient-derived induced pluripotent stem cells (iPSC)
Annelise Bennaceur-Griscelli (Villejuif) to be presented by Ali Turhan (Poitiers)

15.15-15.30 A novel AHI-1-BCR-ABL-JAK2 interaction complex mediates cellular resistance to tyrosine kinase inhibitors in CML stem/progenitor cells
Min Chen (Vancouver)

15.30-15.45 Altered microenvironmental niche regulation of leukemia and normal stem cells in CML
Ravi Bhatia (Duarte)

15.45-16.00 BCL6 is required for the initiation and maintenance of CML
Christian Hurtz (San Francisco) to be presented by Markus M üschen (San Francisco)

16.00-16.25 Coffee break
SESSION 2:
GENETICS, BIOLOGY AND POSSIBLE THERAPIES FOR CML IN BLASTIC TRANSFORMATION
Chair: Pierre Laneuville (Montreal)

16.25 -16.45 **Keynote Lecture:**
Blastic transformation: top ten hits and potential therapies
Danilo Perrotti (Columbus)

16.45-17.00 Awakening dormant human blast crisis leukemia stem cells with a therapeutic sonic hedgehog antagonist
Alice Y. Shih (La Jolla)

17.00-17.15 The pan-BCL2 family inhibitor, sabutoclax, selectively targets bone marrow niche-resident blast crisis CML stem cells while sparing normal progenitor cells
Daniel J. Goff (La Jolla)

17.15-17.30 Elucidation of novel epigenetic mechanisms driving human LSC generation
Anil Sadarangani (San Diego)

17.30-17.45 Targeting of a novel MNK-eIF4E-b-catenin axis in blast crisis CML inhibits leukemia stem cell function
Sharon Lim (Singapore)

17.45-18.15 **Poster viewing (presenters present at their posters)**

18.15-19.00 Poster walk #1 – Poster walks will address separately posters that are primarily biological or primarily clinical.
Poster Walk Leaders Clinical: Jorge Cortes and Tim Hughes
Poster Walk leaders Biological: Connie Eaves, Danilo Perrotti

19.30-21.00 Welcome reception and finger food dinner

Friday 23rd September

08.00-10.00 **SATELLITE SYMPOSIUM** (please refer to the information provided in your conference folder)

08.30-10.00 **Workshop A for non-clinical scientists** (limited attendance, pre-registration required) - Room F7
New approaches to targeting LSCs in chronic and advanced phased
Convenors: Gudmundur Vignir Helgason (Glasgow), Xiaoyan Jiang (Vancouver)

- Proteasome inhibitors in combination with TKI
  Lisa Crawford (Belfast)
- Wnt/b-catenin signaling inhibitors in combination with TKI
  Shinya Kimura (Saga)
- HDAC inhibition in combination with TKI
  David Snyder (Duarte)
- New targets for advanced phase LSCs
  Danilo Perrotti (Columbus)
- Other speakers may be presenting data

10.00-10.30 **Coffee break**

SESSION 3:
ALTERNATIVE AVENUES TO TARGET CML STEM/PROGENITOR CELLS
Chair: Tim Brümmendorf (Aachen)

10.30-10.50 **Keynote Lecture:**
Pharmacological targeting of leukemic stem cells in CML: new insights
Rick van Etten (Boston)

10.50-11.05 Characterization of three novel and non-immunosuppressive FTY720 derivatives that target TKI-resistant quiescent stem and proliferating progenitor CML cells
Paolo Neviani (Columbus)

11.05-11.20 Evaluation of the efficacy and mechanism of action of the JAK2 inhibitor INCB18424 in primary CML stem/progenitor cells
Paoli Gallipoli (Glasgow)
Inhibition of the PI3K/Akt/mTOR pathway induces cell death and protective autophagy in TKI-resistant CML cells

Targeting inhibitory phosphatase signaling in CML

General Discussion

Lunch & poster viewing

**SESSION 4: GENOMIC INSTABILITY AND GENETICS OF CML**

**Chair:** Connie Eaves (Vancouver)

**14.00-14.20 Keynote Lecture:**
Enhanced oxidative DNA damage in CML stem cells: should we inhibit it to prevent genomic instability or use it to eliminate TKI-refractory cells?

**14.20-14.35** Genomic instability originates from leukemia stem cells in a mouse model of CML-CP

**14.35-14.50** DNA repair gene RAD52 is essential for BCR-ABL1-mediated transformation of hematopoietic stem cells

**14.50-15.05** A novel BIM polymorphism mediates resistance to BCR-ABL inhibitors in CML

**15.05-15.20** Identification of novel kinase-activating rearrangements in BCR-ABL1-like ALL by next generation sequencing

**15.20-15.30** General Discussion

**15.30-16.00 Coffee break**

**SESSION 5: ABL TYROSINE KINASE INHIBITORS (1): BIOLOGY AND RESISTANCE**

**Chair:** S. Tiong Ong

**16.00-16.15 Keynote lecture:**
10 years of imatinib resistance- heaps of mutations and a dozen new TKI: what we have learned – a biochemist’s view

**16.15-16.30** Intrinsic and extrinsic survival signals converge upon activation of STAT3 and b-catenin for protection of CML cells from imatinib

**16.30-16.45** Targeting the BCR-ABL/SH2 interface

**16.45-17.00** Irreversible apoptosis commitment of CML cells following acute exposure to tyrosine kinase inhibitors: oncogenic shock, cryptic intracellular retention or both?

**17.00-17.15** Sensitivity to imatinib in BCR-ABL1-positive CML cells is regulated by remaining normal ABL1 kinase

**17.15-17.45 Poster viewing (presenters present at their posters)**

**17.45-18.30** Poster walk #2 - Poster walks will address separately posters that are primarily biological or primarily clinical.

Poster Walk Leaders Clinical: Jorge Cortes and Tim Hughes
Poster Walk leaders Biological: Connie Eaves, Danilo Perrotti
08.00-10.00  **SATELLITE SYMPOSIUM**  (please refer to the information provided in your conference folder)

08.30-10.00  **Workshop B for non-clinical scientists (limited attendance, pre-registration required)** - **Room F7**

*Genome wide technologies in CML: which are approaching clinical use?*

**Convenors:** Simona Soverini (Bologna), Oliver Hantschel (Lausanne)

**Topics in the workshop will include:** Pharmacogenomic technologies, SNP arrays, gene expression profiling and deep sequencing

**Speakers include:** Dennis Kim (Toronto), Charles Mullighan (Memphis), Anna Eiring (Salt Lake City), Alex Kohlmann (Munich)

10.00-10.30: Coffee break & poster viewing

**SESSION 6 : IMMUNOLOGICAL TARGETS AND MONITORING AT LOW LEUKEMIA LEVEL**  
**Chair:** Richard E. Clark (Liverpool)

10.30-10.50  **Keynote lecture:**  
Vaccine and antibody therapy for CML  
**David Scheinberg** (New York)

10.50-11.05  Man versus machine: a semi-automated platform for BCR-ABL QPCR  
**Jerald Radich** (Seattle)

11.05-11.20  **IL1-RAP update**  
**Thoas Fioretos** (Lund)

11.20-11.35  Novel concepts in neoplastic stem cells in CML  
**Peter Valent** (Vienna)

11.35-11.50  Distinct graft-vs-leukemic stem cell effects of early or delayed donor leukocyte infusions in a mouse CML model  
**Yi-Fen Lu** (Boston)

11.50-12.05  Tyrosine kinase inhibitors modulate the B-cell response to vaccination in CML  
**Katy Rezvani** (London)

**SESSION 7: ABL TYROSINE KINASE INHIBITORS (2): BIOLOGY AND RESISTANCE**  
**Chair:** Peter Valent (Vienna)

11.50-12.05  The BELA trial: 18-month update on safety and clinical activity in patients with chronic phase CML treated with bosutinib (SKI-606) or imatinib  
**Carlo Gambacorti-Passerini** (Monza)

12.05-12.20  Multiple non-resistant low-level BCR-ABL1 mutations in CML patients after imatinib resistance predict poor response and high risk of new resistant mutations during second-line kinase inhibitor therapy  
**Susan Branford** (Adelaide)

12.20-12.35  Updated phase 1 data on ponatinib, a pan-BCR-ABL inhibitor, in CML and other hematologic malignancies  
**Jorge Cortes** (Houston)

12.35-12.50  RAF1 is a crucial mediator of BCR-ABL driven leukemogenesis  
**Justus Duyster** (Munich)

12.50-14.00  Lunch & poster viewing
14.00-15.00
**BRIEF ORAL COMMUNICATIONS (BIOLOGY)** - (4 slides, 7 mins)
**Chair:** Jerald Radich (Seattle)

- Use of genetic engineering to model disease progression in CML reveals distinct steps required  
  Ivan Sloma (Villejuif)
- Targeting DNA checkpoint/repair proteins as a strategy for the treatment of CML  
  Mary Scott (Glasgow)
- Targeting STAT5 in CML: Mechanism-of-action of JAK2 tyrosine kinase inhibitors in CML unmask a direct BCR-ABL/STAT5 axis  
  Wolfgang Warsch (Vienna)
- Regulation of mature versus immature conformation of BCR-ABL  
  Yoshiro Maru (Tokyo)
- Rac2 - mitochondrial respiratory chain complex III signaling generates reactive oxygen species causing genomic instability in CML-CP leukemia stem and progenitor cells  
  Piotr Kopinski (Philadelphia)
- Sirt1 co-operates with TGF-b signal to suppress BCR-ABL1-dependent cell growth *in vitro*  
  Hu Ming (London)

15.00-16.00
**BRIEF ORAL COMMUNICATIONS (CLINICAL)** - (4 slides, 7 mins)
**Chair:** Rüdiger Hehlmann

- BCR-ABL compound mutations in CML  
  Jamshid Khorashad (Salt Lake City)
- Correlation of hOCT1 genetic polymorphisms with the clinical outcome of CML patients treated with imatinib  
  Athina Giannoudis (Liverpool)
- Switching to nilotinib vs imatinib dose escalation for patients with suboptimal treatment response to imatinib: 24 month update of the TIDEL-II trial  
  David T Yeung (Adelaide)
- High BCR-ABL1 expression levels at diagnosis and after 3 and 6 months of treatment are associated with an unfavourable response to imatinib  
  Paolo Vigneri (Catania)
- The Prognostic significance of Molecular and Cytogenetic response landmarks after 3 month of Imatinib in the upfront treatment of CML  
  Benjamin Hanfstein (Mannheim)
- Dynamics of the emergence of dasatinib and nilotinib resistance in imatinib resistant CML patients  
  Thomas Ernst (Jena)
- Loss of major molecular response is the most accurate criteria for restarting imatinib after imatinib discontinuation in CP-CML patients with long lasting CMR  
  Philippe Rousselot (Versailles)
- Residual normal stem cells can be detected in newly diagnosed CML patients by a new flow cytometric approach and predict for optimal response to imatinib  
  Jeroen Janssen (Amsterdam)

16.00 - 16.30  **Coffee break**

**SESSION 8:**
**CML CLINICAL ASPECTS AND NEW TRIALS**
**Chair:** François-Xavier Mahon (Bordeaux)

16.30-16.50  **Keynote lecture:**
What questions remain and how can we answer them?  
Jane Apperley (London)

16.50-17.05  Optimising frontline therapy in CML: Developing a treatment algorithm based on sensitivity studies  
Tim Hughes (Adelaide)
17.05-17.20  A Phase 1 study of DCC-2036, an oral novel inhibitor of Abl kinase, in adult patients with Philadelphia Chromosome Positive (Ph+) CML including patients with T315I mutation  
Jorge Cortes (Houston)

17.20-17.35  Assessment of BCR-ABL1 transcripts at 3 months predicts patient outcome  
David Marin (London)

17.35-17.50  The TIDEL II strategy of imatinib dose intensification and nilotinib switch may not overcome the negative impact of a low OCT-1 activity in de-novo CP-CML patients  
Deborah White (Adelaide)

17.50-18.05  How do we define the 'best' front-line therapy for CML and can we afford it?  
Steve O'Brien (Newcastle)

Sunday 25th September

SCIENTIFIC SESSION 9:  
MINI-DEBATES: TOPICAL BIOLOGICAL QUESTIONS  
Chair: Tessa Holyoake (Glasgow)

• There is a definite need to target stem cells
  
8.30-8.40: Yes  
Mhairi Copland (Glasgow)

8.40-8.50: No  
Giovanni Martinelli (Bologna)

8.50-9.00: General Discussion

• Genomic instability can be manipulated to induce LSC to self-destruct
  
9.00-9.10: Yes  
Tomasz Skorski (Philadelphia)

9.10-9.20: No  
Martin Sattler (Boston)

9.30-9.40: General Discussion

• JAK-2 is clearly an important therapeutic target in CML
  
9.40-9.50: Yes  
Min Chen (Vancouver)

10.00-10.10: No  
Wolfgang Warsh (Vienna)

10.10-10.20: General Discussion

10.20-10.50  Coffee break

SCIENTIFIC SESSION 10:  
MINI-DEBATE: TOPICAL CLINICAL QUESTIONS  
Chair: François Guilhot (Poitiers)

• All CML patients should start treatment with 2G-TKI
  
10.50-11.00: Yes  
Giovanni Martinelli (Bologna)

11.00-11.10: No  
Charlie Schiffer (Detroit)

11.10-11.20: General Discussion

• Maintenance of a stable CCyR is an adequate therapeutic target
  
11.20-11.30: Yes  
Michele Baccarani (Bologna)

11.30-11.40: No  
Philippe Rousselot (Versailles)

11.40-11.50: General Discussion

• Stopping TKI can now be recommended in selected patients
  
11.50-12.00: Yes  
François-Xavier Mahon (Bordeaux)

12.00-12.10: No  
Giuseppe Saglio (Torino)

12.10-12.20: General Discussion

12.20-12.30  Closing comments