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 AUGUST 8, 2011 : STILL SUBJECT TO MODIFICATION

Thursday 22nd September

12.00-14.00  Registration & mounting of posters
14.00-14.05  Welcome                                    John Goldman (London)
14.05-14.45  Rowley Prize Presentation
             Chairs: Tim Hughes (Adelaide), Jorge Cortes (Houston)
             CML – Reminiscences and dreams                                    John Goldman (London)
14.45-15.05  Keynote lecture: TBA
             Mike Deininger (Salt lake City)
15.05-15.20  Reconstructing chronic myeloid leukemia (CML) stem cell
             niche using patient-derived induced pluripotent stem cells (iPSC) Annelise Bennaceur-Griscelli (Villejuif)
15.20-15.35  A novel AHI-1-BCR-ABL-JAK2 interaction complex mediates
             cellular resistance to tyrosine kinase inhibitors in CML
             stem/progenitor cells                                            Min Chen (Vancouver)
15.35-15.50  Differential hedgehog pathway activity and response to imatinib Alistair Reid (London)
15.50-16.05  BCL6 is required for the initiation and maintenance of
             chronic myeloid leukemia                                    Christian Hurtz (San Francisco)
16.05-16.30  Coffee break

SESSION 2:
GENETICS, BIOLOGY AND POSSIBLE THERAPIES FOR CML IN BLASTIC TRANSFORMATION
Chair: TBA
Keynote Lecture: Blastic transformation: top ten hits and potential therapies
Danilo Perrotti (Columbus)

16.50-17.05 Awakening dormant human blast crisis leukemia stem cells with a therapeutic sonic hedgehog antagonist
Alice Y. Shih (La Jolla)

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)

Elucidation of novel epigenetic mechanisms driving human LSC generation
Q. Jiang (San Diego)

Targeting of a novel MNK-Elf4E-b-catenin Axis in blast crisis CML inhibits leukemia stem cell function
Sharon Lim (Singapore)

Poster walk (1) and refreshments

Welcome reception and finger food dinner

Friday 23rd September

08.00-10.00 Satellite symposium sponsored by Pfizer

Workshop for non-clinical scientists (limited attendance, preregistration required)
Topic: New approaches to targeting for chronic and advanced phase LSCs.
Chairs: Gudmundur Vignir Helgason (Glasgow), Xiaoyan Jiang (Vancouver)

10.00-10.30 Coffee break

SESSION 3:
ALTERNATIVE AVENUES TO TARGET CML STEM/PROGENITOR CELLS
Chair: Ravi Bhatia

10.30-10.50 Keynote Lecture: Pharmacological Targeting of Leukemic Stem Cells in CML: New Insights
Rick Van Etten (Boston)

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

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
Gudmundur Vignir Helgason (Glasgow)

Targeting inhibitory phosphatase signaling in CML
Seyedmedhi Shojaee (San Francisco)

11.50-12.15 General Discussion

12.15-14.00 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?
Tomasz Skorski (Philadelphia)
14.20-14.35 Genomic instability originates from leukemia stem cells in a mouse model of CML-CP
   Elisabeth Bolton (Philadelphia)

14.35-14.50 DNA repair gene RAD52 is essential for BCR-ABL1-mediated transformation of hematopoietic stem cells
   Kimberly Cramer (Philadelphia)

14.50-15.05 A novel BIM polymorphism mediates resistance to BCR-ABL inhibitors in CML
   King P. Ng (Singapore)

15.05-15.20 Identification novel kinase-activating rearrangements in BCR-ABL1-like ALL by next generation sequencing
   Ryan D. Morin (Memphis)

15.20-15.30 General Discussion

15.30-16.00 Coffee break

16.00-17.30

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

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
   Oliver Hantschel (Lausanne)

16.15-16.30 Intrinsic and extrinsic survival signals converge upon activation of STAT3 and b-catenin for protection of CML cells from imatinib
   Anna M. Eiring (Salt Lake City)

16.30-16.45 Targeting the BCR-ABL/SH2 interface
   Giulio Superti-Furga (Vienna)

16.45-17.00 Irreversible apoptosis commitment of CML cells following acute exposure to tyrosine kinase inhibitors: oncogenic shock, cryptic intracellular retention or both?
   Thomas O’Hare (Salt Lake City)

17.00-17.15 Sensitivity to imatinib in BCR-ABL1-positive CML
   Yashodhara Dasgupta (Philadelphia)

17.15-18.30 Poster walk (2) and refreshments

20.00 Speakers Dinner

Saturday 24th September

08.00-10.00 SATELLITE SYMPOSIUM SPONSORED BY BMS
   Management of CML as a Chronic Disease : Considerations beyond treatment response
   Chair: Francois Guilhot (Poitiers)
   Speakers: Lina Eliasson (London), Joelle Guilhot (Poitiers), Kimmo Porkka (Helsinki), Philippe Rousselet, (Versailles),

08.30-10.00 WORKSHOP FOR NON-CLINICAL SCIENTISTS (limited attendance, preregistration required)
   Suggested: Genetic of CML: GEP, GWAS, miRNA, signal transduction, etc.
   Chairs: Simona Soverini (Bologna), Vivian Oehler (Washington)

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  Distinct graft-vs-leukemic stem cell effects of early
            or delayed donor leukocyte infusions in a mouse CML model
            Y.F. Lu (Boston)

11.35-11.50  B-lymphocytes 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  TBA

12.50-13.05  TBA

13.05-14.00  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)

- On the mechanism of Jak2 activation by Bcr-Abl
  Ralph Arlinghaus (Houston)

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 patient with suboptimal treatment response to imatinib: 24 month update of the TIDEL-II trial
  David T Yeung (Adelaide)

• BCR-ABL transcripts at 3 months predict outcome
  David Marin (London)

• Dynamics of the emergence of dasatinib and nilotinib resistance in imatinib resistant CML patients
  Thomas Ernst (Jena)

• Loss of major molecular response (MMR) 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: TBA
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 Philadelphia chromosome positive (Ph+) CML including patients with a T315I mutation
Jorge Cortes (Houston)

17.20-17.35 TBA
Steve O’Brien (Newcastle)

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)

Sunday 25th September

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

• There is a definite need to target stem cells, but with what?
  8.30-8.40: Yes
  8.40-8.50: No
  8.50- 9.00: General Discussion
  Mhairi Copland (Glasgow)
  Giovanni Martinelli (Bologna)

• Genomic instability can be manipulated to induce LSC to self-destruct?
  9.00-9.10: Yes
  9.10-9.20: No
  9.30-9.40: General Discussion
  Elisabeth Bolton (Philadelphia)
  Martin Sattler (Boston)

• JAK-2 is clearly an important therapeutic target in CML?
  9.40-9.50: Yes
  Min Chen (Vancouver)
SCIENTIFIC SESSION 10:
MINI-DEBATE: TOPICAL CLINICAL QUESTIONS
Chair: François Guilhot (Poitiers)

- All CML patients should start treatment with 2G-TKI
  10.20-10.30: Yes Michele Baccarani (Bologna)
  10.30-10.40: No Charlie Schiffer (Detroit)
  10.40-10.50: General Discussion

- Maintenance of a stable is CCyR is an adequate therapeutic target
  10.50-11.00: Yes Gianantonio Rosti (Bologna)
  11.00-11.10: No TBA
  11.10-11.20: General Discussion

- Stopping TKI can now be recommended in selected patients
  11.20-11.30: Yes François-Xavier Mahon (Bordeaux)
  11.30-11.40: No Giuseppe Saglio (Torino)
  11.40-11.50: General Discussion

11.50-12.00 Closing comments