Over the last 25 to 30 years, detection of minimal residual disease (MRD) has evolved from research tool to a clinical diagnostic test for evaluation of treatment effectiveness in patients with a hematological malignancy. Initially MRD research was focused on technology development, mainly flow cytometry and PCR techniques. Over the last 10 years special attention has been given to standardization, guidelines for interpretation and reporting of results, and quality assurance, all factors that are critically important for clinical implementation of MRD diagnostics. Until recently, quantitative PCR technologies had a preferred position, mainly because of the higher sensitivity and standardization. However the novel 8-colour flow cytometric MRD strategies become highly attractive because of their speed and easy reference database.

Over the last 10 to 15 years, MRD diagnostics has proven to recognize risk groups that differ significantly in prognosis, thereby allowing treatment intervention; in parallel, multiple novel drugs have been developed for patients with a hematological malignancy, resulting in a major increase of overall progression free survival and disease free survival.

MRD is now regarded as an early treatment response marker, but it is still questionable whether MRD might be regarded as a surrogate endpoint of survival. Acceptation of MRD diagnostics to define the primary end point in clinical studies can speed-up the evaluation of novel drugs significantly and improve patient care in hemato-oncology. This requires careful considerations as well as fully standardized and quality controlled MRD diagnostics, approved by EMA and FDA.

The MRD Symposium will address all above topics in five interactive sessions.

Organizing Committee
- J.J.M. van Dongen
- M. Brüggemann
- A. Schrauder
- W.M. Comans-Bitter
- B. van Bodegom
- C. Linther
- B. Beukenkamp

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E-mail: b.beukenkamp@erasusmc.nl
www.hetcongresbureau.nl

Scientific Committee
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- M. Brüggemann
- G. Cazzaniga
- J. Hancock
- M. Koebal
- E. Macintyre
- A. Orfao
- C. Pott
- T. Raff
- B. Schäfer
- A. Schrauder
- T. Szczepanski
- V.H.J. van der Velden

Detection of minimal residual disease (MRD) on flow cytometric analysis of TCR/Ig rearrangements

1st Announcement
International Symposium on Minimal Residual Disease in Hematological Malignancies:
From research tool to primary endpoint in clinical trials
Rotterdam, The Netherlands, 8-9 November 2012
Thursday, 8 November 2012

08:00 – 09:00 Registration and Coffee/Tea

09:00 – 09:10 Welcome – J.J.M. van Dongen

09:10 – 10:30 SESSION 1: MRD techniques: State of the art
Chair: E. Macintyre (Paris, France)
• MRD detection by Ig/TCR targets: State of the art
  J.J.M. van Dongen, Rotterdam, Netherlands (20 min)
• Flow cytometry for MRD detection: State of the art
  A. Orfao, Salamanca, Spain (20 min)
• Comparison between PCR and flow cytometry
  G. Genjia, Monza, Italy (5-10 min)
  H. Cave, Paris, France (5-10 min)
  S. Böttcher, Kiel, Germany (5-10 min)
  V.H.J. van der Velden, Rotterdam, Netherlands (5-10 min)

10:30 – 11:00 Coffee/Tea

11:00 – 12:30 SESSION 2: MRD diagnostics: new developments
Chair: A. Orfao (Salamanca, Spain)
• News from the EuroFlow network: new MRD tubes and bioinformatics-assisted automated analysis
  T. Szczepanski, Zabrze, Poland (10-15 min)
• News from the EuroMRD network: new targets and technical advances
  G. Cazzaniga, Monza, Italy (10-15 min)
• Relevance of subclone detection and implications for targeted therapy in ALL
  M. Brüggemann, Kiel, Germany (10-15 min)
• High Throughput Sequencing of Ig-TCR genes: position for MRD?
  C. Pott, Kiel, Germany (10-15 min)
• High Throughput Sequencing of mutations: targets for MRD?
  T. Hafelfeld, München, Germany (10-15 min)

12:30 – 13:30 Lunch

13:30 – 15:30 SESSION 3: MRD diagnostics for treatment decision in ALL: are the criteria for a valid biomarker status fulfilled?
Chair: V. Conter (Bergamo, Italy) and J.J.M. van Dongen (Rotterdam, Netherlands)
• Criteria for the application of valid biomarkers in haematology-oncology
  Speaker to be confirmed (15-20 min)

ALL
• Introduction on ALL
  V. Conter, Bergamo, Italy (5-10 min)
• Application of MRD diagnostics in the design of childhood ALL protocols
  M. Schnappe, Kiel, Germany (10-15 min)
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• Do we need MRD diagnostics for improving SCT strategies in ALL?
  P. Bader, Frankfurt, Germany (10-15 min)
• MRD-based recognition of low-risk groups for treatment reduction
  R. Pieters, Rotterdam, Netherlands (15-20 min)

15:30 – 16:00 Coffee/Tea

16:00 – 18:00 SESSION 4: MRD diagnostics for treatment decision in mature lymphoid malignancies: how far are we from a valid biomarker status?
Chair: V. Conter (Bergamo, Italy) and J.J.M. van Dongen (Rotterdam, Netherlands)
• Criteria for the application of valid biomarkers in haematology-oncology
  Speaker to be confirmed (15-20 min)

LYMPHOMA
• Introduction on lymphoma
  M. Kneba, Kiel, Germany (5-10 min)
• MRD diagnostics in follicular lymphomas
  M. Lasidlo, Torino, Italy (10-15 min)
• MRD diagnostics in mantle cell lymphoma
  M.H. Damas, Creteil, France (10-15 min)
• MRD strategies in Burkitt lymphoma
  A. Rosen, Padova, Italy (10 min)

CLL and MM
• Introduction on CLL and MM
  P. Sonneveld, Rotterdam, Netherlands (5-10 min)
• MRD application in CLL protocols
  M. Hallek, Cologne, Germany (10-15 min)
• Introduction of MRD diagnostics for stratification in MM protocols
  B. Palva, Salamanca, Spain (10-15 min)

Friday, 9 November 2012

08:30 – 10:30 SESSION 5: MRD as primary endpoint in clinical trials
Chair: J.J.M. van Dongen (Rotterdam, Netherlands)
• Role of MRD diagnostics as surrogate for predicting clinical benefit of novel treatment
  Speaker to be confirmed (20-25 min)
• Challenging the current MRD response criteria in leukemia and lymphoma: is it time for a change?
  Speaker to be confirmed (15-20 min)
• How to assess single drug efficacy in modern treatment protocols
  C.M. Zwaan, Rotterdam, Netherlands (10-15 min)
• MRD diagnostics as surrogate marker for outcome: issues in validation and trial design
  M. G. Visco, Milano, Italy (15-20 min)
• Standardization guidelines and QC
  T. Raff, Kiel, Germany (10-15 min)
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• MRD as primary endpoint in registration trials: position of the regulatory authorities
• Need for worldwide standardization and validation of MRD diagnostics
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  J.J.M. van Dongen

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Thursday, 8 November 2012

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     M.H. Delfau, Creteil, France (10-15 min)
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     A. Bosken, Padova, Italy (10 min)
   - Introduction of MRD diagnostics to stratification in MM protocols
     B. Paiva, Salamanca, Spain (10-15 min)

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     N. Gündüz, Frankfurt, Germany (10-15 min)
   - Do we need MRD diagnostics for improving SCT strategies in ALL?
     R. Bader, Frankfurt, Germany (10-15 min)
   - MRD-based recognition of low-risk groups for treatment reduction
     R. Pieters, Rotterdam, Netherlands (15-15 min)

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Friday, 9 November 2012

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   - Requirement of the current response criteria in leukemia and lymphoma: is it time for a change? Speaker to be confirmed (15-20 min)
   - How to assess single drug efficacy in modern treatment protocols
     M.D. Zaal, Rotterdam, Netherlands (10-15 min)
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The MRD Symposium will address all above topics in fine interactive sessions.

### Information and organization

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- B. van Bodegom
- C. Linker
- B. Beukenkamp

### Scientific Committee

- J.J.M. van Dongen (chair)
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- J. Hancock
- M. Kieboes
- E. Macintyre
- A. Orfao
- C. Pilt
- T. Raff
- B. Schäfer
- A. Schrauder
- T. Szczepanski
- V.H.J. van der Velden

### General Information

**Date**
8-9 November 2012

**Venue**
Congress Centre De Doelen
Jutlaan 31
3000 CA Rotterdam
The Netherlands

**Registration and Information**
For more information, accommodation and registration please check the website: www.hetcongresbureau.nl (congresagenda).

- Registration fees from 30 September 2012: €195,-
- Registration after 30 September 2012: €225,-

**Cancellation and refunds**
All cancellations should be in writing (e-mail) and sent to Ms. Bernice Beukenkamp. In case of cancellation:
- Until September 30, 2012 a refund is possible minus a service charge of €15.
- Between September 30 and October 25, 2012 you will have to pay 50% of the total amount you are registered for.
- After October 25, 2012 no refund will be possible and the full amount will remain due.

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### EuroMRD (ESG-MRD-ALL) Guideline Report


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### Results

- **Detection of minimal residual disease (MRD)**
- **RQ-PCR analysis of TCR/Ig rearrangements**
- **LCM (Leonard et al. 2011)**
- **Detection range**

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### Mini symposium 1

### International Symposium on Minimal Residual Disease in Hematological Malignancies:

**From research tool to primary end point in clinical trials**

Rotterdam, The Netherlands, 8-9 November 2012
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Congress Centre De Doelen
Julianaweg 12
Rotterdam, The Netherlands

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### Scientific Committee

**Detection of minimal residual disease (MRD)**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>% relapse free survival</th>
<th>% overall survival</th>
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**EuroFlow Consortium; Responsible scientist: L. Lhermitte**

**APS 2**

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**3rd Announcement**

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