Present
Ca. 95 participants.

Future meetings

- Second International ELN Workshop on standardization of flow cytometry in MDS, 7th May, 2009 in Patras.
- MDS symposium in Patras, 7th May, 2009: ELN MDS meeting on therapeutic guidelines.
- MDS symposium in Patras, 6th May, 2009: EUMDS low-risk Registry
- The second Workshop on flow cytometry in MDS- will be held on 30-31 Oct 2009 in Munich, Germany (host: Dr. W. Kernn; chair: AA van de Loosdrecht).
- ESH-EHA Scientific Workshop on Experimental Haematopoiesis and Therapeutics 2010? (R. Padua)

Proposal for standardized diagnostic and prognostic procedures in the myelodysplastic syndromes
E. Hellström Lindberg

Jan. 2009 E. Hellström Lindberg and A. Porwit prepared a revised version of the guidelines: updated according to WHO and revised regarding flow cytometry, according to minutes from the previous meeting. The document was sent to all participants of the MDS WP. Many comments were received by email and E. Hellström Lindberg summarized the major comments during the meeting.

Suggested work process:

- Send on to representative for the cytogenetic group?
- A. Porwit suggested to wait for official ELN FACS doc. (and thereafter integrate this in the diagnostic guidelines?).
- Work-up of suspected MDS or mixed MDS/MPNs.
- Include comments (regarding evaluations) that still allows investigation at local center and add some other comments with a ”may”.
- Add clearer statement regarding the target group and reference to the WHO 2008 book.
- It was proposed and agreed (?) to keep the MDS and AML guidelines separated because of the new WHO classification.
- Both IPSS and WPSS will be included in the guidelines (WPSS is less validated compared to IPSS).
- It was proposed and agreed to remove the WHO classification 2001.

E. Hellstrom-Lindberg will prepare a next version of the guidelines using the comments of the MDS WP participants. This next version will be published on the ELN website and evaluated after one year. It was suggested to add a section on the website were participants may comment on the guidelines. In addition, it was proposed to add a summarized version of these guidelines to the therapeutic guidelines which is in preparation for publication.

Standardization of flow cytometry in myelodysplastic syndromes
T. de Witte on behalf of A. van de Loosdrecht

Report from the first ELNet Working Conference on flow cytometry in MDS, Amsterdam 2008.
Goal: Proposals for an ELN standardization protocol of Flow Cytometry in MDS.
The following topics were presented:

- Potential impact of flow cytometry in MDS.
- Proposed antigens of major importance in flow cytometry in MDS.
- Proposed marker combinations for flow cytometry in MDS.
- Proposed Concensus [%] on aberrant antigen expression in MDS.
- Number of aberrancies in the myeloid lineage as assessed by flow cytometry.
- Pathological control samples for flow cytometry: defining specificity towards MDS.

Conclusions:

- Emerging new diagnostic flow cytometric approaches in MDS. Consensus: to be done.
- Definition on scoring e.g. FCSS to be defined.
- MDS Patras; Greece May 2009.

- The second Workshop on flow cytometry in MDS- will be held on 30-31 Oct 2009 in Munich, Germany (host: Dr. W. Kernn; chair: AA van de Loosdrecht).
- Currently: NvC [Dutch WP]: exchange of 'wet' (fresh) samples.

WP10 will be involved in the planned meetings.
A consensus protocol for use within the ELN as well as abroad, was finalized and submitted for publication and will be operational in the beginning of 2009.

Evidence- and consensus-based practice guidelines for the therapy of primary myelodysplastic syndromes
D. Bowen

Two consensus conference were held in Florence in May and in Paris in September 2007, with the aim to reach a definite consensus on question-specific statements and to agree on the appropriateness of some selected scenarios.
Algorithms were presented for treatment of MDS for Low IPSS risk, Intermediate-1 IPSS risk, and Intermediate-2 or High IPSS risk.
It was proposed to present the guidelines on the ELN website, including a comment that these guidelines are still under development. Similar to the diagnostic guidelines, a section on the website may be add were participants may comment on the guidelines.

Added after the meeting (see email Cazzola 21-2-09 and Bowen 4-2-09): It was suggested to include a summary of the existing diagnostic guidelines in the therapeutic guidelines.
L. Malcovati and M. Cazzola will update the last draft of the therapeutic guidelines and will circulate the new version; when?
Availability of the scenario analysis programme on the website?
Meeting in Patras for approving the final version to be submitted to a journal in the mid of May.

A multicentre phase II study of the efficacy and safety of lenalidomide in high-risk myeloid disease (high-risk MDS and AML) with a karyotype including del(5q) or monosomy 5
E. Hellström Lindberg

Study coordinator: Lars Möllgård
- An investigator initiated study with financial support from Celgene
- Sponsor: Nordic MDS Group
- Sweden, Denmark, Norway, Finland and Iceland
- 20 centers
- 50 patients
- Inclusion 2007-2009

Study report:
- 22 patients included
- Responders and non-responders.
- Overall, all GCP rules have been met and it was easier than expected
- NMDSG now working on the next phase II protocol, which will be submitted to authorities in March-April and is planned to start Sept 2009

HOVON89 randomized phase II trial in low/int-I risk MDS; lenalidomide with or without Epo/G-CSF.
T. de Witte on behalf of A. van de Loosdrecht

Design of the study is the result of an extensive discussion. Many translational studies included.
Objective: Extension of the study to other countries will be considered.

A prospective, non-interventional multicenter European Registry on IPSS low and intermediate-1 MDS patients Joint-collaboration ELN– Novartis Oncology Region Europe
D. Bowen

Primary Objective : descriptive epidemiology and disease-management of IPSS low and intermediate-1 MDS patients, classified according to WHO criteria.

Conclusions:

Later added after the meeting: Status at the end of February:

- Study running well with 80% of the sites actively accruing patients (129 sites open, from which 69 sites actively including patients)
- 348 patients have been included so far, the target will hopefully be reached before the end of 2009
- Extension to 2,000 patients foreseen
- Substudies will probably start in first Q3-Q4 of 2009
- A high-risk MDS registry is planned in 2009

Progress of Substudies of Low Risk MDS Registry:

- ✓ Iron pathophysiology: M McKenzie
- ✓ Imaging of iron overload: P. Fenaux
- ✓ Cytomorphologic sub-study: U Germing
- ✓ Geriatric Assessment : R. Stauder
- ✓ Protein Profile substudy: D. Bowen

Blood and urine samples are collected for future substudies.
Several other countries would like to participate in this registry. Before participation, a feasibility check will be performed.

ELN high-risk MDS registry proposal
D. Bowen

Study objectives:

- To capture and describe the epidemiological and demographic data of newly diagnosed patients with MDS of IPSS intermediate-2 and high-risk subtypes, patients with AML with 20-30 percent marrow blasts and multi-lineage dysplasia and patients with CMML with 10-29 percent marrow blasts.
- To capture and describe all treatment outcomes of such newly diagnosed patients.
- Proposal for substudies: To perform relevant scientific research on biological samples.

Study visits:

- Accrual period 12-18 months
- Follow up 6 monthly for 5 years
- Dataset adapted from low-risk registry
- Incorporate patient reported outcome / co-morbidity scoring
- Blood / urine for biological correlative studies

Funding:

- For negotiation with interested companies
- Academic independence paramount: University of Nijmegen as sponsor

The Development of a Frailty Score in AML/MDS: update
B. Deschler

Summary:

- ✓ Multicenter performance feasible
- ✓ Numerical age is not a strong predictor of survival
- ✓ Two prognostically most powerful, independent predictors:
  - ADL (=Barthel Index)
  - Fatigue (= 3 items of the EORTC C30 questionnaire)
- ✓ A simple frailty score (made from ADL and fatigue) discriminates 2 risk groups (across 3 different treatment modalities)
- ✓ Clinical judgement (treatment allocation) can be well related to score

Application of score desired, but first: validation required.

Proposal for validation of the frailty score in prospective MDS studies of:
1. Older MDS Low-Risk Patients (e.g. growth factor or IMiD trials)
2. Older MDS High-Risk Patients
   a) Non-Intensive (e.g. azanucleosides)
   b) intensive treatment (e.g. allografting after RIC)

Incorporation of frailty index in high risk MDS registry.
Findings of substudy low risk MDS registry: Geriatric Assessment (R. Stauder) may help to answer questions regarding frailty index.

Detection of novel genetic lesions in myelodysplastic syndromes
J. Jansen

Detection of chromosomal aberrations in MDS:
High density SNP-array (Affymetrix) analysis

- Bone marrow of 102 MDS patients at diagnosis
  - all MDS subtypes
- Controls:
  - peripheral blood MNC of healthy people (n=231)
- Several novel, recurrently affected regions are detected, as reported during ELN meeting at EHA.

Minimal region on chromosome 4 (4q24) contains two genes: TET2 and PPA2.
TET2 mutations are present in all six patients with SNP-array aberrations at 4q24.
Overall: mutations can be detected in 27/102 MDS patients (bi-allelic in more than half of patients).
Conclusions:

- TET2 is the most frequently mutated gene in MDS known so far, occuring in 25% of the cases.
- All missense mutations in TET2 cluster in two conserved regions, nonsense & frameshift mutations leading to STOP codons are scattered throughout the coding sequence.
- TET2 deletion/mutation may precede other chromosomal aberrations that are well-known in MDS.
- TET2 mutations are more frequent in MDS patients within the low/int-1 IPSS categories (up to 40% in the low-risk category).
- NB: TET2 mutations were also reported by Delhommeau & Vainchenker et al in JAK2 positive MPD (reported at ASH dec 2008).

High expression in hematological tissues. Possibly tumor supressor gene. Mutation acquired during development of disease. Expansion of the cohort is planned.

European Genomic and Epigenetic Study on MDS and AML (EuGESMA COST Action)
R. Padua

Chair: K. Mills

- **WG1:** miRNA/mRNA expression profiling:
  - Lars Bullinger (Germany)/Margarita Guenova (Hungary)
- **WG2:** Whole genome mutation and abnormalities:
  - Sophie Dominique Raynaud (France)/Tiziana Storlazzi (Italy)
- **WG3:** Epigenetic scanning:
  - Brigitte Schlegelberger (Germany)/ Soren Lehmann (Sweden)
- **WG4**: Screening novel drugs:
  - Rose Ann Padua (France)/ Nevena Veljkovic (Serbia)
- **WG5:** Web interface, data integration:
  - Martin Dugas (Germany)/Sakari Knuutila (Finland)

- Coordinated use of resources
  - Technical
  - Samples
  - Knowledge

Translation of laboratory findings into new diagnostic, prognostic and treatment strategies.

Several EU Costs offices in Europe for organization. Two representatives / country / WG.
EU (FP7 program) budget is 400.000 euros / 4 years for meetings. It is possible to apply for separate budget for research projects. 1e kick of meeting was in Nov. 2008. First WG meetings planned in March 2009.

Finances
ELN will continue as a foundation. The EU budget for ELN for the next 2 years is very limited.
Celgene grant: proposal to use this for high risk MDS registry and for meeting/travel costs.