EHASWG
SCIENTIFIC WORKING GROUPS

Annual Report 2016

SWG ACUTE MYELOID LEUKAEMIA

Background

Unraveling the molecular aberrancies underlying the pathogenesis of AML provided, apart from greater insights into disease biology, also useful information predicting the outcome following conventional chemotherapy, leading to the development of risk-stratified treatment approaches. Using novel genomics technologies, such as next generation sequencing (NGS) techniques, major progress has been made in further unravelling the heterogeneity of the disease. On average, AML harbours a median of 13 mutations, with in excess of 200 genes being recurrent mutation targets. However, translating this knowledge into clinical practice is lagging. Treatment still includes the cytostatic drugs that are in use now for over 40 years. Nevertheless outcome has improved mainly due to better supportive care and the broad application of stem cell transplantation. The major indication for alloSCT is AML. Concerted efforts from basic, translational, and clinical hematologists will be required to make major advances in the forthcoming years. Only two new drugs (hypomethylating agents) have been approved for AML in the last twenty years. However many new drugs targeting leukemic drivers or a multitude of deregulated pathways are now introduced for clinical usage. New immunotherapy approaches, such as vaccination, CAR T cells, natural killer (NK) cells, bispecific T-cell engagers, novel mono-clonal antibodies, and immune-conjugates, hold great promise and are investigated now in various clinical trials some already in Phase3 studies.

Mission

- Annual scientific meeting at EHA
- To institute a platform for translational research
- Provide a forum to bridge gaps between basic scientists and clinicians treating patients with AML
- Consideration of the implications of high throughput sequencing technologies and minimal residual disease assessment to clinical trial design
- Close collaboration with ELN AML WP 5

Chairs

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Annual Activity

2016 was a sad year due to the fact that David Grimwade the chair of this SWG passed away.

David Grimwade was Professor of Molecular Hematology in the Department of Medical and Molecular Genetics, King's College London School of Medicine and Honorary Consultant Hematologist in Guy's and St. Thomas' NHS Foundation trust.

In September 2015 David Grimwade was diagnosed esophageal cancer. He was in contact with many scientific friends until weeks before he passed away and kept his sense of humor and scientific enthusiasm till the end.

He was internationally renowned for his translational research, particularly in the field of APL was also greatly involved in many of the scientific activities of the EHA. He was an EHA board member from 2011-2015 and was co-director of the Translational Research Training in Hematology.

He led the MRD WP of the European LeukemiaNet, which comprises a network of 28 labs spread across 12 countries involved in development,

optimization and standardization of quantitative PCR assays to improve the management of patients with myeloid malignancies.

The Board of EHA selected David Grimwade as the winner of the EHA Jean Bernard Life Time Achievement Award 2017, for his many contributions to the diagnosis and management of AML. This will be posthumously awarded during the Opening Ceremony of the 22nd Congress of EHA in Madrid, Spain in June of next year.

The AML Scientific Working Group was formed in 2013 and arranged scientific meetings in 2013 -2015 and a further scientific session at EHA21 entitled “AML from leukemogenesis to treatment”, which was attended very well (over 500 attendants). Professor Jude Fitzgibbon (Center of Haematology-Oncolgy at Barts Cancer institute London) gave a presentation on Genetic predisposition of AML with special emphasis on germ-line mutations in 3 myeloid transcription factors, CEBPA, RUNX1 and GATA2. He showed that while these studies are important to the individual families, they are also helping to understand the molecular evolution of AML, the patterns by which mutations arise and explain the clinical heterogeneity that exists both within and between families.

This talk was very timely given the fact that a new entity is now included in the WHO 2016 classification of AML: Myeloid neoplasms with germ line predisposition without a preexisting disorder or organ dysfunction.

Kimmo Porkka M.D, Ph.D. is a professor of clinical hematology at the University of Helsinki and his current clinical position is Head of the Department of Hematology at the Helsinki University Hospital Comprehensive Cancer Center gave a presentation entitled: “Drug profiling for prediction of disease sensitivity”. His talk focussed on the improvement of therapeutic accuracy by selecting drugs and drug combinations based on signal network analyses and in vitro resistance testing. He discussed a functionalized personal medicine approach to be integrated into an early clinical trial design.

In 2015 and 2016, members of the AML SWG have discussed the preparation of an update to the ELN AML guidelines (Blood, 2010), in close collaboration with ELN. This international group of experts had many productive meetings during this period. The AML recommendations are finalised and are published in Blood February 2017.

Together with some relevant ELN Working Parties (MRD, AML, Diagnostics, NGS) we organized in 2015 and 2016 a couple of meetings to discuss the value of measurable residual disease detection in AML. Especially F2F meetings that were attended by leading AML MRD experts from Europe and USA covering flow cytometric, molecular, NGS and clinical MRD have been very productive. This will result in a manuscript containing recommendations on harmonization of methods to apply MRD detection in clinical trials for AML that will be submitted soon.

The SWG does not organize separate AML SWG meeting because this would be redundant due to the 2-yearly AML meeting organized by ESH and the also every two years organised Munich Acute Leukemia Conference. Both meetings are excellent and it would be redundant to organise another scientific meeting on AML.

It is clear from the activities that close collaborations exist with the AML WP 5 and some other for AML relevant ELN WPs. Many scientists are member of both groups. Formal ‘’fusion” of both scientific groups will be discussed.

SWG relevant publications

Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel.
Döhner H, Estey E, Grimwade D, Amadori S, Appelbaum FR, Büchner T, Dombret H, Ebert BL, Fenaux P, Larson RA, Levine RL, Lo-Coco F, Naoe T, Niederwieser D, Ossenkoppele GJ, Sanz M, Sierra J, Tallman MS, Tien HF, Wei AH, Löwenberg B, Bloomfield CD.
Blood. 2017 Jan 26;129(4):424-447

MRD in AML: does it already guide therapy decision-making?
Ossenkoppele G, Schuurhuis GJ.
Hematology Am Soc Hematol Educ Program. 2016 Dec 2;2016(1):356-365