EHA-SWG SCIENTIFIC MEETING ON INTEGRATED CELL TRACKING IN ONCOHEMATOLOGY: DIAGNOSIS, TARGETED THERAPY AND RESIDUAL DISEASE

November 10-11, 2022 | Bordeaux, France

Meeting Chairs:
MC Béné, Nantes University
G Zini, Università Cattolica S.Cuore - Fondazione Policlinico Gemelli-IRCCS

In the second week of November, the city of Bordeaux; the wine capital and city with its beautiful historical monuments served as the perfect backdrop for the EHA-SWG meeting on Diagnosis. The latter turned out to be a gathering of expert friends bringing the latest updates and approaches of integrated diagnosis in hematological malignancies.

From November 10-12, the chairs Profs MC Béné and G Zini were thus joined by leading experts to present the state of the art and future directions in laboratory and clinical oncohematology. The program contained a mixture of expert lectures, patient input and presentations from submitted abstracts.

The whole meeting was recorded and is available until **December 12, 2022**. Below a summary of the presentations, allowing you to choose what to view.

Day 1 | Tools of the trade

On Thursday, November 10, the day started with the new approaches for the diagnosis of hematological malignancies. Insight was provided on how new parameters on the hematology analyzers allow to suspect myelodysplastic and myeloproliferative syndromes. Morphology requires deep knowledge and remains prone to heuristic errors. In recent years and more likely in the future, digital morphology will help to fix knowledge errors and heuristics and improve patient management. This part was highlighted by numerous examples from Profs. M Eveillard, J Bentham, G Zini and T Haferlach.
It was discussed how morphology remains until today the best starting point for the diagnosis of leukemia and lymphoma. It has however to be complemented by other approaches, especially since targeted therapies require more specific diagnostic workflows. New techniques/anomalies in cytogenetics and high-throughput sequencing as well as expert analytic software were thus discussed with significant examples by Profs. C Mecucci and T Haferlach.
The time points: diagnosis, refractory/relapse (R/R) cases, minimal residual disease (MRD) and medical history (pCT) also have to be considered during diagnostic procedures for hematological diseases.
With the development of unsupervised analysis tools, as shown by Dr F Lacombe, a new era is opening in flow cytometry. Provided that supervised analysis of artificial intelligence proposals is performed, this allows for the discrimination of hematological cell subsets. Advantages are the disappearance of subjective gating, reproducibility of quantitative results and high sensitivity of abnormal cell detection and counting. This is especially useful at later time points of MRD detection of appreciation of the restoration of normal hematopoiesis.

Day 2 | Emphasis on clinical practitioners and the diagnostic of hematological diseases in practice

The second day targeted clinical practitioners and the diagnostic of oncohematological diseases in practice. The day kicked-off with a session focusing on "The blast cell". Prof. A Porwit showed that B-lineage acute leukemia may be distinguished from B-cell lymphoma by flow cytometry instead of genetics and detailed some new concepts from the recent classifications of hematological malignancies. Prof. W Kern highlighted the new classifications of acute myeloid leukemia and emphasized that there are 2 yet very close approaches to diagnosing MRD in multiparametric flow cytometry

- The "Different-from-Normal" (DfN) approach based on the identification of aberrant differentiation/maturation profiles at follow-up
- The LAIP approach: defining "Leukemia Associated Immunophenotypes" at diagnosis and tracking them in subsequent samples

The final presentation in this session was given by Prof Dr. C Müller-Tidow who presented the new therapeutic approaches using T-cell cytotoxicity, namely T-cells engagers and CAR T-Cells. He emphasized the 2 side effects of cytokine release syndrome and neurotoxicity (immune effector cell-associated neurotoxicity syndrome, ICANS), as well as the need to overcome cytopenias.

Profs A Rawstron and LM Fornecker discussed CD5+ malignancies, essentially chronic lymphocytic leukemia and its differential diagnosis from mantle cell lymphoma. The rationale of current therapies based on the pathophysiology of these diseases was also developed.

A lively roundtable allowed to discuss the topic of MRD in hematological malignancies with the questions Why? How? When? Where?.

Prof A Porwit presented the probabilistic Classification tool for Genetic Subtypes of Diffuse Large B Cell Lymphoma with Therapeutic Implications published in 2022 by Wright et al.:

- Diffuse Large B cell Lymphoma (DLBCL) consist of seven genetic subtypes
- The LymphGen algorithm classifies a DLBCL biopsy into one or more genetic subtypes
- The genetic subtypes have distinct clinical outcomes and pathway dependencies
- The genetic subtypes will aid the development of rationally targeted therapy for DLBCL

The chair of the Scientific meeting Prof MC Béné presented the story of the Reed Sternberg cells discovery and elusive immunophenotype as well as the impact of molecular anomalies such as a highly unstable genome, many chromosomal abnormalities, frequent aneuploidy. She also detailed how the Reed Sternberg cells, crippled B-cells refusing to apoptose, manipulate the physiological immunosuppressive functions of the host.

Prof O Tournilhac discussed the conundrum of T-cell lymphoma, with a focus on ALCL molecular classification with ALK+ and ALK- variants and targeted therapy based on this classification.

Prof FX Mahon discussed the rationale of the therapy and therapy cessation in chronic myeloid leukemia. His presentation was highlighted by the testimony of one of his patients, who initially failed to respond to classical therapies, 20 years ago, yet benefited from the second generation of tyrosine kinase inhibitors up to the point that she is now off therapy and doing well. Prof Saussele provided,

by connecting remotely, even more information on the rationale of stopping treatment in this disease and the precautions it requires.

Day 3 | Clinicians and the diagnostic of specific hematological diseases

On the last day, four different conditions were discussed. Prof A van de Loosdrecht explained to the participants the contribution of flow cytometry to the diagnosis and classification of myelodysplastic syndromes. He presented the criteria for the integrated diagnostic in Myelodysplastic Syndromes such as prerequisite criteria, MDS-related Criteria, and Co-criteria.
Prof A Risitano provided a comprehensive review of paroxysmal nocturnal hemoglobinuria, including the exciting new pathophysiological and therapeutic approaches in this condition.
Prof P Valent, from his office in Vienna, gave an exhaustive description of mastocytosis and related conditions, encompassing pathophysiology, integrated diagnosis and therapy.
Finally the modern approaches of multiple myeloma therapy and follow up were reviewed by Prof M Eveillard.

Selected oral presentations
A selection of abstracts was eligible for acceptance during the meeting, the presentation format was in the form of oral presentations or poster presentations. In total, the program included ten insightful oral- and three poster presentations.

EHA would like to thank the chairs, sponsors, faculty, and attendees for their contribution and effort to the meetings success.