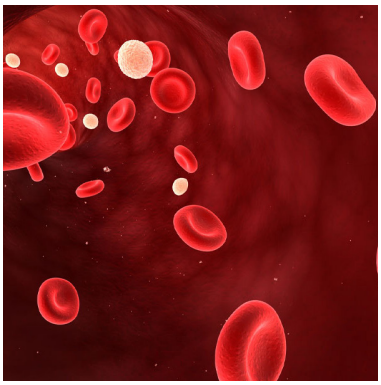
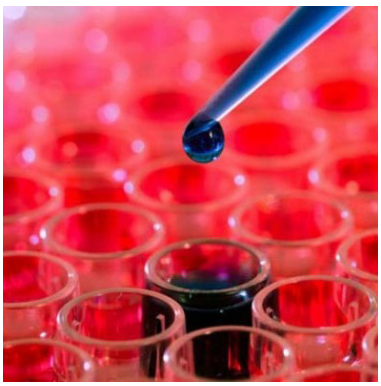
Keynote Forum
August 23, 2018

Hematology 2018

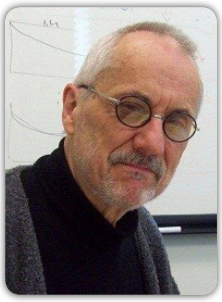



2nd International Conference on

Hematology and Oncology

August 23-24 | London, UK



H Joachim Deeg

University of Washington, USA

Hematopoietic cell transplantation for myelodysplastic syndrome and myeloproliferative neoplasms: issues of age, ethics, and uncertainty

Currently hematopoietic cell transplantation (HCT) is the only therapeutic modality with proven curative potential for patients with myelodysplastic syndrome (MDS) or myeloproliferative neoplasms (MPN). However, HCT is associated with certain, potentially fatal complications, such as graft versus host disease (GVHD). As these disorders occur primarily in older individuals who often present with comorbid conditions, a central question is whether non-transplant therapies might be preferable in regards both quality and quantity of life. This question is enhanced by the recent progress in our understanding of the genetics and pathophysiology of the hematopoietic system, and the development of a rapidly broadening spectrum of novel therapeutic agents, which offer a new outlook to many patients who previously had limited treatment options. Further, the life expectancy of patients with MDS or MPN varies greatly, from a few months to a decade or more, and it may not be appropriate aggressive therapy up-front. Retrospective analyses of date in MDS as well as in MPN have shown that patients with "low risk "disease may not benefit from HCT, and comparison of hypomethylating therapy and HCT in patients with MDS have shown that even in higher risk patients the benefit of HCT may not become apparent for two years or more Therefore, particularly in older individuals, a central question may be whether non-transplant therapies might be preferable regarding the quality and quantity of life. From a different perspective, many of modern non-transplant therapeutics come at an exorbitant cost, and, dependent upon the indication, prolongation of life may only be on the order of months, and, furthermore, the gain in comparison to results with more conventional and less costly drugs may only be incremental. Therefore, important aspects to be addressed by any physician treating these patients are the patients' own priorities including their resources, considering the frequently considerable out-of-pocket expenses, even for patients who do have insurance coverage. The discussions also need to include deliberation of the optimum timing of HCT if it is considered, If HCT is considered in very high-risk patients or in patients who have failed other therapies, the success rate is considerably lower than among good risk patients or patients transplanted early in the disease course. This raises questions as to the cost/benefit ratio and the role of the physician as a financial steward of health resource utilization. Of course, some might argue that in view of the cost of modern anti-cancer drugs, HCT may look like a good deal. Thus, modern treatment of hematologic malignancies is presenting us with enormous challenges in regard the uncertainty of success, the cost to the patient and to society, even though little gain might be expected. These discussions need to involve not only the medical community but our society at large.

Speaker Biography

H Joachim Deeg completed his MD in Wilhelms Universitaet, Germany. Presently he is working as a Professor of medicine in the University of Washington. He is also a member of the Fred Hutchinson Cancer Research Center. He is also a visiting professor at Carl Carus University, Dresden, Germany. His research interests are Pathophysiology, genetics and epigenetics of MDS (role of transcription factors in regulation) Inflammatory responses and GVHD (effects of alpha1 anti-trypsin [AAT]), Separation of GVHD and GVL effects by AAT, Iron and allogeneic responses.

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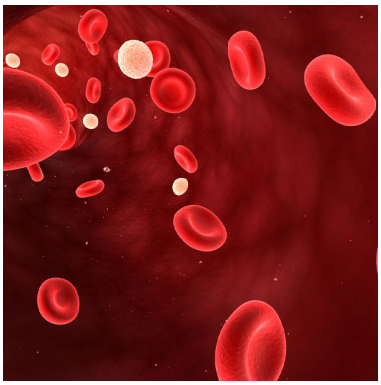


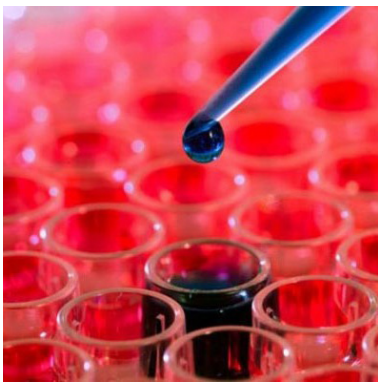


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Jan Michiels

Good Heart Centre, The Netherlands

Evaluation of classical and novel von Willebrand Factor assays in ECLM defined von Willebrand disease patients

A complete set of von Willebrand factor (VWF) assays is used for the diagnosis and classification of von Willebrand disease (VWD) according to European Clinical Laboratory and Molecular (ECLM) criteria (Clinical Applied Thrombosis/Hemostasis 2017;23(6):518). The aim is to evaluated the von Willebrand factor (VWF) assays VWF:GPIbM and VWF:GPIbR in von Willebrand disease (VWD) against the use of ECLM criteria as the gold standard for VWD classification anno 2018. Methods. The complete set of VWF assays include Platelet Function Analyser closure time (PFA-CT) von Willebrand factor (VWF) antigen (Ag), ristocetine cofactor activity (RCo), collagen binding (CB), propeptide (pp), ristocetine induced platelet aggregation (RIPA), the rapid VWF activity assay VWF:GPIbM based on glycoprotein Ib (GPIb) binding to particles coated with G233V and M239V mutants in the absence of ristocetin, the rapid VWF:GPIbR assay in the presence of ristocetine, and the responses to DDAVP of FVIII:C and VWF parameters to pick up secretion and/or clearance defects of VWF.It resulted in VWF:RCo/Ag, VWF:GPIbM/Ag and VWF:GPIbR ratios are completely normal (above 0.7) in all variants of VWD type 1 and Low VWF. The VWF:RCo/Ag, GPIbR/Ag and GPIbM/Ag ratios vary around the cut off level of 0.70 in VWD due to multimerization defect in the D3 domain and therefore diagnosed as either type 1 E or type 2E. The VWF:GPIbM/Ag and VWF:GPIbR/Ag ratios are pronounced decreased as compared to VWF:RCo/Ag and VWF:CB/Ag ratios in dominant VWD 2A and VWD 2B due to proteolytic loss of large and intermediate VWF multimers caused by VWF mutations in the A2 and A1 domain. VWD 2M due to loss of function mutation in the A3 domain is featured by decreased VWF:Rco/Ag ratio and normal VWF:CB/Ag ratio, whereas the VWF:GPIbR/Ag ratio (range 0.14-28) and the VWF:GPIbM/Ag ratio (range 0.32 to 0.36) were decreased indicating the need to retain the VWF:CB assay to make a correct diagnosis of VWD 2M. The introduction of the rapid VWF:GPIbM or VWF:GPIbR assays as compared to the classical VWF:RCo assay did change VWD type 2 into type 1 in about 10 to 12%. VWD type 1 due to a heterozygous mutation in the D1 domain is featured by persistence of proVWF as the cause of VWF secretion/multimerization and FVIII binding defect mimicking VWD type 3 together with decreased values for VWFpp, VWFpp/Ag ratios. The majority of 22 different missense mutations in the D3 domain are of type 1 or 2 E multimerization defect usually associated with an additional secretion defect (increased FVIII:C/VWF:Ag ratio) and or clearance defect (increased VWFpp/Ag ratio). The majority of VWF mutations in the D4 and C1 to C6 are VWD type 1 SD with smeary (1sm) or normal (1m) multimers with no or a minor clearance defect. The heterozygous S2179F mutation in the D4 domain is featured by VWD type 1 secretion and clearance (SCD). Thus it is concluded that a complete set of sensitive FVIII:C and VWF assays related to domain location of the molecular defect is mandatory for correct diagnosis and classification of VWD.

Speaker Biography

Jan Michiels Professor of Nature Medicine & Health Blood Coagulation & Vascular Medicine Center in Netherlands. He also serves as an Editorial board member for many scientific journals.

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