

■ Regulation on clinical trials - Comments and points of interest for academic researchers

Last July, the European Commission prepared a proposal for a regulation on clinical trials for the European Parliament, which will ensure that the new rules, once finalized and adopted, will have an immediate and binding impact across the EU avoiding the fragmentation and vagaries of interpretation that have plagued Directive 2001/20/EC. Furthermore, the European Commission has apparently identified many of shortcomings of the current directive and suggested a number of reasonable approaches for international trials. Nevertheless, there are other very **alarming suggestions** in the rapports from different Committees of the European Parliament which are summarized in the following:

- ✘ Suggestion to upload complete clinical trial information including all CRF information into a publicly accessible data base
- ✘ Suggestion to store trial master files at sponsor sites and participating sites for an indefinite time period
- ✘ Suggestion that only trials registered in a WHO trial registry can even be cited in a trial application
- ✘ Deletion of the definition and alleviations for low-intervention trials

Please use your connections to politically support the interests of investigator initiated trials in the new EU legislation!

For further information, please visit ► [International Trials on the ELN homepage](#).

■ 9th Information Letter online

Thanks to the contributing authors, we can present the 9th Information Letter of the European LeukemiaNet. For the first time, this issue contains summaries of the most important clinical results from oral presentations of the 54th ASH Annual Meeting which were selected and summarized by ELN experts. ► [Information Letter online](#)

■ New participating centers in the ELN

With the enclosure of the five new participating centers - Bornova-Izmir (Turkey), Pilsen (Czech Republic), Beirut (Lebanon), Wroclaw (Poland), and Ankara (Turkey) - the ELN now involves 194 centers in 39 countries. Please have a look at the updated ELN map to see who's at it. ► [ELN participating centers](#)

■ ELN WP10 'Diagnostics' Meeting

From March 15-16, the WP10 'Diagnostics' Meeting takes place in Munich, Germany. The meeting, which is organized and hosted by Marie Christine Béné, Gina Zini, and Torsten Haferlach, respectively, covers aspects of morphology and immunophenotyping. ► [further information](#)

■ Publications from the Network (selected)

Acute lymphoblastic leukemia

- ▶ Giles FJ et al. MK-0457, an Aurora kinase and BCR-ABL inhibitor, is active in patients with BCR-ABL T315I leukemia. *Leukemia*. 2013 Jan;27(1):113-7.
- ▶ Peyrouze P et al. Genetic polymorphisms in ARID5B, CEBPE, IKZF1 and CDKN2A in relation with risk of acute lymphoblastic leukaemia in adults: a Group for Research on Adult Acute Lymphoblastic Leukaemia (GRAALL) study. *Br J Haematol*. 2012 Dec;159(5):599-602.

- ▶ Ribera JM. Optimal approach to treatment of patients with Philadelphia chromosome-positive acute lymphoblastic leukemia: how to best use all the available tools. *Leuk Lymphoma*. 2013 Jan;54(1):21-7.
- ▶ Tanguy-Schmidt A et al. Long-term follow-up of the imatinib GRAAPH-2003 study in newly diagnosed patients with de novo Philadelphia chromosome-positive acute lymphoblastic leukemia: a GRAALL study. *Biol Blood Marrow Transplant*. 2013 Jan;19(1):150-5.
- ▶ Topp MS, Gökbuğet N et al. Long-term follow-up of hematologic relapse-free survival in a phase 2 study of blinatumomab in patients with MRD in B-lineage ALL. *Blood*. 2012 Dec 20;120(26):5185-7.
- ▶ Bassan R. Toward victory in adult ALL: blinatumomab joins in. *Blood*. 2012 Dec 20;120(26):5094-5.

Acute myeloid leukemia

- ▶ Baron F et al. Impact of graft-versus-host disease after reduced-intensity conditioning allogeneic stem cell transplantation for acute myeloid leukemia: a report from the Acute Leukemia Working Party of the European group for blood and marrow transplantation. *Leukemia*. 2012 Dec;26(12):2462-8.
- ▶ Christopheit M et al. Evaluation of BM cytomorphology after allo-SCT in patients with AML. *Bone Marrow Transplant*. 2012 Dec;47(12):1538-44.
- ▶ Gardin C et al. Superior long-term outcome with idarubicin compared with high-dose daunorubicin in patients with acute myeloid leukemia age 50 years and older. *J Clin Oncol*. 2013 Jan 20;31(3):321-7.
- ▶ Greif PA et al. RUNX1 mutations in cytogenetically normal acute myeloid leukemia are associated with a poor prognosis and up-regulation of lymphoid genes. *Haematologica*. 2012 Dec;97(12):1909-15.
- ▶ Grimwade D. The changing paradigm of prognostic factors in acute myeloid leukaemia. *Best Pract Res Clin Haematol*. 2012 Dec;25(4):419-25.
- ▶ Gröschel S et al. Deregulated expression of EVI1 defines a poor prognostic subset of MLL-rearranged acute myeloid leukemias: a study of the German-Austrian Acute Myeloid Leukemia Study Group and the Dutch-Belgian-Swiss HOVON/SAKK Cooperative Group. *J Clin Oncol*. 2013 Jan 1;31(1):95-103.
- ▶ Guièze R et al. Role of autologous hematopoietic stem cell transplantation according to the NPM1/FLT3-ITD molecular status for cytogenetically normal AML patients: a GOELAMS study. *Am J Hematol*. 2012 Dec;87(12):1052-6.
- ▶ Heidel FH et al. The cell fate determinant Llg1 influences HSC fitness and prognosis in AML. *J Exp Med*. 2013 Jan 14;210(1):15-22.
- ▶ Lengfelder E et al. Outcome of elderly patients with acute promyelocytic leukemia: results of the German Acute Myeloid Leukemia Cooperative Group. *Ann Hematol*. 2013 Jan;92(1):41-52.
- ▶ Lichtenegger FS et al. Current strategies in immunotherapy for acute myeloid leukemia. *Immunotherapy*. 2013 Jan;5(1):63-78.
- ▶ Mrózek K et al. Prognostic significance of the European LeukemiaNet standardized system for reporting cytogenetic and molecular alterations in adults with acute myeloid leukemia. *J Clin Oncol*. 2012 Dec 20;30(36):4515-23.
- ▶ Ossenkoppele GJ et al. Addition of bevacizumab to chemotherapy in acute myeloid leukemia at older age: a randomized phase 2 trial of the Dutch-Belgian Cooperative Trial Group for Hemato-Oncology (HOVON) and the Swiss Group for Clinical Cancer Research (SAKK). *Blood*. 2012 Dec 6;120(24):4706-11.
- ▶ Paschka P et al. Secondary genetic lesions in acute myeloid leukemia with inv(16) or t(16;16): a study of the German-Austrian AML Study Group (AMLSG). *Blood*. 2013 Jan 3;121(1):170-7.
- ▶ Schnittger S et al. ASXL1 exon 12 mutations are frequent in AML with intermediate risk karyotype and are independently associated with an adverse outcome. *Leukemia*. 2013 Jan;27(1):82-91.
- ▶ Schoofs T et al. DNA methylation changes are a late event in acute promyelocytic leukemia and coincide with loss of transcription factor binding. *Blood*. 2013 Jan 3;121(1):178-87.
- ▶ Sun SM et al. The prognostic relevance of miR-212 expression with survival in cytogenetically and molecularly heterogeneous AML. *Leukemia*. 2013 Jan;27(1):100-6.

Chronic myeloid leukemia

- ▶ Aduwa E et al. Significant weight gain in patients with chronic myeloid leukemia after imatinib therapy.

Blood. 2012 Dec 13;120(25):5087-8.

- ▶ Branford S et al. Initial molecular response at 3 months may predict both response and event-free survival at 24 months in imatinib-resistant or -intolerant patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase treated with nilotinib. *J Clin Oncol*. 2012 Dec 10;30(35):4323-9.
- ▶ Giles FJ et al. MK-0457, an Aurora kinase and BCR-ABL inhibitor, is active in patients with BCR-ABL T3151 leukemia. *Leukemia*. 2013 Jan;27(1):113-7.
- ▶ Giles FJ et al. Nilotinib in imatinib-resistant or imatinib-intolerant patients with chronic myeloid leukemia in chronic phase: 48-month follow-up results of a phase II study. *Leukemia*. 2013 Jan;27(1):107-12.
- ▶ Horn M et al. Model-based decision rules reduce the risk of molecular relapse after cessation of tyrosine kinase inhibitor therapy in chronic myeloid leukemia. *Blood*. 2013 Jan 10;121(2):378-84.
- ▶ Piazza R et al. Recurrent SETBP1 mutations in atypical chronic myeloid leukemia. *Nat Genet*. 2013 Jan;45(1):18-24.
- ▶ Rousselot P et al. Long-term safety and efficacy of imatinib mesylate (Gleevec®) in elderly patients with chronic phase chronic myelogenous leukemia: results of the AFR04 study. *Am J Hematol*. 2013 Jan;88(1):1-4.

Chronic lymphoblastic leukemia

- ▶ Edelmann J et al. High-resolution genomic profiling of chronic lymphocytic leukemia reveals new recurrent genomic alterations. *Blood*. 2012 Dec 6;120(24):4783-94.
- ▶ Elter T et al. Fludarabine and cyclophosphamide in combination with alemtuzumab in patients with primary high-risk, relapsed or refractory chronic lymphocytic leukemia. *Leukemia*. 2012 Dec;26(12):2549-52.
- ▶ Lutzny G et al. Protein Kinase C- β -Dependent Activation of NF- κ B in Stromal Cells Is Indispensable for the Survival of Chronic Lymphocytic Leukemia B Cells In Vivo. *Cancer Cell*. 2013 Jan 14;23(1):77-92.
- ▶ Rawstron AC et al. Improving efficiency and sensitivity: European Research Initiative in CLL (ERIC) update on the international harmonised approach for flow cytometric residual disease monitoring in CLL. *Leukemia*. 2013 Jan;27(1):142-9.
- ▶ Reinart N et al. Delayed development of chronic lymphocytic leukemia in the absence of macrophage migration inhibitory factor. *Blood*. 2013 Jan 31;121(5):812-21.
- ▶ Schweighofer CD et al. Clinical safety and pharmacological profile of the HLA-DR antibody 1D09C3 in patients with B cell chronic lymphocytic leukemia and lymphoma: results from a phase I study. *Cancer Immunol Immunother*. 2012 Dec;61(12):2367-73.

Chronic myeloproliferative diseases

- ▶ Barbui T et al. Development and validation of an International Prognostic Score of thrombosis in World Health Organization-essential thrombocythemia (IPSET-thrombosis). *Blood*. 2012 Dec 20;120(26):5128-33.
- ▶ Bench AJ et al. Molecular diagnosis of the myeloproliferative neoplasms: UK guidelines for the detection of JAK2 V617F and other relevant mutations. *Br J Haematol*. 2013 Jan;160(1):25-34.
- ▶ Kiladjian JJ et al. Efficacy and Safety of Cytoreductive Therapies in Patients with Essential Thrombocythaemia Aged >80 Years: An Interim Analysis of the EXELS Study. *Clin Drug Investig*. 2013 Jan;33(1):55-63.
- ▶ Marchioli R et al. Cardiovascular events and intensity of treatment in polycythemia vera. *N Engl J Med*. 2013 Jan 3;368(1):22-33.
- ▶ Rosti V et al. Spleen endothelial cells from patients with myelofibrosis harbor the JAK2V617F mutation. *Blood*. 2013 Jan 10;121(2):360-8.

Myelodysplastic syndromes

- ▶ Haferlach T. Molecular genetics in myelodysplastic syndromes. *Leuk Res*. 2012 Dec;36(12):1459-62.
- ▶ Nolte F et al. Results from a 1-year, open-label, single arm, multi-center trial evaluating the efficacy and safety of oral Deferasirox in patients diagnosed with low and int-1 risk myelodysplastic syndrome (MDS)

and transfusion-dependent iron overload. *Ann Hematol.* 2013 Jan;92(2):191-8.

Diagnosics

- ▶ Schnittger S et al. Use of CBL exon 8 and 9 mutations in diagnosis of myeloproliferative neoplasms and myelodysplastic/myeloproliferative disorders: an analysis of 636 cases. *Haematologica.* 2012 Dec;97(12):1890-4.
- ▶ Faber K et al. CDX2-driven leukemogenesis involves KLF4 repression and deregulated PPAR γ signaling. *J Clin Invest.* 2013 Jan 2;123(1):299-314.

Stem cell transplantation

- ▶ Blanes M et al. Intravenous busulfan and melphalan as a conditioning regimen for autologous stem cell transplantation in patients with newly diagnosed multiple myeloma: a matched comparison to a melphalan-only approach. *Biol Blood Marrow Transplant.* 2013 Jan;19(1):69-74.
- ▶ Egli A et al. Human metapneumovirus infection after allogeneic hematopoietic stem cell transplantation. *Infection.* 2012 Dec;40(6):677-84.

Supportive Care

- ▶ Hirsch HH et al. Fourth European Conference on Infections in Leukaemia (ECIL-4): guidelines for diagnosis and treatment of human respiratory syncytial virus, parainfluenza virus, metapneumovirus, rhinovirus, and coronavirus. *Clin Infect Dis.* 2013 Jan;56(2):258-66.
- ▶ Matthes-Martin S et al. European guidelines for diagnosis and treatment of adenovirus infection in leukemia and stem cell transplantation: summary of ECIL-4 (2011). *Transpl Infect Dis.* 2012 Dec;14(6):555-63.

Registries

Hansson MG et al. Medical registries represent vital patient interests and should not be dismantled by stricter regulation. *Cancer Epidemiol.* 2012 Dec;36(6):575-8.

■ New trials in the ELTR

ARCADE A Multicenter, Randomised, Double-blind, Placebo-controlled Study of Darbepoetin Alfa for the Treatment of Anaemic Subjects With Low or Intermediate-1 Risk Myelodysplastic Syndrome (MDS)