Advancing a Field by Building Consortia: The Example of the European LeukemiaNet

Building consortia sounds straightforward and simple because the advantage of consortia for advancement, particularly of rare diseases, appears obvious: achieving goals faster by combining forces and resources. The insight of the individual scientist that cooperation is better than competition for one’s personal career is not so obvious. If one wants to include younger colleagues competing for grants and promotions, it is essential that they realize that consortia not only advance the field but also their careers. A good starting experience for younger colleagues may be participation in clinical study groups of a defined scope. Consortia require interaction between individuals. Even if the reason for the interaction is clear, consortia need individuals (eg, in the case of leukemia, hematologists, medical oncologists, and scientists such as cytogeneticists, molecular biologists, or statisticians) who are motivated to interact.

The strongest motivation for cooperation is success. Consortia need to be structured for the greatest amount of success to the largest possible number of patients to have the optimum impact on the field. Working together successfully requires an atmosphere of cooperation and mutual trust. Regular meetings at little or no cost to the participants are essential to get to know and trust each other and achieve the best possible outcome.

This does not happen by chance at big international conferences such as the American Society of Hematology, European Hematology Association, American Association for Cancer Research, and American Society of Clinical Oncology but rather requires organization and structuring by an established authority or institution of excellence with personal contacts to leading hematologists and scientists. Networks of excellence such as the European LeukemiaNet (ELN) have been proven to serve this purpose well.

Founded in 2002, the ELN originates from a consortium dealing with 1 leukemia in the majority of European countries, the European Investigators on Chronic Myeloid Leukemia (El-CML), and a consortium dealing with all leukemias in 1 country, the German Competence Network for Acute and Chronic Leukemias. Its goal is to cure leukemia through cooperative research. To achieve this goal, the need to accelerate progress by combining resources (patients) was recognized, as well as the need for a “common language” for cooperation (ie, common definitions of diagnosis and outcomes and common standards and data sets [eg, for conducting clinical trials or monitoring treatment]).

For this purpose, leading European hematologists and scientists created the ELN and made use of a call of the European Union within the 6th Framework Program to compete for a network of excellence. The ELN ranked among the top 5% and was awarded funding from 2004 onward. For sustainability, an ELN foundation was established in 2009 and support was solicited from the European Science Foundation from 2010 through 2015. An initial report on the ELN was published in 2011.

To actively include as many participants as possible, working groups (called work packages [WPs]) were established for each major leukemia and related syndrome (ie, CML, acute myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, myelodysplastic syndrome [MDS], and myeloproliferative neoplasms) for each interdisciplinary specialty required for the diagnosis and treatment of leukemia.

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management of all leukemias such as morphology, flow cytometry, cytogenetics, molecular monitoring, gene sequencing, etc, and for several central service areas such as transplantation, biometry of clinical trials, and leukemia information and network management centers.

All WPs are subnetworks of their own, comprising the leading national study groups of the respective leukemias or specialties. Clinical study groups and interdisciplinary partner groups include junior as well as senior investigators. Having a common goal and network structure favors personal input and leadership by excellence.

Each WP is chaired by one or more lead participants who oversee the cooperative research within the WP and participate in the ELN Steering Committee. The ELN itself is chaired by the network coordinator. It may have been helpful in forming the ELN that at the start the coordinator already was at an age and position that excluded competition for his own career. Figure 1 provides an overview of the ELN networking structure. Figure 2 provides a map of the 220 currently participating centers in 44 countries, 3 of which are in the United States.

Key elements of networking are management recommendations at the highest international level. The bases of the recommendations usually are comprehensive reviews of the literature and expert panels selected by the ELN for excellence. This is different from other organizations such as the National Comprehensive Cancer Network. In addition, the term “recommendation” is preferred over “guidelines” in the absence of sufficient randomized evidence. The panels include experts who also are from outside Europe to guarantee high-level expertise and international acceptance. With the increasing number of participants from the Americas and Asia, the ELN has evolved from a European to an international network. Some of the more recent ELN recommendations are listed in Table 1.

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**Table 1**

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Figure 1. Overview of the European LeukemiaNet (ELN) networking structure. The left side shows a list of work packages (WPs) 1 to 15 and 17 (there is no WP 16). The pink insert indicates the cooperation between clinical groups, interdisciplinary basic science groups, and industry. The blue insert indicates the activities of central services (WP 1 and 3 to 17). In the case of industry, large spots indicate large companies and small spots indicate small companies. WP 1 lead participants: Hehlmann, Hochhaus, and Saussele; WP 2 lead participants: Hoelzer, Gokbuget, and Serve; WP 3 lead participant: Dugas; WP 4 lead participants: Baccarani, Guilhot, Hehlmann, Hochhaus, and Simonsson; WP 5 lead participants: Ossenkoppele, Bloomfield, Dochner, and Muller-Tidow; WP 6 lead participants: Hoelzer, Gokbuget, Dombret, Ribera, M. Sanz, Bassan, Willemze, and Foa; WP 7 lead participants: Ghia, Montserrat, and Hallek; WP 8 lead participants: De Witte, Fenaux, and Hellstrom-Lindberg; WP 9 lead participants: Barbu, Barosi, Pahl, and Kiladjian; WP 10 lead participants: Bene and Zini; WP 11 lead participants: Rieder, Haase, and C. Haferlach; WP 12 lead participants: Thiede, M.C. Muller, T. Haferlach, and Hernandez-Rivas; WP 13 lead participants: T. Haferlach and Martinelli; WP 14 lead participants: Niederwieser and Apperley; WP 15 lead participants: Ljungmann and Einsele; WP 17 lead participant: Hasford. ALL indicates acute lymphoblastic leukemia; AML, acute myeloid leukemia; CLL, chronic lymphocytic leukemia; CML, chronic myeloid leukemia; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasms; NGS, next-generation sequencing.
Cooperation with industry was an integral part of networking from the very beginning of the ELN. Visible projects are public-private partnerships (eg, the European Treatment and Outcome Study [EUTOS] for CML or the European MDS registry [EU-MDS]). To advance research on a disease that requires products from pharmaceutical companies, it is important that industry is included. By taking the lead in research and clinical trials, the consortium is in a position to ensure that marketing interests do not become a dominant factor of common research.

A second key element of networking is regular meetings of all participants. To maintain independence with regard to management recommendations and research goals, the meetings are funded publicly or by donations with no service provided in return. Representatives of industry are invited as guests and equal partners (not as sponsors). There have been no commercial exhibitions or satellite symposia permitted at ELN symposia. Public funding has enabled all participants to contribute to ELN research projects free of personal financial considerations.

The greatest efforts in time and resources are directed toward the research projects of the respective WPs (with help from the ELN, some ELN members have even won projects funded by the European Union). Some work has been practice-changing, such as the standardization of BCR-ABL polymerase chain reaction through the definition of conversion factors for interlaboratory comparability (International Scale), or the minimal residual disease-guided treatment of acute lymphoblastic leukemia.

The greatest visibility of the ELN is achieved by its management recommendations and, since 2003, its annual symposia. These 2 activities by far require the largest percentage of the ELN budget, whereas research projects as such are, as a rule, not financed by the ELN directly but are supported by ELN infrastructure and the annual symposium.

The key limitation of the ELN is its budget. The free-for-all symposium for 400 to 500 attendants each year, including housing and travel, may not be sustainable in the long term. Smaller and less costly solutions currently are being considered. An ELN Foundation Circle has been established to provide financial infrastructure support through donations. A task force of ELN lead participants currently is working out new strategies to adapt the ELN for the future.
Take-Away Points

- Building consortia represents an efficient and economical approach to advancing fields in urgent need of progress, such as currently incurable cancers.
- Participants of consortia have a competitive advantage over those not participating.
- The ELN has structured leukemia research internationally through the creation of standards, definitions, and high-level management recommendations and has contributed toward improved outcomes.
- Management recommendations providing definitions and standards have laid the groundwork for cooperative research by clinical study groups and interdisciplinary partner groups.
- The ELN provides an example of advancing a field with little budget and high impact.

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REFERENCES


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Rüdiger Hehlmann, Prof. Dr. med., Dr. hc, was chief of medicine at the Mannheim Medical Faculty of Heidelberg University in Mannheim, Germany, until 2007. In 1982, in cooperation with his colleagues, he founded the German CML [Chronic Myeloid Leukemia] Study Group. In addition, he founded the German Competence Network for Acute and Chronic Leukemias in 1997 and the European LeukemiaNet (ELN) in 2002. Dr. Hehlmann completed his last randomized CML study (CML Study IV) in 2017 and currently manages the ELN Foundation in support of ELN.