LEUKEMIA, LYMPHOMA, & MYELOMA PROGRESS REVIEW REPORT

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Leukemia, Lymphoma, and Myeloma: An Agenda for Action

Report of the Leukemia, Lymphoma, and Myeloma Progress Review Group

Presentation to the National Cancer Advisory Board
September 11, 2001

Charge to the PRG

Help NCI develop an agenda for research in leukemia, lymphoma, and myeloma by-

- Identifying and prioritizing research opportunities and needs to advance medical progress,
- Defining the scientific resources required,
- Comparing and contrasting the priorities with the current NCI research portfolio, and
- Preparing a written report that describes findings and recommendations.

Members of the PRG

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- Clara D. Bloomfield, M.D., Co-chair
- Riccardo Dalla-Favera, M.D., Co-chair
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The Call to Action

- Together, leukemia, lymphoma and myeloma (LLM) constitute the 4th most common form of cancer
- LLM represents a large number of diseases that vary in etiology, pathobiology, treatment and outcome.
- An estimated 60,000 Americans will die of these diseases in 2001.

The Call to Action

- For leukemia, the 5-year survival is only 46%;
  - And is 54% for non-Hodgkin's lymphoma and 28% for multiple myeloma.
  - In the U.S., leukemia and lymphoma are the leading cause of death from disease in children.

The Call to Action

- Death rates for non-Hodgkin's lymphoma and multiple myeloma are increasing.
  - The incidence of non-Hodgkin's lymphoma has increased dramatically, making it one of the fastest rising cancers in the U.S.
  - By comparison, death rates for many other cancers are dropping.

Creating the Agenda for Action

- The LLM Progress Review Group (PRG) was charged to identify and prioritize research areas that could advance progress against leukemia, lymphoma, and myeloma.
- In December 2000, the LLM PRG Roundtable was convened with 180 participants.
- In breakout groups, participants were instructed to identify top research priorities for the next 5-10 years.

Creating the Agenda for Action

Roundtable Breakout Group Topics

- Etiology and Pathobiology: bone marrow biology, lymphoid biology, diagnosis, scientific infrastructure, and epidemiology.
- Therapeutics: preclinical therapeutics, targeted therapeutics, clinical trials methodology, prognosis and disease monitoring, treatment, optimization and integration of emerging and conventional therapies, and partnership platforms.
- Education, Communication and Outcomes: education, communication, behavioral research, and outcomes research.

Creating the Agenda for Action

- Breakout groups were provided with an analysis of the NCI LLM research portfolio and ongoing initiatives.
- Reports from the breakout groups showed a high degree of agreement on many of the crucial needs.
- The PRG used the group reports to identify the highest research priorities, and included the descriptions and justifications for each.

The Agenda for Action

<u>Etiology</u>: Understand the interaction among genotype, immune function, infectious agents, environmental toxins and lifestyle factors that can lead to hematopoietic malignancy.

- **The etiology of LLM is poorly understood, and is required to develop behavioral and pharmacological interventions for prevention.**
- **PRG recommends case-control and cohort investigations that go well beyond a single or limited group of cancers.**

The Agenda for Action

<u>Pathobiology</u>: Identify the basic mechanisms responsible for genomic instability, chromosome translocations and other mutations in hematological malignancies.

Reducing the incidence of LLM requires an understanding of:

- **The causes and mechanisms of DNA damage in LLM,**
- **The role genetic factors on susceptibility to DNA damage,**
- **Repair capacity and other types of cellular responses to DNA damage, and**
- **The role of environment in the broadest sense.**

The Agenda for Action

<u>Pathobiology</u>: Define the relationship between the development of hematologic malignancies and the host biological environment.

- **The stromal microenvironment and the overall host environment are important determinants of tumor initiation, progression, migration, and response to therapy.**
- **These complex phenomena can now be studied with new research tools, which are already providing new insights into the biology of normal and malignant cells.**

The Agenda for Action

<u>Pathobiology</u>: Provide molecular characterization of hematological malignancies, including the global patterns of genetic and epigenetic alterations and RNA and protein expression, as well as the identification of molecular targets necessary for their survival, proliferation, and evolution.

- **Development of a molecular definition of cancer will dramatically improve diagnosis and treatment specificity.**
- **The PRG recommends expansion of several NCI initiatives to promote the application of novel technologies to hematological malignancies, including common and less prevalent subtypes.**

The Agenda for Action

<u>Pathobiology</u>: Further develop research on stem cells, including those from both normal and malignant lineages.

- **Understanding the biology of normal blood cell precursors will provide critical insights into their malignant counterparts.**
- **Presently, it is still not possible to anticipate how specific molecular changes produce disease.**
- **Such information is essential to designing therapies that are curative and nontoxic.**

The Agenda for Action

<u>Drug Development and Therapeutics</u>: Develop the resources to translate "lead" structures and molecules into effective therapeutic agents. Hasten the translation of candidate validated targets to lead compounds and clinical testing, the development of orphan drugs, and rapid FDA approval.

- **The PRG recommends the NCI magnify its efforts to offset the cost of drug development for relatively rare cancers, including leukemia, lymphoma and myeloma.**

The Agenda for Action

<u>Drug Development and Therapeutics</u>: Foster partnerships between the NCI and academia, advocates, cooperative groups, FDA and industry to expedite drug development and availability of therapies.

- **The PRG recommends the NCI form a working group among these partners to enhance cooperation and efficiency.**

The Agenda for Action

Education, Communication, and Survivorship Research: Determine how to provide accurate, and timely information to patients to improve medical decision-making, access to clinical trials, quality of care, and quality of life.

- **Effective health communication improves patient understanding of their disease and treatment options and reduces health disparities among our citizens.**
- **Nevertheless, much of the available information for patients does not specifically address those affected by hematological malignancies.**

The Agenda for Action

<u>Education, Communication, and Survivorship Research</u>: Develop education and training programs for certification of physicians and centers for diagnosis, treatment, and clinical trials in hematological malignancies.

- **Certification will lead to significant improvement in the quality of treatment of hematological cancers.**
- **Patients would have access to specialized physicians and centers where state-of-the-art treatments may be investigated.**

The Agenda for Action

<u>Education, Communication, and Survivorship Research</u>: Identify and target individuals and populations at high risk for adverse long-term outcomes to identify the biological causes, and to facilitate design and testing of intervention and prevention strategies.

- **Patient groups at high risk of adverse treatment outcomes are not well understood.**
- **Outcome research in hematological malignancies is often hampered by small sample sizes, lack of necessary heterogeneity and potential bias in the study populations**

The Agenda for Action

A New Initiative – The Cancer Translational Research Allied Consortium (C-TRAC):

- **Will bring together experts across multiple disciplines and institutions to participate within a formalized infrastructure.**
- **Will encompass the whole spectrum of drug discovery and development: identifying, validating, and credentialing targets; discovery and preclinical testing of agents directed against these targets; and scale-up and testing of promising agents in clinical trials.**

The Agenda for Action

- **The ultimate goal of the C-TRAC will be to shorten drug development time from 5-10 years to 2 years through a novel alliance among academia, industry, government, and patients.**

The Next Steps

- **Meet with NCI Director and staff in two months to –**
  - **Determine the extent to which the PRG recommendations are being addressed or could be addressed by existing efforts,**
  - **Identify the recommendations that ongoing NCI initiatives and projects do not address.**
  - **Discuss strategies for implementing the unmet recommendations.**
- **Assist NCI in tracking progress over the next several years.**

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