2023 Strategic Priorities

Leukemia Steering Committee (LKSC)

Overall Portfolio

The LKSC recognizes the need to streamline clinical trials to facilitate participation by patients with leukemia from diverse populations and geographic areas. It is also recognized that the field can be advanced by utilizing precision medicine approaches, including targeted therapeutics and MRD guided treatment. Leveraging resources to incorporate integral assays for these purposes is critical; therefore, randomized biomarker-based studies are highly prioritized.

Acute Lymphoblastic Leukemia

- Standardization of MRD and development of various platforms to understand which performs best for a given use (e.g., prognosis, stratification, surrogate marker, etc.). The ultimate goal would be multiplex categorization: MRD + genetic abnormalities and the eventual development of up-front molecular screening to classify ALL subtypes.

- A high priority is to focus on the BCR-ABL-1 like phenotype. Identification would be through molecular screening at diagnosis, and patients would be allocated to matched therapy selections and/or allogeneic transplants.

- Optimizing the "backbone" therapy in Adult ALL remains important, so the strategic priority will be to combine age-appropriate backbone therapeutics with novel therapy, in particular immunotherapy:

    - Conjugated antibodies
    - Bi-Specific antibodies
    - CAR-T cell therapy

  The priority is not dependent on the actual immunotherapy bulleted above but rather to test whether the likelihood of a cure can be increased by incorporating them and to determine if it is possible to de-intensify backbone therapy consequent to novel therapy (such as immunotherapy) while maintaining or even improving the cure rate.

- An important question for Ph+ Adult ALL is the relative role of TKI therapy and conventional chemotherapy and whether allogeneic transplantation or other immunotherapeutics improve outcomes following induction to an MRD-negative status. The incorporation of immunotherapeutic approaches is a strategic priority for the portfolio.

The MyeloMATCH Precision Medicine Initiative is a strategic priority of the LKSC. The broad goal of myeloMATCH is to sequentially treat patients targeting increasingly lower remaining disease more effectively. Additional specific priorities for AML and MDS are as stated below.

Acute Myeloid Leukemia

- A critical strategic priority is to improve therapy for older patients with AML. This requires the development and validation of tools to identify patients unlikely to benefit from standard therapy and the development of clinical studies aimed at improving the outcome for this population.
- Validate gene expression and clinical assays for patient selection in clinical trials.
- Progress beyond the multitude of AML genotypic prognostic markers to predictive markers and incorporate them into clinical trials involving targeted therapies appropriate to the markers.
- Systematically prioritize for phase 3 testing based on big phase 2 signals emerging from myeloMATCH.
- Develop randomized phase II / phase III studies to evaluate the addition of novel agents to less intensive therapy in those unlikely to benefit from intensive therapy.

Myelodysplastic Syndrome

Incorporate the mutational spectrum and epigenetic findings of MDS biology into the clinical trial designs:

- Utilize novel agents biologically relevant to the disease based on the identified mutations (and pathways) and epigenetics
- Test whether these agents can augment the action of hypomethylating agents
- Adaptive clinical trial designs with multiple arms that can close early for futility or rapidly inform the subsequent phase III trial
- Include in the trial designs specific arms where there are predictive marker mutations and an available targeted agent specific to the MDS risk features to improve efficiency and more rapidly advance the field.
- Systematically prioritize for phase 3 testing based on big phase 2 signals emerging from myeloMATCH.

CLL

- CLL therapeutics are rapidly advancing. Protocols that investigate treatment strategies using novel biomarkers (e.g., MRD, immune profiling) to determine whether intermittent therapy can be employed without undermining outcomes or can enhance outcomes are a priority.
- BTk failure may comprise a substantial population of patients over time. The strategic plan will be to address therapeutics to prevent and treat ibrutinib resistance. Resistance to other novel therapies developed for CLL will also be important.

CML

The tremendous success of tyrosine kinase inhibitors has made the initiation of phase III trials for chronic phase CML rather difficult. Further discussions regarding potential large trials will be informed by the results of several smaller trials being carried on by pharmaceutical sponsors as well as institutions across the NCTN network groups. The next NCTN trials will revolve around the issue of TKI discontinuation, and the treatment of relapsed and progressive disease.

BMT CTN Collaboration

The 2021 BMT CTN State of the Science Symposium identified high priority areas. The investigation of MRD and genomic-driven maintenance therapies was identified as relevant to myeloMATCH, as the LKSC agrees with this priority. This continues the 2015 LKSC strategic priorities to prevent post-transplant relapse.