

CHRONIC LYMPHOCYTIC LEUKEMIA MOON SHOT

INTRODUCTION

Chronic lymphocytic leukemia (CLL) is a slow developing disease which occurs in lymphocytes, a type of white blood cell important to the immune system. Lymphocytes help the body fight infection and disease. When CLL occurs, the lymphocytes stop functioning properly. It's the most common form of adult leukemia in Europe and North America. In the United States, an estimated 16,000 new cases will be diagnosed this year and about 4,600 people will die of the disease.

- Chemotherapy combinations have greatly improved the cure rate for CLL over the last 25 years, with 10-year disease-free survival moving from zero to 35 percent of patients.
- Side effects remain harsh from cytotoxic chemotherapy. About 45 percent of all CLL deaths are associated with second cancers caused by therapy, including 33 percent of deaths during first remission.
- Development of targeted, biologic drugs in recent years has improved survival and the prospects for less harmful therapy.
- CLL has a strong association with age, ethnicity and family history. The disease progresses in well-characterized steps that include specific survival-related chromosomal and genetic abnormalities.

KEY PROJECTS

MD Anderson's CLL Moon Shot will accelerate gains in survival and develop new approaches to curing CLL. It starts with a critical mass of expertise and resources – the world's largest CLL program, a collaborative team that has led most major therapeutic advances for CLL over the past 25 years, global leadership in clinical trial development, a tissue bank with 1,700 annotated patient samples, a 7,900-patient research database and established genomics resources.

The Moon Shots Program adds access to important new research infrastructure. For example, the CLL Moon Shot will benefit from new platforms in genomics, targeted therapy, including immunology, and drug development.

Projects include:

- Shift treatment from existing combinations to targeted combination therapies and develop new drugs that will double 10-year disease-free survival rates. Have most patients on targeted combinations by the end of the first full year of moon shot operations. Focus on rebuilding patients' immune system and leaving it intact in the first place with new targeted, biologic therapies.

MOON SHOT GOALS

- Increase **10-year disease-free survival rates** from 35 to 75 percent.
- Dramatically **reduce mortality** during the first year of a patient's treatment to less than 2 percent.
- Develop effective therapies for patients with two genomic changes that cause the worst forms of CLL, **doubling survival**.

-more-

- Create a CLL Genomic Atlas to profile all coding and non-coding genes, correlate this data with clinical parameters and use it to build predictors of CLL progression.
- Identify and develop therapies for the most chemotherapy-resistant forms of CLL, which harbor specific genetic and chromosomal abnormalities.
- Explore therapeutic options with micro RNA (miRNA) approaches developed at MD Anderson to block protein synthesis by inhibiting messenger RNA.

THE AIM

The CLL Moon Shot will more efficiently apply existing technology and knowledge to improve survival in the near term while conducting break-through studies to understand and ultimately to cure this cancer.

THE CLL MOON SHOT TEAM

This moon shot gathers a diverse team of experts from across the institution and externally, including leaders in oncology, immunology, genomics, non-coding RNA, stem cell transplantation, pathology, basic science, translational research and drug development.

Moon shot leaders



Michael Keating, M.B., B.S., professor in MD Anderson's Department of Leukemia. Keating and co-leader Plunkett have led the multidisciplinary, collaborative group that has been central to the improvement of CLL therapy and patient survival for 25 years. The team developed the current standard of care for CLL, comprising two chemotherapies and an antibody-based drug. In addition to his work in CLL, Keating is developing rational combinations of new drugs for all leukemias.



William Plunkett, Ph.D., professor in MD Anderson's Department of Experimental Therapeutics. His research focuses on development of novel drugs based on knowledge of cellular responses to DNA damage and on understanding the mechanisms of drug action. Plunkett and co-leader Keating have led the multidisciplinary, collaborative group that has been central to the improvement of CLL therapy and patient survival for 25 years. The team developed the current standard of care for CLL.