


LLS: Blood Cancer Update

May 30, 2015

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fighting blood cancers

Jim Brewer, Executive Director

The Leukemia and Lymphoma Society

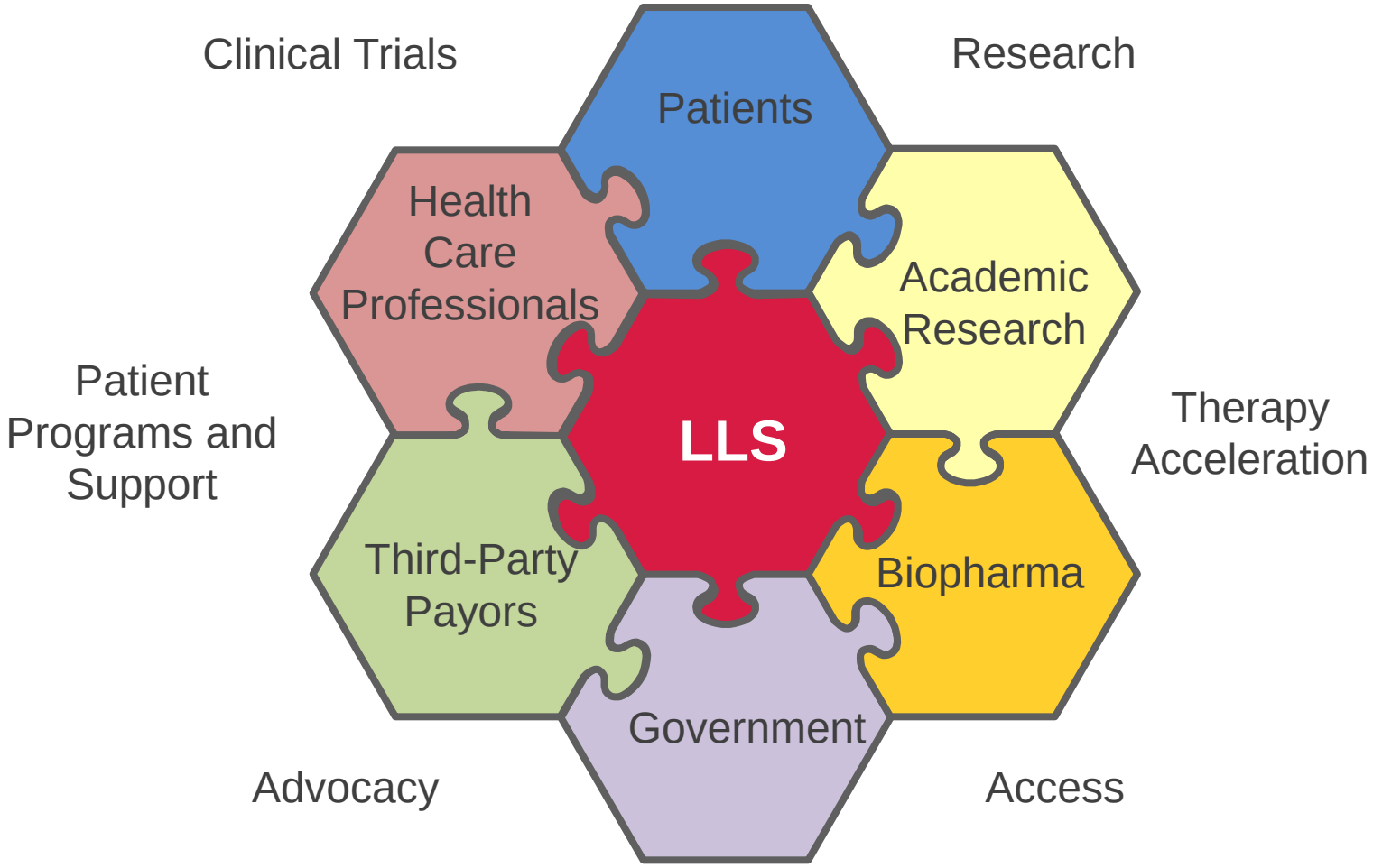
Arizona Chapter

someday is today

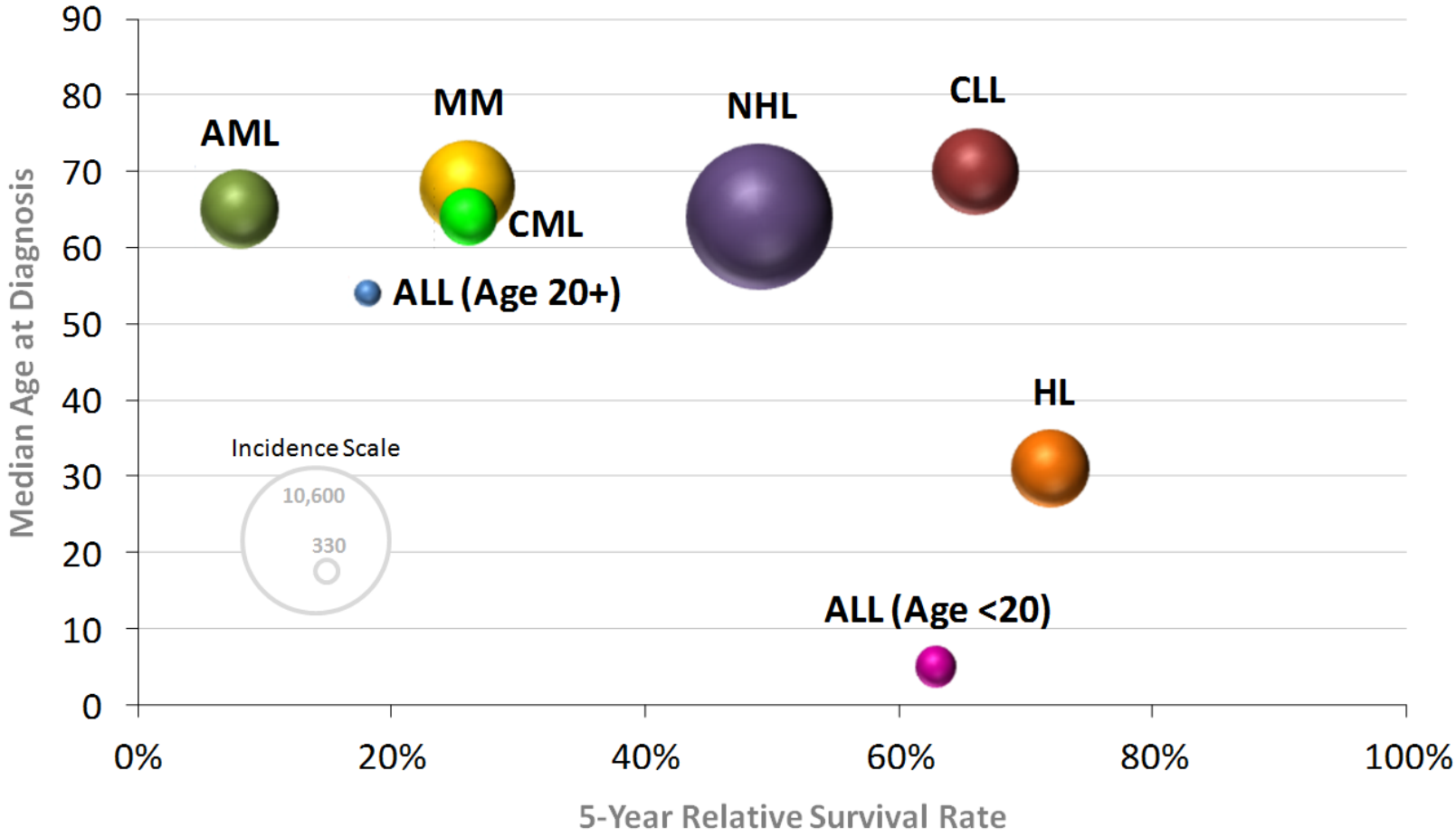
LEUKEMIA & LYMPHOMA SOCIETY®

fighting blood cancers

Aligning the Players in the Innovation Ecosystem

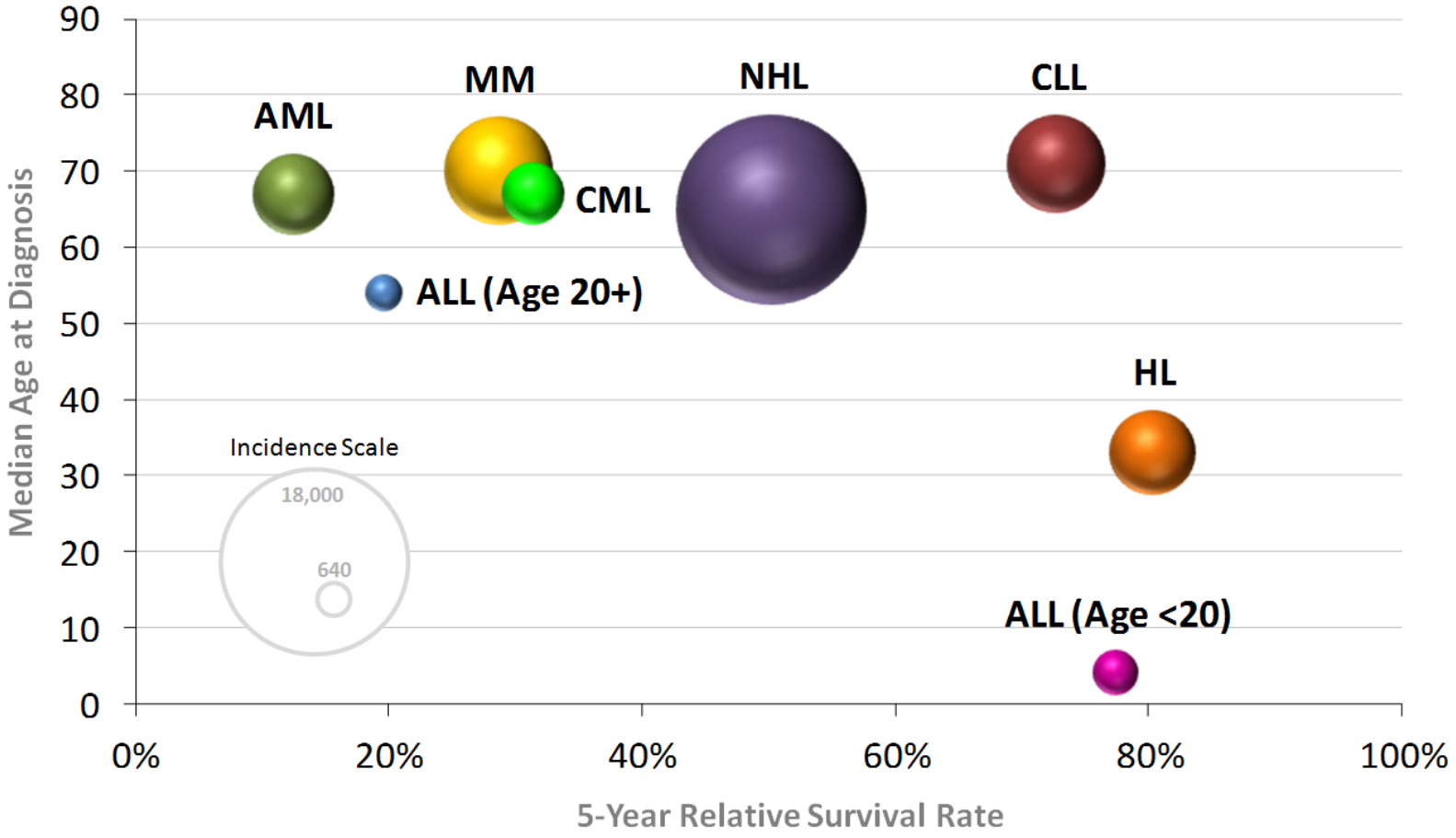


1976 - 1980



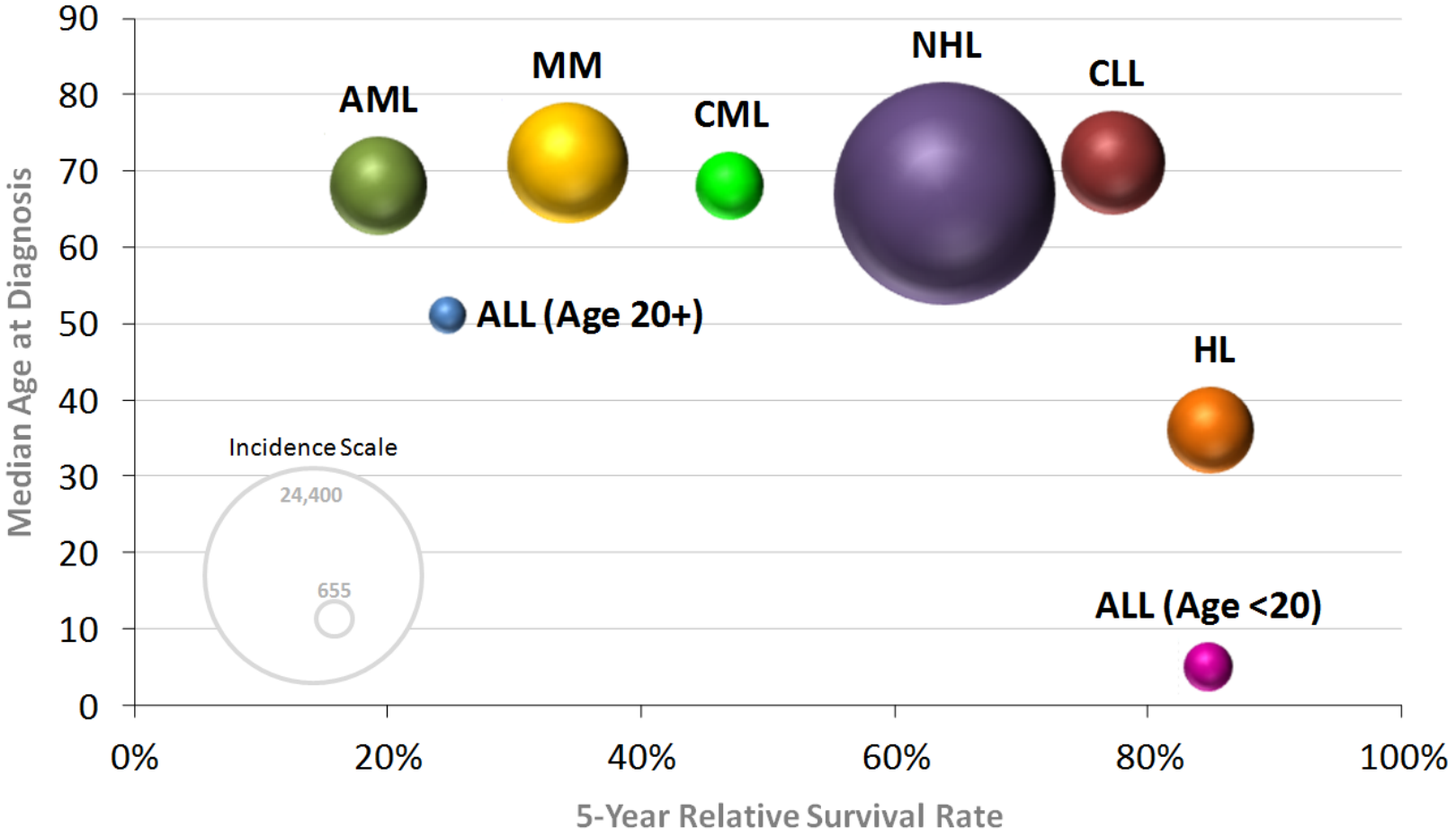
Source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta. Median age and incidence counts include cases diagnosed in 1976-1980. Relative survival rates include cases diagnosed in 1979-1981.

1986 - 1990



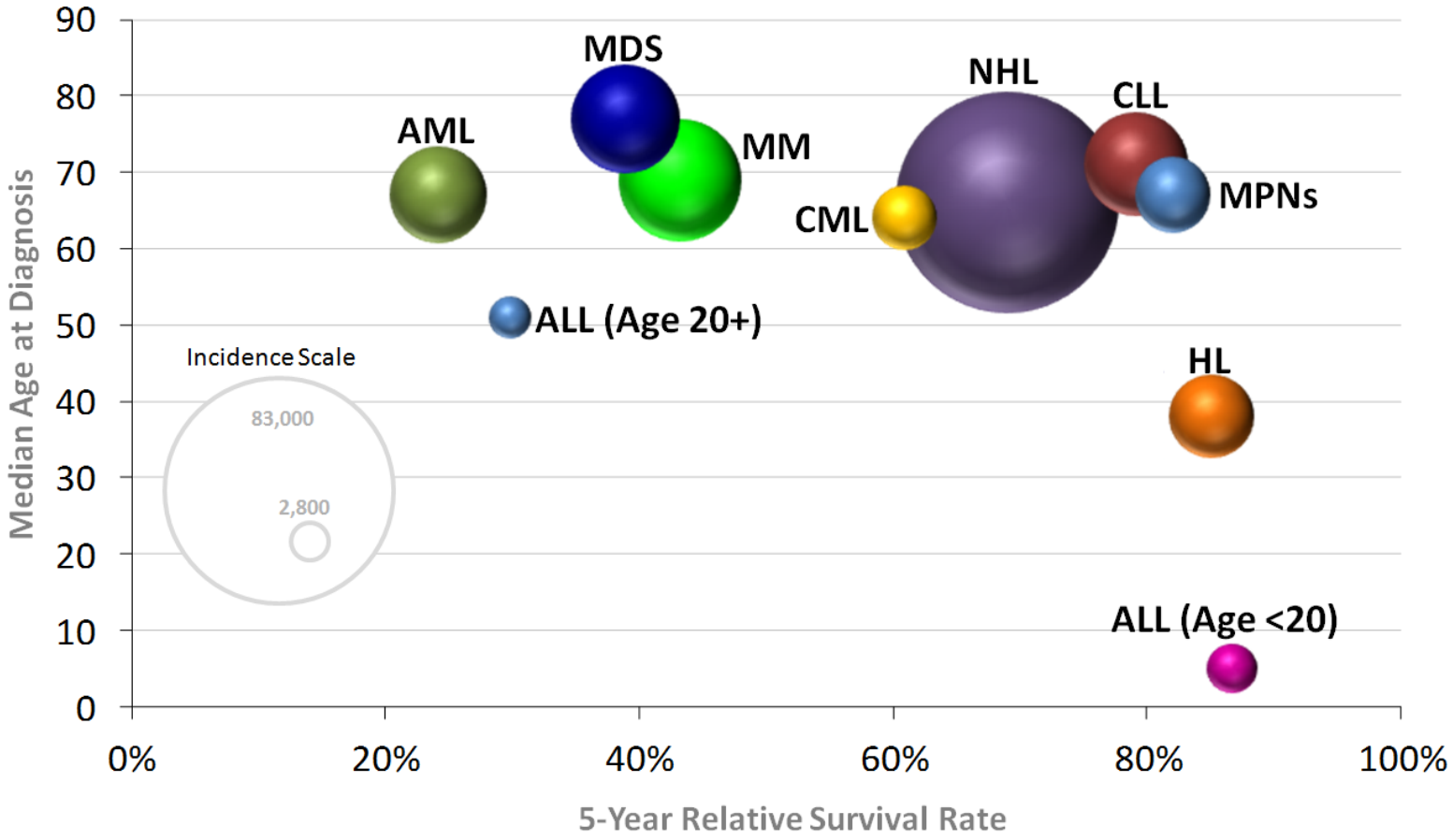
Source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta. Median age and incidence counts include cases diagnosed in 1986-1990. Relative survival rates include cases diagnosed in 1989-1991.

1996 - 2000



Source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta. Median age and incidence counts include cases diagnosed in 1996-2000. Relative survival rates include cases diagnosed in 1999-2001.

2006 - 2010



Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG). Median age and incidence counts include cases diagnosed in 2006-2010. Relative survival rates include cases diagnosed in 2003-2009.

Dr. Ian DeRoock
Ironwood Cancer and Research Center

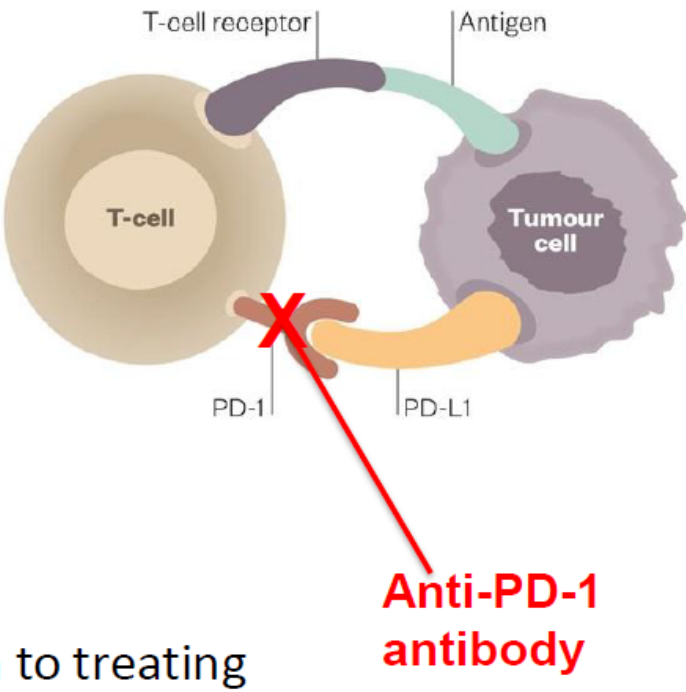
IMMUNE CHECKPOINT INHIBITORS

Disease: Hodgkin Lymphoma

Therapy: Immune checkpoint inhibitors

Findings:

- Two Phase I trials with distinct anti PD-1 antibodies
- Extraordinary response in patients with relapsed Hodgkin lymphoma (overall response rate = 50-87%)
- Well tolerated



Why it's important: This is a promising new approach to treating patients who have very poor prognosis

How did LLS help?

- LLS funded investigators who found very high expression of PD-1 in HL
- Multiple new grant awards in progress to expand utility to other lympyhomas

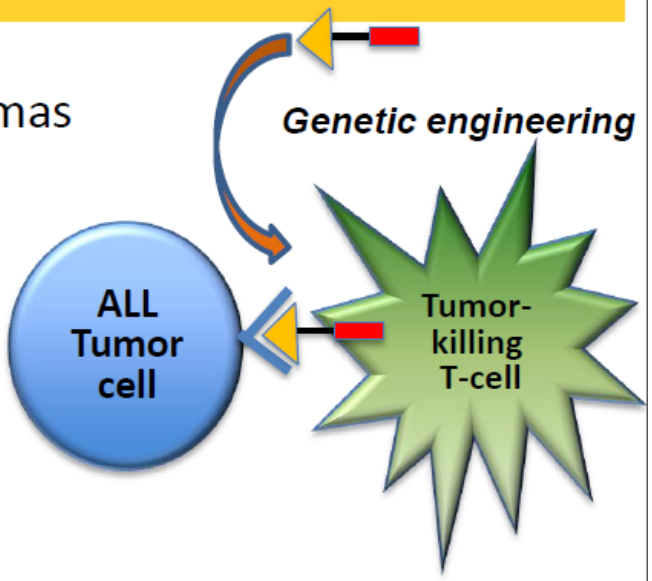
UPDATE ON CAR-T IMMUNOTHERAPY

Disease: Acute Lymphoblastic Leukemia (ALL) & lymphomas

Therapy: CAR-T Immunotherapy

Findings:

- Two phase I clinical trials; 90% response rate in ALL
- Long-term response rates in ALL (> 2 years)
- New data shows utility in patients with B-cell lymphomas



Why it's important? Groundbreaking approach to treating relapsed/refractory patients; durable responses for many of the patients.

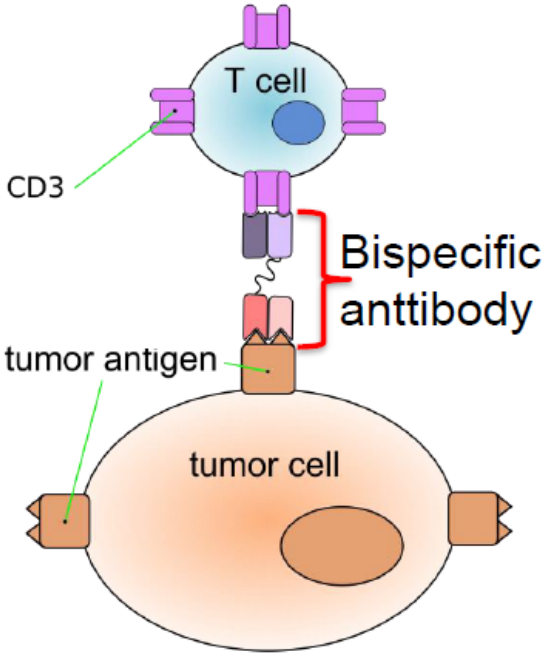
How did LLS help?

- LLS has funded a team at University of Pennsylvania and Children's Hospital of Philadelphia for nearly two decades with a commitment of $21 million
- Numerous on-going grants to expand utility and examine resistance

BLINATUMOMAB APPROVAL

Disease: Acute Lymphoblastic Leukemia (ALL)

Therapy: Blinatumomab: bispecific T-cell antigen



Findings:

- FDA approved on December 3, 2014 for Philadelphia chromosome-negative (PH-) relapsed or refractory B-cell precursor ALL
- Phase II clinical trial presented at ASH2014
- 43% complete response rate; 40% go on to transplant

Why it's important? New option for patients with poor prognosis. First approval for new type of antibody as therapeutic

How did LLS help? LLS did not fund the advance of blinatumomab, but this is a promising advance for patients we serve

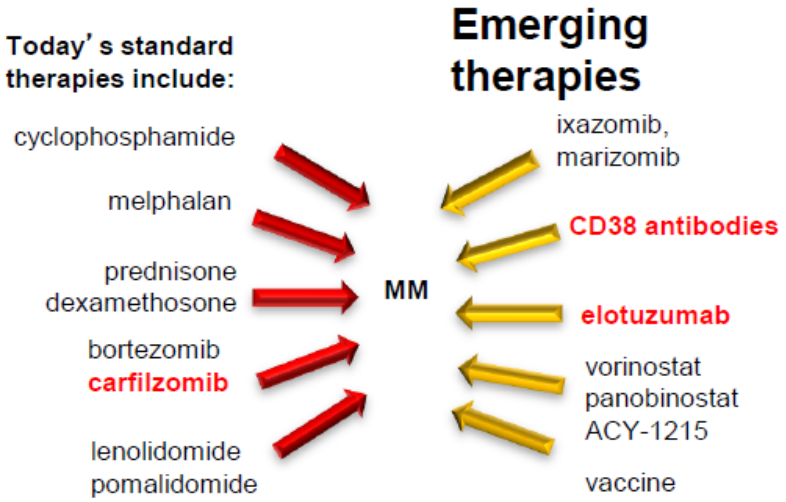
New Therapies Emerging for Myeloma

Disease: Multiple Myeloma (MM)

Therapy: Anti-CD38 antibody, carfilzomib

Findings:

- Encouraging single agent activity with anti-CD38 antibodies
- Phase II studies on-going with anti-CD38 Abs or elotuzuamb + standard therapies likely to increase survival times by multiple years
- Phase III: carfilzomib + standard therapy increase progression-free survival time (+9 mo) compared to standard therapy



Why is this important? New immunotherapy approach to treating myeloma patients has therapeutic effects; additional combinations possible

How did LLS help? LLS did not fund these advances but nicely complements our on going efforts with grants/TAP programs for other MM targets

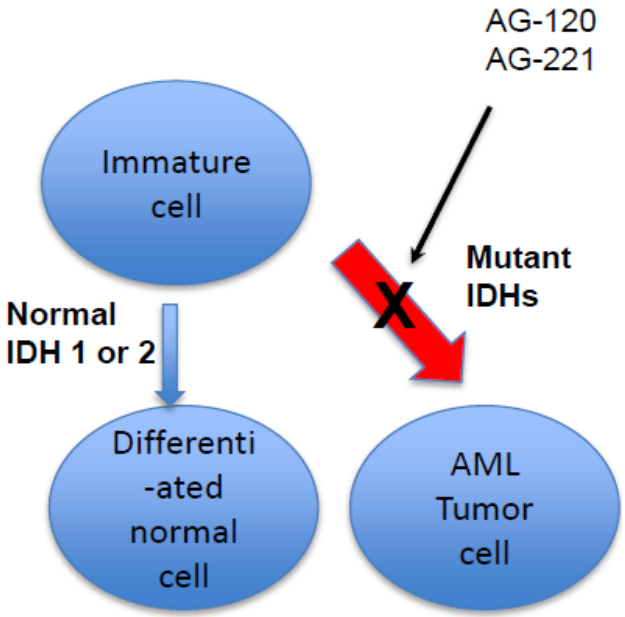
Targeting IDH in Acute Myeloid Leukemia

Disease: Acute Myeloid Leukemia (AML)

Therapy: IDH Inhibitors – AG-221, AG120

Findings:

- About 15-20 % of AML patients have IDH mutations
- Phase I trial with oral (pill) IDH1 or 2 inhibitors show 50-60% response rate in refractory AML patients



Why is this important? Therapy shows promise of durable response for subset of AML patients. No change in standard of therapy for AML in past 40 years

How did LLS help? LLS is funding one of the researchers in the study & LLS has numerous grants in progress studying this target

TARGETING EZH2 IN CHRONIC MYELOID LEUKEMIA

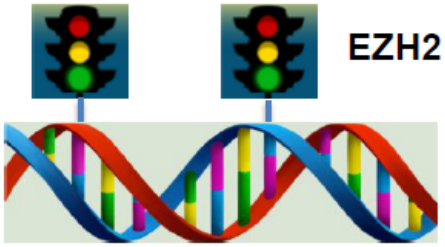
Disease: Chronic Myeloid Leukemia

Therapy: EZH2 Inhibitor

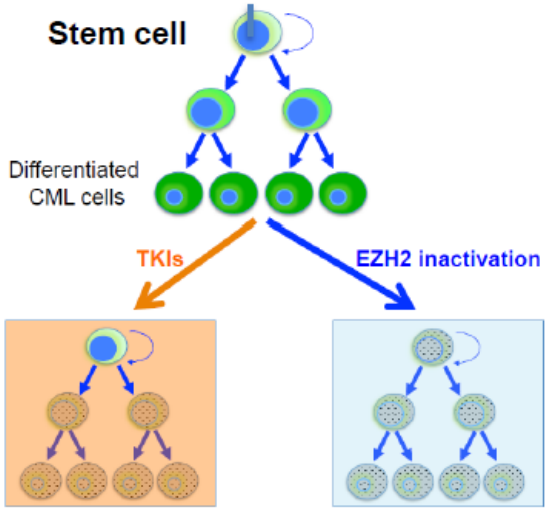
Findings: Pre-clinical evidence that EZH2 inhibitor may eradicate CML leukemia stem cells (LSC)

Why is this important? Experimental therapy targeting the cancer stem cells and may lead to complete eradication of disease (vs. long-term disease control with imatinib)

How did LLS help? LLS is funding a researcher, Huafeng Xie, at Dana-Farber Cancer Institute, through our Career Development Fellow Program. He is planning a clinical trial.



EZH2 controls the "read-out" of DNA



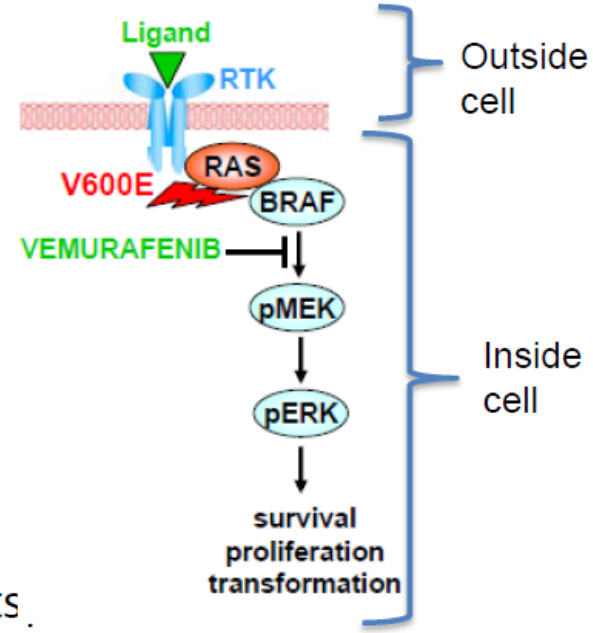
HAIRY CELL LEUKEMIA

Disease: Hairy Cell Leukemia

Therapy: B-RAF inhibitor (vemurafenib)

Findings:

- Two Phase II trials (US and Italy)
- Extraordinarily high response rate (overall response rate= 95-100%) that is rapid and durable



Why is this important?

- Hairy cell leukemia remains incurable with 30-40% pts
- 95%+ patients have activating mutation of B-RAF ("V600E")
- Excellent example of "right patient, right therapy" (like imatinib)
- New treatment alternative with long-term disease control potential

How did LLS help?

- Lead Italian investigator (Dr. Tiacci) is an LLS CDP Scholar funded for this trial
- First author of US trial (Dr. Park) is an LLS CDP Special Fellow in Clinical Research

Clinical Trials Division TAP Pipeline

Blood Cancer Research Partnership (BCRP):
To establish a collaborative partnership between LLS, DFCI, and community oncologists

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DANA-FARBER CANCER INSTITUTE

- **A Phase 1/2 Open-label Study to Assess the Safety, Tolerability and Preliminary Efficacy of TH-302, A Hypoxia-Activated Prodrug, and Dexamethasone with or without Bortezomib in Subjects with Relapsed/Refractory Multiple Myeloma (NCT01522872)**
- **A Phase I/Ib Study of Ipilimumab in Patients with Relapsed Hematologic Malignancies After Allogeneic Hematopoietic Cell Transplantation (NCT01822509)**
- **Open-label Study of the Safety and Activity of Oprozomib in Patients With Hematologic Malignancies (NCT01416428)**

TAP Special Initiatives

A Simple Patient Care Strategy to Reduce Early Deaths in Acute Promyelocytic Leukemia (APL)

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EMORY UNIVERSITY

Precision Medicine to Beat Acute Myeloid Leukemia (AML)

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OHSU KNIGHT CANCER INSTITUTE Oregon Health & Science University

Equity Investment in Multiple Small Molecules and Targets for Hematological Malignancies

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BioTheryX

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