

A photograph of the St. Jude Children's Research Hospital building, a large, modern, multi-story structure with a curved, tiered design and many windows. The building is surrounded by green lawns and trees. A large, semi-transparent blue circle is overlaid on the right side of the image, containing the text and logo.

St. Jude Children's Research Hospital



Innovation Opportunities

Patrick Campbell, MD, PhD
October 30, 2018



St. Jude History

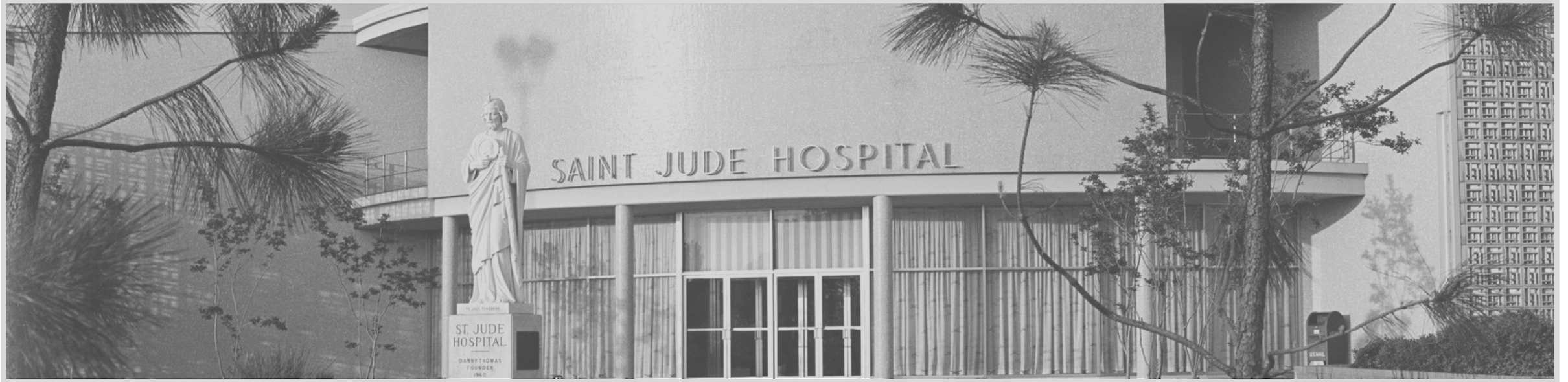
Danny Thomas

St. Jude Founder



***"Show me my way in
life and I will build
you a shrine."***

Danny Thomas said it best: “No child should die in the dawn of life.”



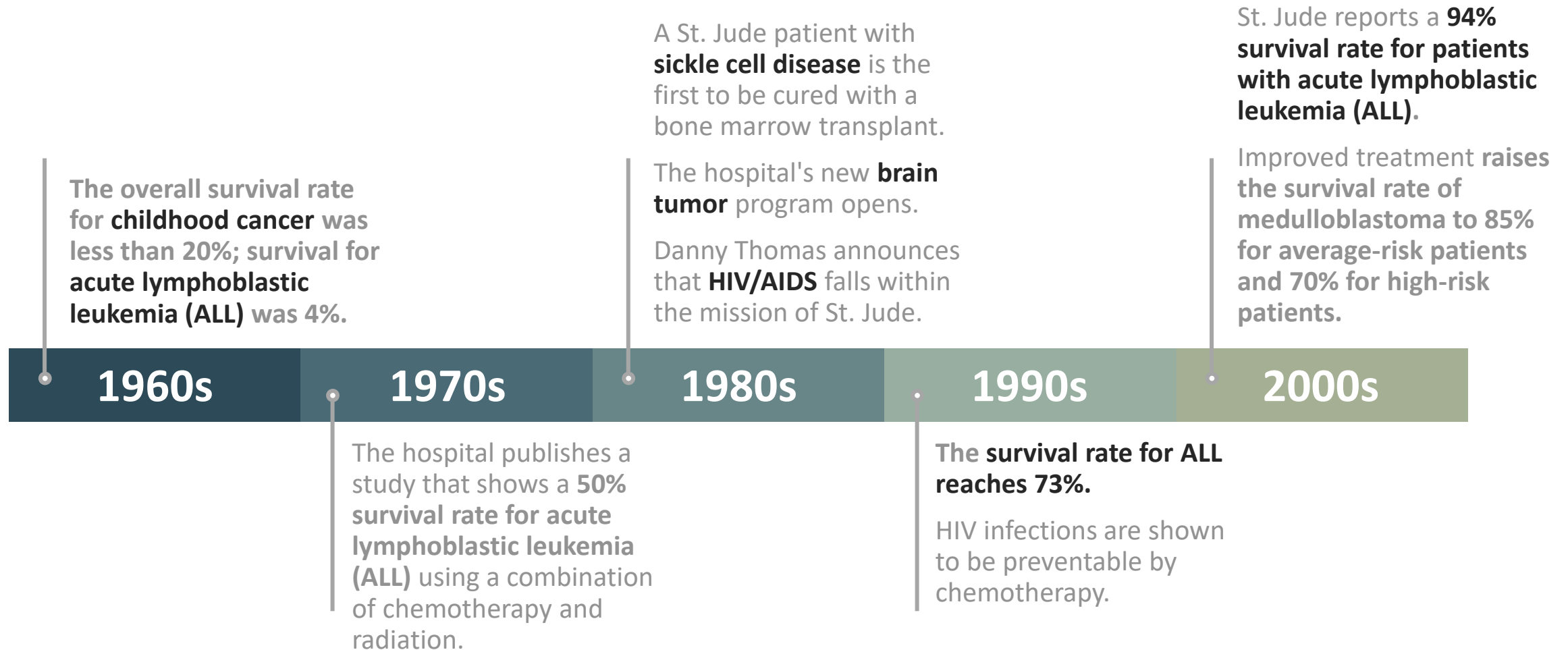
Thomas’ promise became a reality when St. Jude Children's Research Hospital opened in 1962.

During the past five decades, St. Jude has become the world's premier pediatric research institution.

During the next 50 years, St. Jude will continue that quest, further improving survival rates for childhood cancer and other catastrophic diseases. We will not stop until we reach 100%.

St. Jude History

Improving pediatric cancer survival rates



A photograph of the St. Jude Children's Research Hospital building, a large, modern, multi-story structure with a prominent red and white facade. The building features large glass windows and a curved design. In the foreground, a group of children are playing on a grassy area with trees and flowers. The sky is blue with scattered white clouds. The text "St. Jude's Strategic Plan" and "A Vision for the Future" is overlaid on the left side of the image in white, bold font. The text is positioned over a dark, semi-transparent background that covers the left portion of the image. The overall tone is bright and hopeful, reflecting the hospital's mission.

St. Jude's Strategic Plan

A Vision for the Future



Our Vision for the Future

To accelerate progress on a global level

- **20% increase** in the number of new cancer patients treated on campus
- **Double the number** of patients treated on our protocols in the U.S. and worldwide
 - **25% increase** in faculty and **28% increase** in total staff
 - **\$900** million in new construction and renovation



Clinical Priorities

Increase the number
of patients treated
on St. Jude-led
clinical trials here
and worldwide

Set the standard for
pediatric cancer care
delivery

Advance clinical care
programs for
children with non-
malignant
hematologic diseases



Research Priorities

Strengthen basic lab and clinical research programs

Continue to create and run high-complexity protocols

Establish the benchmark for precision medicine

Define the optimal use of proton therapy for brain tumors, solid tumors and Hodgkin lymphoma

Develop a world-class cancer immunotherapy program



St. Jude Global Mission

To improve the survival rates of children with cancer and other catastrophic diseases worldwide through:

- the sharing of knowledge, technology, and organizational skills;
- the implementation of new approaches to treat pediatric cancer globally;
- the generation of international networks committed to eradicating cancer in children.



St. Jude Global Impact





Innovation Opportunities

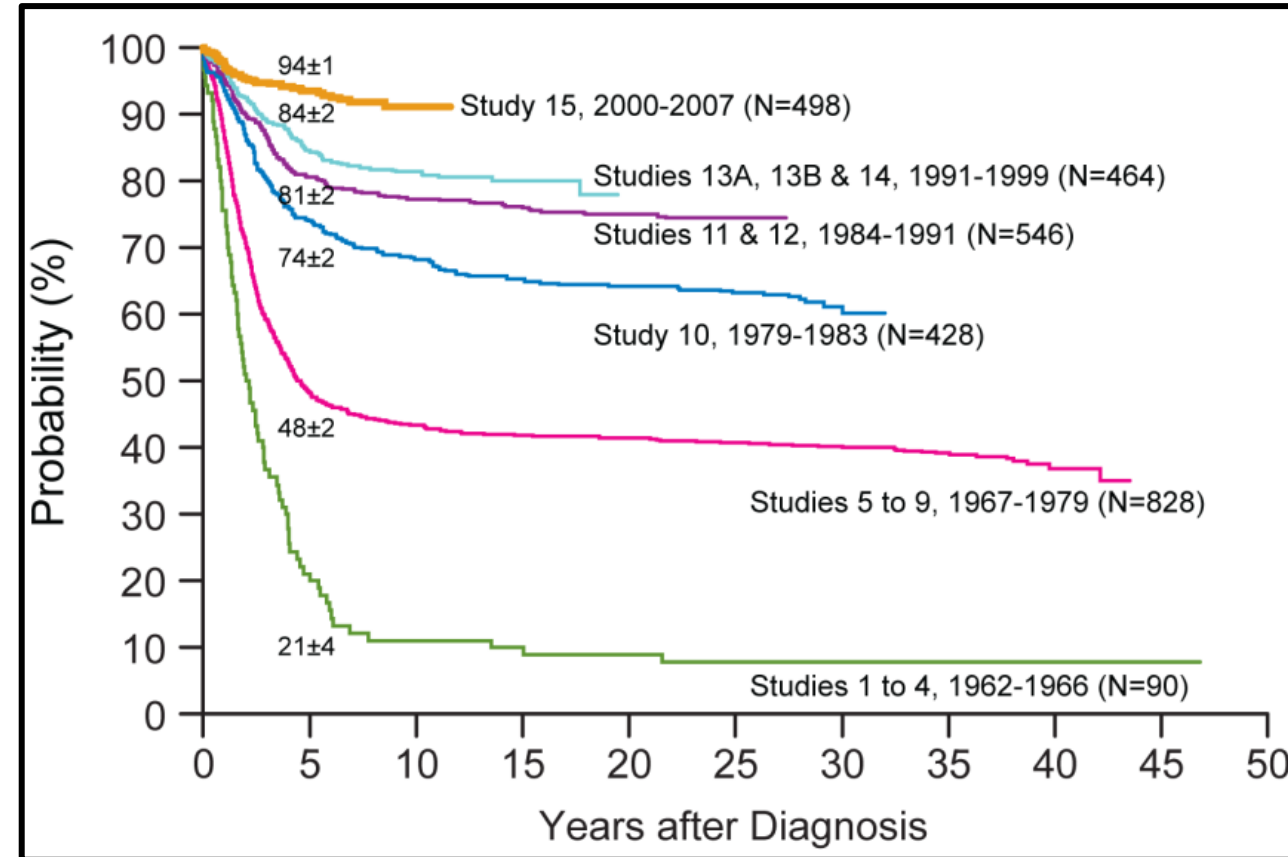
Integration Projects
eConsent



St. Jude Total Therapy trials for pediatric ALL

Survival improved through incremental changes in therapy

- Most drugs developed before 1970
- Duration now ~ 2 ½ years
- CNS-therapy:
 - intrathecal therapy
 - elimination of radiation
- Doses and schedules are optimized
- Improved transplantation procedures for high-risk patients





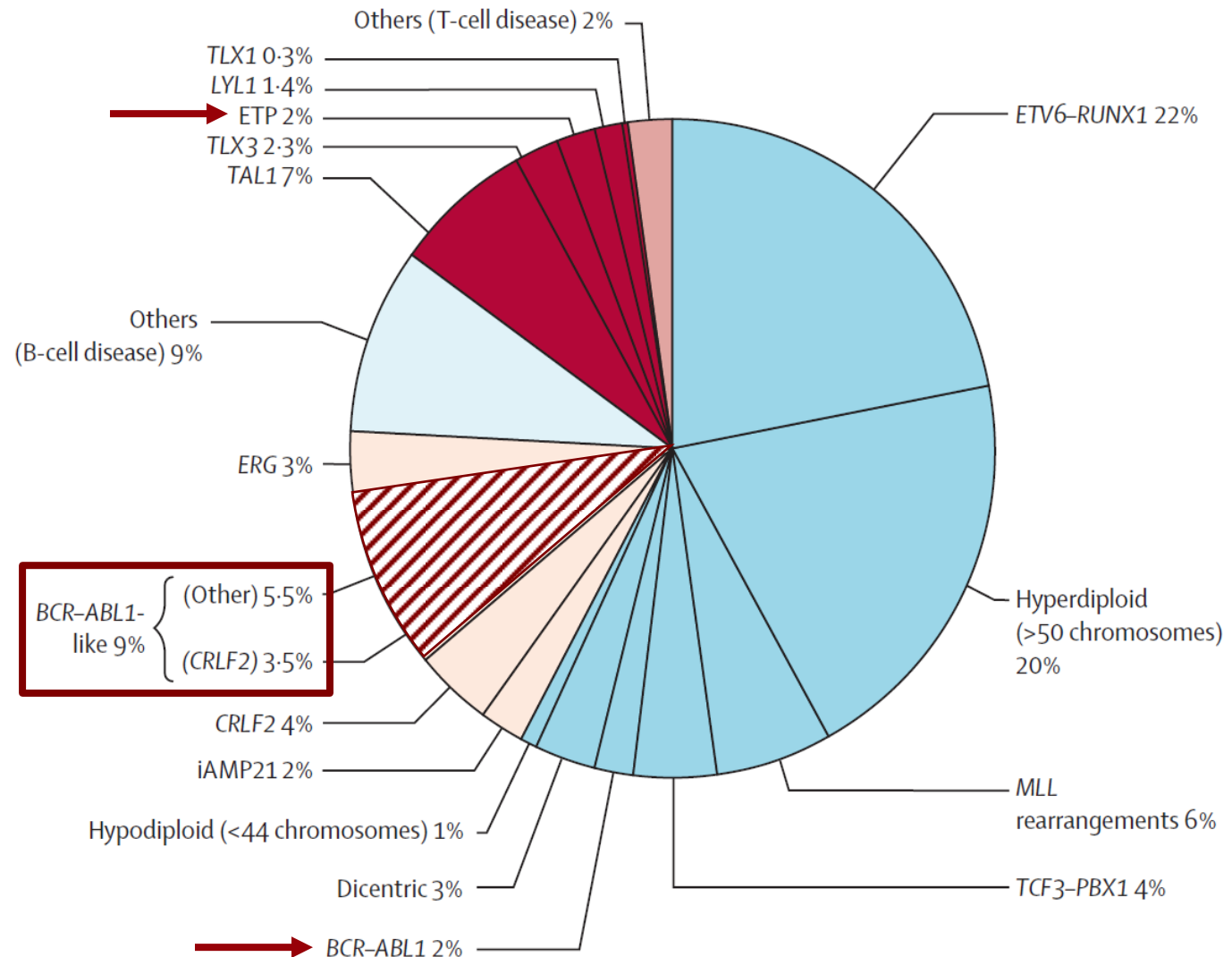
Complex assortment of genetic mutations in pediatric ALL

Rare subtypes of ALL identified with poor outcome

- improved survival with:
 - intensification of therapy
 - use of first therapy targeted to a genetic mutation (Imatinib)

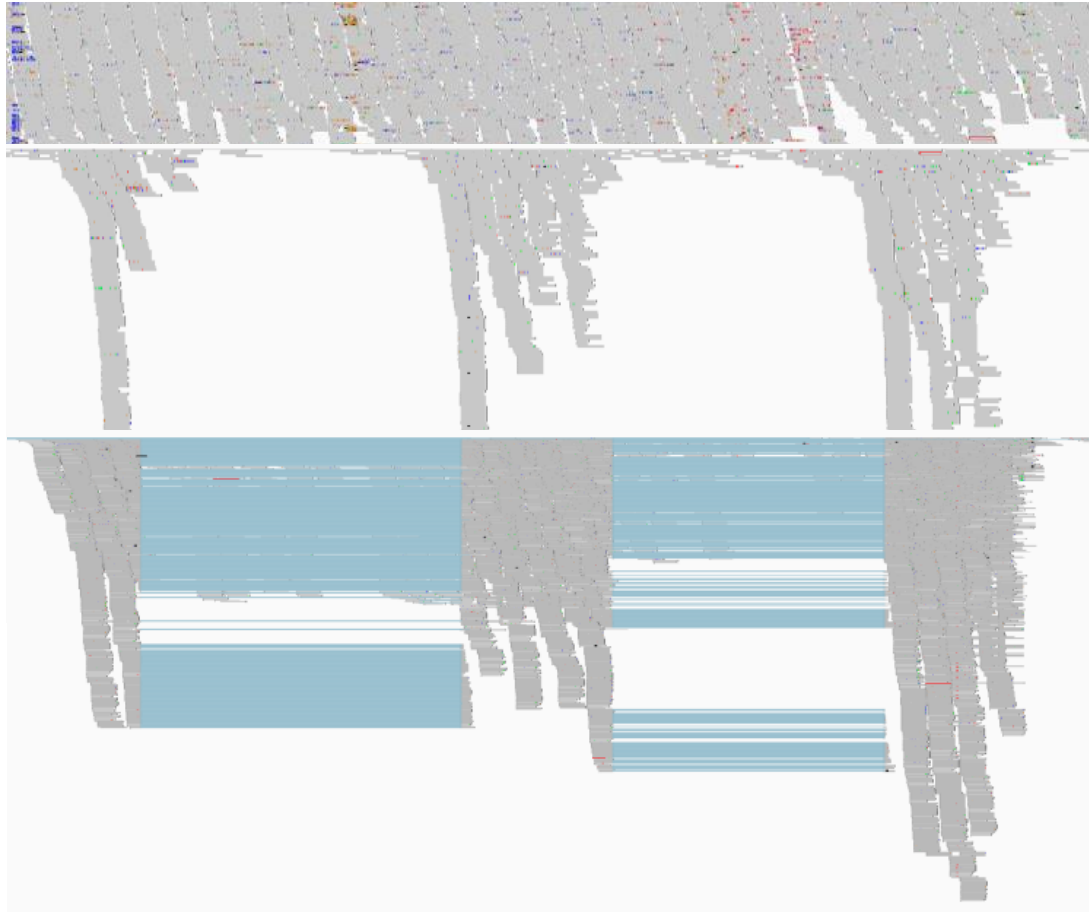
Philadelphia-like ALL

- <10% of all cases
- poor response to standard therapy





Gene sequencing strategy for Total XVII



Whole Genome:
Everything 30-45X

Copy Number

Exome:
Coding sequences
> 45X

Coding Mutations

Transcriptome:
Everything that
is expressed

Gene Fusions /
Structural Disruptions

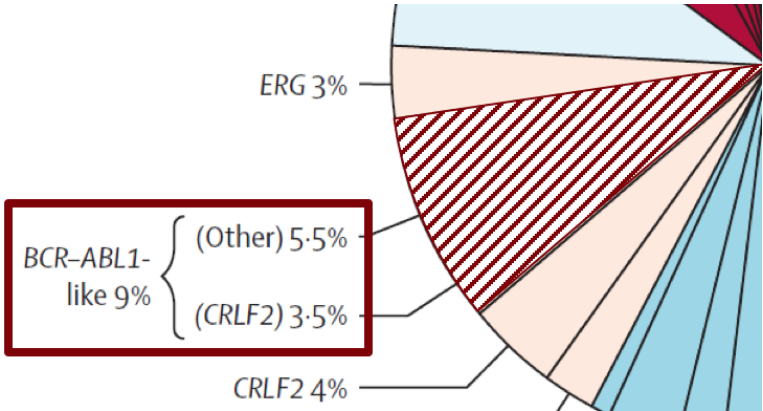
Perform sequencing on every patient:

- Cancer cells and normal cells
- Completed by day 42 of therapy



Identify genetic mutations in Ph-like ALL and add targeted therapy to standard chemo

Kinase	TKIs	Number of partners	Number of cases	5' genes
<i>ABL1</i>	Dasatinib	6	14	<i>ETV6, NUP214, RCSD1, RANBP2, SNX2, ZMIZ1</i>
<i>ABL2</i>	Dasatinib	3	7	<i>PAG1, RCSD1, ZC3HAV1</i>
<i>CSF1R</i>	Dasatinib	1	4	<i>SSBP2</i>
<i>PDGFRB</i>	Dasatinib	4	11	<i>EBF1, SSBP2, TNIP1, ZEB2</i>
<i>CRLF2</i>	JAK2 inhibitor	2	30	<i>IGH, P2RY8</i>
<i>JAK2</i>	JAK2 inhibitor	10	19	<i>ATF7IP, BCR, EBF1, ETV6, PAX5, PPFIBP1, SSBP2, STRN3, TERF2, TPR</i>
<i>EPOR</i>	JAK2 inhibitor	2	18	<i>IGH, IGK</i>
<i>TSLP</i>	JAK2 inhibitor	1	1	<i>IQGAP2</i>
<i>IL2RB</i>	JAK1/JAK3 inhibitor or both	1	1	<i>MYH9</i>
<i>NTRK3</i>	Crizotinib	1	1	<i>ETV6</i>
<i>TYK2</i>	TYK2 inhibitor	1	1	<i>MYB</i>
<i>PTK2B</i>	FAK inhibitor	2	1	<i>KDM6A</i>



Overview of Total XVII

Biologic studies

Genetic sequencing of leukemia cells
Minimal residual disease monitoring



Therapeutic studies

Standard- and high-risk leukemia

Day 15 MRD $\geq 5\%$: **Addition of Targeted Therapy**



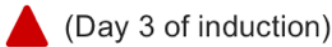
Early Intensification MRD $\geq 0.1\%$ (B-ALL): **Immunotherapy** (CAR-T cells/blinatumomab)



T-ALL: Intensification of early phase of therapy



Rituximab randomization (B-ALL)



Vincristine randomization (based on *CEP72* genotype)



Supportive care studies

Neurocognitive intervention randomization (week 61 of continuation or off therapy)



Low-magnitude high frequency mechanical stimulation randomization



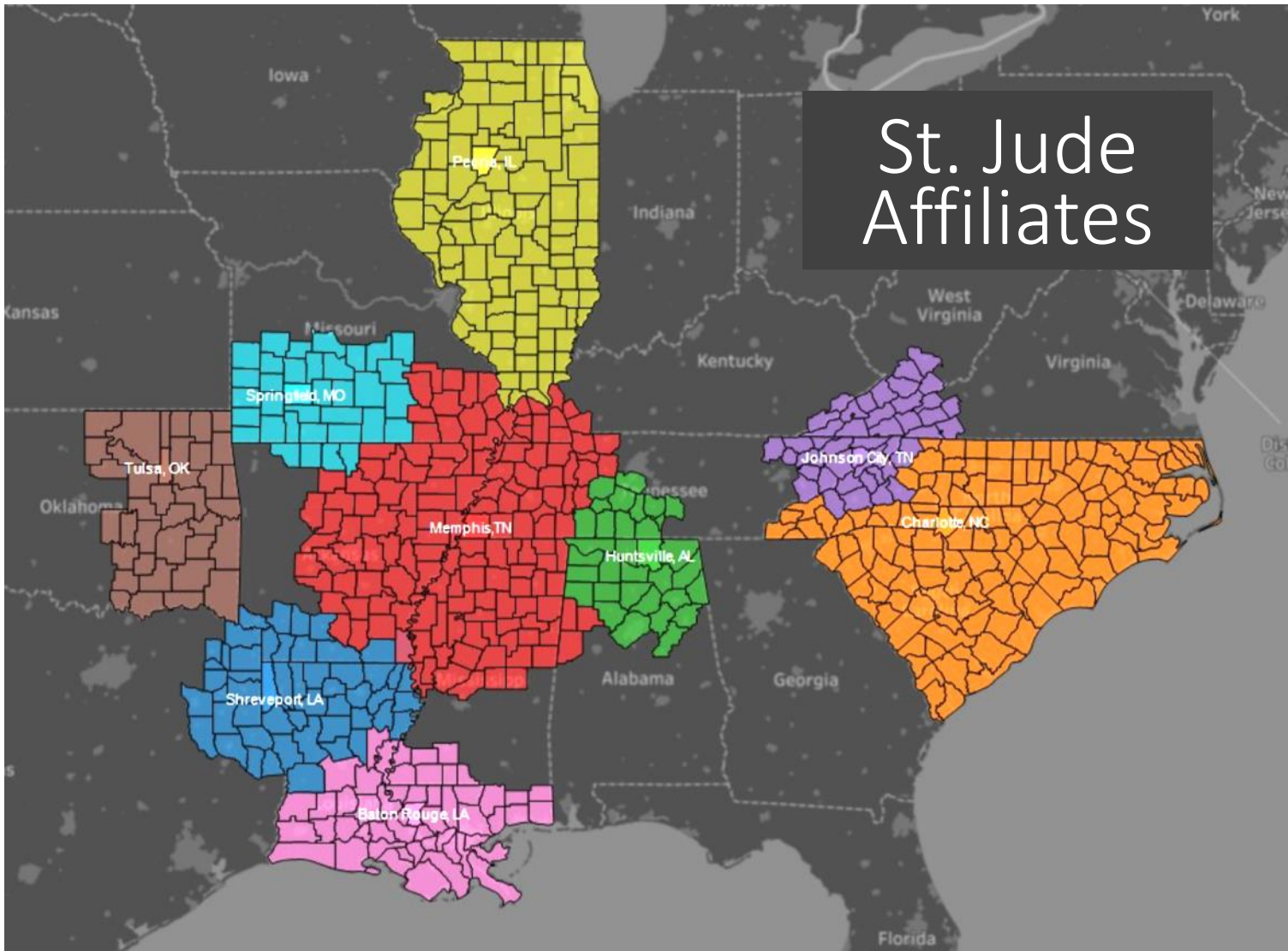


Data Reporting Requirements on Total XVII

- ~2.5 years of therapy
- Routine weekly labs throughout therapy
 - Labs collected multiple times daily during induction and critical illness
- Labs, vitals, and measurements
- Neurologic and physical therapy assessments
- Serial neurocognitive assessments
- Diagnostic imaging interpretations
- Immunopathology and molecular pathology
- Adverse events
- Medications
- ...



Geographic scope of Total 17



Partner sites

Cook Children's Medical Center
Fort Worth, TX

Children's Hospital of Michigan
Detroit, MI

Lucile Packard Children's Hospital
Stanford University , Palo Alto, CA

Rady Children's Hospital
San Diego, CA

Monash Children's Hospital
Victoria, Australia

The Royal Children's Hospital
Melbourne, Australia



Integration Projects

Cerner EMR to OmniComm EDC

EMR to Site/Trial Management platform

EDC to Site/Trial Management

Need to include human decision making in integration platform



Integration for Total XVII and other SJ trials

- Need for EMR-EDC integration
 - Excellent/dedicated research nurses and CRA, but huge volumes of data
 - Need to minimize risk of data entry error
- Challenges
 - Selecting only the data required for protocol – requires manual step in integration
 - Non-discrete data – e.g. pathology/DI reports
 - Increasing development of multi-center trials (more targeted therapy, smaller numbers of eligible patients). How to provide same integration for patients treated at affiliate and partner sites?



EMR to EDC Integration

- Cerner Millennium EMR to OmniComm TrialMaster EDC
- Step1: patient demographics, by HL7
 - Completed relatively easily for basic patient demographics and enrollment
 - Very mature technology but not easily scalable
- Step 2: single instance labs, by FHIR
 - Ongoing – Cerner invested heavily in FHIR, their Ignite API is operational
 - OmniComm is currently investing in this technology, mapping FHIR & LOINC codes
- Step 3: multiple instance labs+, via SMART on FHIR
 - SMART on FHIR is the emerging innovation platform
 - Both companies committed and actively engaged in planning

TaskEditViewPatientChartLinksOptionsCurrentAddHelp

Patient List

Links

New Sticky Note

View Sticky Notes

Tear Off

Change

Charges

Charge Entry

Exit

Calculator

Message Sender

AdHoc

Medication Administration

Doe, Jane

←List→

Recent

Name

🔍

Doe, Jane

Allergies: No Known Medication Allergies

IQHealth: No

PCP: J. Smith, M.D.

Phone:

Age: 6 years

DOB: 2/14/ 2012

Wt:

Sex: Female

Pref. Labs/Diagnostics:

MRN: R12345678

Menu

SMART App Validator DSTU2

Patient Information

Diagnoses and Problems

Histories

SMART TrialMaster

Flowsheet

Document Viewing + Add

Clinical Notes + Add

Reference Text Browser

SMART TrialMaster - Patient Task Menu

User Name: mbell | Role: Coordinator | Session Date: 07-Jan-2018, 15:31

R12345678 > Protocol A > Patient Task Menu

Trial: Protocol A

Site: Metropolis Research Center, 005

Patient: R12345678

Change Protocol

Reconciliation Tasks

Hide Applied

Data Source	Visit	Form	Date Issued	Status
Vital Signs	Pre-Study	Vital Signs	2017-12-01T22:14	Applied
Patient	Pre-Study	Demographics	2017-10-30T11:23	Applied

Start Reconciliation Job

Select from the available visits to begin data entry

Hide Complete

[Pre-Study](#)

[Induction - 11/20/2017](#)

[Early Intensification - 12/29/2017](#)

Exit SMART TrialMaster

Patient Task Menu (Lab Data Example)

1. Select visit

2. Select eCRF
form

3. Select data to
enter into TM

4. Save form to TM

Task Edit View Patient Chart Links Options Current Add Help

Patient List Links

New Sticky Note View Sticky Notes Tear Off Change Charges Charge Entry Exit Calculator Message Sender AdHoc Medication Administration

Doe, Jane ×

← List → Recent Name

Doe, Jane PCP: J. Smith, M.D. DOB: 2/14/2012 Pref. Labs/Diagnostics:
Allergies: No Known Medication Allergies Phone: Wt: MRN: R12345678
IQHealth: No Age: 6 years Sex: Female

Menu ↑

- SMART App Validator DSTU2
- Patient Information
- Diagnoses and Problems
- Histories
- SMART TrialMaster**
- Flowsheet
- Document Viewing + Add
- Clinical Notes + Add
- Reference Text Browser

SMART TrialMaster User Name: mbell | Role: Coordinator | Session Date: 07-Jan-2018, 15:31

R12345678 > Protocol A > Induction - 11/20/2017 > Form Selection

Trial: Protocol A Patient: R12345678
Site: Metropolis Research Center, 005

Induction - 11/20/2017

Select from the available forms Hide Complete

Chemistry	+
CBC	+
Lipid Screen	+ Add form
Chemistry - 11/22/2017	I
CBC - 11/20/2017	C
CBC - 11/24/2017	C
Physical Exam	N
Vital Signs	N
Drug Therapy	I



Patient Task Menu
(Lab Data Example)

1. Select visit



2. Select eCRF
form



3. Select data to
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4. Save form to TM

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Clinical Notes

Reference Text Browser

SMART TrialMaster - Data Selection

User Name: mbell | Role: Coordinator | Session Date: 07-Jan-2018, 15:31

R12345678 > Protocol A > Induction - 11/20/2017 > Lipid Screen > Data Selection

Trial: Protocol A

Site: Metropolis Research Center, 005

Patient: R12345678

Induction - 11/20/2017

Lipid Screen

Displaying matching values between 11/20/2017 and 11/20/2017

Select new date or range: <Start date> <End date>

Select the sample collection date and time of the results you want to enter on the form

Date	Lab Test	Result	Unit	Normal Range
2017-11-20T09:34	Total Cholesterol	90	mg/dL	120-200
2017-11-20T09:34	HDL	54	mg/dL	>55
2017-11-20T09:34	Triglycerides	66	mg/dL	35-114
2017-11-20T09:34	Free Fatty Acid	1.28	mmol/L	N/A
2017-11-20T09:34	Insulin	2.8	uIU/L	6-26
2017-11-20T09:34	25-Hydroxyvitamin D	<5	ng/mL	20-100

Date	Lab Test	Result	Unit	Normal Range
2017-11-20T22:04	Total Cholesterol	104	mg/dL	120-200
2017-11-20T22:04	HDL	57	mg/dL	>55
2017-11-20T22:04	Triglycerides	66	mg/dL	35-114
2017-11-20T22:04	Free Fatty Acid	--	mmol/L	N/A

Review



Patient Task Menu (Lab Data Example)

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SMART TrialMaster User Name: mbell | Role: Coordinator | Session Date: 07-Jan-2018, 15:31

R12345678 > Protocol A > Induction - 11/20/2017 > Lipid Screen > Confirm Selection

Trial: Protocol A Patient: R12345678
 Site: Metropolis Research Center, 005

Induction - 11/20/2017 **Lipid Screen**

Lab Date

Was sample collected? ☒ Yes ☐ No

Date of Sample Collection 11/20/2017
 MM/DD/YYYY

Time of Collection 09:34
 HH:MM

Fields sourced from EMR are read-only. Add note to annotate or cancel to clear form.

Not Done	Test Name	Test Result	Unit
☐	Total Cholesterol	90	mg/dL
☐	HDL	54	mg/dL
☐	Triglycerides	66	mg/dL
☐	Free Fatty Acid	1.28	mmol/L

Rows 6

Incomplete Complete Cancel



Patient Task Menu
(Lab Data Example)

1. Select visit

2. Select eCRF
form

3. Select data to
enter into TM

4. Save form to TM



Impact of real-life on development of SMART app

- If more than one result exists for a specific lab, no algorithm can replace human to select the appropriate result
- Depending on patient situation, any result may be:
 - integrated from St. Jude EMR
 - manually entered by CRA at St. Jude
 - manually entered by team at Affiliate or Partner site
 - faxed from remote site to St. Jude for manual entry into EDC
- Patients may move between Affiliate and St. Jude on a weekly basis
- Single eCRF may have fields requiring manual entry and integration
- Need robust reconciliation step to update EDC values when integrate result changes



eConsent opportunities

Market not stable, opening for vendors?

Clinical Trial/Study Enrollment History for Patient

Protocol Name

- ☐ PGEN5
 - ☐ Amendment 3
- ☐ SJLTFU
 - ☐ Amendment 5
- ☐ TBANK
 - ☐ Amendment 2
- ☐ COGREG
 - ☐ Amendment 2
- ☐ PTSD2
 - ☐ Amendment 3
- ☐ PG4KDS
 - ☐ Amendment 2
- ☐ PRO-CTCAE
 - ☐ Amendment 5
- ☒ TOT17
 - ☐ Initial Protocol
 - ☐ Amendment 1
 - ☐ Amendment 2
- ☐ EPIGUT
 - ☐ Amendment 1
- ☐ NVIROM
 - ☐ Initial Protocol



Unparalleled commitment to Clinical Research

- Approximately 6,500 active patients
 - 95% of patients are <19 years old
- 60% of new cancer patients are enrolled on a treatment trial at the time of diagnosis
- 98% of patients are enrolled on a clinical trial at some point in their treatment and follow-up course
- Discuss eConsent needs related to Total VXII, but scope is much larger



Total XVII protocol consent

- Performed within 1 to 3 days of diagnosis
 - 35 pages long, covers first 6-9 weeks of therapy
 - 13 different chemotherapy drugs with long lists of common toxicities
 - Treatment risks are significant and include death
- Consent performed by attending physicians who have busy schedules
 - Typically requires 1-2 hours of dedicated time with family (range 30 minutes – 2 days)
- Parents typically have had little sleep
 - English is not always primary language
 - Education level varies, consent written at ~ 5th grade level
- Older children and teenage patients are encouraged to participate and asked to assent to treatment plan



Total XVII protocol consent

- 9 optional research studies, families must opt in or out
 - Drug randomizations
 - Optional research tests

Optional randomization for vincristine dose or duration: You can choose to not have vincristine treatment assignment by randomization and you can still take part in the main study. In this case, you will get the standard dose or duration of vincristine.

Please circle your answer: I agree to take part in the randomization for vincristine dose or duration during Continuation Treatment.

YES

NO

2. Optional drug sensitivity research

If you agree to have this extra test, we will use a sample of the bone marrow that was collected during your bone marrow procedure at diagnosis. The bone marrow will be sent to a laboratory at St. Jude for sensitivity to anti-leukemia/lymphoma drugs. If no bone marrow is drawn during routine care, a blood sample drawn at the same time you are having blood drawn for routine care may be used in its place.

Please circle your answer: I agree to allow my bone marrow and blood to be used for drug sensitivity research studies

YES

NO



eConsent product needed to replace current paper consent process

- Video consent delivered on mobile devices
 - add consistency to consent process
 - deliver at pace appropriate for parents
 - remove physician-specific differences in content of consent discussion
 - significant regulatory requirements to documenting consistent and thorough informed consent
- Remote process for re-consent at age of majority
- Multi-lingual platform
- Capture discrete data regarding consent in EMR
 - e.g. agreement to optional testing
 - use to drive clinical decision support and reduce risk of improper research test or medication orders



St. Jude is still looking for an
eConsent product – we are open to
suggestions



Questions?