St. Jude Children's Research Hospital

Innovation Opportunities

Patrick Campbell, MD, PhD
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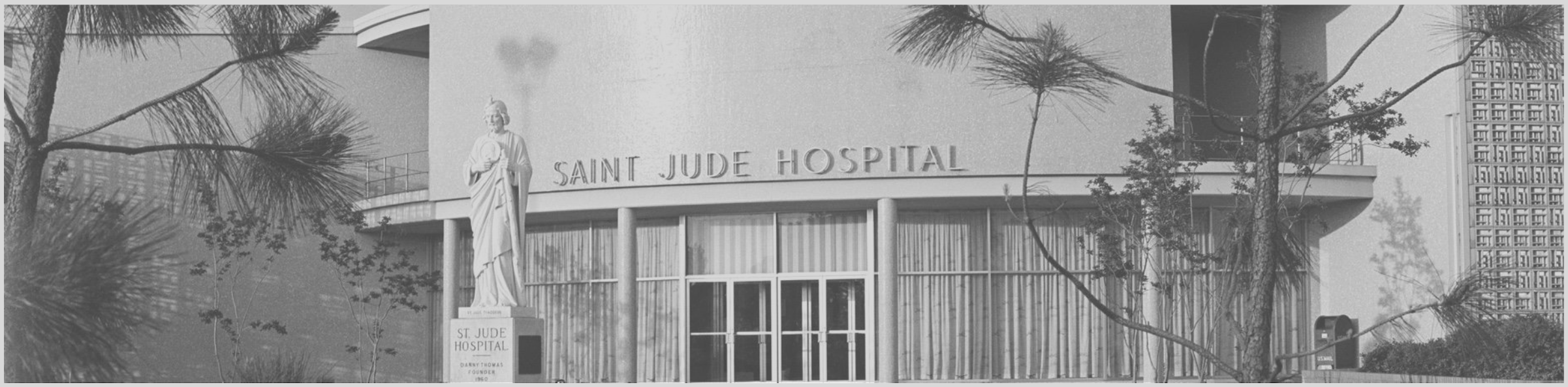
St. Jude History

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.”

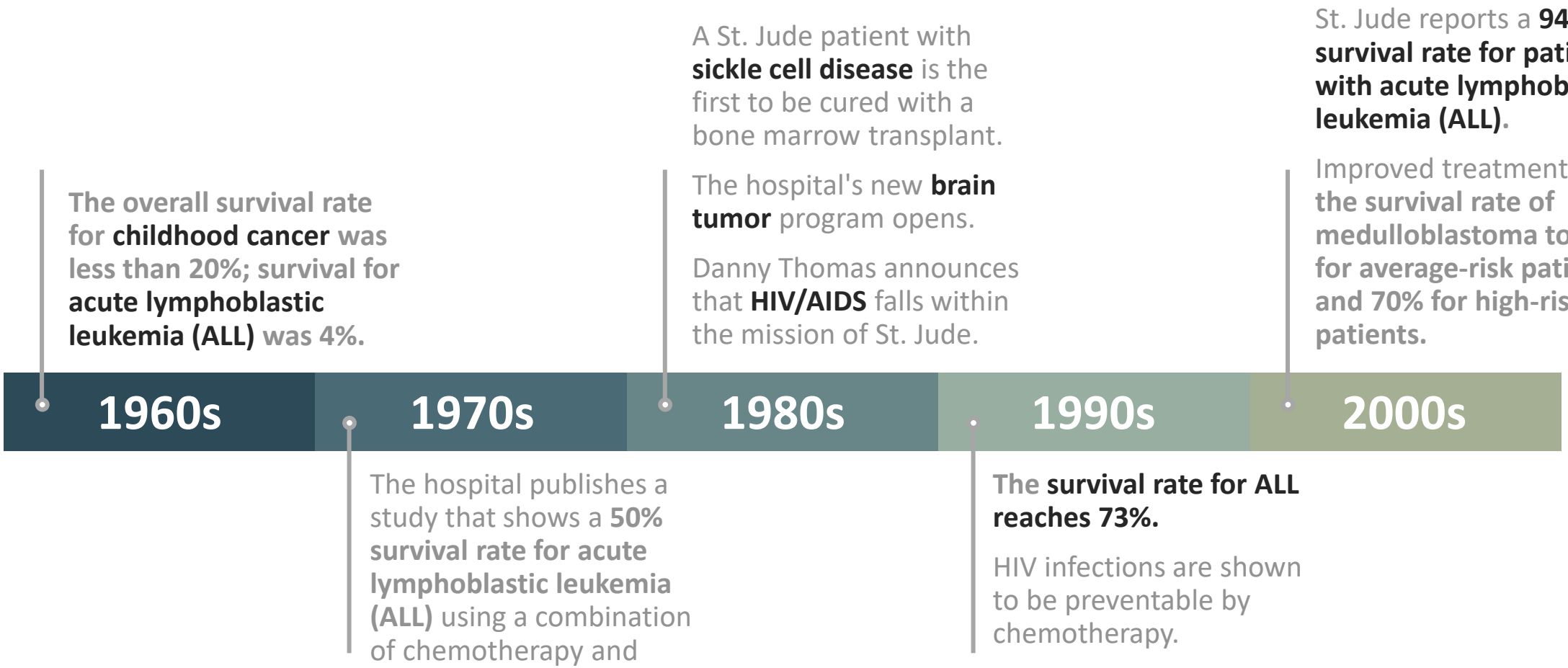


Thomas’ promise became a reality when St. Jude Children's Research Hospital opened in 1962.

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



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

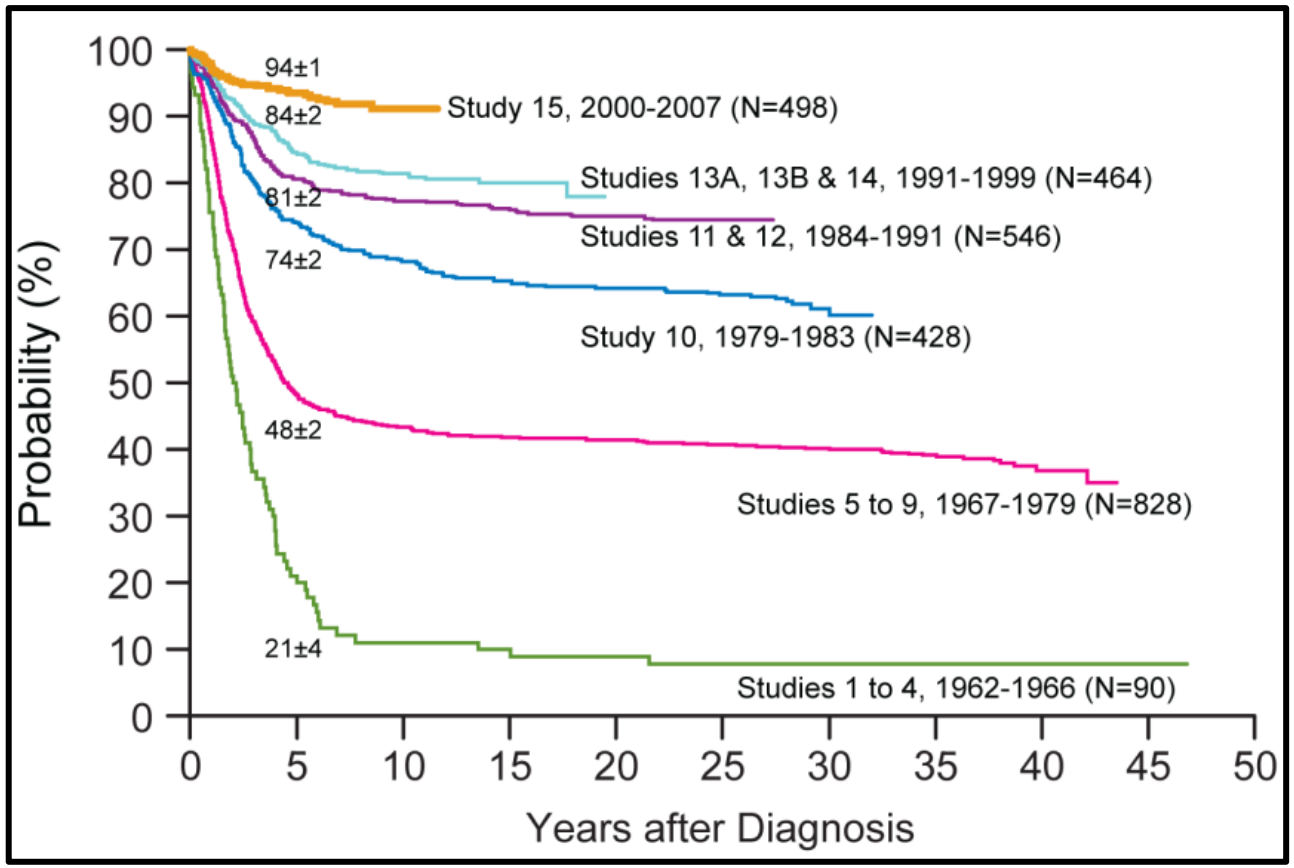
Integration Projects

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



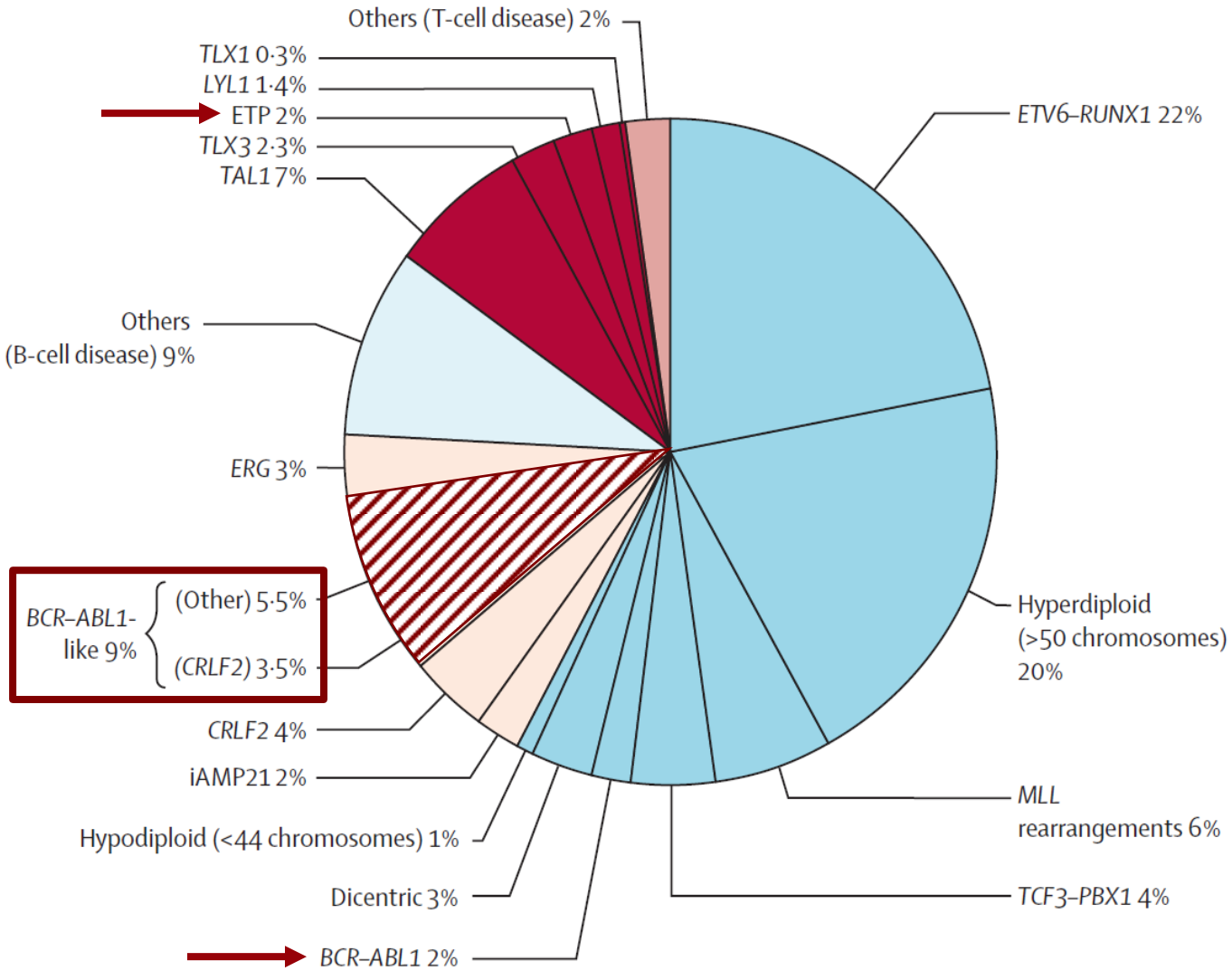
Complex assortment of genetic mutations in pediatric ALL

Rare subtypes of ALL identified with poor outcome

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

<u>Philadelphia-like ALL</u>

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



Hiroto Inaba et al, Lancet 2013

Gene sequencing strategy for Total XVII

Whole Genome:
Everything 30-45X

Exome:
Coding sequences
> 45X

Transcriptome:
Everything that
is expressed

Copy Number

Coding Mutations

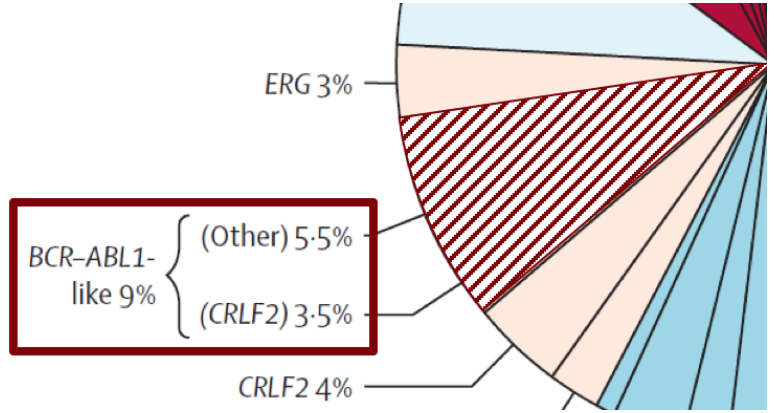
Gene Fusions /
Structural Disruptions

Perform sequencing on every patient:

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

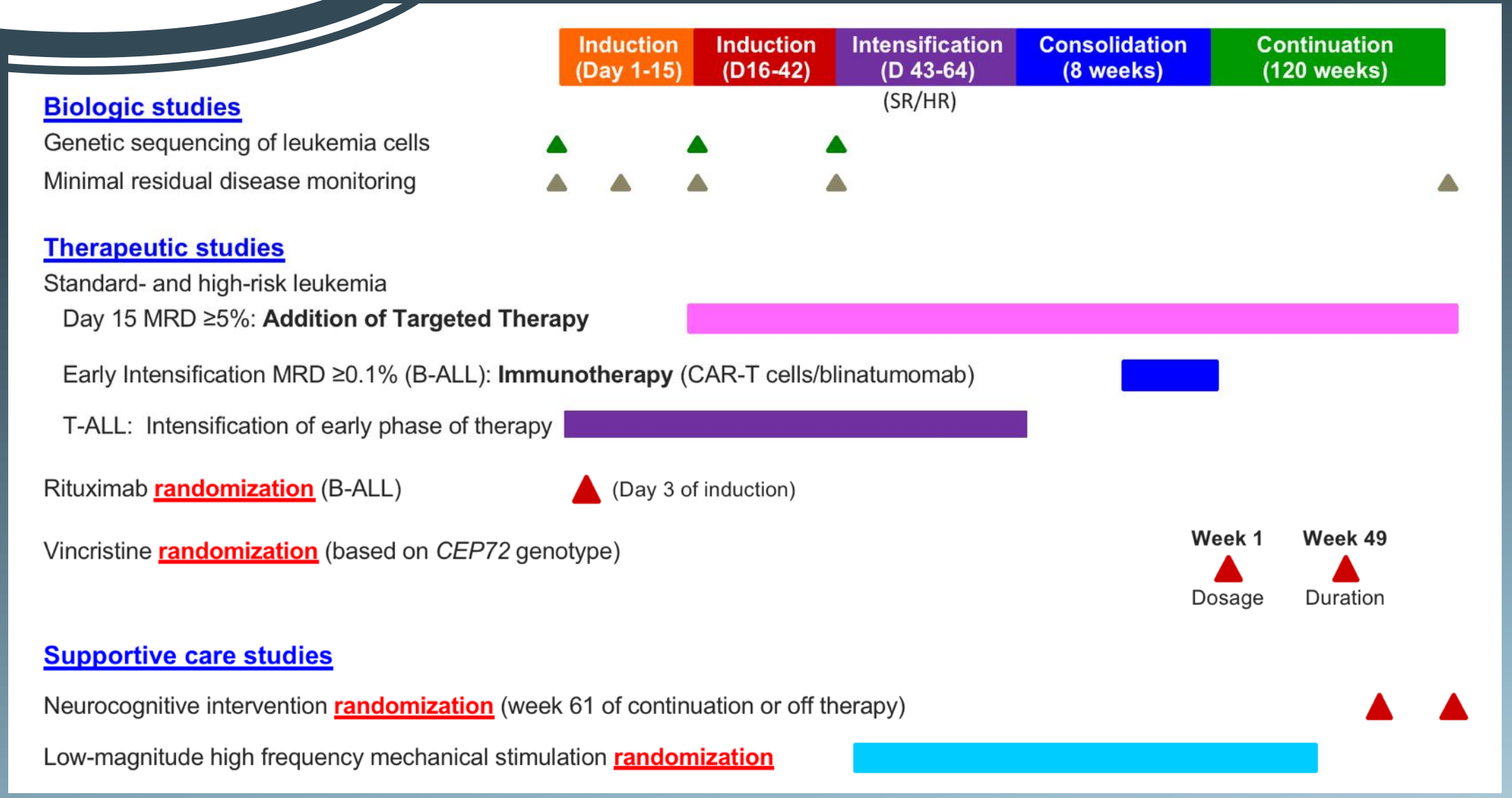
Identify genetic mutations in Ph-like ALL and add targeted therapy to standard chemo

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



Roberts KG et al, NEJM 2014

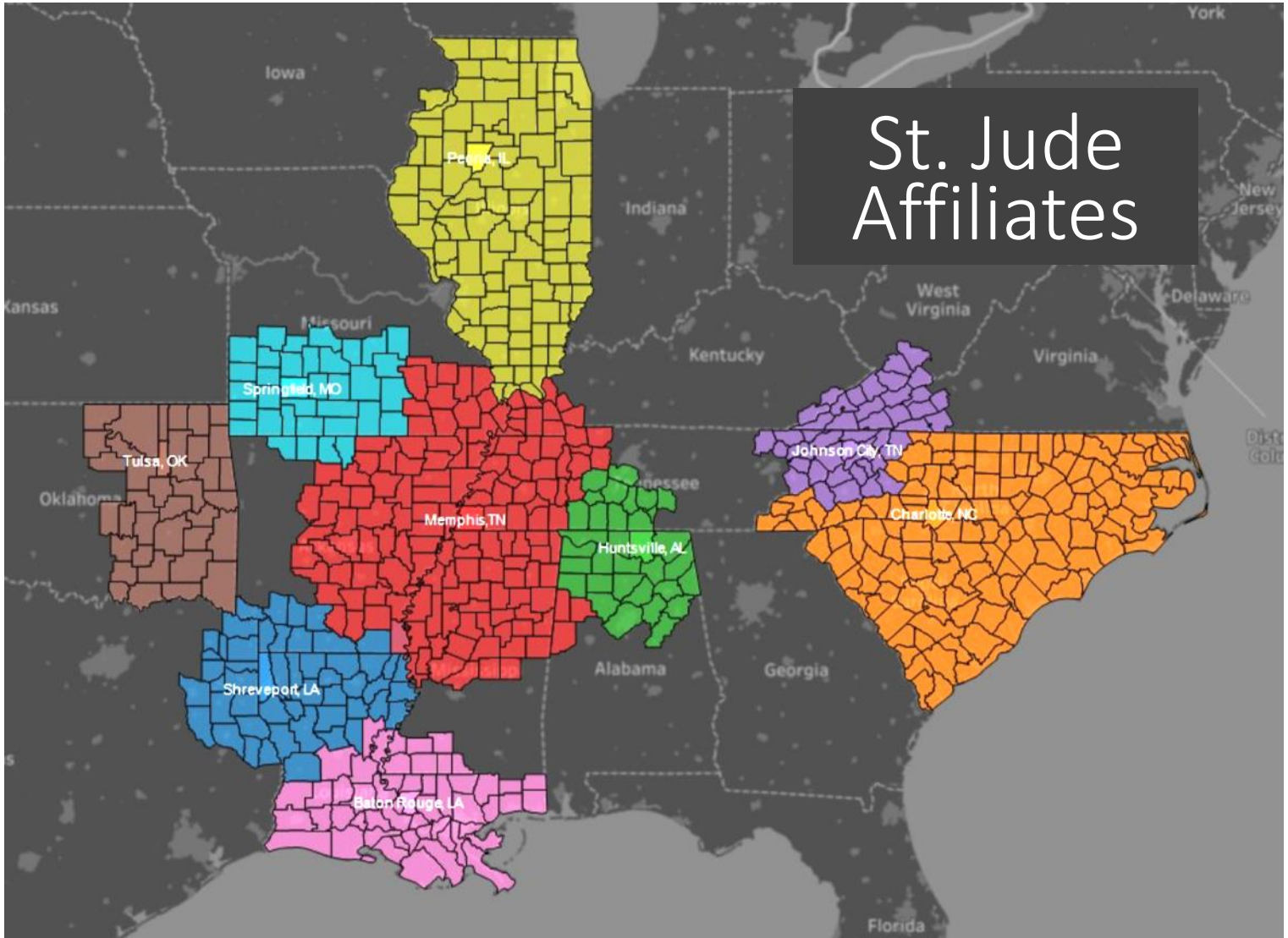
Overview of Total XVII



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

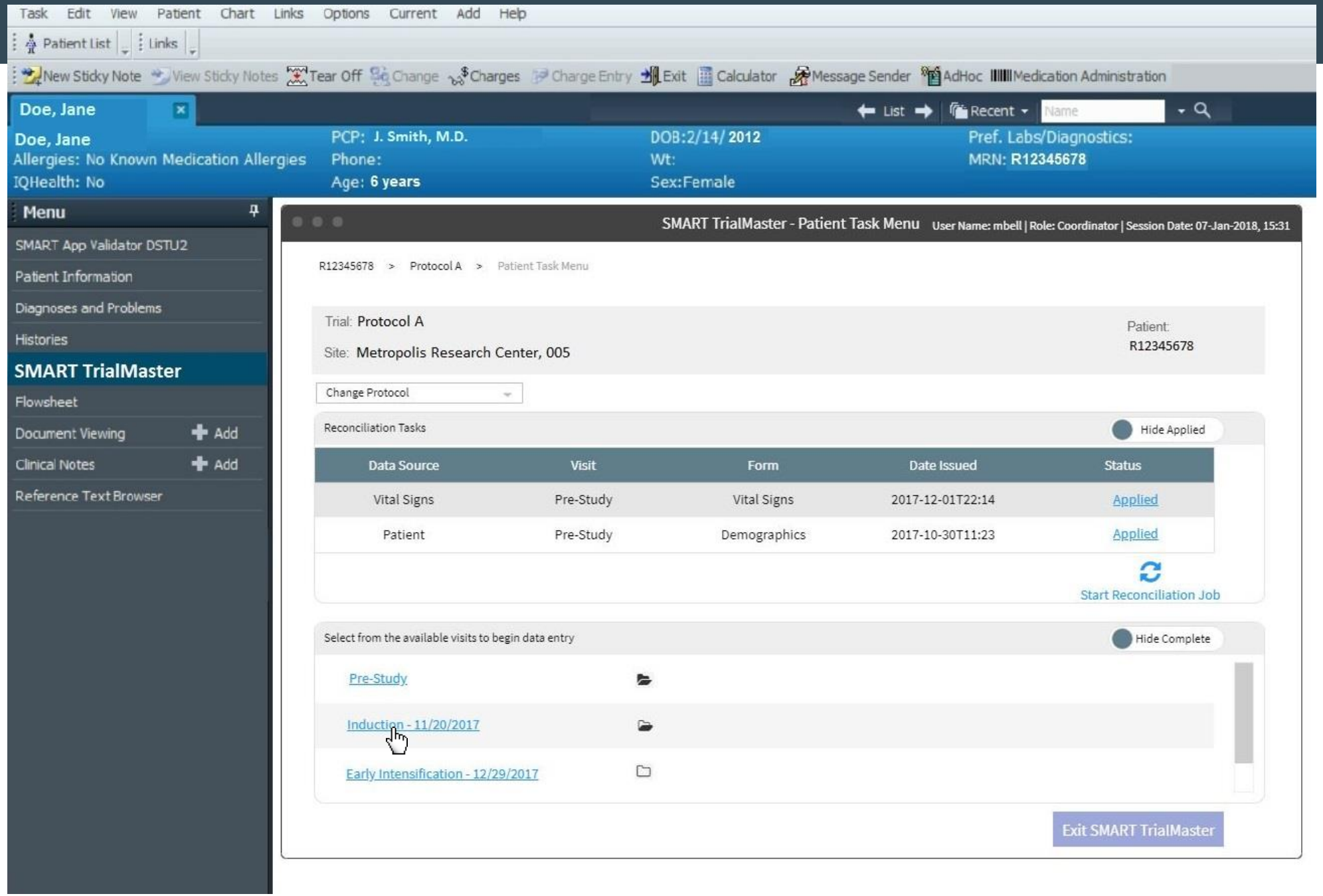
Need to include human decision making in integration platform

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



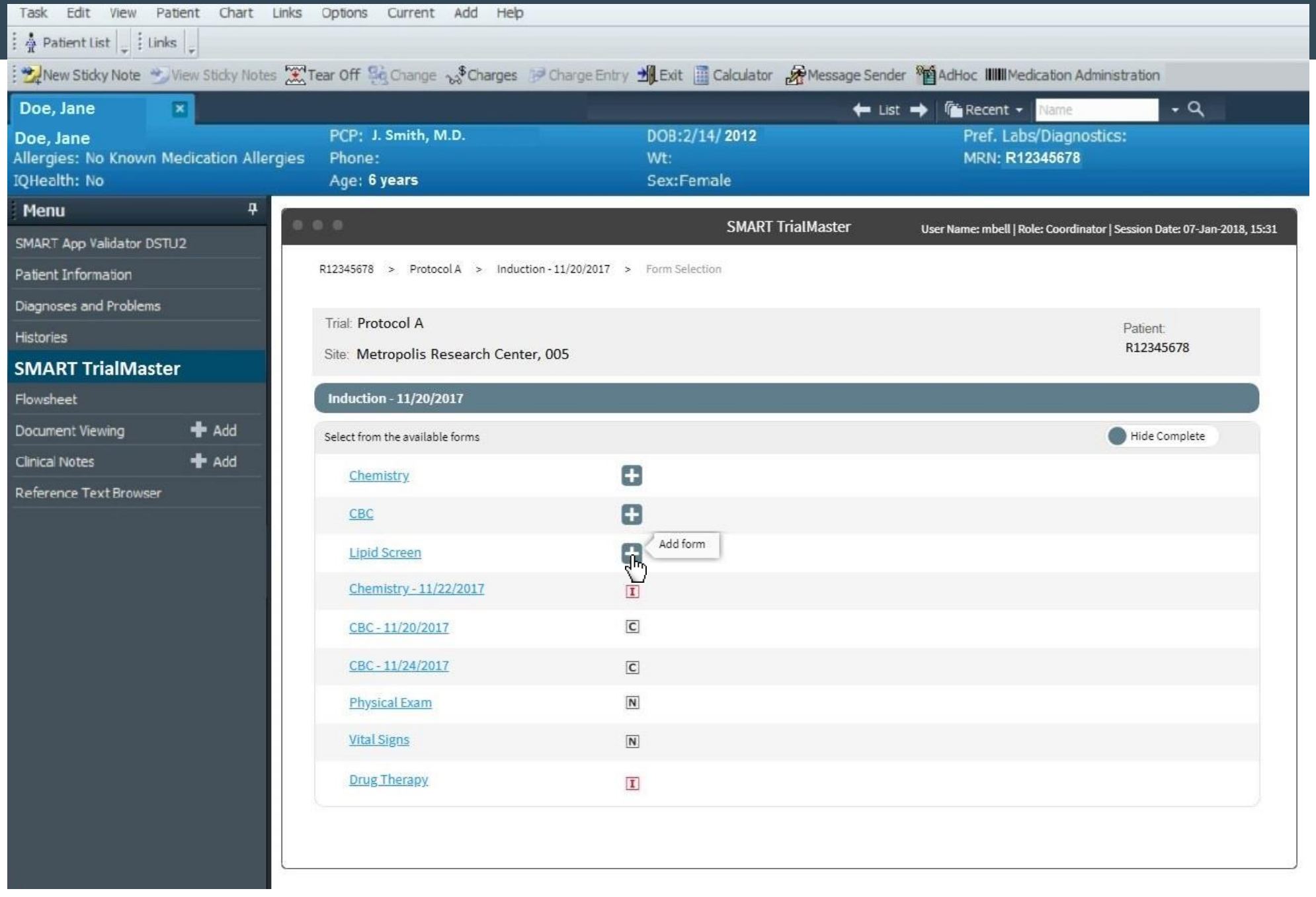
Patient Task Menu (Lab Data Example)

1. Select visit

2. Select eCRF form

3. Select data to enter into TM

4. Save form to TM



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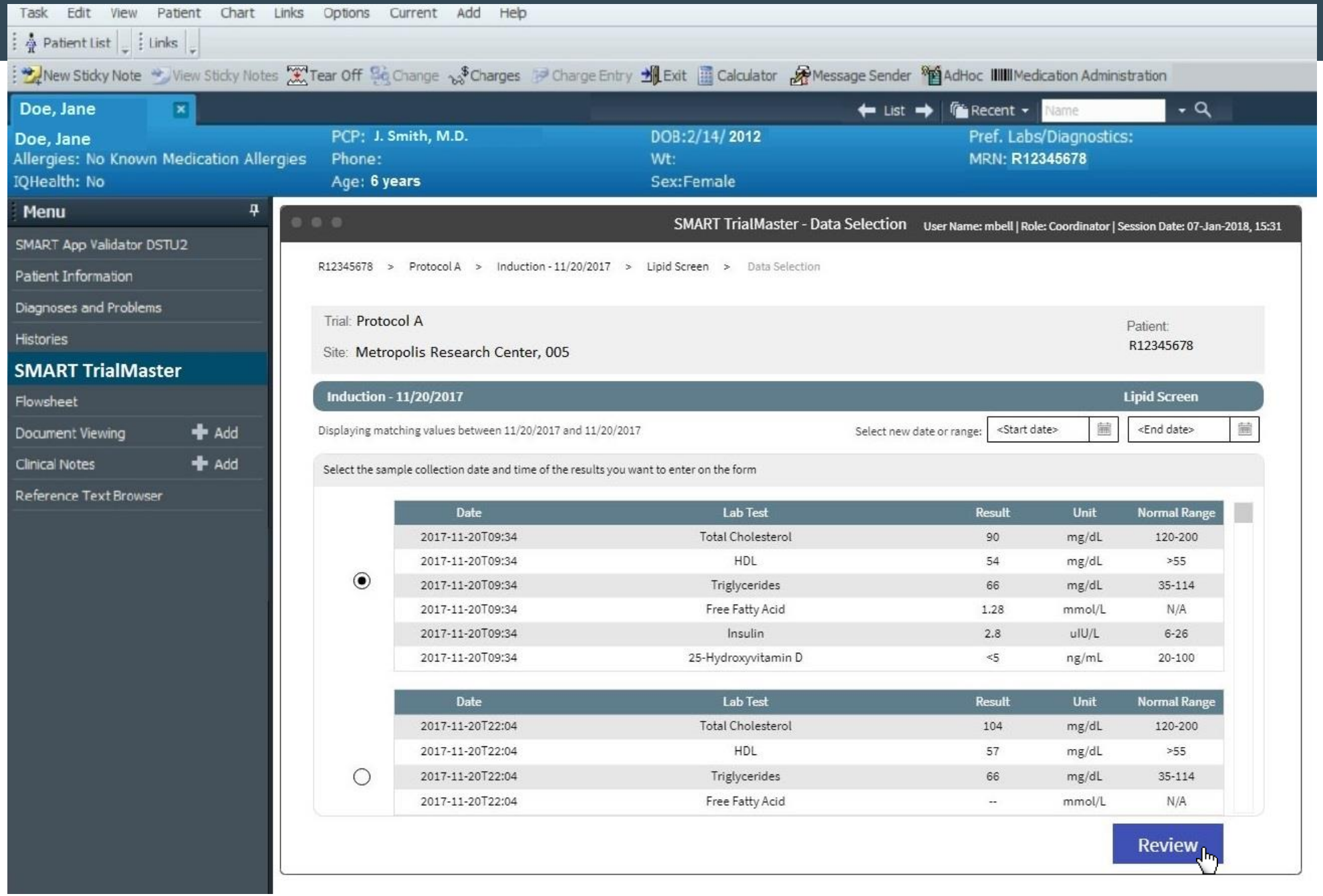

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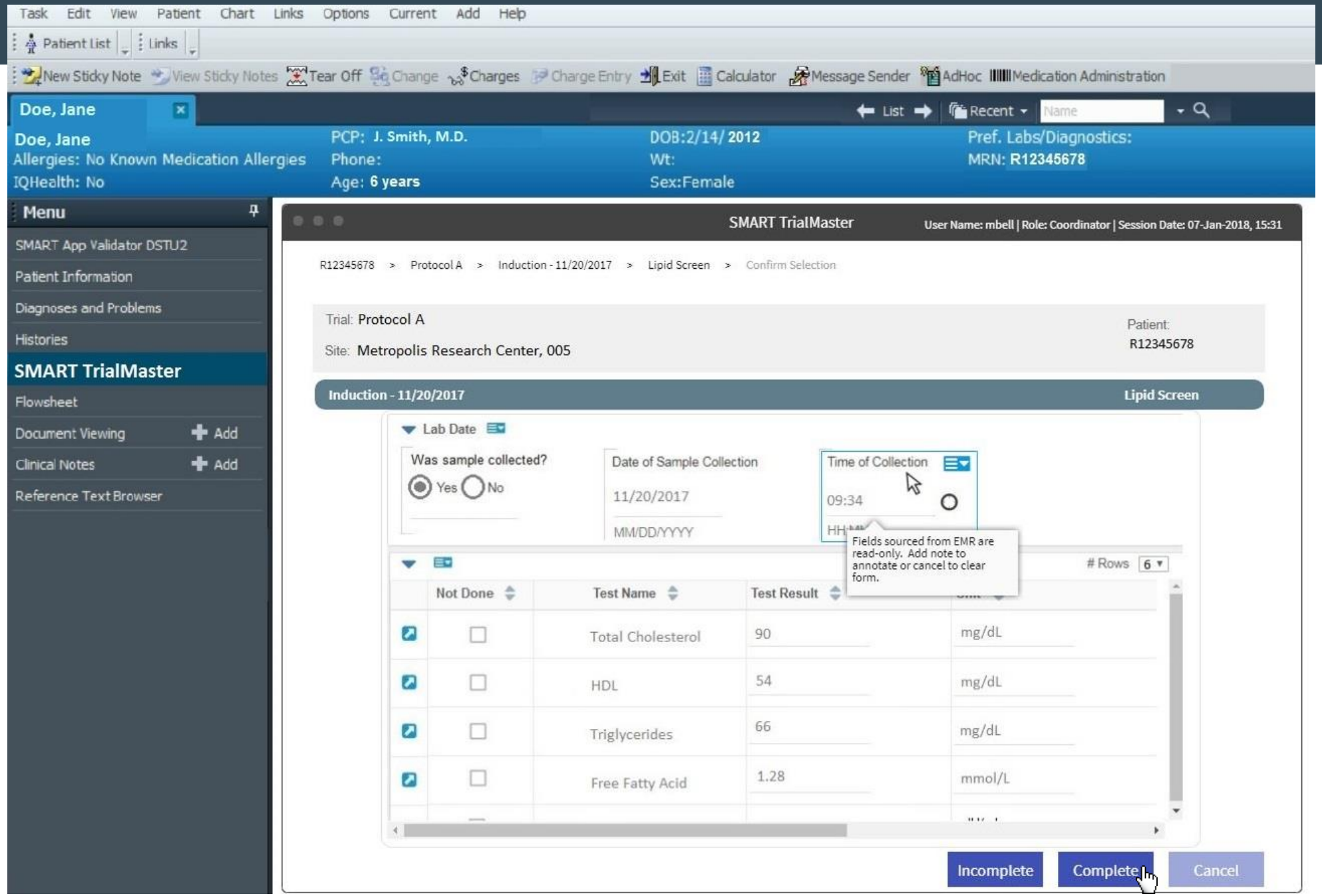

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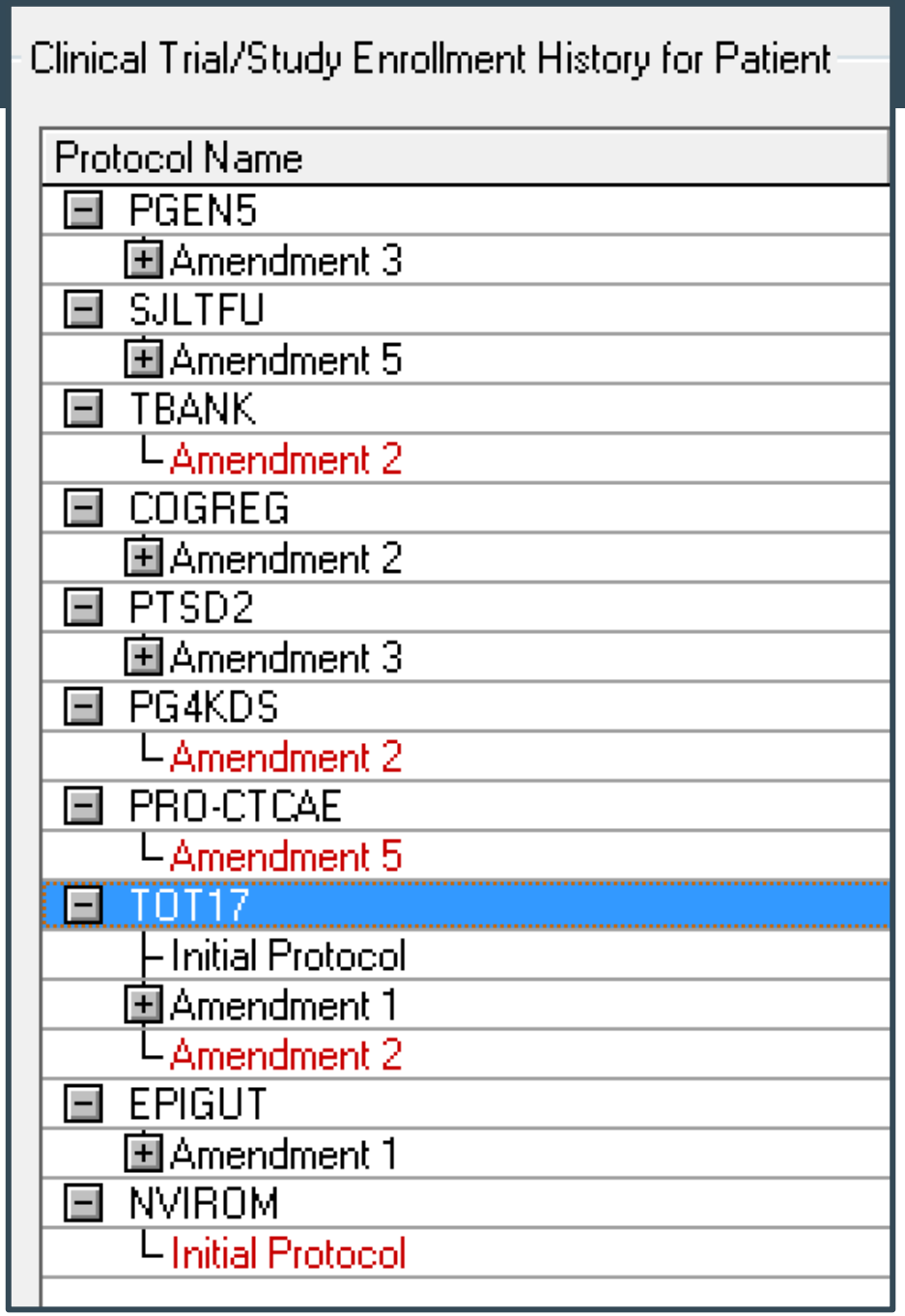
Impact of real-life on development of SMART app

- 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?



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 attendings 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
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 o
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 col
during your bone marrow procedure at diagnosis. The bone marrow will be sent to a lab
at St. Jude for sensitivity to anti-leukemia/lymphoma drugs. If no bone marrow is drawn
routine care, a blood sample drawn at the same time you are having blood drawn for rout
may be used in its place.

Please circle your answer: I agree to allow my bone marrow and blood to be used for dr
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?