Clinical Databases for Observational Research
Weill Cornell Medicine

Beginning
Data Collection

![Excel Spreadsheet]

<table>
<thead>
<tr>
<th>Accession#</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td>1600</td>
</tr>
<tr>
<td>O</td>
<td>1900</td>
</tr>
<tr>
<td>P</td>
<td>3000</td>
</tr>
<tr>
<td>R</td>
<td>6000</td>
</tr>
<tr>
<td>S</td>
<td>9000</td>
</tr>
<tr>
<td>T</td>
<td>12000</td>
</tr>
<tr>
<td>U</td>
<td>15000</td>
</tr>
<tr>
<td>V</td>
<td>18000</td>
</tr>
<tr>
<td>W</td>
<td>21000</td>
</tr>
<tr>
<td>X</td>
<td>24000</td>
</tr>
<tr>
<td>Y</td>
<td>27000</td>
</tr>
<tr>
<td>Z</td>
<td>30000</td>
</tr>
</tbody>
</table>

**Note:** The image shows a Microsoft Excel spreadsheet with various columns and data entries.
Outcome of Deferred Initial Therapy in Mantle-Cell Lymphoma

Peter Martin, Amy Chadburn, Paul Christos, Karen Weil, Richard R. Furman, Jia Ruan, Rebecca Elstrom, Ruben Niesvizky, Scott Ely, Maurizio DiLiberto, Ari Melnick, Daniel M. Knowles, Selina Chen-Kiang, Morton Coleman, and John P. Leonard

ABSTRACT

Purpose
Treatment of mantle-cell lymphoma (MCL) is nonstandardized, though patients are commonly treated immediately at diagnosis. Because data on observation, or “watch and wait,” have not been previously reported, we analyzed the outcome of deferred initial therapy.

Patients and Methods
Inclusion criteria in this retrospective analysis were a diagnosis of MCL between 1997 and 2007 and known date of first treatment. Hospital and research charts were reviewed for prognostic and treatment-related information. Date of death was derived from hospital records and confirmed using an online Social Security death index.
What I learned

Observational studies can yield powerful results.
Observational studies can foster collaboration between departments and between institutions.
Observational studies are useful when clinical trials are not practical.

Data collection can be painful.
Poor quality data can limit results.
Storing patient data on your computer is a violation of HIPAA.
A new beginning
What did we need to do better?

Hardware
• A computer and maybe some sort of server

Software
• For data entry, data storage, data reports

Process
• Work flow in the clinic
• Work flow for sample collection

Personnel
• Coordinators for patient consent, data entry, data retrieval
• Technicians/coordinators for biobanking
What kind of software can we use to store data?

caBIG
REDCap
GE PPM
Heme-Onc database
EPIC

We decided on a home-built solution

- Web-based/secure
- Rapidly customizable
- Data entry AND reporting function

\{ eCRFs/CTMS/EMR are NOT databases \}
Amazing things are happening here
What are we going to collect?
We need help!

History of the Mayo/Iowa Molecular Epidemiology Resource

• Population Science Project in first SPORE was funded as an R01
  – Based on a SEER cohort of NHL patients
  – NCI allowed a replacement project

• Replacement Project 5
  – Future direction in Original Project 5: use SPORE cohort of patients
  – Written and approved as a full population science project; NOGA in spring 2003

• “MER” in second and third SPORE
  – Research resource
  – Population science aim in Project 3 [germline DNA]
  – Population science project 4 [germline and tumor DNA]
What are we going to collect?
We need help

Mayo/Iowa Molecular Epidemiology Resource

Distribution of Patient Residence
<table>
<thead>
<tr>
<th>Name</th>
<th>Required</th>
<th>Type</th>
<th>Question</th>
<th>Choices</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>diagnosis_dt</td>
<td>Yes</td>
<td>DATE</td>
<td>Date of diagnosis</td>
<td></td>
<td>For all patients consented as of 7/1/2015: Date of diagnosis as indicated from positive biopsy results. Use the date (Date of Specimen, NOT Report) of first diagnostic test that shows evidence of disease, regardless of whether subtype is determined. E.g. If an FNA shows lymphoma, and an excisional bx is required to determine subtype, use FNA date. If an exact date of diagnosis cannot be found, keep conservative with the marked date. (For patients consented before 7/1/15, see previous data dictionary dated 9.28.2015).</td>
</tr>
<tr>
<td>sample1</td>
<td>No</td>
<td>CB</td>
<td>Surgical biopsy</td>
<td>Surgical biopsy</td>
<td>Removal of cells or tissue for examination by a pathologist. There are many different types of biopsy procedures. The most common types include: (1) incisional biopsy (removal of small amount of tissue/part of lymph node), in which only a sample of tissue is removed; (2) excisional biopsy (removal of lymph node or resection of involved area), in which an entire lump or suspicious area is removed.</td>
</tr>
<tr>
<td>sample2</td>
<td>No</td>
<td>CB</td>
<td>Core needle biopsy</td>
<td>Core needle biopsies can often be diagnostic. A sample of tissue, cells, or fluid is removed with a needle - often done in the brain or retroperitoneal tissue. Tissue is removed from the lymph node as a core (Hollow circular wide needle).</td>
<td></td>
</tr>
<tr>
<td>sample3</td>
<td>No</td>
<td>CB</td>
<td>Fine needle aspirate</td>
<td>Fine needle aspirate</td>
<td>FNA (Fine Needle Aspirate): A needle biopsy, in which a sample of tissue, cells or fluid is removed from lymph node with a thin needle.</td>
</tr>
<tr>
<td>sample4</td>
<td>No</td>
<td>CB</td>
<td>Bone marrow</td>
<td>Bone marrow</td>
<td>The removal of a sample of tissue from the bone marrow with the use of a needle. The sample is then examined under a microscope by pathology. (Aspirate or Biopsy)</td>
</tr>
<tr>
<td>sample5</td>
<td>No</td>
<td>CB</td>
<td>Fluid</td>
<td></td>
<td>Include pleural fluids, Spinal, Peritoneal, Pericardial and Synovial fluids.</td>
</tr>
<tr>
<td>sample7</td>
<td>No</td>
<td>CB</td>
<td>Other</td>
<td></td>
<td>Example - skin punch biopsy.</td>
</tr>
</tbody>
</table>
NEW PATIENT FLOW CHART

Study Coordinator completes screening of clinic list the week prior.

SC attends weekly Monday meeting to verify eligible new patients for the week.

Eligible New Diagnosis: Patient's lymphoma dx date is no more than 6 months prior to the date of consent; age ≥ 18.

SC emails mol. Path, nurses, and physicians about patients who will be seen in clinic.

SC prepares consent documents, study forms and specimen requirements (prep tubes).

Tubes: Plasma Citrate/Buffy Coat - Light blue top; Serum - Red top; EDTA (Plasma/Cellular Fraction) - Lavender top.

Eligible patients check in at front desk.

Receptionist gives patient general self-assessment form to complete. Receptionist scans document into medical records.

Patient proceeds to exam room.

Nurse (Alison or Susan) pages SC when patient checks in.

Physician sees patient and introduces coordinator.

Physician informs patient of study objectives, procedures, etc. Obtain informed consent.

Patient has study labs drawn by nurse. SC pages mol. path to notify them of upcoming sample.

Patient is given copy of consent form and study items for that day are complete.

Mol. path personnel processes and banks specimens according to protocol. Data is uploaded to lymphoma database.

SC brings specimens to mol. path to be processed and banked.

Patient goes home.

SC enters patient data (enrollment info, FACT-Lym, biospecimen info, on study and treatment info) into Lymphoma Database.

SC emails database listserver re: new patients weekly.

Investigator performs quality control.

SC continues fu with patients every 6 months (patient-reported fu, MD fu, FACT-Lym, subsequent treatments, etc.).
3/20/12: Why do we have so many databases???

Here is my idea:

A unified consent form for all patients seen in the Division of Hematology-Oncology.

It basically says we will collect and store your clinical data. We may contact you and/or your other physicians in the future. We may collect urine/blood/marrow/tissue. The above will be used for research. We can't predict what research it will be used for.

The idea would be that every patient that comes into the clinic would be given the consent form at their first visit at the same time as they receive the self-assessment form.

In lymphoma/CLL/WM, we have a coordinator that will see the patients at the end of the first visit to complete the informed consent process. Other services could do something similar or could just have the physician sign the consent. The ICF will be given to the secretaries and scanned into the medical records at the same time as the self-assessment form.

Advantages:
1) The front desk will give everyone the same form, so there's no chance for error there.
2) The database coordinators won't have to wait around to see the patients or talk with the patients quite as long as they do now.
3) Everyone is doing the same thing
4) Services without databases in existence yet will still be getting consent from patients, making it easier for them to create a database in the future
YOU CAN CATCH FLIES WITH HONEY BUT
YOU CATCH MORE HONEYS
BEIN’ FLY....
Universal Consent

• Initiated September 2013 in hematology and medical oncology
• Permitted to collect data, blood, bone marrow, cheek swab, and questionnaires
• Research only procedures handled with amendment and separate ICF

• This is a data collection study for the purpose of conducting future research. This is not THE research.
What can be collected?

Guidelines for Collection

• Questionnaires – may be administered no more than once per month

• Blood - may only be drawn at the time of other SOC labs; not to exceed 50 mL over 8 weeks

• Cheek swab – not to exceed what is deemed to be clinically safe

• Aspirate – may only be collected at the time of an SOC procedure
Everybody wants to be a bodybuilder

but don't nobody want to lift no heavy-ass weight!
Research Coordinators

- Identify/Recruit new participants
- Facilitate baseline blood collection
- Abstract clinical data
- Facilitate pathology review process
- Collect and enter patient reported follow-ups
- Verify and enter patient reported events
- Collect and abstract cause of death data
Personnel

- Allison Knutson – March 2010 to August 2012
- Tricia Ellis – February 2012 to January 2017
- Erica Bhavsar (CLL) – April 2012 to present
- Joshua Felsenfeld (CLL) – August 2015 to present
- Hannah Campbell – September 2015 to June 2017
- Arcania Garcia – February 2017 to present
- Channy Kong – May 2017 to present
Enrollment 2010-present

- 2010-2017
- 0 to 1800

Graph showing enrollment trends from 2010 to present, with a steady increase over the years.
Another new beginning
PAR-14-160: Core Infrastructure and Methodological Research for Cancer Epidemiology Cohorts (U01)

• The Funding Opportunity Announcement (FOA) invites grant applications for targeted infrastructure support of the core functions of Cancer Epidemiology Cohorts (CECs) and methodological research.

• Through this FOA, the National Cancer Institute (NCI) will support infrastructure and core functions for existing or new CECs.

• This FOA will also lead to support of core functions for CECs currently funded through other grant mechanisms by the Epidemiology and Genomics Research Program (EGRP) and other components of the Division of Cancer Control and Population Sciences (DCCPS) at the NCI.
Rationale: Data Gap

• Most studies of NHL outcomes are based on:
  – Small institutional clinical databases with no epidemiologic data or bank biospecimens; very long enrollment periods; most not prospective; many often do not have written consent.
  – Clinical trials of generally highly selected participants with a relatively short duration of follow-up; often lack biospecimens, particularly DNA (with appropriate consent); epi data or full range of survivorship outcomes; move to focus cooperative groups towards Phase I/II trials
  – Large etiology cohorts that conduct survivor studies of NHL generally lack meaningfully detailed clinical and treatment data, disease progression/relapse endpoints, patient-reported outcomes, and (variably) tumor tissue.
  – National database (e.g., SEER-Medicare) lack access to epidemiologic data, biospecimens, tissue, full range of outcomes; often restricted to certain populations (e.g., age 65+)
Goals

• Develop/maintain registry of newly diagnosed lymphomas
  – Clinical (including treatment) and pathology data
  – Epidemiological data
  – Follow up data
    • Patient reported
    • Validated against medical records

• Develop/maintain bank of serum/plasma, DNA, RNA
• Develop/maintain a bank of FFPE derived DNA/RNA extracted from subset of registry
• Develop/maintain tissue microarrays (TMAs) from formalin fixed paraffin embedded (FFPE) tissue
• Ability to link across information for project design and management
Figure B.3. Organizational Structure of LEO Cohort

Steering Committee
Study Pls: Cerhan, Friedberg, Flowers, Kahl, Link, Lossos, Martin, Nastoupil
Iowa/Mayo SPORE Pl/Co-Pl: Weiner, Witzig
NCI Representative (TBN)

External Advisory Board
Gilles Salles
Dennis Weisenburger
Lindsay Morton
Ben Haines (Patient Advocate)

NCI/CEC

Core A (Administration)
LEO Pls: Cerhan, Flowers
Coordinator: Lunde

Core B (Clinical)
Link, Habermann

Core C (Path & Biospec.)
Feldman, Jaye

Core D (Biostats & Inform.)
Slager

LEO Recruitment Centers:
Cornell
Emory/Grady
Mayo
MD Anderson
U. of Iowa
U. of Miami
U. of Rochester
U. of Wisconsin
Pathology Protocol – at LEO Center

At LEO Centers:
Coordinator organizes consented cases monthly (path report + completed path CRFs + slides)

At LEO Centers:
With coordinator, LEO Center Pathologist reviews case, verifies the WHO diagnosis, and reviews other relevant path variables, and picks a representative block (ranked 1-4)

At LEO Centers:
Coordinator enters pathology data into RAVE
At LEO DCC:
Quarterly manifests are made for each center

At LEO Centers:
Coordinator organizes consented cases monthly (path report + completed path CRFs + slides)

At LEO Centers:
With coordinator, LEO Center Pathologist reviews case, verifies the WHO diagnosis, and reviews other relevant path variables, and picks a representative block (ranked 1-4)

At LEO Path Core:
LEO Coordinator pulls and organizes blocks and sends to Mayo (logged in)

At LEO Path Core:
One 5μm cut for H&E

At LEO Path Core:
TMAs and Tubes to storage; Block returned to LEO site (within 45 days; no depletion)

At LEO Path Core:
Excisional: Four 1mm cores for two sister TMAs; Two 1mm cores for RNA extraction; Two 1mm cores for DNA extraction
Cores: up to ten 5μm sections

At LEO Path Core:
Feldman circles area for punches for excisional

At LEO Path Core:
Feldman reviews Path report, H&E and RAVE data to verify all in order

At LEO Centers:
Coordinator enters pathology data into RAVE
Data and Materials Use

Steering Committee will review and decide on acceptance or rejection of all requests for Cohort Data and samples for a Research Project on behalf of all LEO Cohort Collaborators who provided and/or generated the data and or samples requested

- For an approved research project, Mayo/LEO Cohort shall provide the data and/or samples requested under the terms of MOU.

- Once a research project is complete, data from the research project will be made available to the LEO Cohort Data Coordinating Center and stored in the LEO Cohort Database.
## Research Agenda: Topic Areas

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical endpoints:</strong></td>
<td>EFS, EFS24, transformation, OS, cause-specific survival</td>
</tr>
<tr>
<td><strong>Treatment:</strong></td>
<td>New treatments; subgroups; comparative effectiveness</td>
</tr>
<tr>
<td><strong>Additional Endpoints:</strong></td>
<td>CVD, PE/DVT, stroke, bone, healthy aging</td>
</tr>
<tr>
<td><strong>Patient Reported Outcomes:</strong></td>
<td>QoL, behavioral and psychosocial</td>
</tr>
<tr>
<td><strong>Epidemiologic predictors:</strong></td>
<td>BMI, statins, NSAIDs, metformin, smoking, alcohol, physical activity, diet (basic)</td>
</tr>
<tr>
<td><strong>Serum/Plasma:</strong></td>
<td>Proteomics, metabolomics, free DNA</td>
</tr>
<tr>
<td><strong>Tumor Markers:</strong></td>
<td>IHC, FISH, tumor/microenvironment</td>
</tr>
<tr>
<td><strong>Tumor (Somatic) Genomics:</strong></td>
<td>DNA, RNA, microRNA, epigenetic</td>
</tr>
<tr>
<td><strong>Host (Germline) Genetics:</strong></td>
<td>Predictive/prognostic, pharmacogenomics (including toxicity), second cancers, cardiovascular disease, other chronic diseases</td>
</tr>
<tr>
<td><strong>Basic Science:</strong></td>
<td>Biology of treatment response and early/aggressive disease</td>
</tr>
<tr>
<td><strong>Health Services Research:</strong></td>
<td>Cost, utilization, quality</td>
</tr>
</tbody>
</table>
Strengths and Limitations

• Large cohort of newly diagnosed lymphoma patients
• Good event-free and overall survival
  – Event = progression, retreatment, death
• Good at collecting standard clinical markers
  – Provided the institution is capturing it clinically
• Capturing treatment type, timing, over disease course
• Interaction between clinical data and coordinators
  – Database prompt for FU, clinical verification, etc.
• Incorporate research results into database
• Quality data
• Interactions with CTN (Alliance, SWOG, ECOG)

• Response data
  – Treated off trial, changing response criteria, not doing scan measurements
• Treatment data limited to start date, number of cycles
  – Collect stop date (define?)
  – Do not collect dosing data
  – Toxicity data messy in observational study and beyond scope
# Recruitment – By Center

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayo</td>
<td>329</td>
<td>28</td>
<td>36</td>
<td>25</td>
<td>29</td>
<td>36</td>
<td>36</td>
<td>30</td>
<td>23</td>
<td>22</td>
<td>23</td>
<td>35</td>
<td>27.4</td>
<td>29.5</td>
<td>2.1</td>
<td>632</td>
<td>84</td>
</tr>
<tr>
<td>UIowa</td>
<td>112</td>
<td>7</td>
<td>11</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>10</td>
<td>13</td>
<td>6</td>
<td>7</td>
<td>9</td>
<td>13</td>
<td>9.3</td>
<td>10.2</td>
<td>0.9</td>
<td>189</td>
<td>2</td>
</tr>
<tr>
<td>Cornell</td>
<td>106</td>
<td>8</td>
<td>12</td>
<td>13</td>
<td>18</td>
<td>14</td>
<td>4</td>
<td>15</td>
<td>7</td>
<td>16</td>
<td>23</td>
<td>15</td>
<td>8.8</td>
<td>13.7</td>
<td>4.9</td>
<td>237</td>
<td>60</td>
</tr>
<tr>
<td>URMC</td>
<td>154</td>
<td>0</td>
<td>21</td>
<td>10</td>
<td>15</td>
<td>18</td>
<td>10</td>
<td>6</td>
<td>11</td>
<td>18</td>
<td>16</td>
<td>11</td>
<td>12.8</td>
<td>13.6</td>
<td>0.8</td>
<td>271</td>
<td>14</td>
</tr>
<tr>
<td>Emory</td>
<td>225</td>
<td>0</td>
<td>16</td>
<td>14</td>
<td>20</td>
<td>15</td>
<td>18</td>
<td>13</td>
<td>9</td>
<td>18</td>
<td>10</td>
<td>8</td>
<td>18.8</td>
<td>14.1</td>
<td>-4.7</td>
<td>296</td>
<td>-79</td>
</tr>
<tr>
<td>MDACC</td>
<td>500</td>
<td>0</td>
<td>52</td>
<td>37</td>
<td>64</td>
<td>54</td>
<td>33</td>
<td>19</td>
<td>41</td>
<td>73</td>
<td>42</td>
<td>25</td>
<td>41.7</td>
<td>44.0</td>
<td>2.3</td>
<td>748</td>
<td>-85</td>
</tr>
<tr>
<td>Miami</td>
<td>220</td>
<td>0</td>
<td>12</td>
<td>8</td>
<td>24</td>
<td>12</td>
<td>24</td>
<td>12</td>
<td>11</td>
<td>10</td>
<td>20</td>
<td>13</td>
<td>18.3</td>
<td>14.6</td>
<td>-3.7</td>
<td>205</td>
<td>-162</td>
</tr>
<tr>
<td>WashU</td>
<td>100</td>
<td>0</td>
<td>13</td>
<td>11</td>
<td>12</td>
<td>10</td>
<td>16</td>
<td>16</td>
<td>14</td>
<td>13</td>
<td>8</td>
<td>7</td>
<td>8.3</td>
<td>12.0</td>
<td>3.7</td>
<td>189</td>
<td>22</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1746</strong></td>
<td><strong>43</strong></td>
<td><strong>173</strong></td>
<td><strong>128</strong></td>
<td><strong>193</strong></td>
<td><strong>171</strong></td>
<td><strong>151</strong></td>
<td><strong>124</strong></td>
<td><strong>122</strong></td>
<td><strong>177</strong></td>
<td><strong>151</strong></td>
<td><strong>127</strong></td>
<td><strong>145.5</strong></td>
<td><strong>151.7</strong></td>
<td><strong>6.2</strong></td>
<td><strong>2767</strong></td>
<td><strong>-143</strong></td>
</tr>
</tbody>
</table>
### Recruitment – Subtype/Race/Ethnicity

<table>
<thead>
<tr>
<th>Ethnicity/Race</th>
<th>DLBCL</th>
<th>FL</th>
<th>MCL</th>
<th>MZL</th>
<th>Other NHL</th>
<th>TCL</th>
<th>Comp</th>
<th>Unkn/ Missing</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Race/Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>74</td>
<td>42</td>
<td>16</td>
<td>21</td>
<td>32</td>
<td>20</td>
<td>10</td>
<td>1</td>
<td>216</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>652</td>
<td>450</td>
<td>183</td>
<td>177</td>
<td>337</td>
<td>161</td>
<td>66</td>
<td>66</td>
<td>2092</td>
</tr>
<tr>
<td>UKN/Not reported</td>
<td>7</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td></td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>Missing</td>
<td>34</td>
<td>28</td>
<td>15</td>
<td>15</td>
<td>20</td>
<td>21</td>
<td>1</td>
<td>18</td>
<td>152</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>767</td>
<td>525</td>
<td>216</td>
<td>214</td>
<td>393</td>
<td>203</td>
<td>78</td>
<td>86</td>
<td>2482</td>
</tr>
<tr>
<td>Am Indian/AK Native</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Asian</td>
<td>26</td>
<td>14</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>73</td>
</tr>
<tr>
<td>Native HI/Pac Island</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Black or AA</td>
<td>64</td>
<td>30</td>
<td>5</td>
<td>18</td>
<td>37</td>
<td>46</td>
<td>6</td>
<td>3</td>
<td>209</td>
</tr>
<tr>
<td>White</td>
<td>716</td>
<td>483</td>
<td>207</td>
<td>191</td>
<td>333</td>
<td>146</td>
<td>70</td>
<td>69</td>
<td>2215</td>
</tr>
<tr>
<td>Other/&gt;1 race</td>
<td>16</td>
<td>17</td>
<td>6</td>
<td>7</td>
<td>10</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>64</td>
</tr>
<tr>
<td>UKN/Not reported</td>
<td>8</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>28</td>
</tr>
<tr>
<td>Missing</td>
<td>47</td>
<td>39</td>
<td>16</td>
<td>15</td>
<td>23</td>
<td>22</td>
<td>2</td>
<td>8</td>
<td>172</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>878</td>
<td>593</td>
<td>242</td>
<td>240</td>
<td>417</td>
<td>229</td>
<td>84</td>
<td>84</td>
<td>2767</td>
</tr>
</tbody>
</table>
## LEO Refusal Rate by SITE

### As of April 4, 2017

Excludes CLL/SLL and HL Cases

<table>
<thead>
<tr>
<th>Site</th>
<th>N Consented</th>
<th>N Refused</th>
<th>N Approached</th>
<th>% Refused</th>
</tr>
</thead>
<tbody>
<tr>
<td>CORNELL</td>
<td>240</td>
<td>28</td>
<td>268</td>
<td>10.4</td>
</tr>
<tr>
<td>EMORY</td>
<td>297</td>
<td>33</td>
<td>330</td>
<td>10.0</td>
</tr>
<tr>
<td>IOWA</td>
<td>189</td>
<td>5</td>
<td>194</td>
<td>2.6</td>
</tr>
<tr>
<td>MAYO</td>
<td>634</td>
<td>51</td>
<td>685</td>
<td>7.4</td>
</tr>
<tr>
<td>MDA</td>
<td>752</td>
<td>7</td>
<td>759</td>
<td>0.9</td>
</tr>
<tr>
<td>MIAMI</td>
<td>206</td>
<td>6</td>
<td>212</td>
<td>2.8</td>
</tr>
<tr>
<td>URMC</td>
<td>272</td>
<td>7</td>
<td>279</td>
<td>2.5</td>
</tr>
<tr>
<td>WASHU</td>
<td>189</td>
<td>12</td>
<td>201</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2779</strong></td>
<td><strong>149</strong></td>
<td><strong>2928</strong></td>
<td><strong>5.1</strong></td>
</tr>
</tbody>
</table>
Weill Cornell Medicine

Middle
What can we do better?
Three very simple things:

1. Increase patients
   - Target more patients
   - Improve consent process
   - Improve regulatory processes
   - Improve data capture

2. Increase tissue
   - See point 1
   - Increase in-house open biopsies
   - Acquire outside tissue
   - Do more with less

3. Improve sustainability
   - Find new sources of funding
Increase patients

• Expand eligibility to all patients with lymphoma
  • Not just new diagnosis
• Target all patients with diagnosis made at WCM
  • Not just Lymphoma Program
• Enroll at other NYP/WCM centers
  • Will start at NYP-M in July
• Recruit more patients to come to WCM and Lymphoma Program
  • Retain patients from WCM
  • Market directly to patients
  • Outreach to referring physicians
Increase patients

• Improve consent process
  • Not currently feasible to consent all

• Improve regulatory process
  • Not currently feasible to register all

• Improve data capture
  • Modify EMR to facilitate export
  • New software to simplify collection
  • Have patients enter data directly
Increase tissue

- Increase in-house biopsies
  - See more patients without a diagnosis
  - Send more patients for biopsies
  - Coordinate collection with Surgery/Pathology

- Acquire outside tissue
  - Not just Lymphoma Program

- Do more with less
  - Develop tests/platforms that can use less tissue and/or more accessible tissues
Improve sustainability

- Find new sources of funding
  - Dedicated philanthropy
  - Institutional support
  - Grant support
  - Charge for data/tissue?
  - Industry partnerships?
Has it been worth it so far?
Use of WCM data and tissue

Race/ethnicity data for multiple grants
• SPORE, P01, U01

Six publications

Biological specimens
• 5255 collected so far, 565 distributed to at least 25 investigators

Clinical data
• I’m not sure how many groups have received data
A retrospective study

CLINICAL TRIALS AND OBSERVATIONS

Postibrutinib outcomes in patients with mantle cell lymphoma

Peter Martin,1 Kami Maddocks,2 John P. Leonard,1 Jia Ruan,1 Andre Goy,3 Nina Wagner-Johnston,4 Simon Rule,5 Ranjana Advani,6 David Iberri,6 Tyce Phillips,7 Stephen Spurgeon,8 Eliana Kozin,9 Katherine Noto,1 Zhengming Chen,9 Wojciech Jurczak,10 Rebecca Auer,11 Ewa Chmielowska,12 Stephan Stilgenbauer,13 Johannes Bleehen,13 Craig Portell,14 Michael E. Williams,14 Martin Dreyling,15 Paul M. Barr,16 Selina Chen-Kiang,17 Maurizio DiLiberto,17 Richard R. Furman,1 and Kristie A. Blum2

1Department of Medicine, Weill Cornell Medical College, New York, NY; 2Ohio State University Comprehensive Cancer Center, Columbus, OH; 3Hackensack University Medical Center, Hackensack, NJ; 4Division of Oncology, Washington University School of Medicine, St. Louis, MO; 5Department of Haematology, Plymouth University Peninsula Schools of Medicine and Dentistry and Derriford Hospital, Plymouth, United Kingdom; 6Stanford Cancer Institute, Stanford, CA; 7Department of Internal Medicine, University of Michigan, Ann Arbor, MI; 8Center for Hematologic Malignancies, Oregon Health and Science University, Portland, OR; 9Department of Healthcare Policy and Research, Weill Cornell Medical College, New York, NY; 10Department of Hematology, Jagiellonian University, Krakow, Poland; 11St. Bartholomew’s Hospital, London, United Kingdom; 12Odzia Kliniczny Onkologi, Bydgoszcz, Poland; 13Universitätsklinik Ulm, Ulm, Germany; 14University of Virginia Cancer Center, Charlottesville, VA; 15Klinikum der Universität München, Munich, Germany; 16Department of Medicine, University of Rochester Medical Center, Rochester, NY; and 17Department of Pathology, Weill Cornell Medical College, New York, NY

Despite unprecedented clinical activity in mantle cell lymphoma (MCL), primary and acquired resistance to ibrutinib is common. The outcomes and ideal management of patients who experience ibrutinib failure are unclear. We performed a retrospective cohort study of all patients with MCL who experienced disease progression while receiving ibrutinib across 15 international sites. Medical records were evaluated for clinical characteristics, pathological and radiological data, and therapies used pre- and postibrutinib. A total of 114 subjects met eligibility criteria. The median number of prior therapies was 3 (range, 0-10). The Mantle Cell Lymphoma International Prognostic Index (MIPI) scores at the start of ibrutinib were low, intermediate, and high in 46%, 31%, and 23% of patients, respectively. Of patients with available data prior to ibrutinib and postibrutinib, 34 of 47 and 11 of 12 had a Ki67 >30%. The median time on ibrutinib was 4.7 months (range 0.7-43.6). The median overall survival (OS) following cessation of ibrutinib was 2.9 months (95% confidence interval [CI], 1.6-4.9). Of the 104 patients with data available, 73 underwent subsequent treatment an average of 0.3 months after stopping ibrutinib with a median OS of 5.8 months (95% CI, 3.7-10.4). Multivariate Cox regression analysis of MIPI before postibrutinib treatment, and subsequent treatment with bendamustine, cytarabine, or lenalidomide failed to reveal any association with OS. Poor clinical outcomes were noted in the majority of patients with primary or secondary ibrutinib resistance. We could not identify treatments that clearly improved outcomes. Future trials should focus on understanding the mechanisms of ibrutinib resistance and on treatment after ibrutinib. (Blood. 2016;127(12):1559-1563)
However …

The common rule is changing:

Generally require informed consent for the use of stored biospecimens in secondary research (for example, part of a blood sample that is left over after being drawn for clinical purposes), even if the investigator is not being given information that would enable him or her to identify whose biospecimen it is. That consent would generally be obtained by means of broad consent (i.e., consent for future, unspecified research studies) to the storage and eventual research use of biospecimens.
Conclusions
Conclusions

This is way bigger than I had imagined

• This work has an impact on everyone from basic to clinical scientists
• This is going to be important as we build epidemiology
• This requires collaboration across multiple programs, multiple departments

This is more expensive than I had imagined

• 4 coordinators, support from biobank, and we are still behind

This is a lot less successful (on the surface) than I had imagined

• Lymphoma is incredibly diverse and not always obvious
• There will always be holes in data and tissue collection
• Think of a number and divide it by 3

We are way ahead of the game and need to keep up the momentum

• The changes to the common rule are going to hit everyone hard. We are uniquely prepared.
• Now is the time to push to expand.
Before developing your own database, think about three key ingredients

• Clinical Question
  – Listen to the learners
  – Don’t root for an answer – root for the truth
  – Greatest potential in refining important questions

• Clinical Database
  – Utilize a pre-existing database
  – Build your own

• Tools for interrogating
Acknowledgments

- Erica Bhavsar
- Hannah Campbell
- Joshua Felsenfeld
- Arcania Garcia
- Channy Kong
- Alicia Lewis
- Irene Karpenko
- James McConnell
- John Leonard
- Richard Furman
- Jia Ruan
- Sarah Rutherford
- John Allan
- Kristie Richards
- Lisa Roth
- Melnick lab
- Cerchietti lab
- Chen-Kiang lab
- Elemento lab
- Landau lab
- Hassane lab
- Ighirami lab
Q&A

QAU Contact Information

E-mail: JCTOQAU@med.cornell.edu