Welcome & Introductions

Dr. Brander’s slides are available for download at www.LLS.org/programs

Living with Chronic Lymphocytic Leukemia (CLL)

Danielle M. Brander, MD
Assistant Professor, Division of Hematologic Malignancies & Cellular Therapy
CLL & Indolent Lymphomas Team Leader
Duke Cancer Institute
Durham, NC
Disclosures

Danielle M. Brander, MD, has affiliations with AbbVie, Genentech, Gilead, Pharmacyclics, and Teva Pharmaceuticals (Consultant).

Disclosures (2)

- Content is presented and referenced to the best of our knowledge
- In order to teach to a broad audience, generalizations on CLL are made. However, CLL can vary greatly person to person, and the details of a patient’s CLL are critically important in specific recommendations – I encourage discussion with your doctor if questions arise.
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In the Era of Novel Treatments:

- Even with high risk del17p, patients treated with ibrutinib did well
- Other studies also support that traditional markers in CLL not as predictive in the modern era of treatment options with ibrutinib
**Leukemia in the US: 2016 Diagnoses**

60,140 new cases

- CML: 8,220 (14%)
- ALL: 6,590 (11%)
- CLL: 18,960 (32%)
- AML: 19,950 (33%)
- other: 6,420 (10%)

**NHL in the US: Subtypes**

NHL ~65,000+/year

- B-cell (85%)
- T-cell


7/12/2017
NHL in the US: Subtypes

NHL ~65,000+/year

B-cell (85%)

- Indolent (30-40%)
  - SLL/CLL
  - Follicular (FL)
  - Marginal zone (MZL)
  - Lymphoplasmacytic (LPL)

- Aggressive/Highly Aggressive (60-70%)
  - DLBCL
  - Mantle Cell (MCL)
  - Burkitt

T-cell

US Epidemiology:
- Incidence: ~19,000/year
- US Prevalence: ~130,000 cases
- Median age at diagnosis: 71 years
- Male to female ratio: 2 to 1
- Immunophenotype (CD5+ CD10- CD23+)
  - Differential (FISH)

Chronic Lymphocytic Leukemia

Siegel et al. CA Cancer J Clin. 2015;65(3).
**CLL diagnosis: phenotype**

- Immunophenotype
  - Blood
  - Lymph node Biopsy
  - Bone marrow bx (rarely)

- Generalization for "typical CLL"

- Monoclonal B-cell (light chain restricted)
- CD5+
- CD19+
- CD20 (dim), CD22 (dim), sIg(dim)
- CD23+ (bright)

---

**T-cell marker**

**B-cell markers**

* Generalization for "typical CLL"
**CLL diagnosis: phenotype**

- **Immunophenotype**
  - monoclonal B-cell (light chain restricted)
  - CD5+
  - CD19+
  - CD20 (dim), CD22 (dim), sIg(dim)
  - CD23+(bright)
- **Distinguish from mantle cell lymphoma (MCL)**
  - immunophenotype
  - FISH: t11;14
  - Cyclin D1

* Generalization for “typical CLL”

---

**CLL vs. SLL vs. MBL**

- **CLL**
  - At least $5 \times 10^9$ monoclonal Bcells/L*
  - May or may not be symptomatic
  - Small lymphocytic lymphoma
  - $< 5 \times 10^9$ mBcells/L*
  - + symptoms, cytopenias, LAD, or splenomegaly

* some variation in definition of malignant vs Bcells
**CLL vs. SLL vs. MBL**

**CLL**
- At least $5 \times 10^9$ monoclonal Bcells/L*
- May or may not be symptomatic

**SLL**
- Small lymphocytic lymphoma
- $< 5 \times 10^9$ mBcells/L*
- + symptoms, cytopenias, LAD, or splenomegaly

**MBL**
- Monoclonal B-cell lymphocytosis
- $< 5 \times 10^9$ mBcells/L*
- No symptoms, cytopenias, LAD or splenomegaly
- 1-2%/yr progress to CLL
- 2.5-5% or more of the population

* some variation in definition of malignant vs Bcells

**CLL: Dynamic Monitoring vs Treatment**

- Rationale against treatment on diagnosis for asymptomatic patients
CLL: Dynamic Monitoring vs Treatment

- Rationale against treatment on diagnosis for asymptomatic patients

Rationale on asymptomatic early therapy

1. CLL is treatable, but not curable*
1. CLL is treatable, but not curable*

2. Studies of treatment at diagnosis vs. treatment on indications: no difference in survival

3. Not all patients will require treatment and all treatments have some side effects
Rationale on asymptomatic early therapy

1. CLL is treatable, but not curable*

2. Studies of treatment at diagnosis vs. treatment on indications: no difference in survival

3. Not all patients will require treatment and all treatments have some side effects

4. After treatment, the CLL can come back with more aggressive cells ("clonal evolution")

Treatment indications: Risks vs. Benefits
CLL/SLL: Indications for treatment

- Confirm persistent!

**Disease Symptoms**
- Fatigue
- Night Sweats
- Weight Loss
- + Affecting quality of life

**Cytopenias**
- Platelets <100
- Hgb <11
- Ref autoimmune complications

**Bulky Disease**
- LAD
  - symptomatic
  - >9-10cm
- Splenomegaly
  - symptomatic
  - 6cm+ on exam
- Rapid WBC increase*
  - Doubling (over 30K) <6mo

*No magic WBC threshold in the iwCLL indications!!*
## Traditional Prognostics: Staging Systems

### Rai Findings

<table>
<thead>
<tr>
<th>Stage</th>
<th>Findings</th>
<th>Survival (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Lymphocytosis only</td>
<td>&gt; 120</td>
</tr>
<tr>
<td>I</td>
<td>Lymphocytosis + lymphadenopathy</td>
<td>95</td>
</tr>
<tr>
<td>II</td>
<td>Lymphocytosis + &gt; spleen and/or liver</td>
<td>72</td>
</tr>
<tr>
<td>III</td>
<td>Lymphocytosis + anemia (Hgb &lt; 11.0 g/dL)</td>
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</tr>
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### Binet Findings

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<tr>
<td>A</td>
<td>Hgb ≥ 10, Plts ≥ 100, &lt; 3 involved areas*</td>
<td>&gt; 120</td>
</tr>
<tr>
<td>B</td>
<td>Hgb ≥ 10, Plts ≥ 100, ≥ 3 involved areas*</td>
<td>84</td>
</tr>
<tr>
<td>C</td>
<td>Hgb &lt; 10, or Plts &lt; 100</td>
<td>24</td>
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*Involved areas include cervical, axillary, or inguinal nodes, spleen, or liver.


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## Traditional Prognostics: Staging Systems

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<td><strong>Low risk (Rai 0): &gt; 10 years</strong></td>
</tr>
<tr>
<td>I</td>
<td>Lymphocytosis + lymphadenopathy</td>
<td><strong>Intermediate risk (Rai 1/2): 5-7 years</strong></td>
</tr>
<tr>
<td>II</td>
<td>Lymphocytosis + &gt; spleen and/or liver</td>
<td><strong>High risk (Rai 3/4): 1-3 years</strong></td>
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Treatments and supportive care available very different today

Understanding CLL Heterogeneity

Characterization of CLL Heterogeneity

Understanding CLL Heterogeneity

Characterization of CLL Heterogeneity

Markers Do NOT change need/indications for treatment

IGHV mutational status


Kipps et al. Nat Rev Dis Primers. doi:10.1038/nrdp.2016.96
FISH

- **Late 1980-1990s**: FISH (interphase)

### Table: Chromosome Abnormalities

<table>
<thead>
<tr>
<th></th>
<th>Chromosome banding</th>
<th>Interphase cytogenetics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Trisomy 12</td>
<td>112</td>
<td>19</td>
</tr>
<tr>
<td>Structural 13q aberrations</td>
<td>62</td>
<td>10</td>
</tr>
<tr>
<td>Structural 11q aberrations</td>
<td>49</td>
<td>8</td>
</tr>
<tr>
<td>Structural 6q aberrations</td>
<td>36</td>
<td>6</td>
</tr>
<tr>
<td>Structural 17p aberrations</td>
<td>22</td>
<td>4</td>
</tr>
</tbody>
</table>

(Brief) Summary of Genomic/Molecular Prognostic Factors

- **FISH defects**
  - 17p deletion
  - 11q deletion
  - 12q trisomy
  - Normal
  - 13q deletions

Hierarchy:

- Unfavorable
- Favorable
(Brief) Summary of Genomic/Molecular Prognostic Factors

- **FISH defects**
  - 17p deletion
  - 11q deletion
  - 12q trisomy
  - Normal
  - 13q deletions

- **Immunoglobulin heavy chain variable region (IGHV)**
  - ≤ 2% mutation = unmutated
  - Unmutated: higher risk

- **CD38 status (≥ 30% = higher risk)**
- **ZAP-70 status (≥ 20% = higher risk)**

Often included with flow but IGHV more important and less variable
Responses *IGHV UM* and novel agents - ibrutinib

- Mutated *IGHV* (n=12)
- Unmutated *IGHV* (n=69)

* Included all previously treated patients (median 4 prior)


Responses and Progression rates for patients with CLL & TP53 dysregulation

Rossi et al. Leukemia & Lymphoma. DOI: 10.1080/10428194.2016.1250264
Responses and Progression rates for patients with CLL & TP53 dysregulation

Responses

Progression free at 12 months

Low frequency of FISH/IGHV testing

  - First line (n=889)
  - Second line (n=260)

<table>
<thead>
<tr>
<th>Test</th>
<th>% tested (first line)</th>
<th>% tested (2nd line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metaphase cytogenetics</td>
<td>39%</td>
<td>31.2%</td>
</tr>
<tr>
<td>FISH</td>
<td>58%</td>
<td>40.4%</td>
</tr>
<tr>
<td>IGHV</td>
<td>7.9%</td>
<td>5%</td>
</tr>
</tbody>
</table>
Summary: diagnosis & initial work up

- Flow cytometry
- Laboratory testing
  - CBC, CMP
  - LDH
  - B2M
  - FISH
  - IGHV mutation analysis
  - Others by case (if need treatment: TP53 mutation and full chromosome analysis)

• Imaging
  - Not needed for most patients
    - High risk
    - symptoms

• Bone marrow
  - Not needed unless for low counts or would change treatment recommendations
Highlights of CLL Treatment Options

Clinical Trials!
**Brief History - CLL**

**Approved Treatment Options**

<table>
<thead>
<tr>
<th>Period</th>
<th>1950s/60s</th>
<th>1970s</th>
<th>1980s</th>
<th>1990s</th>
<th>2000s</th>
<th>2010s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alkylating agents - chlorambucil - cyclophosphamide</td>
<td>Purine nucleosides - fludarabine - pentostatin - cladribine</td>
<td>Purine nucleosides and alkylators rituximab</td>
<td>Chemo-immunotherapy (FCR, FR, BR)</td>
<td>obinutuzumab + chlorambucil</td>
<td>BCR inhibitors idelalisib BCL2 inhibitor venetoclax</td>
</tr>
<tr>
<td></td>
<td>5% CR 30-50% ORR</td>
<td>20-30% CR 50-80% ORR</td>
<td>35% CR 75-90% ORR</td>
<td>40-70% CR 90-95% ORR</td>
<td>Variable CR &amp; ORR</td>
<td></td>
</tr>
</tbody>
</table>

**CLINICAL TRIALS**

- Immunotherapy
- Allo HSCT

### Treatment Basics: Chemotherapy vs Targeted Agents

**IV – intravenous**

- **FCR** = Fludarabine + Cyclophosphamide + Rituximab
  - Monday, Tuesday, Wednesday, Thursday, Friday, Saturday
  - For 4-6 total cycles

- **BR** = Bendamustine + Rituximab
  - Monday, Tuesday, Wednesday, Thursday, Friday, Saturday
  - For 4-6 total cycles

- **G-Clb = chlorambucil + obinutuzumab (G)**
  - Monday, Tuesday, Wednesday, Thursday, Friday, Saturday
  - For 4-6 total cycles

**PO – by mouth**

- **ibrutinib**
  - Monday, Tuesday, Wednesday, Thursday, Friday, Saturday
  - Targets BTK

- **idelalisib + rituximab**
  - Monday, Tuesday, Wednesday, Thursday, Friday, Saturday
  - Targets PI3Kdelta
  - Specific rituximab schedule (limited)

- **venetoclax**
  - Monday, Tuesday, Wednesday, Thursday, Friday, Saturday
  - Targets BCL2
  - Dose ramp up (5 weeks)
  - Sometimes given with anti-CD20 antibody

Targeted drug given continuously unless not tolerated or resistance develops.
Treatment Basics: Other Terminology

iwCLL Responses
• Complete Response (CR)
• Partial Response (PR)
• Partial Response + lymphocytosis (PR-L)*
• Stable Disease (SD)
• Progressive Disease (PD)

Duration of Response & Survival
• Progression Free Survival (PFS)
• Overall Survival (OS)

Rationale for frontline chemoimmunotherapy (CIT): durable remissions for some patients

FCR
• MDACC: 300pts received treatment with FCR
  ▫ Plateau in PFS: no relapses beyond 10.4 years in 42 patients with favorable risk (mutated IGHV, no del17p or del11q)

• Similar plateau in CLL8 and Rossi et al FCR studies
**Rationale for frontline chemoimmunotherapy (CIT): durable remissions for some patients**

**Bendamustine and Rituximab**

- **CLL10 (FCR vs BR frontline): 561 randomized**
  - Severe infections all pts: 39.8% vs. 25.4% (NS)
  - Infections older pts: 48.4% vs. 26.8% (p=.001)
  - PFS: NS difference in age > 65yo
  - M-IGHV improved PFS, no interaction with treatment type
  - No difference in OS to date

![Graphs showing progression-free survival](image)


---

**Anti-CD20 antibodies: obinutuzumab (G)**

- 781 CLL, treatment naive
- Randomized 1:1:1
- Median PFS advantage (R-Clb vs G-Clb 15.2 vs 26.7 mo)

![Graphs showing response rates](image)

Chemoimmunotherapy (CIT): Considering the Toxicities

Addressing risks

- Support cytopenias: can recover without complications
  - In long term follow of CLL8, prolonged cytopenias did not translate to increased MDS/AML
- Assessing DAT positivity
  - AIHA in 8% DAT-neg patients; 28% DAT-positive patients
- Prophylaxis for infections


Blood. 2008; 112: 975-980.
**TP53 mutation and del17p**

- Percentage of patients with TP53 mutation and not del17p

---

**Resend FISH, chromosomes, TP53 mutation if CLL relapses!**

- Percentage of patients with TP53 mutation and not del17p
FDA approved in:
1. CLL (all)
2. Waldenstrom’s Macroglobulinemia
3. MCL
4. MZL

ibrutinib in CLL

- Phase Ib/II expansion in CLL/SLL (85 pts; high risk!)
  - Daily dosing of ibrutinib (420mg, 840mg in 34 patients)
  - ORR 71%, plus 15-21% achieved PR-L
  - At 26 months, OS was 83%
- Phase III ibrutinib vs ofatumumab led to approval

**ibrutinib in frontline CLL**

Frontline Ibrutinib Monotherapy

- 31 patients
- Age > 65 years
- Responses: 71% ORR, and 13% PR with lymphocytosis

![Graph showing progression-free survival over time](image)


---

**ibrutinib in CLL: extended follow up**

- Responses continuous, although...
  - Time to best response, median: 7.4 mo (1.7-42.5 mo)
  - Time to CR, median: 21.2 mo (4.6-42.5)
- ORRs very high, but...
  - TN: 84% (23% CR)
  - R/R: 90% (7% CR)

-Blood. 2015;125:2497.
ibrutinib in CLL: extended follow up

- Responses continuous, although...
  - Time to best response, median: 7.4 mo (1.7 - 42.5 mo)
  - Time to CR, median: 21.2 mo (4.6 - 42.5)

- ORRs very high, but...
  - TN: 84% (23% CR)
  - R/R: 90% (7% CR)

- Many do well, but...
  - discontinuations

Best responses take time

CR rates low
ibrutinib in CLL: extended follow up

- Responses continuous, although...
  - Time to best response, median: 7.4 mo (1.7 - 42.5 mo)
  - Time to CR, median: 21.2 mo (4.6 - 42.5)

- ORRs very high, but...
  - TN: CR rates low
  - R/R: discontinuations

- Many do well, but...
  - discontinuations

"Other events" more common reason for discontinuation

Putting it together for Frontline CLL treatment in US: Young (≤65 yo) & fit

- Suitable for systemic therapy: YES
- Clinical trial available & eligible?: YES
- Clinical trial encouraged

- TP53 (other high risk features): No
- BCR inhibitor (ibrutinib based): YES
- HDMP + rituximab

- FCR (especially if M-IGHV, non del17p/11q): NO
- ibrutinib

- Questions: Role of allo HSCT Anti-CD20s
- Questions: IGHV mutation status to make treatment decisions (favor yes)
Frontline CLL in US: >65/70 yo OR any age with renal impairment +/- co-morbidity (90% of all CLL)

Suitable for systemic therapy: YES
Clinical trial available & eligible?: YES
Clinical trial encouraged: YES

No TP53 (other high risk features): YES
BCR inhibitor (ibrutinib based): HDMP + R

Fit?: YES

BR obinutuzumab-chlor ibrutinib
rituximab or ofatumumab + chlor

No: NO

Other?: YES

TP53 (other high risk features): NO
BCR inhibitor (ibrutinib based): HDMP + R

Fit?: NO

Other?: NO

Targeting BCR Signaling: PI3K pathway

- FDA approved for
  1. Relapsed/Refractory CLL (if R alone appropriate)
  2. 3rd line FL
  3. 3rd line SLL

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**Idelalisib**

- Phase III randomized, placebo controlled, rel/ref CLL
  - 220 pts, R +/- idelalisib
  - PFS: 93% vs 46% at 24 wks
  - OS: 92% vs 80% at 52 weeks

Who needs to stop?

Targeting anti-apoptosis with Bcl-2 inhibition

FDA approved for 1. previously treated del17p CLL
venetoclax

• High single agent responses in high risk patients
  ▫ Includes bone marrow CRs

CLL frontline or relapsed/refractory treatments: considering toxicities

Toxicity varies by regimen
• Cytopenias
• Infections
• Autoimmune complications
• Clonal evolution
• Second Malignancies including MDS/AML

chemoimmunotherapy

ibrutinib
bleeding risks
  ▫ phase I/II Studies: ICH: 2%
  ▫ followup (3yr): 7% gr 3
cardiiovascular risks
  ▫ a fib: range up to 16%
  ▫ HTN
other
  ▫ GI/diarrhea
  ▫ rash
  ▫ arthralgia/arthritis
  ▫ infections

venetoclax
tumor lysis
  ▫ Can be rapid
  ▫ dose ramp up & hospitalization needs
cytopenias (gr ³4)
  ▫ neutropenia (41%)
  ▫ anemia (12%)
  ▫ thrombocytopenia (12%)
other (all grades)
  ▫ diarrhea (52%)
  ▫ nausea (47%)
  ▫ fatigue (40%)

idelalisib
• cytopenias
• LFT abnormalities
• colitis (diarrhea)
• pneumonitis
• drug-drug (CYP3A)
• infections
**CLL frontline or relapsed/refractory treatments: considering toxicities**

**chemoimmunotherapy**

Toxicity varies by regimen
- Cytopenias
- Infections
- Autoimmune complications
- Clonal evolution
- Second Malignancies including MDS/AML

### ibrutinib

**bleeding risks**
- phase I/II Studies: ICH: 2%
- followup (3yr): 7% gr 3

**cardiovascular risks**
- a fib: range up to 16%
- HTN

**other**
- GI/diarrhea
- rash
- arthralgia/arthritis
- infections

### idelalisib

- cytopenias
- LFT abnormalities
- colitis (diarrhea)
- pneumonitis
- drug-drug (CYP3A)
- infections

### venetoclax

**tumor lysis**
- Can be rapid
- dose ramp up & hospitalization needs

**cytopenias (gr 3)**
- neutropenia (41%)
- anemia (12%)
- thrombocytopenia (12%)

**other (all grades)**
- diarrhea (52%)
- nausea (47%)
- fatigue (40%)

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**ibrutinib and idelalisib: understanding toxicity**

**Table 3. Most common reasons for kinase inhibitor (KI) discontinuation in patients who have discontinued ibrutinib or idelalisib.**

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<tr>
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<th>ibrutinib</th>
<th>Idelalisib</th>
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<tbody>
<tr>
<td>Toxicity</td>
<td>51% (n=73)</td>
<td>52% (n=18)</td>
</tr>
<tr>
<td>CLL Progression</td>
<td>28% (n=40)</td>
<td>31% (n=11)</td>
</tr>
<tr>
<td>Richter’s transformation</td>
<td>8% (n=11)</td>
<td>6% (n=2)</td>
</tr>
<tr>
<td>Cellular therapies (CAR T cells or allogeneic SCT)</td>
<td>2% (n=3)</td>
<td>0% (n=0)</td>
</tr>
<tr>
<td>Unrelated death / Other</td>
<td>11% (n=16)</td>
<td>11% (n=4)</td>
</tr>
</tbody>
</table>

*note this are reasons for discontinuation, not discontinuation rates
*KI=kinase inhibitor (ibrutinib and idelalisib)*
Ibrutinib Outcomes with Adherence

Dose Intensity (DI)

Progression-free survival, %

- ≥ % Mean DI
- < % Mean DI

<table>
<thead>
<tr>
<th>Median PFS, mo</th>
<th>≥ % Mean Dose Intensity</th>
<th>&lt; % Mean Dose Intensity</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR</td>
<td>6.9</td>
<td>0.0127</td>
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Months

Barr et al. 2017;129:2612

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Treatment with alternate KIs

A

PFS From Start of Alternate KI

B

PFS by Discontinuation Reason (treated with alternate KI)

- Median PFS not reached
- Median PFS 7 months

p= .01

Recurrent Somatic Mutations in CLL

<table>
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<tr>
<th>FISH Cytogenetic Features</th>
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<tbody>
<tr>
<td>del(13q)</td>
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<tr>
<td>Trisomy 12</td>
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<tr>
<td>del(11q)</td>
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<tr>
<td>del(17p)</td>
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<th>Cell cycle or DNA damage</th>
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<tr>
<td>TP53</td>
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<td>ATM</td>
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<th>RNA processing</th>
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<tr>
<td>SF3B1</td>
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<td>DDX31</td>
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<th>Genes with Significant Mutation Frequency and Related Pathways</th>
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<tr>
<td>NOTCH1                        FBOV7</td>
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<th>Inflammatory pathway</th>
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<td>MYD88</td>
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<tr>
<td>MAPK1</td>
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<td>ZMRYM3</td>
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- Some recurrent mutations are associated with known prognostic features


• Mutations detected up to 15 mos b/f progression


Science ↔ Clinical Trials ↔ Practice

Opportunity for monitoring, intervention and clinical trials?

Recognizing power of disease biology (biomarkers) vs therapy in adverse events

• In very favorable risk FCR-treated CLL, life expectancy matched normal general population
• Richter’s syndrome still diagnosed in ibrutinib treated patients (including frontline)

![Graph showing prevalence of second tumors](Blood.2015;126(16):1921)

MRD neg & durable responses

• **MDACC FCR:** MRD marrow
  - Treated for 3-6 cycles, MRD bone marrow assessed at each
  - PFS similar by ending MRD status
    - 3 vs 6 cycles (didn’t matter how much to get there)

![Graph showing population vs PFS](JCO.2012;30:980-988;
Blood.2014;123:3727-3732;
Blood.2015;126(16):1921-1924;
Blood.2016;127(3):303)
MRD neg & durable responses

• **MDACC FCR:** MRD marrow
  - Treated for 3-6 cycles, MRD bone marrow assessed at each
  - PFS similar by ending MRD status
    - 3 vs 6 cycles (didn’t matter how much to get there)

• **CLL8:** MRD on blood & marrow
  - Post treatment “low” MRD associated with longer PFS and OS
    - FCR vs. FC (didn’t matter what to get there)
    - *But* more “low” MRD pts in FCR

BCR/BCL2 Inhibitors: CRRs and MRD

• **Ibrutinib:**
  - Rel/Ref CRs: 0, 2%, 7%, 12%
  - Frontline CRs: 14%
    (23% - longer follow up)
  - MRD: ? As monotherapy

• **Idelalisib + rituximab:**
  - Rel/Ref CR: 0%
  - Frontline CRs: 19%
  - MRD: ? As monotherapy

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JCO. 2012;30:980-988.
Blood. 2015;126(16):1921-1924.

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Brander et al, ivCLL 2017
Lancet Oncol 2017; 18: 230
BCR/BCL2 Inhibitors: CRRs and MRD

- Venetoclax + rituximab (n=49):
  - Ability to stop therapy in CR or MRD-negative status and maintain
  - MRD-rate: 59%

Brander et al, iwCLL 2017
Lancet Oncol 2017; 18: 230

Thank you for your attention, and thank you to our patients and care team members

Danielle M. Brander, MD
Assistant Professor
Duke University
Division of Hematologic Malignancies & Cellular Therapy
Q&A Session

Ask a question by phone:
- Press star (*) then the number 1 on your keypad.

Ask a question by web:
- Click “Ask a question”
- Type your question
- Click “Submit”

Due to time constraints, we can take only one (1) question per person. Once you’ve asked your question, the operator will transfer you back into the audience line.

SUPPORT RESOURCES

- Online chats: Online moderated chat forums: www.LLS.org/chat
- What to ask: Questions to ask your treatment team: www.LLS.org/whattoask
- Free education materials: www.LLS.org/booklets
- Past CLL education programs: www.LLS.org/programs
- For information on leukemia: www.LLS.org/leukemia
- Information Resource Center: Speak one-on-one with an Information Specialist who can assist you through cancer treatment, financial, and social challenges.
  - E-MAIL: infocenter@LLS.org
  - TOLL-FREE PHONE: (800) 955-4572