Welcome & Introductions

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

What’s on the Horizon for Chronic Myeloid Leukemia?

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Disclosure

Michael J. Mauro, MD, has affiliations with Bristol Myers Squibb and Pfizer (Consulting); Novartis Oncology and Takeda (Grant Support).
Almost 20 y have passed: STI571 pt 0101 (first Portland patient, 1998) from chaos to rapid hematologic response

300 mg/day imatinib

WBC \times 10^3

Days

0 50 100 150 200 250

0 10 20 30 40 50 60

0

250

200

150

100

50

0

10

20

30

40

50

60

Adapted from Hehlmann R., German CML Study Group. Imatinib changed the way we treated CML and was the beginning of a new era

German CML study III/IIIA/IV data

Best available therapy 5-year OS

Frontline imatinib\(^a\) 93%

IFN-\(\alpha\) or SCT plus 2nd line imatinib\(^b\) 71%

IFN-\(\alpha\) or SCT\(^c\) 63%

IFN-\(\alpha\) 52%

Hydroxyurea 46%

Busulfan 38%

Years After Diagnosis

Survival Probability

0 2 4 6 8 10 12 14 16 18 20 22

0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

1983-1994, Busulfan

1983-1994, Hydroxyurea

1986-2003, IFN-\(\alpha\)

1995-2008, IFN-\(\alpha\) or SCT\(^c\)

1997-2008, IFN-\(\alpha\) or SCT plus 2nd line imatinib\(^b\)

2002-2008, Frontline imatinib\(^a\)

Adapted from Hehlmann R., German CML Study Group.
The history of CML is long, the kinase inhibitor era short

1845: First description of CML by John Hughes Bennett reported a "Case of Hypertrophy of the Spleen and Liver in which Death Took Place from Suppuration of the Blood" in the Edinburgh Medical Journal; Virchow in Germany wrote up a similar observation.

1865: Fowlers's solution - 1% arsenic trioxide

1879: Staining methods for blood

1903: Radiotherapy

1933: Busulfan

1965: Hydroxyurea

1968: BMT

1983: Interferon

1998: After seminal preclinical work first clinical trials commence with STI571 (imatinib); 1999, target inhibition validated, resistance identified (T315I)

2001: Imatinib

2006: Dasatinib

2012: Bosutinib

2016: Generic Imatinib

CML is an increasingly prevalent and survivable cancer

Incidence 4700 per year
Age-matched mortality ratio vs normal population = 1.50
Accounts for increased US population to 410 million in 2050

10x greater steady state number of CML patients in US by 2050

CML response not different in presence of other health problems: ‘Comorbidity Index’ Study

As measured by the Charleson Comorbidity Index (CCI)

Living with CML:
Other health issues more important (impact longevity)

Charlson Comorbidity Index (CCI) calculated age included

Internist before Hematologist: Taking care of the whole patient

Charlson Comorbidity Index (CCI) calculated age not included
How common are other health problems in CML patients?

Table 3. All countries, chronic phase, baseline characteristics, recorded before any therapy (n = 2388)

<table>
<thead>
<tr>
<th>Hematologic values</th>
<th>Stem</th>
<th>Comorbidities (% n = 2388)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb, g/dL, males, median (n = 1280)</td>
<td>12.5</td>
<td>0 hypoesthesia</td>
</tr>
<tr>
<td>Hb, males, &lt; 12.0</td>
<td>3.0</td>
<td>53.5</td>
</tr>
<tr>
<td>Hb, males, &gt; 12.0</td>
<td>39.9</td>
<td>15.6%</td>
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<tr>
<td>Hb, females, &gt; 12.0</td>
<td>57.2%</td>
<td>11.8%</td>
</tr>
<tr>
<td>Hb, females, &lt; 12.0</td>
<td>5.71</td>
<td>15.2%</td>
</tr>
<tr>
<td>Platelet count, x 10^9/L, median (n = 2388)</td>
<td>497.0</td>
<td>Molecular data—type of transcript (n = 1333)</td>
</tr>
<tr>
<td>Platelet count, &lt; 10^9/L</td>
<td>155</td>
<td>30.9%</td>
</tr>
<tr>
<td>Platelet count, &gt; 10^9/L</td>
<td>450 to 1000</td>
<td>52.0%</td>
</tr>
<tr>
<td>Platelet count, &gt; 10^9/L</td>
<td>1000</td>
<td>34.7%</td>
</tr>
<tr>
<td>WBC count x 10^9/L, median (n = 2388)</td>
<td>84.6</td>
<td>96% with comorbidities</td>
</tr>
<tr>
<td>WBC count &lt; 10^9/L</td>
<td>50</td>
<td>2.7%</td>
</tr>
<tr>
<td>WBC count &gt; 10^9/L</td>
<td>50 to 100</td>
<td>23.0%</td>
</tr>
<tr>
<td>WBC count &gt; 10^9/L</td>
<td>100 to 200</td>
<td>24.5%</td>
</tr>
<tr>
<td>WBC count &gt; 10^9/L</td>
<td>&gt; 200</td>
<td>25.9%</td>
</tr>
<tr>
<td>Blast cells, %, median (n = 2358)</td>
<td>1.0</td>
<td>EURO score (n = 2292)</td>
</tr>
<tr>
<td>Basophils, %, median (n = 2359)</td>
<td>3.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Eosinophils, %, median (n = 2353)</td>
<td>2.0</td>
<td>EURO low</td>
</tr>
<tr>
<td>Eosinophils, %, median (n = 2353)</td>
<td>2.0</td>
<td>EURO intermediate</td>
</tr>
<tr>
<td>Abbreviations: CCA, clonal chromosome abnormalities; ECOG, Eastern Cooperative Oncology Groups; EUFOS, European Treatment and Outcome Study for chronic myeloid leukemia; WBC, white blood cell; WHO, World Health Organization. * cm below costal margin.</td>
<td></td>
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</tr>
</tbody>
</table>

Hoffmann VS et al, Leukemia 29: 1336-43, 2015

NCCN Guidelines Version 1.2018
Chronic Myeloid Leukemia

Step 1: precise diagnosis, baseline measurements (PCR)
Step 2: informed and careful discussion and choice of therapy
At present, five oral, small molecular kinase inhibitors approved in the US for Ph+ Leukemia: a ‘spoil of riches’; more on the way?

1st Gen. TKI
- Imatinib (STI571)
- 2001 Novartis (1st line)

2nd Gen. TKIs
- Dasatinib (BMS354825)
- 2007/2010 BMS (1st, 2nd line)
- Nilotinib (AMN107)
- 2007/2010 Novartis (1st, 2nd line)
- Bosutinib (SKI606)
- 2012 Pfizer (2nd/3rd line)

South Korea only
- Radotinib (IY5511)
- 2012/2015 IL-YANG: (1st, 2nd line)

3rd Gen. TKI
- Ponatinib
- 2012 Ariad (2nd/3rd line)

4th Gen. TKI (allosteric): ABL001
- 2017
- 1st/2nd/3rd line?

Choosing your tools: comparing TKI toxicity in CML

<table>
<thead>
<tr>
<th>Issue</th>
<th>Imatinib</th>
<th>Nilotinib</th>
<th>Dasatinib</th>
<th>Bosutinib</th>
<th>Ponatinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing</td>
<td>QD/BID, with food</td>
<td>BID, without food (2h)</td>
<td>QD, w/o or w/o food</td>
<td>QD, with food</td>
<td>QD, w/o or w/o food</td>
</tr>
<tr>
<td>Long term safety</td>
<td>Most extensive</td>
<td>Extensive; Emerging toxicity</td>
<td>Extensive; Emerging toxicity</td>
<td>Extensive, No emerging toxicity</td>
<td>More limited but increasing; Emerging toxicity</td>
</tr>
<tr>
<td>Heme toxicity</td>
<td>Intermediate</td>
<td>Least</td>
<td>Most severe; ASA-like effect; lymphocytosis</td>
<td>–dasatinib in 2nd, 3rd line; –nilotinib in 1st line</td>
<td>–thrombocytopenia ASA-like effect</td>
</tr>
<tr>
<td>Non-Heme toxicity</td>
<td>Edema, GI effects, Phos</td>
<td>↑lipase, ↑bili, ↑chol, ↑glu Black box: QT prolongation; screening req’d</td>
<td>Pleural / pericardial effusions</td>
<td>Diarrhea; transaminitis</td>
<td>↑lipase, pancreatitis; rash; hypertension; Black box: vascular occlusion, heart failure, and hepatotoxicity</td>
</tr>
<tr>
<td>Emerging toxicities</td>
<td>early question re: CHF; ?late renal effects</td>
<td>Vascular events (ICVE, IHD, PAD)</td>
<td>PAH (pulmonary arterial hypertension)</td>
<td>? Mild renal effects</td>
<td>Vascular events (ICVE, IHD, PAD, VTE)</td>
</tr>
</tbody>
</table>
Figure 1: Average wholesale price of Gleevec per year at 400 mg per day—typical dosing for chronic myelogenous leukemia maintenance therapy—from 2005 to 2015, according to Redbook data. Prices were adjusted to 2015 USD using the US Department of Labor’s Consumer Price Index.

**Fig 1.** Average wholesale price of Gleevec per year at 400 mg per day—typical dosing for chronic myelogenous leukemia maintenance therapy—from 2005 to 2015, according to Redbook data. Prices were adjusted to 2015 USD using the US Department of Labor’s Consumer Price Index.

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**Reality check: Cost of Therapy**

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**What do we know about generic imatinib?**

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**Table 1: Patient Demographics and Clinical Characteristics of Study Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Innovator Imatinib (n = 107)</th>
<th>Generic Imatinib (n = 144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>Median 40</td>
<td>Median 36</td>
</tr>
<tr>
<td>Range</td>
<td>10.68</td>
<td>2.75</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td>Male 62 (58)</td>
<td>Male 87 (60)</td>
</tr>
<tr>
<td>White cell count, 10^3</td>
<td>Median 189,000</td>
<td>Median 142,070</td>
</tr>
<tr>
<td>Range</td>
<td>2800-6,008,000</td>
<td>4900-619,000</td>
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<tr>
<td>Platelet count, 10^3</td>
<td>Median 340,000</td>
<td>Median 341,000</td>
</tr>
<tr>
<td>Range</td>
<td>20,000-2,130,000</td>
<td>70,000-1,370,000</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>Median 9.9</td>
<td>Median 10.2</td>
</tr>
<tr>
<td>Range</td>
<td>31-186</td>
<td>52-183</td>
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<tr>
<td>Periph. blast cells, %</td>
<td>Median 2</td>
<td>Median 2</td>
</tr>
<tr>
<td>Range</td>
<td>0.21-0.29</td>
<td>0.12-0.19</td>
</tr>
<tr>
<td>Periph. blast blasts, %</td>
<td>Median 3</td>
<td>Median 2</td>
</tr>
<tr>
<td>Range</td>
<td>0.41-0.75</td>
<td>0.15-0.36</td>
</tr>
<tr>
<td>Splenomegaly, n (%)</td>
<td>Median 663</td>
<td>Median 74</td>
</tr>
</tbody>
</table>

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**References:**

- Chen CT, Kesselheim AS, JOP 13: 352-355, 2017

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Branded vs. generic imatinib: toxicity

- Remember generic substitutions can rotate (different manufacturer with each Rx)
- Closer side effect monitoring prudent
- Shorter term PCR monitoring after switch may be advisable also

International Standard (IS) qPCR

10% 1% 0.1% 0.01% 0.0032%

Early Molecular Response: <10% or 1-log (10x) drop from starting level
Complete Cytogenetic Response: <1% or 2-log (100x) drop
Major Molecular Response: <0.1% or 3-log (1000x) drop
MR4, 'CMR'

Complete Molecular Remission: <0.0032%; below the level of detection for standard labs eligible for 'treatment free remission' trials

Plainly stated:
1. PCR at diagnosis = very important, like a timing chip when you run a race (where did you start?)
2. Early response at 3mo should be 'on track', 10x lower than start, ~10% (if you start ~100%)
3. Complete cytogenetic response (~1% on the PCR scale; 100x lower) is very important and protective
4. Major molecular response (MMR, ~0.1% on the PCR scale; 1000x lower) adds further protection
5. Deep Molecular remission: aiming for 0.01% or lower (10,000x lower than start) and staying that way

'Shrinking the iceberg': response expectations

Figure 2: A. Hematological Adverse Events, B. Hematological Adverse Events

Overall Survival
Progression-Free Survival
Failure-Free Survival

Major Molecular Response
Complete Molecular Response

Mutation Status

Predictive molecular tools in CML

Early Molecular Response (EMR)

Overall (N=862)
US (n=573)
Europe (n=289)

Patients not tested for CyR at 12 months

Patients not tested for MR by 12 months

About 1 in every 5 patients are not tested for MR at 12 months and almost half are not tested for CyR

Age <65 years at initiation of first-line TKI, patients who had switched from first-line TKI and those seen in academic centres were more likely to be monitored by 12 months (p<0.05)


The most significant ‘late effects’: 
CML TKI Associated Cardiovascular Adverse Effects

- Cardiomyopathy
- Congestive Heart Failure
- Cerebrovascular Disease
- Coronary Heart Disease
- Myocardial Infarction
- Venous Thrombosis
- Pulmonary Arterial Hypertension
- Peripheral Arterial Disease

Other:
- Fatigue
- Musculoskeletal Sx / Cramping
- Exercise-Induced Symptoms

Morbidity and mortality; ? Effect on survival observations in front-line studies?
? Delay/deferral of advantageous therapy both in front-line and salvage

Guidelines in active development for CML patients and CV risk

‘ABCDE’ Step Approach to CV Intervention

- A: Awareness of cardiovascular disease signs and symptoms
- B: Aspirin (in select patients)
- A: Ankle-brachial index measurement at baseline and follow-up to document peripheral arterial disease
- B: Blood pressure control
- C: Cigarette/tobacco cessation
- C: Cholesterol (regular monitoring and treatment if indicated)
- D: Diabetes mellitus (regular monitoring, dose of radiation/chemotherapy, and treatment if indicated)
- D: Diet and weight management
- E: Exercise (echocardiogram)

Barber M, Mauro M and Moslehi J, in press

Baseline Assessment

<table>
<thead>
<tr>
<th></th>
<th>Imatinib</th>
<th>Bosutinib</th>
<th>Dasatinib</th>
<th>Nilotinib</th>
<th>Ponatinib</th>
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<tr>
<td>Cardiovascular assessment</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<td>Blood pressure check</td>
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<tr>
<td>Fasting glucose</td>
<td></td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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<tr>
<td>Fasting lipid panel</td>
<td>✔️</td>
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<td>Echocardiogram</td>
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<td>✔️</td>
<td>✔️</td>
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<td>Electrocardiogram</td>
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<td>Ankle-brachial index</td>
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1-month follow up

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<th>Imatinib</th>
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<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
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3- to 6-month follow up

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<td>Blood pressure check</td>
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<tr>
<td>Fasting glucose</td>
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<td>Fasting lipid panel</td>
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<td>Echocardiogram</td>
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<tr>
<td>Electrocardiogram</td>
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*Patients treated with dasatinib should be considered for echocardiogram if cardiopulmonary symptoms are present.
Prospective study of cardiovascular and metabolic risk in newly diagnosed CML (CA180-653, sponsored by BMS)

ABL001: Novel 3rd generation ABL kinase inhibitor

- ABL001 is a new potent, specific inhibitor for CML with a distinct ‘allosteric’ mechanism of action
- Binds a different and separate region of the kinase domain: the myristate-binding pocket, holding Bcr-Abl in the inactive conformation
- Has potential to be combined with the currently available TKIs — the first instance where there is rationale for combinations...
In the case of CML / t(9;22) and Bcr-Abl fusion the inactivation of the kinase is blocked.

How ABL001 works

ABL001 allosterically blocks BCR-ABL1 kinase activity

- ABL001 in cells in the lab selectively inhibits (blocks) Bcr-Abl
- In animal studies it was able to prevent resistance development
- In human cells when very small amounts of ABL001 were added, smaller amounts standard TKIs were needed to block Bcr-Abl
47 of 77 (61%) patients with CML treated with single-agent ABL001 BID were resistant to their last TKI.

**Primary outcome:** estimation of MTD/RDE

**Secondary outcomes:** safety, tolerability, preliminary anti-CML activity, pharmacodynamics, pharmacokinetic profile

ALL, acute lymphocytic leukemia; BID, twice daily; BP, blast phase; CML, chronic myeloid leukemia; MTD, maximum tolerated dose; Ph+, Philadelphia chromosome-positive; po, peroral; QD, once daily; RDE, recommended dose for expansion


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**Responses in Patients With CML Treated With Single-Agent BID ABL001 With ≥3 Months Exposure on Study**

**Hematologic Response Within 6 mo**

- CHR: 88% (14/16)

**Cytogenetic Response Within 6 mo**

- CCyR: 75% (9/12)

**Molecular Response Within 6 mo**

- MMR: 20% (10/50)
- ≥1-log reduction: 30% (10/33)

**Molecular Response Within 12 mo**

- MMR: 42% (46/108)
- ≥1-log reduction: 40% (21/53)

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**Low blood counts and pancreas enzyme elevation are main side effects of higher intensity seen to date**

- 13.3% and 37.5% achieved MMR by 6 and 12 months
- 29.4% and 42.9% achieved ≥1-log reduction by 6 and 12 mo
- 8 of 10 (80%) patients with >35% Ph+ achieved CCyR by 6 mo

**Disease Status at Baseline**

- CCyR: complete cytogenetic response; CHR, complete hematologic response; IS, International Scale; MMR, major molecular response; mo, months
- *a* Patients had 6 months of treatment exposure or achieved response within 6 months
- *b* NCR: ABL1 IS reduction achieved
- *c* Patients had ≥12 months of treatment exposure or achieved response within 12 months

CABL001A2301 (Planned): Study Design
A phase 3, Multicenter, Open-label, Randomized Study of ABL001 Versus Bosutinib

- **Primary endpoints:** Major Molecular Response (MMR) rate at 24 weeks
- **Key secondary endpoint:** MMR rate at 96 weeks

**Randomization**
- CML CP patients (N = 222 planned), previously treated with ≥ 2 ATP binding TKIs

**ABL001**
- 40 mg BID
- Lack of response
- Failure/Intolerance

**Bosutinib**
- 500 mg QD
- Lack of response
- Failure/Intolerance

**Survival Follow-up**

*BID,* twice daily; CML, chronic myeloid leukemia; CP, chronic phase; QD, once daily; TKI, tyrosine kinase inhibitor

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**EURO-SKI: Survival without loss of MMR**
- n=205, MR4 or greater, >2y (inclusion)
- Relapses, n=86
- Relapses within 6 months, n=77

**Relapse-free survival at 6 months:** 61% (54-68)

**EURO-SKI: Survival without loss of MMR**
- Median time to molecular recurrence: 2.5 mo. (range, 0.8 to 22.2)
- 57 out of the 61 pts restarted TKI (imatinib, n=66; dasatinib, n=1) and 55 achieved 2nd CMR at a median of 4.2 months
- Median follow-up of 63 mo.:
  - None of the MR patients have CML progression event

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*A Cancer Drug Gave Me This Life. Can I Survive Without It?*
Criteria for consideration of treatment free remission (TKI cessation): *the rules as noted by the National Comprehensive Cancer Network (NCCN)*

Age ≥18 years.

Chronic phase CML. No prior history of accelerated or blast phase CML.

On approved TKI therapy (imatinib, dasatinib, nilotinib, bosutinib, or ponatinib) for at least three years.

Prior evidence of quantifiable BCR-ABL1 transcript.

Stable molecular response (MR4; ≤0.01% IS) for ≥2 years, as documented on at least four tests, performed at least three months apart.

No history of resistance to any TKI.

Access to a reliable QPCR test with a sensitivity of detection of ≥4.5 logs that reports results on the IS and provides results within 2 weeks.

Monthly molecular monitoring for the first six months following discontinuation, bimonthly during months 7–24, and quarterly thereafter (indefinitely) for patients who remain in MMR (MR3; ≤0.1% IS).

Consultation with a CML Specialty Center to review the appropriateness for TKI discontinuation and potential risks and benefits of treatment discontinuation, including TKI withdrawal syndrome.

Prompt resumption of TKI, with a monthly molecular monitoring for the first six months following resumption of TKI and every 3 months thereafter is recommended indefinitely for patients with a loss of MMR. For those who fail to achieve MMR after six months of TKI resumption, BCR-ABL1 kinase domain mutation testing should be performed, and monthly molecular monitoring should be continued for another six months.

Reporting of the following to a member of the NCCN CML panel is strongly encouraged:

- Any significant adverse event believed to be related to treatment discontinuation.
- Progression to accelerated or blast phase CML at any time.

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Criteria for consideration of treatment free remission (TKI cessation): *patient specifics*

Age ≥18 years.

Chronic phase CML. No prior history of accelerated or blast phase CML.

On approved TKI therapy (imatinib, dasatinib, nilotinib, bosutinib, or ponatinib) for at least three years.

Prior evidence of quantifiable BCR-ABL1 transcript.

Stable molecular response (MR4; ≤0.01% IS) for ≥2 years, as documented on at least four tests, performed at least three months apart.

No history of resistance to any TKI.

Access to a reliable QPCR test with a sensitivity of detection of ≥4.5 logs that reports results on the IS and provides results within 2 weeks.

Monthly molecular monitoring for the first six months following discontinuation, bimonthly during months 7–24, and quarterly thereafter (indefinitely) for patients who remain in MMR (MR3; ≤0.1% IS).

Consultation with a CML Specialty Center to review the appropriateness for TKI discontinuation and potential risks and benefits of treatment discontinuation, including TKI withdrawal syndrome.

Prompt resumption of TKI, with a monthly molecular monitoring for the first six months following resumption of TKI and every 3 months thereafter is recommended indefinitely for patients with a loss of MMR. For those who fail to achieve MMR after six months of TKI resumption, BCR-ABL1 kinase domain mutation testing should be performed, and monthly molecular monitoring should be continued for another six months.

Reporting of the following to a member of the NCCN CML panel is strongly encouraged:

- Any significant adverse event believed to be related to treatment discontinuation.
- Progression to accelerated or blast phase CML at any time.
Criteria for consideration of treatment free remission (TKI cessation): **PCR criteria and assay**

Age ≥18 years.
Chronic phase CML. No prior history of accelerated or blast phase CML.
On approved TKI therapy (imatinib, dasatinib, nilotinib, bosutinib, or ponatinib) for at least three years.
Prior evidence of quantifiable BCR-ABL1 transcript.
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No history of resistance to any TKI.
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Reporting of the following to a member of the NCCN CML panel is strongly encouraged:
- Any significant adverse event believed to be related to treatment discontinuation.
- Progression to accelerated or blast phase CML at any time.

Criteria for consideration of treatment free remission (TKI cessation): **monitoring rules**

Age ≥18 years.
Chronic phase CML. No prior history of accelerated or blast phase CML.
On approved TKI therapy (imatinib, dasatinib, nilotinib, bosutinib, or ponatinib) for at least three years.
Prior evidence of quantifiable BCR-ABL1 transcript.
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Reporting of the following to a member of the NCCN CML panel is strongly encouraged:
- Any significant adverse event believed to be related to treatment discontinuation.
- Progression to accelerated or blast phase CML at any time.
Criteria for consideration of treatment free remission (TKI cessation): CML specialty center / NCCN feedback

Age ≥18 years.
Chronic phase CML. No prior history of accelerated or blast phase CML.
On approved TKI therapy (imatinib, dasatinib, nilotinib, bosutinib, or ponatinib) for at least three years.
Prior evidence of quantifiable BCR-ABL1 transcript.
Stable molecular response (MR4; ≤0.01% IS) for ≥2 years, as documented on at least four tests, performed at least three months apart.
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- Progression to accelerated or blast phase CML at any time.

Do Adverse Events Occur With TKI Withdrawal?

N=200; 222 AEs in 98 patients were reported
57 AEs in 31 patients were related to treatment stop, no grade 4

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patients All Grade (n)</th>
<th>Patients Grade 3 (n)</th>
<th>AEs All Grade (n)</th>
<th>AEs Grade 3 (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal pain, joint pain, arthralgia</td>
<td>23</td>
<td>3</td>
<td>39</td>
<td>6</td>
</tr>
<tr>
<td>Other (sweating, skin disorders, folliculitis, depressive episodes, fatigue, urticaria, weight loss)</td>
<td>8</td>
<td>0</td>
<td>18</td>
<td>3</td>
</tr>
</tbody>
</table>

Musculoskeletal pain in CML patients after discontinuation of imatinib: a tyrosine kinase inhibitor withdrawal syndrome?

Tyrosine kinase inhibitor withdrawal syndrome: a matter of c-kit?
Response to Richter et al.
Ph. Rousselot et al.

Mahon FX et al, Blood 2014 124:155
Repurposing imatinib: other Abl targets

Imatinib Ameliorates Neuroinflammation in a Rat Model of Multiple Sclerosis by Enhancing Blood-Brain Barrier Integrity and by Modulating the Peripheral Immune Response

Abelson Kinase Inhibitors Are Potent Inhibitors of Severe Acute Respiratory Syndrome Coronavirus and Middle East Respiratory Syndrome Coronavirus Fusion
We need your help to better our research

Go to www.curecml.org and click on ‘survey’

HAS YOUR LIFE BEEN AFFECTED BY CML?

We want to know what you think the research priorities should be.

The 5-10 minute survey is voluntary and anonymous.

SURVEY LINK
mcw.edu/CML_survey

CML in 2017 and beyond...

• CML is highly treatable; ‘functional cure’ appears feasible
• Generic imatinib is here; let science overcome fears
• TKIs should be carefully chosen (risk/benefit)
• Monitoring needs to happen, mutations can drive treatment choice and resistance is treatable
• Even more new agents on the horizon (ABL001)
• SCT still needed as an option; don’t under-utilize
• The past and the future have been VERY bright........
Thank you for your attention!

Questions?
212-639-3107

What’s on the Horizon for Chronic Myeloid Leukemia?

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 only take one question per person. Once you’ve asked your question, the operator will transfer you back into the audience line.

Wednesday, September 27, 2017
What's on the Horizon for Chronic Myeloid Leukemia?

SUPPORT RESOURCES

- **LLS Community**: Online community of people living with or supporting someone with blood cancer: [www.LLS.org/community](http://www.LLS.org/community)
- **What to ask**: Questions to ask your treatment team: [www.LLS.org/whattoask](http://www.LLS.org/whattoask)
- **Free education materials**: [www.LLS.org/booklets](http://www.LLS.org/booklets)
- **Past CML education programs**: [www.LLS.org/programs](http://www.LLS.org/programs)
- **Online CML Chat**: [www.LLS.org/chat](http://www.LLS.org/chat)
- **Information Resource Center**: Speak one-on-one with an Information Specialist who can assist you through cancer treatment, financial, and social challenges.
  - **EMAIL**: infocenter@LLS.org
  - **TOLL-FREE PHONE**: (800) 955-4572

Wednesday, September 27, 2017