ADVANCES IN CHRONIC MYELOGENOUS LEUKEMIA

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How the Experts Treat Hematologic Malignancies
Las Vegas, NV
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Disclosures

- Consultant for Ariad, BMS, Gilead, and Incyte
- We do not intend to discuss the unlabeled use of a product or a product under investigational use.
Objectives

- Discuss the process of diagnosing Chronic Myelogenous Leukemia (CML)
- Describe clinical challenges associated with the management of CML
- Evaluate factors that inform evidence-based treatment planning
- Recognize the clinical application of novel therapies in the treatment of newly diagnosed CML
- Assess side-effect profile of novel therapies for CML
- Discuss interventions to manage side-effects related to TKI therapy
- Evaluate when it is appropriate to discontinue TKI therapy
2001

TIME

THERE IS NEW AMMUNITION IN THE WAR AGAINST CANCER. THESE ARE THE BULLETS.

Revolutionary new pills like GLEEVEC combat cancer by targeting only the diseased cells. Is this the breakthrough we've been waiting for?

2016

DAILY Mirror

CML TREXIT

WE'RE OUT

We vote to quit TKIs
Chronic Myelogenous Leukemia

- Chronic myelogenous leukemia (CML) accounts for 15% of adult leukemias.
- The median age of disease onset is 67 years; however, CML occurs in all age groups (SEER statistics).
- In 2015, an estimated 6,660 people will be diagnosed with CML in the United States, and 1,140 people will die from the disease.
- CML is characterized by the presence of Philadelphia chromosome (Ph) resulting from a reciprocal translocation between chromosomes 9 and 22 [t(9;22)].
The Ph Chromosome and the \textit{Bcr-Abl} Gene

\textbf{t}(9;22) translocation

\textit{Bcr-Abl} gene structure

**Diagnosing CML**

**NCCN Guidelines Version 1.2017**

Chronic Myeloid Leukemia

**WORKUP**

- H&P, including spleen size by palpation (cm below costal margin)
- CBC with differential, platelets
- Chemistry profile
- Bone marrow evaluation
  - Aspirate and biopsy for morphologic review
- Cytogenetics
  - FISH (blood, if bone marrow not available)
- Molecular
  - Quantitative RT-PCR (QPCR) using International Scale (IS) for BCR-ABL1 (blood)
  - ECG for prolonged QTc
  - Hepatitis panel

**CLINICAL PRESENTATION**

- Chronic phase CML
  - Ph positive or BCR-ABL1 positive
- Advanced phase CML
- Blastic phase CML
  - Ph negative and BCR-ABL1 negative
  - Evaluate for diseases other than CML (See NCCN Guidelines for Myeloproliferative Neoplasms)

**ADDITIONAL EVALUATION**

- Determine risk score (See Risk Calculation Table CML-A)
  - See Primary Treatment (CML-2)
- Accelerated phase
  - Additional testing
    - Flow cytometry to determine cell lineage
    - Mutational analysis
    - HLA testing, if considering allogeneic HCT (See CML-6)
  - See Primary Treatment (CML-4)
Phases of CML

- **Chronic**
  - Average duration of 5 to 6 years
  - There are mostly mature leukemia WBCs in the blood and bone marrow and there may be no symptoms of leukemia.

- **Accelerated**
  - Average duration of 6 to 9 months
  - There are some immature leukemia WBCs in the blood and bone marrow (between 5 percent and 30 percent). Patients may have fever, poor appetite and weight loss.

- **Blast**
  - Average duration of 3 to 6 months
  - In this phase, there are mostly immature WBCs in the blood and bone marrow. Symptoms such as anemia and recurring infections are typical.
<table>
<thead>
<tr>
<th>Study</th>
<th>Calculation</th>
<th>Risk Definition by Calculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sokal et al, 1984</td>
<td>Exp 0.0116 x (age in years - 43.4) + (spleen - 7.51) + 0.188 x [(platelet count ÷ 700)² - 0.563] + 0.0887 x (blast cells - 2.10)</td>
<td>Low &lt;0.8 Intermediate 0.8 - 1.2 High &gt;1.2</td>
</tr>
<tr>
<td>Hasford et al, 1998</td>
<td>0.666 when age ≥ 50 years + (0.042 x spleen) + 1.0956 when platelet count &gt; 1500 x 10⁹/L + (0.0584 x blast cells) + 0.20399 when basophils &gt; 3% + (0.0413 x eosinophils) x 100</td>
<td>Low ≤780 Intermediate 781 - 1480 High &gt;1480</td>
</tr>
</tbody>
</table>
Primary Treatment

NCCN Guidelines Version 1.2017
Chronic Myeloid Leukemia

**CLINICAL PRESENTATION**

- Low-risk score (See Risk Calculation Table CML-A)
  - Chronic phase CML

**PRIMARY TREATMENT**

- **Dasatinib** 100 mg QD (category 1)
- **Imatinib** 400 mg QD (category 1)
- **Nilotinib** 300 mg BID (category 1)
  - Clinical trial

Treatment Considerations:
- Patient comorbidities and drug toxicities
- Monitor response
- Evaluate patient compliance and drug interactions
- Early toxicity monitoring

- Intermediate- or high-risk score (See Risk Calculation Table CML-A)
  - **Dasatinib** 100 mg QD (preferred)
  - **Nilotinib** 300 mg BID (preferred)
  - **Imatinib** 400 mg QD
  - Clinical trial

See Response Milestones and Treatment Options (CML-3)
Primary Treatment (cont.)

NCCN Guidelines Version 1.2017
Chronic Myeloid Leukemia

CLINICAL PRESENTATION

- Advanced phase CML
  - Accelerated phase
  - Blast phase

- Lymphoid
- Myeloid

PRIMARY TREATMENT

- Clinical trial or TKI (CML-G) or Omacetaxine (CML-G)

- Clinical trial
- ALL-type induction chemotherapy + TKI (CML-G)
  (See NCCN Guidelines for Acute Lymphoblastic Leukemia)
  or TKI (CML-G) + steroids

- Clinical trial
- AML-type induction chemotherapy + TKI (CML-G)
  (See NCCN Guidelines for Acute Myeloid Leukemia)
  or TKI (CML-G)

Treatment Considerations

- Role of allogeneic HCT should be discussed based on response.
- Disease progression to advanced phase while on TKI therapy has worse prognosis than presenting with advanced phase CML.
- Treatment options are based on patient comorbidities and age.
- Selection of TKI is based on prior therapy and/or BCR-ABL mutation profile.
- CNS involvement has been described in blast phase CML. Lumbar puncture and CNS prophylaxis is recommended for lymphoid blast phase.
## Defining Response

<table>
<thead>
<tr>
<th>Type of Response</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHR</td>
<td>Complete Hematologic Response</td>
</tr>
<tr>
<td></td>
<td>Normal differential, WBC, platelets $\leq$ ULN</td>
</tr>
<tr>
<td>MCyR</td>
<td>Major Cytogenetic Response</td>
</tr>
<tr>
<td></td>
<td>0-35% Ph+ marrow metaphases</td>
</tr>
<tr>
<td>CCyR</td>
<td>Complete Cytogenetic Response</td>
</tr>
<tr>
<td></td>
<td>0% Ph+ marrow metaphases</td>
</tr>
<tr>
<td>MMR</td>
<td>Major Molecular Response</td>
</tr>
<tr>
<td></td>
<td>BCR-ABL/ABL $\leq$ 0.1% (International Scale)</td>
</tr>
<tr>
<td>CMR</td>
<td>Complete Molecular Response</td>
</tr>
<tr>
<td></td>
<td>Undetectable BCR-ABL (test of sensitivity $\geq$ 4.5 logs)</td>
</tr>
</tbody>
</table>
### Response Milestones

**BCR-ABL1 (IS)**

<table>
<thead>
<tr>
<th></th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
<th>&gt;12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10%</td>
<td>YELLOW</td>
<td>RED</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1%-10%</td>
<td>GREEN</td>
<td>YELLOW</td>
<td>RED</td>
<td></td>
</tr>
<tr>
<td>0.1%-&lt;1%</td>
<td>GREEN</td>
<td></td>
<td>YELLOW</td>
<td></td>
</tr>
<tr>
<td>&lt;0.1%</td>
<td>GREEN</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Clinical Considerations

**RED**

- Evaluate patient compliance and drug interactions
- Mutational analysis

**YELLOW**

- Evaluate patient compliance and drug interactions
- Mutational analysis

**GREEN**

- Monitor response and side effects

#### Second-Line and Subsequent Treatment Options

**RED**

- Switch to alternate TKI (CML-5) and Evaluate for HCT (CML-6)

**YELLOW**

- Switch to alternate TKI (CML-5) or Continue same TKI (CML-G)
- Dose escalation of imatinib (to a max of 800 mg) and Evaluate for HCT (CML-6)

**GREEN**

- Continue same TKI (CML-G)
# Monitoring Response to TKI Therapy and Mutational Analysis

<table>
<thead>
<tr>
<th>Test</th>
<th>Recommendation</th>
</tr>
</thead>
</table>
| Bone Marrow Cytogenetics                          | • At diagnosis  
• Failure to reach response milestones  
• Any sign of loss of response (defined as hematologic or cytogenetic relapse) |
| Quantitative RT-PCR (QPCR) using IS                | • At diagnosis  
• Every 3 months after initiating treatment. After BCR-ABL1 0.1% – <1% (IS) has been achieved, every 3 months for 2 years and every 3–6 months thereafter  
• If there is 1-log increase in BCR-ABL1 transcript levels with MMR, QPCR should be repeated in 1–3 months |
| BCR-ABL kinase domain mutation analysis            | • Chronic phase  
➢ Failure to reach response milestones  
➢ Any sign of loss of response (defined as hematologic or cytogenetic relapse)  
➢ 1-log increase in BCR-ABL1 transcript levels and loss of MMR  
• Disease progression to accelerated or blast phase |
Response Summary

- >10% at 3 months is a poor risk category
- Not all patients with a BCR-ABL1 value >10% at 3 months have a high ongoing risk of treatment failure.
- Any reduction below 10% by 6 months may improve outcome.
- The rate of reduction over the first 3 months is an important factor for outcome and could be considered in therapeutic decisions.
The Spectrum of CML TKI Toxicities

**Imatinib**
- Fluid retention (ascites, edema, pleural and pericardial effusion)
- Muscle Cramps
- Hypophosphatemia
- GI effects (diarrhea, nausea)
- Renal changes
- Hepatotoxicity

**Bosutinib**
- Diarrhea/nausea
- Transaminitis
- Fluid Retention (ascites, edema, pleural and pericardial effusion)

**Ponatinib**
- Vascular Occlusion
- Heart Failure, Hypertension
- Hepatotoxicity, Pancreatic enzyme elevation
- Fluid retention (ascites, edema, pleural and pericardial effusion)

**Nilotinib**
- Peripheral Arterial Occlusive Disease (PAOD)
- Hyperglycemia, ↑Lipids
- QT Interval Prolongation
- Hyperglycemia
- Pancreatic enzyme elevation
- Hepatotoxicity

**Dasatinib**
- Fluid Retention (ascites, edema, pleural and pericardial effusion)
- Pulmonary Arterial Hypertension (PAH)
- GI Upset

**Myelosupression**
- Electrolyte Δ’s
- Rash
Interventions to Manage Toxicities

**Imatinib**
- Diuretics, Supportive Care, Echo
- Calcium Supplement, Tonic Water
- Antidiarrheal, Antinausea meds
- Take with food, large glass of water
- Monitor Renal Function
- Monitor LFTs

**Ponatinib**
- Interrupt or stop immediately for vascular occlusion or heart failure
- Monitor and manage blood pressure
- Monitor LFTs and pancreatic enzymes
- Diuretics, Supportive Care

**Nilotinib**
- Evaluate for PAOD and if diagnosed, D/C permanently
- Monitor glucose level
  (antiglycemic agents if indicated)
- Monitor LFTs and pancreatic enzymes
- Avoid food 2 hrs before and 1 hour after taking dose

**Bosutinib**
- Antidiarrheal, Antinausea meds
- Take with food, large glass of water
- Diuretics, Supportive Care
- Monitor LFTs

**Dasatinib**
- Diuretics, Supportive Care
- Steroids if pleural or pericardial effusion causing significant symptoms
- D/C permanently if PAH diagnosed
- Take with food, large glass of water

Monitor Laboratory Studies (CBC, CMP, Electrolytes)
- Topical or systemic steroids

Monitor Renal Function

Monitor LFTs
## What Is the Standard? Comparative Results: Imatinib 400/600, Nilotinib, Dasatinib

<table>
<thead>
<tr>
<th></th>
<th>IRIS (IM400)</th>
<th>IM400 ENEST/DASISION</th>
<th>TIDEL I (IM600)</th>
<th>TIDEL II (IM600)</th>
<th>SPIRIT FRANCE (IM600)</th>
<th>ENESTnd (NIL)</th>
<th>DASISION (DAS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10% at 3 mos</td>
<td>---</td>
<td>33%/36%</td>
<td>24%</td>
<td>12%</td>
<td>---</td>
<td>9%</td>
<td>16%</td>
</tr>
<tr>
<td>CCyR at 12mos</td>
<td>69%</td>
<td>65%/73%</td>
<td>88%</td>
<td>87%</td>
<td>65%</td>
<td>80%</td>
<td>85%</td>
</tr>
<tr>
<td>MMR at 12mos</td>
<td>40%</td>
<td>27%/28%</td>
<td>47%</td>
<td>64%</td>
<td>49%</td>
<td>55%</td>
<td>46%</td>
</tr>
<tr>
<td>MMR at 24 mos</td>
<td>55%</td>
<td>44%/46%</td>
<td>73%</td>
<td>73%</td>
<td>53%</td>
<td>71%</td>
<td>64%</td>
</tr>
<tr>
<td>MR4.5 at 12mos</td>
<td>---</td>
<td>4%/-</td>
<td>18%</td>
<td>19%</td>
<td>22%</td>
<td>11%</td>
<td>5%</td>
</tr>
<tr>
<td>MR4.5 at 24mos</td>
<td>---</td>
<td>9%/8%</td>
<td>---</td>
<td>34%</td>
<td>26%</td>
<td>25%</td>
<td>17%</td>
</tr>
<tr>
<td>OS at 3 yrs</td>
<td>92%</td>
<td>94%/93%</td>
<td>---</td>
<td>96%</td>
<td>---</td>
<td>95%</td>
<td>94%</td>
</tr>
</tbody>
</table>
Choice of TKI After Resistance

**BCR-ABL1 Kinase Domain (KD) Mutations**

<table>
<thead>
<tr>
<th>Mutation</th>
<th>IC50 Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native BCR-ABL</td>
<td>imatinib (nM)</td>
</tr>
<tr>
<td>M244V</td>
<td>260</td>
</tr>
<tr>
<td>G250E</td>
<td>2000</td>
</tr>
<tr>
<td>Q252H</td>
<td>1350</td>
</tr>
<tr>
<td>Y253F</td>
<td>1325</td>
</tr>
<tr>
<td>Y253H</td>
<td>&gt;6400</td>
</tr>
<tr>
<td>E255K</td>
<td>5200</td>
</tr>
<tr>
<td>E255V</td>
<td>&gt;6400</td>
</tr>
<tr>
<td>V299L</td>
<td>3475</td>
</tr>
<tr>
<td>F311L</td>
<td>540</td>
</tr>
<tr>
<td>T315I</td>
<td>480</td>
</tr>
<tr>
<td>T315A</td>
<td>971</td>
</tr>
<tr>
<td>T315I</td>
<td>&gt;6400</td>
</tr>
<tr>
<td>F317L</td>
<td>1050</td>
</tr>
<tr>
<td>F317V</td>
<td>850</td>
</tr>
<tr>
<td>M315T</td>
<td>15</td>
</tr>
<tr>
<td>E355G</td>
<td>2300</td>
</tr>
<tr>
<td>F359V</td>
<td>1825</td>
</tr>
<tr>
<td>V379L</td>
<td>1630</td>
</tr>
<tr>
<td>L387M</td>
<td>1000</td>
</tr>
<tr>
<td>H396P</td>
<td>850</td>
</tr>
<tr>
<td>H396R</td>
<td>1750</td>
</tr>
</tbody>
</table>

- **Sensitive**
- **Intermediate sensitivity**
- **Insensitive**

Second Generation TKIs Have Improved Response But not Changed Overall Survival Over Imatinib

<table>
<thead>
<tr>
<th>Response Landmarks</th>
<th>ENESTnd</th>
<th>DASISION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Imatinib</td>
<td>Nilotinib</td>
</tr>
<tr>
<td>Complete cytogenetic response at 12 mos</td>
<td>65%</td>
<td>80%</td>
</tr>
<tr>
<td>Major molecular response at 12 mos</td>
<td>27%</td>
<td>55%</td>
</tr>
<tr>
<td>Major molecular response at 60 mos</td>
<td>60%</td>
<td>77%</td>
</tr>
<tr>
<td>Complete molecular response at 60 mos</td>
<td>31%</td>
<td>54%</td>
</tr>
<tr>
<td>Overall survival at 60 mos</td>
<td>91.7%</td>
<td>93.7%</td>
</tr>
</tbody>
</table>

Green Indicates Statistically Significant Difference  
Red Indicates Nonsignificant Difference
## Second Generation TKIs after Imatinib in Chronic Phase CML

<table>
<thead>
<tr>
<th></th>
<th>Dasatinib</th>
<th>Bosutinib</th>
<th>Nilotinib</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Months follow-up</strong></td>
<td>&gt;24</td>
<td>Median of 24</td>
<td>&gt;24</td>
</tr>
<tr>
<td><strong>Complete Hematologic Response</strong></td>
<td>89%</td>
<td>86%</td>
<td>77%</td>
</tr>
<tr>
<td><strong>Major Cytogenetic Response</strong></td>
<td>59%</td>
<td>54%</td>
<td>56%</td>
</tr>
<tr>
<td><strong>Complete Cytogenetic Response</strong></td>
<td>44%</td>
<td>41%</td>
<td>41%</td>
</tr>
<tr>
<td><strong>2-year Progression Free Survival</strong></td>
<td>80%</td>
<td>79%</td>
<td>64%</td>
</tr>
<tr>
<td><strong>2-year Overall Survival</strong></td>
<td>91%</td>
<td>92%</td>
<td>87%</td>
</tr>
</tbody>
</table>
Ponatinib After Second Generation TKI Failure

Source: Lipton et al, ASH 2013

Figure represents proportion of patients achieving CCyR (post 2G-TKI setting).
Node size represents patient numbers, line signifies derived 95% confidence interval.
Practical Approach to a Patient With Resistance (or Intolerance +/- Resistance)

- First determine what the disease state requires
  - Disease phase
  - Prior TKI exposure
  - Mutational Status
  - T315I unique
  - Select mutations may support role of specific 2nd generation TKIs
  - Predictive potential imprecise
  - “Iceberg” phenomenon
  - More detailed assays forthcoming (like ultra deep sequencing)

- Next balance therapy risk and toxicity potential with known comorbidities
  - Are there true contraindications?
  - Does risk outweigh benefit expected from therapy?
  - Can risk be mitigated or anticipated?
  - Enlist the patient’s insight, trust, and awareness.
Discontinuation of TKI Therapy

- Discontinuation of TKI therapy appears to be safe in select CML patients.
- Clinical studies that have evaluated the safety and efficacy of TKI discontinuation have employed strict eligibility criteria and have mandated more frequent molecular monitoring than typically recommended for patients on TKI therapy.
- Some patients have experienced significant adverse events that are believed to be due to TKI discontinuation.
- Discontinuation of TKI therapy should only be performed in consenting patients after a thorough discussion of the potential risks and benefits.
- Outside of a clinical trial, TKI discontinuation should be considered only if ALL of the criteria are met.
Reasons to Discontinue TKI

1. Ongoing Toxicity- Fatigue, arthralgias, GI upset, etc.
2. Financial toxicity
3. Female patient and pregnancy
## Criteria for TKI Discontinuation

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Green</th>
<th>Yellow</th>
<th>Red</th>
</tr>
</thead>
<tbody>
<tr>
<td>Institutional criteria met</td>
<td>Yes</td>
<td>-</td>
<td>No</td>
</tr>
<tr>
<td>Sokal score at diagnosis</td>
<td>Non-high</td>
<td>High</td>
<td>-</td>
</tr>
<tr>
<td>BCR-ABL transcript at diagnosis</td>
<td>Typical - B2A2 or B3A2 (e13a2 or e14a2)</td>
<td>Atypical, but can be accurately quantified</td>
<td>Not quantifiable</td>
</tr>
<tr>
<td>CML past history</td>
<td>CP only</td>
<td>Resistance or KD mutation</td>
<td>Prior AP or BC</td>
</tr>
<tr>
<td>Response to first line TKI therapy</td>
<td>Optimal</td>
<td>Warning</td>
<td>Failure</td>
</tr>
<tr>
<td>Duration of all TKI therapy</td>
<td>&gt; 8 years</td>
<td>3–8 years</td>
<td>&lt; 3 years</td>
</tr>
<tr>
<td>Depth of deep molecular response</td>
<td>MR4.5</td>
<td>MR4.0</td>
<td>Not in MR4.0</td>
</tr>
<tr>
<td>Duration of deep molecular response monitored in a standardized laboratory</td>
<td>&gt; 2 years</td>
<td>1–2 years</td>
<td>&lt; 1 year</td>
</tr>
</tbody>
</table>

**All green lights:** strong recommendation to consider TKI withdrawal  
**Any yellow lights:** only consider TKI withdrawal in high priority circumstances (e.g., significant toxicity or planned pregnancy)  
**Any red lights:** TKI withdrawal not recommended except in clinical trial
# Summary of Imatinib Discontinuation Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number</th>
<th>Treatment before disc.</th>
<th>Response required</th>
<th>Definition of relapse</th>
<th>TFR (different FU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STIM1</td>
<td>100</td>
<td>IFN then Imatinib for ≥3 years</td>
<td>CMR</td>
<td>Loss of MMR or ≥1-log increase in BCR-ABL&lt;sup&gt;a&lt;/sup&gt;</td>
<td>39 %</td>
</tr>
<tr>
<td>STIM2</td>
<td>200</td>
<td>Imatinib for ≥3 years</td>
<td>As for STIM</td>
<td>As for STIM</td>
<td>46 %</td>
</tr>
<tr>
<td>ALLG CML8</td>
<td>40</td>
<td>Imatinib for ≥3 years</td>
<td>UMRD ≥2 years</td>
<td>Loss of MMR or confirmed loss of MR&lt;sup&gt;4.5&lt;/sup&gt;</td>
<td>45 %</td>
</tr>
<tr>
<td>According to STIM</td>
<td>80</td>
<td>Imatinib for ≥3 years</td>
<td>As for STIM; occasional positive samples eligible</td>
<td>Loss of MMR</td>
<td>64 %</td>
</tr>
<tr>
<td>EUROSKI</td>
<td>868</td>
<td>Imatinib, nilotinib, dasatinib</td>
<td>MR&lt;sup&gt;a&lt;/sup&gt; for ≥1 year; TKI for ≥3 years</td>
<td>Loss of MMR</td>
<td>54 %</td>
</tr>
<tr>
<td>ISTAV</td>
<td>112</td>
<td>Imatinib</td>
<td>Undetectable PCR (3 PCRs)</td>
<td>Loss of MMR</td>
<td>52%</td>
</tr>
<tr>
<td>DESTINY</td>
<td>168</td>
<td>Imatinib, nilotinib or dasatinib</td>
<td>MR4 and stable response under half standard dose for 12 months</td>
<td>Loss of MMR</td>
<td>In progress</td>
</tr>
</tbody>
</table>

<sup>a</sup> BCR-ABL: Breakpoint Cluster Region–Abelson tyrosine kinase; CMR: Complete Major Response; UMRD: Undetectable Major Residual Disease; TFR: Time to First Relapse; MR: Major Response; TKI: Tyrosine Kinase Inhibitor; PCR: Polymerase Chain Reaction; MIRACLE: Medical Institute for Research and Clinical Excellence; SOUL: Society of Oncological Sciences of the USA; City of Hope.
Key Takeaways

- CML is a highly treatable condition
- Generic Imatinib is here; combinations still hold promise
- Early response increasingly predictive of long term success
- Resistance based on mutations can drive treatment choice but is likely quite complex; Novel agents in study (ABL001)
- Second-line therapy can be highly effective; third-line therapy needs to be carefully chosen (risk/benefit of ponatinib vs other alternatives)
- SCT still needed option


References (cont.)


Mauro, MJ ( ). Chronic Myelogenous Leukemia: applying emerging evidence in practice (PowerPoint slides)
References (cont.)


