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**DISCLOSURES**  
Advances in Chronic Myeloid Leukemia

PAGE 2

**Alison Wakoff Loren, MD, MSCE, has no affiliations to disclose.**

BEATING CANCER IS IN OUR BLOOD.




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### Learning Objectives

- Treatment advances for chronic myeloid leukemia (CML)
- The concept of treatment-free remission
- Supportive care and side-effects management
- How communicating with your healthcare team can improve your quality-of-life

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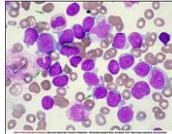
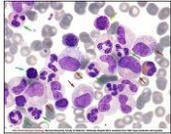
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### A Few Basics: What is CML?

- Cancer of bone marrow stem cells
- Three phases: chronic, accelerated, blast
- Most patients are diagnosed in chronic phase
  - Often without symptoms
- Untreated, all patients progress to accelerated / blast phase within 3-5 years



Atlas of Haematological Cytology (online). 2016 [cit. 2018-9-16]. Available from WWW: <http://www.leukemia-cell.org/Atlas>.

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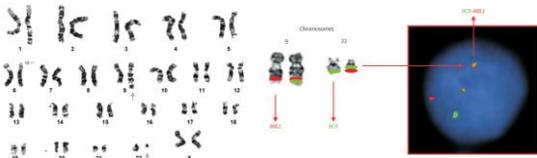
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### A Few Basics: What is CML?

- Characterized by a translocation between chromosomes 9 and 22, denoted as t(9;22) which results in an abnormal juxtaposition of two genes, bcr and abl



Images courtesy of Spandidos Publications and The Lancet

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### How Do We Know If Treatment is Working?

- Hematologic response (CBC [complete blood count])
  - Normal blood counts
- Cytogenetic response (bone marrow cytogenetics ["karyotype"])
  - Major (MCyR): < 35% of cells have the Philadelphia chromosome
  - Complete (CCyR): 0% of cells have the Philadelphia chromosome
- Molecular response (Quantitative PCR, International Scale [qPCR, IS])
  - MR3 (0.1%) aka "major molecular response" or MMR
  - MR4.5 (0.01 – 0.001%)
  - Complete or deep molecular response (CMR or DMR): no detectable bcr/abl

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### Treatment Advances for CML: TKIs

- Ponatinib
  - The only commercially available TKI effective for patients with T315I mutations
  - Significant cardiovascular risks
- Radotinib\*
  - Structurally similar to imatinib and nilotinib
  - Approved in Korea for 1<sup>st</sup> line and later therapy
  - 2<sup>nd</sup> line: 77 patients (2014)
    - MCyR 65%, CCyR 47%, MMR 14% at 12 months
  - 1<sup>st</sup> line radotinib 300 mg vs imatinib 400 mg: 241 patients
    - MMR 52% (R) vs 32% (I), CCyR 91% (R) vs 77% (I)

\*Radotinib is not FDA-approved

Kim SH et al. Haematologica 99(7): 1191-1196, 2014.  
Kwak JY et al. Clin Cancer Res Dec 2017, Epub ahead of print.

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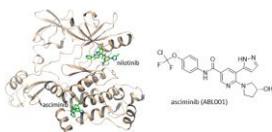
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### Treatment Advances for CML

- Asciminib (ABL001)\*
  - Potent and selective inhibitor of BCR-ABL
  - Different site from other TKIs, allowing possible co-treatment
  - Promising early data
  - Resistance may occur
    - ABL mutations
    - Proteins that pump drug out of the cells
  - 4 open clinical trials, alone or in combination with existing TKIs



\*Asciminib is not FDA approved

Schoepfer J et al. J Med Chem, Sep 2018. Epub ahead of print.

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### Treatment Advances for CML

- Targeting leukemic stem cells (LSCs)
  - JAK2 and STAT3 pathways: ruxolitinib
  - PPARγ inhibitors: pioglitazone
  - Autophagy inhibitors: hydroxychloroquine
  - Immune activation: IFNα, IL-1 receptor antagonists, others

Bhatia R. Hematology Am Soc Hematol Educ Program. 2017 Dec 8;2017(1):115-120

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### Treatment Free Remission: How to monitor?

- Most patients relapse within 6-9 months
- qPCR for bcr/abl in IS lab with prompt results:
  - Every 4 weeks during year 1
  - Every 6 weeks during year 2
  - Every 12 weeks during year 3 and thereafter
- Upon loss of response, re-initiate effective TKI therapy immediately and monitor bcr/abl every 2 weeks until MMR is regained / sustained
- Nilotinib (and imatinib) withdrawal syndromes have been described
- Not all patients wish to discontinue therapy

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### Supportive Care: Managing Side Effects

- Unfortunately, most patients with CML will not be eligible for a trial of treatment-free remission
- How to live well on these medications?
- Side effects are common (60-80% of patients)
- 3 areas of concern
  - Physical (side effects and health risks)
  - Psychological
  - Financial ("TKI handcuffs")

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### Supportive Care: Side Effects

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|---|---|
| <ul style="list-style-type: none"> <li>• Imatinib                             <ul style="list-style-type: none"> <li>• Once daily, with or without food</li> <li>• Muscle cramps, swelling, rash, nausea/diarrhea</li> </ul> </li> <li>• Dasatinib                             <ul style="list-style-type: none"> <li>• Once daily, with or without food</li> <li>• Fluid around lungs (pleural effusion) in up to 30% of patients</li> <li>• Low blood counts, especially platelets</li> </ul> </li> <li>• Nilotinib                             <ul style="list-style-type: none"> <li>• Twice daily, 1 hour before / 2 hours after eating</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>• Ponatinib                             <ul style="list-style-type: none"> <li>• Once daily</li> <li>• Rash, constipation, nausea</li> </ul> </li> <li>• Bosutinib                             <ul style="list-style-type: none"> <li>• Once daily</li> <li>• Diarrhea major side effect (85% although most cases mild/moderate)</li> <li>• Nausea</li> <li>• Low platelets</li> </ul> </li> </ul> |
|---|---|

**ALL: FATIGUE!!!!**

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	Imatinib Once daily	Dasatinib Once daily	Nilotinib Twice daily, empty stomach	Treatment
Cramps/myalgia	+++	+	+	Hydration, electrolytes
Fluid retention	+++	+	+	Diuretics, dose adjust
GI: Nausea, diarrhea	++	+	+	I and D with small meals, N fasting propranolol/Lorazepam
Pleural effusion	-	++	-	Hold, diuretics, steroids, decrease dose
Prolonged QTc	+	+	++	Electrolytes, EKG monitoring
Pancreatitis	+	+	++	Hold, decrease dose
Rash	+	+	++	Topical steroids, hold
Neutropenia	++	+	+	Hold, dose adjust, growth factors
Thrombocytopenia	+	++	+	Hold, dose adjust




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Supportive Care: Medical Risks

- All TKIs except imatinib increase risk of cardiac events:
  - Prolonged "QTc" interval
  - Congestive heart failure
- Dasatinib
  - Pleural effusions
  - Pulmonary hypertension

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Supportive Care: Medical Risks

- Nilotinib
  - Metabolic risks: elevated blood glucose, lipids
- Ponatinib
  - High blood pressure
  - Arterial clots (heart attack, stroke, clots in other blood vessels) in up to 33% of patients
- Patients should consider routine cardiology care and/or referral to an "onco-cardiologist"

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Q&A SESSION

Advances in Chronic Myeloid Leukemia

- **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.

BEATING CANCER IS IN OUR BLOOD.




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LLS EDUCATION & SUPPORT RESOURCES

- **Information Specialists**  
Master's level oncology professionals, available to help cancer survivors navigate the best route from diagnosis through treatment, clinical trials and survivorship.
  - EMAIL: [infocenter@LLS.org](mailto:infocenter@LLS.org)
  - TOLL-FREE PHONE: 1-800-955-4572
- **Free Education Booklets:**
  - [www.LLS.org/booklets](http://www.LLS.org/booklets)
- **Free Telephone/Web Programs:**
  - [www.LLS.org/programs](http://www.LLS.org/programs)
- **Live, weekly Online Chats:**
  - [www.LLS.org/chat](http://www.LLS.org/chat)



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LLS EDUCATION & SUPPORT RESOURCES



- **LLS Podcast, *The Bloodline with LLS***  
Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients: [www.thebloodline.org](http://www.thebloodline.org)



- **Education Videos**  
Free education videos about survivorship, treatment, disease updates and other topics: [www.LLS.org/education/videos](http://www.LLS.org/education/videos)
- **Patti Robinson Kaufmann First Connection Program**  
Peer-to-peer program that matches newly diagnosed patients and their families: [www.LLS.org/firstconnection](http://www.LLS.org/firstconnection)
- **Free Nutrition Consults**  
Telephone and email consultations with a Registered Dietitian: [www.LLS.org/nutrition](http://www.LLS.org/nutrition)
- **What to Ask**  
Questions to ask your treatment team: [www.LLS.org/whattoask](http://www.LLS.org/whattoask)
- **Other Support Resources**  
LLS Community, discussion boards, blogs, support groups, financial assistance and more: [www.LLS.org/support](http://www.LLS.org/support)

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