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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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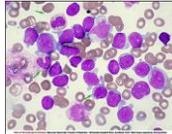
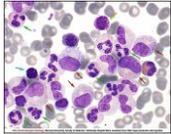
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### A Few Basics: What is CML?

- 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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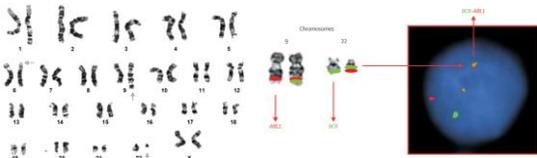
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### A Few Basics: What is CML?

- 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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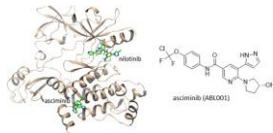
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### Treatment Advances for CML

- 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 STAT5 pathways: ruxolitinib
  - PPAR $\gamma$  inhibitors: pioglitazone
  - Autophagy inhibitors: hydroxychloroquine
  - Immune activation: IFN $\alpha$ , 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.

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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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