THE CML TKI REGISTER & DECLARATION ON GENERICS

Jelena Cugurovic
CML Association of Serbia

On CML Horizons 2013 in Prague first session about generic drugs was held.

The story of generic drugs had just started: Serbia was the first European country with generics, Canada was preparing for generics.

We agreed to open special page for generics called Resource & Knowledge Center on CML generics, copy drugs & substandard drugs. 
www.cmladvocates.net/generics
CML GENERICS ON
WWW.CMLADVOCATES.NET/GENERICS
THE TKI REGISTER

- The TKI register is an unofficial register of CML Tyrosine Kinase Inhibitors.
- There are 5 original drugs & 77 generic drugs in it!
- It is patient-driven and made from the information provided by CML advocates around the world.
- Its main goal is to increase transparency and provide easy accesses to generic drug information to advocates. It is not commercial!
- The information about each CML drug is: name, type, active substance, manufacturers name, availability & authorisation status, publications and indications.
THE TKI REGISTER

<table>
<thead>
<tr>
<th>Medicine Name</th>
<th>Type</th>
<th>Active Substance</th>
<th>Manufacturer/Supplier</th>
<th>Availability &amp; Authorization Status</th>
<th>Publicly available documentation (1/2)</th>
<th>Publicly available documentation (2/2)</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gleevec (Imatinib)</td>
<td>OEC</td>
<td>4,5-Dihydroimidazole</td>
<td>Novartis</td>
<td>Authorized by EMA (Europe), FDA, other countries</td>
<td>See EMA website</td>
<td>03/05/2001 (EMA)</td>
<td>Ph−BCR−abl, positive CML in all phases</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>Indication</td>
</tr>
<tr>
<td>Imatinib-Admac</td>
<td>Genesys</td>
<td>Imatinib</td>
<td>Accord Healthcare</td>
<td>Authorized by FDA (USA) (for all EOCs) &amp; European EMA (Europe)</td>
<td>See Genesys website</td>
<td>02/15/2013 (EMA)</td>
<td>Ph−BCR−abl, positive CML (only adult blast phase, and pediatric)</td>
</tr>
<tr>
<td>Imatinib-Novartis</td>
<td>Novartis</td>
<td>Imatinib</td>
<td>Novartis</td>
<td>Authorized by EMA (Europe), FDA, other countries</td>
<td>See Novartis website</td>
<td>12/09/2013 (EMA)</td>
<td>Ph−BCR−abl, positive CML (only adult blast phase, and pediatric)</td>
</tr>
<tr>
<td>Imatinib-Neo</td>
<td>NeoPharma R.N.</td>
<td>Imatinib</td>
<td>NeoPharma</td>
<td>Authorized by FDA (USA) (for all EOCs) &amp; European EMA (Europe)</td>
<td>See NeoPharma website</td>
<td>08/29/2011 (EMA)</td>
<td>Ph−BCR−abl, positive CML (only adult blast phase, and pediatric)</td>
</tr>
<tr>
<td>Vexat</td>
<td>Genetic</td>
<td>Imatinib</td>
<td>India</td>
<td>Drug available in India, China, India, India, India, India, India (All grades in all countries)</td>
<td>See Vexat website</td>
<td>03/05/2011 (EMA)</td>
<td>CML</td>
</tr>
<tr>
<td>Imatinib-Novartis</td>
<td>Novartis</td>
<td>Imatinib</td>
<td>Novartis</td>
<td>Authorized by EMA (Europe), FDA, other countries</td>
<td>See Novartis website</td>
<td>03/05/2011 (EMA)</td>
<td>Children with chronic myeloid leukemia (CML) in first chronic phase (CP), patients with Philadelphia (Ph) chromosome-positive (CP) or chronic myeloid leukemia (CML) in chronic phase (CP)</td>
</tr>
<tr>
<td>Telgria</td>
<td>Gleevec (Imatinib patented)</td>
<td>nitrosourea</td>
<td>Novartis</td>
<td>Authorized by FDA (Europe), FDA, other countries</td>
<td>See Telgria website</td>
<td>10/21/2007 (EMA)</td>
<td>Ph−BCR−abl, positive CML</td>
</tr>
<tr>
<td>Stivarga</td>
<td>Gleevec (Imatinib patented)</td>
<td>4,5-Dihydroimidazole</td>
<td>Bristol-Myers Squibb Pharmacology</td>
<td>Authorized by FDA (Europe), FDA, other countries</td>
<td>See Stivarga website</td>
<td>10/21/2007 (EMA)</td>
<td>Ph−BCR−abl, positive CML</td>
</tr>
<tr>
<td>Rasuvo</td>
<td>Gleevec (Imatinib patented)</td>
<td>4,5-Dihydroimidazole</td>
<td>Dr. Reddy’s Ltd.</td>
<td>Authorized by FDA (Europe), FDA, other countries</td>
<td>See Rasuvo website</td>
<td>10/21/2007 (EMA)</td>
<td>Ph−BCR−abl, positive CML</td>
</tr>
</tbody>
</table>
The TKI register is important not only for advocates to quickly find information about specific drug, but for doctors and HCP as well.

The TKI register has some value only if it is up-to-date, because it should provide relevant information to the users.

This is a call for all advocates to provide us with the NEW information about drugs they have and UPDATE those we already have!
CML Society of Canada & CML Serbia provided a toolbox with tips and tricks of:
- how to fight the generic drugs
- how to address different groups (patients, media, public,...).

This is a 2nd call for all advocates to share with us their experiences of how to address generic issues!
SESSIONS ON GENERICS FROM CONFERENCES

CML. The page provides information on the product name, common name, registration status of all NDS available on the international market, the names of the respective manufacturers and the Mailing Authorization Holder (MAH) and the specific indication of each drug. If available, it also provides links to publicly available documentation.

Session at European Hematology Association (EHA) Congress 2014:
“Generics in Haematology: The doctors’ and patients’ perspective”

This session at the EHA’s Patient_Hematology focus, in which the CML Advocates Network co-chaired, addressed the issue of drug quality in generics, substandard drugs, and copyfacts from a pharmacology perspective, how the issue of drug quality is being addressed with governments, how the change in generics is being handled on a clinical level by hematologists, and the challenges and opportunities from a patient perspective.

- Drug quality in generics, substandard drugs, copyfacts – the pharmacology perspective (Dr. Alih Johnson, UK) - PDF
- Use of generic drugs and guidelines with the government on drug quality (Dr. Mohammad Rashid, Iran) - PDF
- The hematologists’ clinical perspective (Dr. Navin Gwule, India) - PDF
- The patient’s perspective (Sainus Rasidz, Lithuania) - PDF

Session at CML Horizons 2014:
“The new reality: Generics and Copy Drugs in CML”

Please see the videos and PDF files of our session “CML Horizons 2014”

- Generics, copyfacts & substandard drugs, how to ensure quality of drugs and labs (Prof. Yosuke Tsukao, Pharmacology) - PDF / Video Stream
- CML, generics from a patient perspective (Cheryl Anne Simmoneau, CML Society of Canada) - PDF / Video Stream
- CML, generics from a hematologist perspective (Dr. Rina Baptista, Portugal) - PDF / Video Stream
- CML, generics from a hematologist perspective (N. O. Hulsmann, Germany) - PDF / Video Stream

Session at CML Horizons 2013:
“Drug World vs. Reality: New Challenges with Substandard Drugs & Generics”

Please see the videos and PDF files of our session “CML Horizons 2013” which was addressing the new challenges with substandard drug, copyfacts and generics in CML. We are also showing the European survey of the data collected in our generic survey in March 2013.

- Generics, copyfacts, copyfacts, substandard drugs: efficacy, efficiency, availability and quality? What is the different? (Salome Hoep, Molecure Quality Assurance Programme, Haiku)
- PDF / Video Stream
- Original, generics, copyfacts: Results of the CML Advocates Network Survey (Jens Stockard, CML Advocates Network) - PDF / Video Stream
- United summary of survey data (Gutto) - PDF / Video Stream
- Actions of CML, contours: Fighting against Amlodip, a generic drug (Jens Skovgaard, Sentery)
- PDF / Video Stream

Scientific publications on efficacy and bioequivalence of generic and copy drugs in CML

We are collecting all scientific publications and other credible articles that give some evidence on the quality, bioequivalence or efficacy of generic CML drugs or copy drugs. Please see the list of publications that are known to us so far. If you come across additional publications, please let us know to get them shared!

“Best Practice Toolbox” for patient advocacy on generics, copy drugs and substandard drugs

We invite our CML Advocates Network members to check out our newly created “Best Practice Toolbox on CML Generics” for registered members, after login only. The Toolbox intends to provide CML patient groups with some guidance as advocacy initiatives that they may consider when planning activities on generics in your country. We will get started with a toolbox provided by our members organisations CML Advocates of India who kindly accepted our invitation to share their experience or how to advocate for quality drugs or CML. This is a community-driven initiative and intended to grow over time.
THE DECLARATION ON GENERICS

- In May 2014 patient organisations from 58 countries met in Serbia and discussed with health professionals the introduction of generics in CML treatment.

- Patients welcome that generics will provide more affordable access to treatment in many countries.

- But, patients are worried about the impact on their cancer when switched from one drug to another for non-medical reasons.
Generics are used in 32 countries and patients agreed to call governments, health authorities and healthcare professionals to minimize potential uncertainties and risks for patients with the following 5 measures:

1. No generic drug to treat CML should be provided to patients without reliable proof of quality as well as equivalence of pharmacokinetics and bioavailability. Generic drugs should be approved by the appropriate authorities of the respective country or region, also reflecting a narrow therapeutic range of these cancer drugs.

THE DECLARATION ON GENERICS
THE DECLARATION ON GENERICS

2. When treating severe cancer diseases like leukemias with generics, further **comparative clinical data** should be collected, demanded by regulatory bodies, and published, to ensure comparable clinical efficacy of products with the same compound.

3. A CML patient should **not be switched between products** with the same compound for non-medical reasons, provided this patient already responds optimally to the current product and tolerates it well.
4. If a switch for non-medical reasons between products with the same compound is enforced, this should not happen **more frequently than once in a year**, to allow a consistent follow-up of responses and side effects on the same CML treatment. If a patient loses its response or experiences a significant increase of toxicities after switching to the other product, the patient must have the option to return to the previous treatment, or switch to another treatment if available.
THE DECLARATION ON GENERICS

5. After switching between products with the same compound, **more frequent monitoring** should be conducted to detect potential differences in effectiveness or side effects early.
We (patients and patients` groups) should not fight against generic drugs, because it is or it will be a reality, but we should fight for GOOD GENERIC DRUGS PRODUCED BY REALIBLE PHARMACEUTICALS!

Focus the fight on non switching the drug for non-medical reasons! If switching must be done than it must be under doctors control.

Regular monitoring! Most doctors do not have any experiences in treating patents with generics or switching from one drug to another.
BEYOND THE DECLARATION

- Fight always to have next line of therapy in your country! (Who has 1\textsuperscript{st} fight for 2\textsuperscript{nd}, who has 1\textsuperscript{st} and 2\textsuperscript{nd} fight for 3\textsuperscript{rd}, ...).

- Be informed! Get as much information about the generic drugs in your country (available and those to come). Formal and informal information (TKI register, other advocates experiences, rumors,...)!

  Knowledge is power!
RESULTS AFTER 18 MONTHS ON GENERIC DRUG

- Generic drug: Anzovip® (imatinib) by Actavis
- Period: August 2012 to March 2014
- Number of patients: 49 newly diagnosed patients & 55 switched patients
- Country: Serbia

Data provided by: Dr Andrija Bogdanovic et al., (abstract submitted to EHA20) & Dr Ivana Urosevic, (presentation on EHA19)
INSTEAD OF A CONCLUSION

<table>
<thead>
<tr>
<th></th>
<th>18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>49 newly diagnosed</td>
</tr>
<tr>
<td>CCgR (optimal response)</td>
<td>30</td>
</tr>
<tr>
<td>No major CgR</td>
<td>16</td>
</tr>
<tr>
<td>Molecular response (at least MR3)</td>
<td>25</td>
</tr>
<tr>
<td>No molecular response</td>
<td>5</td>
</tr>
</tbody>
</table>

**Conclusion:** According to these data generic imatinib (Anzovip) is not much inferior to branded imatinib comparing to IRIS study, but the number of patients monitored is very small!

- **2012**
  - 1st line: Glivec
  - 2nd line: Tasigna

- **2012 - 2014**
  - 1st line: Anzovip
  - 2nd line: Tasigna

- **2014 - 2015**
  - 1st line: Alvotinib
  - 2nd line: Tasigna

- **2015 - 2016**
  - 1st line: Anzovip & Tasigna
  - 2nd line: Tasigna
IT IS JUST A BEGINNING ... OF A NEW ERA

THERE IS NO NEED TO BE AFRAID JUST TO BE WISE!
THANK YOU!

&

QUESTIONS

contact:
Jelena Cugurovic
CML Association of Serbia
cml@cml.rs