THE CML TKI REGISTER & DECLARATION ON GENERICS

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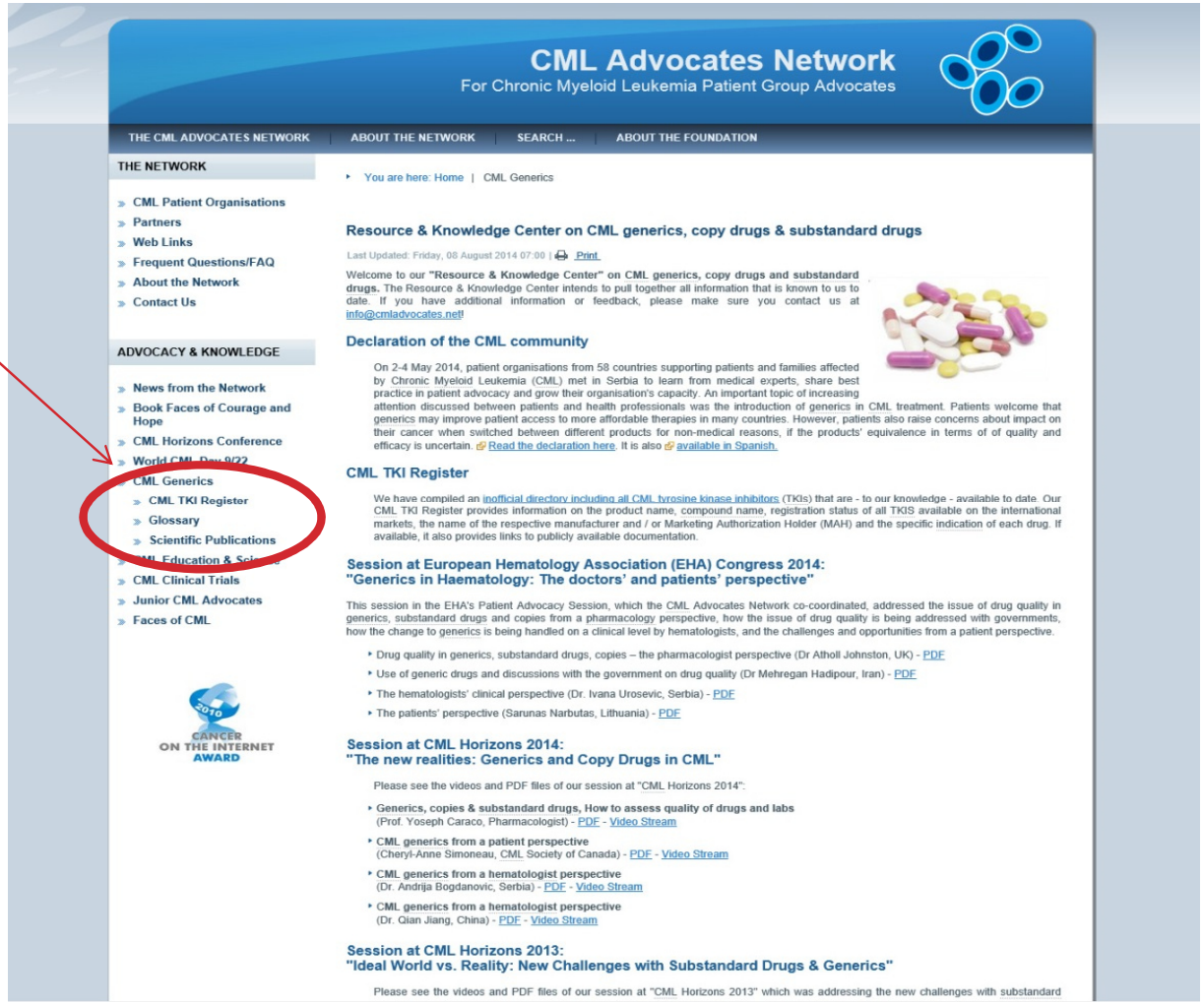
CML GENERICS ON CMLADVOCATES.NET

- 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

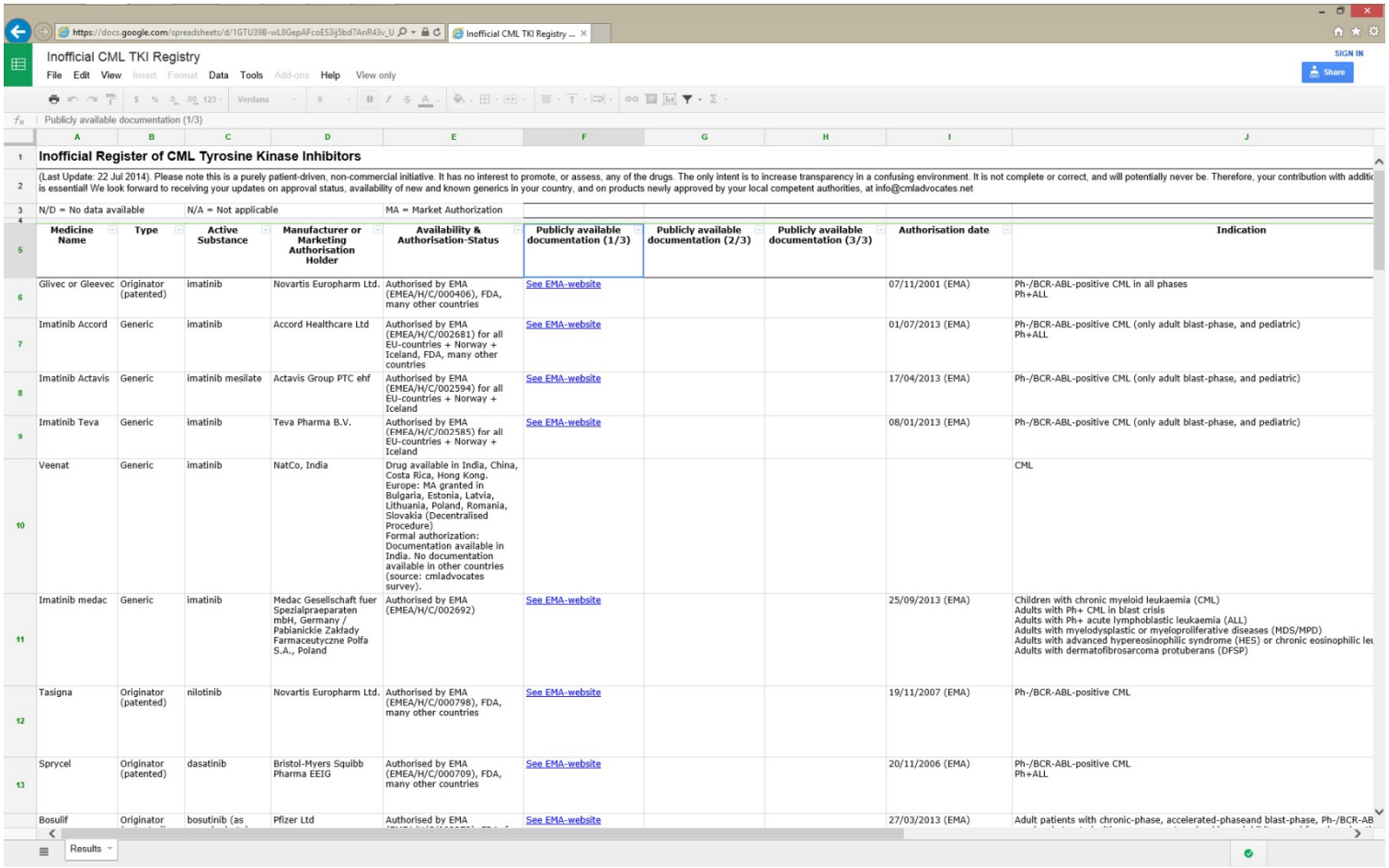
CML GENERICS ON
WWW.CMLADVOCATES.NET/GENERICS



THE TKI REGISTER

- The TKI register is an inofficial 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



Inofficial CML TKI Registry

File Edit View Insert Format Data Tools Add-ons Help View only

Publicly available documentation (1/3)

Inofficial Register of CML Tyrosine Kinase Inhibitors

(Last Update: 22 Jul 2014). Please note this is a purely patient-driven, non-commercial initiative. It has no interest to promote, or assess, any of the drugs. The only intent is to increase transparency in a confusing environment. It is not complete or correct, and will potentially never be. Therefore, your contribution with additi is essential! We look forward to receiving your updates on approval status, availability of new and known generics in your country, and on products newly approved by your local competent authorities, at info@cmladvocates.net

N/D = No data available | N/A = Not applicable | MA = Market Authorization

Medicine Name	Type	Active Substance	Manufacturer or Marketing Authorisation Holder	Availability & Authorisation-Status	Publicly available documentation (1/3)	Publicly available documentation (2/3)	Publicly available documentation (3/3)	Authorisation date	Indication
Glivec or Gleevec	Originator (patented)	imatinib	Novartis Europharm Ltd.	Authorised by EMA (EMEA/H/C/000406), FDA, many other countries	See EMA-website			07/11/2001 (EMA)	Ph-/BCR-ABL-positive CML in all phases Ph+ALL
Imatinib Accord	Generic	imatinib	Accord Healthcare Ltd	Authorised by EMA (EMEA/H/C/002681) for all EU-countries + Norway + Iceland, FDA, many other countries	See EMA-website			01/07/2013 (EMA)	Ph-/BCR-ABL-positive CML (only adult blast-phase, and pediatric) Ph+ALL
Imatinib Actavis	Generic	imatinib mesilate	Actavis Group PTC ehf	Authorised by EMA (EMEA/H/C/002594) for all EU-countries + Norway + Iceland	See EMA-website			17/04/2013 (EMA)	Ph-/BCR-ABL-positive CML (only adult blast-phase, and pediatric)
Imatinib Teva	Generic	imatinib	Teva Pharma B.V.	Authorised by EMA (EMEA/H/C/002585) for all EU-countries + Norway + Iceland	See EMA-website			08/01/2013 (EMA)	Ph-/BCR-ABL-positive CML (only adult blast-phase, and pediatric)
Veenat	Generic	imatinib	NatCo, India	Drug available in India, China, Costa Rica, Hong Kong. Europe: MA granted in Bulgaria, Estonia, Latvia, Lithuania, Poland, Romania, Slovakia (Decentralised Procedure) Formal authorization: Documentation available in India. No documentation available in other countries (source: cmladvocates survey).					CML
Imatinib medac	Generic	imatinib	Medac Gesellschaft fuer Spezialpraeparaten mbH, Germany / Pabianickie Zakłady Farmaceutyczne Polfa S.A., Poland	Authorised by EMA (EMEA/H/C/002692)	See EMA-website			25/09/2013 (EMA)	Children with chronic myeloid leukaemia (CML) Adults with Ph+ CML in blast crisis Adults with Ph+ acute lymphoblastic leukaemia (ALL) Adults with myelodysplastic or myeloproliferative diseases (MDS/MPD) Adults with advanced hypereosinophilic syndrome (HES) or chronic eosinophilic le Adults with dermatofibrosarcoma protuberans (DFSP)
Tasigna	Originator (patented)	nilotinib	Novartis Europharm Ltd.	Authorised by EMA (EMEA/H/C/000798), FDA, many other countries	See EMA-website			19/11/2007 (EMA)	Ph-/BCR-ABL-positive CML
Sprycel	Originator (patented)	dasatinib	Bristol-Myers Squibb Pharma EEIG	Authorised by EMA (EMEA/H/C/000709), FDA, many other countries	See EMA-website			20/11/2006 (EMA)	Ph-/BCR-ABL-positive CML Ph+ALL
Bosulif	Originator	bosutinib (as	Pfizer Ltd	Authorised by EMA	See EMA-website			27/03/2013 (EMA)	Adult patients with chronic-phase, accelerated-phaseand blast-phase, Ph-/BCR-AB

Results

THE TKI REGISTER

- 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.

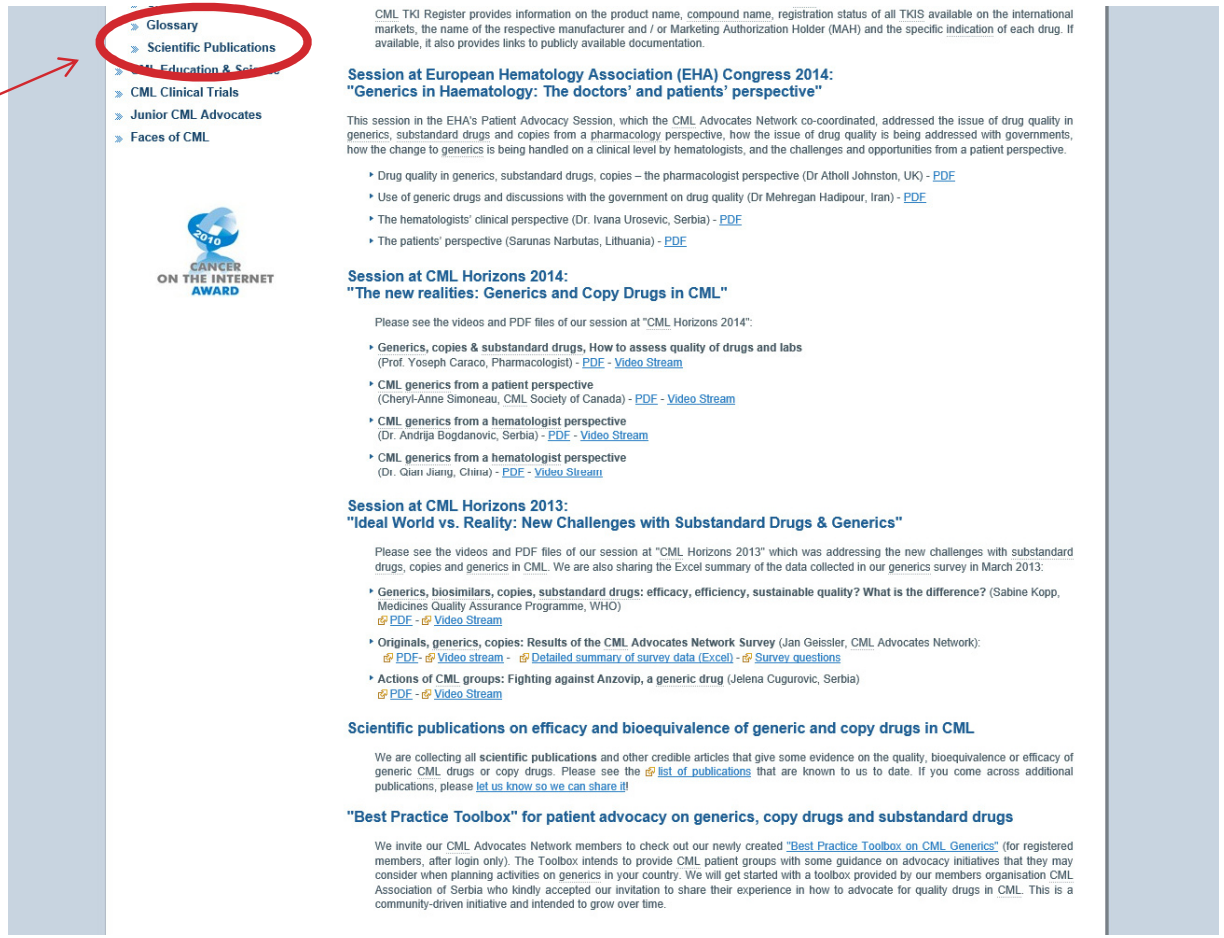
- This is a call for all advocates to provide us with the NEW information about drugs they have and UPDATE those we already have!

THE TKI (GENERIC) TOOLBOX

- 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



- Glossary
- Scientific Publications
- CML Clinical Trials
- Junior CML Advocates
- Faces of CML

2010 CANCER ON THE INTERNET AWARD

CML TKI Register provides information on the product name, compound name, registration status of all TKIS available on the international markets, the name of the respective manufacturer and / or Marketing 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 in the EHA's Patient Advocacy Session, which the CML Advocates Network co-coordinated, addressed the issue of drug quality in generics, substandard drugs and copies from a pharmacology perspective, how the issue of drug quality is being addressed with governments, how the change to 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, copies – the pharmacologist perspective (Dr Atholl Johnston, UK) - PDF
- Use of generic drugs and discussions with the government on drug quality (Dr Mehregan Hadipour, Iran) - PDF
- The hematologists' clinical perspective (Dr. Ivana Urosevic, Serbia) - PDF
- The patients' perspective (Sarunas Narbutas, Lithuania) - PDF

Session at CML Horizons 2014: "The new realities: Generics and Copy Drugs in CML"

Please see the videos and PDF files of our session at "CML Horizons 2014":

- **Generics, copies & substandard drugs, How to assess quality of drugs and labs** (Prof. Yoseph Caraco, Pharmacologist) - PDF - Video Stream
- **CML generics from a patient perspective** (Cheryl-Anne Simoneau, CML Society of Canada) - PDF - Video Stream
- **CML generics from a hematologist perspective** (Dr. Andrija Bogdanovic, Serbia) - PDF - Video Stream
- **CML generics from a hematologist perspective** (Dr. Qian Jiang, China) - PDF - Video Stream

Session at CML Horizons 2013: "Ideal World vs. Reality: New Challenges with Substandard Drugs & Generics"

Please see the videos and PDF files of our session at "CML Horizons 2013" which was addressing the new challenges with substandard drugs, copies and generics in CML. We are also sharing the Excel summary of the data collected in our generics survey in March 2013:

- **Generics, biosimilars, copies, substandard drugs: efficacy, efficiency, sustainable quality? What is the difference?** (Sabine Kopp, Medicines Quality Assurance Programme, WHO) PDF - Video Stream
- **Originals, generics, copies: Results of the CML Advocates Network Survey** (Jan Geissler, CML Advocates Network): PDF- Video stream - Detailed summary of survey data (Excel) - Survey questions
- **Actions of CML groups: Fighting against Anzovip, a generic drug** (Jelena Cugurovic, Serbia) 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 to date. If you come across additional publications, please let us know so we can share it!

"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 on 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 organisation CML Association of Serbia who kindly accepted our invitation to share their experience in how to advocate for quality drugs in 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.

THE DECLARATION ON GENERICS

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

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.

THE DECLARATION ON GENERICS

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.

BEYOND
THE DECLARATION

- 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 1st fight for 2nd, who has 1st and 2nd fight for 3rd, …).

- 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!

INSTEAD OF A CONCLUSION

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)

Abstract Submission

8. Chronic myeloid leukemia - Clinical

EHA-5599

OUTCOME OF FRONTLINE TREATMENT WITH GENERIC IMATINIB ACCORDING TO ELN 2009 BASED NATIONAL GUIDELINES. EXPERIENCE FROM UNIVERSITY CLINIC OF HEMATOLOGY, CLINICAL CENTER OF SERBIA, BELGRADE

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INSTEAD OF A CONCLUSION

	18 months	
Number of patients	**49 newly diagnosed**	**55 switched patients**
CCgR *(optimal response)*	30	45
No major CgR	16	10
Molecular response (at least MR3)	25	
No molecular response	5	

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!

INSTEAD OF A CONCLUSION

- Drug situation in Serbia in May 2015.

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

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