Clinicians Perspectives on CML Generics

Example Latin America

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Non branded imatinib: an issue impacting in patient safety?

- ✓ Non branded are purported to be “comparable” to branded imatinib, but have not been rigorously tested for clinical equivalence.
- ✓ Unlike generic drugs in the USA, non branded drugs do not necessarily contain the same active compound and are not required to meet the same quality standards as branded drugs.
- ✓ No bioequivalence has been established between non branded imatinib and the branded one, by any regulatory agency, as is required prior to approval of a generic drug in the USA.

Saavedra D. et al. Lek & Lymph. 55(12): 2813-16, 2014

Deleterious effects of non branded versions of imatinib used for the treatment of patients with CML in CP

N: 12 patients exposed to Non branded IM.
63% (5/8) treatment failure and 75% (6/8) severe adverse events

	Duration of branded iM therapy (mo)	Best response to branded	Reasons to switch to non branded	Reasons for switch to Nilo or Dasa
1	85	MMR, CCyR	HMO policy	Failure
2	22	MMR, CCyR	HMO policy	Failure
3	65	MMR, CCyR	HMO policy	Intolerance
4	23	MCyR	HMO policy	F and I
5	24	MMR, CCyR	HMO policy	F and I
6	41	CCyR	HMO policy	Intolerance
7	62	CCyR	HMO policy	Intolerance
8	73	MMR, CCyR	HMO policy	Failure

Saavedra D. et al. Lek & Lymph. 55(12): 2813-16, 2014

Generics in Argentina

- ➔ The regulatory entity in Argentina: ANMAT approved the generic law in 2002.
- ➔ With the approval of this law many new laboratories started with generic manufacturing.
- ➔ The INAME still “guarantees bioequivalence and biodisponibility in all copies with respect to original drug”
- ➔ Regulation in Argentina: disposition 5040/2006 of ANMAT

Argentina Non branded Imatinib: more than 20

Product	Commercialized by
– Timab	LKM
– Imatinib GC Pharm	GC PHARM
– Agacel	TUTEUR
– VEK 400	DOSA
– Imatib	ASPEN
– Tagonib	MICROSULES ARG
– Ziatir	RICHMOND
– Mesinib	VARIFARMA
– Imatinib	ELEA*

Argentina Dasatinib generic: 10

Private practice vs Public practice
Branded IM vs non branded IM

	Private Practice with Branded Imatinib FUNDALEU	Public Practice with Non branded Imatinib Hospital Ramos Mejia
N	106	150
CCyR at 6 mo	84%	31%
MMR at 24 m	64%	21%
Death	5% (5/106) CML 3 Progression 2 other	25%

But: … this results are influenced by:

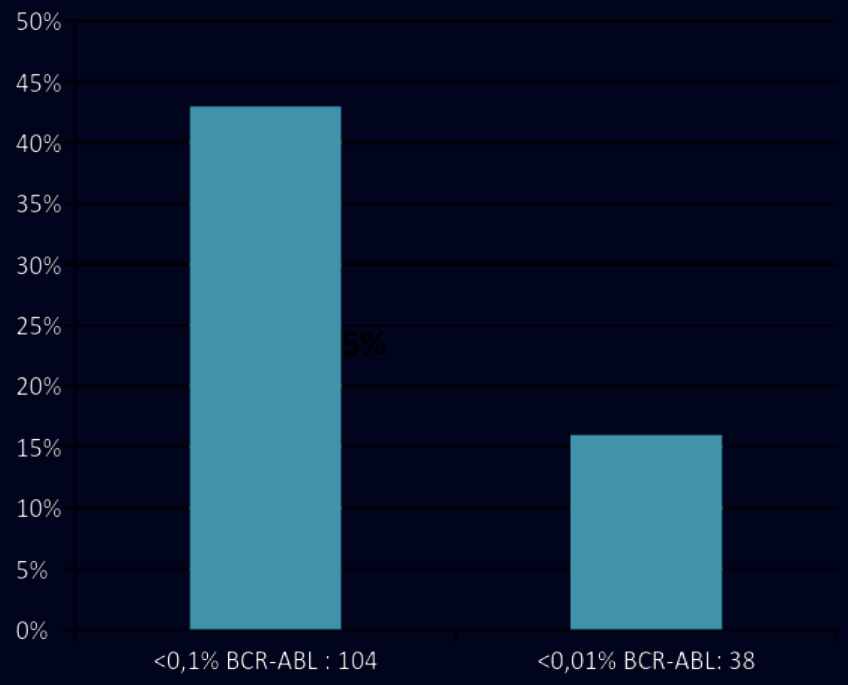
- **Low Adherence due to adverse events**
- **Switching between different generics**
- **Availabilty, problems to drug access**

Argentine Experience: Data Collection

- Questionaire was emailed to 40 hematologists from Argentina
- Objective: collect data about non-branded imatinib efficacy and side effects
- 34 answered

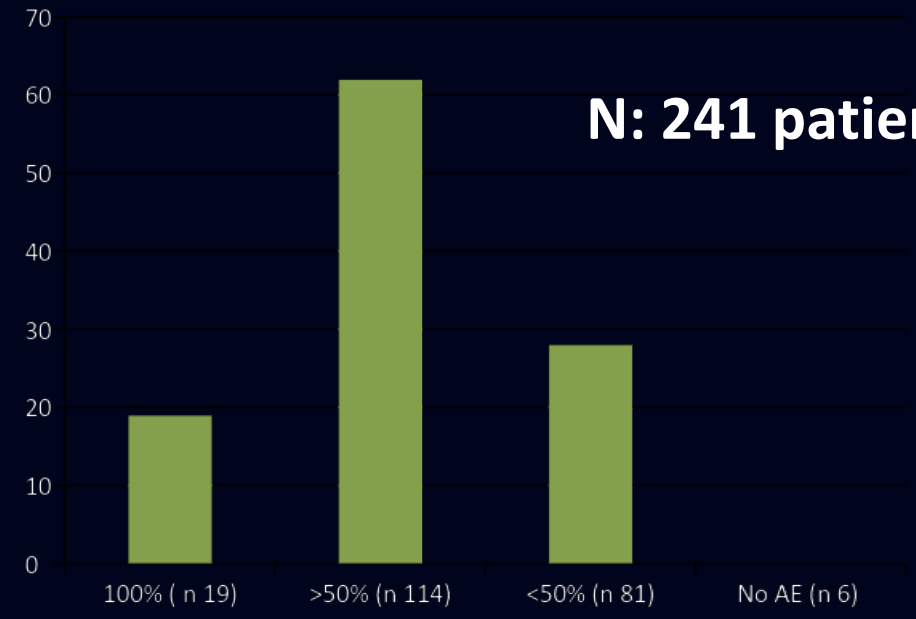
Argentine Experience: Data Collection

- 29 participating centers in Argentina
- N 602 patients under Imatinib treatment
- 40% (241) Non-branded Imatinib therapy
- 50% centers from Buenos Aires
- 62% Public Hospital , 38% Private Practice

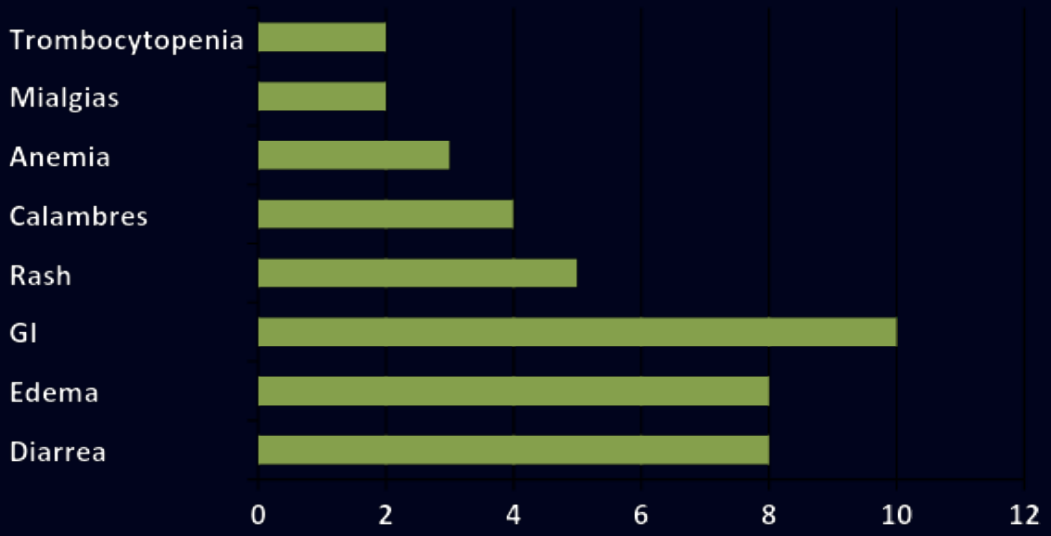


Molecular Response Evaluation N 241 59% optimal responses	
MMR (<0,1% BCR-ABL)	104 (43%)
MR 4/ 4.5 (<0,01 % BCR-ABL)	38 (16%)

Adverse Events in CML patients with generic Imatinib



N: 241 patients



- Gastrointestinal events were the most common side effects: leading to several interruptions and possible lack of efficacy
- Different non branded IM in the same patient
- Different quality of drug copie

In vitro comparative study of original Imatinib apoptotic activity with a pharmacologic bioequivalent

Palmitelli Micaela, de Campos Nebel Marcelo, González Cid Marcela. Larripa Irene. IMEX-CONICET . Academia Nacional de Medicina, Argentina

- **Objective: Evaluate biologic efficacy of a generic inhibitor (imatinib Elea) compared to branded imatinib (imatinib Glivec), describing the analyses of apoptosis (celular death) in vitro in a celular line.**

- **TKI imatinib Elea vs Glivec did not show significative differences, indicating a similar biologic response .**

Some aspects to be considered about Generics:

- ✓ Are generics safe? YES
- ✓ ….”But only if you live in a country with strict regulatory control of medicines…”
- ✓ Is their quality as good as that of corresponding brand?...

What must we expect for generic therapies in LatinAmerica ?

- ✓ We need Pharmacokinetics and pharmacovigilance data, not available now.
- ✓ Need for greater regulation and oversight of generic molecules being introduced in different health care systems, and the need for processes to be put in place to monitor therapy when such changes are made.
- ✓ The Mechanism of approval and continued monitoring of the quality of the generic drug being supplied are not well established.
- ✓ Is there a reason for concern regarding current generic regulations in Argentina ? YES……

What must we expect for generic therapies as a physician ?

- ✓ Strict monitoring with RQ-PCR so as to detect loss of response sooner .
- ✓ Report side effects during non branded IM treatment.
- ✓ If intolerance: switch immediately to branded treatment

Aknowledgements	
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ALMA: Asociation for CML patients

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And many others not named who answered my questions