Clinic of hematology
Clinical centre Vojvodina

School of Medicine
University of Novi Sad,
Serbia

The perspective of generic drugs in chronic myeloid leukemia

Ivana Urosevic

Generic Imatinib

The potential impact of different crystal forms of Imatinib used in Gleevec (beta) vs. Generic Imatinib (alpha)

Bioequivalence in children

Different absorption due to gastrectomy and change in gastric acidity in patients with GIST

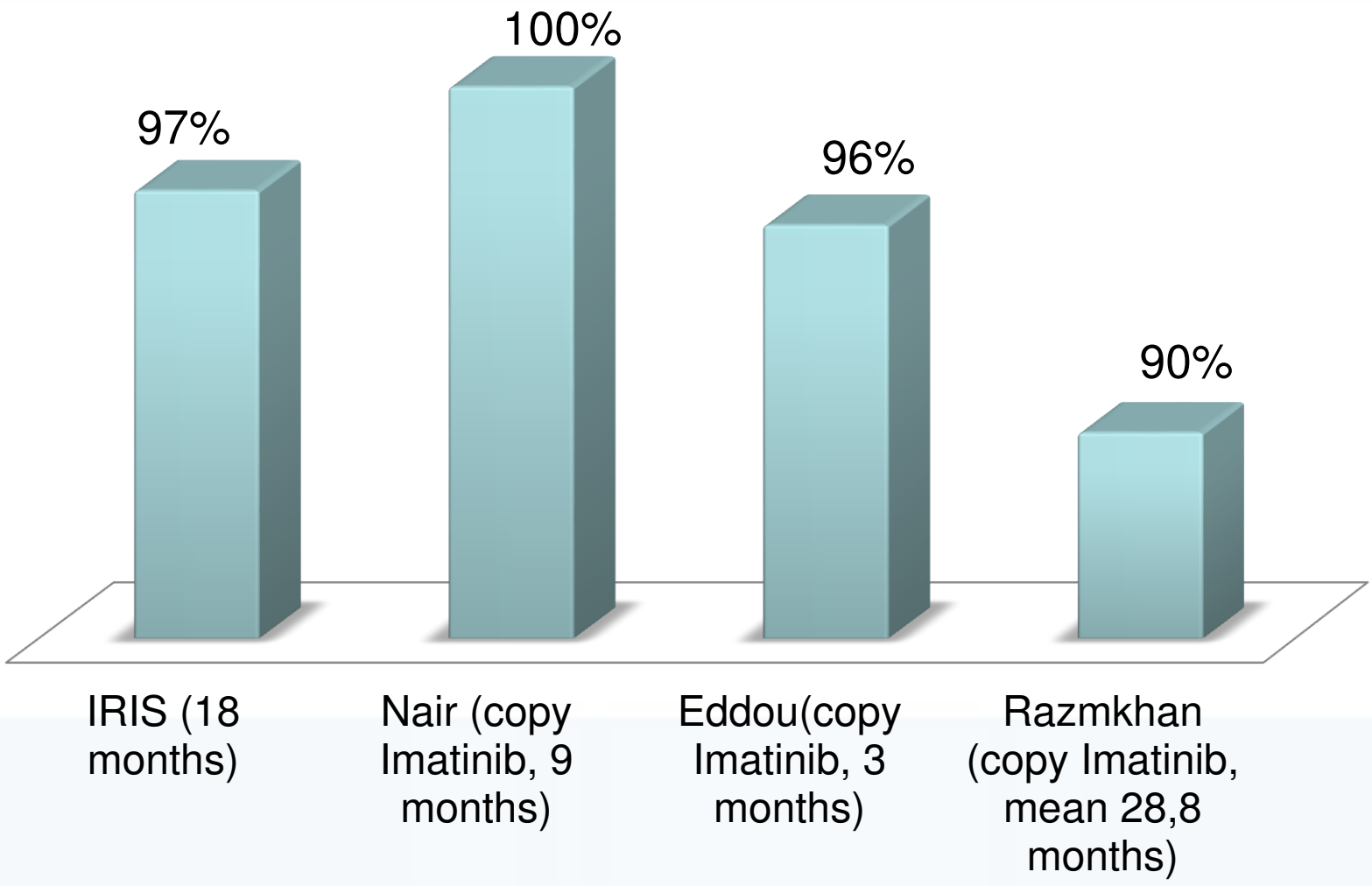
Imatinib copy- clinical case reports

Case reports	Population	Details
Asfour, 2009	N-2, Egypt	CHR on Gleevec Hematologic relaps with copy version
Goubran, 2009	N-1, Egypt	CHR on Gleevec Hematologic relaps with IM-alpha crystal CHR resumed with Gleevec
Chouffal, 2010	N-1, Morocco	CHR on hydroxyurea+INF Hematologic relaps with IM-COPER CHR resumed with Gleevec+hydroxyurea
Mattar, 2010	N-1, Egypt	CHR on Gleevec Hematologic relaps with IM-alpha crystal CHR resumed with Gleevec

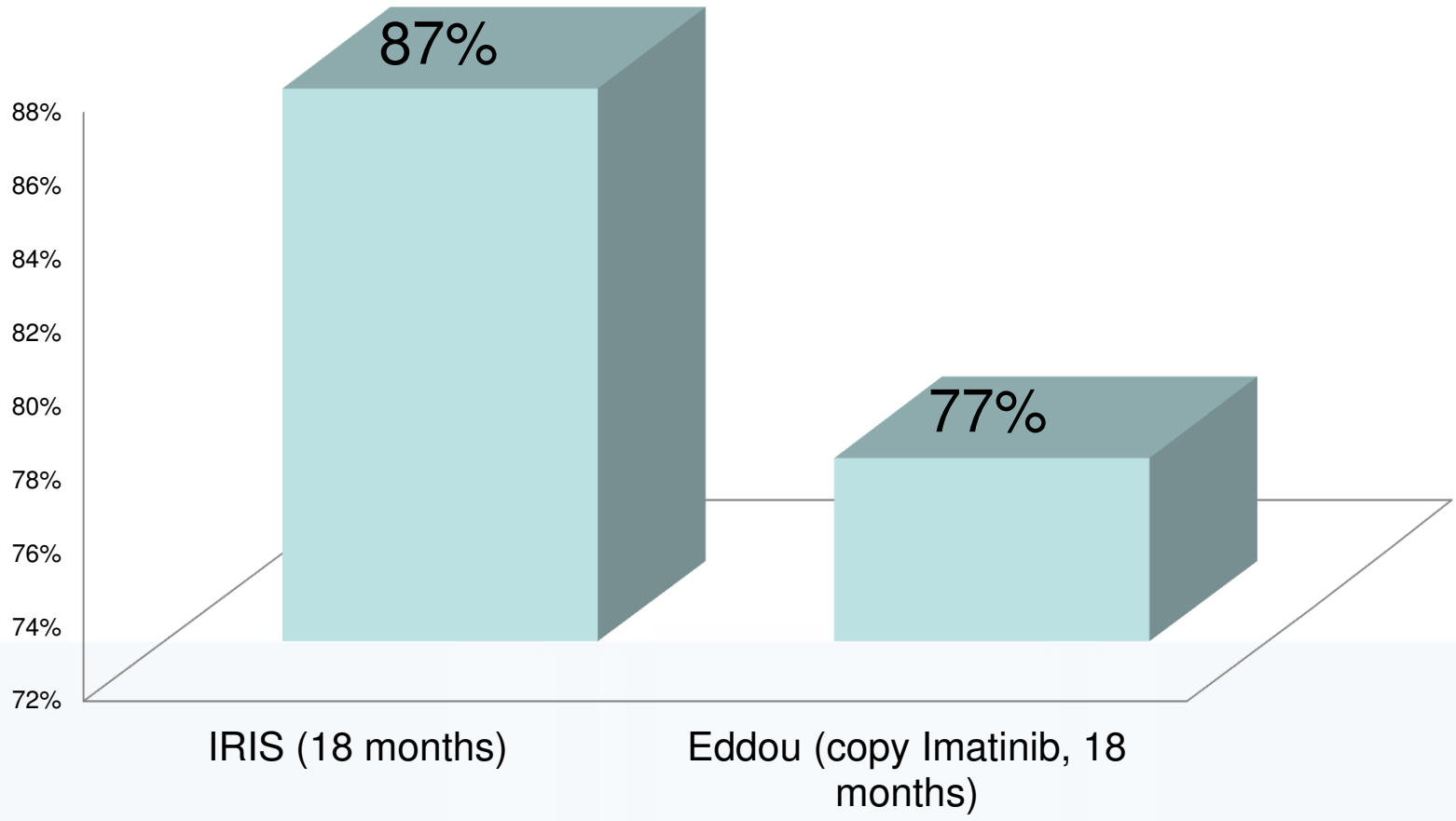
Imatinib copy- observational study

Observational study	Populations	Details
Razmkhan 2009	N-30, Iran	90% CHR with Imatinib alpha crystal
Alwan et al 2011	N-126, Iraq	CHR on Gleevec 33% hematologic relapse with IM copy
Nair et al 2008	N-100, India	100% CHR at 9 months
Eddou et al 2011	N-26, Morocco	96% CHR at 3 months 77% MCgR at 18 months
Saavedra et all 2014	N-12, Colombia 8 switched 4 de novo	63% treatment failure (switched) 75% AE (switched) 100% resistence or suboptimal (de novo) 75% AE (de novo)

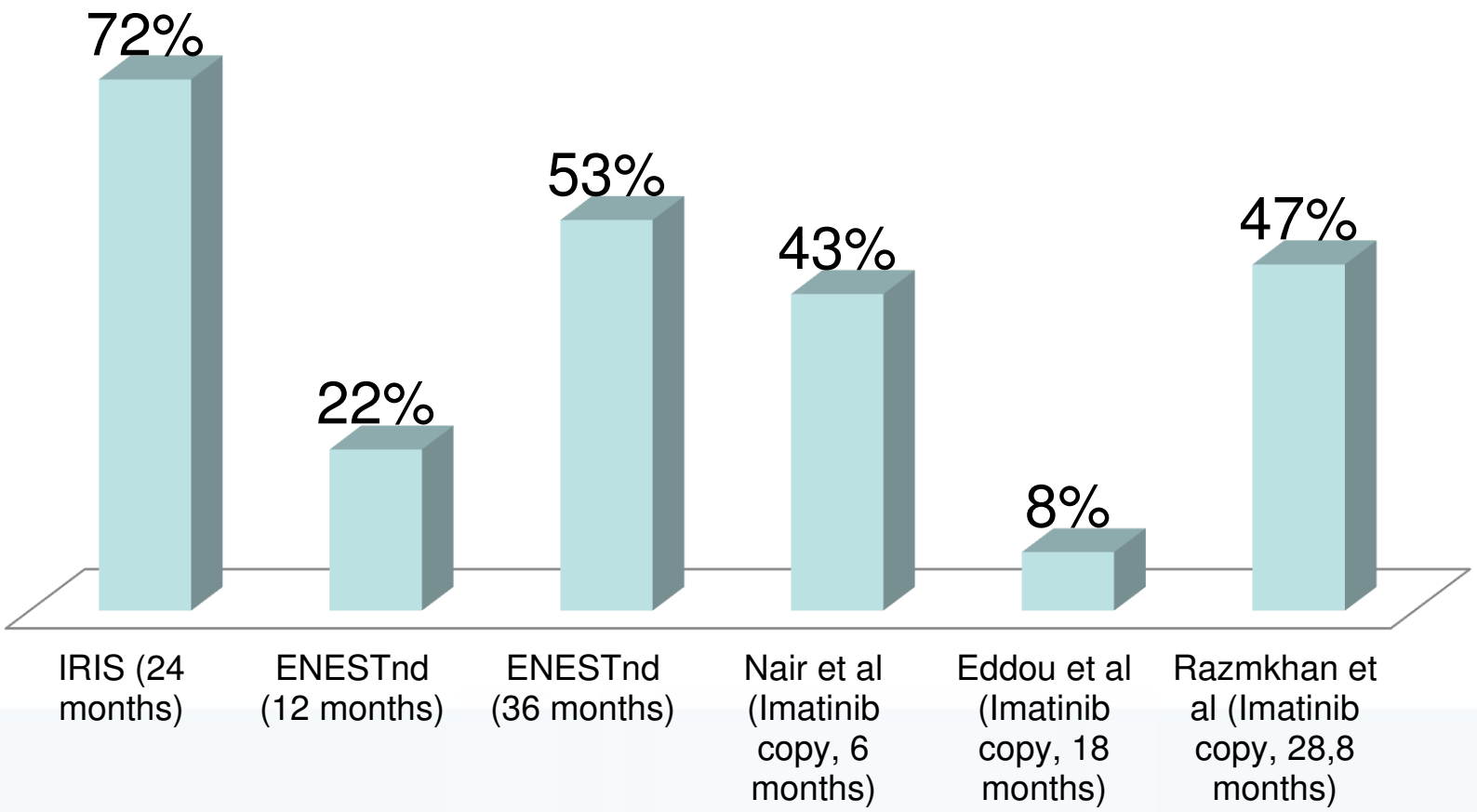
Comparasion of CHR rates



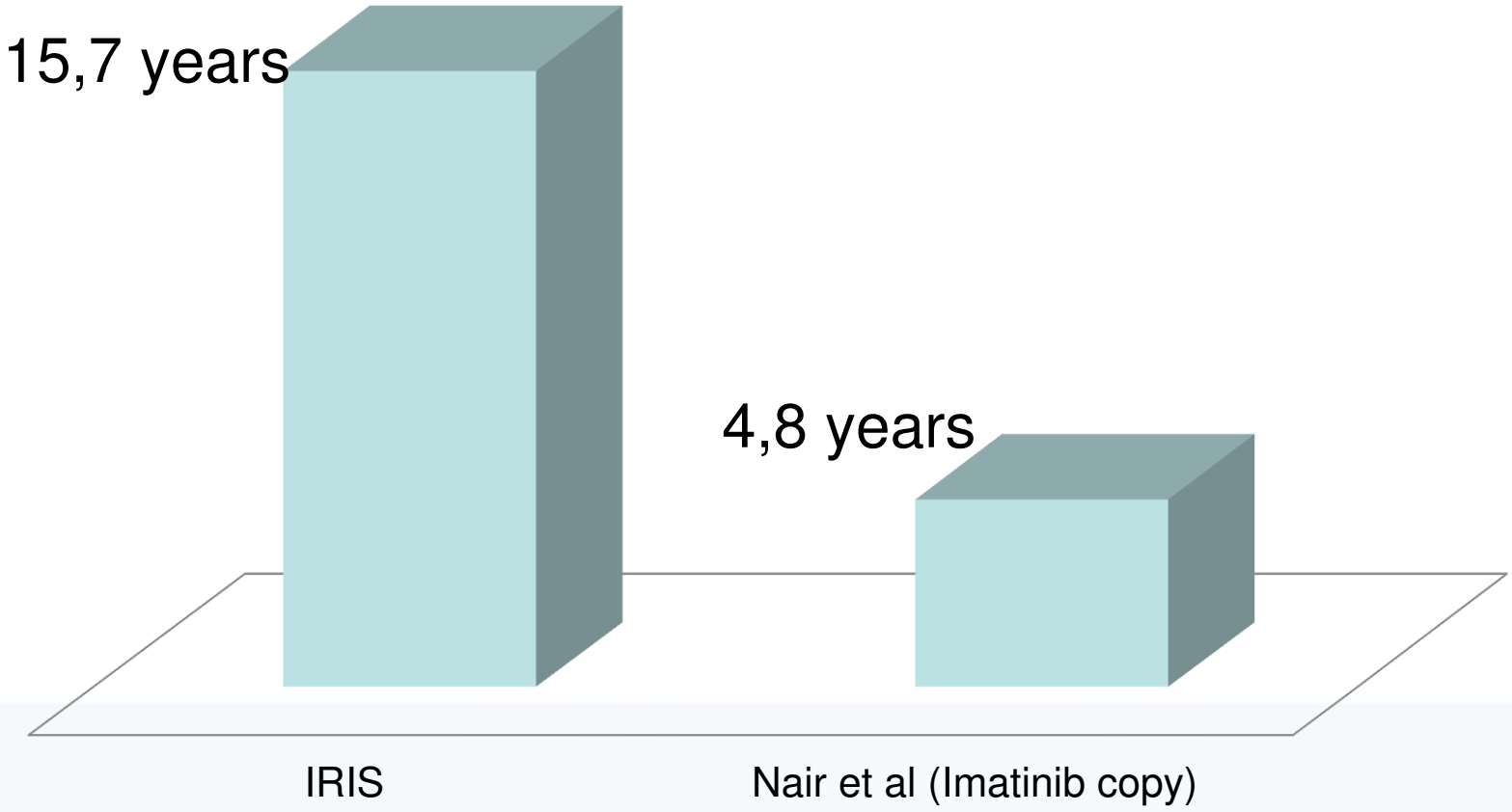
Comparison of MCgR rates



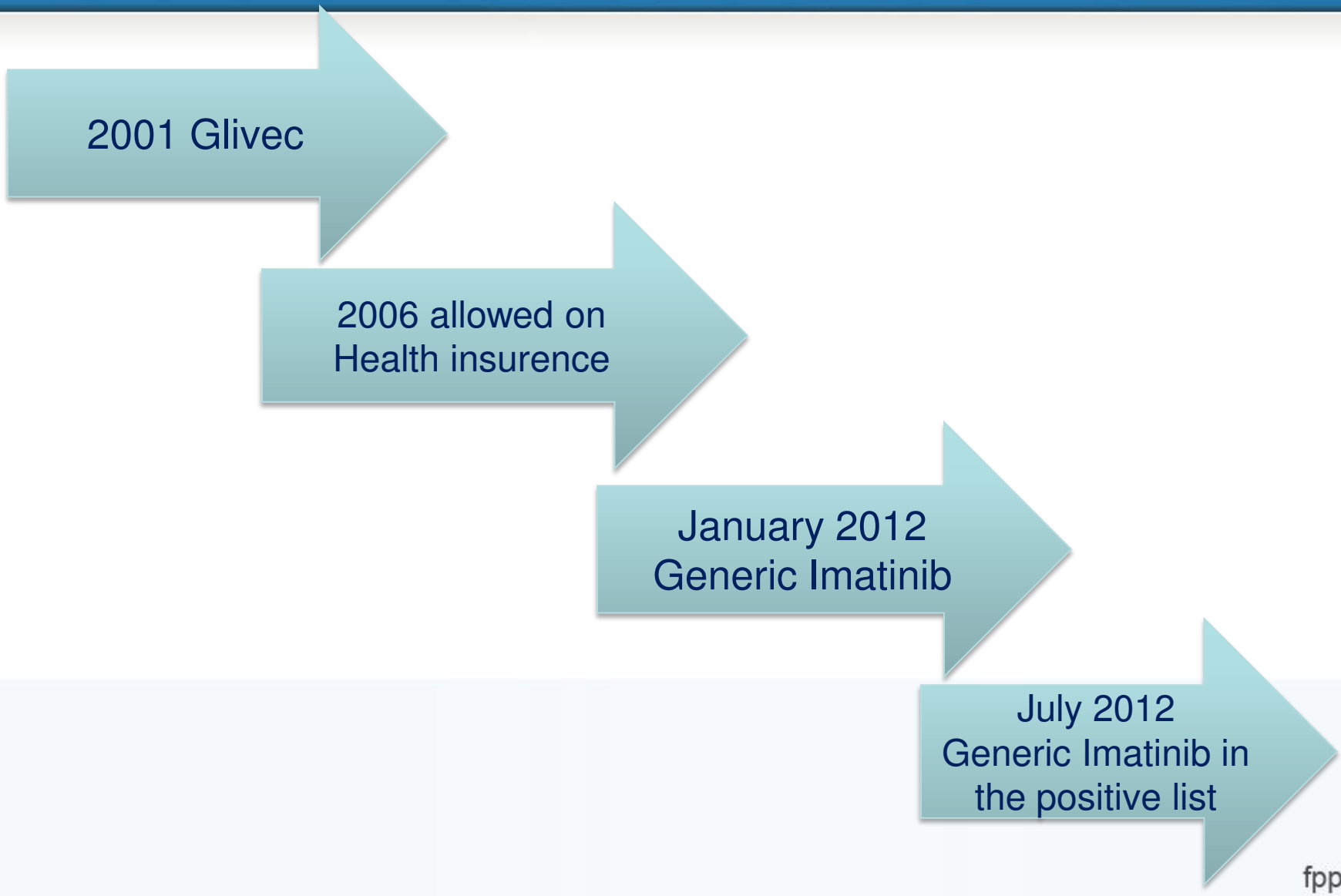
Comparison of MMR rates



Comparison of mean projected survival



What is the situation like in Serbia?



What is the situation like in Serbia?

- The TKI drugs on the positive list in NHIF until June 2014:

  - Imatinib (Glivec, Anzovip, Imatinib Pharma Swiss, Alvotinib) as a 1st line therapy

  - Nilotinib (Tasigna) as a 2nd line therapy

- 220 patients were on Glivec until 2012 in Serbia
- 45 patients on Tasigna

Experiences of our centre - Clinic of hemathology, Clinical centre Vojvodina

- During August and September 2012 all patients were switched from Glivec to Anzovip.
- These are the results of using Anzovip after 18 months.
- Two groups of patients were monitored:
- **55 CML patients on Glivec → Anzovip**
- **15 newly diagnosed CML patients**

Results

- 55 patients treated with branded Imatinib were switched to generic Imatinib

- 10 patients **(18,1%)** had lost complete cytogenetics response they already had, but without signs of biological illness transformation → they were switched to 2nd line therapy nilotinib

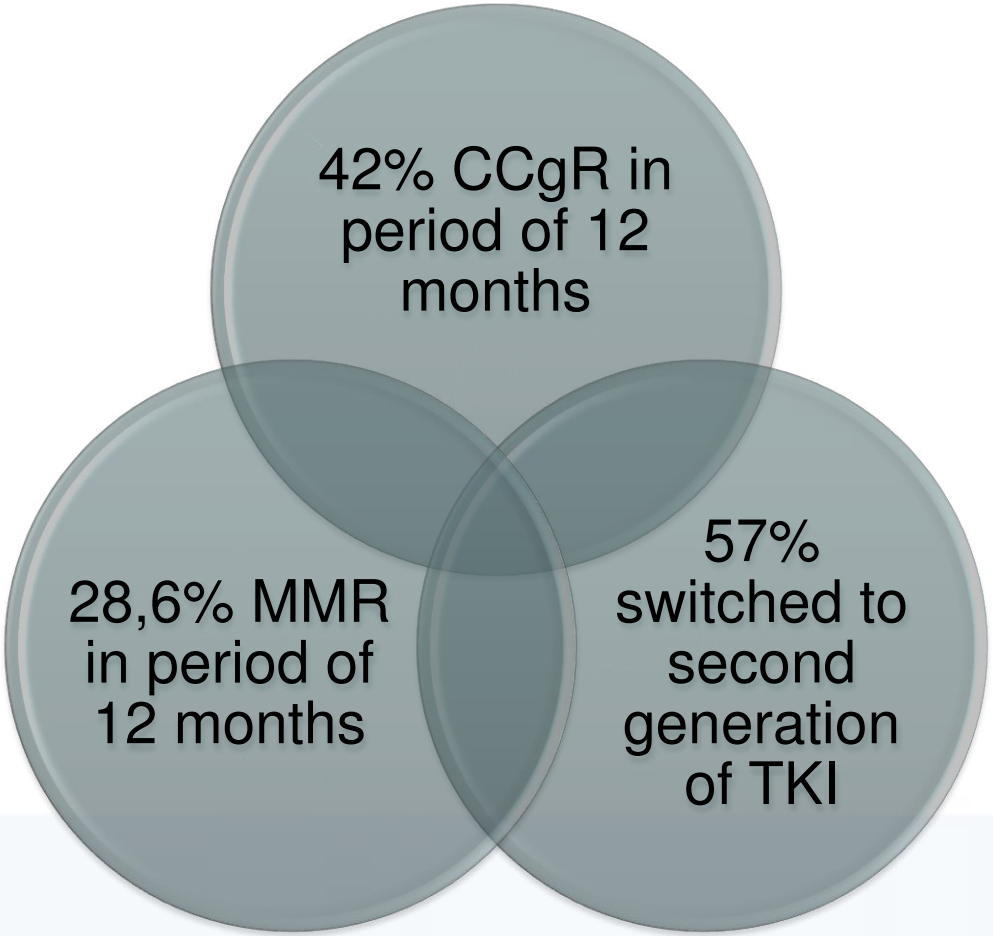
Results- de novo CML patients

- 15 newly diagnosed pts from septembar 2012 to april 2014
- 7 patients – median follow up 12 months (9-18 months)
- Median age 27 (19-60)
- Median duration of Imatinib generic 12 months (9-18 months)
- The patients belonged to intermediate and high Sokal risk group.

Patients characteristics

Patients	Sex	Age at diagnosis	Duration of Anzovip therapy (months)	Reason for switch to II line th	Detalis
1	F	59	18	-	PCgR at CCgR, escalated dose II at 800 after 9 months, CCgR at 18 months
2	F	25	12	-	PCgR at 6m CCgR at 12 months
3	M	19	11	failure	Minor CgR at 6 months, 19% bcr/abl transcript at 9 months
4	M	60	10	Failure	No CgR at 6 months
5	M	27	9	intolerancy	PCgR at 6 months
6	M	21	12	failure	PCgR at 12 months
7	F	56	12	-	CCgR at 12 months

Results



Instead of conclusion

- The safety and efficancy of the copy drug has not been established in randomized clinical trials
- It is unknown whether patients, who responded to branded Imatinib and than switched to its copy versions, will tolerate the copy drug and maintain the previous response
- Careful follow up of a selected patients several months after the switch to generic imatinib
- Despite of the small number of patients our results in term of hematologic and cytogenetic response were close to the international series.

Thank You for Your attention!