

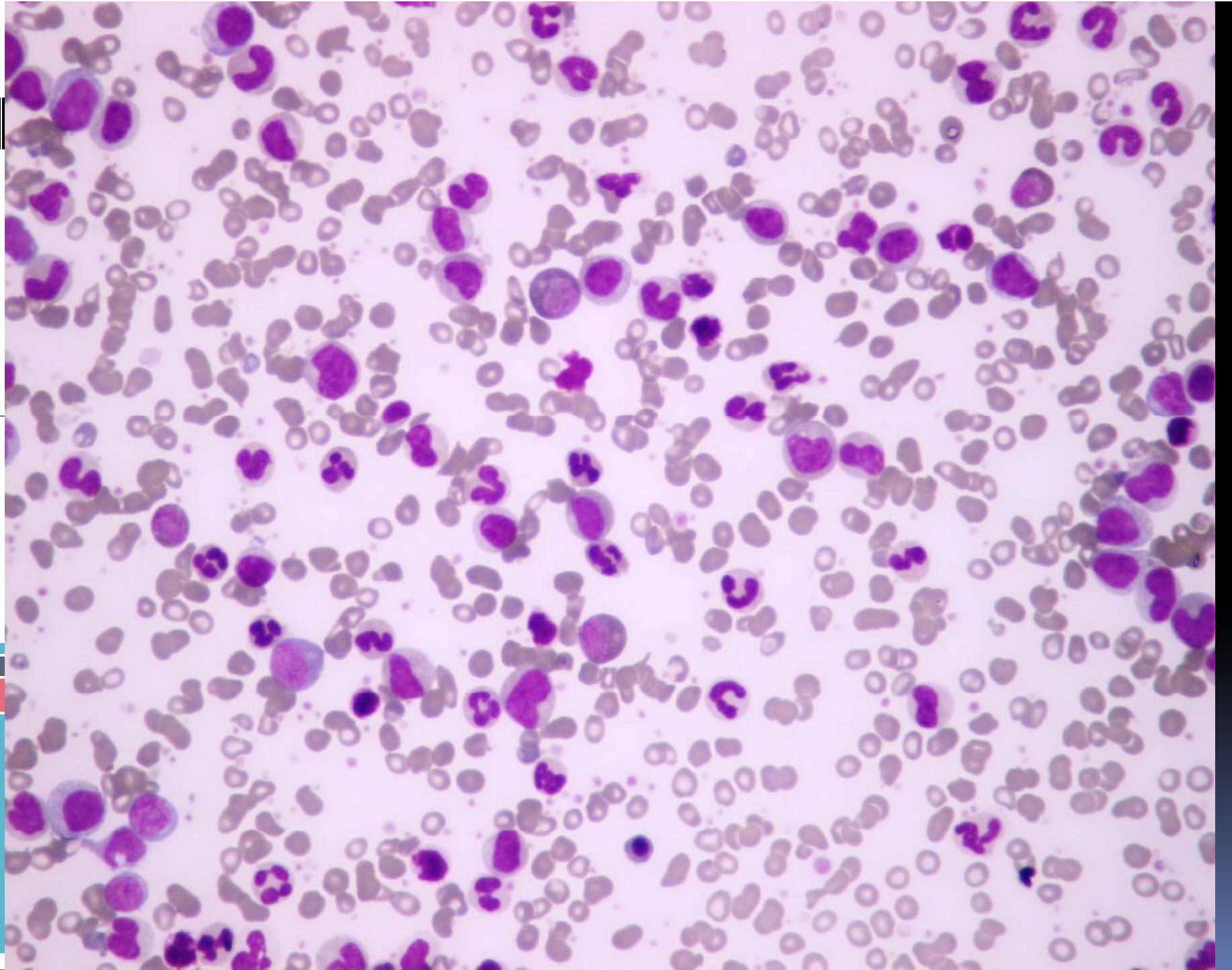
**RESPONSE OF IMATINIB IN
PEDIATRIC AND ADOLESCENT
CHRONIC MYELOID LEUKEMIA –
A SINGLE CENTRE EXPERIENCE.**

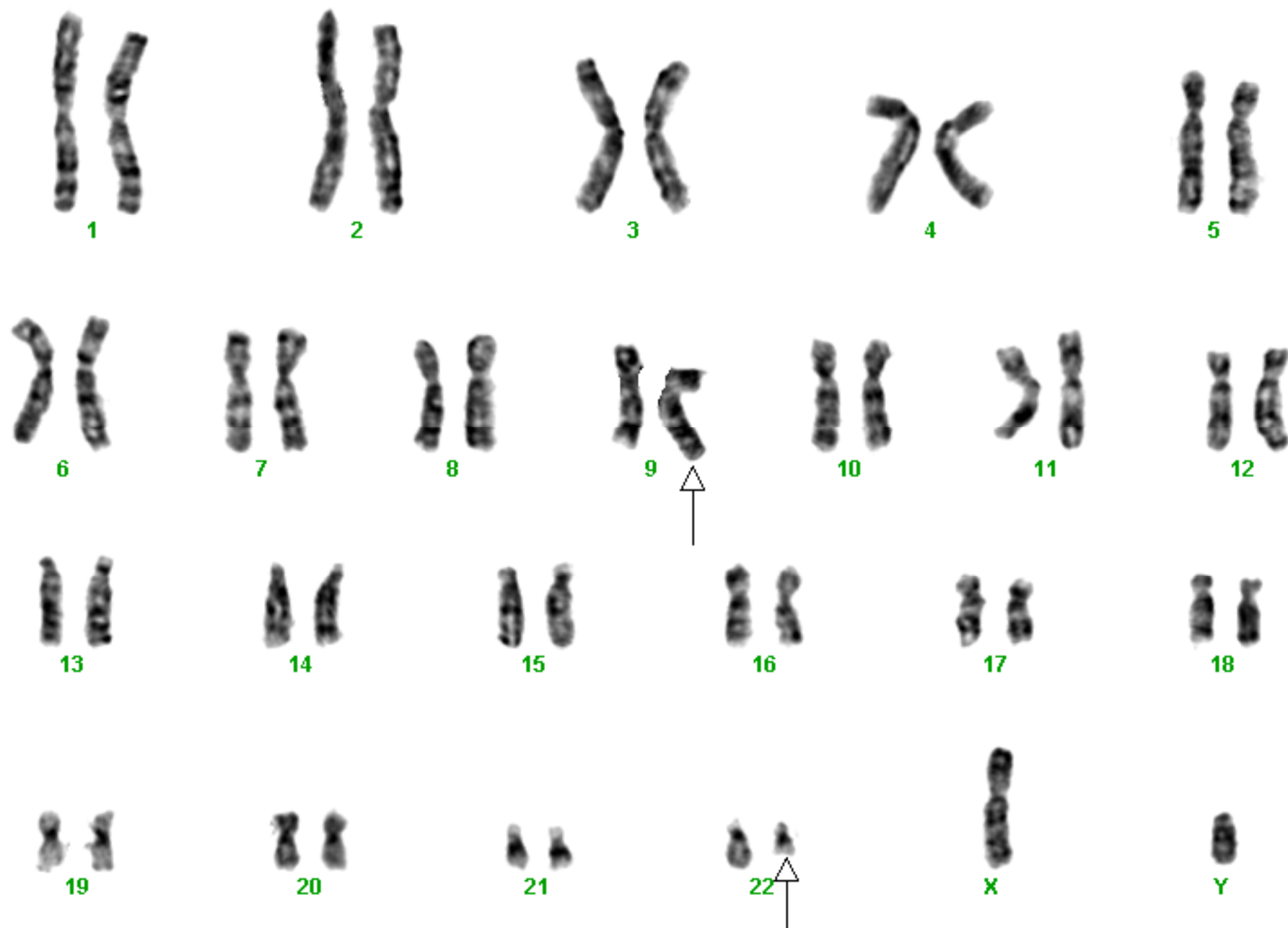


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Introduction

- CML is a hematopoietic stem cell disorder.
- Characterized by the balanced reciprocal translocation $t(9:22)$.
- Fusion gene, the BCR-ABL, is responsible for oncogenesis





46,XY,t(9;22)(q34;q11.2)[20].

BCR-Abl affects multiple cell functions

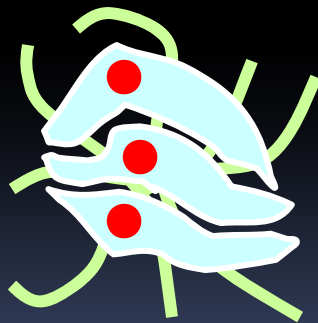
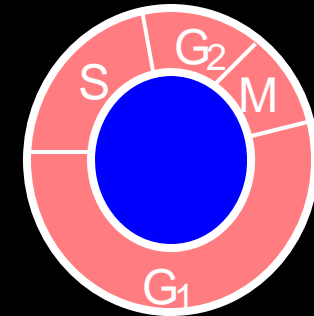
Proliferation & differentiation ↑



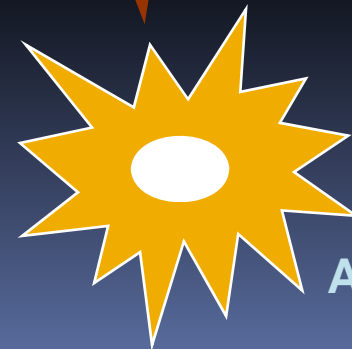
Stem cell turnover ↑



BCR-Abl



Cytoskeleton/
adhesion defects



Apoptosis ↓




Introduction

- CML in childhood is biologically the same disease as in adults.
- Rare disease in childhood (2%-3% of childhood leukemias).
- No predilection for sex and race.
- No association with genetic syndromes / infections.



Introduction


- Studies in adults provide authentic information for the management of CML in pediatric patients.
 - Therefore many years of follow-up are needed to assess the impact of therapeutic strategies.
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BMT Vs Imatinib

- The potential curative therapy is allogeneic marrow transplant in children.
- Imatinib mesylate is a novel targeted therapy for CML discovered in the past decade.
- Approved by FDA in 2003 for childhood CML.



The Study

- The main objective of this study was to evaluate the safety and efficacy of imatinib in children and adolescent group.
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Patients and Methods

- The study was conducted at Aga Khan University Hospital.
- Patients with the age of less than 18 years and Philadelphia chromosome positive CML were included in the study.
- Patients were analyzed weekly/ monthly for hematological response and at the end of 6 months for the cytogenetic response.

Response Assessment

- Complete hematologic response (CHR) –
- Complete cytogenetic response (CCyR) –
- Major cytogenetic response (MajCyR) –
- Minor cytogenetic response (MinCyR) –
- No cytogenetic response (NCyR) –

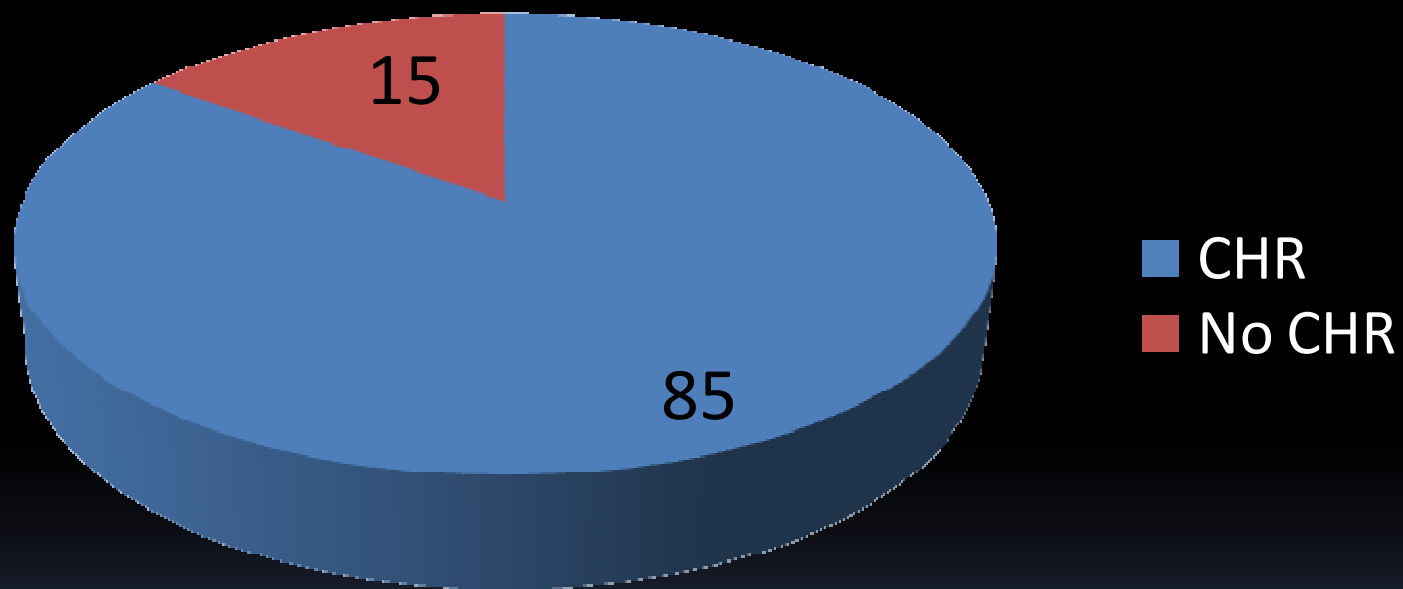
Patients characteristics

Number of Patients	20
Age (Mean)	15.2 yrs
Age (Range)	9 – 18 yrs
Male :Female	1.5:1
Hemoglobin	9.7 gm/dl
TLC	196 x 10 ⁹ /L
Platelets	473 x 10 ⁹ /L
Splenomegaly	85 %

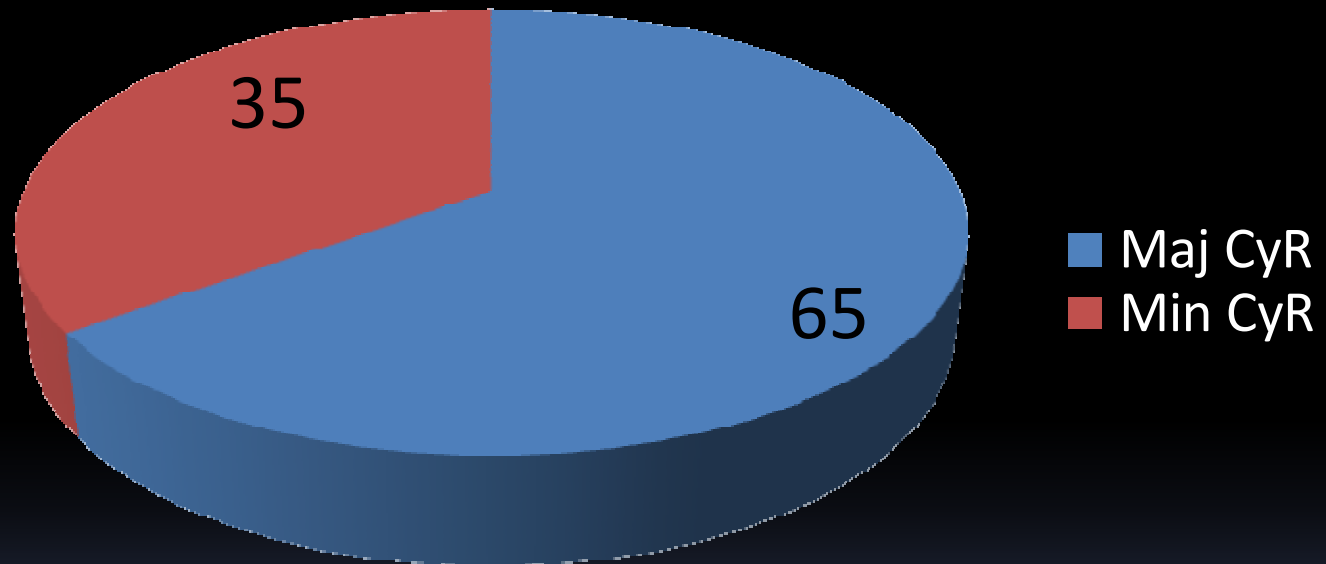
Patients characteristics

Phase	No.
Chronic	16
Accelerated	3
Blast Crisis	1

Hematological Response



Cytogenetic Response



Response

Phase	CHR	Maj Cy R	Min Cy R
Chronic	14	12	4
Accelerated	2	1	2
Blast Crisis	1	0	1

Side effects

Side effects	No.	Percentage
<u>Hematological</u>		
Anemia	1	5
Neutropenia	3	15
Thrombocytopenia	2	10
<u>Non hematological</u>		
Skin rash	1	5
Weight gain	1	5
Muscle cramps	3	15

Data Comparison

Trial	No of patients	Dose/duration	Response (Maj Cy R)
Anders Kolb et al	5	240 - 360 mg/m ²	80%
Martin A et al	14	400 mg	83%
Millot et al	30	300-400 mg	60%
<i>Present study</i>	<i>20</i>	<i>300 - 400 mg</i>	<i>65%</i>

Conclusion

- In Paediatric and adolescents patients with CML imatinib mesylate was well tolerated and good response rates .
- However the debate is still on, considering the younger age of patients, among the choices of imatinib vs. Allo-SCT.

Thank you.