



Pilot Study on a Response Directed Switch from Nilotinib to Imatinib in Newly Diagnosed Chronic Myeloid Leukemia.

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Background

- The treatment of newly diagnosed chronic phase chronic myeloid leukemia (CML) with nilotinib has resulted in a higher rate of major molecular (MMR) and complete cytogenetic response (CCyR) at 12 months compared to imatinib.
- However, long-term toxicities related to nilotinib is of significant concern, particularly cardiovascular events that occurred in about 20% of patients over a 10-year period.
- In addition to cumulative TKI costs as a substantial economic burden, especially in developing countries.

Objective

- The aim of the study is to evaluate the efficacy and safety of a response-directed switch from nilotinib to imatinib in patients newly diagnosed with CP-CML.

Design

- This is a single arm interventional phase 2 clinical trial conducted at the American University of Beirut Medical center (AUBMC), Beirut, Lebanon

Treatment Plan

- Patients were treated with nilotinib at the standard dose of 300 mg orally twice daily for 12 months, and who achieved CCyR or partial cytogenetic response (PCyR) were shifted to imatinib at a dose of 400 mg orally once daily, with regular follow ups at 3, 6, 12 months, then every 6 months thereafter.

Clinical Endpoints

- The primary endpoint was to evaluate the efficacy of imatinib in maintaining molecular responses achieved at 12 months after nilotinib treatment.
- Secondary endpoints were to assess the safety of such strategy.

Results

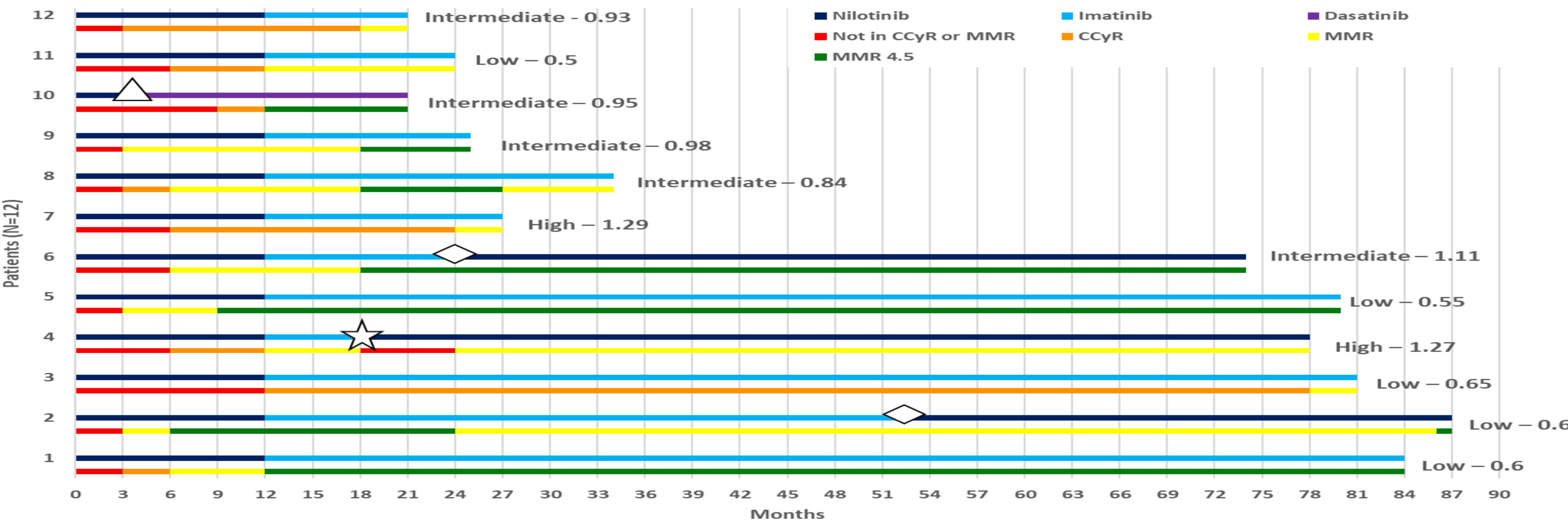
- Thirteen patients were enrolled in the study.
- Eleven patients completed one year of nilotinib and switched to imatinib 400mg daily as per protocol.

Baseline Characteristics

Variable	N (%) – median (range)
No. evaluable patients	12
Male gender	8 (67)
ECOG performance status ≤ 2	1 (0-2)
Sokal risk score	
Low	5 (42)
Intermediate	5 (42)
High	2 (16)
Smoking status	5 (42)
Age – years	51 (31-85)
WBCs - /mm ³	91750 (19500-464000)
Platelets - /mm ³	284000 (152000-794000)
Median time from diagnosis to treatment, days	9 (2-32)
Median Follow-up in months	54 (21-87)

Results

Response Milestones



- At 3 months, all patients achieved a complete hematologic response, with 7 (54%) patients had early molecular response.
- At 12 months, all patients achieved CCyR, of whom 5 (45%) and 4 (36%) patients achieved MMR and MR4.5, respectively.
- Three (27%) patients switched back to nilotinib after 18, 24, and 51 months respectively: one patient lost CCyR after 18 months, and two patients were imatinib intolerant.
- After a median follow-up of 60 months, all patients (n=12) were alive and in MMR, 6 (50%) of them in continuous MR4.5.
- No new safety concerns emerged in the study.

Conclusion

- These findings suggest that response-directed switch from nilotinib to imatinib at 12 months is capable of maintaining long-term CCyR, with manageable side effects.
- This study serves as a pilot study for a later research to be carried out investigating alternative approaches like a response – directed switch from nilotinib to imatinib, or even lowering the dose of nilotinib to 150 mg twice daily beyond 12 months..