Impact of Imatinib interruption & duration of prior Hydroxyurea on treatment outcome in CML patients

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INTRODUCTION

- CML is a myeloproliferative neoplasm characterized by presence of BCR-ABL fusion gene resulting in uncontrolled proliferation of mature and maturing granulocytes.

- CML accounts for 15-20% of leukemias in adults.

- It has an annual incidence of 1-2 cases per 100,000, with a slight male predominance.

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INTRODUCTION

- The management of CML has undergone a profound evolution over a relatively short period of time, with the introduction of Imatinib in 1998.

- Imatinib produced significantly higher hematologic and cytogenetic response rates with deeper, more durable responses, and much less toxicity than interferon therapy, which had been standard of care prior to availability of Imatinib.

- Optimal response requires that patients should be maintained on the drug continuously.

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Aim of work

- Evaluation the impact of Imatinib interruption and prior Hydroxyurea use on response and progression free survival of patients with CML in chronic phase.

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Patients and Methods

- Between January 2010 and December 2013, all patients with chronic phase CML who received Imatinib at our department were included in a retrospective analysis.
- The patients were analyzed with respect to the demographic profile, EUTOS score, molecular response and survival.
- Patients were divided into 2 groups according to prior Hydroxyurea administration or Imatinib interruption.

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Patients and Methods

- The 2009 European Leukemia Net (ELN) response criteria was adopted to define chronic, accelerated, blastic phases and to assess the response.

- PFS was defined as time from start of Imatinib to onset of an accelerated or blastic phase, discontinuation of Imatinib due to failure, sub-optimal response or death.

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Results

- During study period, 60 patients were included. 33 patients (55%) received Imatinib upfront, while 27 (45%) received Imatinib post Hydroxyurea.

- On the other hand, half of patients (30 patients) received the drug regularly without interruption while the other half had interruption of more than 7 days over 3 months period.

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Baseline characteristics

		Number (%)
Total number		60 (100)
Age	Median (range)	46 (18 – 86)
Gender	Male	30 (50)
	Female	30 (50)
EUTOS score	low	45 (75)
	high	15 (25)
TLC	Median (range)	150 (29.8 – 500)
Hgb	Median (range)	10 (6.4 – 12.6)
Plt	Median (range)	271 (93 – 797)

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Response evaluation according to prior Hydroxyurea use

	Upfront Imatinib	Prior Hydroxyurea	P value
	N= 33	N= 27	
CHR at 3 mo	31 (94%)	24 (89%)	0.234
MMR at 6 mo	19 (57.5%)	15 (55.5%)	0.757
CMR at 12 mo	9 (27%)	6 (22%)	0.462

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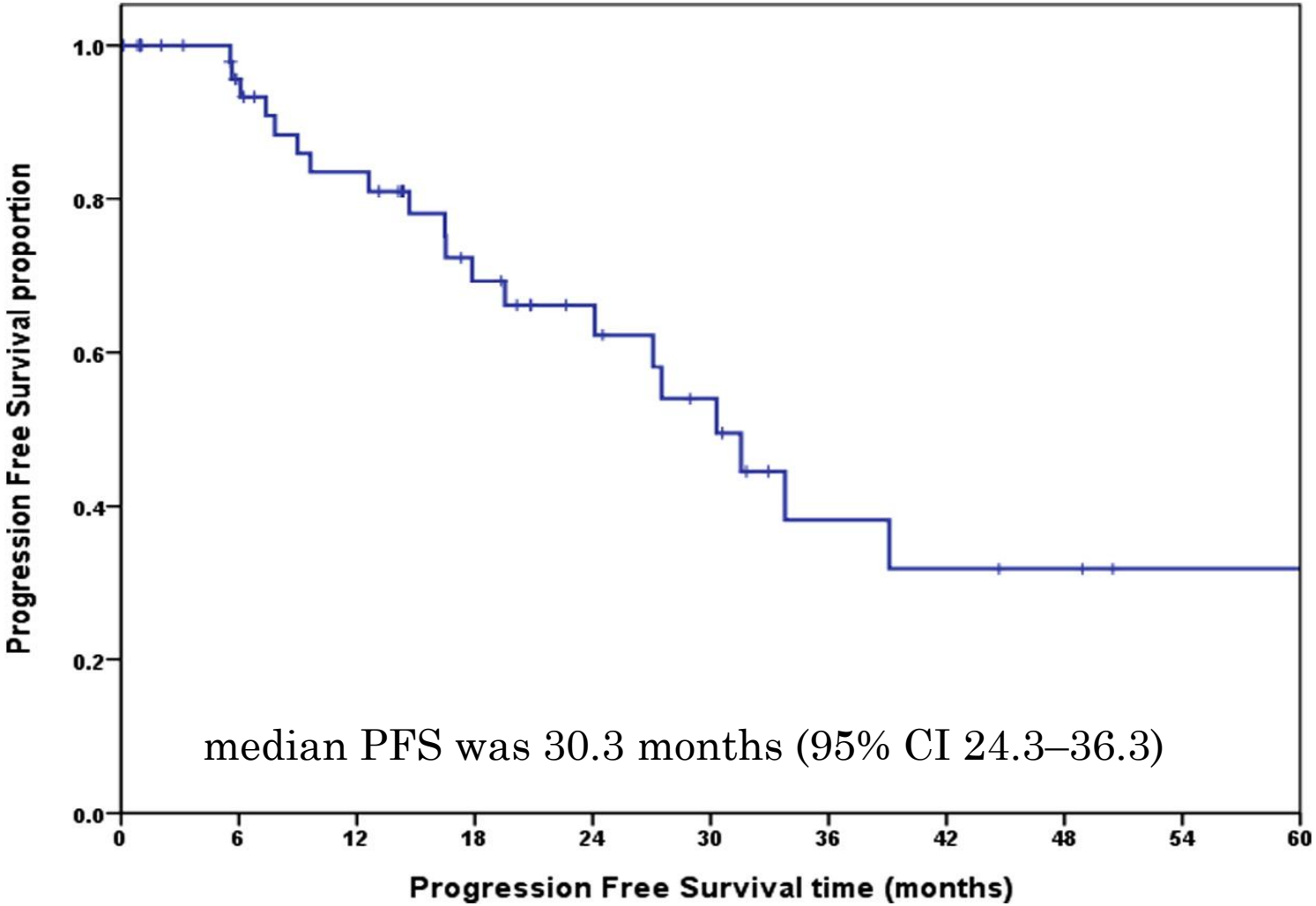
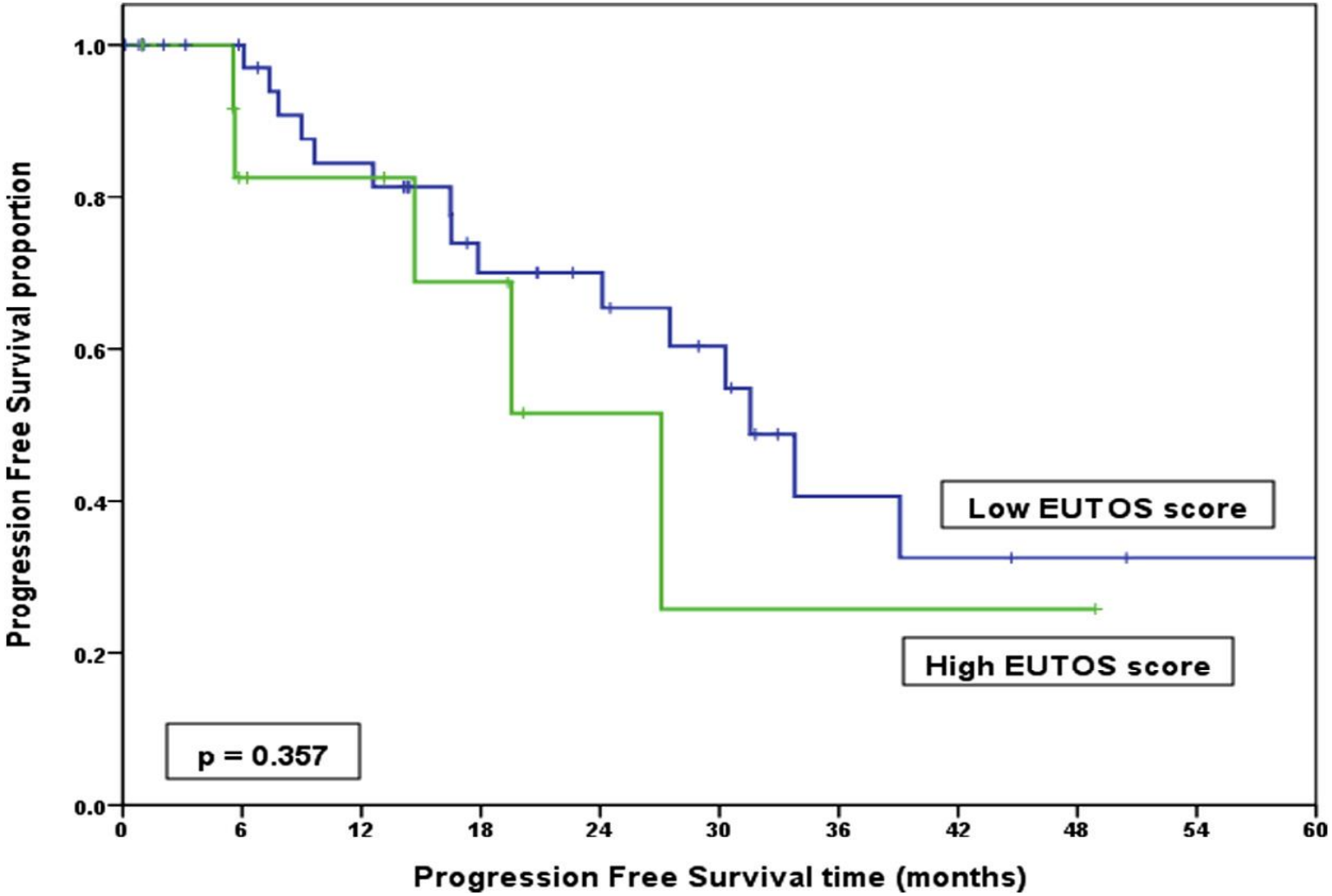
Response evaluation according to Drug Interruption

	No interruption	Interruption	P value
	N= 30	N= 30	
CHR at 3 mo	28 (93%)	27 (90%)	0.234
MMR at 6 mo	21 (70%)	9 (30%)	<0.001
CMR at 12 mo	13 (43.3%)	0 (0%)	<0.001

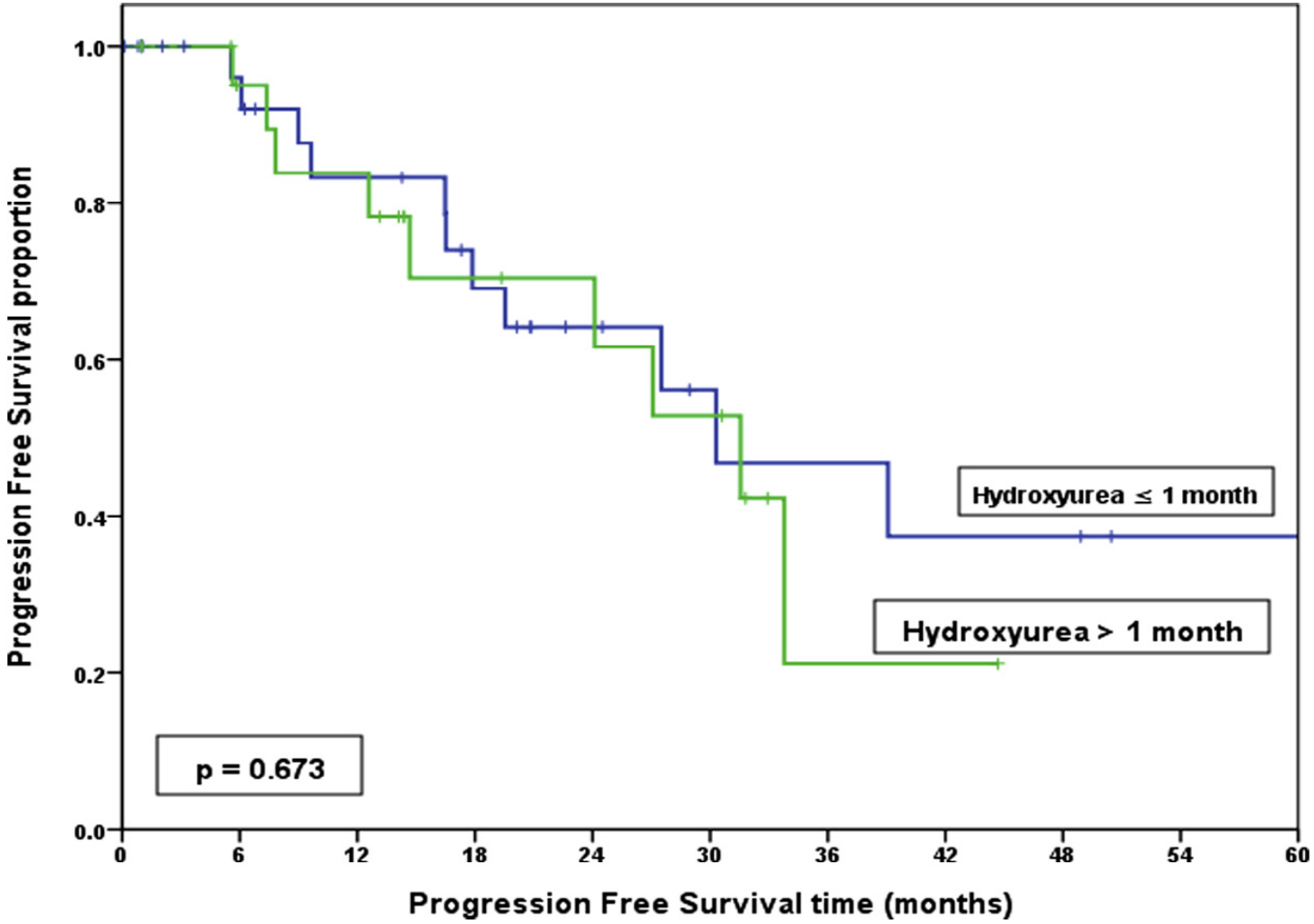
Survival analysis



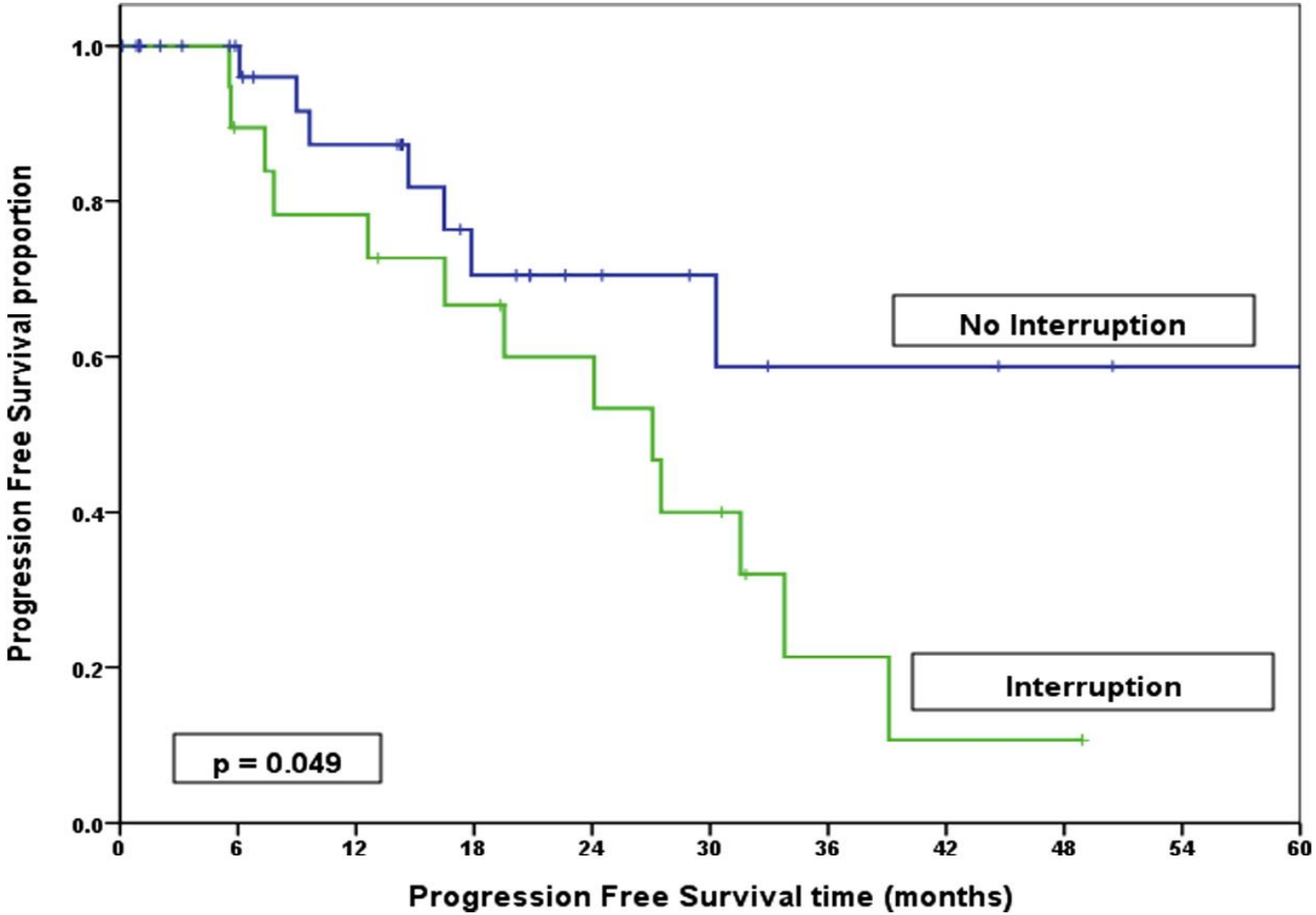
PFS according to EUTOS score



PFS acc to prior Hydroxyurea use



PFS according to Drug Interruption



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CONCLUSIONS

- In conclusion, duration of prior Hydroxyurea had no impact on response or PFS.
- Patients regular on Imatinib had statistically significant higher MMR, CMR and PFS, compared to those who had periods of drug interruption.
- Thus, we need more governmental support to supply the drug without interruption to improve treatment outcome for our CML patients.

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	P value	HR	95% CI
Imatinib (prior Hydroxyurea vs. no)	0.673	1.21	0.49 – 2.96
Drug administration (Interruption vs. No)	0.049	2.38	1.01 – 5.99
EUTOS score (High vs. Low)	0.360	1.61	0.58 – 4.48