EHA18ABSSUB-5460

IN CML PATIENTS TREATED FRONTLINE WITH IMATINIB, WITH A BCR-ABL RATIO HIGHER THAN 10% AT 3 MONTHS, THE CHANGE TO A 2ND GTKI IS ASSOCIATED WITH IMPROVEMENT OF CYTOGENETIC RESPONSE, BUT NOT WITH MMR

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Poster Presentation

Background: A cut-off value of BCR-ABL ratio of more than 10% at 3 months discriminates patients with an ulterior worse outcome in treatments with Imatinib, Dasatinib, Nilotinib, and Bosutinib. There is limited data about how this outcome is affected by change to a 2GTKI.

In our registry of Imatinib front-line treated patients, 156 out of 374 (41,7 %) had been molecularly evaluated at 3 months.

Aims: To asses the influence of treatment change to 2GTKI in the outcome of patients with mollecular evaluation at 3 months.

Methods: Demographics. 93 M, 63 F, median age: 54,2 y (15-86). 7 received HD Imatinib upfront.

Results: Among 156 patients evaluable, 50 (32%) had a ratio of > 10% . Sokal, Hasford, or EUTOS risk score were not significantly associated with this cut-off.

Response: The Probability of obtaining CCyR while on Imatinib was 89% for those patients with ratio of 10% or less (vs 66% with > 10%) p< 0.**0001**.

The probability of CCyR, considering all TKI treatments was 92% for those patients with ratio of 10% or less (vs 77% with > 10%) p=0.**007**.

The probability of obtaining MMR while on Imatinib was 80% for those patients with ratio of 10% or less (vs 47% with > 10%) p< 0.**0001**.

The probability of MMR, considering all TKI treatments was 88% for those patients with ratio of 10% or less (vs 58% with > 10%) p< 0.**0001**.

Response after changing therapy

43 patients changed to a 2GTKI (30 to Dasatinib, 13 to Nilotinib). The median time to change was 15 months (3-82m). 19 patients changed during the 1 st year,and 13 beyond 2 years.

Among the 106 patients with a ratio of 10% or less, 23 (22%) changed to a 2GTKI. The most frequent causes were intolerance (44%) and lost of response (39%). The probability of obtaining a CCyR and MMR after changing to a 2GTKI were 87% and 65%, respectively.

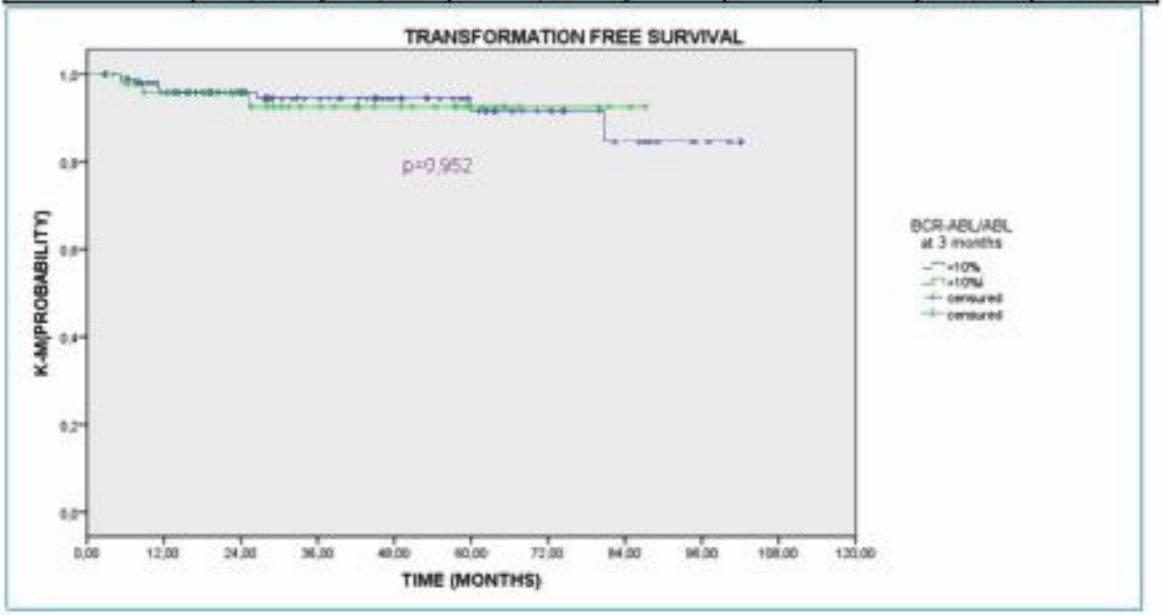
Among the 50 patients with a ratio of more than 10% , 20 (40%) changed to a 2GTKI, mostly because of intolerance (40%) or primary resistance (55%). The probability of obtaining a CCyR and MMR after change were 75 % and 45%, respectively.

Survival outcomes

PFS and OS were not significantly different across the 10% threshold at 3 months,(91,6 vs 92,5%) and (93,5 vs 02,8%) by 7 years, respectively

Image / Pictures:

	Best response with imatinib				Best response with imatinib or I+2ªGTKI				
BCR-ABL/ABL at 3 months	CCyR	MMR	Switch 2ªGTKI		CCyR	MMR	Events	CCyR all	MMR all
Less than 10% 106/156(68%)	94/106 (89%)	85/106 (80%)	yes	23/106 (22%)	20/23 (87%)	20/23 (65%)	3/23 (13%)	98/106 (92%)	93/106 (88%)
			no	83/106 (88%)	78/83 (94%)	73/83 (88%)	4/83 (5%)		
More than 10% 50/156(32%)	31/47 (66%)	23/49 (47%)	yes	20/50 (40%)	15/20 (75%)	9/20 (45%)	2/20 (10%)	37/48 (77%)	29/50 (58%)
			no	30/50 (60%)	22/28 (79%)	20/30 (67%)	2/30 (7%)		
	P<0,0001	P<0,0001	P=0,017					P=0,007	P<0,0001



Summary / Conclusion: In the setting of a multicentric, hospital based registry, only 42% of the CML patients treated with imatinib frontline were molecularly evaluated. The 10% BCR-ABL ratio threshold at 3 months discriminates the probability of obtaining CCyR and MMR thereafter, not only with imatinib, but with sequential TKI therapy. Although the reasons for changing to a 2GTKI in patients having £10% and > 10% ratio differ, the improvement is small, and confined to cytogenetic response, whereas molecular response is not increased. But the proportion of transformation or death was not increased in any of the groups.

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Keywords: Chronic myeloid leukemia, Imatinib