Imatinib dose reduction in major molecular response of chronic myeloid leukemia: results from the German Chronic Myeloid Leukemia-Study IV

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Supplementary material

Molecular analyses

Molecular diagnostics for residual BCR-ABL transcripts followed the procedures and definitions of Hughes et al. [1] and Cross et al. [2] and were performed in two standardized and accredited laboratories with defined conversion factors for equivalence of tests (Mannheim and MLL Munich) [3].

The analysis of molecular end points was restricted to patients expressing b2a2 and/or b3a2 transcripts. MMR, MR^4 and $MR^{4.5}$ were defined as previously described [2, 4].

To be considered for this analysis, in accordance with its meaning for later deep MR, the last molecular response in the high-dose treatment interval before reduction to 400 mg/day had to be at least MMR. Results of molecular samples taken within one month after stopping high-dose treatment were still attributed to the high-dose therapy. Molecular diagnostics dating from one month after start of reduced imatinib therapy with 400 mg/day to 14 days after end of reduced therapy were rated as results linkable to the reduction period. This fortnight was not considered, if end of reduction therapy meant the restart of 600 or 800 mg/day or start of a second-generation TKI. Treatment breaks within the reduction period of not more than six weeks were acceptable and not particularly considered. In contrast, treatment breaks of more than six weeks were not regarded as a part of the reduced-treatment interval. In this situation, only the first period with reduced therapy was evaluated with regard to continued molecular response.

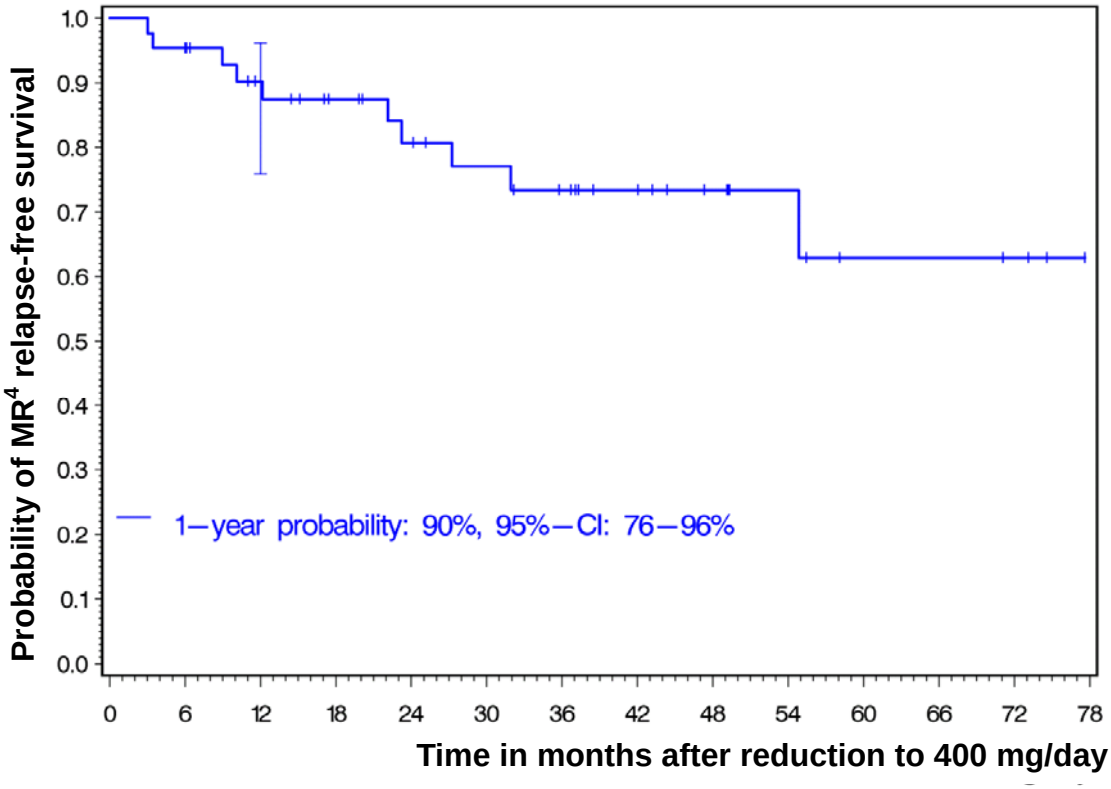
Supplementary Table 1. Characteristics of the 68 patients included in the study

Characteristic, unit	Median (range) or n (%)	Mean (standard deviation)
Variables recorded at diagnosis		
Age (years)	52 (20-81)	50 (13)
Sex (number and proportion of males)	48 (71%)	
Spleen size cm below costal margin (cm)	2 (0-18)	3 (4)
White blood cell count (x10^9/L)	74 (3-497)	111 (111)
Blasts in peripheral blood (%)	0 (0-12)	2 (2)
Eosinophils in peripheral blood (%)	2 (0-16)	3 (3)
Basophils in peripheral blood (%)	3 (0-19)	4 (4)
Platelet count (x10^9/L)	358 (123-1535)	417 (247)
Sokal score		
Low risk	29 (43%)	
Intermediate risk	27 (40%)	
High risk	12 (18%)	
Euro score		
Low risk	30 (44%)	
Intermediate risk	34 (50%)	
High risk	4 (6%)	
EUTOS score		
Low risk	62 (91%)	
High risk	6 (9%)	
ELTS Score		
Low risk	44 (65%)	
Intermediate risk	19 (28%)	
High risk	5 (7%)	

Variables recorded under treatment		
Time with 800mg dosage, months	31 (6-98)	35 (20)
Time from start of 800mg until MMR, months	5 (0-23)	7 (5)
Time from MMR until end of 800mg, months	23 (0-93)	28 (20)
Time with 400mg dosage, months	34 (6-78)	32 (19)

MMR=Major molecular remission.

Supplementary Figure 1. Probability of MR^4 relapse-free survival after dose reduction to imatinib at 400mg / day (n=43 pat., at least in MR^4, at stop of high-dose treatment)



Number of patients still at risk (n) at different months of observation

Months	**0**	**12**	**24**	**36**	**48**	**60**	**72**	**78**
Patients at risk, n	43	33	24	18	10	4	3	0

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