Abstract: P713

Title: EUROPEAN LEUKEMIANET MILESTONES AND THEIR PROGNOSTIC RELEVANCE FOR ACHIEVING DEEP MOLECULAR RESPONSE AND TREATMENT-FREE REMISSION IN ROUTINE CARE: RESULTS OF THE GERMAN CML REGISTRY

Abstract Type: Poster Presentation

Topic: Chronic myeloid leukemia - Clinical

Background:

Tyrosine kinase inhibitor (TKI) induced molecular response (MR) within the first months after diagnosis of chronic myeloid leukemia (CML) is critical for long-term outcome prediction.

Aims:

To analyze the prognostic relevance of MR according to European Leukemia Net (ELN) treatment milestones in CML patients in routine care with regard to the different TKI.

Methods:

Within the German CML registry, adult patients (pts) with CML newly diagnosed between 2013 and 2019 were registered and followed annually. Endpoints included time to MR, progression and death. MR was analyzed according to the ELN recommendations 2013 with the focus on the *BCR::ABL1* (International Scale, IS) levels <10% (EMR, early molecular response) at 3 months (mo, M3), <1% (MR2) at 6 mo (M6) and <0.1% (MMR, major molecular response) at 12 mo (M12) using the cumulative incidence function. MR at milestones were correlated to DMR (deep molecular response, defined as *BCR::ABL1IS* <0.01%) and TKI treatment.

Results:

A total of 540 pts have been registered from 91 centers. 30 pts had to be excluded (inclusion failure), 510 pts were evaluable for baseline analyses. Median age at diagnosis was 59 years (range (r) 16-100), 264 pts (52%) were male. Median follow-up was 5.4 years. First-line treatment included imatinib ([n=209 (41%)], nilotinib [n=141 (28%)], dasatinib [n=144 (28%)], other and unknown [n=16 (3,%)].

For MR analyses 481 pts were evaluable. Of these 479 (99,6%) achieved an EMR after a median of 3 mo [r 0-54], 461 (95,8%) pts MR2 [median 5 mo (r 1-54)], and 449 (93,3%) pts MMR [median of 9 mo (r1-82)]. DMR was achieved in a total of 385 (80,0%) pts after a median of 15 mo (r 1-96) of which at least 282 (58,6%) had a MR level according to MR4.5 (BCR::ABL1 <0.0032%).

Pts on imatinib treatment achieved DMR in 74% (n=154) of which 52% (n=109) achieved MR4.5: On dasatinib and nilotinib this was achieved by 74% (n=106) and 84% (n=119) pts for DMR, respectively and 51% (n=74) and 70% (98 pts) for MR4.5, respectively

At M3, 311 pts were evaluable, at M6 366 pts and at M12 410 pts. Milestones M3, M6, and M12 were achieved in 275 (88%), 311 (85%), and 301 (73%) pts.

Milestones were achieved in a higher percentage of pts on dasatinib and nilotinib compared to imatinib (Table 1). DMR was achieved in 235 (85%), 268 (86%) and 275 (91%) pts who reached M3, M6, and M12, respectively. In pts who did not reach M3, M6, and M12 only 16 (44%), 25 (45%), and 56 (51%) pts achieved DMR. 93 (19%) pts stopped TKI-treatment with the aim of treatment-free remission (TFR). Thereby TFR approach after imatinib (n=29, 14%) and dasatinib (n=19, 13%) in 1st-line was observed much less frequently than after nilotinib (n=45, 32%). After reaching M3, M6, and M12 TFR-approach was observed in 24%, 23%, and 26%, respectively. Both results were favorable for pts on nilotinib compared to imatinib and dasatinib.

Pts who failed the milestones started a TFR approach in only 3-6%. These pts were mostly treated with imatinib.

Pts who had missed the milestones after imatinib and achieved a TFR, switched except for one pt before TFR to a 2nd generation TKI (Table 1).

Summary/Conclusion:

In routine care, achieving ELN milestones in CML was associated with higher DMR rates. As DMR is a prerequisite for stopping treatment in CML, the rate of pts who could start TFR after achieving the ELN-milestones was 4-5 times higher than of pts who failed milestones. The rate for DMR after reaching the milestones is comparable for all TKI, however the rate of pts with TFR-approach after nilotinib was higher than after dasatinib and imatinib.

Table 1

M3	All Patients					Imatinib in 1st-line					Dasatinib in 1st-line					Nilotinib in 1st-line					Other
		DMR		TFR			DMR		TFR			DMR		TFR			DMR		TFR		
	total	n	%	n	%	total	n	%	n	%	total	n	%	n	%	total	n	%	n	%	
M3 achieved	275	235	85%	66	24%	88 (77%)	77	88%	17	19%	86 (91%)	70	81%	16	19%	97 (96%)	84	87%	33	34%	4
M3 failed	36	16	44%	1	3%	26 (23%)	10	38%	2	8%	6 (7%)	3	50%	0	0%	4 (4%)	3	75%	0	0%	0
M3 evaluable	311	247	79%	67	22%	114 (100%)	87	76%	19	17%	92 (100%)	73	79%	16	17%	101 (100%)	87	86%	33	33%	4
M6																					Other
M6 achieved	311	268	86%	72	23%	98 (73%)	86	88%	18	18%	96 (88%)	84	88%	18	19%	112 (97%)	98	88%	36	32%	5
M6 failed	55	25	45%	3	5%	37 (27%)	18	49%	4	11%	13 (12%)	5	38%	0	0%	4 (3%)	2	50%	0	0%	1
M6 evaluable	366	293	80%	75	20%	135 (100%)	104	77%	22	16%	109 (100%)	89	82%	18	17%	116 (100%)	100	86%	36	31%	6
M12																					Other
M12 achieved	301	275	91%	77	26%	106 (65%)	97	92%	22	21%	92 (78%)	86	93%	18	20%	98 (79%)	92	94%	37	38%	5
M12 failed	109	56	51%	7	6%	57 (35%)	28	49%	4	7%	26 (21%)	13	50%	0	0%	26 (21%%)	15	58%	3	12%	0
M12 evaluable	410	331	81%	84	20%	163 (100%)	125	77%	26	16%	118 (100%)	99	84%	18	15%	124 (100%)	107	86%	40	32%	5

Other: HU, Interferon, not specified
DMR: deep molecular response, defined as BCR-ABL1IS <0.01%
TFR: stopped TKI-treatment with the aim of treatment-free remission (TFR)

Keywords: treatment-free remission, Molecular response, Prognostic factor, Chronic myeloid leukemia