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POSTER ABSTRACTS

632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

The Use of 2 nd Generation TKIs As First Line Therapy Does Not Prevent CML Related Deaths: Results of an Italian CML Campus Prospective Study in 1277 Patients Treated First Line with Imatinib or 2 nd Generation TKIs

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Background: In the last decades prognosis and survival of chronic myeloid leukemia (CML) patients have dramatically improved, thanks to a wider therapeutic armamentarium. Molecular responses are the milestones that guide clinical decisions; however, some information is still lacking and what we know derives mainly from investigational trials: it is still unclear if real-life management could lead to comparable results. For this reason, a prospective observational study was conducted by a CML Italian network to analyze molecular responses in a real-life setting.
Methods: A web-based database (www.epiclin.it/lmc) was used to collect clinical and biological data on newly diagnosed CML prospective consecutive patients enrolled in 24 Italian Hematology Centers from January 2013 onwards. Patients were treated according to the policy of the center and the molecular data were obtained by performing tests in accordance with the IS% parameters.
Results: A total of 1277 patients were enrolled (Tab. 1) with a median follow up of 4,1 years. There was a significant difference in the median age of patients who started with imatinib (IMA) or 2 nd gen TKIs (II-TKI): 70 vs 52, respectively.
The Overall Survival (OS) of the whole cohort at 5 years was 80% for the IMA and 94% for II-TKI treated patients respectively. Out of the total 86 deaths observed in the IMA treated cohort only 11 (12.7%) were due to CML related causes, whereas out of the 32 deaths observed in the II-TKI treated cohort 12 (37.5%) were due to CML. Out of the 607 patients who were on first line IMA, 422/607 (69%) did not switch therapy and have an OS of 81% at 5 years. One hundred and eighty-five out of 607 (31%) changed therapy and showed an OS of 80% at 5 years. Out of 670 patients who started with II-TKI, 492 (73%) continued the same treatment and 178/670 (27%) changed therapy, showing a 5-year OS of 96% and 89%, respectively. In summary, patients who remain in the same type of therapy in which they were initially started show a 5-year OS of 81% and 96% for IMA and II-TKI respectively and only 9 of the total 73 deaths observed in this group of 914 patients were CML related (8 of 58 II-TKI treated patients). Patients who switched to another therapy showed 80% and 89% 5-year OS on IMA and II-TKI group, respectively. Of the 45 deaths observed in this group of 363 patients, 14 were CML related (3 on IMA and 11 on II-TKI) (Tab. 2).
In IMA treated patients, 5-year OS according to 6- and 12-months molecular response was worse for patients with BCR::ABL1 >1% compared to those with values between 1 and 0.1% and <0.1% BCR::ABL1 patients (looking at 12 months response, OS was 65% vs 85% vs 90%, Fig. 1A). At 24 months there was a statistical difference in OS between patients with BCR::ABL1 between 1 and 0.1% versus those <0.1% (OS at 3 years was 82% vs 92%) (Fig. 1B).
Among II-TKI treated patients, no significant differences in OS were observed, but there was only a generic trend for those with deeper molecular responses between patients with BCR::ABL1 >0.1 versus patients with BCR::ABL1 < 0.1% at all timepoints; to note, the deaths are few and were observed within the first year, independently from the molecular response achieved: at 6 months, 10 deaths on 113 patients of which 7 CML related; at 12 months, 5 deaths on 48 patients of which 4 CML related. Row comparisons of OS were confirmed with multivariable Cox models including main prognostic factors.
Conclusions: The real-life data collected by this observational study support the good prognosis of CML patients obtained in our days independently by the TKI used in first line. Indeed, most of the deaths observed are due to CML unrelated causes and the use of II-TKIs does not seem to prevent the CML related deaths, whose number is similar in both cohorts. The fact that the OS is similar in those who remain in IMA therapy versus to those who switch could also simply reflect the presence of unfavorable prognostic factors at diagnosis not controlled by IMA nor by II-TKIs. In this scenario, the observation that the achievement of <1% at 12 months and of MMR at 24 months in patients treated with imatinib is endowed with a statistically significant better OS could simply represent an association rather than a determining factor. Early NGS study would probably provide helpful information at this regard and for identifying patients that, even if treated first line with II-TKIs, could benefit of an early switch, since 11 of the 12 progressions were observed in this group.

Disclosures Giai: *Sobi:* Membership on an entity's Board of Directors or advisory committees; *Alexion:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Membership on an entity's Board of Directors or advisory committees. **Stagno:** *Incyte, Novartis, Pfizer:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Speakers Bureau. **Castagnetti:** *Bristol Myers Squibb:* Honoraria; *Incyte:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria, Research Funding; *Novartis:* Consultancy, Honoraria, Research Funding. **Bonifacio:** *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board of Directors or advisory committees; *Clinigen:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Membership on an entity's Board of Directors or advisory committees; *Incyte:* Membership on an entity's Board of Directors or advisory committees. **Galimberti:** *Abbvie, Janssen, Novartis, Roche, Jazz, Astra Zeneca, Pfizer, Incyte:* Speakers Bureau. **Bocchia:** *Novartis:* Honoraria; *Incyte:*

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		ALL		IMA		II-TKI	
n		1277		607		670	
		n	%	n	%	n	%
Sex	Female	532	41.66	242	39.87	290	43.28
	Male	745	58.34	365	60.13	380	56.72
Age	Median	58		70		52	
ELTS	Low	761	59	305	50.25	456	68.06
	Intermediate	361	28	218	35.91	143	21.34
	High	153	12	83	13.67	70	10.45
CCI	Low (2)	908	71.10	341	56.18	567	84.63
	Intermediate (3-4)	293	22.94	209	34.44	84	12.54
	High (>5)	72	5.64	53	8.73	19	2.84
ACA	all	179	14	79	13	100	14.9
	Major routes	80	6.3	26	4.3	54	8

Table 1: Patients characterics.
CCI: Charlson Comorbidity Index; ACA: additional cytogenetic abnormalities

	5-year OS (%)		CML related death		
	IMA	II-TKI	IMA	II-TKI	Tot deaths
1 line	81	96	8/58	1/14	72
> 1 line	80	89	3/27	11/17	44

Table 2: OS and CML related death in patients treated with 1 therapy or > 1 therapy, starting with IMA or II-TKI

Fig.1A: OS according to 12 months molecular response in IMA patients

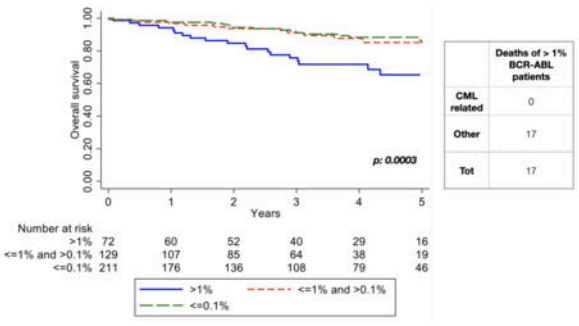

Fig. 1B: OS according to 24 months molecular response in IMA patients

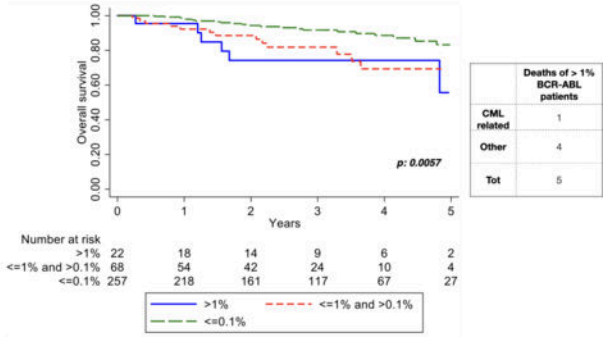

Figure 1

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