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POSTER ABSTRACTS

632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

3-YEARS and Beyond Study Completion Results of the Otpkima Randomized Clinical Trial in Elderly CML Patients

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The goal of Treatment Free Remission (TFR) is achievable in no more than 25-30% of patients with Ph+ Chronic Myeloid Leukemia (CML) treated with Tyrosine Kinase Inhibitors (TKIs). Thus, for the great majority of patients, particularly for the elderly, the options are to continue TKI therapy life-long or to enter an intermittent TKI administration, as previously published (*Russo D et al, Blood 2013; Russo et al Blood Adv 2015*). The probability of major molecular response (MMR or MR3.0)

maintenance while on intermittent 1 month on/1 month off TKI at 1 year is 80%, as reported recently in the first interime analysis of the Italian prospective randomized OPTkIMA trial *(Malagola M et al, Cancer Med 2021)*.

This is the second interim report of OPTkIMA trial, in which elderly patients with Ph+ CML in sustained (≥ 2 years) confirmed major molecular response (MMR or MR3.0) or deep molecular response (MR4.0 or deeper) were randomly assigned to receive a FIXED intermittent schedule (1 month on/1 month off) vs a PROGRESSIVE intermittent schedule (1 month on/1 month off for the 1 st year, 1 month on/2 months off for the 2 nd year, 1 month on/3 months off for the 3 rd year). After the 3 rd year, clinicians were free to decide if maintain the intermittent schedule, discontinue TKI or resume TKI daily (*Malagola M et al, Cancer Med 2021*).

At last follow up, 203 patients are evaluable after randomization (104 FIXED vs 99 PROGRESSIVE). At 3 rd year (end of study protocol), by intention to treat, 28/104 (27%) and 45/99 (45%) patients discontinued OPTkIMA because of MR3.0 loss in the FIXED vs PROGRESSIVE arm, respectively (p=0.005). The percentages of patients who discontinued OPTkIMA because of MR3.0 loss at 1 st, 2 nd and 3 rd year in the FIXED vs PROGRESSIVE arm were: 24% in both arms (p=0.97), 1% vs 22% (p=0.001) and 3% vs 15% (p=0.01), respectively (Figure 1). The probability of survival without MR3.0 loss at 1, 2 and 3 years in the FIXED vs PROGRESSIVE arm were: 81%, 69% and 66% vs 81%, 59% and 53%, respectively (Figure 2; p=0.13). None of the patients who lost MR3.0 progressed to accelerated or blastic phase (AP/BP) and all of the patients regained the MR3.0 after continuous TKI resumption within 9 months.

At the end of the 3 rd year from randomization, 61/104 (59%) and 36/99 (36%) patients were in MR3.0 or deeper response in the FIXED vs PROGRESSIVE arm, respectively (p=0.001). For these patients, comparing the two arms, Clinicians' choice was to maintain the ongoing intermittent schedule in 46% vs 28% of the cases (p=0.01), discontinue TKI with the goal of TFR in 36% vs 58% (p=0.03), and resume the TKI continuously in 18% vs 14% of the patients (p=0.59).

The results of the OPTkIMA trial clearly confirm that a policy of intermittent TKI administration in elderly patients with Ph+ CML in MR3.0 or deeper response is safe, as no progression to AP/BP was observed. Furthermore, the great majority of protocol discontinuation for MR3.0 loss were recorded in the 1 st year (one month on and one month off in both arms). Then the cumulative incidence of patients who lost MR3.0 beyond the 1 st year was significantly higher in the PROGRESSIVE arm with a trend towards a higher probability of survival without MR3.0 loss in the FIXED arm (Figure 1). Finally, at the end of the study protocol (3 rd year), patients in MR3.0 or deeper response after a FIXED intermittent schedule were more likely addressed to maintain the same program, whereas patients included in the PROGRESSIVE arm were more frequently discontinued with the goal of TFR. This last observation represents a "real-life" CML management by Clinicians. It suggests that after a PROGRESSIVE intermittent therapy, patients were considered at high probability to safely maintain the TFR.

Disclosures Malagola: *Biotest, MSD:* Consultancy, Honoraria. **Iurlo:** *Novartis, Pfizer, Incyte, BMS, GSK, AOP Health:* Honoraria. **Bucelli:** *Novartis/Incyte:* Honoraria. **Abruzzese:** *Takeda:* Consultancy; *Novartis:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *Pfizer:* Consultancy; *Incyte:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *BMS:* Consultancy, Membership on an entity's Board of Directors or advisory committees. **Bonifacio:** *Novartis:* Membership on an entity's Board of Directors or advisory committees; *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; *Incyte:* 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. **Rosti:** *Novartis, Pfizer, and Incyte:* Honoraria. **Roccaro:** *Italian Foundation for Cancer Research; Transcan2-ERANET; AstraZeneca:* Research Funding; *Amgen, Celgene, Janssen. Takeda:* Consultancy. **Polverelli:** *BMS:* Honoraria; *GSK:* Honoraria; *Abbvie:* Honoraria; *Novartis:* Honoraria. **Russo:** *MSD, Novartis, Gilead, BMS, Medac:* Honoraria; *Medac, Abbvie, MSD, Jazz Pharma, Gilead, Novartis:* Membership on an entity's Board of Directors or advisory committees.

Figure 1. Intention to treat distribution of OPTkIMA discontinuation causes during the 3 years of the trial duration and follow up beyond the 3rd year

Patients	FIXED (n=104)	%	PROGRESSIVE (n=99)	%	P
Total OUT	101/104	97	98/99	99	0.33
- OUT for MR3 loss	28/104	27	45/99	45	**0.005**
- OUT for study completion	61/104	59	36/99	36	**0.001**
- OUT for other reasons	12/104	11	17/99	7	0.25
1st year OUT	32/104	31	30/99	30	0.94
- OUT for MR3.0 loss	25/104	24	24/99	24	0.97
- OUT for other reasons	7/104	7	6/99	6	0.84
On OPTkIMA	72/104	69	69/99	70	
2nd year OUT	6/72	8	23/69	33	**0.002**
- OUT for MR3.0 loss	1/72	1	15/69	22	**0.001**
- OUT for other reasons	5/72	7	8/69	12	**0.34**
On OPTkIMA	66/104	64	46/99	46	
3rd year OUT	63/66	95	45/46	98	0.5
- OUT for MR3.0 loss	2/66	3	7/46	15	**0.01**
- OUT for other reasons*	61/66	92	38/46	83	0.11
Clinicians' choice after 3rd year for patients in MR3.0 or deeper who completed the study					
OUT for study completion	61/104	59	36/99	36	**0.001**
Maintain the intermittent schedule	28/61	46	10/36	28	**0.01**
TKI discontinuation	22/61	36	21/36	58	**0.03**
Resume TKI daily	11/61	18	5/36	14	0.59

Figure 2. Probability of Survival without MR3.0 loss (Probability of survival without MR3.0 loss at 1, 2 and 3 years in the FIXED vs PROGRESSIVE arm were: 81%, 69% and 66% vs 81%, 59% and 53%, respectively - p=0.13)

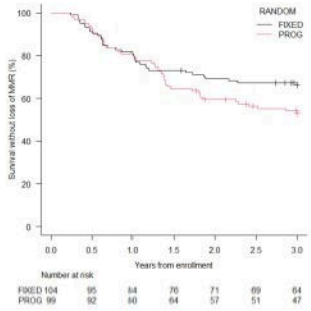

Figure 1

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