

**CLINICAL EXPERIENCE OF BOSUTINIB UNDER COMPASIONATE USE PROGRAM IN CHRONIC MYELOID LEUKEMIA PATIENTS WITH RESISTANCE OR INTOLERANCE TO IMATINIB, DASATINIB AND NILOTINIB**

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Abstract:

**ABSSUB-5596: CLINICAL EXPERIENCE OF BOSUTINIB UNDER COMPASIONATE USE PROGRAM IN CHRONIC MYELOID LEUKEMIA PATIENTS WITH RESISTANCE OR INTOLERANCE TO IMATINIB, DASATINIB AND NILOTINIB**

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**Abstract topic:** 8. Chronic myeloid leukemia - Clinical

**Background:** Bosutinib (BOS) is a dual Src/Abl tyrosine kinase inhibitor that has confirmed a potent activity in patients (pts) resistant or intolerant to previous tyrosine kinase (TKI) inhibitors with a good safety profile. However, the European Medical Agency has approved BOS only for patients (pts) resistant or intolerant to imatinib (IM) and for whom nilotinib (NI) and dasatinib (DA) are not considered appropriate treatment options. Efficacy and safety data have been published of 115 pts who had been pretreated with imatinib followed by dasatinib or nilotini, however only data of 3 pts have been collected in fourth-line setting.

**Aims:** The aim of this study is to present the first data reported of pts treated in Spain with BOS in previous heavily treated patients.

**Methods:** We have collected data of 29 pts among the 35 pts (85%) that have been treated with BOS since 2012 under a Spanish Compassionate Use Program in 16 centers. The study was approved by regulatory authorities and all pts signed informed consent document. Four patients (13%) received BOS in third line (after failure or intolerance to IM and NI or DA) while 25 pts were treated with BOS after receiving IM, DA and NI (one also received ponatinib). The most common indication was pts intolerant to three previous TKI (38%), while 24% were resistant to the 3 TKIs. Patients disposition and main baseline characteristics are shown in table 1.

**Results:** Considering those pts in fourth line (25), the median follow up was 7.23 months RI=[3,67\_9,17]. Time to best response was 5.13 months RI=[2.10-8.32]. BOS was discontinued in 3 pts (12%): 1 death (after progression to advanced phase) (4%), 1 resistance (4%) and 1 intolerance (4%). Event free survival (Guilhot J, et al. Blood 119(25): 5963-5971) was 88%. BOS was usually well tolerated. Grade 3-4 anemia, neutropenia and thrombocytopenia occurred in 6%, 8% and 8% respectively. The most common nonhematological toxicities were diarrhea (48%), nausea (20%), rash (8%), increased ALT/AST (12%) and abdominal pain (12%). Grade 3-4 nonhematological toxicities were observed in 4 pts (1 nausea, 1 gastrointestinal bleeding, 1 ALT/AST elevation and 1 diarrhea). BOS has been proved to be a useful treatment option regardless the indication of use. Patients were classified according to the status when BOS was started. Group 1 consisted of 12 patients (46%) who started treatment as failures (less than CCyR); while 13 patients in group 2 (54%) started treatment with at least CCyR. Responses in group 1 were: CCyR 25% (3/12), MMR 16% (2/12), 75% (9/12) maintained baseline response and 8% (1 patient) progressed. For patients in group 2, probabilities of improve molecular response, sustained baseline response and progression were: 50% (4/8), 77% (10/13) and 15% (2/13) respectively.

**Image/Pictures:**

		IM+NI-I +DA-R	IMA+NI-R +DA-R	IM+NI-I +DA-I	IM+NI-R +DA-I	IM+NI/ DA	TOTAL
Pts, N(%)		3 (10)	7 (24)	11 (38)	4 (14)	4 (14)	29 (100)
Age of diagnosis, med yr		41	47	55	61	54	54
Age of BOS initiation, med yr		47	61	67	72	65	65
Sokal index at diagnosis, N	High	0	1	0	1	0	2
	Intermediate	1	2	5	1	1	10
	Low	1	4	6	1	2	14
Time from first TKI to BOS, med yr		6	10	10	11	11	10
Duration of IM treatment, med, mo		16	33	22	62	87	30
Duration of DA treatment, med, mo		17	16	26	27	27	23
Duration of NI treatment, med, mo		30	14	10	29	24	16

**Summary/Conclusion:** We are presenting (to our knowledge) the largest series of patients treated with BOS fourth line). Our study shows the results in 25 patients treated with bosutinib after failure or intolerance to 3 previous TKIs. In resistant patients, BOS has shown probabilities of CCyR and MMR (25% and 16%, respectively), similar to those described in third line. Bosutinib has also shown a very good safety profile in patients intolerant to 3 previous TKI, and one-half of them improved the response after switching to Bosutinib. Our results show Bosutinib is a safe and effective option for those patients in 4rd line of TKIs, Ongoing analysis of a larger series will be presented at the meeting.

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**Disclosure of Interest:** None Declared

**Keywords:** None