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P663 MULTICENTER, PROSPECTIVE AND RETROSPECTIVE OBSERVATIONAL COHORT STUDY OF PONATINIB IN PATIENTS WITH CML IN ITALY: LONG-TERM FOLLOW-UP RESULTS OF THE OITI TRIAL

Topic: 8. Chronic myeloid leukemia - Clinical

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Background:

Ponatinib is a 3rd-generation TKI indicated for adults with resistant or intolerant CP, AP or BP CML or carrying the T315I mutation. Ponatinib, approved by EMA in 2013 and reimbursed in Italy in 2015, is now a well-established treatment in CML clinical practice.

Aims:

The goal of the Observational study of Iclusig® (ponatinib) Treatment in patients with CML in Italy (OITI) was to evaluate treatment patterns and outcomes, including safety and efficacy, in CML patients treated in Italy since ponatinib approval.

Methods:

This non-interventional study included patients ≥18 years with CP, AP or BP CML who started ponatinib treatment in clinical practice across 26 Italian centers, and comprised 3 different cohorts: prospective, retrospective and retrospective/prospective.

Demographic, efficacy and safety data were collected from patient medical charts at study entry and routine visits. The primary endpoint was the CCyR rate in CP CML patients by 6 months after ponatinib start. In the absence of cytogenetic evaluation, molecular assessment was used, considering patients in MR2 or better to be in CCyR. Here, we present the updated analysis of all evaluable patients (median follow-up 40.9 mo [IQR 31.6–59.0]).

Results:

120 patients (111 CP, 6 AP, 3 BP CML; median age 60 [19–93] years) were analyzed. 60 (50%) received ponatinib in 2L, 42 (35%) in 3L and 18 (15%) in ≥4L. Last TKI before starting ponatinib was: dasatinib 63 (52.5%), nilotinib 39 (32.5%), bosutinib 9 (7.5%), imatinib 8 (6.7%), asciminib 1 (0.8%). Most common reasons for switching to ponatinib were intolerance 40 (33%), primary resistance 29 (24%), secondary resistance 19 (16%). Of 70 evaluated patients, 6 (8.6%) had the T315I mutation whereas 17 (24%) had other ABL1 mutations. Ponatinib starting doses were 45mg (36%), 30mg (41%) or 15mg (23%). Median treatment duration was 33.5 (1.3–89.7) mo. Focusing the analyses on CP patients, at baseline, 54 (50%) patients had less than CCyR and 55 (50%) were in CCyR or better. Baseline data were unavailable for 2 patients. At 6 mo, 82/109 (75%) evaluable patients were in CCyR; 29/54 (54%) achieved and 52/54 (96%) maintained at least a CCyR or improved response vs baseline. Additionally, 38/109 (35%) achieved a major molecular response (MR3) and 21/109 (19%) a DMR (≥MR4) (Table). PFS rates at 24 and 36 mo were 87.7% (95% CI 81.6–94.2%) and 83.0% (95% CI 75.9–90.8%). Corresponding OS rates were 90.4% (95% CI 84.9–96.3%) and 86.7% (95% CI 80.2–93.8%).

In the whole cohort, 64/120 (53%) experienced at least one treatment-related AE, most commonly hypertension (8.3%), increased lipase (5.0%) and thrombocytopenia (5.8%). Only 2 treatment-related arterial occlusive events were reported. Dose modifications occurred in 76 patients: 29 (38%) due to AEs, of which 4 were CV AEs; 22 (29%) due to medical decisions; 16 (21%) reduced the dose after at least an MCyR; 8 (11%) increased the dose due to lack of efficacy and 1 (1%) for other reasons. Median time to first dose modification was 1.84 (0.03–30.30) mo. Among 54 patients who permanently discontinued ponatinib, main reasons were AEs 19/54 (35%), progression or death 12/54 (22%), other therapies 7/54 (13%), and other reasons 7/54 (13%), e.g. nonadherence, loss to follow up.

Summary/Conclusion:

Ponatinib confirmed a favorable efficacy and long-term manageable safety profile in CML patients treated in clinical practice. By 6 mo, 75% of evaluable patients were in CCyR, and 54% achieved at least MMR. The probability of survival at 3 years was 87%. No new safety signals emerged with ponatinib in longer follow-up. Early ponatinib use and dose optimization appear key to the outcomes observed in this real-world study.

Table. Molecular response outcomes in patients with CP CML overall and according to treatment line.

	CP CML			
Cohort	**Overall (N=111)**	**2L (n=56)**	**3L (n=38)**	**>3L (n=17)**
MR2, n/n (%)				
3 mo	12/80 (15.0)	4/44 (9.1)	7/26 (27.0)	1/10 (10.0)
6 mo	23/109 (21.0)	9/55 (16.0)	8/37 (22.0)	6/17 (35.0)
12 mo	10/69 (14.0)	4/33 (13.0)	4/26 (15.0)	2/12 (17.0)
24 mo	7/53 (13.0)	1/22 (4.5)	3/22 (14.0)	3/9 (33.0)
36 mo	6/42 (14.0)	3/15 (20.0)	1/18 (5.6)	2/9 (22.0)
MR3, n/n (%)				
3 mo	18/80 (22.0)	10/44 (23.0)	8/26 (31.0)	0/10 (0)
6 mo	38/109 (35.0)	18/55 (33.0)	14/37 (38.0)	6/17 (35.0)
12 mo	30/69 (43.0)	16/33 (52.0)	9/26 (35.0)	5/12 (42.0)
24 mo	20/53 (38.0)	12/22 (55.0)	4/22 (18.0)	4/9 (44.0)
36 mo	13/42 (31.0)	5/15 (33.0)	4/18 (22.0)	4/9 (44.0)
DMR (MR4–MR5), n/n (%)				
3 mo	13/80 (16.2)	7/44 (15.5)	5/26 (19.7)	1/10 (10.0)
6 mo	21/109 (19.4)	11/55 (19.6)	4/37 (21.8)	2/17 (11.6)
12 mo	18/69 (25.5)	8/33 (25.7)	9/26 (33.8)	1/12 (8.3)
24 mo	21/53 (39.4)	9/22 (41.1)	10/22 (45.1)	2/9 (22.0)
36 mo	21/42 (50.1)	7/15 (46.7)	11/18 (60.6)	3/9 (33.0)

Abbreviations: 2L, 2nd-line; 3L, 3rd-line; 4L, 4th-line; AE, adverse event; AP, accelerated phase; BP, blast phase; CCyR, complete cytogenetic response; CI, confidence interval; CML, chronic myeloid leukemia; CP, chronic phase; CV, cardiovascular; DMR, deep molecular response; EMA, European Medicines Agency; IQR, interquartile range; MCyR, major cytogenetic response; MMR, major molecular response; mo, months; MR, molecular response; OS, overall survival; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.