Outcomes of Patients with Blast Phase Chronic Myeloid Leukemia Following Ponatinib-Based Therapy

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Background

- Outcomes of CML in myeloid blast phase (MBP) are poor (historical median OS <1 year)
- Current consensus guidelines recommend AML-like chemotherapy combined with a potent TKI
- Ponatinib is effective in CML with resistance mutations, including the T315I mutation, and is commonly used in CML-MBP
- Outcomes of ponatinib-based combination regimens in CML-MBP remain largely unknown

Methods

- Retrospective analysis of 76 pts with CML-MBP who received ponatinib-based regimen at MDACC between 1/2008 and 8/2023
  - Pts could have received ponatinib as any line of therapy for CML-MBP
  - Evaluated response rates, survival outcomes and characteristics at relapse/failure

Results

Baseline Characteristics

Characteristic (N = 76)	n (%); median [range]
Age (years)	50 [20-90]
Age >60 years	23 (30)
Male	49 (64)
Line of therapy	
Newly diagnosed MBP	50 (66)
Relapsed/refractory MBP	26 (34)
Prior ponatinib exposure	8 (11)
Additional chromosomal abnormality (ACA)	57 (75)
***ABL1* KD mutation status at first ponatinib therapy (n=68)**	
Negative	36 (53)
T315I	8 (12)
Others	24 (35)
First MBP regimen	
IC+ven+ponatinib	28 (37)
IC+ponatinib	7 (9)
HMA+ven+ponatinib	18 (23)
HMA+ponatinib	6 (8)
Ponatinib monotherapy	17 (22)

Response Rates

Response (N=76)	n (%)
CR	20 (26)
CRi	10 (13)
CR/CRi	**30 (40)**
MLFS	7 (9)
ORR (CR/CRi/MLFS)	**37 (49)**
No response	31 (41)
Inevaluable	4 (5)
Early death	4 (5)

- 12/61 pts (20%) achieved MMR or better
- 14/51 pts (28%) achieved CCyR

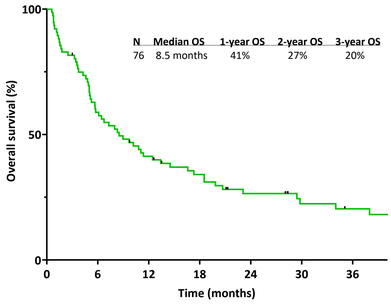
Response Rates by Subgroup

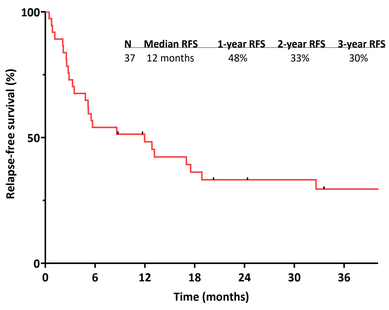
Subgroup	ORR, n (%)	CR/CRi, n (%)
Line of therapy		
Newly diagnosed MBP	30 (60)	25 (50)
Relapsed/refractory MBP	7 (27)	5 (19)
Type of therapy		
Combination therapy	32 (54)	26 (44)
Ponatinib monotherapy	5 (29)	4 (24)
ABL1 KD mutation		
Present	18 (56)	16 (50)
Absent	15 (42)	11 (31)

ORR and CR/CRi rates significantly higher in newly diagnosed MBP than in R/R MBP (P=0.006 and P=0.007, respectively)

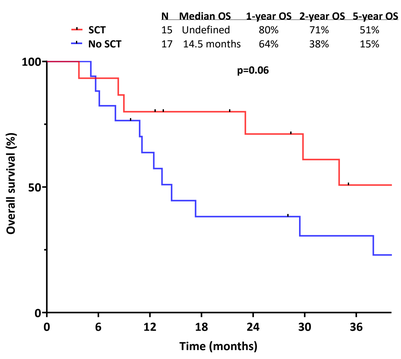
Results

Overall Survival and Relapse-free Survival

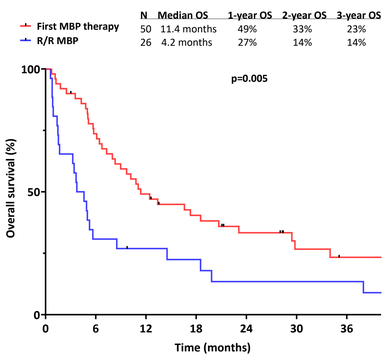




SCT Landmark analysis



OS by Line of Therapy



- Median time to SCT: 2.5 months (range, 1-12 months)
- 10/15 pts (67%) received a post-SCT TKI (ponatinib in 8 and dasatinib and bosutinib in 1 each) for a median duration of 20.1 months

Baseline Characteristics of Patients after Ponatinib Failure

Characteristic N = 49	n (%); median [range]
Age, years	50 [26-90]
Age >60 years	13 (27)
Type of ponatinib failure	
Refractory	31 (63)
Relapse	18 (37)
Duration of response (months)	4.2 [0.8-18.8]
New ABL1 KD mutation(s) at relapse	
T315I	2/8 (25)
Q271H+Y272H	1/8 (13)
None	5/8 (63)
Cytogenetic evolution at relapse	3/11 (27)
Type of relapse	
BM only	13 (72)
CNS only	3 (17)
BM + CNS	1 (6)
BM + non-CNS extramedullary	1 (6)
TKI received after ponatinib failure (n=40)	
Ponatinib	26 (65)
Asciminib	3 (8)
Dasatinib	3 (8)
Bosutinib	2 (5)
Nilotinib	1 (3)
None	5 (13)
Backbone therapy received after ponatinib failure (n=40)	
High intensity chemotherapy	13 (50)
Low intensity chemotherapy	2 (8)
HMA+venetoclax	6 (23)
HMA	3 (12)
Venetoclax	2 (8)

Outcomes After Ponatinib Failure

- 40 pts (82%) received salvage therapy after ponatinib failure
- ORR was 25% and CR/CRi rate was 20%
- OS was poor after ponatinib failure (median OS 3.9 months; 1-year OS rate 21%)

Conclusions

- Ponatinib-based therapies result in high rates of response in CML-MBP
- Best response rates were observed when given as first therapy for CML-MBP (ORR 60%) and when used in combination with other agents
- Pts bridged to SCT have the best outcomes (2-year OS 71%)
- Outcomes are dismal after failure of ponatinib, highlighting the need for more effective treatment strategies of CML-MBP

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