Characteristics and treatment of blast crisis in chronic myeloid leukemia

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Introduction.

The Chronic myeloid leukemia blast crisis (CML BC) is a rare clinical and biologically heterogeneous condition often characterized by aggressive clinical course. In spite of successful use of tyrosine kinase inhibitors (TKIs) some patients with CML still develop a BC. There is no standard approach to BC treatment and outcomes are generally unsatisfactory with long-term overall survival rarely exceeding 10% (Saxena K et al.).

Objective.

This study is aimed to evaluate treatment outcomes, mainly overall survival (OS), in patients with CML BC.

Materials and methods.

A total of 87 patients (65 male and 22 female) with verified CML receiving treatment in RM Gorbacheva Research Institute for 1st or subsequent BC were included in this retrospective cohort. Therapy efficacy was evaluated according to the European LeukemiaNet (ELN) criteria.

Results.

The median age at the time of diagnosis was 42 (18 – 62) years. In 66% of cases (n=57) the diagnosis was established in chronic phase (CP), in 19% (n=17) in acceleration phase (AP), and in 15% (n=13) as a de novo BC, which was myeloid in 9% and lymphoid in 6% of patients. The cytogenetics data at diagnosis was available in 85 (98%) cases. Additional chromosomal aberration (ACAs) were present in 31 (37%) cases, most frequently trisomy 8 (29%), 3q26 rearrangement (23%), monosomy 7 / 7q deletion (17%), trisomy 19 (13%), additional Ph-chromosome (13%), and complex karyotype (55%). The median age at the first BC was 44.5 (21 - 76) years with a median time since diagnosis of 39.5 (0 – 248.5) months. Most (79.3%) BC were myeloid, extramedullary lesions were seen in 8% of cases. Most patients received complex therapy regimens combining chemotherapy and TKIs (56%), in 30% cases chemotherapy-only, and in 14% cases TKIs-only regimens (in 75% of cases dasatinib) regimens were used. Allogeneic hematopoietic stem cell transplantation was not performed due to progression, severity of condition, presence of significant concomitant pathology, lack of donors, patient refusal. The response was evaluated in 78% of cases with 47% of patients being resistant to 1st-line therapy and 31% of patients reaching CP (complete hematologic response in 100%, cytogenetic response in 30%, and molecular response in 19% of cases). In 22 % of cases a 2nd BC developed. The median OS was 11.5 months since 1st BC (Fig. 1). The median time from 1st BC1 till 2nd BC or death evaluated in 72 patients was 7.8 (0.6 – 107.2) months. At the time of the last evaluation 16% of patients were alive and 84% died of disease progression (82%), other documented reasons (1.4%) or due to unknown cause (17.4%).

Conclusion.

The outcomes of patients with CML BC remain poor, with a median time till 2nd BC development or death being less than 1 year. Prompt diagnosis and treatment initiation as well as timely transition to allogeneic hematopoietic stem cell transplantation are crucial to achieve a response.

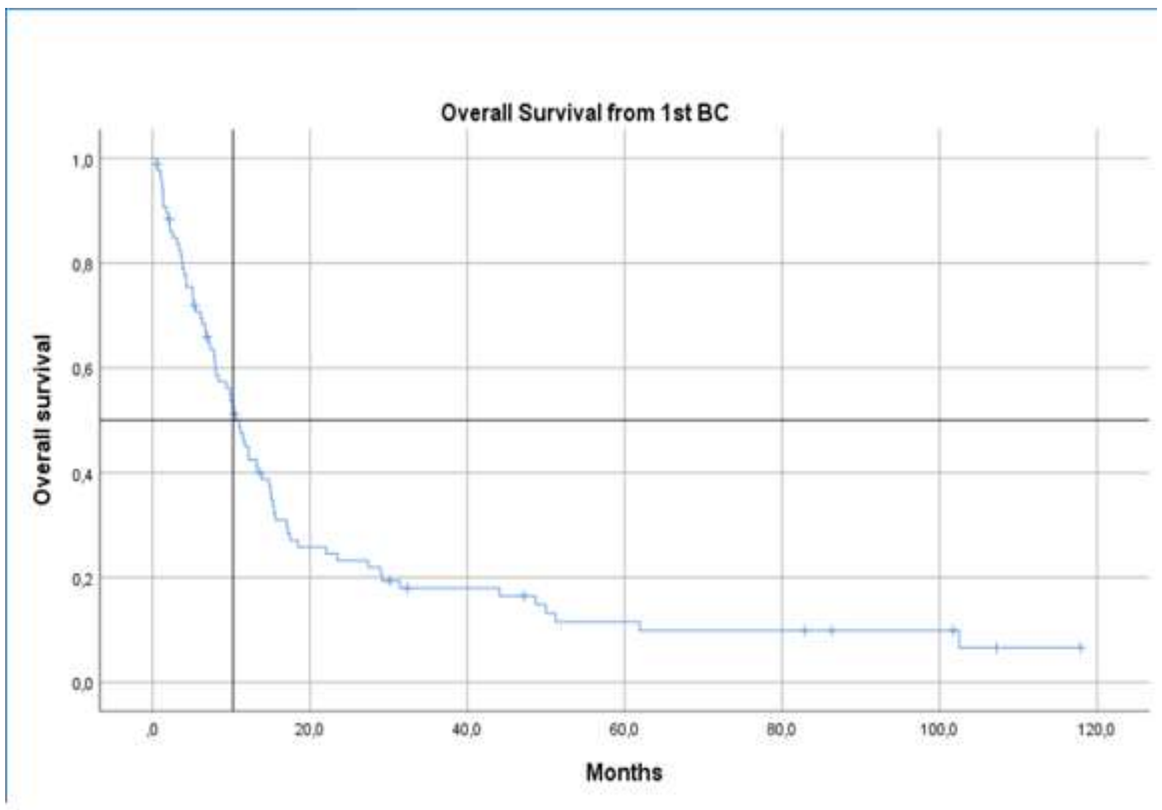

Fig. 1 Overall survival from 1st BC

Characteristic of 87 patients	N (%); median [range]
Male / Female	65 (75%) / 22 (25%)
Age at diagnosis, years	42 (18 - 62)
Phase at the onset of the disease: - Chronic phase - Acceleration phase - Blast crisis	 57 (66%) 17 (19%) 13 (15%)
Age at 1st BC, years	44,5 (21 - 76)
Additional cytogenetic abnormalities	31 (37%)
Extramedullary disease	7 (8%)
Therapy: - Tyrosine kinase inhibitors (TKIs) - Chemotherapy (CT) - TKIs + CT	 12 (14%) 26 (30%) 49 (56%)
Median overall survival (OS) from 1st BC, months	11,5
Reasons for not performing allogeneic hematopoietic stem cell transplantation: - Progression - Significant concomitant pathology - Lack of donors - Late referral to a transplant center - Patient's refusal	

Fig. 2 Characteristic of 87 patients