

TREATMENT WITH BTK INHIBITORS IN PATIENTS AFFECTED BY CHRONIC LYMPHOCYTIC LEUKEMIA: SAFETY AND HEMOSTASIS.

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Background and Aims: The treatment of chronic lymphocytic leukemia (CLL) with Bruton's tyrosine kinase (BTK) inhibitor Ibrutinib is a widely used and effective therapy, with a good safety profile. However, studies and post-marketing surveillance showed an increased risk of bleeding (up to 30% of the patients) and heart rhythm disorders (up to 6% of the patients). In the last few years new BTK inhibitor agents were produced, trying to improve the efficacy and safety of Ibrutinib. The aim of this retrospective monocentric study was to analyze the safety of the treatment with different BTK inhibitors, with particular reference to bleeding complications.

Methods: We collected the data of 114 patients with the diagnosis of chronic lymphocytic leukemia treated with BTK inhibitors in the Azienda Ospedaliero Universitaria delle Marche and authorized by the Internal ethical committee and General affair committee from 2009 to 2024.

Results: The median age at diagnosis was 68.5 years (standard deviation 10.3 years). 75 of the patients (66%) were male and 23 patients (20%) already had a known cardiac disease (not including arterial hypertension). 78 patients (68%)

were treated with Ibrutinib (34 as a first line treatment, 28 as a second line, 13 as a third line, 3 as a fourth line); 28 with Acalabrutinib (22 as a first line, 5 as a second line, 1 as a third line); 10 with Zanubrutinib (5 as a first line, 4 as a second line, 1 as a third line) and 1 with Pirtobrutinib (as a third line treatment). 11 patients (10%) had a concomitant treatment with anticoagulants. Bleeding occurred in 5 patients, but only 2 were majors, and none was fatal. 2 events were in patients treated with Ibrutinib, 2 with Zanubrutinib, 1 with Acalabrutinib. Only one of bleeding events occurred during anticoagulant therapy. 8 patients (7%) had an atrial fibrillation onset or resurgence, all during the Ibrutinib treatment.

Conclusions: In this study the treatment with BTK inhibitors had a cardiac safety profile comparable to known data (7% vs 6%), but none of the events was associated with the new inhibitors. The bleeding safety profile was significantly better than the one reported with Ibrutinib (4% vs 20%), but almost all BTK inhibitors had at least one event. This study confirms the safety of the new agents, of which post-marketing surveillance data are still to be known.

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