# (PB3671) CHEMO-FREE FIRST-LINE THERAPY IN FRAIL PATIENTS WITH MARGINAL AND MANTLE CELL NON-HODGKIN LYMPHOMA: OUR EXPERIENCE

**Topic:** 18. Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

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## Background

BKT inhibitors (iBKT) in the treatment of some non-Hodgkin's lymphomas are shifting the balance in the therapeutic approach to these diseases, increasingly moving towards chemotherapy-free treatment. The lymphomas that already have approval for the use of iBKT are mantle cell lymphoma (mNHL) and marginal lymphoma (MNHL) with good results but used only as monotherapy and from second line(1,2). In mNHL, studies in the first-line setting in combination with chemotherapy(3,4). Have documented response rates and safety that will lead to changes in first-line treatments.
An unmet medical need is how to treat frail (often undertreated) elderly patients in the first line with iBTK and without (potentially less toxic) chemotherapy, to achieve maximum response with minimal toxicity and improve responses and quality of life in this patient cohort.

## Aims

The aim of our study is to treat frail patients diagnosed with mNHL or MNHL with a single dose of bendamustine 70 mg/m2 immediately discontinued, followed by one weekly cycle of rituximab 375 mg/m2, after which iBKT (zanubrutinib for MNHL and acalabrutinib for mNHL) was added concurrently with immunotherapy (Rituxmab 375 mg/m2, one dose every 28 days for 4 administrations). Subsequently, they were reevaluated and, if in response, the program includes iBTK and rituximab 375 mg/m2 every 2 months for 2 years or until unacceptable toxicity or disease recurrence.

## Methods

From September 2023 to February 2026, we treated 22 patients (7 mNHL and 15 MNHL) in our division. Nine females and 16 males had a median age of 78 years (range: 61-88 years) and a median performance status of 2 (range: 1-3). Sixteen patients (75%) were evaluable after 6 months of treatment.

## Results

Two patients died: one due to mucor infection (after 1 month from the start of treatment) and one due to complications unrelated to treatment at month +3.
Of the 16 evaluable patients, the ORR at 6 months was 100%: 5 CR (30%); 5 VgPR (30%) and 6 PR (40%).
At 12 months, 15 patients were evaluable, with a confirmed ORR of 100%, with improved complete remissions: 11 CR (75%) and 4 RP (25%) (fig. 1).
No patients experienced grade >2 cardiac adverse events; 3/22 patients (14%) experienced grade >2 bleeding events that led to iBKT discontinuation with subsequent resumption at a 50% reduced dose; no patients experienced >2 hematological toxicity; no patients experienced CMV reactivation (from retrospective data from our center, approximately 25% of patients treated with R-Benda had developed CMV reactivation); 2 patients (9%) developed serious fungal infection (maxillary sinus mucormycosis with death and pulmonary aspergilloma treated with isavuconazole).
4/22 patients (18%) discontinued treatment: 2 due to death and 2 due to the development of a second neoplasm (1 breast carcinoma and 1 intestinal carcinoma).
No disease progression has been documented and the projected 30-months overall survival (OS) is 90% (whit a median follow-up of 13 monts). (figure 1)

## Summary/Conclusion

In conclusion, even if small cohort and with a short follow-up, the first-line chemotherapy-free treatment (combination of immunotherapy and iBKT) in frail patients with marginal and mantle cell lymphoma has proven to be very active with good compliance and an excellent quality of life.

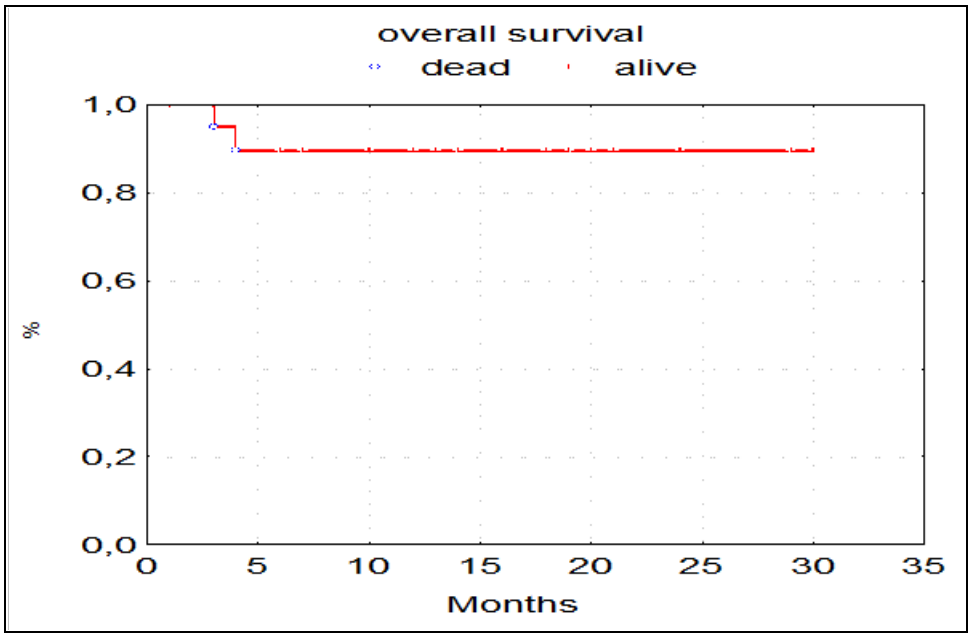


Figure1: Overall survival: Total Evaluable 22/22 patients: 2 patients died, one due to mucor mycosis infection and one due to causes not related to treatment No disease progression has been documented and the projected 30-month overall survival (OS) is 90% (with a median follow-up of 13 months).