IBRUTINIB AND VENETOCLAX FOLLOWED BY CAR-T CELL THERAPY AS FIRST-LINE TREATMENT IN AN ELDERLY PATIENT WITH MANTLE CELL LYMPHOMA WITH A TP53 GENE MUTATION AND HYPERLEUKOCYTOSIS

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INTRODUCTION

Main prognostic factors considered as high-risk in mantle cell lymphoma (MCL) include TP53 lesions (17p13 deletions or TP53 mutations), blastoid/pleomorphic histology, hyperleukocytosis, high Ki-67 index, and complex karyotype. The consensus on managing elderly patients with high-risk MCL is not yet elaborated. Intense approaches including allogeneic stem cell transplantation (allo-SCT) are not feasible in elderly patients with comorbidities. Dual targeting of BTK and BCL2 with ibrutinib and venetoclax as first-line therapy is the most rational approach in this group of patients. As a consolidation for elderly patients with high-risk MCL, especially in the presence of mutations in the TP53 gene, CAR-T cell therapy is a promising option.

AIM

To share the experience of using combination ibrutinib and venetoclax followed by CAR-T cell therapy in the first-line treatment in an elderly patient with high-risk MCL with a TP53 gene mutation and hyperleukocytosis.

METHOD

A 68-year-old patient was diagnosed with MCL. Examination revealed hyperleukocytosis (978 × 109/l) (fig.1), anemia (55 g/l), thrombocytopenia (30 × 109/l), and splenomegaly (250 × 180 mm) (fig.2). Among the unfavorable prognostic factors are a complex karyotype, 17p13 and 13q14 deletions, and a p.R248W mutation in the 7th exon of the TP53 gene (VAF = 26%).

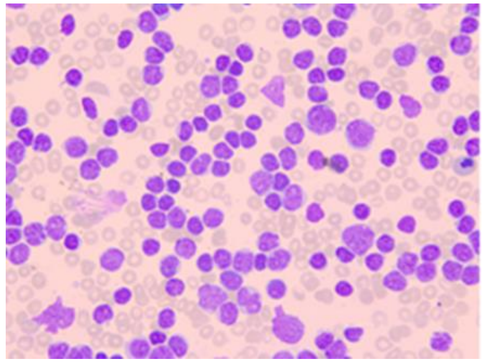


Figure 1. Cytological examination of a peripheral blood smear at the onset,
magnification ×100, azure-eosin staining

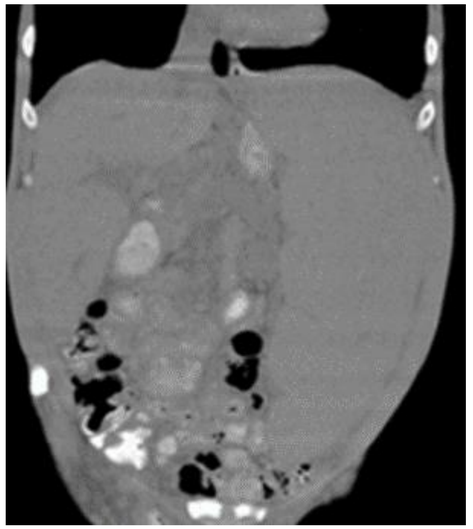


Figure 2. Computed tomography of the abdomen: splenomegaly 250 × 180 mm

RESULTS

After 2 sessions of leukapheresis, ibrutinib therapy was started at 420 mg/day and venetoclax at 100 mg/day, which led to the development of tumor lysis syndrome. After 7 days of therapy, the leukocyte counts were 2.5 × 109/l, neutrophils were 70%, platelets were 90 × 109/l, and hemoglobin was 95 g/l. MRD affecting 4% of blood cells was detected with 0.8% VAF for TP53 gene mutation. The patient underwent anti-CD19 CAR-T-cell therapy and achieved complete remission. After 18 months of the therapy, MRD-negative remission continues.

CONCLUSIONS

Combining targeted and cell therapy in elderly patients with high-risk MCL with TP53 gene mutation is an effective and potentially curative strategy.

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