MONOCLONAL ANTI-CD20 ANTIBODY OBINUTUZUMAB IN RELAPSED AND REFRACTORY HAIRY CELL LEUKEMIA

L. Al-Radi, S. Smirnova, T. Moiseeva, H. Julhakyan, B.Biderman, A. Kokhno
National research center for hematology, Russian, Moscow

Introduction

The gold standard for the treatment of hairy cell leukemia (HCL) are purine analogues (cladribine, pentstatin), as complete remissions are achieved in most patients (about 90%). Purine analogues are also recommended for the treatment of late relapses of HCL, but they are less effective in the treatment of early relapses. Alternative treatment is required for refractory/relapsed forms of HCL. One of the possible approaches is to add a monoclonal anti-CD20 to purine analogues, but rituximab is sometimes unsuccessful. The effectiveness of the second-generation anti-CD20 antibody obinutuzumab in HCL is unknown and currently being studied.

To present our experience and evaluate the efficacy of using the second-generation anti-CD20 antibody obinutuzumab in practice for patients with refractory/relapsed HCL

Methods

Obinutuzumab was used in 9 patients with refractory/relapsed HCL (m:f = 5:4; age range 29-54 years (median 41 years)). Two patients in 1-st relapse, 4 patients in 2-nd relapse, 1 patient in 3-d relapse, 2 patients in 4-th relapse. All patients had classic HCL with V600E B-RAF mutation. In the previous lines of therapy Cladribine + Rituximab were used in all patients, Vemurafenib - in 3 patients.

The response to therapy was evaluated by control of cytopenia, neutrophil count, size of the spleen and lymph nodes, assessment of MRD in bone marrow.

Obinutuzumab was used in a dose of 1000 mg every three months in a total of 4-6 intravenous injections. The first administration of Obinutuzumab was performed immediately after a course of Cladribine in 5 patients, or in combination with Vemurafenib in 4 patients.

Results

The treatment using combination with Obinutuzumab was successful in 7 of 9 cases (78%), achieving complete remissions (CR) in all the patients (5 MRD-negative CR, 1 MRD-positive CR, 1 MRD unknown CR). Median follow up 16 months (1 – 75 months). No relapses have been detected yet. There was a failure of therapy in 2 cases (22%) of heavily pretreated patients in 4-th relapse, one of them V4-34 variant.

Summary

Obinutuzumab in combination with standard therapy may be a promising option in the treatment of patients with refractory/relapsed forms of HCL.

Discussion

This study presents preliminary clinical evidence suggesting that obinutuzumab, a type II anti-CD20 monoclonal antibody, holds promise in the treatment of relapsed/refractory hairy cell leukemia when combined with cladribine or vemurafenib. The observed overall response rate of 78% (7/9 patients) with complete remissions achieved in all responders is clinically significant, particularly given the pretreated the cohort. Five of these CRs were MRD-negative, underscoring the potential depth of response attainable with this approach.

Notably, these responses occurred in patients who had universally failed prior cladribine-rituximab therapy. This suggests that obinutuzumab's distinct mechanism of action—including enhanced antibody-dependent cellular cytotoxicity (ADCC), direct induction of non-apoptotic cell death, and reduced complement-dependent cytotoxicity compared to rituximab—may overcome resistance associated with first-generation anti-CD20 antibodies in HCL. The successful combination with both chemotherapy (cladribine) and targeted therapy (vemurafenib) further highlights its versatility.

The two treatment failures occurred in patients with exceptionally advanced disease (4-th relapse), including one with the VH4-34 variant—a known poor prognostic factor in HCL. This aligns with existing literature indicating diminishing returns with successive lines of therapy and suggests that obinutuzumab-based regimens may be most effective in earlier relapses or less refractory settings.

References

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