Insight Medical Publishing

JOURNAL OF INFECTIOUS DISEASES AND TREATMENT

A novel anti-CD20 monoclonal antibody shows favorable pharmacodynamic effects and acceptable safety profile in patients with multiple sclerosis

Maria Morozova

BIOCAD, Russia

Abstract

Introduction: Anti-CD20 monoclonal antibodies (mAbs) induce the B cells depletion due to Fc-mediated Antibody-Dependent Cellular Cytotoxicity (ADCC), Complement-Dependent Cytotoxicity (CDC), or direct cells death. We developed BCD-132, a novel humanized anti-CD20 IgG1 mAb. Materials and methods: Bio-layer interferometry, cell-based assays and aggregation stability studies proved that BCD-132 interacts with extracellular part of CD20 antigen with nanomolar affinity. The hallmark of the new molecule is the modified Fc fragment glycosylation. The absence of fucose determines increased affinity to the FcγRIII B cells receptors compared to rituximab (74 nM and 19.3 nM vs. 633 nM and 105 nM for the FcγRIIIa-158F and FcγRIIIa-158V receptors, respectively, BCD-132 vs. rituximab), leads to pronounced ADCC effect. Biological activity was established in Macaca fascicularis model of autoimmune encephalomyelitis which also showed satisfactory drug toxicity and immunogenicity. The phase 1 (3+3 design) clinical trial sequentially included 24 patients with Remitting Multiple Sclerosis (RMS). In each of 4 cohorts participants received the assigned dose of BCD-132 (100, 250, 500 or 1000 mg) as one or two (14-day interval) intravenous infusions. Results: We observed the rapid depletion of CD19+/CD20+ cells within 12 hours after the BCD-132 infusion. At day 14 the median of the CD19+ cells was 0%. There was a slight repopulation of the cells pool after 6 months (0 or <5% from baseline in BCD-132 500 mg and 1000 mg groups). There was no significant change in the T-cells (CD3+) count. Adverse events (AEs) were not dose dependent. Severe AEs were registered in 2 (8.3%) patients (grade 3 neutropenia). Infusion-related reactions (grades 1-2) were registered in 6 (25%) patients, lasted 24 hours or less. Conclusion: BCD-132 has the expected dose-dependent pharmacodynamic effect, in all studied doses mediates the long-term depletion of CD19+/CD20+ B lymphocytes and possesses the acceptable safety profile in RMS patients.

Biography:

Maria Morozova, PhD, has over 10 years of clinical practice experience in gastroenterology. Now works as a medical expert in R&D department specializing in the field of autoimmune and rare diseases in JSC BIOCAD.

European Congress on Immunology | Edinburgh, Scotland | March 04-05, 2020

Citation: Maria Morozova, *A novel anti-CD20 monoclonal antibody shows favorable pharmacodynamic effects and acceptable safety profile in patients with multiple sclerosis*, Euro Immunology 2020, European Congress on Immunology, Edinburgh, Scotland, March 4 -5 , 2020, 10