INTRODUCTION

BION-1301 is a first-in-class human anti-human antibody targeting APRIL (TNFSF13). We demonstrated that BION-1301 inhibits proliferation and survival of human cells and alleviates both APRIL-mediated drug resistance and immune suppression in preclinical multiple myeloma (MM) models (Ref. 2). BION-1301 inhibits APRIL-dependent cell survival in both tumor lines (Raji cells) and non-tumor cells (Caco-2), with differential effects from BION-1301 (TNFSF13) targeting distinct approaches to MM management. Here, we report on the preclinical safety, pharmacokinetics (PK) pharmacodynamics (PD) relationship and pharmacodynamic analysis of BION-1301.

Fig. 1 Study design single and multiple dose IV BION-1301 in Non Human Primates; no BION-1301 related Toxicity

Fig. 2 BION-1301 Pharmacokinetics.

Fig. 3 BION-1301 suppresses IgA, IgG and IgM level in NHP

Fig. 4 BION-1301 predicted FIH dose using PK/ PD modeling

Pharmacokinetics (PK) anti-drug antibodies (ADA) after a single intravenous dose of BION-1301 to cynomolgus monkey. A cytokometric ELISA method was utilized to measure the concentration of BION-1301 in serum from cynomolgus monkey serum samples. For detection of anti-drug antibody (ADA), targeted sera were obtained from cynomolgus monkeys (3 weeks after treatment) and were treated with biotinylated anti-drug monoclonal antibody (BDMA) as a capture antibody. The intensity of the color indicates the ADA titer. Light blue indicates that ADA was not confirmed and has a low ADA titer. The light blue indicates the lower limit of quantifications. A blue color of an area on the dose group 5 only was visible in 2 out of 3 animals at the highest dose group 30 mg/kg.

CONCLUSION

BION-1301 was well tolerated and binding of APRIL in non-human primates resulted in decreased IgA, IgG and IgM production. Furthermore, BION-1301 suppresses the T cell independent (I) B cell response in NHP, confirming preclinical activity in the TI mouse model. PK and target engagement results predict that BION-1301 may be suitable as a lead therapeutic for multiple myeloma, which was shown preclinically to inhibit MM proliferation, survival, drug resistance and evaded immune suppression activity in the TI mouse model. PK and target engagement results predict that BION-1301 may be suitable as a lead therapeutic for multiple myeloma, which was shown preclinically to inhibit MM proliferation, survival, drug resistance and evaded immune suppression activity in the TI mouse model.

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