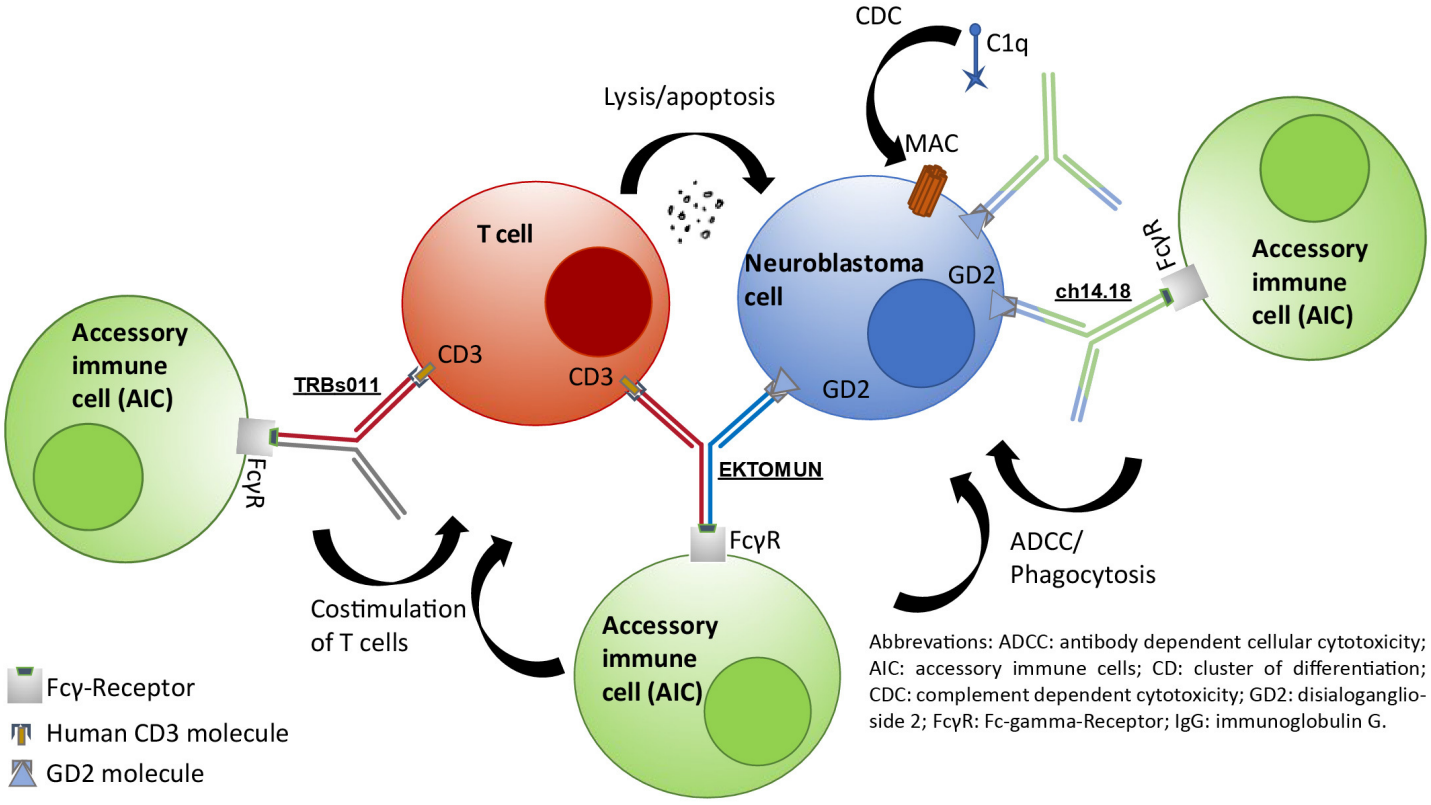
Graphical abstract

GD2-directed bispecific trifunctional antibody outperforms dinutuximab beta in a murine model for aggressive metastasized neuroblastoma



Abbrevations: ADCC: antibody dependent cellular cytotoxicity; AIC: accessory immune cells; CD: cluster of differentiation; CDC: complement dependent cytotoxicity; GD2: disialoganglioside 2; FcγR: Fc-gamma-Receptor; IgG: immunoglobulin G.

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In Brief: T cells are redirected to and activated at GD2 positive neuroblastoma cells by bispecific trifunctional antibody EKTOMUN. In addition, the Fc-region of bispecific trifunctional antibodies interacts simultaneously or subsequently with Fc-gamma receptor positive accessory immune cells such as natural killer cells, macrophages or dendritic cells and thus provide a co-stimulatory signal to activate T cells. In this way, tumor cells can be effectively eradicated by a combined action of T cells and accessory immune cells expoiting different mechanisms, such as antibody dependent cellular cytotoxicity (ADCC), phagocytosis, or perforin/granzyme-mediated lysis and apoptosis induction. The primary mode of action of the monoclonal antibody ch14.18 is either mediating ADCC or inducing the formation of a membrane attack complex (MAC) via complement activation.