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An alternative nonclinical approach to support the first-in-human clinical trial of a T-cell bispecific targeting EGFRvIII

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Abstract

As a tumor specific protein, EGFRvIII represents an ideal target for targeted cancer immunotherapies. Here we report the nonclinical evaluation of EGFRvIII-TCB, a novel EGFRvIII-targeted T-cell bispecific antibody designed for glioblastoma treatment. The antibody exhibited high specificity for EGFRvIII, with no effects on EGFR wild-type cells. In the absence of a relevant species, the nonclinical safety assessment to support its first-in-human clinical trial, was conducted applying an alternative in vitro strategy to predict potential off-target toxicity. A 3D blood-brain barrier-glioblastoma model was used to optimize the starting dose. Our translational strategy addressed regulatory feedback received from the Danish Health and Medicines Agency (DKMA) and the FDA to further increase confidence in the applied in vitro approach and ultimately led to the regulatory approval of our Ph1 study protocol across multiple countries.

Keywords: EGFRvIII; MABEL; T cell bispecific; blood-brain-barrier; glioblastoma; new approach methodologies.