Clinical Cancer Research

GA201: A Novel Humanized and Glycoengineered Anti-EGFR Antibody—Response

Christian A. Gerdes and Pablo Umaña

We are pleased that Dr. Modjtahedi found our work on GA201 interesting. The origin of the CDR sequences of GA201 based on the published sequences of the ICR62 antibody is clearly mentioned in our publication (1). Likewise, previous publications describing the properties of ICR62 were also cited in the article.

Equivalent EGFR binding of the humanized antibody versus the chimeric antibody with the original, complete variable regions of ICR62 is shown in Fig. 1. Increased binding affinity to FcgRIII as a result of Fc glycoengineering is clearly documented in this and many other publications (1–3). The safety profile and initial clinical activity of GA201 in humans has been described (4). Finally, regarding the contribution of glycoengineering to the superior efficacy of GA201 versus cetuximab in preclinical tumor models, please see demonstration in Fig. 2. *In vitro* activity comparisons and additional *in vivo* comparisons are already described in our publication (ref. 1, figs. 3 and 4).

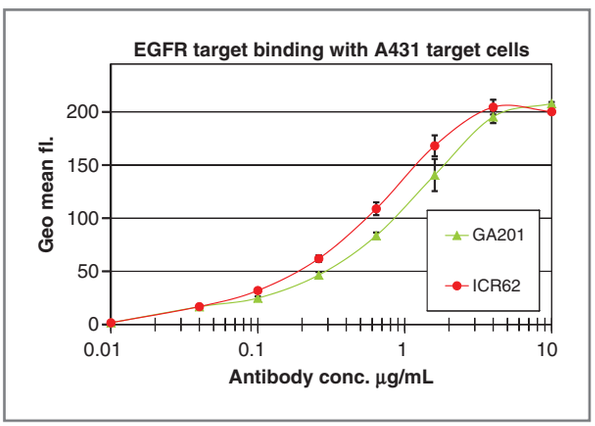

Figure 1. Binding of GA201 (clone name: IHHD) was compared with an antibody with the sequence of the V-domains of ICR62. Both antibodies carry a human IgG1/κ constant part. Binding intensity was determined by flow cytometry via a secondary antibody directed against the constant human IgG1 portion.

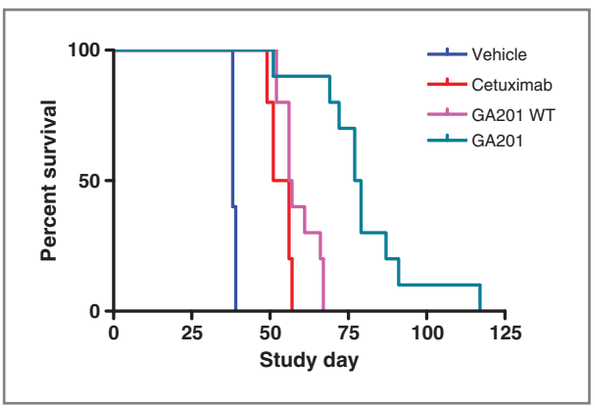

Figure 2. Superior efficacy of GA201 versus cetuximab and the wild type, nonglycoengineered version of GA201 in the A549 lung adenocarcinoma xenograft model in SCID/beige mice. All animals ($n = 10$ per treatment group) were treated therapeutically with 25 mg/kg antibody once weekly for 3 weeks. Dosing began on day 7 after injection of tumor cells, once tumor was detectable. The data show that GA201 achieved a significantly superior median OS compared with cetuximab, and the wild type nonglycoengineered version of GA201.

Authors' Affiliation: Roche Glycart AG, pRED, Schlieren, Switzerland

Corresponding Authors: Christian A. Gerdes, Roche Glycart AG, Wagistrasse 18 CH-8952 Schlieren, Switzerland. Phone: 41-44-755-6148; Fax: 41-44-755-6165; E-mail: christian.gerdes@roche.com; and Pablo Umaña, pablo.umana@roche.com

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Disclosure of Potential Conflicts of Interest

C.A. Gerdes is employed (other than primary affiliation; e.g., consulting) as a head of pharmacology in Roche Glycart. No potential conflicts of interest were disclosed by the other author.

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