Letter to the Editor

Reply: In vitro and in vivo anticancer efficacy of unconjugated humanised anti-CEA monoclonal antibodies

Sir,

In response to Blumenthal et al, we would like to further clarify a few points that have been raised. The main one relates to the statement made in our paper that ‘there are so far no unconjugated or ‘naked’ antibodies to carcinoembryonic antigen (CEA) being used for the treatment of colorectal cancer’ (Conaghan et al, 2008).

Blumenthal et al suggest that this is not correct; however, they fail to provide evidence to the contrary in their letter. They quote three published articles in support of their argument. However, the first one relates to a targeting study using MN-14 (Sharkey et al, 1995).

In the 1980s, radiolabelled murine PR1A3 was also demonstrated to be highly specific for human colorectal lesions (Granowska et al, 1989). The other two papers present data relating to the use of a radioconjugate form of MN-14 (Hajjar et al, 2002; Liersch et al, 2005). In the letter from Blumenthal et al, there is reference to unpublished results with unconjugated MN-14 being used in patients. It is however difficult to make an informed response regarding unpublished data. Thus, to our knowledge, the point made in our paper still holds true: no unconjugated antibody that targets CEA has been licensed in the treatment of colorectal cancer in humans by the clinical licensing authorities in the United Kingdom or United States. This, of course, includes MN-14.

We acknowledge the in vitro and preclinical work that has been published using MN-14 (labetuzumab), which has been followed with interest over the years. A reference is actually made to this antibody in the introduction of our paper (Liersch et al, 2007; Conaghan et al, 2008). On a broader note, there are in fact over 200 antibodies that are under clinical testing in oncology (Reichert and Valge-Archer, 2007). Eight of these use CEA as a target, including T84.66, which, like MN14, have been used in clinical trials as radioconjugates (Wong et al, 2004; Reichert and Valge-Archer, 2007). Our study further defines NK cells as an important effector cell type in eliciting this response in humans. Significantly, PR1A3-induced NK-cell-mediated killing of colorectal cancer cells is not inhibited by free CEA, which is an important characteristic for any anti-CEA antibody to be successful in vivo. This can be explained by the specific binding of PR1A3 to membrane-bound CEA. Previous work has identified the B3-GPI anchor of CEA as being the epitope of PR1A3 (Durbin et al, 1994; Stewart et al, 1999). The authors feel that this information can be used to further engineer PR1A3 for maximal clinical effectiveness in humans. Like Blumenthal et al, we would envisage this happening in partnership with current chemotherapeutic regimens.

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