Letters to the Editor

HER2 (ErbB2) receptors, a potential therapeutic target in squamous cell carcinoma of oesophagus

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Sir,

We read with great interest a recent article by Gibault et al (2005) regarding the role of various molecular markers in squamous cell carcinoma of oesophagus (SCCO). We agree with their conclusions that ErbB1 receptors are involved in oesophageal carcinogenesis and prognosis, thus they may be potential targets for immunotherapy of SCCO. However, we have a different view on one of the issues addressed by the group regarding the role of HER2 (ErbB2) in SCCO. In their article, they suggested that their results are consistent with other studies but note a lack of comparative data simply because, to their knowledge, studies concerning ErbB2 expressions are very scarce since a study reported by Shiga et al (1993). They therefore concluded that HER2 receptors are very scarce as a study reported by Shiga et al (1993). They therefore concluded that HER2 receptors nevertheless appear to be of poor interest as potential therapeutic targets in SCCO.

Traditionally ErbB1 has been considered to be associated with SCCO and majority of the studies have shown it to be overexpressed and associated with poor prognosis in SCCO. However, there is growing body of evidence showing ErbB2 is also abnormally expressed in SCCO and associated with poor prognosis. We reviewed studies reported since 1993 that have analysed ErbB2 expression in SCCO in association with outcome of the disease. Six studies have analysed ErbB2 overexpression in SCCO using immunohistochemistry and ErbB2 has been found to be overexpressed in 9% of cases in one study (Sunpaweravong et al, 2005) and 26–64% of cases in the other five studies (Hardwick et al, 1997; Friess et al, 1999; Wang et al, 1999; Akamatsu et al, 2003; Mimura et al, 2005b). This rate of overexpression is greater than the one reported by Gibault et al (2.8%), suggesting that ErbB2 is overexpressed to a greater extent in SCCO. Of the six studies described above, two reported a statistically significant association of ErbB2 overexpression with poor prognosis (Mimura et al, 2005b; Sunpaweravong et al, 2005). ErbB2 overexpression has also been shown to be a marker of chemoradioresistance (Akamatsu et al, 2003). Two studies, since 1993 have detected ErbB2 mRNA expression using PCR and reported overexpression in 25 and 28% of cases (Tanaka et al, 1997; Miyazono et al, 2004). In these two studies ErbB2 overexpression has also been associated with extramucosal tumour invasion and poor response to chemoradiation.

Although methodologies used in these studies to detect ErbB2 expression are different but all of them clearly suggest that ErbB2 receptors are overexpressed in SCCO to a greater extent as reported by Gibault et al. ErbB2 overexpression has also been associated with invasive disease, poor response to treatment and outcome. Early preclinical studies using Herceptin (anti HER2 monoclonal antibody) in SCCO cell lines have shown that it does have inhibitory effect on growth of cells, either alone or in combination with conventional treatments (Mimura et al, 2005a; Sato et al, 2005). On the basis of current evidence, which suggests abnormalities of ErbB2 expression, its association with poor prognosis and evidence that targeting it could be of therapeutic benefit in SCCO, we cannot exclude the possibility of significant role of HER2 receptors in oesophageal squamous cell carcinogenesis, disease progression and its potential value as therapeutic target, along with ErbB1.

ErbB2-targeted therapies are still in an early stages of development in reference to SCCO and at this stage we look forward to results evaluating its effects in other cancers, where these therapies are in a relatively advanced stages of development. We hope that further research in this field will help determine the value of ErbB1 and ErbB2 targeted therapies in SCCO.

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Sir,

At first, we would like to thank you for giving us the opportunity to reply to this letter. It may be worth reminding that our study shows a potential impact of EGFR status, and HER2 was found to be overexpressed in esophageal squamous cell carcinoma. Our experiments were aimed at gaining insight, from only immunohistochemical data, into the potential impact of several targets such as EGFR, Her2 (ErbB2) receptors, a potential therapeutic target in squamous cell carcinoma of the oesophagus. We totally agree with them about the fact that several analyses of HER2 carried out by immunohistochemistry or other methods (Shiga et al, 1999; Hardwick et al, 1997; Tanaka et al, 1999; Friess et al, 1999; Wang et al, 1999; Akatmatsu et al, 2003; Miyazono et al, 2004; Mimura et al, 2005a; b; Sato et al, 2005; Sunpaweravong et al, 2005) have all found rates of overexpression greater than 2.8%. To our opinion, the differences observed between these different studies have several origins: the first of them, as clearly said by Khan and co-workers, in addition to immunochemistry they performed a coexpression study of several factors which could explain the differences observed between these different studies have a correlation with HER2 expression. However, by a careful reading of their paper, it seems that after the study of squamous cell lines, they analysed Her-2 amplification or with GATA-3 transcription factor expression. Anticancer Res 15: 1293 – 1301

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Reply: Her2 (ErbB2) receptors, a potential therapeutic target in squamous cell carcinoma of oesophagus?

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