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Edrecolomab (Monoclonal Antibody 17-1A)

A Viewpoint by Harry Bleiberg

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Because chemotherapy for colorectal cancer is still of limited efficacy, major efforts are being made to develop other therapeutic strategies. During the last few decades the huge advance in molecular biology, especially in the fields of genetics and immunology, has brought an enormous wealth of information that will have a major impact on the treatment of cancer.

Immunotherapy is currently divided into 2 major categories: active and passive. Active immunotherapy involves stimulating the antitumoural immunity of the host. This may be achieved either directly by using vaccines to produce an antitumour response against tumour antigens or indirectly using immunomodulators such as Bacillus Calmette-Guérin or cytokines. Passive immunotherapy involves the administration of agents with spontaneous antitumour properties such as monoclonal antibodies, or the administration of *in vitro* induced cells such as lymphokine-activated cells or tumour-infiltrating lymphocytes.

Edrecolomab is a mouse-derived immunoglobulin G (class 2a) that recognises the tumour-associated antigen CO17-1A. Eight phase I or II studies have been conducted in patients with metastatic colorectal cancer. More than 200 patients received between 1 and 10 doses of edrecolomab (200 to 400mg per dose) and objective responses were seen in 4 to 7% of patients which unfortunately was insignificant.

In vitro, the lytic activity of effector cells can be stimulated by the addition of cytokines such as granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon-γ (IFNγ) and interleukin-2. In humans with metastatic colorectal cancer, 4 trials combining edrecolomab and IFNγ produced negative results. In contrast, the combination of edrecolomab and GM-CSF produced 2 durable responses.

The rationale for using monoclonal antibodies alone as adjuvant treatment after surgery is strong. After a 7-year follow-up period, treatment with edrecolomab produced a relative reduction in overall mortality of 32% in patients with colorectal cancer ($p = 0.01$ *vs* surgery alone). However, due to the small number of patients and the mix of colon and rectal cancer, confirmatory studies are required.

The major drawback of immunotherapeutic trials is that they are evaluated as chemotherapeutic studies, with tumour reduction the main objective. Other efficacy criteria need to be identified.

A greater understanding of the antitumour immunity of the host and the search for better ways to stimulate the immune response should improve the use of this interesting approach. ▲