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First gene-based asthma drug almost ready

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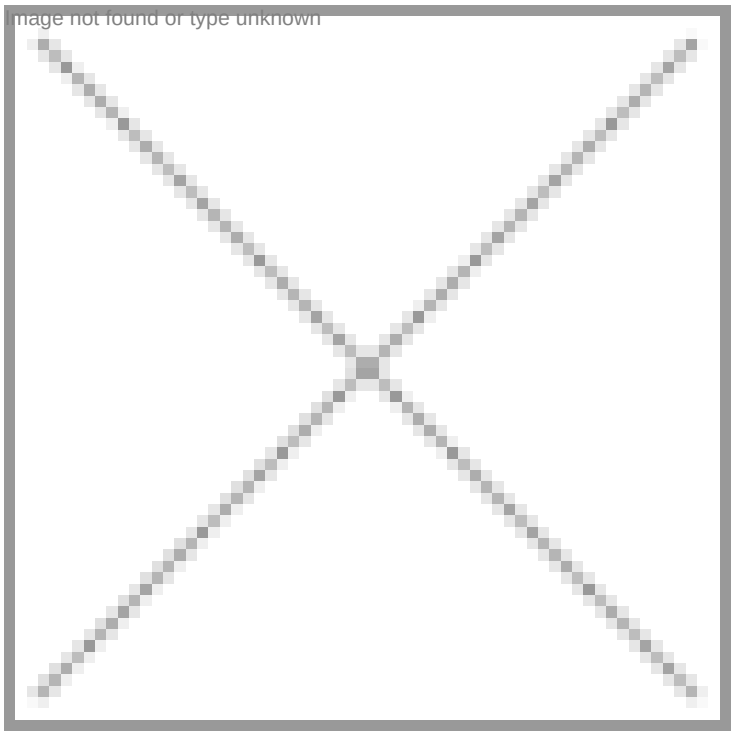

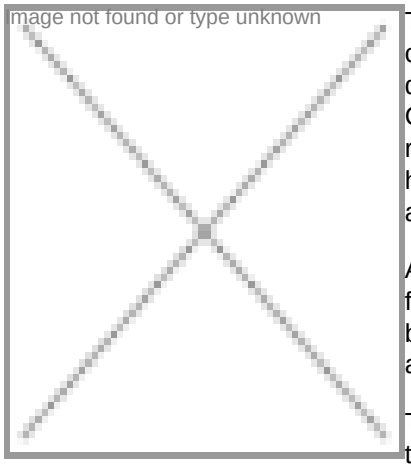

The panel had recommended that the drug's intended benefits may outweigh some concerns about its potential to cause cancer in some patients. In June 2002, Australia's drug regulator had given marketing approvals for Xolair, jointly developed by Novartis, Genentech and Tanox. However, an approval by FDA, one of the world's leading drug regulators, will pave the way for the drug's acceptance in global markets. The FDA panel has restricted the use of Xolair to teenage children and adults mainly due to the non-availability of adequate data for this group now.

According to media reports, the recommendation by FDA's advisory panel was among the final steps leading to the formal approval of the drug by the authorities. Though FDA is not bound to accept the panel's recommendation, it has rarely rejected such a committee's advice. A formal approval may happen by June-end.

The drug, omalizumab, known by its brand name Xolair, is an immunoglobulin E (IgE)-targeting monoclonal antibody. A complex protein, it works by disabling a naturally occurring antibody called IgE that triggers the release of some chemicals. These chemicals are known to cause inflammation and provoke asthma and allergy attacks.

The consortium of companies expect to market Xolair in early 2004 after getting all the approvals. The price of the drug has not been announced. However, analysts expect the full treatment in a year (it may involve injection of Xolair once or twice a

month) may cost about $ 10,000 (Rs 5 lakh).

According to Genentech, Xolair is the first in a new class of therapies that target IgE in the treatment of an allergic disease. Xolair is designed to inhibit IgE before it has the opportunity to bind to the mast cell, thereby interrupting the cascade of asthma or allergic events.

Asthma is a potentially life-threatening chronic inflammatory lung disease. Asthma is often triggered by allergies and is characterized by airway obstruction, wheezing and coughing. Millions of people of all age groups suffer from this disease worldwide every year. In the US alone over 17 million people suffer from asthma including five million children. Additionally, asthma accounts for as many as 500,000 hospitalizations each year. Allergens, such as pollen and mold, and irritants such as dust and tobacco smoke are among the major "triggers" for the breathing problems in asthma patients.

Five Phase III clinical trials were conducted to determine the effectiveness of Xolair in asthma (two studies) and seasonal allergic rhinitis (three studies). In the studies, adults (ages 12-75 years) and pediatric patients (approx. ages 6-12 years) were given either Xolair or placebo in conjunction with other medications â€" either inhaled steroids for asthma or antihistamines for seasonal allergic rhinitis (SAR). A study of its impact on perennial allergic rhinitis (year-round allergies caused by allergens such as dust, mold and animal dander) was also done.

A Washington Post report said FDA experts were concerned about the data that indicated Xolair may increase the risk of cancer in about 0.5 percent of the patients. The companies said there was no definite link between the drug and the enhancement of cancer in the patients. Most of the various malignancies detected in such cases were solid tumors and most were diagnosed within six months of starting Xolair therapy which suggests they were present before the treatment started. Most tumors develop over several years.

In the US alone over 17 million people suffer from asthma including five million children. Additionally, asthma accounts for as many as 500,000 hospitalizations each year. Xolair gives a ray of hope to these patients

Dr Graca Dores, a panel member and fellow at the National Cancer Institute told The Washington Post that there were too few cases to draw a conclusion. "I don't think there's sufficient information one way or another to say Xolair increases risk or does not increase risk of malignancy," she said, adding that Xolair patients should be closely monitored for cancer.

"We are impressed with Xolair's magnitude of treatment effect as demonstrated already in multiple U.S and European peer-reviewed publications," said Btech News, a biotech analyst publication.

"Xolair reduces the need for corticosteroids and minimizes asthma exacerbations in atopic ("allergic") asthmatic children. Endpoints of school days lost and unscheduled asthma-related medical visits were significantly fewer in Xolair treated children versus their placebo-treated counterparts. The frequency and severity of adverse events were similar between Xolair and placebo and there were no serious treatment-related adverse events," said the August 2001 electronic issue of the journal Pediatrics.

The Journal of Allergy and Clinical Immunology (August 2001) wrote that Xolair both reduces the frequency of asthma exacerbations and decreases the use of inhaled corticosteroid and rescue medication when added to standard asthma therapy. Moreover, Xolair had an adverse effect profile similar to that of placebo. This publication provided confirmation of analogous results for adults published and presented in multiple medical society forums.

The Journal of the American Medical Association (JAMA) said, "Xolair significantly reduces symptoms of seasonal allergic rhinitis (hay fever) in patients between the ages of 12 and 75 years old who had at least a two-year history of moderate to severe ragweed-induced allergic rhinitis and baseline IgE levels between 30 IU/mL and 700 IU/mL. Xolair provided a linear dose-response relationship for average daily nasal symptom severity scores."

An accompanying commentary by Dr Marshall Plaut of the National Institute of Allergy and Infectious Diseases stressed that many children with allergic rhinitis go on to develop asthma within two to five years and that "it will be important for future research to evaluate whether (Xolair) blocks the onset of asthma." If this proves to be the case, then not only will Xolair be used for the treatment of asthma and hay fever (chronic rhinitis) but also for the prevention of asthma in those predisposed by virtue of their having hay fever.

" Xolair treatment effect profiles against other IgE-mediated disorders such as atopic dermatitis and food allergies are also being studied. In multiple studies, Xolair has demonstrated an unequivocally clinically important treatment effect and thus far has demonstrated a reassuring safety profile in both adults and children. The potential blockbuster, a key driver of the monoclonal antibody sector has a considerably greater than average probability of gaining FDA approval," wrote Dr Leon Henderson, Dr Bennett Weintraub and Christopher Martin in Btech news.

Analysts expect Xolair sales in the first year to be around $30 million and eventually stabilize around $750 million annually

after a few years.

N Suresh in Cleveland, Ohio