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Epidermal Growth Factor Receptor: A Novel Target for Anticancer Treatment

Manoj Pandey* and K Chandramohan

Address: Assistant Professor, Department of Surgical Oncology, Regional Cancer Centre, Medical College P.O., Thiruvananthapuram, Kerala 695 011, India

Email: Manoj Pandey* - manojpandey@vsnl.com; K Chandramohan - cm@vsnl.com

* Corresponding author

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The process of cell division, growth, differentiation and death is a highly regulated process. Several class of trans membrane receptors play a pivot role in this process, of these, epidermal growth factor receptor (EGFR) a member of Receptor Tyrosine Kinase (RTK) family are best known. These comprises of four receptors Erb B1/HER 1, Erb B2 / HER 2, Erb B3/ HER 3, and Erb B4 / HER 4. Of these HER 2 is the most favoured target.

Monoclonal Antibodies against EGFR

To target aberrant signalling through EGFR, monoclonal antibodies were the first approach to be investigated. Laboratory studies with murine monoclonal antibodies MAb 528 and MAB 225 demonstrated high affinity. IMC 225 [1], was the first antibody for clinical use that binds to extra cellular domain of EGFR and blocks the binding of activating ligands like EGFR and TGF-α. This inhibits autophosphorylation of receptor, induces internalisation of receptor and degradation of EGFR. This also causes p 27 inhibition and G_1 cell cycle arrest.

The second antibody to be tested was ABX-EGF, which is a human immunoglobulin G2 monoclonal antibody. The mechanism of action is similar to that of IMC-225, however being completely human it does not produce immunogenic response against antibody, which improves efficacy and reduces premature termination of treatment due to side effects. Its safety has been demonstrated in phase I studies [2–5].

Small molecule inhibitors

An alternate strategy is to inhibit EGFR TK activity using small molecules [6], like ZD 1839 (gefitinib, 'Iressa™'; Astra Zeneca) approved for use in lung cancer [7,1] and several such other molecules like OSI-774, CI-1033 (PD 183805) and PKI-166 have been evaluated in phase I and II trials while several others like EKB – 569, PD 168393, GW 2016 and CGP 59326 are in pre-clinical trials. These molecules act by inhibiting EGFR-TK thus inhibiting autophosphorylation of EGFR [8,3].

The dream of inhibiting EGFR for its potential clinical use has become a reality. The day is not for when anti EGFR strategies will become another arrow in the quiver of anticancer armamentarium of clinical oncologists.

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