Monoclonal Antibody Therapy of Solid Tumors

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Recently, two monoclonal antibodies (trastuzumab and rituximab) have been approved by the US Food and Drug Administration (FDA) for routine use in cancer patients.

Trastuzumab (Herceptin, Genetech, Inc) is a humanized antibody that recognizes the human oncoprotein HER-2/neu or c-erbB-2 which is over expressed in 25-30% of breast cancer, increasing the aggressiveness of the tumor. Phase I and phase II clinical trials showed the antibody is safe and many women with HER2-positive metastatic breast cancer who had relapsed after chemotherapy had a response to trastuzumab treatment. Randomized trials also showed the combination of either doxorubicin/cyclophosphamide plus trastuzumab or paclitaxel plus trastuzumab resulted in not only a significantly greater overall response rate but also improved overall survival than either chemotherapeutic regimen alone in metastatic breast cancer. However, there were increased risk of cardiac toxicities with combination of trastuzumab and chemotherapy.

Rituximab (Rituxan; Genetech, Inc) is genetically engineered chimeric monoclonal antibody containing murine light and heavy chain variable regions and human IgG1 heavy chain and kappa light chain constant region. Rituximab binds to CD-20, a differentiating antigen found exclusively on B cells and on more than 95% of B-cell Non-Hodgkin’s Lymphoma (NHL). A number of phase I and II trials showed safety and significant antitumor effect in patients with relapsed or refractory follicular CD-20 positive NHL. In subsequent clinical trials, rituximab treatment, either alone or in combination with conventional chemotherapy, also showed encouraging antitumor effect in patients with bulky disease and intermediate or high grade CD-20 positive NHL. Data on the durability of responses to rituximab, given alone or in combination with conventional chemotherapy are awaited. Most common side effects associated with rituximab were related to intravenous infusion itself and involved mild to moderate flu like symptoms.

Radioimmunotherapy, radioactive isotopes coupled with monoclonal antibodies for solid tumors has not been entirely successful. Limited responses were observed in the most radiosensitive cancers. Development of human antimouse antibody response, poor tissue penetration, hematologic toxicities were major obstacles of radioimmunotherapy.

In conclusion, recently approved two monoclonal antibodies showed considerable promise in specific disease and under special circumstances. Possible synergistic or additive effect of these monoclonal antibodies in combination with chemotherapy, and use in low-volume disease (ie, following bone marrow transplantation), or in the adjuvant setting should be resolved in the future trials.