OVERVIEW
Pertuzumab

Introduction

Pertuzumab is a humanized monoclonal antibody to the human epidermal growth factor receptor 2 (HER2) which is used in combination with other antineoplastic agents in the therapy of refractory, advanced breast cancer. Pertuzumab has been implicated in rare instances of transient, occasionally marked serum enzyme elevations, but has not been linked to instances of clinically apparent liver injury with jaundice.

Background

Pertuzumab (per tooz' ue mab) is humanized monoclonal antibody to HER2 which is a growth factor receptor that is overexpressed in 20% to 25% of breast cancers. The interaction of epidermal growth factor (EGF) with HER2 results in rapid cell growth and proliferation via intracellular pathways that include MAP and PI3 kinase. Blockage of this pathway results in cell cycle arrest and cell death. Pertuzumab binds to the dimerization site on the HER2 receptor and prevents pairing of receptors and blocks their intracellular signaling. Because the binding site for pertuzumab is different from that of trastuzumab (another monoclonal antibody to HER2), they can be used together and are believed to have additive antitumor effects. Pertuzumab in combination with trastuzumab and docetaxel has been shown to increase the rate of pathological complete responses in women with advanced HER2 positive breast cancer and it was approved for this indication in 2012. Pertuzumab is available in multiple use vials of 420 mg under the brand name Perjeta. The typical dose is 840 mg intravenously initially, followed by 420 mg every three weeks. Common side effects include diarrhea, nausea, fatigue, rash, abdominal pain and cardiac dysfunction. Rare, but serious side effects include infusion reactions (usually with the initial dose), cardiomyopathy (especially when combined with an anthracycline), pneumonitis and fetal toxicity.

Hepatotoxicity

In large registration trials of pertuzumab for breast and other cancers, rates of serum enzyme elevations were usually not reported, although elevations in ALT above 5 times the ULN have been reported in studies of pertuzumab combined with carboplatin, docetaxel and trastuzumab or with trastuzumab emtansine. A single instance of acute liver failure was reported in a patient who received pertuzumab, trastuzumab and docetaxel in a clinical trial, but few details were given. In all of these situations, the role of pertuzumab as opposed to the other antineoplastic agents being used was

uncertain. Since its approval and wider scale use, there have been no reports of serum ALT elevations or clinically apparent, acute liver injury with jaundice attributed to pertuzumab.

Mechanism of Injury

Pertuzumab is a human monoclonal antibody and is unlikely to have intrinsic hepatotoxicity, but it may interact with endothelial growth factor receptors present on normal cells and cause injury by its direct cellular effects on epithelial growth factor pathways.

Outcome and Management

The liver injury attributed to pertuzumab has not been well characterized and there is no information on possible cross sensitivity to the injury among different monoclonal antibodies or therapies directed at epidermal growth factor receptors.

Drug Class: Antineoplastic Agents, Monoclonal Antibodies

PRODUCT INFORMATION
Pertuzumab

REPRESENTATIVE TRADE NAMES

Pertuzumab – Perjeta®

DRUG CLASS

Antineoplastic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE
Pertuzumab

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Pertuzumab	380610-27-5	Monoclonal Antibody	Not Available