FDA approves pertuzumab for HER-2 positive metastatic breast cancer

On 8th June 2012, the U.S. Food and Drug Administration approved pertuzumab (Perjeta), a HER2/neu receptor antagonist indicated in combination with trastuzumab and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

In HER2-positive breast cancers, the increased amount of the HER2 protein contributes to cancer cell growth and survival. About 20% of breast cancers have increased amounts of the HER2 protein. Pertuzumab is a humanized monoclonal antibody, believed to work by targeting a different part of the HER-protein than trastuzumab, resulting in further reduction in growth and survival of HER2-positive breast cancer cells.

Pertuzumab was reviewed under the agency's priority review program, which provides for an expedited six-month review of drugs that may offer major advances in treatment. The safety and effectiveness of pertuzumab were evaluated in a single clinical trial involving 808 patients with HER2-positive metastatic breast cancer. Patients were randomly assigned to receive pertuzumab, trastuzumab and docetaxel or trastuzumab and docetaxel with a placebo. Those treated with the combination containing pertuzumab had a median progression-free survival (PFS) of 18.5 months, while those treated with the combination containing placebo had a median PFS of 12.4 months.

The most common side effects observed in patients receiving pertuzumab in combination with trastuzumab and docetaxel were diarrhea, hair loss, neutropenia, nausea, fatigue, rash, and peripheral sensory neuropathy. Pertuzumab is being approved with a Boxed Warning alerting patients and health care professionals to the potential risk embryo-fetal death and birth defects. Patients must be advised of these risks and the need for effective contraception.

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DO YOU KNOW.....? (answer)

Aldactone A is also a product of G.D. Searle & Co., the original manufacturer of Aldactone, i.e. Spironolactone oral tablet. The story has to be traced all the way back to 1960s. Aldactone A was designed to preserve the small particle size of spironolactone, and was claimed to be effective in one quarter of the dosage of the older preparation, 'Aldactone'[1]. This reduction in dosage may be particularly useful in treating ascites of cirrhosis as in those days 20-40% patients may require up to 800-1200mg per day of spironolactone1. Nowadays, the maximum daily dose of spironolactone in the same setting seldom exceeds 400mg when used with frusemide[2] .

The reason why by preserving the small particle size of spironolactone enhances its absorption was not fully understood. Several mechanisms have been proposed such as the smaller particle size favours a more rapid absorption in the gut, and a shorter disintegration time for the tablet as compared to the original product of Aldactone1. Another possible reason may be the addition of Tween 80, a surfactant, into the formulation. However, Tween 80 itself has no direct effect on enhancing oral absorption of spironolactone and it was thought that Tween 80 only encapsulated to preserve the small particle size of spironolactone in the Aldactone A preparation[1].

All in all, are Aldactone A and the Aldactone we are using now the same preparation? We do not know. Interestingly, Aldactone A is still being marketed in some countries including Japan, Argentina, Peru, Spain, Turkey and Guyana under Pfizer (as Searle was acquired by Pharmacia and Upjohn, which was later acquired by Pfizer). The dosage recommendation in the Argentinian Package Insert of Aldactone A is not different from that of Aldactone, and clinical studies that support dosages of spironolactone in certain conditions, such as RALES, have been quoted[3] .

References

1. Shaldon S, Ryder JA, Garsenstein M. A comparison of the use of Aldactone and Aldactone A in the treatment of hepatic ascites. Gut. 1963;4:16-9
2. Runyon BA. AASLD Practice Guideline Management of adult patients with ascites due to cirrhosis: An update. Hepatology. 2009; 49(6): 2087–2107
3. ALDACTONE-A ESPIRONOLACTONA Comprimidos. Last updated August 2009. Accessed via http://www.pfizer.com.ar/Productos/.../Aldactone-A.pdf. Last viewed 29 June 2012.

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