Fulvestrant Antiestrogen for Treatment of Breast Cancer

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In April 2002, the U.S. Food and Drug Administration (FDA) approved fulvestrant injection (Faslodex®, AstraZeneca Pharmaceuticals LP, Wilmington, DE) for the treatment of hormone receptor-positive, metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy (i.e., tamoxifen, Nolvadex® [AstraZeneca Pharmaceuticals LP]). Fulvestrant is the first in a new class of steroidal antiestrogens, the estrogen receptor downregulators. It targets and degrades the estrogen receptors in breast cancer cells and is the only antiestrogen that has demonstrated efficacy following tamoxifen failure (Bundred et al., 2002).

Clinical Trials

The efficacy of fulvestrant was demonstrated in clinical trials comparing the drug to the aromatase inhibitor anastrozole (Arimidex®, AstraZeneca Pharmaceuticals LP). Two randomized trials in North America and Europe were conducted in postmenopausal women with locally advanced or metastatic breast cancer. The double-blind, North American trial included 400 women, whereas the open, randomized, European trial included 451 women. All patients had progressed after previous therapy with an antiestrogen or progestin for breast cancer in the adjuvant or advanced disease setting. Subjects were randomized to receive either fulvestrant 250 mg intramuscularly once a month or anastrozole 1 mg orally each day. The effectiveness of fulvestrant was determined by comparing response rates (RRs) and times to progression (TTPs). In the North American trial, objective tumor RR were 17% for both the fulvestrant and anastrozole treatment groups. In the European trial, fulvestrant produced a 20.3% objective tumor RR, compared to 14.9% for the anastrozole group. TTP for fulvestrant versus anastrozole was 5.5 months versus 3.5 months in the North American trial and 5.5 months versus 5.1 months in the European trial (Howell et al., 2002; Osborne et al., 2002).

No randomized trials have been conducted to demonstrate the efficacy of fulvestrant in premenopausal women with advanced breast cancer. Fulvestrant is contraindicated in pregnant women (Howell, 2001; Howell, Osborne, Morris, & Wakeling, 2000).

Dosage and Administration

The recommended dosage of fulvestrant is 250 mg intramuscularly at one-month intervals. It can be administered as either a single 5 ml injection or two 2.5 ml injections. Fulvestrant is supplied in 2.5 ml and 5 ml prefilled glass barrels. The syringes are presented in a tray with a polystyrene plunger rod and a safety needle (e.g., Safety Glide™, Becton Dickinson and Company, Franklin Lakes, NJ) for connection to the barrel.

Side-Effect Profile

In the North American and European clinical trials, the most common adverse events related to the use of fulvestrant were gastrointestinal symptoms (nausea 26% and 25.3%, vomiting 13% and 11.8%, constipation 12.5% and 10.6%, diarrhea 12.3% and 12.8%, abdominal pain 11.8% and 11.6%, respectively). Other reported side effects were headache, back pain, and injection site discomfort or irritation.

Vaginal bleeding has been reported (less than 1%) most commonly in patients during the first six weeks after changing from existing hormonal therapy to fulvestrant (AstraZeneca Pharmaceuticals LP, 2002).

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Clinical Update