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Tykerb™ (lapatinib ditosylate) plus letrozole significantly delayed disease progression in post-menopausal women with ErbB2 positive metastatic breast cancer

Findings from one of the largest studies in hormone receptor positive women determined clinical benefit with first-line oral treatment regimen

MISSISSAUGA, ON (December 12, 2008) – New results from a study in metastatic breast cancer presented today at the 31st Annual CTRC-AACR San Antonio Breast Cancer Symposium showed that the combination of Tykerb™ (lapatinib ditosylate) plus letrozole, as a first line treatment regimen, provided a significant improvement in delaying disease progression when compared to treatment with Femara® (letrozole) alone.¹ In the study, women diagnosed with post-menopausal, hormone receptor positive (HR+) and ErbB2 positive (ErbB2+ / HER2+) metastatic breast cancer experienced a 5.2 month increase in median progression free survival (PFS) compared to women treated with letrozole alone.

This double blind, placebo controlled study (EGF30008) randomized 1,286 post-menopausal women with HR+ breast cancer to treatment with lapatinib plus letrozole or to letrozole alone. Letrozole, an aromatase inhibitor (AI), is a recognized therapy in the treatment of HR+ breast cancer. The ErbB2 status of patients was not required for randomization into the study, however PFS was the primary endpoint in the HR+ and ErbB2 positive patient post study analysis.

Via independent central testing, 219 patients were deemed ErbB2 positive.¹ Current treatment regimens for women who are HR+ and ErbB2 positive include chemotherapy with a monoclonal antibody. In the study, women in this patient population who received combination therapy with lapatinib and letrozole experienced a significantly increased median PFS, compared to treatment with letrozole alone (8.2 months versus 3.0 months respectively, HR=0.71, (95%CI: 0.53, 0.96) p=0.019) - an improvement of 41 per cent.

“The encouraging positive results seen in women who are HR+ and ErbB2 positive shows that the lapatinib and letrozole combination has the potential to become a first-line, oral treatment option for clinicians and patients in this setting,” says Paolo Paoletti, SVP Oncology Global R&D, GSK. “We plan to discuss these data with regulators in the near future.”

Results from the intent to treat group (ITT; all patients, irrespective of ErbB2 status) showed that lapatinib plus letrozole provided, on average, an additional month before disease progression compared to letrozole treatment alone (11.9 months versus 10.9 months, HR=0.86 (95%CI: 0.76, 0.98), p=0.026). Within the ITT group there was therefore a small subset of HR+ ErbB2 negative women who may have benefited from this treatment combination, but further investigations into this specific group of women are warranted.

The combination of letrozole and lapatinib was manageable, and no new safety issues were identified. Grade 3 / 4 adverse events that occurred in more than two per cent of patients in either the combination arm or monotherapy arm included diarrhoea (9 per cent vs. <1 per cent, respectively); back pain (2 per cent vs. 2 per cent, respectively); fatigue (2 per cent vs. < 1 per cent, respectively); increased ALT (2 per cent vs. <1 per cent, respectively) and increased AST (2 per cent vs. <1 per cent, respectively).

Growth factor receptors such as those in the ErbB family play a key role in cell growth and survival.² Targeting these protein receptors is a way in which cancer cells can be killed and tumour growth curtailed. Approximately 70 per cent of all breast cancer cases are HR+³ and only a third of all HR+ tumours respond to first-line treatment with AIs. Furthermore, tumours that initially respond to AIs can become resistant, leading to disease progression and ultimately, patient death.⁴ Recent studies have revealed interactions between HR and ErbB receptors as a primary contributor to the development of resistance, and served as the hypothesis basis for this study.⁵

Breast cancer is the most common cancer among Canadian women. In 2008, an estimated 22,400 women will be diagnosed with breast cancer and 5,300 will die of it.⁶

About EGF30008

EGF30008 is a Phase III, randomized, double-blind, placebo-controlled trial in 1,286 post-menopausal women with HR+ metastatic breast cancer. Women in the study were randomized to compare the efficacy of first-line therapy with lapatinib, a small molecule dual tyrosine kinase inhibitor, and the aromatase inhibitor letrozole, versus letrozole monotherapy. At randomization patients received either letrozole 2.5 mg once daily (QD) plus lapatinib 1500 mg QD, or letrozole 2.5 mg QD plus placebo. The primary endpoint of EGF30008 was PFS in the HR+/ErbB2+ population, and secondarily in the overall ITT population. Secondary endpoints included overall response rate (ORR), clinical benefit rate (CBR), time to response, duration of response, overall survival, safety assessments, and quality of life. Hormonal therapy was allowed in the adjuvant setting only (1 year prior to study entry) and crossover was not permitted.

About Tykerb™

Tykerb™ tablets have been approved in 63 countries around the world, including the United States, Europe and Australia. Tykerb™ has not been approved for commercial use in Canada.

Tykerb™ is an investigational drug that is in a class of cancer treatments called targeted therapies. It is an oral small-molecule inhibitor of the ErbB2 tyrosine kinase receptor. Stimulation of ErbB2 is associated with cell proliferation, tumour progression and the development of metastases. Overexpression of this receptor has been reported in a variety of human tumours and is associated with poor prognosis and reduced overall survival.⁷

Tykerb™ Clinical Trials

GSK has a comprehensive clinical trial program that is actively studying Tykerb™ in other breast cancer settings and other cancers to better identify patient populations that may respond to this therapy.

About GlaxoSmithKline

GlaxoSmithKline – one of the world's leading research-based pharmaceutical and health-care companies – is committed to improving the quality of human life by enabling people to do more, feel better and live longer. GSK is Canada's largest biopharmaceutical employer, and has been consistently recognized as one of the 50 Best Employers in Canada. GSK is an Imagine Caring Company and is among the top 15 investors in Canadian research and development, investing more than \$178 million in 2007 alone. For company information, please visit www.gsk.ca.

- 30 -

Notes to Editors:

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