Novartis drug Afinitor® helps women with advanced breast cancer live significantly longer without their disease progressing

Media release

- Everolimus combined with hormonal therapy more than doubled time without tumor growth and reduced risk of progression by 57% vs hormonal therapy alone (1).
- Study shows everolimus significantly enhances benefit from hormonal therapy, representing important advance for women with postmenopausal ER+ breast cancer (1, 2).
- Worldwide regulatory filings planned by the end of 2011 based on these data, marking the first submission for everolimus in breast cancer.

_Basel, September 26, 2011_ – A pivotal Phase III study shows Afinitor® (everolimus) tablets plus exemestane, a hormonal therapy, more than doubled the time women lived without tumor growth (progression-free survival; PFS) and significantly reduced the risk of cancer progression by 57% versus exemestane alone in patients with advanced breast cancer (1).

“Everolimus is the first drug to show significant efficacy when combined with hormonal therapy in women with ER+HER2-advanced breast cancer, where there continues to be a critical unmet need,” said Hervé Hoppenot, President, Novartis Oncology. “The magnitude of benefit seen in these patients, despite their resistance to previous hormonal therapies, shows everolimus represents a potential important new treatment approach.”

BOLERO-2 (Breast cancer trials of Oral EveroLimus-2) examined the safety and efficacy of everolimus in combination with exemestane versus exemestane alone in postmenopausal women with ER+HER2-advanced breast cancer who recurred or progressed while on or following previous treatment with hormonal therapies, letrozole or anastrozole (1). Findings from the trial will be presented today during a Presidential Symposium at the 2011 European Multidisciplinary Cancer Congress in Stockholm, Sweden.

At a pre-planned analysis, the trial met its primary endpoint of PFS showing treatment with everolimus improved PFS to 6.9 months compared to 2.8 months (hazard ratio 0.43 [95% confidence interval (CI): 0.35 to 0.54]; p < 0.0001) by local investigator assessment. This significant improvement was consistent across all subgroups including number of prior therapies, presence of visceral disease, bone metastases and prior use of chemotherapy (1).

Hormonal therapy remains the cornerstone of treatment for women with advanced breast cancer but most women with metastatic disease do not respond to initial treatment with hormonal therapy, and almost all initial responders develop resistance (2, 3). Additionally, life expectancy is significantly shortened due to the worsening of the disease (3).

Everolimus targets mTOR in cancer cells, a protein that acts as an important regulator of tumor cell division, blood vessel growth and cell metabolism4. Resistance to hormonal therapy in breast cancer has been associated with over-activation of the mTOR pathway (3).

Data from BOLERO-2 support worldwide regulatory submissions, which are planned by the end of 2011. Additional data from BOLERO-2 will be presented at upcoming medical congresses this year.

Worldwide, there are approximately 220 000 newly diagnosed cases of ER+HER2-advanced breast cancer each year (5, 6). Everolimus is also being investigated for the treatment of patients with HER2+ advanced breast cancer (7, 8).

About BOLERO-2

BOLERO-2 is a Phase III, randomized, double-blind, placebo-controlled, multicenter study. The trial was conducted at 189 sites worldwide and enrolled 724 patients (1). Patients who met the study criteria were randomized (2:1) to receive either everolimus 10 mg/day orally (n= 485), or placebo, plus oral exemestane 25 mg/day (n = 239) (1).

The primary endpoint was PFS based on local investigator radiology assessment. Additional analysis by an independent central radiology review committee showed everolimus extended PFS to 10.6 months compared to 4.1 months (hazard ratio 0.36; [95% CI 0.27 to 0.47]; p < 0.0001). Other endpoints include overall survival, overall response rate, safety, patient reported outcome, clinical benefit rate and changes in markers of bone metabolism (1). These data are being evaluated and will be submitted for publication or presentation in a peer-reviewed forum.

The side effects observed were consistent with those previously reported with everolimus with the most common grade 3 or 4 adverse events including stomatitis (7.7%), anemia (5.8%), dyspnea (3.9%), hyperglycemia (4.3%), fatigue (3.7%), non-infectious pneumonitis (3.1%) and increase in liver enzymes (3.1%) (1).

About everolimus

Afinitor® (everolimus) tablets is approved in more than 70 countries and regions including the United States and the European Union in the oncology settings of advanced renal cell carcinoma (RCC) following vascular endothelial growth factor (VEGF)-targeted therapy and advanced progressive neuroendocrine tumors of pancreatic origin (pNET).

References

1. Baselga J. Everolimus in combination with exemestane for postmenopausal women with advanced breast cancer who are refractory to letrozole or anastrozole: results of the BOLE-RO-2 phase III trial. 2011 European Multidisciplinary Cancer Congress. Presentation of late breaking abstract No. 9LBA. September 26, 2011.


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