

Primary results of LORELEI study presented at ESMO 2017 Congress

(European Society for Medical Oncology, Madrid-Spain, 8/09/2017)

The LORELEI study shows taselisib and letrozole given prior to surgery significantly increases objective response rates compared to letrozole alone in women with ER-positive, HER2-negative early breast cancer

Brussels, 8 September 2017 - The Breast International Group (BIG), the Austrian Breast & Colorectal Cancer Study Group (ABCSCG), and the SOLTI Breast Cancer Research Group today announced positive results from the randomised phase II LORELEI study. The study, sponsored by Genentech, a member of the Roche group, was designed to evaluate taselisib plus letrozole versus placebo plus letrozole given prior to surgery (neoadjuvant treatment) in postmenopausal women with ER-positive/HER2-negative early-stage breast cancer. LORELEI has met its primary objective and showed that the addition of taselisib increased the objective response rate (ORR) from 38% to 56.2% in patients with *PIK3CA* mutation and from 39.3% to 50% across all patients in the study. No significant difference was observed for pathologic complete response (pCR) rate with the addition of taselisib to letrozole. LORELEI is the first randomised study testing the addition of a selective PI3K inhibitor in combination with endocrine therapy and utilising centrally assessed MRI to evaluate tumour response in a neoadjuvant endocrine trial for patients with early breast cancer. The safety profile was manageable.

Taselisib is an oral selective PI3-kinase (PI3K) inhibitor with enhanced activity against *PIK3CA* mutant cancer cells via a novel mechanism of action. PI3K pathway is critical for cell-cycle modulation, cell growth, metabolism, motility, and survival. *PIK3CA* mutation, as one of the major mechanisms leading to PI3K pathway activation, is found in approximately 40-45% of ER-positive breast cancers. Additionally, preclinical evidence suggests that elevated PI3K pathway activity is associated with resistance to endocrine therapy. Thus, it is believed that blocking PI3K signalling may stop or slow the growth of certain breast cancers and potentially other types of tumours. Clinical data from early trials have demonstrated anti-tumour activity in patients with *PIK3CA* mutant breast cancer treated with taselisib either as a single agent or combined with endocrine therapy.

Results of the LORELEI primary analysis were presented in an oral session today at the European Society for Medical Oncology (ESMO) Congress in Madrid (Spain) by Cristina Saura, M.D., PhD, study primary investigator (Abstract #LBA10), and is featured in ESMO's official press programme.

Dr. Saura (Vall d'Hebrón University Hospital and Vall d'Hebrón Institut of Oncology Barcelona, Spain) added: "The LORELEI study demonstrates the importance of industry-academic collaborations and their crucial role in finding treatments and improving care for people affected by breast cancer. The study incorporates an extensive biomarker programme to guide further clinical development, both in the early and metastatic breast cancer settings. This is an important clinical trial, and to accrue patients successfully, the support of patients and researchers internationally was absolutely essential. BIG, together with ABCSG and SOLTI, have been instrumental in facilitating this international collaboration. The results of the LORELEI study will help guide further clinical research in ER-positive/HER2-negative breast cancer."

About the LORELEI study

LORELEI: a phase II randomised, double-blind study of neoadjuvant letrozole plus taselisib versus letrozole plus placebo in postmenopausal women with ER-positive/HER2-negative early-stage breast cancer

- **Co-primary endpoints: ORR (Objective Response Rate) by centrally assessed breast MRI (via modified RECIST criteria) and pathologic complete response (pCR) rate in breast and axilla at time of surgery, in all randomised patients and in patients with *PIK3CA* mutant tumours.**
- **Key secondary endpoints: ORR (Objective Response Rate) by centrally-assessed MRI in patients with *PIK3CA* wild-type tumours, pCR rate in patients with *PIK3CA* wild-type tumours, and safety overall.**

Study methods: 334 postmenopausal women with newly diagnosed ER-positive/HER2-negative-, untreated, Stage I-III operable breast cancer and evaluable tumour tissue for *PIK3CA* genotyping were randomised (1:1) in 85 sites across 22 countries to receive letrozole (2.5 mg daily) with either taselisib (4 mg on a 5 days on/ 2 days off schedule) or placebo for 16 weeks, followed by surgery. The co-primary endpoints were overall objective response rate (ORR) by centrally assessed breast magnetic resonance imaging (MRI) and pathologic complete response (pCR) rate in breast and axilla at surgery, in all randomised patients and in patients with *PIK3CA* mutant tumours. One planned interim safety analysis and two safety monitoring meetings have been conducted by an Independent Data Monitoring Committee (IDMC), with the recommendation to continue the trial without modifications.

- **Collaborative study partners:** the Breast International Group (BIG), the Austrian Breast & Colorectal Cancer Study Group (ABCSG), and the SOLTI Breast Cancer Research Group
- **Pharmaceutical partner and sponsor:** Genentech, a member of the Roche group, and study sponsor, provided funding for this study

- Groups enrolling patients: **ABCSG** (Austrian Breast & Colorectal Cancer Study Group), **ANZBCTG** (Australia and New Zealand Breast Cancer Trials Group), **EORTC** (European Organisation for Research and Treatment of Cancer), **GECOPERU** (Grupo de Estudios Clínicos Oncológicos Peruano), **GOIRC** (Gruppo Oncologico Italiano di Ricerca Clinica - Italian Oncology Group of Clinical Research), **IBCSG** (International Breast Cancer Study Group), **LACOG** (Latin American Cooperative Oncology Group), and **SOLTI** (Spanish Breast Cancer Research Group)
- Sites: 85 sites worldwide in 22 countries, including 8 BIG Groups, are participating in the study
- Clinical trial information: NCT02273973

About ER-positive/HER2-negative Breast Cancer

ER-positive/HER2-negative breast cancer is the most common subtype of this disease, characterised by expression of ER (oestrogen receptor) and lack of expression of HER2 (human epidermal growth factor receptor 2). Tumours that are ER-positive are much more likely to respond to treatments that block oestrogen. The most common treatment for ER-positive and HER2-negative breast cancer is hormone blocking therapy. The prognosis for patients with ER-positive and HER2-negative breast cancer depends on how advanced the cancer was when it was detected. Prognosis is also influenced by the size of the tumour and if the cancer has spread to other organs. Despite the favourable prognosis of patients with early stage ER-positive, HER2-negative breast cancer receiving endocrine therapy, a substantial proportion of them will experience recurrence of their disease. Resistance to endocrine treatment can be fuelled by several alternative oncogenic signalling pathways, with an abundance of evidence identifying activation of PI3K signalling as mediator of such resistance.

About the Breast International Group (BIG)

The Breast International Group (BIG) is an international not-for-profit organisation for academic breast cancer research groups from around the world, based in Brussels, Belgium.

Global collaboration is crucial to make significant advances in breast cancer research, reduce unnecessary duplication of effort, share data, contribute to the faster development of better treatments, and increase the likelihood of cures for patients. Therefore, BIG facilitates breast cancer research at international level, by stimulating cooperation between its members and other academic networks, and collaborating with, but working independently from, the pharmaceutical industry.

Founded by leading European opinion leaders in 1999, BIG now constitutes a network of 59 collaborative groups from Europe, Canada, Latin America, Asia and Australasia. These entities are tied to several thousand specialised hospitals and research centres worldwide. More than 30 clinical trials are run or are under development under the BIG umbrella at any one time. BIG also works closely with the US National Cancer Institute (NCI) and the North American Breast Cancer Groups (NABCG), so that together they act as a strong integrating force in the breast cancer research arena. For more information, visit www.BIGagainstbreastcancer.org.

About ABCSG

The Austrian Breast & Colorectal Cancer Study Group (ABCSG), a not-for-profit organisation, is Austria's biggest and best-established academic research organisation that successfully performs international clinical trials focusing on the subject of breast and colorectal cancer, and more recently also on pancreatic cancer and liver metastasis. ABCSG has over time and with great dedication achieved a very highly positive public reputation and patient commitment. In some indications, more than 35 percent of all breast cancer patients with a given diagnosis are recruited into ABCSG trials. Their findings have received international recognition and have made a significant contribution towards improving patients' chances of recovery and survival. Since 1984, more than 25,300 patients have participated in ABCSG studies, and over 900 physicians are part of the extensive ABCSG network. For further information, please visit www.abcsbg.com.

About SOLTI

SOLTI is a non-profit association with more than 20 years of experience in conducting innovative clinical and translational research to address unmet medical needs in breast cancer that answer questions of major scientific interest and relevance in the field of oncology. SOLTI has a network of more than 260 professionals, mostly medical oncologists, distributed in over 70 hospitals in Spain, Portugal, France and Italy. For more information, please visit: www.gruposolti.org.

Note to the editor - not for publication:

For further information on this media release, or should you wish to have an interview with Dr. Cristina Saura, Principal Investigator of the LORELEI study, please contact:

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