

Press Release

PANACEA study suggests immunotherapy may help to overcome trastuzumab-resistant breast cancer

Brussels, 6 December 2017 – **At the San Antonio Breast Cancer Symposium (Texas/USA), results from the international phase Ib/II study PANACEA (BIG 4-13/IBCSG 45-13) were presented, suggesting that immunotherapy may help to overcome trastuzumab-resistant breast cancer.**

In addition to surgery, chemotherapy, radiotherapy and hormonal treatments, cancer immunotherapy holds substantial potential as a well-tolerated, sustainable therapeutic option personalised to patients' specific tumour characteristics.

Dr. Sherene Loi, MD, PhD, associate professor at Peter MacCallum Cancer Centre in Melbourne, Australia, working with the International Breast Cancer Study Group (IBCSG), says "The results of the PANACEA study are very encouraging. There is a clear need to develop new therapeutic approaches for patients presenting with HER2-positive metastatic breast cancer that has become resistant to trastuzumab. A significant amount of preclinical and correlative clinical data suggest that such cases could be amenable to immunotherapy."

The PANACEA Study

PANACEA is an international phase Ib/II study set up to evaluate the safety and efficacy of using immunotherapy with pembrolizumab, an anti-PD-1 monoclonal antibody targeting the T-cell checkpoint protein programmed death-1 (PD-1), in combination with the standard therapy trastuzumab in patients with HER2 (human epidermal growth factor receptor 2)-positive metastatic breast cancer. The study hypothesis is that pembrolizumab can reverse trastuzumab resistance in patients whose cancer is progressing on trastuzumab.

In total, 58 patients participated in this Phase Ib/ Phase II study, for which all tumours were centrally assessed for HER2 positivity, PD-1 ligand (PD-L1) status, and quantity of tumour-infiltrating lymphocytes (TILs).

The dose-escalating Phase Ib part of the study of pembrolizumab, used with the standard dose of trastuzumab, showed no dose-limiting toxicities. The Phase II part of the study involved two patient cohorts, one of 40 patients with tumours expressing PD-L1 positivity and a second cohort of 12 patients with PD-L1 negative tumours. Patients received 200 mg of pembrolizumab every three weeks in combination with the standard dose of trastuzumab for 24 months or until disease progression.

Primary objective was met

In the PD-L1-positive cohort, the trial met its primary objective, observing an objective response rate of 15 percent and a disease control rate of 25 percent. At the time of the analysis, 4 patients were without progression of disease for a range of 13 to 22 months since starting treatment. In a subgroup of the PD-L1 positive cohort having 5 percent or more TILs present in the metastatic tumour, the objective response rate was 39 percent and the disease control rate was 47 percent, suggesting that quantification of TILs may help identify patients who will most benefit from this treatment. No objective responses were observed in the PD-L1 negative cohort.

Pembrolizumab with trastuzumab was well tolerated, with grade 1-2 fatigue as the most commonly reported treatment-related adverse event (21 percent of patients). The most common immune adverse events reported were hyper and hypo-thyroidism (grade 1 or 2: 6.9%) and pneumonitis (grade 3 or 4: 3.4%).

“Observations suggest that the PD-1/PD-L1 pathway plays an important role in the trastuzumab resistance that we see in patients with metastatic HER2-positive breast cancer, and the PANACEA study provides proof-of principle evidence that PD-1 inhibition like pembrolizumab can help reverse this,” said Dr Loi. “Moreover, the quantification of TILs seems to be a meaningful way for us to identify those who would benefit most from an immunotherapeutic approach.”

Study Partners

The PANACEA study is sponsored and managed by the International Breast Cancer Study Group (IBCSG), in collaboration with the Breast International Group (BIG) and funded by Merck & Co., Inc., Kenilworth, N.J., USA (known as MSD outside the United States and Canada), through a subsidiary. Eleven institutions from Australia, Austria, Belgium, France, and Italy are involved in the study, with participating investigators active in BIG’s Immunotherapy Task Force. The study is being run according to BIG’s Principles of Research Conduct.

About 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 the 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 about 60 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 International Breast Cancer Study Group (IBCSG)

The IBCSG is one of the world’s leading groups in breast cancer research. The IBCSG pioneers research in combined hormonal therapy and chemotherapy, timing and duration of adjuvant therapies and quality of life of breast cancer patients. The latest generation of clinical trials in the adjuvant setting addresses tailored treatment for subgroups of patients, as IBCSG also expands its research into neoadjuvant treatment and therapy for advanced disease. In addition to clinical trials, IBCSG conducts extensive programs in translational research, database studies, quality of life and statistical methodology. The goal of clinical research within IBCSG is to give the patients a longer survival and symptom-free period after primary treatment, and to improve their quality of life.

For more information, visit <http://www.ibcsg.org>



Breast International Group

Note to the editor - not for publication:

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