

## **APHINITY six-year results strengthen evidence of clinical benefit with Roche's Perjeta-based regimen**

- **Greatest improvement in invasive disease-free survival (iDFS) remains in patients at high risk of recurrence, such as those with lymph node-positive disease with a 28% reduction in the risk of recurrence or death, corresponding to an absolute iDFS benefit of 4.5% at six years**
- **With longer follow-up, treatment effect is seen regardless of hormone receptor status**
- **Fewer deaths seen in Perjeta-based regimen arm, however overall survival data remain immature and statistical significance has not been reached at this interim analysis**

Basel, 11 December 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY), the Breast International Group (BIG), Institut Jules Bordet Clinical Trials Support Unit (IJB-CTSU) and Frontier Science Foundation (FS) today announced data from a second interim overall survival (OS) analysis of the phase III APHINITY study, evaluating the combination of Perjeta® (pertuzumab), Herceptin® (trastuzumab) and chemotherapy (the Perjeta-based regimen) as an adjuvant (after surgery) treatment for patients with HER2-positive early breast cancer (eBC). This latest interim OS analysis was conducted after a median follow-up of approximately 74 months, compared to approximately 45 months for the primary analysis in 2017, and includes updated descriptive iDFS and cardiac safety data. [1]

“The goal of adjuvant treatment is to give each person with early breast cancer the best chance of a cure,” said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. “These new data with longer follow-up show the continued effect of the Perjeta-based regimen and an increased invasive disease-free survival benefit.”

Martine Piccart, M.D., Ph.D., BIG co-founder and Scientific Director at Institut Jules Bordet, added: “These results demonstrate the importance of longer follow-up of APHINITY and further confirm the Perjeta-based regimen as the standard of care for people with HER2-positive early breast cancer at high risk of recurrence, such as those with lymph node-positive disease.”

At this latest planned analysis, in the overall study population, the Perjeta-based regimen reduced the risk of breast cancer recurrence or death by 24%, compared to Herceptin, chemotherapy and placebo (HR=0.76; 95% CI 0.64-0.91). At six years, 90.6% of patients in the Perjeta arm have not seen their breast cancer return, compared to 87.8% in the placebo arm, an absolute benefit of 2.8%. [1]

Consistent with the primary analysis, the greatest effect continues to be observed in patients at high risk of recurrence, such as those with lymph node (LN)-positive disease. In these patients there was a 28% reduction in the risk of recurrence or death with the Perjeta-based regimen compared to Herceptin, chemotherapy and placebo (HR=0.72; 95% CI 0.59-0.87). This corresponds to an absolute improvement in iDFS at six years of 4.5% (87.9% vs. 83.4%). With longer follow-up, the treatment effect of the Perjeta-based regimen is seen regardless of hormone receptor (HR) status. The iDFS hazard ratio for HR-positive patients is 0.73 (95% CI 0.59-0.92). The iDFS hazard ratio for HR-negative patients is 0.83 (95% CI 0.63–1.10). [1]

Hazard ratio (95% CI) for iDFS in the ITT population and in subgroups based on LN and HR status [1,2]			iDFS at six years from randomisation (database with a median follow-up of 74.1 months) [1]		
Population	Primary Analysis (median follow-up 45.4 months; 2017)	Updated Analysis (median follow-up 74.1 months; 2019)	Perjeta + Herceptin + chemo (Perjeta-based regimen)	Herceptin + chemo + placebo	Absolute benefit
ITT	0.81 (0.66-1.00)	0.76 (0.64-0.91)	90.6%	87.8%	2.8%
LN-positive	0.77 (0.62-0.96)	0.72 (0.59-0.87)	87.9%	83.4%	4.5%
LN-negative	1.13 (0.68-1.86)	1.02 (0.69-1.53)	95.0%	94.9%	0.1%
HR-positive	0.86 (0.66-1.13)	0.73 (0.59-0.92)	91.2%	88.2%	3.0%
HR-negative	0.76 (0.56-1.04)	0.83 (0.63-1.10)	89.5%	87.0%	2.5%

Fewer deaths have been observed in the Perjeta-based regimen arm (125 vs. 147 [HR=0.85; 95% CI: 0.67-1.07]); however, data remain immature at this time. The APHINITY study continues as planned with the third interim analysis of OS scheduled for 2022. Continued follow-up of these patients is very important to determine a possible OS benefit. [1]

No new cardiac safety concerns emerged. The safety profile of the Perjeta-based regimen was consistent with that seen at primary analysis and in previous studies, with a low incidence of cardiac events. The percentage of primary cardiac events recorded in the Perjeta-based regimen arm was 0.8% vs. 0.3% in the placebo arm. [1,2]

Based on the primary study analysis in 2017, the clinical value of the Perjeta-based regimen for patients with HER2-positive eBC has been recognised by regulatory bodies around the world. This regimen is now approved for the treatment of eBC for people at a high risk of recurrence in more than 86 countries, including the US and across the EU. To date, more than 150,000 patients have been treated with the Perjeta-based regimen in this setting. [3] The regimen has also been recognised in multiple international treatment guidelines, including those from St Gallen International Breast Cancer Conference, NCCN, ASCO and ESMO, which recommend it as an adjuvant standard treatment for patients with HER2-positive eBC at high risk of recurrence. [4,5,6,7]

These results from APHINITY will be presented in an oral session on Wednesday 11 December at 09.30 CT at the 2019 San Antonio Breast Cancer Symposium (SABCS) in San Antonio, Texas, US, by Dr Martine Piccart (Abstract #GS1-04). The data will also be featured in SABCS' official press programme.

### About APHINITY

APHINITY (Adjuvant Pertuzumab and Herceptin IN Initial TherapY in Breast Cancer, NCT01358877/ BO25126/ BIG 4-11) is an international, phase III, randomised, double-blind, placebo-controlled, two-arm study evaluating the efficacy and safety of Perjeta plus Herceptin and chemotherapy, compared to Herceptin and chemotherapy, as adjuvant therapy in 4,805 people with operable HER2-positive eBC. The primary efficacy endpoint of the APHINITY study is iDFS, which in this study is defined as the time a patient lives without return of invasive breast cancer at any site, or death from any cause after adjuvant treatment. Secondary endpoints include cardiac and overall safety, OS, disease-free survival and health-related quality of life. The study will continue to follow participants for ten years. [2,8]

### **About Perjeta**

Perjeta is a medicine that targets the HER2 receptor, a protein found on the outside of many normal cells and in high quantities on the outside of cancer cells in HER2-positive cancers. Perjeta is designed specifically to prevent the HER2 receptor from pairing (or 'dimerising') with other HER receptors (EGFR/HER1, HER3 and HER4) on the surface of cells, a process that is believed to play a role in tumour growth and survival. [9] Binding of Perjeta to HER2 may also signal the body's immune system to destroy the cancer cells. The mechanisms of action of Perjeta and Herceptin are believed to complement each other, as both bind to the HER2 receptor, but to different locations. The combination of Perjeta and Herceptin is thought to provide a more comprehensive, dual blockade of HER signalling pathways, thus preventing tumour cell growth and survival. [10]

### **About Roche's medicines for HER2-positive breast cancer**

Roche has been leading research into the HER2 pathway for over 30 years and is committed to improving the health, quality of life and survival of people with both early and metastatic HER2-positive disease. HER2-positive breast cancer is a particularly aggressive form of the disease that affects approximately 15-20% of patients. [11] Roche has developed three innovative medicines that have helped transform the treatment of HER2-positive breast cancer: Herceptin® (trastuzumab), Perjeta® (pertuzumab) and Kadcyca® (trastuzumab emtansine). Eligibility for treatment with Roche's HER2-targeted medicines is determined via a diagnostic test which identifies people who will likely benefit from these medicines at the onset of their disease.

### **About Roche**

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the eleventh consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices.

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2018 employed about 94,000 people worldwide. In 2018, Roche invested CHF 11 billion in R&D and posted sales of CHF 56.8 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit [www.roche.com](http://www.roche.com).

### **About Breast International Group**

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. BIG's international network of collaborative academic research groups dedicated to breast cancer research has proven to be crucial in the high-speed recruitment of 4,800 patients from 42 countries and in achieving robust study results from a large multinational trial like APHINITY.

Founded by leading European opinion leaders in 1999, BIG now constitutes a network of 57 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](http://www.BIGagainstbreastcancer.org)

#### **About Frontier Science Foundation**

Frontier Science Foundation (FS) is a not-for-profit corporation that has gained an international reputation as a highly capable data management and statistical organisation, collaborating with research networks, pharmaceutical companies and others in the design, conduct and execution of clinical trials and long-term observation studies.

Founded in 1975, Frontier Science provides innovative data management and analysis for clinical trials in a variety of disease settings throughout the world. Some of the significant advancements in the treatment of AIDS and cancer have resulted from studies in which Frontier Science played a major role.

Frontier Science has biostatistics, IT, data management and support staff in five locations in the United States, Greece and Scotland.

For more information, visit [www.frontierscience.org](http://www.frontierscience.org)

#### **About Institut Jules Bordet Clinical Trials Support Unit**

As an academic non-profit organisation, the Clinical Trials Support Unit (CTSU) of the comprehensive cancer centre Institut Jules Bordet (IJB) is fighting cancer through the design, set-up and conduct of innovative clinical trials that matter to patients. IJB-CTSU's multidisciplinary team strongly believes that its work contributes to improve the understanding of the disease and to optimise diagnosis, care and cancer treatments.

The IJB-CTSU manages the operational activities both for investigator-initiated trials and for clinical trials sponsored by pharmaceutical companies, biotech companies or other academic institutions.

The IJB-CTSU expertise covers project management, regulatory affairs, contract management, pharmacovigilance, data management, sites monitoring, central imaging review and biosamples management. Moreover, the IJB-CTSU benefits from a close collaboration with the IJB medical team and IJB statistical team.

In 2013, the BrEAST (Breast Adjuvant Study Team) joined the IJB-CTSU as its data

management unit. This unit is responsible for the data management activities implemented for all clinical studies managed by the IJB-CTSU.

For more information, please visit <https://ctsu.bordet.be>

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## References

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