

Roche's ipatasertib in combination with Tecentriq and chemotherapy shows promising anti-tumour activity in triple-negative breast cancer in early phase trial

- Data from Phase Ib study to be presented at American Association for Cancer Research (AACR) 2019 annual congress
- 73% overall response rate (ORR) irrespective of PD-L1 status or PI3KCA/AKT1/PTEN alteration status

Basel, 01 April 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) will today present the initial results from a Phase Ib study evaluating the efficacy and safety for the combination of ipatasertib, Tecentriq® (atezolizumab) and chemotherapy (paclitaxel or *nab*-paclitaxel (Abraxane® [paclitaxel albumin-bound particles for injectable suspension]) as a first-line treatment option for people with advanced triple-negative breast cancer (TNBC). Combination treatment demonstrated a confirmed objective response rate (ORR) of 73% (95% CI 53-88%), irrespective of tumour biomarker status. The median duration of follow-up was 6.1 months (range 3.1–10.6). Grade ≥ 3 adverse events occurred in 14 people (54%); the most common all-grade adverse events were diarrhea (88%; grade ≥ 3 19%) and rash (69%; grade ≥ 3 27%).

“We are enthusiastic about the potential of this combination in triple-negative breast cancer, an aggressive type of breast cancer,” said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. “These early results support the contribution of ipatasertib to our combination treatment approach in TNBC and reinforce our vision to develop medicines that may benefit patients with this challenging disease.”

Preliminary efficacy data for the first 26 patients (18 paclitaxel, 8 *nab*-paclitaxel) show confirmed responses in 19/26 patients, giving a confirmed ORR of 73%. Responses were seen irrespective of PD-L1 status (9/11 [82%] PD-L1+; 6/8 [75%] PD-L1-; 4/7 [57%] PD-L1 unknown) or *PIK3CA/AKT1/PTEN* alteration status (5/7 [71%] Dx+, 9/11 [82%] Dx-, 5/8 [63%] Dx unknown).

Activation of the PI3K/AKT pathway has been implicated in resistance to chemotherapies and hormonal therapies in multiple tumour types and loss of PTEN, a negative regulator of AKT, has emerged as a potential mechanism for resistance to checkpoint inhibitor therapy. By inhibiting the PI3K/AKT pathway, ipatasertib may contribute to reversal of T-cell-mediated immunotherapy resistance. These results and the potential benefit that ipatasertib plus the Tecentriq/taxane combination may bring to patients are encouraging and add to the Roche development program in triple-negative breast cancer following the approval of the Tecentriq combination.

Trial enrolment for the Phase Ib study is ongoing. Later this year, Roche will initiate a pivotal multi-center, randomised, double-blind Phase III study investigating the combination of ipatasertib, atezolizumab and paclitaxel as first-line therapy for locally advanced/metastatic triple-negative breast cancer.

About the study

The Phase Ib study is an open-label, multicentre study evaluating the safety and efficacy of ipatasertib in combination with atezolizumab and paclitaxel or *nab*-paclitaxel for patients with locally advanced or metastatic triple-negative breast cancer who have not previously received chemotherapy in the advanced setting. Two triplets: ipatasertib in combination with atezolizumab and paclitaxel (Paclitaxel arm) and ipatasertib in combination with atezolizumab and *nab*-paclitaxel (*nab*-Paclitaxel arm) are being evaluated for first-line treatment for advanced TNBC. A second cohort, which is enrolling now, will allow collection of tumour biopsies to assess treatment-related biomarker changes in TNBC patients who have progressed after at least one line of chemotherapy in the advanced setting.

About ipatasertib

Ipatasertib is an oral, highly specific, investigational medicine designed to target and bind to all three isoforms of AKT, which blocks the PI3K/AKT signaling pathway and may prevent cancer cell growth and survival.

Ipatasertib is being studied in tumours that are frequently found to have activation of the PI3K/AKT pathway, including breast and prostate cancers. Pivotal studies are ongoing to evaluate the efficacy and safety of ipatasertib and the opportunity it may provide to address significant unmet needs for patients with these diseases. Ipatasertib has demonstrated clinically meaningful activity in both breast and prostate cancers, with a manageable safety profile.

Ipatasertib was discovered at Genentech in partnership with Array BioPharma Inc.

About Triple-Negative breast cancer

Breast cancer is the most common cancer among women with more than 2 million diagnosed worldwide each year.^[1] TNBC represents 15% of all breast cancers and is more common in women under the age of 50, compared with other forms of breast cancer.^[2;3;4] It is defined by the lack of expression and/or amplification of the targetable receptors for oestrogen, progesterone and HER2 amplification.^[5] Patients with metastatic TNBC generally experience rapid progression and shorter overall survival (OS) compared to other subtypes of breast cancer.^[3]

About Roche in breast cancer

Roche has been advancing breast cancer research for more than 30 years with the goal of helping as many people with the disease as possible. Our medicines, along with companion diagnostic tests, have contributed to bringing breakthrough innovations in the HER2 -positive breast cancer. As our understanding of breast cancer biology rapidly improves, we are working to identify new biomarkers and approaches to treatment for all forms of early and advanced breast cancer, including triple-negative and hormone receptor-positive.

Our targeted medicines Herceptin, Perjeta and Kadcyla are continuing to transform the treatment of early and advanced HER2-positive breast cancer and, through our Tecentriq and ipatasertib clinical programmes, we hope to bring new treatment combinations to people with breast cancer, ultimately improving outcomes.

In the United States Tecentriq in combination with nab-paclitaxel is approved for treatment of PD-L1-positive metastatic triple-negative breast cancer. Roche currently has seven phase III studies in TNBC.

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. 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 tenth consecutive year, Roche has been recognised as the most sustainable company in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

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.

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Roche Group Media Relations

Phone: +41 61 688 8888 / e-mail: media.relations@roche.com

- Nicolas Dunant (Head)
- Patrick Barth
- Ulrike Engels-Lange
- Simone Oeschger
- Anja von Treskow