

Roche receives positive CHMP opinion for Tecentriq in combination with Avastin for the treatment of people with the most common form of liver cancer

- **Recommendation is based on the results of the IMbrave150 study, in which the Tecentriq combination improved overall survival and progression-free survival compared with the previous standard of care**

Basel, 18 September 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has recommended the approval of Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab) for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy. Based on this recommendation, a final decision regarding approval of Tecentriq in combination with Avastin in this disease setting, along with the full details of the approved indication, is expected from the European Commission in the near future.

“Today’s recommendation by the CHMP is a major step towards bringing Tecentriq in combination with Avastin to people in Europe who suffer from advanced or unresectable hepatocellular carcinoma,” said Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development. “This represents an important milestone in a deadly malignancy and is part of our long-term commitment to improve the lives of people with various types and stages of liver disease.”

“After more than a decade of therapeutic stagnation, the results of the IMbrave150 study are likely to change the way we treat patients with liver cancer who are diagnosed at or reach the advanced stage,” said Professor Bruno Sangro, Director of the Liver Unit and Coordinator of the HPB Oncology Area at Clinica Universidad de Navarra in Pamplona, Spain. “The data from the study showed that the combination of Tecentriq and Avastin results in longer survival with better quality of life than any current choice of tyrosine kinase inhibitor and, for a large subset of patients, is able to induce deep, durable and sometimes complete tumour remissions.”

The recommendation from the CHMP is based on results from the Phase III IMbrave150 study, which showed that Tecentriq in combination with Avastin reduced the risk of death (overall survival [OS]) by 42% (hazard ratio [HR]=0.58; 95% CI: 0.42–0.79; p=0.0006) and reduced the risk of disease worsening or death (progression-free survival [PFS]) by 41% (HR=0.59; 95% CI: 0.47–0.76; p<0.0001), compared with sorafenib. IMbrave150 is the first Phase III cancer immunotherapy study to show an improvement in both OS and PFS in people with unresectable HCC compared with sorafenib. Grade 3–4 adverse events occurred in 57% of people receiving Tecentriq and Avastin and 55% of people receiving sorafenib. The most frequent serious adverse reactions (≥2%) were bleeding in the gastrointestinal tract and fever. These results were published in the New England Journal of Medicine on 14 May 2020.

In May 2020, the US Food and Drug Administration approved Tecentriq in combination with Avastin for the treatment of people with unresectable or metastatic HCC who have not received prior systemic therapy and

in September 2020 the China National Medical Products Administration approved the combination for the treatment of people with unresectable HCC who have not received prior systemic therapy. Tecentriq in combination with Avastin was also recently included as a class I, A recommendation by the European Society for Medical Oncology (ESMO) for the treatment of unresectable HCC, as well as by many clinical practice guidelines globally.

Roche is committed to tackling liver disease right across the disease journey, from the earliest stages through to advanced disease, with the ultimate goal of one day stopping chronic liver disease.

Roche has an extensive development programme for Tecentriq, including multiple ongoing and planned Phase III studies, across several types of lung, genitourinary, skin, breast, gastrointestinal, gynaecological, and head and neck cancers. This includes studies evaluating Tecentriq both alone and in combination with other medicines.

About the IMbrave150 study

IMbrave150 is a global Phase III, multicentre, open-label study of 501 people with unresectable HCC who had not received prior systemic therapy. People were randomised 2:1 to receive the combination of Tecentriq and Avastin or sorafenib. Tecentriq was administered intravenously (IV), 1200mg on day 1 of each 21-day cycle, and Avastin was administered IV, 15mg/kg on day 1 of each 21-day cycle. Sorafenib was administered by mouth, 400mg twice per day, on days 1-21 of each 21-day cycle. People received the combination or the control arm treatment until disease progression or unacceptable toxicity. The two primary endpoints were OS and independent review facility (IRF)-assessed PFS per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1). Additional study endpoints included IRF-assessed overall response rate (ORR) per RECIST v1.1 and HCC mRECIST.

About hepatocellular carcinoma

HCC is an aggressive cancer with limited treatment options and is a major cause of cancer deaths worldwide.¹ Every year, more than 750,000 people worldwide are diagnosed with HCC,^{1,2} with the majority of cases in Asia and almost half of all cases in China.^{2,3} In the US, the number of liver cancer cases have more than tripled since 1980 and HCC represents the fastest-rising cause of cancer-related death, while in Europe, liver cancer is also on the rise, accounting for more than 80,000 diagnoses and approximately 77,000 deaths each year.⁴⁻⁷ HCC develops predominantly in people with cirrhosis due to chronic hepatitis (B or C) or alcohol consumption, and typically presents at an advanced stage.¹ The prognosis for unresectable HCC remains poor, with few systemic therapeutic options and a 1-year survival rate of less than 50% following diagnosis.⁸

About the Tecentriq and Avastin combination

There is a strong scientific rationale to support the use of Tecentriq plus Avastin in combination. The Tecentriq and Avastin regimen may enhance the potential of the immune system to combat a broad range of cancers. Avastin, in addition to its established anti-angiogenic effects, may further enhance Tecentriq's ability

to restore anti-cancer immunity, by inhibiting vascular endothelial growth factor (VEGF)-related immunosuppression, promoting T-cell tumour infiltration and enabling priming and activation of T-cell responses against tumour antigens.

About Tecentriq

Tecentriq is a monoclonal antibody designed to bind with a protein called PD-L1, which is expressed on tumour cells and tumour-infiltrating immune cells, blocking its interactions with both PD-1 and B7.1 receptors. By inhibiting PD-L1, Tecentriq may enable the activation of T-cells. Tecentriq is a cancer immunotherapy that has the potential to be used as a foundational combination partner with other immunotherapies, targeted medicines and various chemotherapies across a broad range of cancers. The development of Tecentriq and its clinical programme is based on our greater understanding of how the immune system interacts with tumours and how harnessing a person's immune system combats cancer more effectively.

Tecentriq is approved in the US, EU and countries around the world, either alone or in combination with targeted therapies and/or chemotherapies in various forms of non-small cell lung cancer, small cell lung cancer, certain types of metastatic urothelial cancer and in PD-L1-positive metastatic triple-negative breast cancer. In the US, and several other countries Tecentriq in combination with Avastin® (bevacizumab) is approved for people with unresectable or metastatic hepatocellular carcinoma. In the US, Tecentriq is also approved in combination with Cotellic® (cobimetinib) and Zelboraf® (vemurafenib) for the treatment of people with BRAF V600 mutation-positive advanced melanoma.

About Avastin

Avastin is a prescription-only medicine that is a solution for intravenous infusion. It is a biologic antibody designed to specifically bind to a protein called VEGF that plays an important role throughout the lifecycle of the tumour to develop and maintain blood vessels, a process known as angiogenesis. Avastin is designed to interfere with the tumour blood supply by directly binding to the VEGF protein to prevent interactions with receptors on blood vessel cells. The tumour blood supply is thought to be critical to a tumour's ability to grow and spread in the body (metastasise).

About Roche in cancer immunotherapy

Roche's rigorous pursuit of groundbreaking science has contributed to major therapeutic and diagnostic advances in oncology over the last 50 years, and today, realising the full potential of cancer immunotherapy is a major area of focus. With over 20 molecules in development, Roche is investigating the potential benefits of immunotherapy alone, and in combination with chemotherapy, targeted therapies or other immunotherapies with the goal of providing each person with a treatment tailored to harness their own unique immune system to attack their cancer. Our scientific expertise, coupled with innovative pipeline and extensive partnerships, gives us the confidence to continue pursuing the vision of finding a cure for cancer by ensuring the right treatment for the right patient at the right time.

In addition to Roche's approved PD-L1 checkpoint inhibitor, Tecentriq® (atezolizumab), Roche's broad cancer immunotherapy pipeline includes other checkpoint inhibitors, such as tiragolumab, a novel cancer immunotherapy designed to bind to TIGIT, individualised neoantigen therapies and T-cell bispecific antibodies. To learn more about Roche's scientific-led approach to cancer immunotherapy, please follow this link:

http://www.roche.com/research_and_development/what_we_are_working_on/oncology/cancer-immunotherapy.htm

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 (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 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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