

Roche to present updated data confirming Tecentriq in combination with Avastin substantially improves overall survival in people with the most common form of liver cancer

- **Tecentriq in combination with Avastin provides the longest overall survival seen in a front-line Phase III study in unresectable hepatocellular carcinoma (HCC)**
- **Liver cancer is the 6th most common cancer and in 2020 was the third leading cause of cancer deaths worldwide**
- **Results to be presented at the 2021 Gastrointestinal Cancers Symposium organised by the American Society of Clinical Oncology (ASCO), January 2021**

Basel, 12 January 2021 - Roche (SIX: RO, ROG; OTCQX: RHHBY) will present updated overall survival (OS) data from the Phase III IMbrave150 study evaluating Tecentriq® (atezolizumab) in combination with Avastin® (bevacizumab), compared with sorafenib, in people with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

After a median follow-up of 15.6 months, an updated analysis showed that Tecentriq in combination with Avastin reduced the risk of death (OS) by 34%, with a median OS of 19.2 months, compared with 13.4 months for sorafenib (hazard ratio [HR]=0.66; 95% CI: 0.52–0.85). The updated OS, along with progression free survival (PFS) and objective response rate (ORR) results, were consistent with the primary analysis and support the use of the combination in HCC. Safety data for Tecentriq and Avastin were consistent with the known safety profiles of each individual drug, with no new safety signals identified.

“These results show that Tecentriq in combination with Avastin provides the longest survival that we’ve ever seen in a front-line Phase III study in unresectable HCC,” said Levi Garraway, M.D., Ph.D., Roche’s Chief Medical Officer and Head of Global Product Development. “The combination, which has now been approved in more than 60 countries around the world, represents a significant treatment advancement for patients with this challenging malignancy.”

“After an additional year of follow-up, these data confirm the superiority of Tecentriq in combination with Avastin compared to sorafenib in patients with advanced HCC,” said Dr Laura Kulik, Professor of Medicine, Interventional Radiology and Transplant, Feinberg School of Medicine, Northwestern University and member of the ASCO GI programme committee. “These results provide further confidence for physicians and patients in the use of this combination as first-line therapy.”

These data will be presented in the Rapid Abstract Session: Hepatobiliary Cancer, Neuroendocrine/Carcinoid, Pancreatic Cancer, and Small Bowel Cancer at the Gastrointestinal Cancers Symposium on Sunday 17 January at 15:30-16:15 ET.

Tecentriq in combination with Avastin is now approved around the world, including in the US, China, Japan and the EU, for people with unresectable HCC and is recommended in 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.

Updated OS, PFS, response and duration of response data		
Global results		
	Tecentriq + Avastin (n=336)	Sorafenib (n=165)
Median OS (95% CI), mo	19.2 (17.0–23.7)	13.4 (11.4–16.9)
OS, HR (95% CI), mo	0.66 (0.52–0.85)	
	Tecentriq + Avastin (n=336)	Sorafenib (n=165)
Median PFS (95% CI), mo	6.9 (5.7–8.6)	4.3 (4.0–5.6)
PFS, HR (95% CI), mo	0.65 (0.53–0.81)	
	Tecentriq + Avastin (n=326)	Sorafenib (n=159)
Confirmed ORR (95% CI) (%)	30% (25–35)	11% (7–17)
CR, n (%)	25 (8%)	1 (< 1%)

PR, n (%)	72 (22%)	17 (11%)
SD, n (%)	144 (44%)	69 (43%)
Ongoing response, n (%)	54 (56%)	5 (28%)
	Tecentriq + Avastin (n=97)	Sorafenib (n=18)
Median DOR (95% CI), mo	18.1 (14.6, NE)	14.9 (4.9–17.0)
Overall survival results in the Chinese subpopulation		
	Tecentriq + Avastin (n=133)	Sorafenib (n=61)
Median OS (95%CI), mo – Chinese subpopulation	24.0 (17.1, NE)	11.4 (6.7–16.1)
OS, HR (95% CI), mo	0.53 (0.35–0.80)	

PFS and all response data are reported by RECIST v1.1 assessed by an independent review facility.

Median follow-up: 15.6 months.

CR, complete response; DOR, duration of response; HR, hazard ratio; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression free response; PR, partial response; SD, stable disease.

See below for OS data from the primary analysis.

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), 1200 mg on day 1 of each 21-day cycle, and Avastin was administered IV, 15 mg/kg on day 1 of each 21-day cycle. Sorafenib was administered by mouth, 400 mg 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.

The primary analysis from the IMbrave150 study showed that after 8.6 months follow-up, Tecentriq in combination with Avastin reduced the risk of death (OS) by 42% (HR=0.58; 95% CI: 0.42–0.79; p=0.0006).

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 815,000 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 87,000 diagnoses and approximately 78,000 deaths in 2020.⁴⁻⁷ 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, in PD-L1-positive metastatic triple-negative breast cancer and for 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

For more than 50 years, Roche has been developing medicines with the goal to redefine treatment in oncology. Today, we're investing more than ever in our effort to bring innovative treatment options that help a person's own immune system fight cancer.

By applying our seminal research in immune tumour profiling within the framework of the Roche-devised cancer immunity cycle, we are accelerating and expanding the transformative benefits with Tecentriq to a greater number of people living with cancer. Our cancer immunotherapy development programme takes a comprehensive approach in pursuing the goal of restoring cancer immunity to improve outcomes for patients.

To learn more about the Roche 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 twelfth 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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