

CHMP recommends EU approval of Roche's Tecentriq in combination with Avastin and chemotherapy as an initial treatment for lung cancer

- **Recommendation based on the Phase III IMpower150 study which showed that Tecentriq (atezolizumab) in combination with Avastin (bevacizumab) and chemotherapy (paclitaxel and carboplatin) helped people with an advanced form of lung cancer live significantly longer compared with Avastin and chemotherapy**

Basel, 01 February 2019 – 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), paclitaxel and carboplatin, for the first-line treatment of adults with metastatic non-squamous non-small cell lung cancer (NSCLC). In people with EGFR mutant or ALK-positive NSCLC, Tecentriq, in combination with Avastin, paclitaxel and carboplatin, is indicated only after failure of appropriate targeted therapies. Based on the positive CHMP recommendation, a final decision regarding the approval of this Tecentriq-based combination is expected from the European Commission in the near future.

The CHMP recommendation is based on results from the Phase III IMpower150 study, which showed that Tecentriq in combination with Avastin, paclitaxel and carboplatin helped people live significantly longer, compared with Avastin and chemotherapy (median overall survival [OS]=19.8 versus 14.9 months; hazard ratio [HR]=0.76; 95% CI: 0.63–0.93; p=0.006) in the intention-to-treat (ITT) population.^[1] The safety profile of the Tecentriq combination was consistent with that observed in previous studies.

“We are pleased to receive a positive opinion from the CHMP for this Tecentriq-based combination, which represents a significant step towards bringing a new treatment option to people across Europe with advanced, non-squamous non-small cell lung cancer,” said Sandra Horning, MD, Roche's Chief Medical Officer and Head of Global Product Development. “The IMpower150 study, on which this opinion is based, demonstrated an overall survival benefit, including those in key populations such as people with EGFR- or ALK-positive mutations or liver metastases.”

About the IMpower150 study

IMpower150 is a multicentre, open-label, randomised, controlled Phase III study evaluating the efficacy and safety of Tecentriq in combination with chemotherapy (carboplatin and paclitaxel) with or without Avastin in people with stage IV or recurrent metastatic non-squamous NSCLC who had not been treated with chemotherapy for their advanced disease. A total of 1,202 people were enrolled and randomised (1:1:1) to receive:

- Tecentriq plus carboplatin and paclitaxel (Arm A), or
- Tecentriq and Avastin plus carboplatin and paclitaxel (Arm B), or
- Avastin plus carboplatin and paclitaxel (Arm C, control arm).

The co-primary endpoints comparing Arms B and C were OS and progression-free survival (PFS), as determined by the investigator using Response Evaluation Criteria in Solid Tumours Version 1.1 (RECIST v1.1) and assessed in the ITT-WT subpopulation. Key secondary endpoints included investigator-assessed PFS, OS and safety in the ITT population.

A summary of the ITT data from the IMpower150 study that support this recommendation is included below:^[1]

- Tecentriq in combination with Avastin and chemotherapy helped people live significantly longer, compared with Avastin and chemotherapy (median OS=19.8 versus 14.9 months; HR=0.76; 95% CI: 0.63–0.93; p=0.006).
- In addition, Tecentriq in combination with Avastin and chemotherapy reduced the risk of disease worsening or death (PFS) by 41% compared with Avastin and chemotherapy (HR=0.59; 95% CI: 0.50–0.69, p<0.0001).
- Tecentriq in combination with Avastin and chemotherapy shrank tumours (overall response rate [ORR]) in 56.4% of people (95% CI: 51.4–61.4) compared with 40.2% of people (95% CI: 35.3–45.2) on Avastin and chemotherapy.
 - 2.8% of people receiving Tecentriq in combination with Avastin and chemotherapy experienced a complete response (CR), and 53.7% of people experienced a partial response (PR).
- The median duration of response (DoR) for people receiving Tecentriq in combination with Avastin and chemotherapy was 11.5 months (95% CI: 8.9–15.7) compared with 6.0 months (95% CI: 5.5–6.9) for people on Avastin and chemotherapy.
- The most common adverse reactions (≥20%) in people receiving Tecentriq in combination with Avastin and chemotherapy were fatigue and lack of energy (asthenia; 50%), hair loss (alopecia; 48%), nausea (39%), diarrhoea (32%), constipation (30%), decreased appetite (29%), joint pain (arthralgia; 26%), hypertension (25%), and pain from nerve damage (peripheral neuropathy; 24%).

About NSCLC

Lung cancer is the leading cause of cancer death globally.^[2] Each year 1.76 million people die as a result of the disease; this translates into more than 4,800 deaths worldwide every day.^[2] Lung cancer can be broadly divided into two major types: NSCLC and small cell lung cancer. NSCLC is the most prevalent type, accounting for around 85% of all cases.^[3] NSCLC comprises non-squamous and squamous-cell lung cancer, the squamous form of which is characterised by flat cells covering the airway surface when viewed under a microscope.^[3]

About the Tecentriq (atezolizumab) and Avastin (bevacizumab) 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 first-line advanced NSCLC. Avastin, in addition to its established anti-angiogenic effects, may further enhance Tecentriq's ability to restore anti-cancer immunity, by inhibiting VEGF-related immunosuppression, promoting T cell tumour infiltration and enabling priming and activation of T cell responses against tumour antigens.

About Tecentriq (atezolizumab)

Tecentriq is a monoclonal antibody designed to bind with a protein called PD-L1 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 has the potential to be used as a foundational combination partner with cancer immunotherapies, targeted medicines and various chemotherapies across a broad range of cancers.

Currently, Roche has nine Phase III lung cancer studies underway, evaluating Tecentriq alone or in combination with other medicines.

Tecentriq is already approved in the European Union, United States and more than 85 countries for people with previously treated metastatic NSCLC and for certain types of untreated or previously treated metastatic urothelial carcinoma (mUC). Tecentriq in combination with Avastin and chemotherapy was also recently approved in the United States for the initial treatment of people with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumour aberrations.

About Avastin (bevacizumab)

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 vascular endothelial growth factor (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 (metastasis).

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. 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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References

- [1] Tecentriq SmPC.
- [2] GLOBOCAN 2018; Lung Cancer: Estimated cancer incidence, mortality and prevalence worldwide. World Health Organization. Available from: <http://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf>. Accessed January 2019.
- [3] American Cancer Society; What Is Non-Small Cell Lung Cancer? [Internet]: Available from: <https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html>. Accessed January 2019.

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