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Phase III IMpower150 study showed Roche's Tecentriq and Avastin plus carboplatin and paclitaxel helped people with a specific type of metastatic lung cancer live significantly longer compared to Avastin plus carboplatin and paclitaxel

- A survival advantage for the Tecentriq and Avastin combination regimen was observed in all pre-specified exploratory patient subgroups analysed, including people with EGFR and ALK mutations, liver metastases and those with varying levels of PD-L1 expression
- Data will be presented at American Society of Clinical Oncology (ASCO) Annual Meeting on June 4, 2018

Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced positive results from the Phase III IMpower150 study of Tecentriq® (atezolizumab) and Avastin® (bevacizumab) plus carboplatin and paclitaxel (chemotherapy) for the initial (first-line) treatment of chemotherapy-naïve people with metastatic non-squamous non-small cell lung cancer (NSCLC). This interim analysis showed that Tecentriq and Avastin plus carboplatin and paclitaxel helped people live significantly longer compared with Avastin plus carboplatin and paclitaxel (median overall survival [OS] = 19.2 versus 14.7 months; hazard ratio [HR] = 0.78, 95% CI: 0.64-0.96; p=0.016) in the intention-to-treat wild-type (ITT-WT) population, a co-primary endpoint of the study.¹ An OS advantage was observed in all pre-specified exploratory biomarker-selected subgroups analysed, which included people with EGFR- and ALK-positive mutations who had received an appropriate targeted therapy, and those with varying levels of PD-L1 expression or with negative PD-L1 expression. People with liver metastases treated with the Tecentriq combination also had a survival advantage. The safety profile of the Tecentriq and Avastin plus carboplatin and paclitaxel combination was consistent with the safety profiles of the individual medicines, and no new safety signals were identified with the combination.

“The IMpower150 study results showed a significant survival benefit, adding to the clinical evidence supporting the combination of Tecentriq and Avastin as an initial treatment for metastatic non-squamous non-small cell lung cancer. An overall survival benefit was also observed in key populations such as people with EGFR- and ALK-positive mutations and those with liver metastases,” said Sandra Horning, MD, Roche’s Chief Medical Officer and Head of Global Product Development. “We are working with health authorities around the world to bring this potential Tecentriq combination regimen to people living with this disease.”

At this interim analysis, the combination of Tecentriq plus carboplatin and paclitaxel (Arm A) did not show a statistically significant OS benefit when compared to the combination of Avastin plus carboplatin and paclitaxel (Arm C). Arm A will continue as planned to the final analysis. Safety in the Tecentriq plus carboplatin and paclitaxel arm appeared consistent with the known safety profile of the individual medicines, and no new safety signals were identified with the combination.

The official data presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting will be on Monday, June 4, 2018, at 15:45 – 15:57 p.m. CDT (Abstract #9002).

The combination of Tecentriq and Avastin plus carboplatin and paclitaxel was recently granted Priority Review from the U.S. Food and Drug Administration (FDA) for the initial (first-line) treatment of chemotherapy-naïve people with metastatic non-squamous NSCLC. The FDA is expected to make a decision on approval by September 5th, 2018.

IMpower150 is one of eight Phase III lung cancer studies underway, evaluating Tecentriq alone or in combination with other medicines. Following the IMpower150 and IMpower131 studies, three more Phase III lung cancer studies are expected to report this year.

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. It enrolled 1,202 people of which those with ALK and EGFR mutations were excluded from the primary ITT analysis. People were 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).

During the treatment-induction phase, people in Arm A received Tecentriq administered intravenously at 1200 mg in combination with intravenous infusion of carboplatin and paclitaxel on Day 1 of a 3-week treatment cycle for 4 or 6 cycles. Following the induction phase, people received maintenance treatment with Tecentriq (1200 mg every 3 weeks) until loss of clinical benefit or disease progression. IMpower150 was designed to formally compare Tecentriq plus chemotherapy (Arm A) versus Avastin plus chemotherapy (Arm C), only if Tecentriq and Avastin plus chemotherapy (Arm B) is shown to improve OS in the ITT-WT population compared to Avastin plus chemotherapy (Arm C).

People in Arm B received induction treatment with Tecentriq (1200 mg) and Avastin administered intravenously at 15 mg/kg in combination with intravenous infusion of carboplatin and paclitaxel on Day 1 of a 3-week treatment cycle for 4 or 6 cycles. People then received maintenance treatment with the Tecentriq Avastin regimen until disease progression (Avastin) or loss of clinical benefit/disease progression (Tecentriq).

People in Arm C received induction treatment with Avastin administered intravenously at 15 mg/kg plus intravenous infusion of carboplatin and paclitaxel on Day 1 of a 3-week treatment cycle for 4 or 6 cycles. This was followed by maintenance treatment with Avastin alone until disease progression.

The co-primary endpoints were PFS and OS, as determined by the investigator using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1). The co-primary OS endpoint in IMpower150 was assessed in all randomised people without an EGFR or ALK genetic mutation (intention-to-treat wild-type). Key secondary endpoints included investigator-assessed PFS, OS and safety in the ITT population and in EGFR and ALK mutation subgroups. The study met its co-primary endpoints of OS and PFS per study protocol.

A summary of OS results is included below.

Table. Arm B (Tecentriq and Avastin plus chemotherapy) vs Arm C (Avastin plus chemotherapy) OS in Populations of Interest				
Population	No. of Pts	HR (95% CI)	mOS, mo	
			Arm B	Arm C
ITT-WT ^a	696	0.78 (0.64, 0.96)	19.2	14.7
ITT	800	0.76 (0.63, 0.93)	19.8	14.9
EGFR/ALK+	104	0.54 (0.29, 1.03)	NR	17.5
Liver metastases ^b	94	0.54 (0.33, 0.88)	13.2	9.1
Subgroups in ITT-WT				
TC1/2/3 or ICI1/2/3	357	0.77 (0.58, 1.04)	22.5	16.4
TC0 and IC0	339	0.82 (0.62, 1.08)	17.1	14.1
Teff-high	285	0.83 (0.59, 1.17)	25.0	16.7
Teff-low	377	0.78 (0.60, 1.02)	17.6	14.3
IC, tumour-infiltrating immune cells; NE, not estimable; TC, tumour cells. ^a WT excludes patients with EGFR or ALK genomic alterations. ^b Present at baseline . TC1/2/3 or ICI1/2/3 = PD-L1+ ≥ 1% of TC or IC; TC0 and IC0 = PD-L1+ < 1% of TC and IC.				

The safety profile of the Tecentriq and Avastin plus carboplatin and paclitaxel combination was consistent with the safety profiles of the individual medicines, and no new safety signals were identified with the combination. Serious adverse events (Grade 3-4) related to treatment were observed in 57% of people who received Tecentriq and Avastin plus carboplatin and paclitaxel compared to 49% of those who received Avastin plus carboplatin and paclitaxel.

About NSCLC

Lung cancer is the leading cause of cancer death globally.² Each year 1.59 million people die as a result of the disease; this translates into more than 4,350 deaths worldwide every day.³ 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. The squamous form tends to grow near the centre of the lung, and accounts for approximately 25-30% of all NSCLC cases.⁴

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 eight 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 70 countries for people with previously treated metastatic NSCLC and for people with locally advanced or metastatic urothelial cancer (mUC) who are not eligible for cisplatin chemotherapy, or who have had disease progression during or following platinum-containing therapy.

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 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 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. Roche has been recognised as the Group Leader in sustainability within the Pharmaceuticals, Biotechnology & Life Sciences Industry nine years in a row by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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-global.com

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

*EGFR: Epidermal Growth Factor Receptor

†ALK: Anaplastic Lymphoma Kinase

References

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