Avastin® in non small cell lung cancer: Summary of clinical data

It is estimated that over 1.5 million people worldwide are newly diagnosed with lung cancer every year with almost 1.3 million deaths due to the disease[1]. The majority of patients with lung cancer are diagnosed when the disease is at an advanced stage[2] and has spread to other parts of the body (metastasised). Unfortunately, less than 5% of patients with advanced non-small cell lung cancer (NSCLC) survive for five years after diagnosis[3] and most die within one year.

Roche has an extensive research and clinical trial programme to improve treatment options for patients with lung cancer, specifically focusing on NSCLC, the most common form of the disease[2]. Avastin (bevacizumab) is an important therapy for lung cancer and has been shown to deliver an outstanding survival time in NSCLC, without the side effects usually associated with chemotherapy such as hair loss, nausea and vomiting.

Avastin is an antibody that specifically binds and blocks VEGF (vascular endothelial growth factor). VEGF is the key driver of tumour angiogenesis – an essential process of development and maintenance of blood vessels which is required for a tumour to grow and to spread to other parts of the body. Avastin's precise mode of action helps control tumour growth and metastases and does not add to the side effects usually associated with chemotherapy.

More than 500,000 patients have been treated with Avastin so far. A comprehensive clinical programme with more than 450 clinical trials is investigating the use of Avastin in various tumour types (including colorectal, breast, lung, brain, gastric, ovarian, prostate and others) and different settings (advanced or early stage disease). Outlined below is key information from clinical trials of Avastin in NSCLC.

E4599

Key findings

- Avastin + chemotherapy significantly improved OS compared to chemotherapy alone, increasing OS by 25%.
- Avastin was effective and well tolerated in combination with platinum-based chemotherapy.

The E4599 trial evaluated the efficacy of Avastin in combination with chemotherapy in more than 800 patients with locally advanced, metastatic or recurrent non squamous NSCLC. Results from the E4599 study showed that treatment with Avastin in combination with chemotherapy significantly improved overall survival (OS) of NSCLC patients compared with chemotherapy alone[4]. Patients treated with Avastin in combination with chemotherapy had a median OS of 12.3 months compared to 10.3 months in patients treated with chemotherapy alone. These results were important because it was the first time therapy had extended survival beyond the one year barrier. In addition, patients with adenocarcinoma of lung, the most common form of NSCLC[5], experienced an even greater benefit

from Avastin in combination with chemotherapy, with a median OS of 14.2 months compared to 10.3 months with chemotherapy alone[6].

AVAiL

More than 1,000 patients with advanced non squamous NSCLC were enrolled in AVAiL. The study demonstrated that Avastin in combination with chemotherapy extended the length of time that patients lived without their disease getting worse[7], otherwise known as progression free survival, or PFS. Although the study was not designed to demonstrate an OS benefit, it was analysed as a secondary endpoint. Analysis of the AVAiL trial showed that while the increase in OS was not statistically significant, the median OS for patients in all arms of the study exceeded 13 months.

Key findings

- The addition of Avastin to chemotherapy led to a 25% reduction in the risk of death or progression.
- Avastin is compatible with platinum based chemotherapies.
- No new safety signals observed.

SAiL

SAiL was a phase IV international trial in a broad population of over 2,000 patients with advanced or recurrent non-squamous NSCLC, representative of daily clinical practice, including the elderly, hypertensive patients and those with brain metastases. The results showed outstanding median OS across this real-world clinical population of patients receiving Avastin in combination with a variety of chemotherapy, and confirmed Avastin's well established and manageable safety profile.

Key findings

- Avastin-based therapy in SAiL resulted in an outstanding median OS.
- SAiL and ARIES confirm Avastin's well established and manageable safety profile in a real-world population, including the elderly, hypertensive patients and those with brain metastases.

ARIES

The ARIES study is a U.S. prospective, observational cohort study enrolling approximately 2,000 patients with advanced NSCLC, including the elderly, those with brain metastases and patients on anticoagulants. Interim data confirm Avastin's well established and manageable safety profile in real-world clinical population.

ATLAS

The ATLAS study aimed to show that treatment with Avastin in combination with chemotherapy followed by combined maintenance treatment with Avastin and Tarceva® (erlotinib) can extend PFS. The vast majority of patients in the ATLAS trial had non squamous NSCLC. Over 1,000 patients received first line Avastin in combination with chemotherapy for at least four cycles, followed by Avastin with the addition of placebo or with the addition of Tarceva until disease progression. Interim data show that patients experienced a 39% improvement in the time they lived without their disease advancing (PFS, the primary endpoint of the study), compared with those who received Avastin and placebo. On the strength of these data, all patients enrolled in the ATLAS trial were offered combined maintenance treatment with Avastin and Tarceva.

BeTaLUNG

The BeTaLUNG study aimed to demonstrate the ability of Avastin in combination with Tarceva to extend duration of life in patients who have previously received treatment for their advanced disease. Over 600 patients, the vast majority of whom had non squamous NSCLC, participated in BeTaLUNG. The addition of Avastin to Tarceva doubled the time that patients with advanced NSCLC lived without their disease getting worse[8] In addition, the combination of Avastin and Tarceva more than doubled the response rate (a measure of tumour shrinkage)[8].

Key findings

- Avastin + Tarceva doubled PFS to 3.4 months from 1.7 months with Tarceva alone.
- Patients receiving Avastin + Tarceva had a response rate of 12.6% compared to 6.2% for patients receiving Tarceva alone.
- No new safety signals were observed.
- Demonstrated the clinical activity of the combination of Avastin + Tarceva.

Upcoming clinical trials of Avastin in earlier stage (non metastatic) lung cancer

The clinical studies outlined above focus on Avastin's use in patients with advanced or metastatic lung cancer. The potential of Avastin is also being assessed in patients with early stage lung cancer, when Avastin based therapy is given directly after the surgical removal of a patient's tumour. This method of treatment is often referred to as adjuvant therapy. The aim of treatment with Avastin in these patients is to increase the chance of curing their lung cancer.

E1505

The E1505 study aims to demonstrate the ability of Avastin to extend the lives of patients with early (stages IB to IIIA) non squamous NSCLC who have had their tumours completely removed by surgery prior to treatment. Avastin administered post surgery aims to prevent the cancer from returning by eliminating any remaining cancerous cells. In this trial, Avastin is being combined with a range of standard chemotherapies. Enrolment is currently ongoing.

Summary

Avastin in combination with chemotherapy was the first therapy in more than ten years to improve upon standard first line treatment for NSCLC. Avastin in combination with chemotherapy as first line treatment of NSCLC provides patients with outstanding survival time, and allows patients to remain free from progression of their disease for longer. These studies have also demonstrated that Avastin can be combined with a wide range of chemotherapies, which allows greater flexibility for physicians to optimise patient care. In addition, Avastin is well tolerated by patients and does not add to the side effects usually associated with chemotherapy such as hair loss, nausea and vomiting.

Current international clinical trials are exploring the benefits of Avastin in patients with earlier stage lung cancer, in the adjuvant setting. These studies offer great hope for patients with lung cancer, and aim to demonstrate Avastin's proven benefits to even more patients.

Glossary

- Non small cell lung cancer: A term used to describe a number of distinct forms of lung cancer, including squamous cell carcinoma, adenocarcinoma and large cell carcinoma.
- Locally advanced: Describes cancer that has spread to nearby tissue and / or lymph nodes but has not metastasised.
- Recurrent: Refers to cancer that has come back at, or near, the same place as the original tumour.
- Non squamous NSCLC: A term used to describe all lung cancers that are not defined as squamous NSCLC.
- Platinum based chemotherapy: A class of chemotherapy derived from the metal platinum. Platinum based chemotherapies include cisplatin and oxaliplatin.
- Adenocarcinoma: A cancer that develops from glandular (mucus secreting) cells.
- Early stage: Refers to cancer that hasn't spread to the lymph nodes and / or other parts of the body.

End

To download images and videos relating to Avastin and non small cell cancer please visit: www.thenewsmarket.com

References

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