Effects of tepotinib in patients with a particular type of lung cancer that has an alteration in a gene called *MET* (*MET* exon 14 skipping), who participated in the VISION clinical study

What is the purpose of this VISION study analysis?

What is *MET* exon 14 skipping advanced NSCLC?

Non-small cell lung cancer, also called NSCLC, is a disease in which cancer cells form in the tissues of the lungs. The symptoms of lung cancer include a cough that gets worse over time, shortness of breath, wheezing, and chest pain. A cancer is considered 'advanced' if the cancer spreads, or metasasizes, to other parts of the body. Only 3–4% of people with NSCLC have certain alterations (mutations) in their *MET* gene called *MET* exon 14 skipping. Many patients with NSCLC have other gene alterations.

What is tepotinib?

Tepotinib is a type of drug called a MET inhibitor and is currently approved for treating adult patients with *MET* exon 14 skipping advanced NSCLC, the gene alteration that is described above. During a clinical study called VISION, patients took 500 mg of tepotinib, orally and once a day, until their cancer worsened, or they had intolerable side effects, or they chose to leave the study.

What questions did the researchers want to answer?

Understanding the effects of a drug in different groups of patients with lung cancer can help guide doctors to make treatment decisions. Compared to patients with NSCLC with different gene alterations, patients with *MET* exon 14 skipping advanced NSCLC are generally older, and may also be receiving additional medication for other illnesses. These patients might have taken different types of anticancer treatments, and may have cancers that have spread to the brain. These factors may make it less likely that these patients will respond to treatment, and make it harder to control or treat their cancer.

The questions that the researchers wanted to answer relate to the effects of tepotinib on NSCLC in specific groups of patients, or 'subgroups', in the VISION study:

- Was tepotinib effective in elderly patients?
- Was tepotinib effective in patients who had received other anticancer drugs before tepotinib?
- Was tepotinib effective in patients who had cancer that had spread to their brain (also known as 'brain metastases')?

Who was included in this analysis?

This analysis included 152 patients with *MET* exon 14 skipping NSCLC who participated in the VISION study. The patients were aged from 41 to 94 years, with about half of the patients being over the age of 73 years. About half of the patients had previously received anticancer treatment.

What were the main results of this analysis?

Of the 152 patients, about **45%** had cancer that disappeared or shrunk after treatment with tepotinib. This percentage is extremely good in NSCLC. The questions that researchers answered by analyzing the results of patient subgroups are summarized in the following paragraphs.

Was tepotinib effective in elderly patients?

Sixty-eight of the 152 patients were at least 75 years of age or older, while 84 patients were younger than 75 years. About **40% of patients** who were at least 75 years old had cancer that disappeared or shrunk after treatment with tepotinib. In the group who were under 75 years old, about **49% of patients** had cancer that disappeared or shrunk after treatment with tepotinib. These results were reassuring, as they showed that tepotinib was effective in treating patients across the age groups, including those with advanced age.

Was tepotinib effective in patients who had received other anticancer drugs before tepotinib?

About **45% of patients** who had not received previous anticancer treatment had cancer that disappeared or shrunk after treatment with tepotinib. About **45% of patients** who had received previous anticancer treatment had cancer that disappeared or shrunk after treatment with tepotinib. Once again, these results were reassuring as irrespective of previous treatment, the same percentage of patients had cancer that disappeared or shrunk after tepotinib treatment.

Was tepotinib effective in patients who had cancer that had spread to their brain (also known as 'brain metastases')?

Of the 15 patients with cancer that spread to their brain and whose brain cancer could be measured, **13 patients** showed 'disease control' in the brain after treatment. Disease control means that the drug was efficacious and their brain cancer remained stable in size, shrunk, or disappeared after tepotinib treatment, but did not grow.

What side effects did patients have during the VISION study?

The safety results included 255 patients. The majority of side effects, related to tepotinib treatment, were mild to moderate. The most common side effects that happened in the VISION study are presented in the table below.

Side effects *are medical problems (such as headache) that happened during the study, which the study doctor thought could be related to the study treatment (tepotinib).*

About 11% of patients stopped taking tepotinib because of side effects. Three patients died due to side effects. Overall, the frequency of side effects was similar across the age and previous cancer treatment subgroups.

Most common side effects reported in more than 10% of patients in the VISION study	
Side effect	**Number of patients affected (%)**
Swelling of lower legs or hands (peripheral edema)	138 out of 255 (54%)
Feeling sick (nausea)	51 out of 255 (20%)
Diarrhea	50 out of 255 (20%)
Increased levels of a protein called creatinine in the blood, which may mean the kidneys are not working well (blood creatinine increased)	45 out of 255 (18%)
Low levels of a protein called albumin in the blood, which may mean malnutrition (hypoalbuminemia)	37 out of 255 (15%)

How was this analysis useful?

The analysis of the VISION study, reported in this manuscript (Le *et al*, 2021), showed that tepotinib had meaningful activity in patients with *MET* exon 14 skipping advanced NSCLC, regardless of their age or whether they had previous cancer treatment or not. Tepotinib also benefited patients whose cancer had spread to the brain. Side effects of tepotinib were generally manageable, with only a few patients stopping their treatment due to side effects.