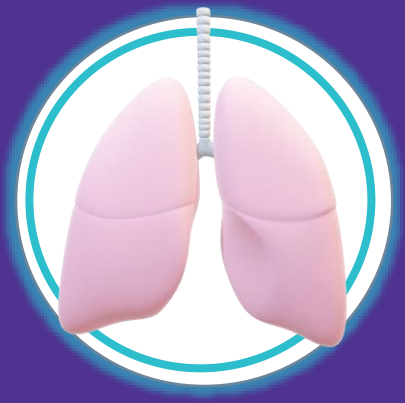

A study to learn about the effects and safety of tepotinib plus osimertinib in patients with *MET*-amplified non-small cell lung cancer that has progressed after treatment with osimertinib (INSIGHT 2)

Date of summary:
December 2021

Study number: NCT03940703

Study dates:
Study start date:
September 19, 2019
Estimated date for completing collection of data for the main aim of the study: November 30, 2022
Estimated study end date:
March 30, 2023

Key words:

- **NSCLC**: Non-small cell lung cancer
- **EGFR**: Epidermal growth factor receptor
- ***MET*:** Mesenchymal-epithelial transition factor
- ***MET*amp**: *MET* amplification
- **TKI**: Tyrosine kinase inhibitor
- **Osimertinib**
- **Tepotinib**

How to say
Osimertinib: O-si-mer-ti-nib
Tepotinib: Tep-o-ti-nib

Who is sponsoring the INSIGHT 2 study?
Merck Healthcare KGaA, Darmstadt, Germany is sponsoring the INSIGHT 2 study.

Full title of the article

INSIGHT 2: A Phase II study of tepotinib plus osimertinib in *MET*-amplified NSCLC and first-line osimertinib resistance

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Who should read this article?

This article, Smit EF, et al. Future Oncol. 2022, may be helpful for patients with a type of lung cancer called non-small cell lung cancer (NSCLC) and their family members or caregivers. It may also be helpful for patient advocates and healthcare professionals who are looking for treatment options for patients with advanced NSCLC.

Summary

Osimertinib is used to treat a type of lung cancer that has specific changes (mutations) in a gene called epidermal growth factor receptor (*EGFR*). Although tumors will usually shrink (respond) during treatment with osimertinib, they can stop responding, or become resistant, to osimertinib. A common cause of resistance is '*MET* amplification (*MET*amp)', which describes when extra copies of a gene called MET are present. Lung cancer that is resistant to osimertinib due to *MET*amp could be treated by combining osimertinib with a treatment that blocks MET, such as tepotinib. INSIGHT 2 is an ongoing study that is designed to learn about the effects and safety of tepotinib combined with osimertinib, in patients with lung cancer that has stopped responding to osimertinib because of *MET*amp.

What is *EGFR*-mutant NSCLC and *MET*-amplified 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.

Epidermal growth factor receptor (EGFR) is a protein expressed on the surface of cells. The *EGFR* gene is responsible for providing a blueprint that instructs cells to create the EGFR protein on a cell's surface. An *EGFR* gene mutation (change) can negatively affect how the EGFR protein functions. Some patients with NSCLC have a mutation in the *EGFR* gene. This type of lung cancer is called *EGFR*-mutated NSCLC.

MET amplification (*MET*amp) describes when extra copies of the *MET* gene are present in the cancer cells; making cancer cells grow more rapidly. This is known as *MET*-amplified NSCLC.

What is osimertinib?

Osimertinib is an approved treatment that inhibits the growth of NSCLC tumors with a specific mutation in the *EGFR* gene.

What is tepotinib?

Tepotinib is a treatment used to treat adults with NSCLC that has spread to other parts of the body and has a certain mutation in the *MET* gene.

Why is the INSIGHT 2 study needed?

While osimertinib can provide effective disease control in patients with NSCLC, most patients develop resistance to it after about a year of treatment. One of the most common causes for resistance to osimertinib is *MET*amp, occurring in up to 30% of patients.

Chemotherapy is another treatment option available, however, results with chemotherapy are not very encouraging as the effect does not last long. Hence, there is a need for newer treatments for patients with NSCLC, that are resistant to EGFR-targeted treatments due to *MET*amp. These treatments are called tyrosine kinase inhibitors or TKIs. In patients with NSCLC with *EGFR* gene mutation and *MET*amp, blocking both *MET* and *EGFR* at the same time may be helpful in overcoming resistance to EGFR TKI treatment when given alone.

What is the purpose of the INSIGHT 2 study?

The **main question** researchers want to answer at the end of the study is:

- **How many patients will show a response to the study treatment?**

  'Response' *means the cancer completely disappears or the size of the tumor decreases by at least 30%.*
  This is also called 'objective response'.

The **other questions** researchers want to answer at the end of the study are:

- **For patients who show a response, how long does the effect last?**

  This is also called 'duration of response'.

- **How long will patients live with their cancer before it gets worse or the patient dies due to any cause?**

  This is also called 'progression-free survival'.

- **How long will patients live after starting the study treatment?**

  This is also called 'overall survival'.

- **How will be the overall health and quality of life of the patients during the study?**

  This is also called 'health-related quality of life'.

- **What medical problems do the patients develop during the study?**

  This is also called 'safety'.

Who is being included in the INSIGHT 2 study?

The INSIGHT 2 study is expected to enroll approximately 120 patients.

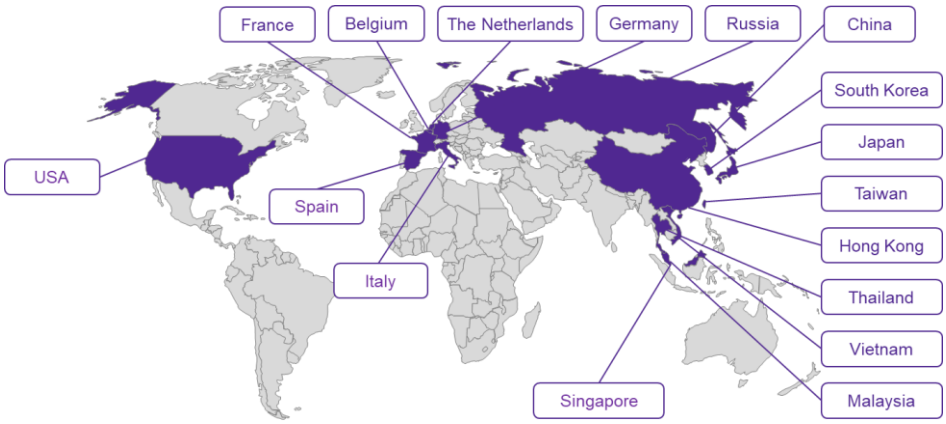
It will enroll patients who:

- have *EGFR*-mutant NSCLC that has spread to other parts of the body,
- are 18 years or older in age,
- have received only first-line treatment with osimertinib and have become resistant to it,
- are fully active or are restricted in physically tiring activity but are able to walk,
- do not have history of lung damage,
- have normal organ function, and
- have *METamp* confirmed by either fluorescence in situ hybridization (FISH) testing (central or local) on tumor tissue or central blood-based next generation sequencing (NGS).

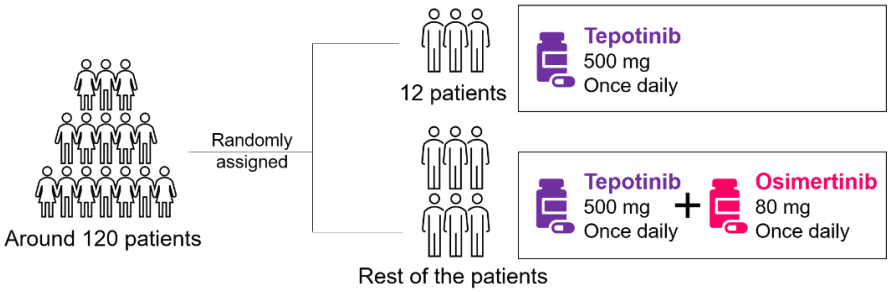
Fluorescence in situ hybridization (FISH) and next-generation sequencing (NGS) are techniques used to detect and locate a specific DNA sequence.

Where is the INSIGHT 2 study taking place?

As of October 2021, the INSIGHT 2 study is active at 114 sites across 17 countries in Europe, Asia, and North America.



What is happening in the INSIGHT 2 study?



At the start of the study, patients will go through a cycle of treatment to confirm the safest dose of osimertinib and tepotinib to be taken together.

Patients assigned to the tepotinib only group will get the chance to switch over to the combination treatment, if their cancer worsens.

Treatment will continue as long as the cancer does not get worse, the patient does not have any medical problems leading to stopping the treatment, or the patient dies. The study doctor may also decide to stop the treatment, or the patient may decide to stop participating in the study.

Further information

Link to full scientific article: https://www.futuremedicine.com/doi/10.2217/FON-2021-1406

Registrations: The INSIGHT 2 study is registered with

- www.clinicaltrials.gov
  Use the study identifier NCT03940703
- www.clinicaltrialsregister.eu
  Use the study identifier 2019-001538-33

For more details on the INSIGHT 2 study, please visit: https://www.insight2lungcancerstudy.com/#!/

What is happening in the INSIGHT 2 study? Cont.

All patients will be monitored by the study doctor, to study the effects and safety of the treatments. Health monitoring will continue until 3 years after the first dose of the last patient enrolled in the study, or until all the patients stop taking the treatment and two-thirds of the patients have died, whichever comes first.

The study is expected to continue till March 2023.

How is the INSIGHT 2 study useful?

Combining an EGFR TKI treatment with a MET inhibitor treatment may overcome MET-related resistance and may be a better option than chemotherapy.

The results from the INSIGHT 2 study will help doctors understand the effects and safety of tepotinib in combination with osimertinib for patients with *EGFR*-mutant NSCLC with *MET*amp who develop resistance to osimertinib.

Acknowledgements:
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