A comparison of atezolizumab + nab-paclitaxel with placebo + nab-paclitaxel for the treatment of triple-negative breast cancer (TNBC): summary of the clinical trial

ClinicalTrials.gov study title: A Study of Atezolizumab in Combination With Nab-Paclitaxel Compared With Placebo With Nab-Paclitaxel for Participants With Previously Untreated Metastatic Triple-Negative Breast Cancer (IMpassion130).

The summary of the Phase 3 clinical trial called IMpassion130 (NCT02425891) was prepared in January 2019 to provide trial participants with information on why the trial was done, and the first results from the trial. The IMpassion130 trial is still ongoing.

F. Hoffmann-La Roche Ltd, the sponsor of this trial, would like to thank the participants for their contribution. If you have any queries about treatment options in your country, please speak with your doctor.

Why was this clinical trial carried out?

Triple-negative breast cancer (TNBC) is a type of breast cancer. There are different types of breast cancer, based on the presence or absence of receptors on the cells of the tumour. Knowing the characteristics of the cancer can help decide which treatments are likely to be successful. Patients who took part in this trial had TNBC, which does not have receptors for the hormones, oestrogen and progesterone, or the human epidermal growth factor receptor 2 (HER2) protein. Although therapies that target these receptors can be used to treat other types of breast cancer, these treatments do not work in patients with TNBC.

This study included TNBC patients with metastatic disease, where the cancer has spread to other parts of the body. For TNBC patients with metastatic disease, chemotherapy is the only treatment option. The new cancer immunotherapy drug atezolizumab was investigated in combination with nab-paclitaxel (a chemotherapy), as an alternative to nab-paclitaxel alone, for patients who have not received any other treatment for their metastatic TNBC.

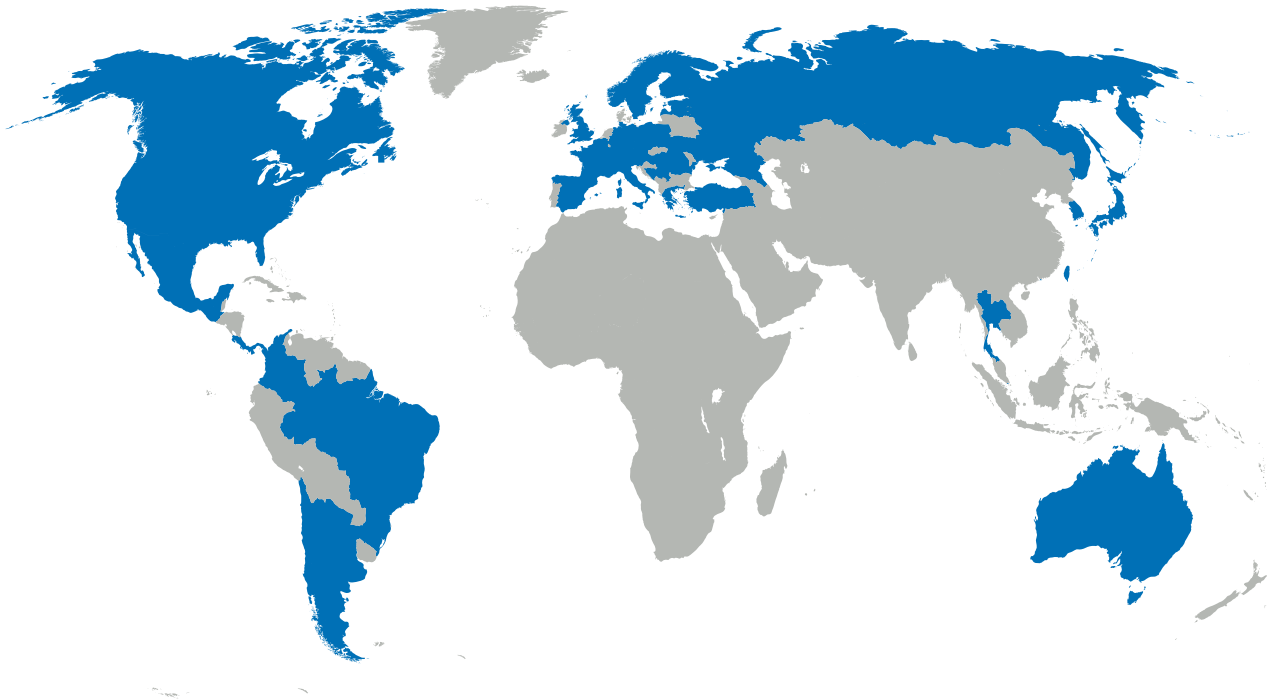
This Phase 3 trial looked at whether atezolizumab combined with nab-paclitaxel can slow down the cancer from getting worse or prolong a patient's life compared with nab-paclitaxel alone. The trial also assessed the safety (the adverse reactions associated with a drug or treatment) of the two drugs when given to patients together. The objective of the trial was to see if atezolizumab should be offered with chemotherapy as treatment instead of chemotherapy alone for patients who have not received any other treatment for their metastatic TNBC.

Who took part?

The trial started in June 2015 and here we report results from April 2018. In total, 902 participants from 41 countries across Europe, the United States and Canada, Asia, Latin America and Australia took part in the trial.

Patients who took part in the trial met all of the following criteria:

- Aged over 18 years
- Diagnosed with metastatic or inoperable, locally advanced TNBC
- Had a tumour that could be accurately measured in size
- Had not received any other therapy for their advanced TNBC
- Fully physically active or restricted in only physically strenuous activity (ECOG PS 0–1)



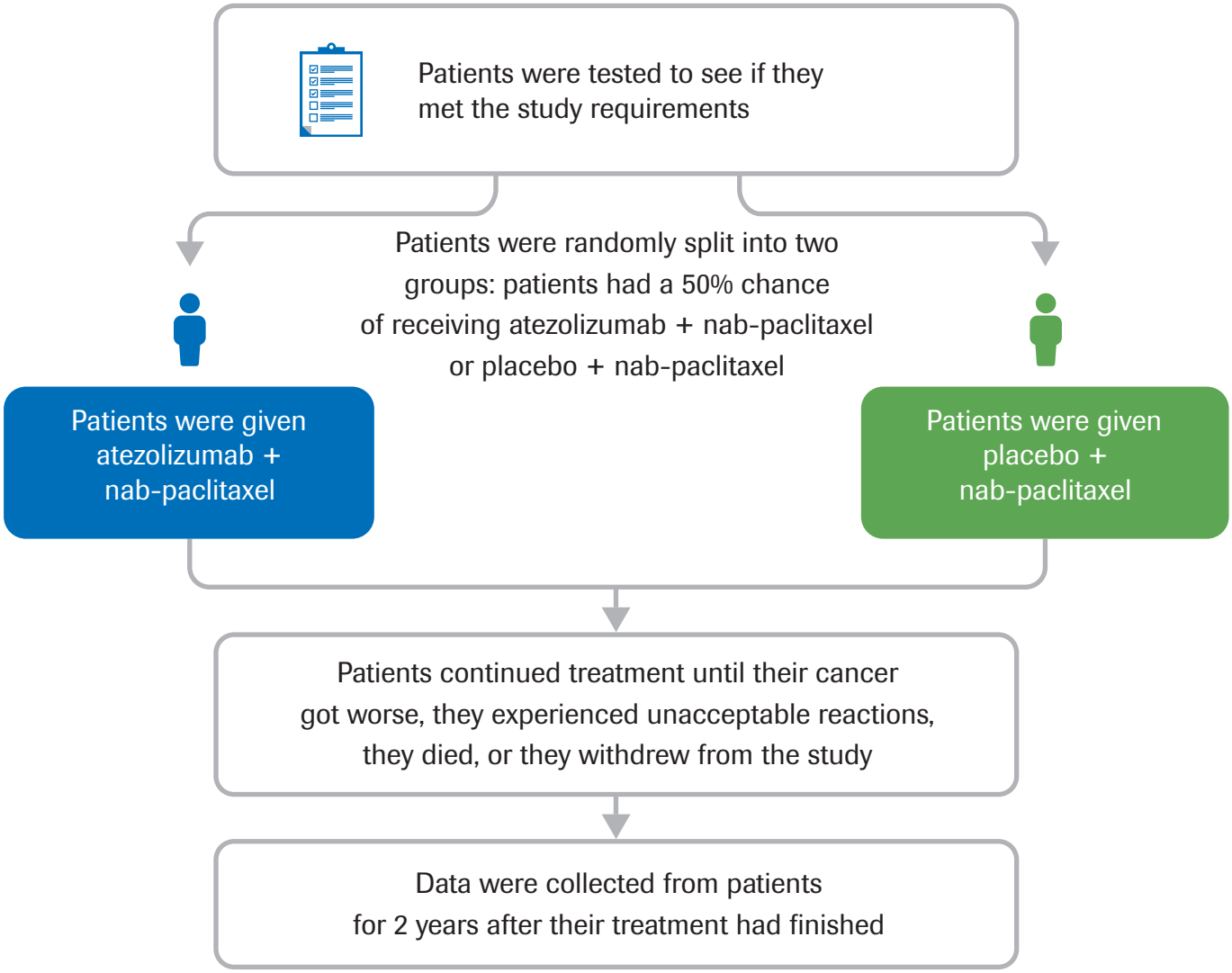
902
patients

246
centres

41
countries

What happened during the trial?

Patients were treated with either atezolizumab + nab-paclitaxel or placebo (no active drug) + nab-paclitaxel. The treatment option was chosen at random. Patients were treated until their cancer got worse, they experienced undesirable reactions from the treatment that caused them to withdraw from the treatment, they died or they (or their doctor) decided they should not continue in the study. The effects of combining atezolizumab with nab-paclitaxel were assessed in all patients enrolled in the study as a whole, and in a subgroup of patients whose tumours contained immune cells that expressed a protein called PD-L1. PD-L1 is found on the surface of some cancer cells and can help cancer cells to avoid attack by the immune system. Atezolizumab targets PD-L1 and this allows the immune cell to become active and be able to fight the cancer cells.



What were the results?

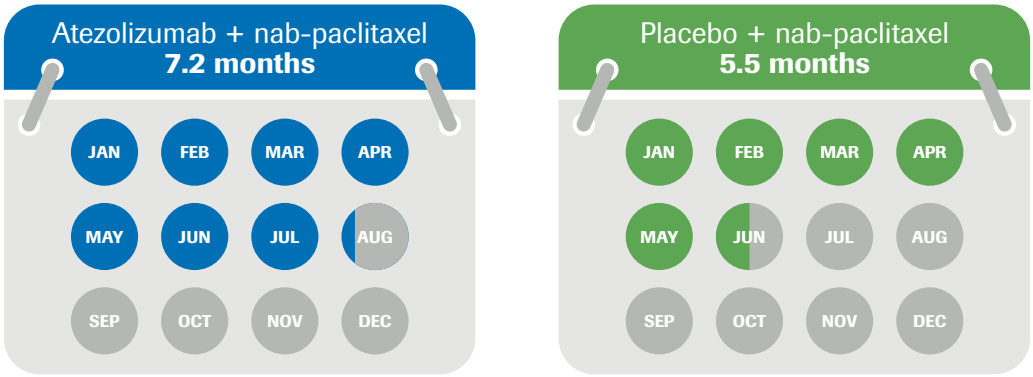
Here, we report the first results from IMpassion130. Of the 902 patients in the study, 451 received atezolizumab + nab-paclitaxel and 451 received placebo + nab-paclitaxel. A total of 185 patients who received atezolizumab + nab-paclitaxel had tumours containing immune cells that expressed PD-L1, and of the patients who received placebo + nab-paclitaxel, 184 had PD-L1 expression. An equal number of patients in each treatment group had PD-L1 present on their tumour immune cells.

How long did patients live without their cancer getting worse?

A key objective of this trial was to measure how long it took from the start of treatment with atezolizumab + nab-paclitaxel or placebo + nab-paclitaxel until a patient's cancer got worse, the patient experienced undesirable reactions from the treatment that caused them to withdraw from the study, or until the patient died. This is known as progression-free survival.

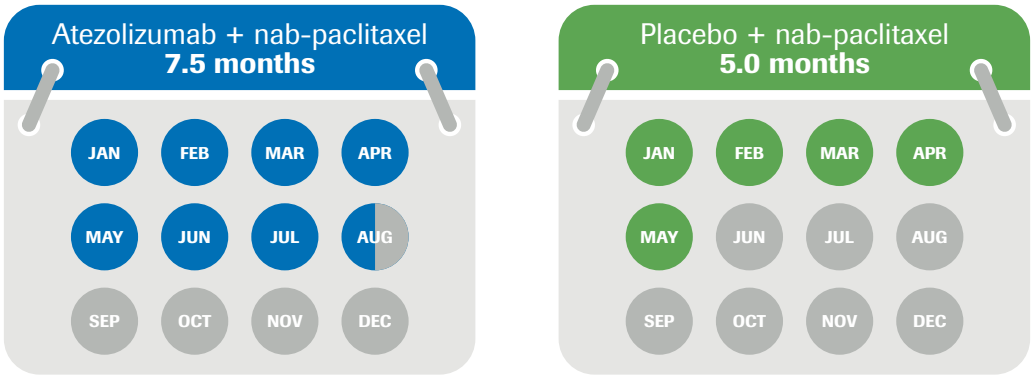
When atezolizumab was given with nab-paclitaxel, it took on average between 7 and 8 months for the cancer to get worse. For patients who received placebo + nab-paclitaxel, it took on average between 5 and 6 months for their cancer to get worse.

All treated patients



In the subgroup of patients whose tumour immune cells expressed PD-L1, those who received atezolizumab + nab-paclitaxel took on average between 7 and 8 months for the cancer to get worse, compared with 5 months when placebo + nab-paclitaxel was given.

Patients whose tumour immune cells expressed PD-L1

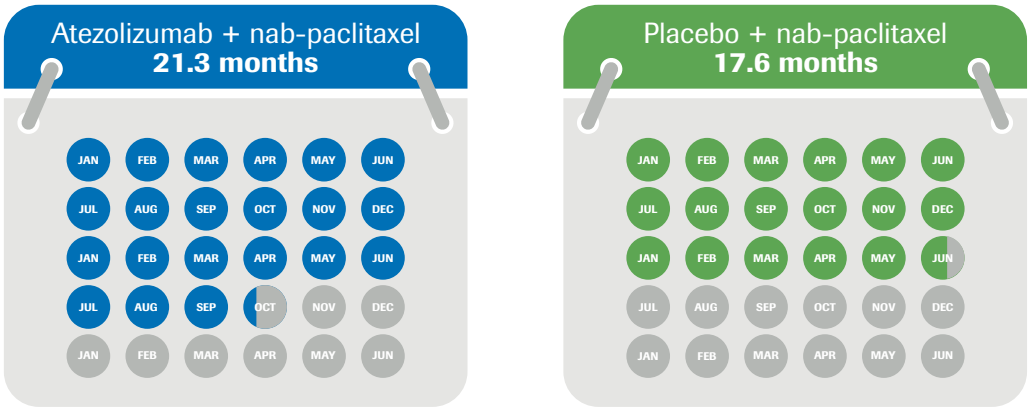


How long did patients live?

A second key objective of IMpassion130 was overall survival. This is the number of patients who died from any cause, not only due to their TNBC, while they were involved in the trial. The overall survival results in this trial are preliminary as patients need to be followed-up for longer before a final analysis can take place.

Preliminary results show that, in patients who received atezolizumab + nab-paclitaxel, patients lived for between 21 and 22 months, on average. In comparison, patients who received placebo + nab-paclitaxel lived for between 17 and 18 months. Statistical analysis showed that the addition of atezolizumab to nab-paclitaxel had a similar outcome on survival as placebo + nab-paclitaxel.

All treated patients



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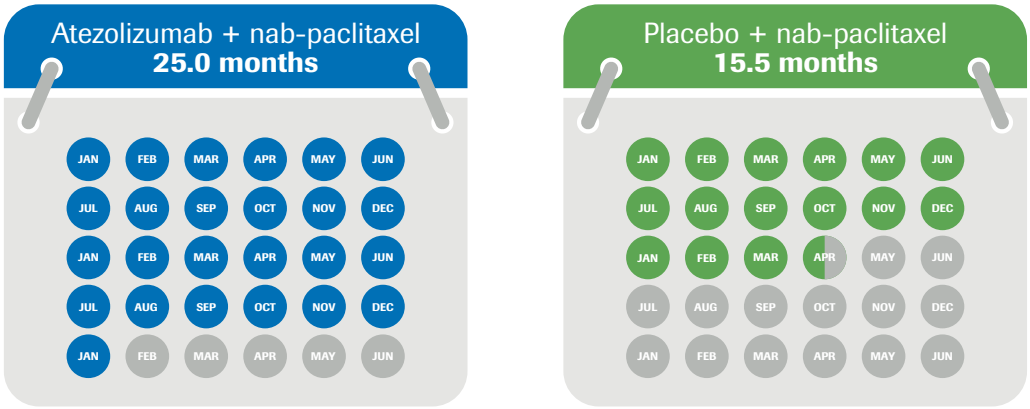
Study WO29522, Zinc Approval Number: NP/TCNGI/1901/0001
Zinc Approval Date: 22-02-2019

In the subgroup of patients whose tumour immune cells expressed PD-L1, those who were treated with atezolizumab + nab-paclitaxel lived for 25 months, on average. In comparison, those who received placebo + nab-paclitaxel lived, on average, for between 15 and 16 months. These survival results have not been formally tested.

Patients whose tumour immune cells expressed PD-L1

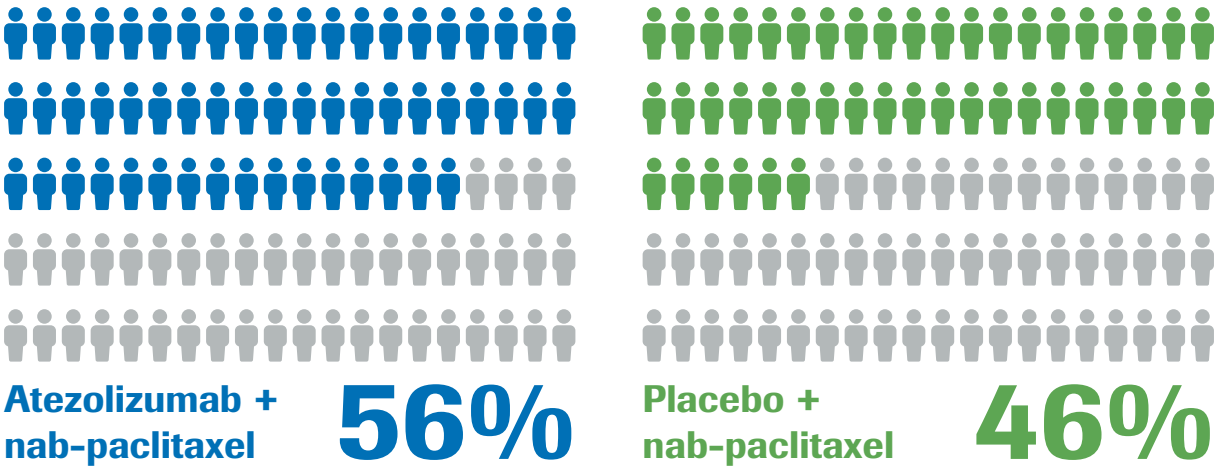


Were the size of the tumours reduced?

Another important measure of a treatment working is whether the tumour is reduced in size. In this study, more patients treated with atezolizumab + nab-paclitaxel had a reduction in the size of their tumour compared with patients treated with placebo + nab-paclitaxel.

In patients who received atezolizumab + nab-paclitaxel, over half (56%) had a reduction in their tumour size. In patients who received placebo + nab-paclitaxel, 46% had a reduction in their tumour size.

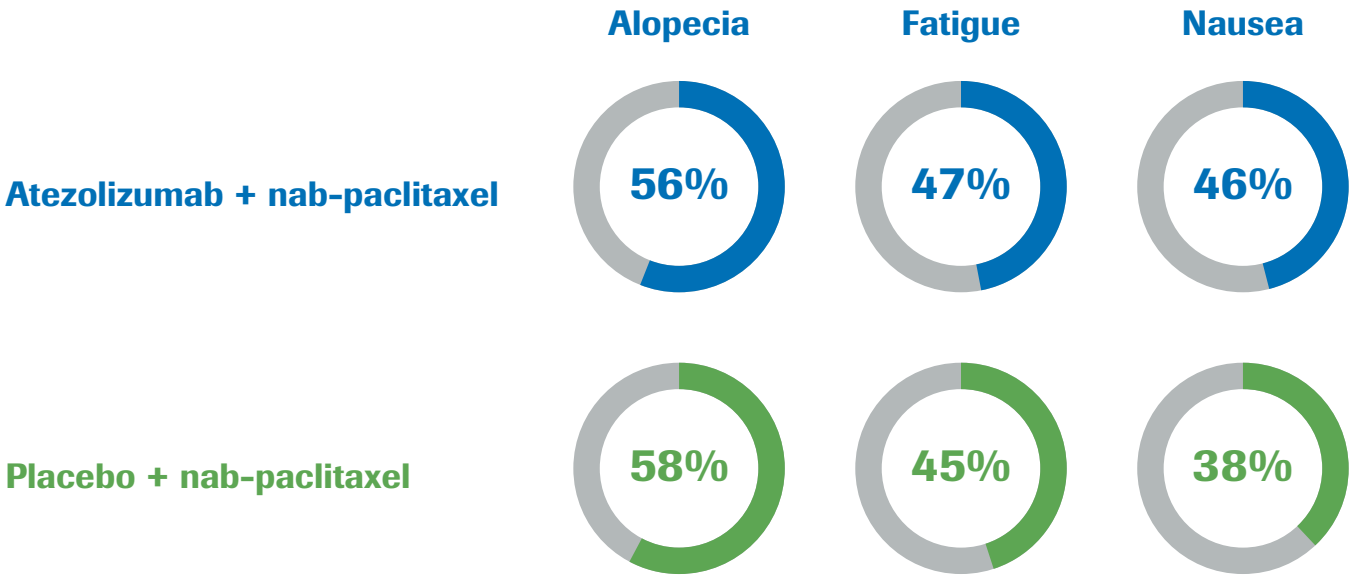
In patients who received atezolizumab + nab-paclitaxel and also had tumour immune cells that expressed PD-L1, 59% had a reduction in their tumour size.



What adverse reactions did the participants have?

An adverse reaction is an unfavourable medical occurrence associated with the use of a drug; it may or may not be thought to be related to the drug. Adverse reactions are different from side effects, which are known effects of a drug beyond the intended effect. Moderate adverse reactions are those that are not life-threatening, but result in a patient needing additional treatment. Severe adverse reactions are those that may result in death, or require or prolong inpatient hospitalisation. It may be possible to reduce the number and severity of adverse reactions, for example, by lowering the dose of study drug received, or with supportive treatment.

The trial looked at the safety of atezolizumab + nab-paclitaxel compared with placebo + nab-paclitaxel, by measuring the number and type of adverse reactions in all patients. More patients who received atezolizumab + nab-paclitaxel had adverse reactions compared with patients who received placebo + nab-paclitaxel. The most common adverse reactions in both treatment arms were alopecia (hair loss), fatigue (overwhelming tiredness) and nausea (feeling sick).



Serious adverse reactions were experienced in 103 patients (23%) in the atezolizumab + nab-paclitaxel group and 80 patients (18%) in the placebo + nab-paclitaxel group. The most common serious adverse reactions were pneumonia (inflammation of the lungs), dyspnoea (shortness of breath) and pyrexia (fever). The most common adverse reactions related to the immune system were hepatitis (inflammation of the liver), and hypothyroidism (underactive thyroid). The number of adverse reactions that caused patients to stop treatment was higher with atezolizumab + nab-paclitaxel (16%), than with placebo + nab-paclitaxel (8%).

What was the overall outcome?

Atezolizumab + nab-paclitaxel was shown to be a more effective treatment than placebo + nab-paclitaxel in patients with metastatic TNBC who had not received any treatment for their disease. Patients who received atezolizumab + nab-paclitaxel lived for longer before their cancer got worse, and responded better to treatment. Patients whose tumour immune cells expressed PD-L1 also lived for longer and responded better to treatment if they received atezolizumab + nab-paclitaxel compared with placebo + nab-paclitaxel. The survival results are preliminary and longer follow-up is needed to confirm the results. It is estimated that final results will be available in 2020.

Patients who received atezolizumab + nab-paclitaxel had adverse reactions similar to those expected, based on other clinical trials.

The results of this trial suggest that the addition of atezolizumab to nab-paclitaxel can slow down the rate at which the cancer gets worse, compared to standard nab-paclitaxel alone in patients with TNBC who have not had any other treatment for their disease.

Any more questions?

Information on this trial can be found on ClinicalTrials.gov by following this link or by using the trial number, NCT02425891. If you have any further questions, please contact your doctor or a representative at your local Roche office https://www.roche.com/about/business/roche_worldwide.htm