NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of PDR001 and standard chemotherapy when given with or without ACZ885 in people with non-small cell lung cancer

Clinical trial protocol number: CPDR001C2101

Thank you!

Thank you to the participants who took part in this clinical trial for the drug **PDR001**, also known as **spartalizumab**, and **ACZ885**, also known as **canakinumab**.

All of the participants helped researchers learn more about how **PDR001** and **ACZ885** work in people with **non-small cell lung cancer**. Novartis sponsored this trial and believes it is important to share the results of the trial with the participants and the public.

We hope this helps the participants understand their important role in medical research.

If you participated in the trial and have questions about the results, please talk to the doctor or staff at your trial site.

Why was the research needed?

Researchers are looking for better ways to treat **non-small cell lung cancer** (**NSCLC**), which is the most common type of lung cancer. Chemotherapy (**chemo**) is often used as a standard treatment for NSCLC, but they do not always work to shrink tumors. Researchers are exploring new drugs to give along with chemo to help shrink tumors.

Immunotherapy is a cancer treatment that uses the body's own immune system to find and fight cancer cells. **PDR001** and **ACZ885** are immunotherapy drugs that block proteins in the immune system. Researchers suspect that they may help shrink NSCLC tumors when given with chemo.

Trial purpose

The main purpose of this 2-part trial was to confirm the dose and learn about the safety of PDR001 and chemo when given with or without ACZ885 in people with NSCLC:

- **Part 1** learned if certain doses of PDR001 and chemo given with or without ACZ885 had risk of harm
- **Part 2** looked at how many participants had their tumors shrink or disappear during treatment

The main questions the researchers wanted to answer in this trial were:

- Could participants receive PDR001 and chemo with or without ACZ885 without risk of serious harm?
- What percent of participants had their tumors shrink or disappear during treatment?
- What medical problems did the participants have during the trial?

Trial drugs

The treatments in this trial were:

PDR001, also known as **spartalizumab:** A trial drug designed to help the immune system fight cancer by blocking a protein called PD-1. PD-1 can prevent the immune system from killing cancer cells. It was given as 300 milligrams (mg) every 3 weeks (3-week cycles) through a needle in a vein as an intravenous (IV) infusion.

ACZ885, also known as **canakinumab:** A trial drug designed to block an immune system protein called IL 1β. It is approved to treat certain immune system diseases involving inflammation, such as certain types of arthritis. It is not approved to treat cancer. It was given as 200 mg every 3 weeks, through 2 injections.

Chemotherapy (chemo): 3 standard treatments for NSCLC given as IV infusions in treatment cycles. Based on their type of NSCLC, participants received one of these:

- **Chemo A**: Cisplatin and gemcitabine once every 3 weeks up to 4 times (4 cycles)
- **Chemo B**: Cisplatin and pemetrexed once every 3 weeks up to 4 times (cisplatin for 4 cycles, pemetrexed could be given longer)
- **Chemo C**: Carboplatin and paclitaxel once every 3 weeks up to 4 times (4 cycles)

How long was this trial?

This trial was designed so that each participant could take part until one of these happened:

- Their cancer got worse
- They started a new treatment
- They had a severe medical problem
- They decided to leave the trial

The participants took their trial treatments for up to 3 years. The trial started in May 2017 and Novartis ended the trial early in July 2021.

Why did the sponsor stop recruitment early?

The trial planned to have up to 140 participants. However, the researchers did not complete this trial as planned because the sponsor stopped recruitment early after 111 participants had joined.

During this trial, more treatments that help the immune system fight NSCLC were approved. Because the participants in this trial could not have received these other types of treatment before starting this trial, it became more difficult to recruit participants for this trial. This led to the sponsor's decision to not recruit more participants. The decision to end recruitment was not related to safety.

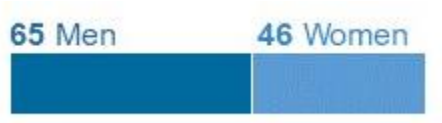
Participants who were taking trial treatment had the option to join another trial, CPDR001X2X01B, after completing at least 5 treatment cycles in this trial. 12 participants joined CPDR001X2X01B.

When the trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

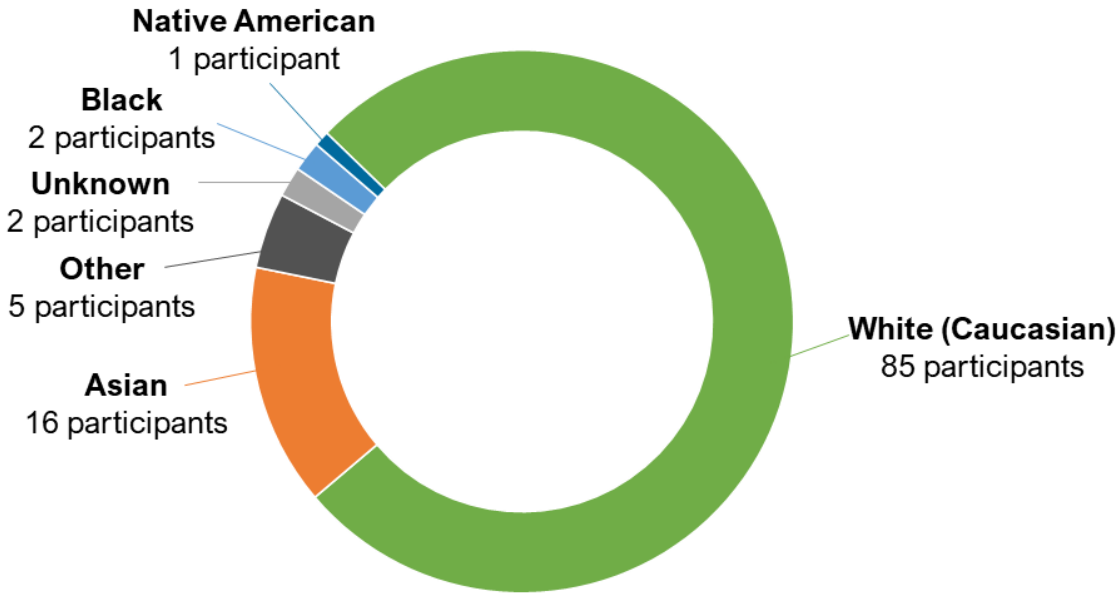
Who was in this trial?

111 participants with NSCLC were in this trial. Their ages ranged from 36 to 82 years. Their average age was 62 years.

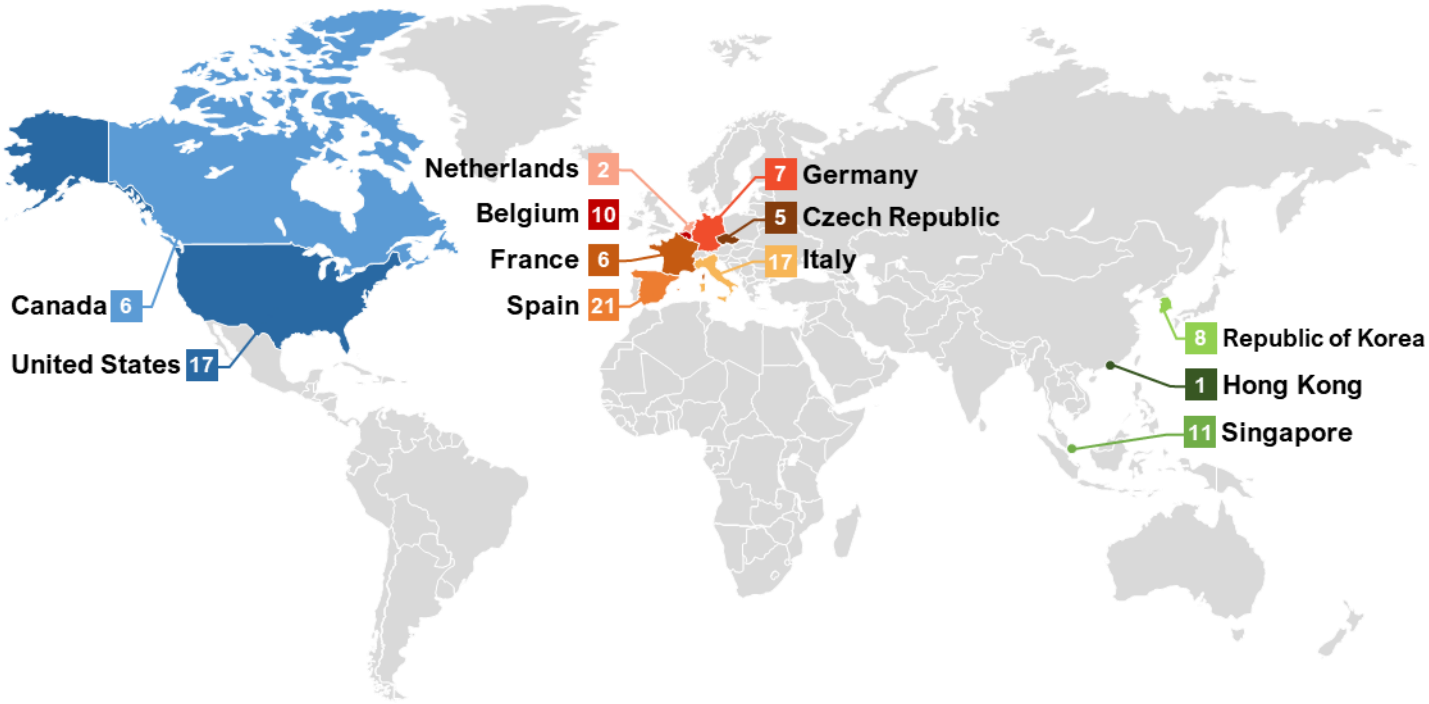
They reported their gender as:



They reported their race as:



111 participants took part at 23 trial sites. The map below shows how many participants took part in each country:



The participants' NSCLC was any of these types:

- **Squamous**, which starts in thin, flat cells that line the inside airways of the lungs
- **Non-squamous**, which includes:
    - **Adenocarcinoma**, which starts in cells that make mucus in the lungs
    - **Large cell**, which starts in larger cells in any part of the lung

The participants could take part in this trial if their NSCLC was either:

- **Stage 3B**, which means lung cancer spread to other parts of the lung or chest but has **not** spread to other parts of the body, and **relapsed locally advanced,** which means it spread after a previous treatment
- **Stage 4**, which means lung cancer has spread to other parts of the body (**metastatic**)

The participants also:

- Could not have taken an immunotherapy to treat their NSCLC
- Did not have certain other serious health problems

What kind of trial was this?

This was an open-label trial, which means that the participants and clinical trial team knew what treatment each participant took.

What happened during this trial?

Up to **4 weeks** before treatment

During screening

Trial doctors checked participants' health and NSCLC to make sure they could be in this clinical trial.

111 participants took part in this trial.

Up to **3 years**

During treatment

The participants were assigned to **1 of 4 groups:**

Group and number of participants	Trial drugs received	Chemo received	Type of NSCLC
Group A 33 participants	PDR001	Chemo A	Squamous
Group B 38 participants	PDR001	Chemo B	Non-squamous
Group C 33 participants	PDR001	Chemo C	Squamous or non-squamous
Group E 7 participants	PDR001 and ACZ885	Chemo B	Non-squamous

Trial doctors could lower a participants' dose of PDR001 or pause their trial treatment, if needed.

Researchers checked the participants' NSCLC and general health throughout the trial.

5 months after treatment or until the end of the trial

During follow-up

Trial staff followed up with participants by phone or in-person visits to check their health and survival until the end of the trial.

What were the main results of this trial?

This is a summary of the overall results for all participants. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total

group of participants. More details on the results can be found on the websites listed at the end of this summary.

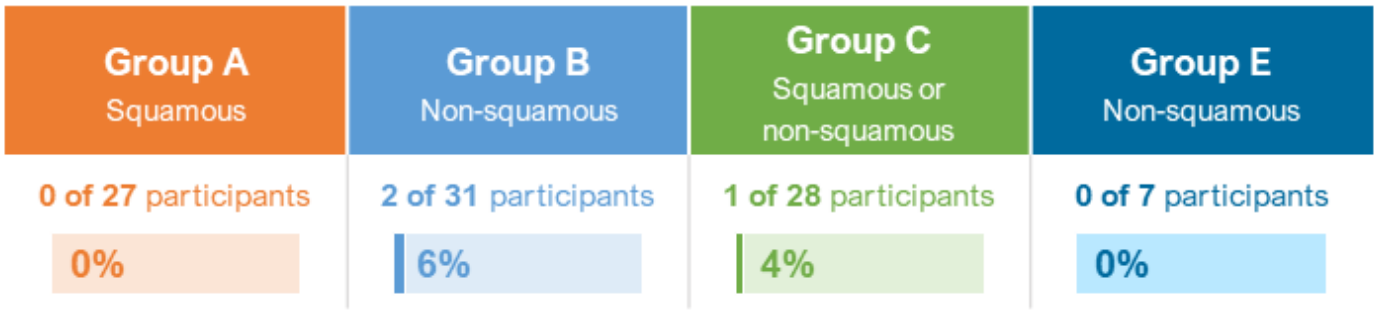
Could participants receive PDR001 and ACZ885 with chemo without risk of serious harm?

Yes. Researchers concluded that 300 mg of PDR001 each treatment cycle given with each chemo did not have risk of serious harm in this trial. 200 mg of ACZ885 given with PDR001 and Chemo B also did not have risk of serious harm.

To find this out, researchers counted each participant's **dose limiting toxicities**. Dose limiting toxicities are medical problems that had risk of serious harm if the dose went up. Before this trial started, the researchers decided which medical problems had risk of serious harm based on their type, severity, and timing. Trial doctors kept track of dose limiting toxicities that happened during the first 2 treatment cycles, which was a total of 6 weeks.

3 of 93 participants (3%) reported dose limiting toxicities. The table below shows the participants with dose limiting toxicities in each group:

Participants in each group who had dose limiting toxicities



These dose limiting toxicities included:

- 1 participant in Group B had **low levels of sodium in the blood** (hyponatremia)
- 1 participant in Group B had a **sudden, severe nervous system disorder that causes symptoms like headache, throwing up, and seizures** (posterior reversible encephalopathy syndrome or PRES)
- 1 participant in Group C had a **type of severe inflammation in the intestines** (neutropenic colitis)

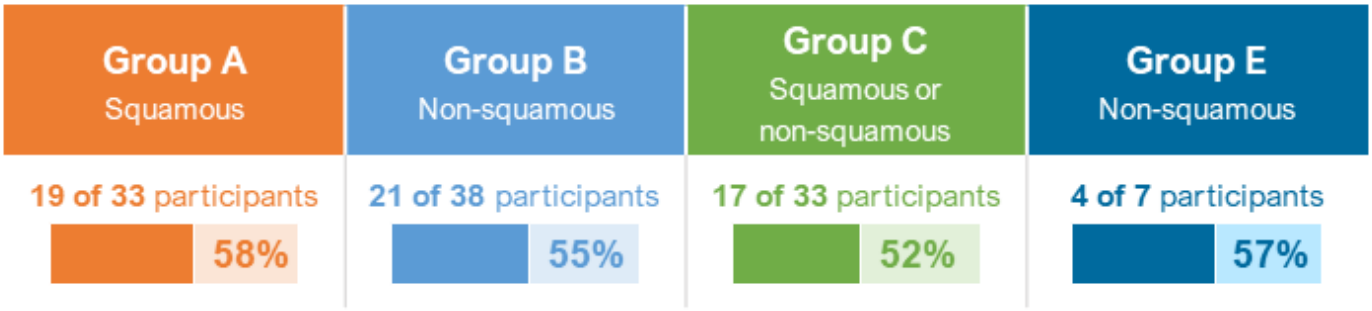
Because the number of dose limiting toxicities reported from each treatment group was small, researchers concluded that the trial treatments did not have risk of serious harm for the participants in this trial.

What percent of participants in each group had their tumors shrink or disappear during treatment?

In each group, a little more than half of the participants had their tumors shrink or disappear during treatment.

To find this out, researchers kept track of the percent of participants whose tumors shrank or disappeared at any time during treatment, even if the tumors grew back later. This is called the **overall response rate (ORR).** The table below gives the percent of participants in each group.

Percent of participants whose tumors shrank or disappeared



What were the other results of this trial?

The researchers also used other measures to look at the effects of the trial treatments on the participants' cancer. These measures included:

- The number of participants whose cancer did not get worse during treatment (disease control rate, or DCR)
- The length of time from the start of treatment until participants' tumors shrank (time to response, or TRR)
- The length of time from when a participants' tumors shrank to when they grew again or the participant died (duration of response, or DOR; progression free survival, or PFS; and overall survival, or OS)

In all groups, most participants' cancer did not get worse during treatment. The participants in Group B survived the longest without their cancer getting worse and had the longest length of time before their tumors grew again or the participant died. Tumors grew back more quickly in the participants in Group E. Because there were only a small number of participants in this group, the team couldn't conclude if this was meaningful.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "**adverse events**".

A lot of research is needed to know whether a drug causes an adverse event. So, when new drugs are being studied, researchers keep track of all adverse events the participants have, whether or not they are thought to be caused by the trial drug.

> An **adverse event** is any sign or symptom that participants have during a trial. An adverse event is considered "**serious**" when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

This section is a summary of the adverse events that happened **during treatment** (from first dose of treatment to 30 days after the last dose) and **during follow-up** (31 to 150 days after the last dose). The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

What were the serious adverse events?

During treatment and up to 30 days after last dose

54 participants had serious adverse events during treatment, and 8 of these participants died. Most of the deaths were due to cancer or health problems related to cancer.

Serious adverse events that happened during treatment in 3 or more participants in any group:

	Group A Squamous	**Group B** Non-squamous	**Group C** Squamous or non-squamous	**Group E** Non-squamous
	Out of 33 participants (percent %)	**Out of 38 participants** (percent %)	**Out of 33 participants** (percent %)	**Out of 7 participants** (percent %)
Trouble breathing Dyspnea	**0** (0%)	**0** (0%)	**3** (9%)	**0** (0%)
Low levels of blood cells Pancytopenia	**0** (0%)	**3** (8%)	**0** (0%)	**0** (0%)
Fever Pyrexia	**3** (9%)	**0** (0%)	**0** (0%)	**0** (0%)
Throwing up Vomiting	**0** (0%)	**3** (8%)	**0** (0%)	**0** (0%)

During follow-up, from day 31 to 150 after last dose

8 participants had serious adverse events during follow-up, and 29 participants died. Each **serious adverse event** happened in one participant, but each participant may have had more than one serious adverse event.

In **Group A (Squamous)**, 2 participants had one or more of these:

- **Heart attack** (acute myocardial infarction)
- **Fever** (pyrexia)
- **Feeling sleepy have having low energy** (lethargy)

In **Group B (Non-squamous)**, 3 participants had one or more of these:

- **The heart cannot pump enough blood to the brain and other organs** (cardiogenic shock)
- **Inflammation in the lining of the colon** (colitis)
- **Loose or watery stool** (diarrhea)
- **A type of lung infection** (pneumonia)
- **Lung cancer** (lung neoplasm malignant)

In **Group C (Squamous or non-squamous)**, 3 participants had one or more of these:

- **An existing health condition gets worse** (condition aggravated)
- **General health gets worse** (general physical health deterioration)
- **Inflammation from the immune system attacking the liver** (autoimmune hepatitis)
- **Back pain**
- **Blood clot** (pulmonary embolism)

No participants in **Group E (Non-squamous)** had serious adverse events during follow-up.

What were the most common non-serious adverse events?

During treatment and up to 30 days after last dose

All participants in the trial had at least one adverse event that was not considered serious during treatment.

The table below shows the **non-serious adverse events** that happened during treatment in at least 50% of participants in any group:

	Group A Squamous	**Group B** Non-squamous	**Group C** Squamous or non-squamous	**Group E** Non-squamous
	Out of 33 participants (percent %)	**Out of 38 participants** (percent %)	**Out of 33 participants** (percent %)	**Out of 7 participants** (percent %)
Low levels of red blood cells Anemia	**20** (61%)	**16** (42%)	**18** (55%)	**4** (57%)
Low levels of white blood cells Neutropenia	**19** (58%)	**19** (50%)	**19** (58%)	**3** (43%)
Feeling sick to the stomach Nausea	**13** (39%)	**28** (74%)	**12** (36%)	**2** (29%)
Feeling tired Fatigue	**9** (27%)	**8** (21%)	**9** (27%)	**4** (57%)
Feeling less hungry Decreased appetite	**7** (21%)	**8** (21%)	**11** (33%)	**4** (57%)

During follow-up, from day 31 to 150 after last dose

18 participants had non-serious adverse events during follow-up.

The table below shows the **non-serious adverse events** that happened during follow-up in at least 5% of participants in any group:

	Group A Squamous	**Group B** Non-squamous	**Group C** Squamous or non-squamous	**Group E** Non-squamous
	Out of 33 participants (percent %)	**Out of 38 participants** (percent %)	**Out of 33 participants** (percent %)	**Out of 7 participants** (percent %)
Back pain	**0** (0%)	**1** (3%)	**2** (6%)	**0** (0%)
Shortness of breath Dyspnoea	**0** (0%)	**1** (3%)	**2** (6%)	**0** (0%)
Possible sign of liver damage Gamma-glutamyltransferase increased	**0** (0%)	**2** (5%)	**0** (0%)	**0** (0%)

How has this trial helped?

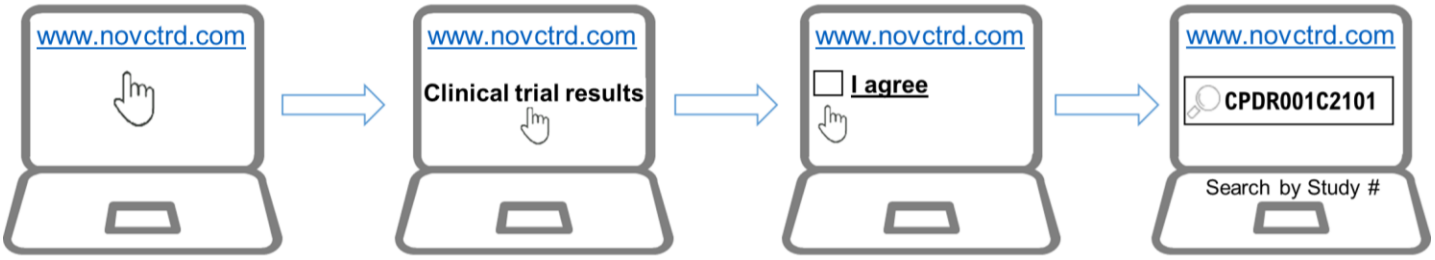
This trial helped researchers learn how PDR001 and standard chemo with or without ACZ885 work and if they can be given without risk of serious harm to people with stage 3B or stage 4 NSCLC. The researchers concluded that PDR001 given with chemo was safe and might shrink tumors more than chemo alone. However, adding ACZ885 to PDR001 and chemo did not shrink tumors for as long. Because of the small number of participants who took ACZ885, the team couldn't conclude if this was meaningful.

The participants who received PDR001 with cisplatin and pemetrexed (Group B) survived the longest without their cancer getting worse and had the longest length of time before their tumors grew again or the participants died. Results from this trial may be used to seek future approval to give PDR001 to people with cancer.

Please remember, this summary only shows the results of one clinical trial. Other clinical trials may have different results. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com).



You can find more information about this trial on this website:

- www.clinicaltrials.gov. Use the NCT identifier **NCT03064854** in the search field.

Full clinical trial title: Phase Ib, multicenter, open label study of PDR001 in combination with platinum doublet chemotherapy and other immunooncology agents in PD-L1 unselected, metastatic NSCLC patients

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

NOVARTIS

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

1-888-669-6682 (US); +41-61-324 1111 (EU);
www.novartisclinicaltrials.com