Plasma cell-targeted treatment with daratumumab in ME/CFS

[An unauthorized translation of Plasma cell-targeted treatment with daratumumab in ME/CFS - Helse Bergen HF](https://www.helse-bergen.no/kliniske-studier/plasmacelle-rettet-behandling-med-daratumumab-ved-mecfs/) for readers not living in Norway

The aim of this study is to investigate whether treatment with daratumumab has a clinically beneficial effect on symptoms in patients with moderate to severe ME/CFS compared with placebo, and to obtain further data on tolerance and side effects.

## About the study

We have conducted an initial pilot study in which 14 patients with moderate to severe ME/CFS received treatment with the drug daratumumab, an antibody that acts on the mature plasma cells of the immune system. The participants in the pilot study have tolerated the medicine well, and several patients experienced a significant improvement in their symptoms. We are therefore conducting this study, where we compare the effect of daratumumab and placebo (injections with saline).

The main aim is to investigate whether injections with daratumumab have a clinical effect on symptoms in patients with moderate to severe ME/CFS. We also want to investigate whether the patients tolerate the treatment well and therefore record any side effects. To get the most reliable answer possible on how well the medicine works, one third of the participants will receive injections of saline (placebo). A computer program will randomly divide the participants into groups, and neither you nor the researchers will know which medicine you have received until the end of the study.

Information about participation - The study is open for recruitment from 06.06.2025 until 01.12.2026

## Who can participate?

To participate in the study, you must be diagnosed with ME/CFS according to the Canada criteria from 2003. You must be between 18 and 64 years of age, with a disease duration of at least two years. The degree of illness must be from moderate (essentially housebound) to severe (essentially bedridden). In addition, the ME/CFS disease must have started at a defined time, typically after an infection.

In order to apply and participate the patients need to read an information page and sign a consent form.

## Information and consent form KTS-11.pdf

Initial information to the patient and her GP is provided as follows:

## General practitioner information

The patient must be diagnosed with ME/CFS according to Canadian diagnostic criteria, and other possible causes of the symptoms must have been excluded as part of the investigation.

### Inclusion criteria:

1. ME/CFS according to Canadian criteria; severity moderate (mainly housebound) to severe (partially bedridden)

2. Age 18 to 64 years.

3. Signed informed consent.

4. Duration of ME/CFS disease at least two years.

5. A defined time of onset of ME/CFS, after a triggering infection or other immunological event.

6. For women of childbearing age: Negative pregnancy test.

7. Women of childbearing age must use a highly reliable method of contraception from at least four weeks before the first treatment until 24 weeks after the last treatment in the study.

8. Baseline NK cell count must be ≥ 125 x109/L

### Exclusion criteria:

1. Very severe ME/CFS, where the patient cannot travel to hospital for assessment and treatment.

2. Participation in a clinical trial with drug intervention aimed at ME/CFS in the last three years.

3. Hypogammaglobulinemia (serum IgG < 5.0 g/L at baseline)

4. Endogenous depression

5. Known multi-allergy with clinically assessed risk of hypersensitivity to daratumumab.

6. Known contraindication to daratumumab.

7. Significant comorbidity including reduced organ function (kidney, liver, heart, lungs, blood)

8. Use of long-term systemic treatment with immunosuppressive agents in the last two years, except short-term steroid treatment for e.g. obstructive pulmonary disease.

9. Chronic infection, including chronic hepatitis B or C, HIV, or other relevant infection.

10. Previous or current malignant disease, with the exception of basal cell carcinoma of the skin or precancerous lesions (carcinoma in situ) of the cervix.

11. Pregnancy or breastfeeding

12. Inability to complete the study including follow-up according to the protocol.

## What does the study involve?

Potential candidates for the study are asked to complete a set of questionnaires online, and then undergo a medical examination with a clinical examination, interview and blood tests to rule out other diseases or a weakened immune system. If you are included in the study, physical tests will also be carried out before and towards the end of the study to record any changes. We adapt the physical tests as best we can to the individual participant's activity level and tolerance. Both initial and final examinations in the study will be carried out at Haukeland University Hospital.

The total duration of the study for each participant is 72 weeks. Throughout the study, we will ask you to regularly answer questionnaires in the study portal, as well as to use a Fitbit watch to record your activity level (number of steps per day and heart rate). You fill out the form from home in a secure online portal, and you will be given your own username and password for this. To map your "normal" symptom and activity pattern, you will not receive active treatment for the first 12 weeks of the study, but will only record symptoms and activity. After that, treatment will start with either active medicine or placebo.

Assessment, sampling and physical examinations are carried out in the Cancer Clinic at Haukeland University Hospital. Treatment is given at the Clinical Research Post at Haukeland, or at the Cancer Department's outpatient clinic at Radium Hospital. We give daratumumab as an injection under the skin of the abdomen three times with two-week intervals, and then twice after 24 and 26 weeks. We take blood tests before each treatment, and a doctor or nurse will record whether you have experienced side effects since the last one. When you have finished treatment, you will have regular follow-up conversations with the study nurse (by telephone) and you will also be called in for two doctor's consultations with blood tests and physical examinations.

Total duration of the study from inclusion to the last visit will be approximately 17 months. After this, we will ask you to participate in a telephone conversation and fill out a form once every six months for three years after the start.

This study is funded by private donations and funds collected by patients and patient associations for research into the treatment of ME/CFS. We do not provide any compensation to participants in the study. There is no deductible for visits or treatments at the hospital. Parking at Haukeland University Hospital is free, and reimbursement for travel expenses can be sought from Patient Travel at the usual rates.