

## **COVER PAGE**

# **INFORMED CONSENT (DETECT)**

**29.3.2017**

**NCT03192020**

**TRIAL NOTICE*****Trial on the treatment strategy of Dupuytren's contracture***

The trial name in English:	DupuytrEn Treatment EffeCtiveness Trial (DETECT): prospective, randomised, controlled, outcome assessor-blinded, three armed parallel 1:1:1, multicentre trial comparing efficacy and cost-effectiveness of collagenase clostridium histolyticum, percutaneous needle fasciotomy and limited fasciectomy as a short- and long-term treatment strategy in mild or moderate Dupuytren's contracture
Trial code:	5.5
EudraCT number:	2016-005215-41

***Request to take part in the trial***

You have been diagnosed with Dupuytren's contracture that requires treatment. You are requested to take part in the trial aiming to assess the long-term results of three different treatment approaches. Each form of treatment has been in use for a long time, but there is a shortage of comparative studies on their long-term results. The forms of treatment to be studied are 1) collagenase clostridium histolyticum injection to dismantle the affected fascia, 2) percutaneous needle fasciotomy of the affected fascia and 3) surgical limited fasciectomy. We have assessed that you would be a suitable candidate for the trial because the fascia contracting your finger(s) causes an extension deficiency meeting the treatment criteria. You also meet the other admittance criteria of the trial, and there are no reasons to exclude you. This notice describes the trial and your possible part in it.

***Voluntary participation***

Participation in this trial is voluntary. You may refuse to take part in the trial, discontinue your participation or cancel your consent without any justification at any point of the trial without any effect on your right to receive the treatment you need.

You do not need to take part in this trial in order to receive treatment. Your doctor will explain the treatment options for your disease to you.

Read this notice carefully. If you have any questions, you may contact the researcher doctor or other trial personnel (the contact information are provided at the end of this document). If you decide to participate in the trial, you are requested to sign the consent form provided on the last page.

***Executors of the trial***

This trial is executed by the university central hospitals of Helsinki, Kuopio, Oulu, Tampere and Turku, Central Finland Central Hospital and Tampere Hatanpää Hospital. The trial is coordinated by Tampere University Central Hospital. The person in charge of the trial is Doctor of Medicine (MD) Olli Leppänen. The person in charge at Helsinki University Central Hospital is MD Susanna Stjärnberg-Salmela, at Kuopio Licentiate of Medicine (ML) Minna Lappalainen, at Oulu ML Janne Soikkeli, at Tampere ML Antti Kaivorinne and at Turku MD Markus Pääkkönen, at Central Finland Central Hospital MD Teemu Karjalainen and at Tampere Hatanpää Hospital ML Niina Ruopsa. The ordering party is Tampere University Hospital. The controller of the trial is Tampere University

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Hospital and the person in charge is MD Olli Leppänen, who ensures the lawfulness of personal data processing taking place in connection with the trial.

### **Background and purpose of the trial**

The objective of this trial is to determine which of the three treatment forms is the most efficient in the treatment of Dupuytren's contracture in long-term monitoring. In addition, the aim is to determine the most cost-effective treatment form.

The studied drug (Xiapex®) is a pharmaceutical preparation, which has been used in the treatment of Dupuytren's contracture in Finland since 2011. Xiapex® is manufactured from the collagenase enzyme produced by the bacterium *Clostridium histolyticum* that dismantles the affected fascia. The percutaneous needle fasciotomy of the affected fascia and the surgical procedure involving limited fasciectomy have been used in the treatment of Dupuytren's contracture for over 100 years. The effect and tolerance of all three treatment forms have been studied before, but the three treatments have not been previously compared against each other. The trial is considered necessary because it is not known, which of the treatment forms offers the best long-term result for patients.

Several thousands of patients have been treated with the above-mentioned treatment forms in Finland.

Persons who are between the ages of 18 and 79, affected by an extension deficiency of over 20° due to Dupuytren's contracture in one or more fingers, the contracting fascia of whom can be identified by touching and who can answer questionnaires in Finnish are requested to participate in the trial. The exclusion criteria of the trial are a recurred disease, nervous system disease having an impact on the finger to be treated, contraindication to the Xiapex® drug, pregnancy or breastfeeding, extension deficiency exceeding 135° in the finger to be treated, rheumatoid arthritis or a previous fracture in the finger to be treated having an impact on the range of motion of the proximal phalanx or middle phalanx.

The aim of the trial is to involve approximately 300 research subjects from Finland.

### **Research methods and procedures**

The participation in the trial lasts approximately 10 years.

The trial involves approximately 6–8 visits at the reception. The trial personnel may also contact you by phone.

The trial will be implemented so that the trial participation will be mapped during the first visit at the reception. The trial notice and patient consent you have received by post. The doctor-in-charge of the research centre will call the trial nurse of the centre coordinating the trial who will perform the randomisation. The probability of each treatment form is 1/3 in the randomisation. The injection treatment or percutaneous needle fasciotomy of the affected fascia will be performed during the same visit. In the injection treatment, the finger will be extended in 1–3 days following the administration of the injection. The appointment for the extension will be given to you during the first visit. If your form of treatment is surgery, the time of your surgery will be given to you during the first visit.

According to the normal treatment practice, a follow-up visit will take place 3 months after the treatment of Dupuytren's contracture. For trial purposes, follow-up visits will also be programmed to take place 2, 5 and 10 years after the treatment. In addition, you are asked to fill in questionnaires measuring your quality of life and the functional ability of the hand as a part of the

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trial. During the follow-up visit, the assessor of the treatment result will not be aware of your treatment form. A protective glove will be used to cover the treated hand before the follow-up visit so that the person assessing the treatment result will not become aware of which of the three treatments has been implemented while performing the examination. If the injection treatment fails to provide the desired treatment result (extension deficiency of under 20°), the treatment can be repeated twice. In case the disease recurs and causes during the monitoring period an increase of extension deficiency of over 20° by the 3-month follow-up visit, the treatment selected for you may be repeated. In that case, you may also select the surgical treatment instead of the subcutaneous treatments.

After all the treatments, you will be fitted with a night-time splint for two months that will keep the treated finger(s) extended.

Because the effects of the trial drug (Xiapex®) are not fully known among those who are pregnant or breastfeed, those who are pregnant, breastfeed or plan a pregnancy cannot take part in this trial.

***Possible benefits of the trial***

It is possible that you will not benefit from taking part in this trial, even if there is clear proven evidence of the benefit of each treatment form in the decreasing of the extension deficiency of the finger. Useful information may also be gained from the studied disease. The trial results can be seen from the articles that will be published about the trial. If necessary, we will provide you with the articles or assist in finding them.

***Possible disadvantages of and inconveniences caused by the trial***

The treatment forms applied in the trial are well established, and disadvantages are more or less equally common in all the treatment forms according to current knowledge. The most common disadvantages (more than one in ten patients) of the trial treatment forms include a skin laceration, hematoma, redness and swelling of the procedure area, pain and tenderness, itching, a burning sensation, partial loss of the sense of touch, tingling or numbness. In addition, the Xiapex drug may cause enlarged and cystic lymph nodes. The rare, severe side effects (less than one in hundred patients) include tendon rupture, neural and vascular injury, reflex sympathetic dystrophy, severe hematoma or inflammation caused by the procedure.

The researcher doctor can inform you of the other possible disadvantages.

If during the trial new information on the treatment forms essential to your safety or the continuation of the trial is gained, the researcher doctor will contact you immediately and discuss with you whether you wish to continue in the trial.

***Information confidentiality and privacy protection***

In the course of the trial, your identity is only known by the trial personnel, and they are all obligated to maintain secrecy. All the information collected about you and all the samples taken from you will be processed in a coded format, and your individual information will not be recognisable from the trial results, reports or publications that are related to the trial.

Only personal data necessary in view of the purpose of the trial will be recorded in the trial register. Your name, personal identity code and contact information will be kept on the server of the ordering party of the trial. In the trial results and other documents, you will only be referred to as an identification code. The register is kept on the server of the ordering party of the trial for 15

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years after the end of the trial. A file description according to the Personal Data Act has been prepared on the trial register, and you can review the file description upon request.

Information regarding your health and essential to the trial may also be collected with your consent from the other health care units (Finnish primary health care and private health care units) and person registers containing health records (My Kanta). In such a case, the researcher doctor may acquire the required information with the help of your personal identity code. In Finland, the authority for regulating pharmaceuticals (Finnish Medicines Agency Fimea) is entitled to verify that the trial has been implemented in an appropriate manner. Foreign authorities for regulating pharmaceuticals and representatives of the ordering party of the trial may also perform inspections. In order to confirm the correctness of the trial data, it is compared against the original patient records among other things. In such cases, the data is processed under the supervision and responsibility of the researcher doctor or some other member of the trial personnel. The data can also be handed over to the pharmaceuticals authority for a safety assessment of the drug. In all cases, your data will be processed confidentially.

Your data may also be handed over to some other researcher for the original purpose. In that case as well, all parties are bound by the above-mentioned confidentiality obligations. The data will not be handed over to any other parties, e.g., the pharmaceutical industry or insurance company.

Scientific journals publishing the articles may require that the trial data is available for the scientific assessment of the results.

If you decide to cancel your consent, the data collected up to the time of cancellation will be used as a part of the trial data. It is necessary in order to confirm the trial results.

### ***Trial costs and financial reports***

The trial drug and trial-related procedures are free of charge to you.

The funding of the trial is ensured by associations and foundations. In addition, financing has been applied from the State Research Funding and will be applied from the Academy of Finland. Financing will not be offered by or applied from the private sector. The available grants will be used to pay the trial-related costs and a reasonable compensation to the researcher doctors for their time. Biostatistician Hannu Kautiainen will work in the trial via Medcare Oy, and MD, Docent Antti Malmivaara is employed by the National Institute for Health and Welfare. The other researchers are employed by the centres participating in the trial. The researchers do not have any other engagements or interests.

### ***Insurance cover of the trial subjects***

If the trial drug or procedure performed in the trial causes you a personal injury, you can apply for compensation.

In the case of a trial drug-related injury, the compensation is applied from the Pharmaceutical injuries insurance. The Pharmaceutical injuries insurance compensates for unexpected injuries caused by the trial drug according to the specific preconditions of the insurance terms.

In the case of other personal injuries caused by the trial procedures, compensation is applied from the insurance against treatment injury of the research centre in question. It compensates for personal injuries caused in connection with health care procedures according to the preconditions of the Patient Injuries Act. The Patient Insurance Centre ensures the compensation processing of patient injuries.

**End of the trial**

The researcher doctor or the ordering party of the trial may also be forced to discontinue your participation prematurely. If this were to take place, the procedures involved in the discontinuation would be discussed with you.

**Further information**

If you have any questions about the trial, you may contact the researcher doctor or other trial personnel.

You can discuss with them all side effects and suspicious symptoms that may manifest during the trial and all other matters occupying your mind.

Contact information:

Junior Researcher, ML, eMBA Mikko Räisänen, Tampere University Central Hospital, P. O. Box 2000, FI-33521 Tampere, +358 3 311 611, mikko.raisanen@pshp.fi

Person in charge of the trial, MD Olli Leppänen, Tampere University Central Hospital, P. O. Box 2000, FI-33521 Tampere, +358 3 311 611, olli.leppanen@pshp.fi

Person in charge of the trial, MD Teemu Karjalainen, Central Finland Central Hospital, Keskussairaalantie 19, FI-40620 Jyväskylä, +358 14 269 1811, teemu.karjalainen@ksshp.fi

Trial Nurse, Nurse Seija Rautiainen, Tampere University Central Hospital, P. O. Box 2000, FI-33521 Tampere, +358 3 311 611, seija.rautiainen@pshp.fi

**TRIAL CONSENT**

I have been requested to participate in the trial concerning the treatment strategy of Dupuytren's contracture (EudraCT number 2016-005215-41).

I have read the above notice and received sufficient information about the trial and the collection, processing and handling over of information that will take place in its connection. The contents of the trial have also been explained to me verbally, and I have received adequate answers to all my trial-related questions. The clarifications were provided by \_\_\_\_\_. I have had sufficient time to consider my participation in the trial.

I understand that my participation in this trial is voluntary. I am entitled to discontinue my participation in the trial or cancel my consent to take part in the trial at any point of the trial without any justification. The discontinuation of the trial or cancellation of my consent will not cause any negative consequences to me and has no impact on my status as a health care client. I am aware that the data collected up to the point of my discontinuation or cancellation of consent will be used as part of the trial documentation and safety assessment of the drug.

**With my signature I confirm that I will participate in the trial described in this document and I give my voluntary consent for becoming a trial subject. I give my consent to retrieving my information from My Kanta. I give my consent to the processing of my personal data in connection with an inspection carried out by a foreign authority and quality assurance activities carried out by a representative of the ordering party.**

\_\_\_\_\_  
*Signature*

\_\_\_\_\_  
*Date*

\_\_\_\_\_  
*Name in print*

\_\_\_\_\_  
*personal identity code*

\_\_\_\_\_  
*Date of birth or*

\_\_\_\_\_  
*Address*

**Consent received**

\_\_\_\_\_  
*Signature of the consent recipient*

\_\_\_\_\_  
*Date*

\_\_\_\_\_  
*Name in print*

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The original signed document will be kept in an archive of the researcher doctor, and a copy will be provided to the trial subject.