Clinical trial results:
A pragmatic multi-centre randomised controlled non-inferiority, cost effectiveness trial comparing injections of collagenase into the cord to surgical correction in the treatment of moderate Dupuytren's Contracture in adult patients.

Summary

EudraCT number	2016-004251-76
Trial protocol	GB
Global end of trial date	31 July 2022

Results information

Result version number	v1 (current)
This version publication date	12 June 2025
First version publication date	12 June 2025

Trial information

Trial identification

Sponsor protocol code	87230

Additional study identifiers

ISRCTN number	ISRCTN18254597
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University Hospitals of Leicester NHS Trust
Sponsor organisation address	Trust HQ, Level 3 Balmoral Building, Leicester Royal Infirmary, Leicester, United Kingdom, LS1 5WW
Public contact	Catherine Arundel, York Trials Unit, University of York, catherine.arundel@york.ac.uk
Scientific contact	Catherine Arundel , York Trials Unit, University of York, catherine.arundel@york.ac.uk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2022
Global end of trial reached?	Yes
Global end of trial date	31 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate whether collagenase injection is as good as surgery (limited fasciectomy) in the correction of Dupuytren’s contracture of the hand

Protection of trial subjects:

Treated in routine UK NHS Care

Background therapy:

Not applicable

Evidence for comparator:

Dupuytren’s disease affects over 2 million UK adults; cords pull the fingers down towards the palm. This interferes with hand function and dexterity, impacting on quality of life.
Current treatments to remove, dissolve or break the cords include surgical correction (limited fasciectomy), collagenase injection (an enzyme injected into the cord), and percutaneous needle fasciotomy (a needle is used to puncture, weaken, and cut the cord). None of these treatments cure the tendency to develop DC and so the cords and contracture can recur over time.
Collagenase has some benefits over limited fasciectomy (LF) surgery including shorter recovery and no dependence on operating theatre availability for delivery of the intervention. There is, however, limited robust evidence comparing surgical correction and collagenase injection in terms of clinical effectiveness, cost effectiveness and in terms of patient’s experiences and preferences.

Actual start date of recruitment	01 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 672
Worldwide total number of subjects	672
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	268
From 65 to 84 years	396
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

The DISC trial was a multicenter, open-label, pragmatic, parallel two-arm randomized controlled non-inferiority trial. The 31 recruiting sites were UK National Health Service hand units. Participants were recruited from 31st July 2017 to 28th September 2021.

Pre-assignment

Screening details:

Patients aged 18 years and over with a discrete, palpable Dupuytren's cord causing contracture of ≥30° and who were appropriate for both study treatments were eligible for inclusion.

Period 1

Period 1 title	Intervention (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Given the pragmatic nature of the trial, and the surgical and injection interventions used, it was not possible to blind clinicians or participants to study allocation. It was also not possible to blind the analysing statistician to trial allocation due to the way in which data were collected. To mitigate any impact of this, a statistical analysis plan (available at: https://www.isrctn.com/ISRCTN18254597) pre-specified all analyses and any changes made to the data set prior to analysis were docu

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention - Collagenase Clostridium Histolyticum

Arm description:

Collagenase clostridium histolyticum

Arm type	Experimental
Investigational medicinal product name	Collagenase Clostridium Histolyticum
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Injection

Dosage and administration details:

Depending on the cord affected 0.25ml or 0.20ml of reconstituted solution (0.58mg Collagenase Clostridium histolyticum) was injected as three aliquots: 0.25ml for cord in a metacarpophalangeal joint, 0.20ml for cord in a proximal interphalangeal joint.

The three aliquots were distributed via injection into an affected cord at set anatomical points through a single needle puncture at a single time point. If separate cords were to be injected at the same treatment visit, this was be permitted but a reference cord (i.e. predominant) must be identified.

Arm title	Control - Limited Fasciectomy

Arm description:

Limited Fasciectomy

Arm type	Active comparator
Investigational medicinal product name	Surgical Intervention
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Unknown use

Dosage and administration details:

The control treatment for the DISC trial was limited fasciectomy, a standard technique in Europe for

treatment of Dupuytren’s contracture. This procedure involves the removal, under anaesthesia, of the diseased fascia, nodule and cord, or a part of it, to correct the contracture of the joint. Tourniquet control may be used if required.

Number of subjects in period 1	Intervention - Collagenase Clostridium Histolyticum	Control - Limited Fasciectomy
Started	336	336
Completed	324	286
Not completed	12	50
Consent withdrawn by subject	4	23
Received a non trial treatment	1	2
Received intervention treatment instead	-	7
Treatment not delivered	6	18
Received control treatment instead	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Intervention - Collagenase Clostridium Histolyticum
Reporting group description: Collagenase clostridium histolyticum	
Reporting group title	Control - Limited Fasciectomy
Reporting group description: Limited Fasciectomy	

Reporting group values	Intervention - Collagenase Clostridium Histolyticum	Control - Limited Fasciectomy	Total
Number of subjects	336	336	672
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	67.4	66.9	
inter-quartile range (Q1-Q3)	61.0 to 72.7	61.3 to 72.8	-
Gender categorical Units: Subjects			
Male	270	263	533
Female	66	73	139

Subject analysis sets	
Subject analysis set title	Primary Analysis - Intervention Group
Subject analysis set type	Intention-to-treat
Subject analysis set description: Primary analysis subject set 314 intervention participants who provided primary outcome data that contributed to the primary analysis	
Subject analysis set title	Primary Analysis - Control Group
Subject analysis set type	Intention-to-treat
Subject analysis set description: Primary outcome analysis of 285 control participants who provided primary outcome data that contributed to the primary analysis,	

Reporting group values	Primary Analysis - Intervention Group	Primary Analysis - Control Group	
Number of subjects	314	285	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
median	66.8	66.8	
inter-quartile range (Q1-Q3)	60.3 to 72.6	61.7 to 72.6	
Gender categorical Units: Subjects			
Male	256	219	
Female	58	66	

End points

End points reporting groups

Reporting group title	Intervention - Collagenase Clostridium Histolyticum
Reporting group description: Collagenase clostridium histolyticum	
Reporting group title	Control - Limited Fasciectomy
Reporting group description: Limited Fasciectomy	
Subject analysis set title	Primary Analysis - Intervention Group
Subject analysis set type	Intention-to-treat
Subject analysis set description: Primary analysis subject set 314 intervention participants who provided primary outcome data that contributed to the primary analysis	
Subject analysis set title	Primary Analysis - Control Group
Subject analysis set type	Intention-to-treat
Subject analysis set description: Primary outcome analysis of 285 control participants who provided primary outcome data that contributed to the primary analysis,	

Primary: PRIMARY OUTCOME Change in PEM score between Baseline and 1 year post treatment

End point title	PRIMARY OUTCOME Change in PEM score between Baseline and 1 year post treatment
End point description: The primary endpoint was the score obtained for the 11 items in part two of the PEM at 1 year after treatment (0 – 100, with higher scores indicating worse outcome).	
End point type	Primary
End point timeframe: Change in score between Baseline and 1 year post treatment	

End point values	Intervention - Collagenase Clostridium Histolyticum	Control - Limited Fasciectomy	Primary Analysis - Intervention Group	Primary Analysis - Control Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	314	285	314	285
Units: Patient reported outcome measure - PEM	314	285	314	285

Statistical analyses

Statistical analysis title	Primary outcome analysis - Analysis Sets

Statistical analysis description:

A covariance pattern model, with all PEM measurements taken after treatment included as outcomes, was used to estimate the between group differences (Collagenase – LF) in expected PEM score at each time point after treatment. Treatment group and time point and their interaction were included as fixed effects. This model also included fixed effects for study reference joint (stratification factor) and baseline PEM score and a random intercept of recruiting site

Comparison groups	Primary Analysis - Intervention Group v Primary Analysis - Control Group
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.49
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	8.8

Statistical analysis title	Primary outcome analysis - Reporting Groups

Statistical analysis description:

A covariance pattern model, with all PEM measurements taken after treatment included as outcomes, was used to estimate the between group differences (Collagenase – LF) in expected PEM score at each time point after treatment. Treatment group and time point and their interaction were included as fixed effects. This model also included fixed effects for study reference joint (stratification factor) and baseline PEM score and a random intercept of recruiting site

Comparison groups	Intervention - Collagenase Clostridium Histolyticum v Control - Limited Fasciectomy
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.49
Method	t-test, 1-sided
Parameter estimate	Mean difference (final values)
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	8.8

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 24 months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10
Reporting groups	
Reporting group title	Intervention - Collagenase Clostridium Histolyticum
Reporting group description: Collagenase clostridium histolyticum	
Reporting group title	Control - Limited Fasciectomy
Reporting group description: Limited Fasciectomy	

Serious adverse events	Intervention - Collagenase Clostridium Histolyticum	Control - Limited Fasciectomy	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 324 (2.47%)	0 / 286 (0.00%)	
number of deaths (all causes)	8	0	
number of deaths resulting from adverse events	0		
Surgical and medical procedures			
Complications following unrelated surgery			
subjects affected / exposed	2 / 324 (0.62%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	2 / 2	0 / 0	
Nervous system disorders			
Brain Hemorrhage			
subjects affected / exposed	1 / 324 (0.31%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Social circumstances			
Pre-existing medical condition (information unknown)			
subjects affected / exposed	1 / 324 (0.31%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

No information available			
subjects affected / exposed	1 / 324 (0.31%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Lung cancer			
subjects affected / exposed	1 / 324 (0.31%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 324 (0.62%)	0 / 286 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Intervention - Collagenase Clostridium Histolyticum	Control - Limited Fasciectomy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	207 / 324 (63.89%)	157 / 286 (54.90%)	
Surgical and medical procedures			
Amputation			
subjects affected / exposed	0 / 324 (0.00%)	1 / 286 (0.35%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	1 / 324 (0.31%)	1 / 286 (0.35%)	
occurrences (all)	1	1	
Delayed discharge			
subjects affected / exposed	0 / 324 (0.00%)	1 / 286 (0.35%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pain Swelling and Stiffness			
subjects affected / exposed	70 / 324 (21.60%)	48 / 286 (16.78%)	
occurrences (all)	70	48	

Instability			
subjects affected / exposed	1 / 324 (0.31%)	0 / 286 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 324 (0.31%)	0 / 286 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	1 / 324 (0.31%)	0 / 286 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Circulation or Bleeding			
subjects affected / exposed	46 / 324 (14.20%)	13 / 286 (4.55%)	
occurrences (all)	46	13	
Raynauds			
subjects affected / exposed	2 / 324 (0.62%)	5 / 286 (1.75%)	
occurrences (all)	2	5	
Lymph related			
subjects affected / exposed	5 / 324 (1.54%)	0 / 286 (0.00%)	
occurrences (all)	5	0	
Skin and subcutaneous tissue disorders			
Scar skin or wound related (excluding infection)			
subjects affected / exposed	59 / 324 (18.21%)	36 / 286 (12.59%)	
occurrences (all)	59	36	
Nerve related			
subjects affected / exposed	18 / 324 (5.56%)	42 / 286 (14.69%)	
occurrences (all)	18	42	
Complex regional pain syndrome			
subjects affected / exposed	0 / 324 (0.00%)	2 / 286 (0.70%)	
occurrences (all)	0	2	
Puritis			
subjects affected / exposed	3 / 324 (0.93%)	1 / 286 (0.35%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Cubital tunnel or carpal tunnel			
subjects affected / exposed	3 / 324 (0.93%)	2 / 286 (0.70%)	
occurrences (all)	3	2	

Infections and infestations Wound infection subjects affected / exposed occurrences (all)	 0 / 324 (0.00%) 0	 6 / 286 (2.10%) 6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 July 2018	Amendment to study to implement revised (updated) Simplified Product Characteristics (SmPC) document for the associated IMP (Xiapex). The changes made to the SmPC were as follows: - Addition of a further uncommon event to the list of adverse reactions for Dupuytren's Contracture (General disorders and administration site conditions - Cold intolerance to treated fingers) - Reformatting of Annex 1 - Section 6.6 to separate information relating to reconstitution of the IMP for Peyronies disease and Dupuytren's contracture (This amendment did not impact on the DISC Trial)
16 October 2018	Amendments made to study protocol requiring regulatory authority approval. This substantial amendment included changes to the protocol, to improve recruitment conversion rates and pathways and to reduce the activity burden on study sites, and to the PIS to reflect amendments made to the protocol and to include GDPR transparency information.
14 July 2020	This substantial amendment included revisions to monitoring plan for the study (as originally detailed in the DISC MHRA Risk Assessment and Safety Monitoring) and a revised (updated) Simplified Product Characteristics (SPC) for the study IMP (Xiapex). Changes to the SPC, relevant to Dupuytren's Contracture inclued: - Addition of further precautions, for use in treatment of Dupuytren's contracture (i.e. reported cases of finger necrosis linked to pre-existing reduced peripheral circulation; cases of digital phalangeal fractures following finger manipulation in patients with bone fragility) and Peyronie's disease (i.e. to reduce risk of Corporal rupture) (Annex 1 - Section 4.4) - Addition of a further two events to the list of adverse reactions for Dupuytren's contracture of an unknown incidence (i.e. digital necrosis and digital fracture). - Combining of information relating to treatment area selection for Peyronie's disease and Dupuytren's contracture (Annex 1 – Section 6.6) - Addition of information to the patient leaflet warning of the risk of finger necrosis or fracture and advising patients to inform their doctor if they have a condition affecting their bones. Addition of side effects for Dupuytren's contracture where frequency is not known (i.e. fractures finger and loss of finger or finger parts) (Annex III – Section B) - Reformatting of the order of information for healthcare professionals (Annex III – Section B)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
19 March 2020	Pause to recruitment activity across all sites due to impacts of the SARS COV-19 (COVID-19) pandemic. Recommencement of activity at individual sites was assessed and agreed with local governance before activity recommenced.	15 July 2020

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/39383454

http://www.ncbi.nlm.nih.gov/pubmed/39644138