

# Prospective randomised sibling-oocyte study using recombinant human hyaluronidase Cumulase® versus Sigma hyaluronidase in intracytoplasmic sperm injection patients

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<b>Registration date</b> 27/06/2007	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 25/10/2021	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

EudraCT/CTIS number

IRAS number

**ClinicalTrials.gov number**

**Secondary identifying numbers**

Protocol number: HZ2-05-07, NL953 (NTR979)

## **Study information**

### **Scientific Title**

Prospective randomised sibling-oocyte study using recombinant human hyaluronidase Cumulase® versus Sigma hyaluronidase in intracytoplasmic sperm injection patients

### **Study objectives**

Non-inferiority trial in order to evaluate the effectiveness of the new compound (recombinant human hyaluronidase or Cumulase®), effectiveness being defined by intactness after Intracytoplasmic Sperm Injection (ICSI) and fertilisation rate.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approval received from the local medical ethics committee (Academisch Ziekenhuis - Vrije Universiteit Brussel) on the 2nd March 2006 (ref: Protocol HZ2-05-07, version 1.0 dd. 27/12 /2005).

### **Study design**

Randomised, active controlled, parallel group trial

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Not specified

### **Study type(s)**

Treatment

### **Participant information sheet**

### **Health condition(s) or problem(s) studied**

Intracytoplasmic Sperm Injection (ICSI), Hyaluronidase

### **Interventions**

Oocyte collection and denudation:

At the moment of oocyte retrieval (day 0), sibling Cumulus Oocyte Complexes(COC's) were allocated to two separate oocyte collection dishes in an alternating way. A computer generated random list (balanced blocks of six) was used for allocation of the first dish to either Cumulase® or bovine hyaluronidase denudation.

Collection and denudation of the oocytes was done in Hepes buffered Human Tubal Fluid (HTF) medium (Cambrex Bioscience, Verviers, Belgium) supplemented with Synthetic Serum Supplement (SSS) (Irvine Scientific, Wicklow, Ireland). Cumulase® denudation (Halozyme Therapeutics Inc., San Diego, USA) involved incubation in 80 U/ml, including Pasteur pipetting of all sibling COCs together (time of incubation to be determined during the study). When most of the cumulus was removed, oocytes were rinsed twice in HTF medium prior to further mechanical decoronation in the absence of the enzyme. The level of additional mechanical stripping was quantified by counting the number of times that individual oocytes had to be pipetted in and out of a small hand-made pipette (inner diameter 135 µm) using a Swemed pipette holder (Vitrolife, Kungsbacka, Sweden). Denudation in bovine hyaluronidase (Type VIII, Sigma Chemical Company, St Louis, USA) was done similarly except for using a 40 U/ml concentration of the enzyme, because of long-term laboratory experience with this concentration. Incubation time and level of mechanical stripping were evaluated similarly.

Incubation time of the cumulus oocyte complexes was 62 and 63 seconds for Cumulase® and bovine hyaluronidase respectively. Duration of follow up was until positive human Chorionic Gonadotropin (hCG) (i.e. 14 to 17 days post oocyte retrieval).

Baseline outcome measures:

Enzyme incubation time, mechanical denudation and number of mature oocytes available for ICSI are measured at the moment of oocyte denudation, which takes place immediately or  $\pm$  2 hours after oocyte retrieval (day 0). ICSI is performed on mature oocytes immediately after denudation.

### **Intervention Type**

Drug

### **Phase**

Not Specified

### **Drug/device/biological/vaccine name(s)**

Cumulase®, sigma hyaluronidase

### **Primary outcome measure**

1. Oocyte intactness after ICSI, measured  $\pm$  18 - 20 hours after ICSI (day 1 of culture)
2. Fertilisation rate, measured  $\pm$  18 - 20 hours after ICSI (day 1 of culture)

### **Secondary outcome measures**

1. Embryo development:
  - 1.1. Day 3 embryo development is assessed on day 3 of embryo culture
  - 1.2. Day 5 embryo development is assessed on day 5 of embryo culture
2. Positive human Chorionic Gonadotropin (hCG) after embryo transfer, measured in two blood samples given day 14 and day 17 after oocyte retrieval (day 0)

### **Overall study start date**

01/05/2006

### **Completion date**

28/02/2007

# Eligibility

## Key inclusion criteria

Women undergoing ICSI treatment with fresh ejaculate sperm cells, no older than 38 years of age and presenting between 8 and 16 Cumulus Oocyte Complexes (COC's) at ovum pick up.

## Participant type(s)

Patient

## Age group

Adult

## Sex

Female

## Target number of participants

135

## Key exclusion criteria

1. Surgically extracted sperm preparations
2. Embryo biopsy cycles
3. Women older than 38 years
4. Women with less than 8 or more than 16 COC's

## Date of first enrolment

01/05/2006

## Date of final enrolment

28/02/2007

# Locations

## Countries of recruitment

Belgium

Netherlands

## Study participating centre

### Laboratory Director

Brussels

Belgium

B-1090

# Sponsor information

**Organisation**

University Hospital Brussels (Universitair Ziekenhuis Brussel [UZ Brussel]) (Belgium)

**Sponsor details**

Centrum Medische Genetica en Centrum Reproductieve Geneeskunde  
Brussels  
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**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.uzbrussel.be>

**ROR**

<https://ror.org/038f7y939>

**Funder(s)****Funder type**

Industry

**Funder Name**

Halozyne Therapeutics Inc. (USA)

**Funder Name**

University Hospital Brussels (Universitair Ziekenhuis Brussel [UZ Brussel]) (Belgium)

**Results and Publications****Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date****Individual participant data (IPD) sharing plan**

Not provided at time of registration

**IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Abstract results</a>		01/06/2007	25/10/2021	No	No