Abstract title 25: Number of trophoectoderm cells removed for biopsy is correlated with first trimester miscarriage.

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### Study question 50:

Trophectoderm biopsy provides the possibility of removing several cells, which allows more accurate genetic diagnosis by array-CGH. Although it is recommended not to remove more than 10 cells, in many cases, the technique itself makes it difficult. This could affect implantation and miscarriage in early stages, despite being euploid embryos.

#### Summary answer 50:

The removal of more than 10 cells during trophectoderm biopsy increases the rate of miscarriage in the first trimester in euploid embryos after comprehensive chromosome screening (CCS).

## What is known already 75:

Day 3 biopsy is considered to be harmful to the embryo. The risk of misdiagnosis due to mosaicism and the aggression for the embryo decreasing dramatically the implantation rate making it unacceptable. In contrast, trophectoderm biopsy offers the possibility of obtaining several cells without apparent embryo damage. However, we have not enough information to ascertain which is the number of cells that can be drawn without affect clinical outcomes.

## Study design, size, duration 50:

Prospective study. We include the known clinical results of 161 euploid embryos transferred coming from 98 women that underwent CCS treatments from January to September 2014.

## Participants, materials, settings, methods 50:

At least one euploid embryo was transferred to 98 patients. Assisted hatching was performed on day 3 using laser pulses (Saturn Active, Research Instruments). On day 5 of development, conventional trophoectoderm biopsy was done. Images were recorded using Cronus software, and trophoectoderm cells were counted. Clinical outcomes were evaluated.

#### Main results and the role of chance 125:

We removed ≤10 cels in 105 blastocysts (group I), and more than 10 in 56 (group II) according to the hatching of the embryos. These embryos were chromosomally analyzed by array-CGH. Euploidies embryos were transferred on day 6. The global clinical pregnancy rate (sac visualization after 6 weeks of gestation) was 51.8%. There was no statistically significant difference in the clinical pregnancy rate between groups I and II. However, an increase in the first trimester miscarriage was strongly associated with the biopsy of more than 10 cells (6.3 % in group I vs 25% in group II, with an odds ratio 6.45, 95% confidence interval 1.26-32.90).

#### Limitations reasons for caution 50:

Study currently under development to increase the number of cases and test this assertion and to ascertain which is the ideal number of trophoectoderm cells for biopsy.

# Wider implications of the findings 75:

The results obtained in this preliminary study confirm that the cells that give rise to the placenta and extraembryonic tissues play a crucial role in the maintenance of early stages of embryo development. The biopsy of more than 10 cells in the blastocyst stage may be detrimental, perhaps not for the embryo implantation, but for the later development. According to our results we should remove less than 10 cells.