The STAR Trial

A randomized controlled trial (RCT) comparing pregnancy rates following VeriSeq™ PGS versus standard morphology for elective single embryo transfer (eSET)

What is PGS?

Preimplantation genetic screening (PGS), also known as preimplantation genetic testing for aneuploidy (PGT-A), is a test for chromosome copy number that can be used during *in vitro* fertilization (IVF) to help determine the chromosomal status of an embryo from a biopsy of one or more cells. The results of PGS aid in the selection of an embryo likely to have a normal number of chromosomes (euploid) for transfer and help avoid those with abnormal copy number (aneuploid) that may result in IVF failure or miscarriage.[1]

What is VeriSeq PGS?

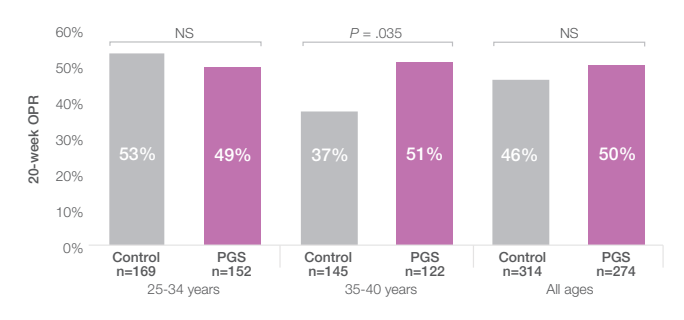
VeriSeq PGS is the Illumina next-generation sequencing (NGS) solution for PGS. VeriSeq PGS provides comprehensive testing for copy number on all 24 chromosomes from the embryo biopsy.

What is the Single Embryo TrAnsfeR of Euploid Embryo (STAR) Trial?[2,3]

- The STAR Trial was an RCT designed to evaluate the effectiveness of VeriSeq PGS to optimize selection of embryos for eSET.
- The primary study outcome was ongoing pregnancy rate (OPR) at 20 weeks gestation in the PGS arm versus standard morphological selection alone in the control arm.
- Key differentiators of this trial
  - Global (4 countries)
  - Multicenter (34 clinical sites and 9 genetic laboratories)
  - One of the largest RCTs undertaken to date in the field of assisted reproduction with over 650 subjects randomized

Results

Figure 1: 20-week ongoing pregnancy rate



NS: not significant

- The primary outcome of the study was the ongoing pregnancy rate at 20 weeks of gestation, which was not significantly different overall between the two study arms (Figure 1).
- Subgroup analysis revealed that the 20-week ongoing pregnancy rate was significantly increased by PGS in women aged 35–40 years but not in women aged 25–34 years.
- All women with an ongoing pregnancy at 20 weeks gestation went on to have a live birth.

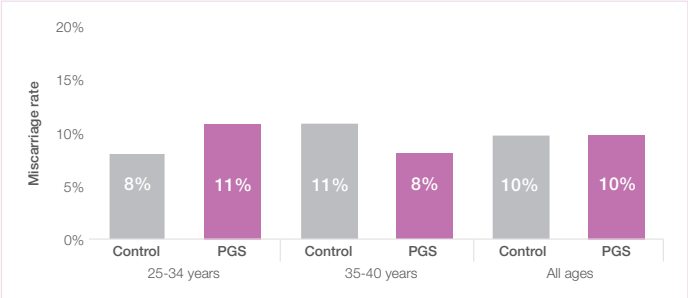
Key takeaways

- While there was no statistically significant improvement in ongoing pregnancy rates in the cohort that included all women, there was a statistically significant improvement in ongoing pregnancy rates of 14% for women aged 35–40 in the PGS arm.
  - Findings are consistent with 2014 Society for Assisted Reproductive Technology (SART) data and other published studies.[4]
- Standardization of clinical and laboratory protocols is recommended for future studies evaluating IVF technologies.

STAR
single embryo transfer of euploid embryo

Results (continued)

Figure 2: Miscarriage rates*



*Miscarriage rate was defined as the loss of a viable intrauterine pregnancy before 20 weeks of gestation.

- There was no significant difference in the overall miscarriage rates between the two study arms (Figure 2).
- The overall miscarriage rates in both groups were low.

Figure 3: Variability in euploid rate by lab

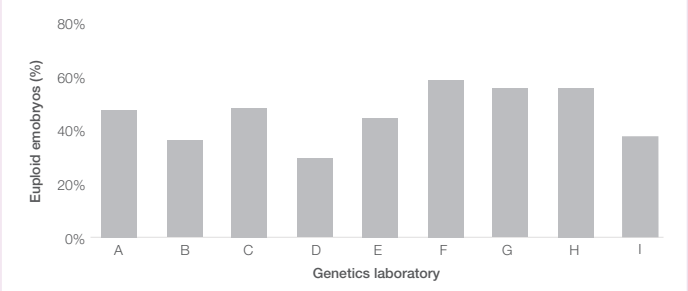
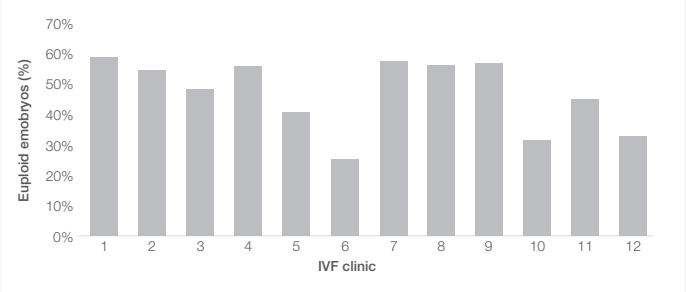


Figure 4: Variability in euploid rate at top-enrolling clinics†



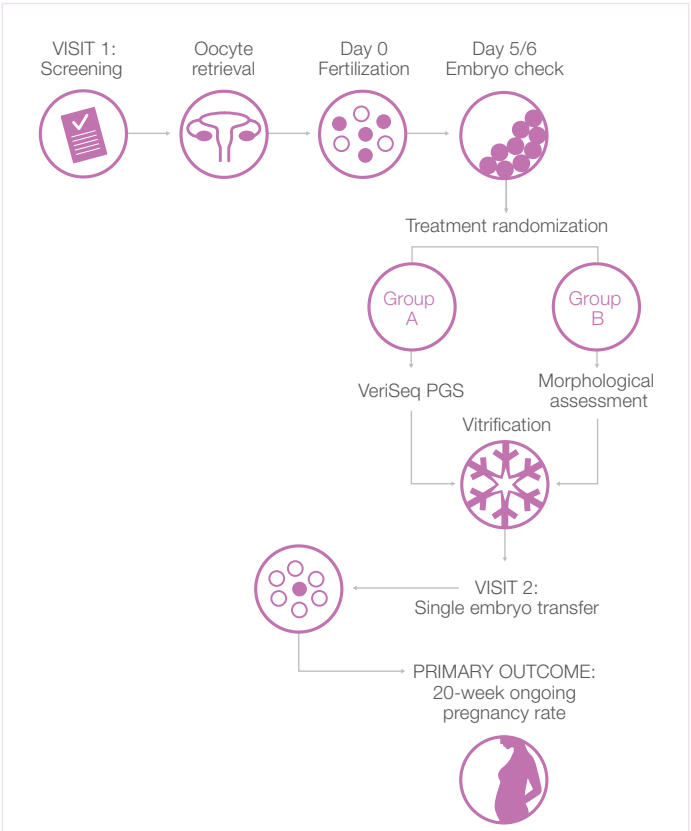
†Top-enrolling clinics had at least 20 embryos transferred.

- Baseline euploid rates were variable among the individual genetics laboratories (range: 30–60%, P = .0081, Figure 3) and IVF clinics (range: 26–60%, P < .001, Figure 4).
- Variability in clinical and laboratory practices as part of the trial may have contributed to the lack of overall significance in the study.

Study design

Inclusion criteria	Exclusion criteria
Female aged 25–40 years	Severe oligospermia and/or surgical requirement for microsurgical sperm retrieval
≤ 2 prior failed IVF cycles	Diminished ovarian reserve
≤ 1 prior miscarriage	Using donor oocyte or gestational carrier
Not a known carrier of a single gene disorder nor a chromosome abnormality	Undergoing preimplantation genetic screening/diagnosis outside of this study

STAR Trial subject flowchart



For questions about the STAR Trial, email MedicalAffairs@illumina.com.

Preimplantation genetic screening (PGS) is a screening test; it is not diagnostic. Aneuploidy screening and diagnostic testing should be offered to all pregnant women following PGS.

1. Rubio C, Bellver J, Rodrigo L, et al. In vitro fertilization with preimplantation genetic diagnosis for aneuploidies in advanced maternal age: a randomized, controlled study. *Fertil Steril*. 2017;107(5):0-7. doi:10.1016/j.fertnstert.2017.03.011. 2. Illumina Inc. Single Embryo TrAnsfeR of Euploid Embryo (STAR), NCT02268786. 2014; clinicaltrials.gov/ct2/show/NCT02268786?id=NCT02268786&rank=1. Accessed August 24, 2017. 3. Munne S, Kaplan B, Frattarelli JL, et al. Global multicenter randomized controlled trial comparing single embryo transfer with embryo selected by preimplantation genetic screening using next-generation sequencing versus morphologic assessment. *Fertil Steril*. 2017;108(3):e19. 4. SART National Summary Report: Preliminary CSR for 2014. 2017. www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?ClinicPKID=0. Accessed April 27, 2017.

Pub. No. 1576-2017-045