1. TITLE (25 words)

Array-CGH vs. FISH for PGS in Recurrent Miscarriage couples

2. Study question (50 words):

Is there a benefit in clinical outcome when performing day-3 biopsy and array-CGH analysis compare fluorescence in situ hybridization (FISH) with a 9 chromosomes panel?

3. Summary answer (50 words):

PGS with array-CGH results in significantly higher implantation and ongoing pregnancy rates per cycle than FISH for nine chromosomes. The better selection of euploid embryos was shown by the fact that with array-CGH, a higher proportion of embryos abnormal for all 23 chromosome pairs were identified and discarded for transfer.

4. What is known already (75 words):

Recurrent miscarriage of unknown etiology occurs in up to 5% of women at reproductive age. Chromosomal abnormalities are present in over 50% of spontaneous miscarriages. Therefore, aneuploidy screening was proposed to improve reproductive outcome of these couples by selecting euploid embryos for transfer. Several studies has been published so far using FISH for different chromosomes, but no comparison with new technologies for comprehensive chromosome screening has been reported.

5. Study design, size, duration (50 words):

Retrospective study performed from January 2010 to December 2012 in couples with 2 or more first trimester miscarriages and negative infertility work-up were included. Female age was below 40 years of age. In 141 cycles chromosomal analysis was done by FISH and 190 cycles by array-CGH.

6. Participants/materials, setting, methods (50 words):

Day-3 embryo biopsies were performed by laser. FISH analysis included probes for chromosomes 13, 15, 16, 17, 18, 21, 22, X and Y (Vysis). Comprehensive chromosome screening was performed by array-CGH (BlueGnome). Embryo transfer was scheduled on day-5. Reproductive outcome was compared between the two groups by Fisher’s exact test.

7. Main results and the role of chance (125 words):

Both groups were comparable in terms of women age (36.0 vs. 36.1 years) and mean number of embryos transferred (1.5 vs. 1.2). Aneuploidy rates were significantly higher in the array-CGH group (67.8 vs. 58.8; p=0.0001), mainly due to abnormalities for chromosomes not included in the FISH panel (18.4% of the embryos had aneuploidy only for chromosomes different from the FISH ones). The better selection of euploid embryos resulted in significantly higher ongoing pregnancy rate per cycle (43.1 vs.
29.8; p=0.0158) and significant increase in implantation rate (36.8 vs. 48.2; p=0.0158; p=0.0324 in the array-CGH group compared to the FISH group.

8. Limitations, reasons for caution (50 words):

This is retrospective study with the intrinsic limitations to draw stronger conclusions. A prospective study could not be designed due to the theoretical superiority attributed and described for comprehensive chromosome screening compared to FISH for a limited number of chromosomes.

9. Wider implications of the findings (75 words):

Despite this is a retrospective study, our results are reassuring in two important aspect: on one side, PGS with array-CGH is offering high ongoing pregnancy rates in this poor reproductive prognosis group of patients; on the other side, improved clinical outcome has been observed when compared with FISH for 9 chromosomes.

10. Study funding/competing interest(s) (30 words): NO

11. Trial registration number (20 words): NO

Autores: Rubio C1,3, Rodrigo L1, Mateu E1, Mercader A2,3, Peinado V1, Buendia P2, Milan M1, Delgado A21, Al-Asmar N4, Escrich L2, Campos-Galindo I1, Poo ME1, Garcia-Herrero S1, Mir P1, Simón C1,2,3,5.

1IVIOMICS Valencia, Spain; 2Instituto Universitario IVI, Valencia; 3INCLIVA, Valencia University; 4IVIOMICS Miami, USA; 5Fundación Instituto Valenciano de Infertilidad (FIVI) Valencia, Spain