BIOPSIES. J. M. Eccles, A. Iturriaga, H. M. Garnsey, J. N. Landis, COMPREHENSIVE CHROMOSOME SCREENING EXPERIENCE WITH A TARGETED NEXT GENERATION SEQUENCING VERSUS MORPHOLOGICAL ASSESSMENT. S. Munne, B. Kaplan, J. L. Frattarelli, M. Gysler, T. J. Child, G. Nakhuda, F. N. Shamama, K. Silverberg, T. Kalista, K. Oliver, M. Katz-Jaffe, D. Wells, T. Gordon, S. Willman. Cooper-Genomics, Livingston, NJ; FCU, Highland Park, IL; Fertility Institute of Hawaii, Honolulu, HI; The Reproductive Care Centre, Mississauga, ON, Canada; Oxford Fertility, Oxford, United Kingdom; Olive Fertility Centre, Vancouver, BC, Canada; REI, IVF Michigan, Bloomfield Hills, MI; Texas Fertility Center, Austin, TX; Illumina, Inc., San Francisco, CA; Colorado Center for Reproductive Medicine, Lone Tree, CO; Reprogenetics, Oxford, United Kingdom; Cooper-Genomics, London, United Kingdom; Reproductive Science Center, Orinda, CA.

OBJECTIVE: The aim of this study was to assess the potential benefit of preimplantation genetic screening (PGS) across multiple international clinical sites and testing laboratories. DESIGN: Blinded, multicenter, randomized, controlled trial of women undergoing IVF with frozen embryo transfer: Control arm: embryo selection based on morphology; intervention arm: embryo selection by next-generation sequencing (NGS)-based PGS. MATERIALS AND METHODS: The study included 323 women aged 25-34, 170 women aged 35-37, and 95 women aged 38-40 years undergoing IVF at multiple clinical sites between 2014 and 2016. Subjects were enrolled from 34 sites in 4 countries, with PGS performed at 9 laboratories. Each clinical site followed its own standard of care for IVF procedures. Each genetics laboratory followed its own internally validated testing and reporting processes, including the reporting of mosaicism. Eligibility criteria included a range of prognostic indicators. Patients were randomized 1:1 on day 5 or 6 of embryo culture. Trophoectoderm biopsy was performed in the intervention arm followed by PGS using the VeriSeq™ PGS Solution (Illumina). In both arms, blastocyst-stage embryos underwent vitrification for single embryo transfer in a later cycle. Mosaic embryos were not replaced. The primary study outcome was ongoing pregnancy rate (OPR) at 20 weeks’ gestation.

RESULTS: A total of 588 eligible women with a mean age of 34 years had an embryo transfer—274 in the PGS arm and 314 in the control arm. The 20 week OPR was 49.6% (136/274) in the PGS arm and 45.9% (144/314; P=0.3369) in the control arm. A post-hoc subgroup analysis revealed that women aged 35-40 had an OPR of 50.8% (62/122) in the PGS arm vs 37.2% (54/145) in the control arm (p=0.0349), with miscarriage rates of 8.2% (10/122) and 11.0% (16/145), respectively.

CONCLUSIONS: This multicenter study, which predominantly enrolled women aged 25 to 34 years, did not replicate earlier, more tightly controlled, single-center studies which showed a benefit of PGS in all patients. These results suggest that standardization of clinical and laboratory protocols is essential for future studies. A benefit with PGS in women 35 years and older, despite the low miscarriage rate in the control arm, is consistent with the 2014 SART data1.

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OBJECTIVE: There is a broad range in the reported frequencies of mosaic and segmental aneuploidies detected in embryo biopsies by NGS-based platforms. Thus, we sought to evaluate the overall test performance of a proprietary tNGS platform, including the frequency of reported abnormalities.

DESIGN: Retrospective analysis of clinical results.

MATERIALS AND METHODS: Between July 1, 2016 and May 1, 2017, 16,127 embryo biopsies were submitted for CCS testing by NGS from several referring IVF centers. The frequencies of each result category were calculated. Segmental abnormalities are classified as segments that are either mosaic or full range gains or losses that are less than an entire chromosome. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal. Mosaic results are classified as full chromosome aneuploidy where the copy number is between normal and abnormal.

RESULTS: Of the 16,127 embryo biopsies tested, 97.5% produced a conclusive result (15,725/16,127), while 1.5% (242/16,127) were nonconcurrent and 1% (160/16,127) were unamplified. Of the samples that yielded conclusive results, the overall euploid rate was 55.1% (8,666/15,725) and 24.9% (3,921/15,725), respectively. A small portion of samples (0.7%, 103/15,725) were positive for at least one mosaic range chromosome and a segmental abnormality on a separate chromosome, without any other aneuploidy. The remaining samples, 7.2% (1,27/15,725) were due to at least one mosaic range chromosome abnormality, but also had mosaic range and/or segmental aneuploidies.

CONCLUSIONS: This study is designed to further define the frequency of reported abnormalities on NGS-based aneuploidy screening within a large sample cohort. These frequencies can be used for counseling patients on their expectation of result outcomes when submitting samples for CCS testing via a tNGS platform.

References:

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PGS ANALYSIS OF OVER 100,000 BLASTOCYSTS USING HIGH RESOLUTION NEXT GENERATION SEQUENCING (HR-NGS) STRATIFIED BY AGE AND LABORATORY. S. S. Zimmerman, D. Wells, T. Escudero, L. Ribustello, J. Blazek, S. Munne. aCooper-Genomics, Livingston, NJ; aGenesis Genetics, Plymouth, MI; bReprogenetics UK, Oxford, United Kingdom; bReprogenetics, Oxford, United Kingdom; bReprogenetics, Livingston, NJ; Operations, CooperGenomics, Houston, TX.

OBJECTIVE: To determine the types and frequency of abnormalities in human blastocyst detected by high resolution next generation sequencing (hr-NGS) stratified by age and laboratory. DESIGN: Retrospective analysis of PGS procedures involving TE biopsy and hr-NGS performed by two large genetic reference laboratories serving over 250 fertility clinics over three years. A total of 109,716 embryos were analyzed, with 53599 from Lab 1 and 55757 from Lab 2.

MATERIALS AND METHODS: Samples were amplified by SurePlex, sequenced with VeriSeq PGS assay (Illumina) on MiSeq (Illumina) and analyzed with BlueFuse Multi analysis (Illumina). Embryos with one or two aneuploid chromosomes or one aneuploid chromosome and one mosaic chromosome were called aneuploid. Embryos with 3 chromosome abnormalities were considered complex abnormal. Lab 1 considered embryos as mosaic if they had 10-90% abnormal cells, euploid if less and aneuploid if more. Lab 2 considered mosaicism as 20-80% abnormal cells.

RESULTS: Aneuploidy rates between the two labs were in general similar, with those for egg donors being 16% vs. 22% (Av. 18%), <35 years old (Av. 20%, 20% vs. 21%), 35-37 (Av. 28%, 27% vs. 29%), 38-40 (Av. 38%, 37% vs. 39%), 41-42 (Av. 41%, 42% vs. 41%), and >42 years old (Av. 33%, 35% vs. 31%). Complex abnormal embryo frequencies were also similar for egg donors (Av. 7%, 6% vs. 8%), <35 years old (Av. 8%, 8% vs. 9%), 35-37 (Av. 10%, 9% vs. 10%).