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Salvaging euploid blastocysts from abnormal fertilised zygote in IVF through biparental testing and ploidy assessment

PGDIS 2024

PRESENTED BY

STEVEN YAP

SENIOR GENETICIST

Introduction

- Abnormal fertilisation
  - One, Three or more pronucei (PN) in a zygote
  - Two normal-sized PNs and smaller PN
- Usually discarded
  - Abnormal single set (haploid) or multiple sets (polyploid) of chromosome constitution
  - Increased risk of miscarriage, implantation failure, or hydatidiform mole development
- Patient with no 2PN blastocysts for transfer
  - Had well developed abnormal fertilised blastocysts

Several studies have shown successful pregnancies and live births resulting from these blastocysts

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Introduction

FERTILITY & REPRODUCTION

Embryos Arising from Apronuclear (0PN) and Unipronuclear (1PN) Have Similar Euploidy Rates with Those from 2PN and Should be Considered for Transfer

Adelle Yun Xin Lim, Colin Soon Soo Lee

IVF Laboratory, Alpha Fertility Centre, Petaling Jaya, Selangor 47810, Malaysia

J Assist Reprod Genet
DOI 10.1007/s10815-015-0518-y

CASE REPORT

Birth of nine normal healthy babies following transfer of blastocysts derived from human single-pronucleate zygotes

Fumiaki Itoi[1,3] · Yukiko Asano[2] · Masashi Shimizu[3] · Hiroyuki Honnma[4] · Yasutaka Murata[3]

Article | Open access | Published: 23 May 2023

Live birth rate following a failed first in vitro fertilization cycle with no embryos for transfer

Xiaohui Dong & Xia Xue

Scientific Reports **13**, Article number: 8343 (2023) | Cite this article

3798 Accesses | **1** Altmetric | Metrics

Case Report / Olgu Sunumu

DOI: 10.4274/tjod.45144
Turk J Obstet Gynecol 2016;13:95-8

Live birth after transfer of a tripronuclear embryo: An intracytoplasmic sperm injection as a combination of microarray and time-lapse technology

Tripronükleer bir embriyonun transferiyle elde edilen canlı doğum: Mikroarray ve time lapse teknolojisinin kombinasyonu olan bir intra-sitoplazmik sperm enjeksiyonu olgusu

Ender Yalçınkaya, Alev Özay, Elif G. Ergin, Zeynep Öztel, Hakan Özörnek

Eurofertil In Vitro Fertilization Center, Embryology Laboratory, İstanbul, Turkey

JOURNAL ARTICLE

Healthy live birth following embryo transfer of a blastocyst of tetrapronuclear (4PN) origin: a case report

Get access ›

Peter Bredbacka ✉, Antonio Capalbo ✉, Kirsi Kananen, Ludovica Picchetta, Candido Tomás

Human Reproduction, Volume 38, Issue 9, September 2023, Pages 1700–1704,
https://doi.org/10.1093/humrep/dead151
Published: 01 August 2023 **Article history** ▾

Objectives

Retrospective study assessing:

- The chromosomal and ploidy status of blastocysts derived from abnormally fertilised zygotes
- The corresponding clinical outcomes post-embryo transfer.

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Material & Methods

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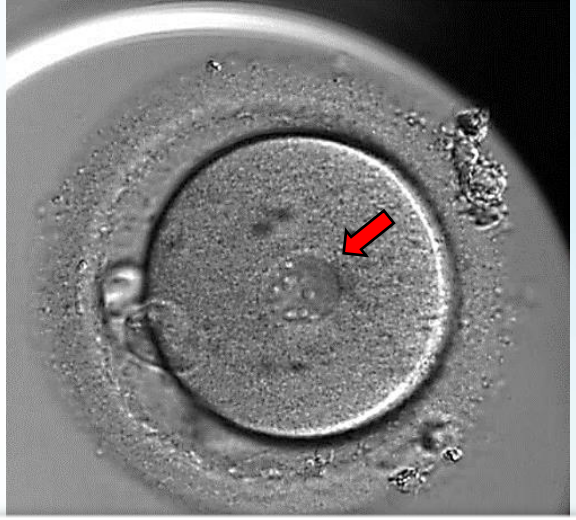
Material & Methods

- July 2020 – December 2023
- 131 patients
- MII Oocytes (n = 2016) -> ICSI (single sperm)
- Time-lapsed incubator
- Fert Check: 16 - 18 hours post-insemination



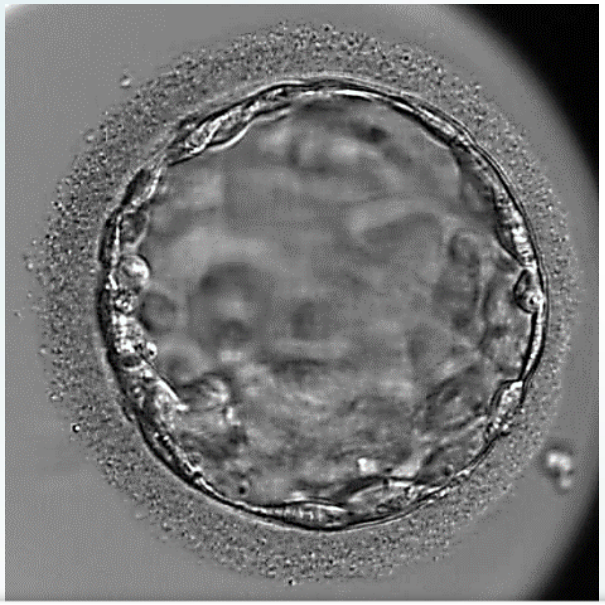
1PN

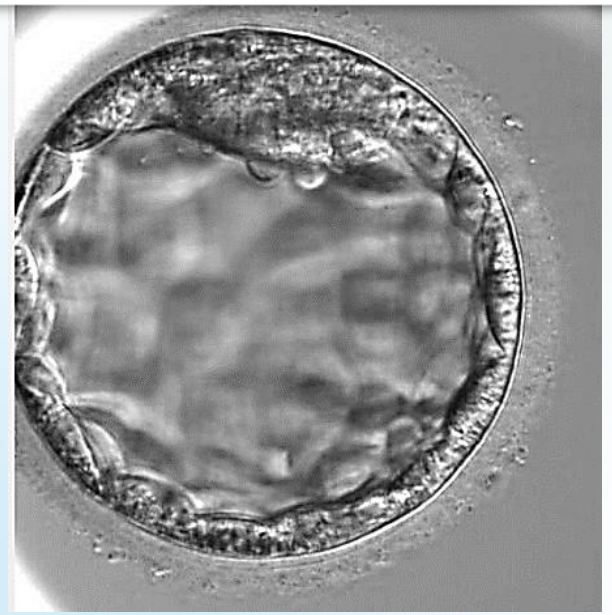
>2PN

2.1, 2.2, 2.3PN

3PN, 4PN

Blastocyst Culture





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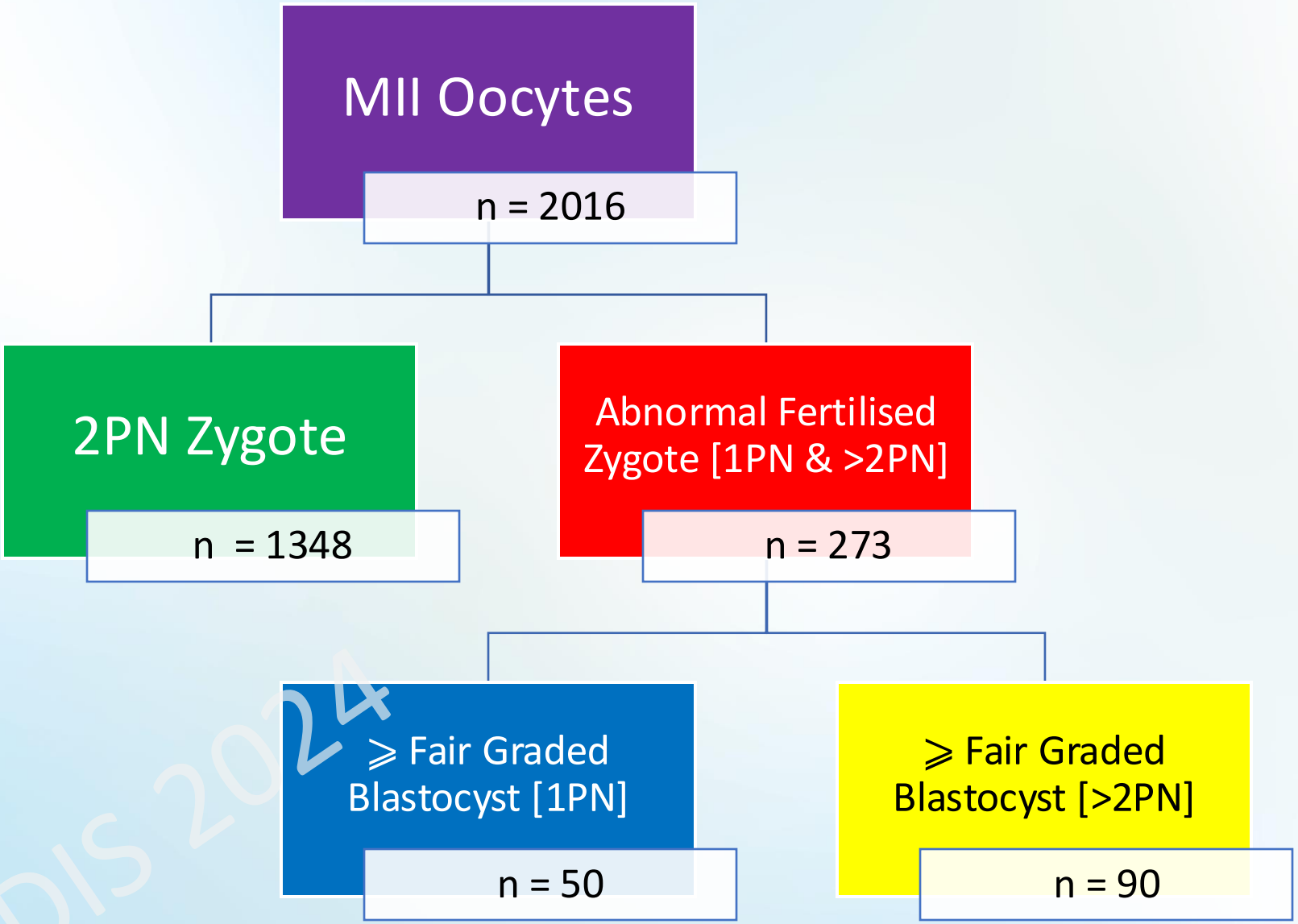
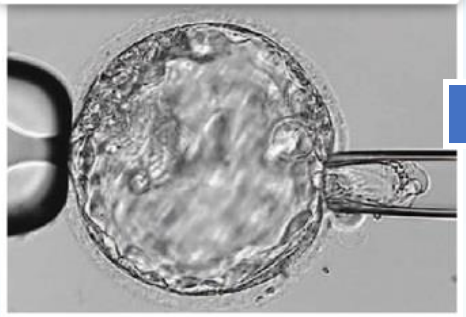
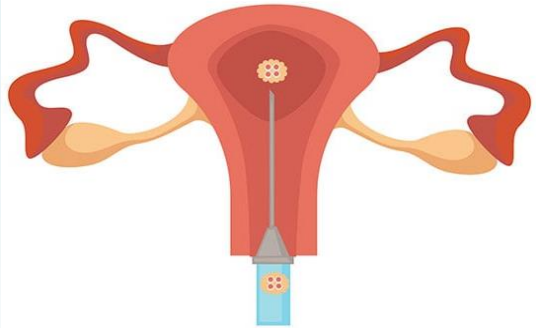


Blastocyst Biopsy

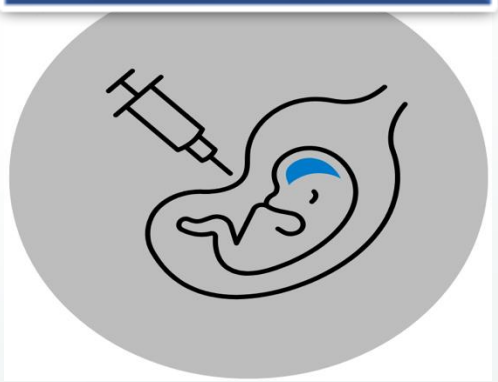


Blastocyst Freezing

Frozen Embryo Transfer



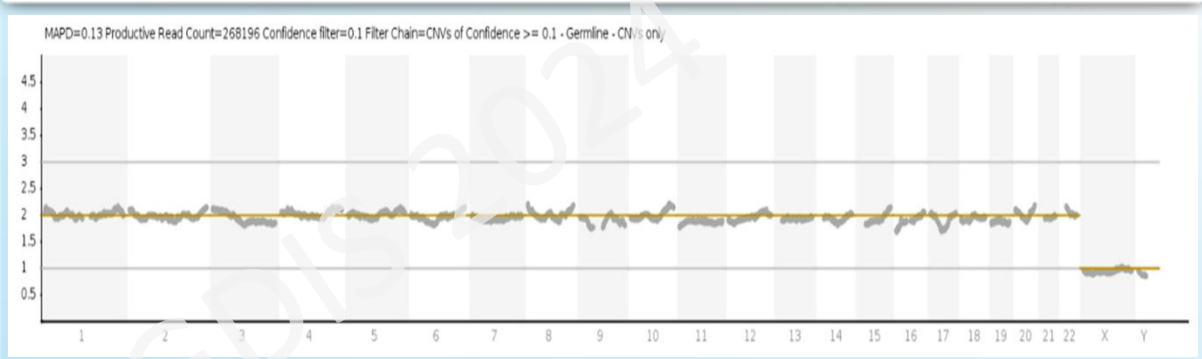
Amniocentesis



MDA WGA

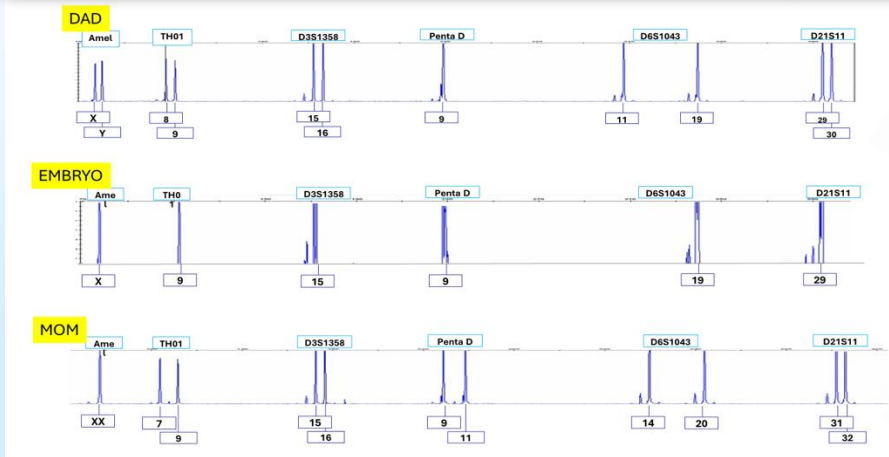
Diploid

Preimplantation Genetic Testing for Aneuploidy



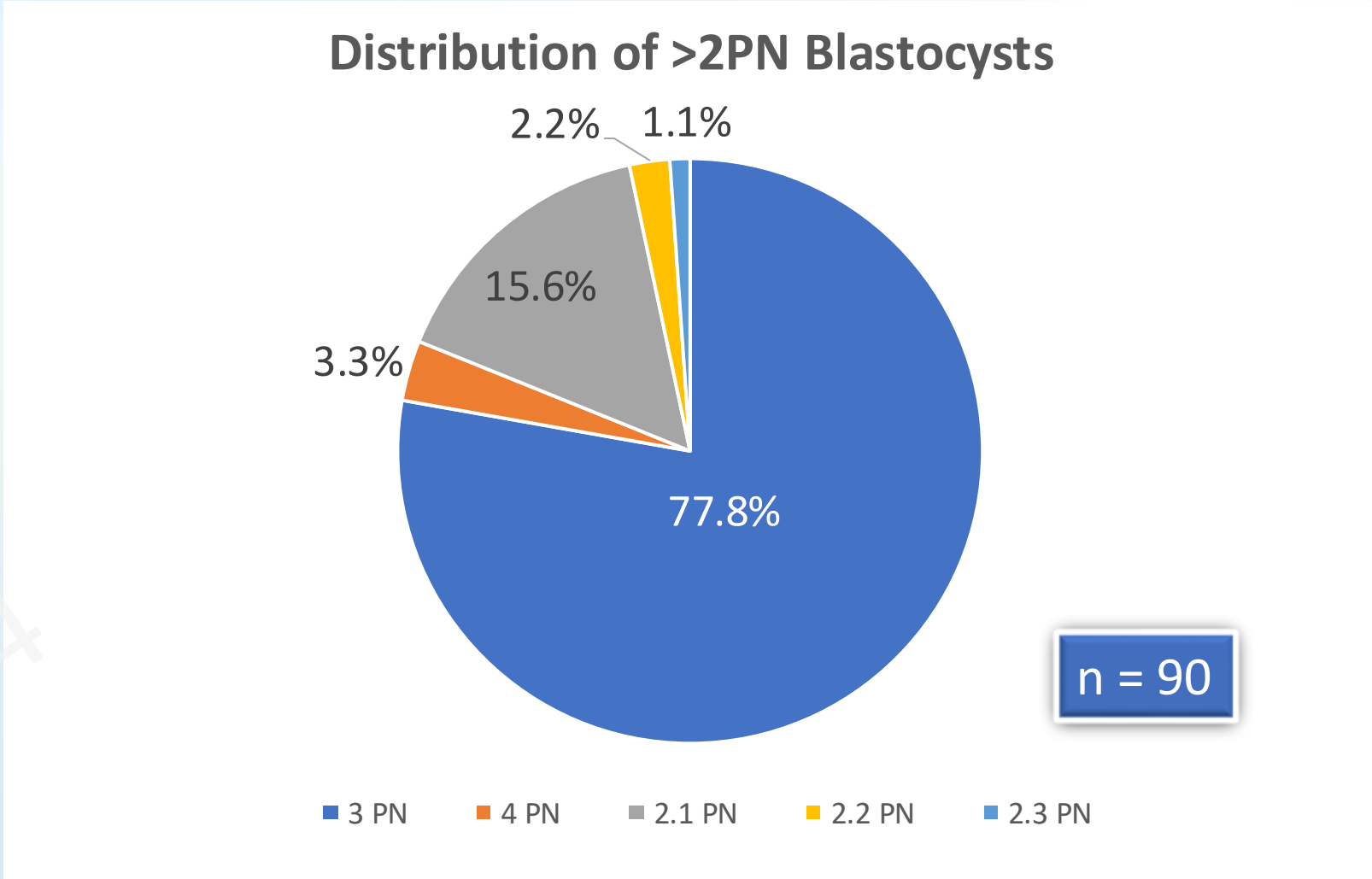
consented

Biparental and ploidy assessment (24 STR Markers)



Results

Results



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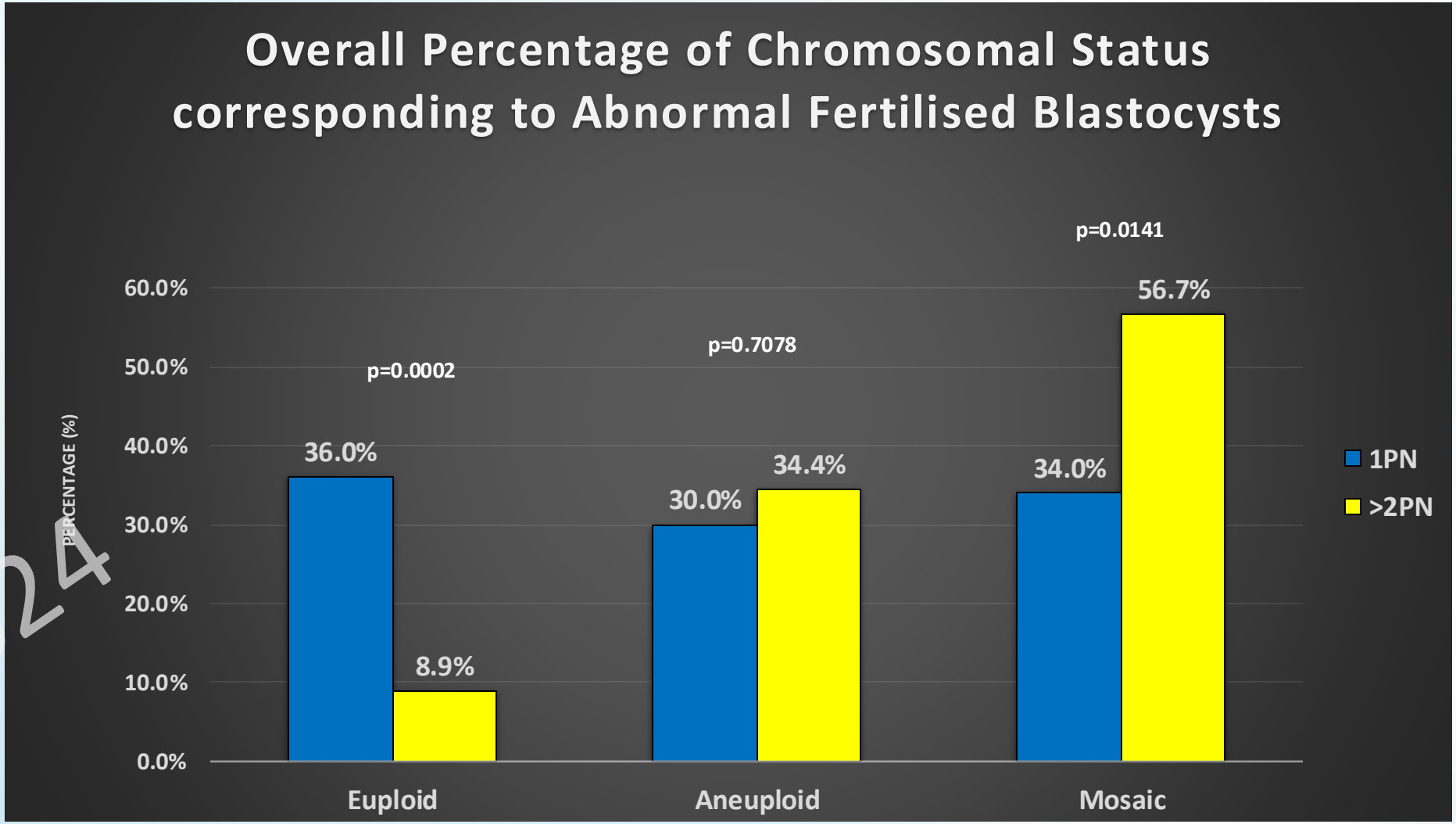
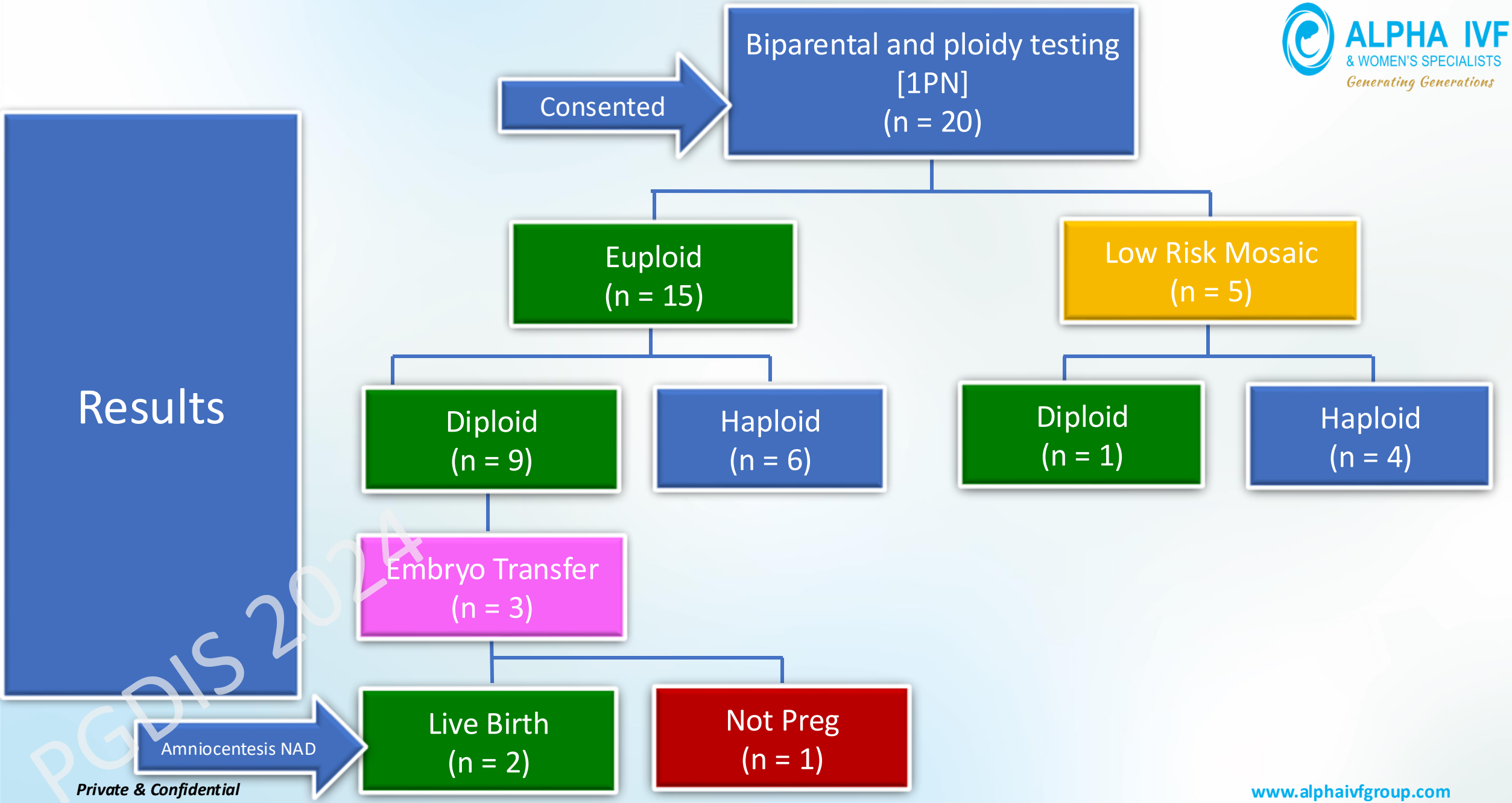
Results





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Results

Consented

Biparental and ploidy testing
[>2PN]
(n = 7)

- Euploid (n = 4)
  - Diploid (n = 4)
  - Embryo Transfer (n = 2)
    - Miscarriage (n = 1) 3PN
    - Not Preg (n = 1) 3PN
- Low Risk Mosaic (n = 2)
  - Triploid (n = 2)
- High Risk Mosaic (n = 1)
  - Diploid (n = 1)
  - Embryo Transfer (n = 1)
  - Not Preg (n = 1) 4PN

Discussions

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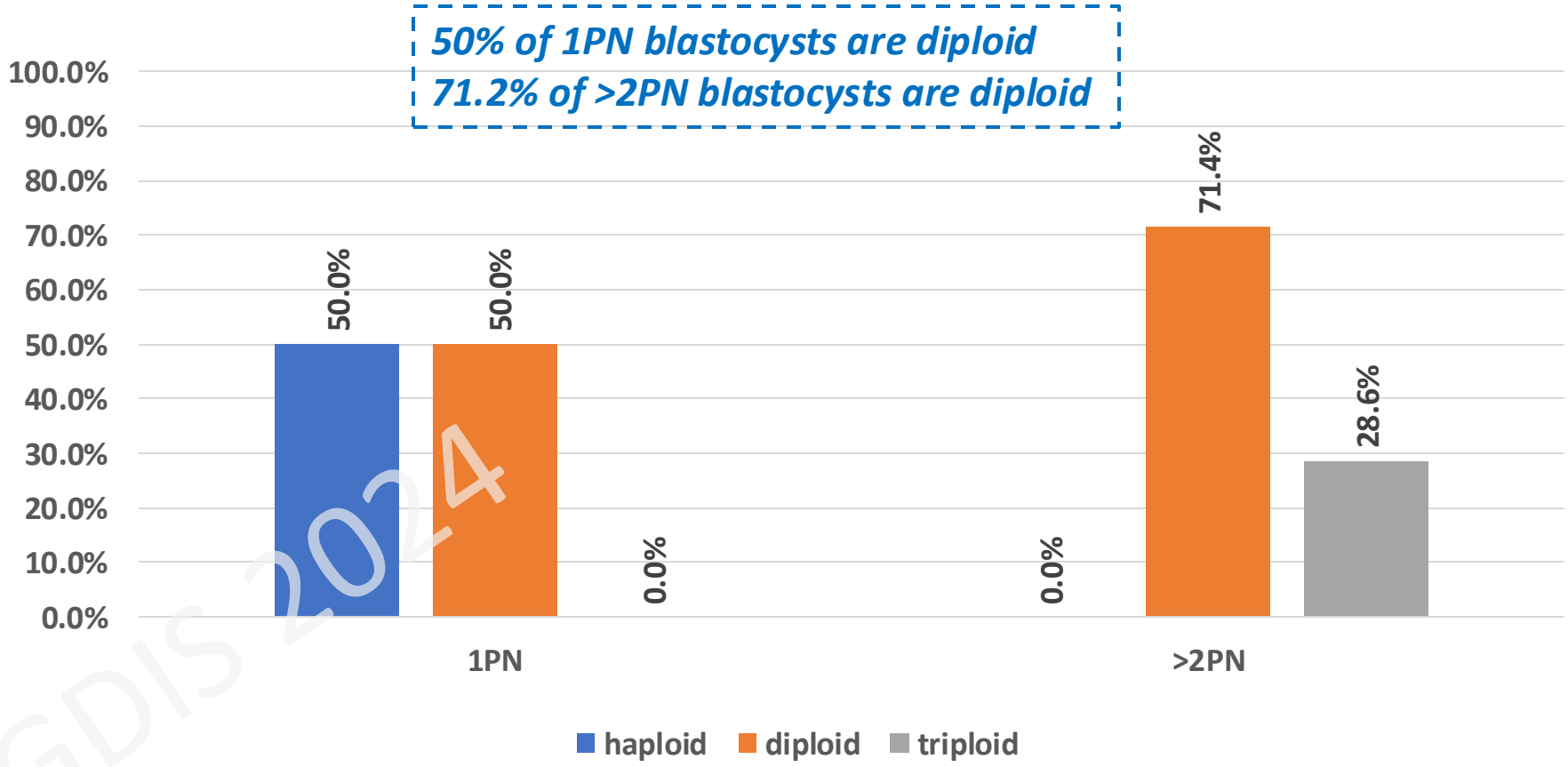
Distribution of ploidy status among abnormal fertilised blastocysts



Discussion

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- Significantly higher **euploidy rates** in 1PN blastocysts
  - Two pronuclei (2PN) formed within one large nuclear envelope
  - Parthenogenetic oocyte activation
    - Possibly normalisation of sample reads to reference of normal samples in PGT-A testing
    - PGT-A using NGS – shallow sequencing, insufficient for ploidy assessment (Treff and Zimmerman, 2017)

- Significantly higher **mosaic rates** in >2PN blastocysts
  - Origin of mosaicism is unclear
  - Phenomenon of trophoblast differentiation (Bielanska et al. 2002)
  - Micronuclei – lagging chromosome
    - Susceptible to severe DNA damage & improper segregation (McCoy R. C. 2017)

Discussion

Diploids in 3PN Blastocysts

- Digynic zygote (ICSI) – extrusion failure of second polar body
- Additional maternal pronucleus
- Self-correction mechanism hypothesis – triploidy to diploidy at zygote stage (Grau et al. 2011)
  - Paternal pronuclei in these embryo facilitate normal progression of first cell division
- Further studies needed to confirm this hypothesis

Discussion

1PN blastocysts

- Presence of chromosome Y – assumed normal fertilisation
- All possible ploidy configurations (Capalbo et al. 2017)
  - Haploid / Diploid / **Triploid**

- Recommended to perform ploidy assessment on 1PN blastocysts prior clinical use

Discussion

Other Salvaging Technologies in Alpha IVF

- 0PN, 1PN, >2PN
- Delayed-ICSI on Day 1 oocyte (immature oocyte on Day 0)
- Extended embryo culture to Day 7

Discussion

Delayed-ICSI on Day 1

- *JP Sam, SK Gan, CSS Lee. Obtaining a fresh sperm sample for Delayed-ICSI: Does it matter? Accepted at the upcoming ESHRE 38th Annual Meeting, 3-6 July 2022, Milan, Italy*
- *Sam JP, Lim AYX, Tee ZQ, Lee CSS. IVF cycle outcomes of Day1-matured oocytes for Delayed-Intracytoplasmic Sperm Injection (delayed-ICSI) in different age groups. Accepted at the upcoming 13th Alpha Biennial Conference, Alpha Conference, 6th - 9th October 2022*
- *Tee ZQ, Sam JP, Lim AYX, Lee CSS. Delayed-ICSI on day1-matured oocytes in low responders of different age groups. Presented at 37th Virtual Annual Meeting of European Society of Human Reproduction and Embryology (ESHRE), 26 June to 1 July 2021*
- *JP Sam, AYX Lim, ZQ Tee, C.S.S. Lee. Successful pregnancies following transfer of blastocysts derived from delayed-intracytoplasmic sperm injection (delayed-ICSI). Presented at 36th Virtual Annual Meeting of European Society of Human Reproduction and Embryology (ESHRE), 05-08 July 2020*

P-203 Successful pregnancies following transfer of blastocysts derived from delayed-intracytoplasmic sperm injection (delayed-ICSI)

J.P. Sam[1], A.Y.X. Lim[1], Z.Q. Tee[1], C.S.S. Lee[2]

[1]Alpha IVF & Women's Specialists, IVF laboratory, Petaling Jaya, Malaysia ;
[2]Alpha IVF & Women's Specialists, Medical Director, Petaling Jaya, Malaysia

Study question: To evaluate the clinical outcome of delayed-ICSI on day1-matured oocytes.

Summary answer: Blastocysts derived from day1-matured oocytes can result in successful pregnancies and thus can be considered for transfer when there is no blastocyst available from day0-ICSI.

JP Sam et al, ESHRE, 2020

Discussion

Extended Embryo Culture to Day 7

ELSEVIER

Reproductive BioMedicine Online
Volume 39, Supplement 1, August 2019, Page e45

P-30

30. LIVE BIRTHS FOLLOWING DAY 7 BLASTOCYST TRANSFER AFTER PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A)

C.W. Chan, Y.X. Lim, M.W. Lim, C.S.S. Lee, C.S. Tan

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https://doi.org/10.1016/j.rbmo.2019.04.083 Get rights and content

Introduction

Extended culture to blastocyst stage is being adopted in many IVF clinics, with the aim to improve embryo selection and promoting single embryo transfer. Selection of these blastocysts usually occurs up to Day 6 of embryo culture. However, a study (Su et al., 2016) has revealed that Day 7 blastocysts can be euploid and can result in healthy live births. In this study, we evaluate the euploidy rate of Day 7 blastocysts and the clinical outcome of transferring these euploid Day 7 vitrified-warmed blastocysts in Alpha Fertility Centre.

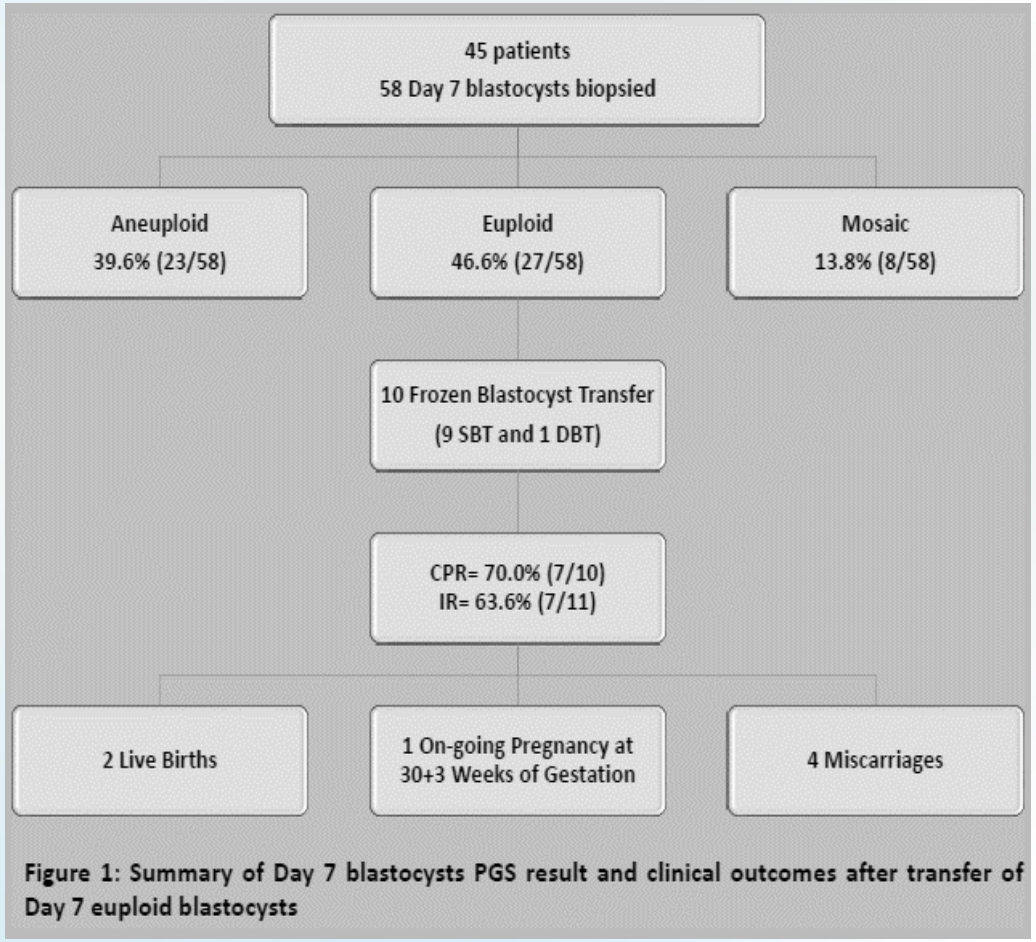

Figure 1: Summary of Day 7 blastocysts PGS result and clinical outcomes after transfer of Day 7 euploid blastocysts

Discussion

Conclusions

- Abnormal fertilisation can lead to a significant number of euploid embryos with confirmed diploidy and biparental origin.
- Transferring these blastocysts has shown potential for successful embryo implantation and healthy live births in IVF.
- Patients without usable blastocysts from normally fertilised zygotes may seek to utilise blastocysts from abnormally fertilised zygotes.

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THANK YOU!