EMBRYO DEVELOPMENT RATE, EUPLOIDY AND PREGNANCY OUTCOMES

BIRGIT WAGER

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Merck

TIME OF MORULATION AND TROPHECTODERM QUALITY ARE ASSOCIATED WITH LIVE BIRTH AFTER EUPLOID BLASTOCYST TRANSFER: A MULTICENTER STUDY

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Time of morulation and trophectoderm quality are associated with live birth

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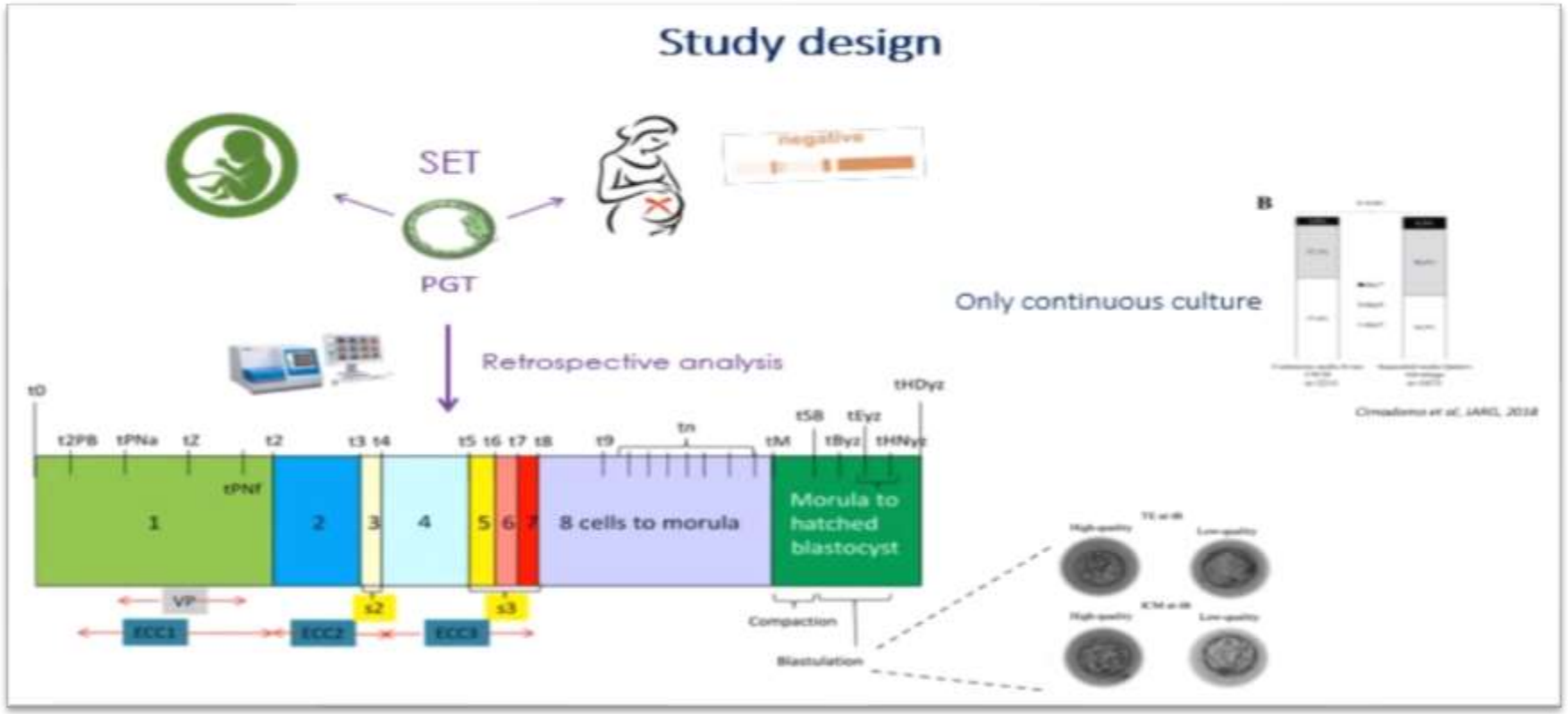
35th Annual Meeting
Vienna, Austria, 23-26 June 2019

Introduction and overview

Study Question:

- Does the morpho-dynamic characterization of human euploid blastocysts' preimplantation development increase the prognostic value upon their reproductive competence?



- In Phase1, 511 SETs, FET Cycles (N=147 center1; N=364 center2; training set) from 1069 PGT-A cycles were retrospectively recruited. A **predictive model** of **LB** was defined.
- In Phase2, this model was tested in a validation set including 319 consecutive SETs from 546 PGT-A cycles performed in 3 IVF centres.
- The ongoing pregnancy rate (OPR) was defined as primary outcome

Main Results

- The average LB rates was 40%
- The euploid blastocysts resulting in a LB showed concordant significantly faster development than non-implanted/miscarried ones for tPB2, t4, t5, t8, s3, cc3, tM and tSB
- High-quality ICM and the TE at tB were concordant as positively associated with a LB
- However, the multivariate logistic regression outlined only tM and TE quality as putative predictors
- A model was then created based on TE quality (high or low) and tM (<80hr or ≥80hr)
  (SAUC of 0.65 from the ROC curve analysis)
- High-quality TE at tB and a tM <80hr resulted in an OPR of 61.2% (N=41/67)
- Low-quality TE at tB and a tM≥80hr resulted in an OPR of 30.0% (N=15/50; p<0.01)
  (ROC curve showed a poorly clinically-significant AUC of 0.59)

Conclusions

- The TE Quality at tB was the only parameter deriving from a static morphological evaluation associated with euploid blastocysts reproductive competence. The ICM in a multivariate analysis was not.
- TM was the only parameter deriving from morpho-dynamic evaluation associated with euploid blastocysts reproductive competence

SLOW EMBRYO DEVELOPMENT PREDICTS HIGH ANEUPLOIDY RATES AMONG HIGH GRADE BLASTOCYSTS BUT DOES NOT INFLUENCE PREGNANCY OUTCOMES IN EUPLOID BLASTOCYST TRANSFER CYCLES

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Slow embryo development predicts higher aneuploidy rates among high grade

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Introduction and Overview

Study Question:

- Is there a relationship between day of blastocyst expansion and embryonic ploidy status?
- In euploid SET cycles, does earlier blastocyst development correlate with improved pregnancy outcome?

Study Description

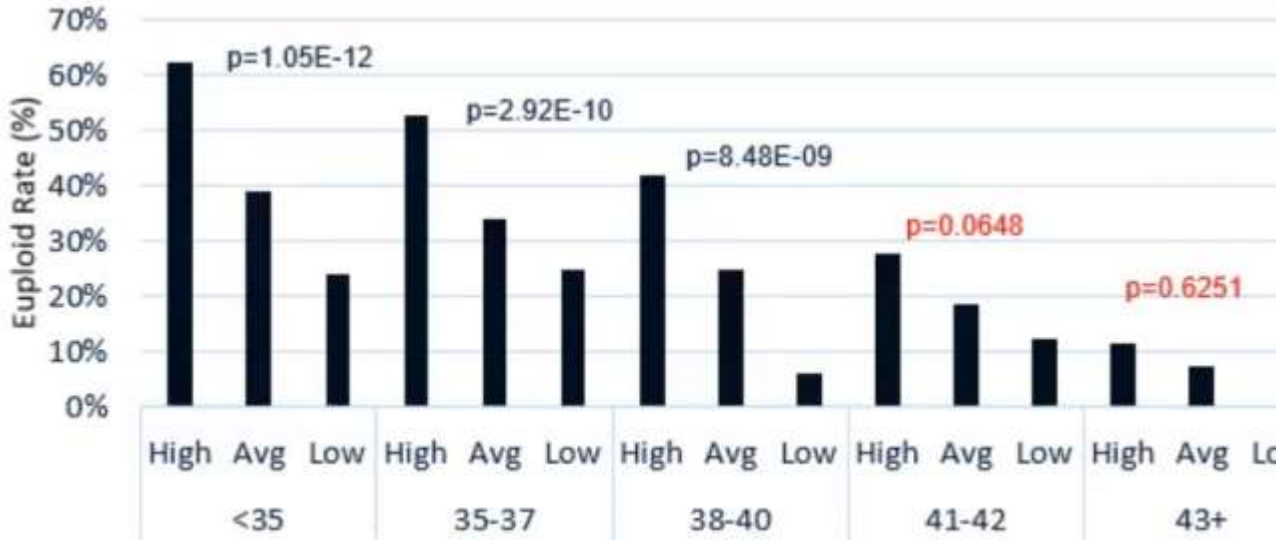
- Retrospective cohort study
- 535 patients undergoing IVF and PGT-A between 2014-2018.
- 4761 embryos were biopsied on day 5 (n=3871) or day 6 (n=890)
- **Euploid rate** was the primary outcome of interest and was calculated according to the day of biopsy and stratified by morphologic grading (good: 5/6AA-BB, average: 5/6BC-CC, poor: 3/4BB-CB) and patient age
- Secondary outcomes included implantation (IR) and ongoing pregnancy rate (OPR) in subsequent euploid transfer cycles
- **Implantation rate** was calculated based on a positive pregnancy test after ET
- **Ongoing pregnancy rate** was defined by the presence of a viable fetal heart rate >7 weeks' gestation

Results

- A higher euploidy rate was observed among day 5 compared to day 6 blastocysts overall (53.01 vs. 39.75%, p<0.0001).
- Aneuploidy rates ↑ with maternal age and no difference in euploid rates was observed among day 5 vs. 6 blastocysts in women 41-years-old (33.33 vs. 23.17%, p=0.22).
- Significantly ↑ euploid rate was also observed among high grade embryos compared to low grade embryos (47.43% vs. 28.23%, p<0.0001);

RESULTS – EUPLOID RATES

Embryo Grade	Total Embryos	Euploids	95% CI	P-valu
High	3688	48.70%	(47.07, 50.33)	< 2.2e-
Average	913	29.03%	(26.12, 32.11)	
Low	160	17.50%	(12.13, 24.47)	



Results Continued

- Day 5 biopsied blastocysts demonstrated a significantly ↑ euploid rate compared to day 6 biopsied blastocysts among high grade embryos (55.15% vs. 44.87%, p=0.0002),
- No difference in euploid rates was observed among lower grade embryos (23.68 vs. 28.64%, p=0.64).
- Overall, no significant difference in IR or OPR between day 5 and day 6 blastocysts was observed (72.41 vs. 70.91% and 71.42 vs. 65.63%, respectively).
- High grade embryos demonstrated improved IR compared to lower grade embryos (73.20 vs. 62.50%, p=0.047) but OPR were not significantly different (69.35 vs. 55.00%, p=0.10).
- High grade embryos biopsied on day 5 yielded similar IR and OPR compared to day 6 (72.29 vs. 73.47%, p=0.87, and 71.67 vs. 68.06%, p=0.57, respectively).

Conclusion

- Euploid Rates decreased with increasing maternal age and lower morphological grading.
- These results demonstrate that early blastocyst formation is only associated with higher euploidy rates among high-grade embryos in women <40-years-old.
- This supports the selection of day 5 over later developing embryos as they are more likely to be euploid.
- Early embryo development does not predict improved pregnancy outcomes in PGT-A cycles, but may be a useful embryo selection adjunct to morphologic grading in non-biopsied cycles.
- Differences in pregnancy outcomes between day 5 and day 6 blastocysts may be the result of higher aneuploidy rates; once this is eliminated the pregnancy outcomes are the same