MEDIA WITH ULTRA-LONG SHELF LIFE SUPPORTS GOOD CLINICAL OUTCOMES

> INTRODUCTION

The culture medium plays a crucial role in any embryo culture system, providing essential nutrients and physiological support to gametes and embryos to facilitate fertilisation and development until embryo transfer. Interestingly, the shelf life of commercially available culture media varies significantly among manufacturers, ranging from 2 to 12 months *(Fig. 1)*.

The Genea Biomedx Gems® Culture Medium suite has been designed and verified for ultra-long shelf life by utilizing stable forms of key ingredients combined with controlled manufacturing processes and extensive quality control. This extended shelf life offers numerous advantages for modern IVF clinics.

AIM

The aim of this paper is to present clinical data from Genea Group clinics on the impact of culture media age on Day 5 usable blastocyst rate, total blastocyst rate and cumulative pregnancy rate. The primary objective is to demonstrate that Geri® culture medium retains its effectiveness in supporting embryo development and viability throughout its shelf life.

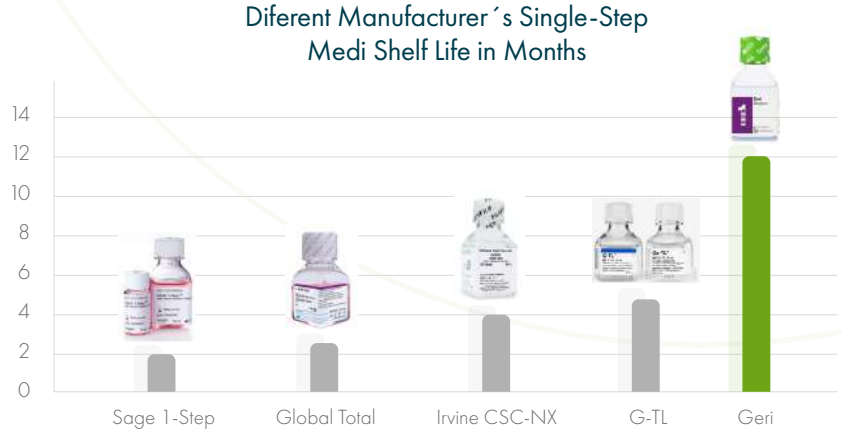

Fig. 1: Shelf life of different manufacturer's single step (continuous) embryo culture media (months from the date of manufacture as stated by the manufacturer)

> MATERIALS AND METHODS

This study is based on a retrospective analysis of IVF data from Genea Pty, Ltd, using the Babysentry EMR dataset collected between 2020 and 2023.

The data includes cycles utilising Geri® continuous culture media for embryo culture from Day 1 to Day 5 or 6. Oocytes were aspirated following standard stimulation protocols, fertilised by IVF or ICSI, and cultured in the Geri® timelapse system until Day 5 or 6. Inclusion criteria for this study were autologous cycles including both PGT and non-PGT cycles of all patient ages. Exclusion criteria included donor oocyte cycles, cycles with no usable oocytes or cycles with failed fertilisation.

A total of 12,680 cycles from 2020 to 2023 from eight clinics within the Genea Group were analysed. Cycle outcomes were assessed using multivariate logistic regression (JMP, SAS, Inc.).

Parameters included in the outcomes were:

- Day 5 Usable Embryo Rate (D5BR): Genea Grade B22 (Gardner 3BB) or better divided by the number of 2PN fertilised oocytes.
- Total Usable Blastocyst Rate (TBUR): Transferred/Cryopreserved Blastocysts at Day 5 or 6 divided by the number of 2PN fertilised oocytes.
- Cumulative Pregnancy Rate: Positive fetal heartbeat at ultrasound examination 6 weeks after embryo transfer.

KEY MESSAGES

Data collected from Genea Group clinics between 2020 and 2023, encompassing 12,680 cycles, analysed the effect of the age of Geri® culture media on clinical outcomes. The analysis showed no significant differences in blastocyst development or cumulative pregnancy rates between media used within 2 months from the manufacturing date and media used after 10 months from the manufacturing date. These results support the use of extended shelf life media to the last drop, optimising operational and practical efficiencies without compromising clinical outcomes. These results provide support to the usage of extended shelf life media, thus optimising operational and practical efficiences achieved with such media without compromising clinical outcomes.

> RESULTS

The average age of the Geri® Culture Medium used in the study was approximately 6 ± 2 months (185 ± 61 days). The distribution percentages of cycles utilising media of different ages were 0.1%, 10.0%, 47.3%, 22.0%, 14.6%, and 6.0% for media within <2, 2-4, 4-6, 6-8, 8-10, and 10-11 months from the date of manufacture, respectively *(Fig. 2)*.

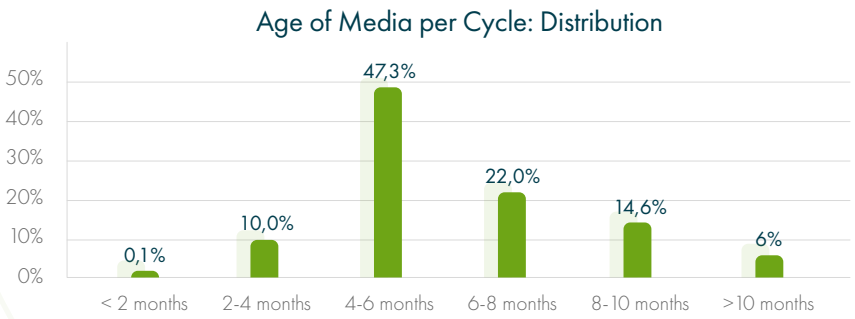

Fig. 2: Distribution of Culture Media Age (months)

Blastocyst rates at Day 5 and total blastocyst rates at Days 5/6 are shown in *Fig. 3*, indicating no significant differences between different media age groups (p=0.396).

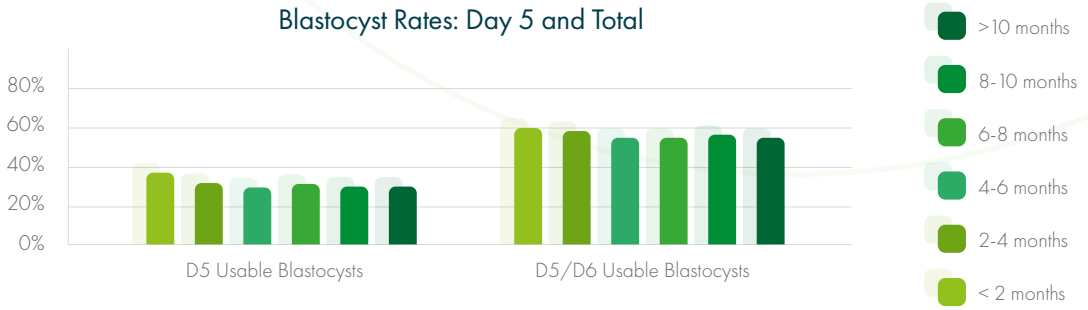

Fig. 3: Day 5 usable and total usable blastocyst rates at Days 5/6 by the age of culture medium (p=0.396)

Cumulative pregnancy rates were not influenced by media age when controlling for patient age, cycle number, number of oocytes collected, ICSI vs. IVF and the individual clinic. Day 5 good quality usable blastocyst rates were 29.4% vs. 30.4%, total usable blastocyst rates were 56.2% vs. 56.1% and cumulative ongoing pregnancy rates were 32.9% vs. 32.4% for media aged under half of its shelf life (≤ 6 months) vs. media aged over half of its shelf life (>6 months), respectively. Cumulative pregnancy rates across different patient age groups are shown in *Fig. 4*, with no statistically significant differences detected between the groups (p=0.446).

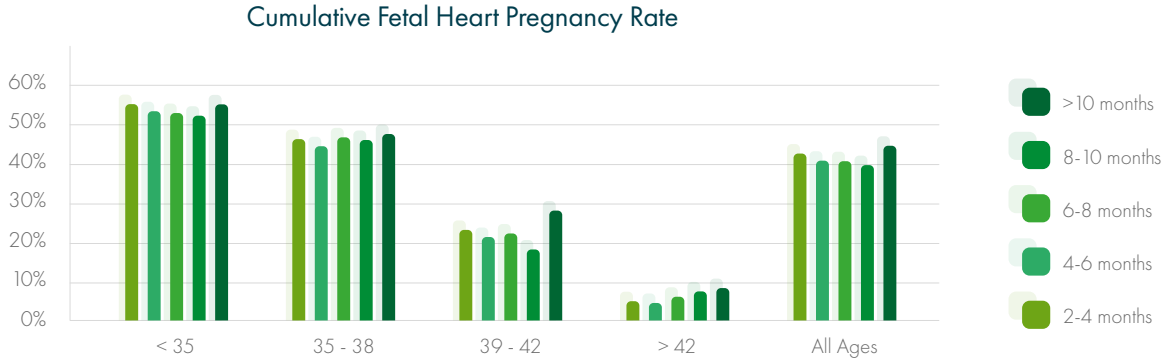

Fig. 4: Cumulative Fetal Heart pregnancy rates across the range of patient ages and by the age of culture medium (p=0.446)

> DISCUSSION AND CONCLUSIONS

The shelf life of embryo culture media has traditionally been limited, possibly reflecting the origins of modern human IVF media that were initially manufactured mostly by clinics themselves under varying conditions and with a variety of ingredients. Even when manufacturing moved to professional facilities under commercial media manufacturers, some of that initial cautiousness may have persisted, especially before further studies illuminated key factors impacting shelf life.

These factors include, for example, the notoriously unstable amino acid glutamine, which breaks down in media over time, leading to the accumulation of harmful ammonium[1,2]. However, extending media shelf life is possible by replacing labile components with their more stable counterparts, such as glutamine with L-alanyl-L-glutamine, and by conducting media manufacturing under carefully controlled conditions and processes, followed by extensive quality control before product release. By utilising these strategies, Genea Biomedx Gems Medium Suite products have extended their shelf life from the usual few months up to 12 months from the date of manufacture, in practice resulting 10-11 months usable shelf life for the users.

Extended media shelf life provides many advantages for clinics, including reduction of waste, improved inventory planning leading to cost savings, operational flexibility and batch consistency, which all assist in optimising clinical processes as well as improve sustainability of the operations[3].

The results of this study show that Geri® culture media renders equivalent clinical outcomes even when approaching the end of its extended shelf life at 11 months.

These results give further confidence that Gems media's extended shelf life allows clinics to use media to their full potential to optimise their operations without concerns about possible impacts on clinical outcomes.

> NOTES

This White Paper is based on studies conducted at Genea Pty Ltd, Australia, and is presented with the permission of the Genea Group.

Some of the data has been presented at the Fertility Society of Australia and New Zealand Annual Conference 2024, Perth, WA, Australia, 14-17 September 2024 (Morbeck D, Hesketh N, Fisk K & Murray A. (2024): "Good to The Last Drop? Impact of Culture Media Age on Blastocyst Development and Implantation Rates").

At the time of the first release of this document, full paper with further data and details is under preparation by the Genea Group.

> REFERENCES

1. *Kliejkers, S.H., van Montfoort, A.P., Bekers, O., Coonen, E., Derhaag, J.G., Evers, J.L., Dumoulin, J.C. Ammonium accumulation in commercially available embryo culture media and protein supplements during storage at 2-8 degrees C and during incubation at 37 degrees C. Hum. Reprod. 2016, 31:1192-1199.*
2. *Hashimoto, S. (IVF N. C., Nishihara, T., Murata, Y., Oku, H., Nakaoka, Y., Fukuda, A., & Morimoto, Y. (2008). Medium without ammonium accumulation supports the developmental competence of human embryos. Journal of Reproduction and Development, 54(5), 370–374.*
3. *Farlie, F., et. Al. Sustainability in the IVF laboratory: recommendations of an expert panel. RBMO 2024 48: DOI:1016/j.rbmo.2023.103600.*

ADVANTAGES OF EXTENDED IVF MEDIUM SHELF LIFE

Batch consistency

Use of one medium batch over a longer period simplifies laboratory performance and KPI tracking, eliminating the need for consideration of batch changes.

Increased operational efficiency

Fewer batch changes and media orders reduce operational and administrative burden for clinics.

Improved inventory planning

Larger volume purchases improve inventory planning and control.

Cost savings

Fewer orders saves administration costs and when applicable, delivery costs.

Waste reduction

Less expired inventory to discard saves costs.

Operational flexibility

Ample inventory allows more flexibility in case of varying number of cases.