

SAGE 1-STEP™ GM-CSF MEDIA

Put your patients one step ahead



SAGE 1-Step™ GM-CSF Media

Providing a new opportunity for patients in need

As patient demographics change and the desire for personalized treatment increases, the need for impactful solutions has grown.

Based on the long established and clinically proven SAGE 1-Step medium, SAGE 1-Step GM-CSF medium sets a new standard as the first single-step culture and transfer medium containing hyaluronan and the GM-CSF cytokine.



Pro-survival cytokines, such as Granulocyte-macrophage colony-stimulating factor (GM-CSF), drive the dialogue between the embryo and endometrium and profoundly influences embryo development and implantation success.



Upgrade your lab with innovation that matters and stand out in the landscape of IVF clinics, all in one step, with SAGE 1-Step GM-CSF.



Innovation with impact

SAGE 1-Step™ GM-CSF media has a unique formula, developed to mimic the natural environment *in vivo*.



In women with normal reproductive function, the GM-CSF cytokine is secreted into the fallopian tube and uterus, where it supports the developing embryo from the zygote to the implanting blastocyst stage and through to ongoing pregnancy.

Patients

GM-CSF-containing media have been shown to be particularly impactful for:

- Women experiencing implantation failure
- Women experiencing miscarriage
- Women of advanced maternal age

Application

SAGE 1-Step™ GM-CSF can be used alone as an advanced transfer medium or as a combined culture and transfer medium

- Post warming culture and transfer
- Fresh culture and transfer cycles

GM-CSF: The great communicator

Pregnancy requires a receptive immunological system.¹ Cytokines are shown to play a central role in immune suppression for embryo implantation and trophoblast invasion.²

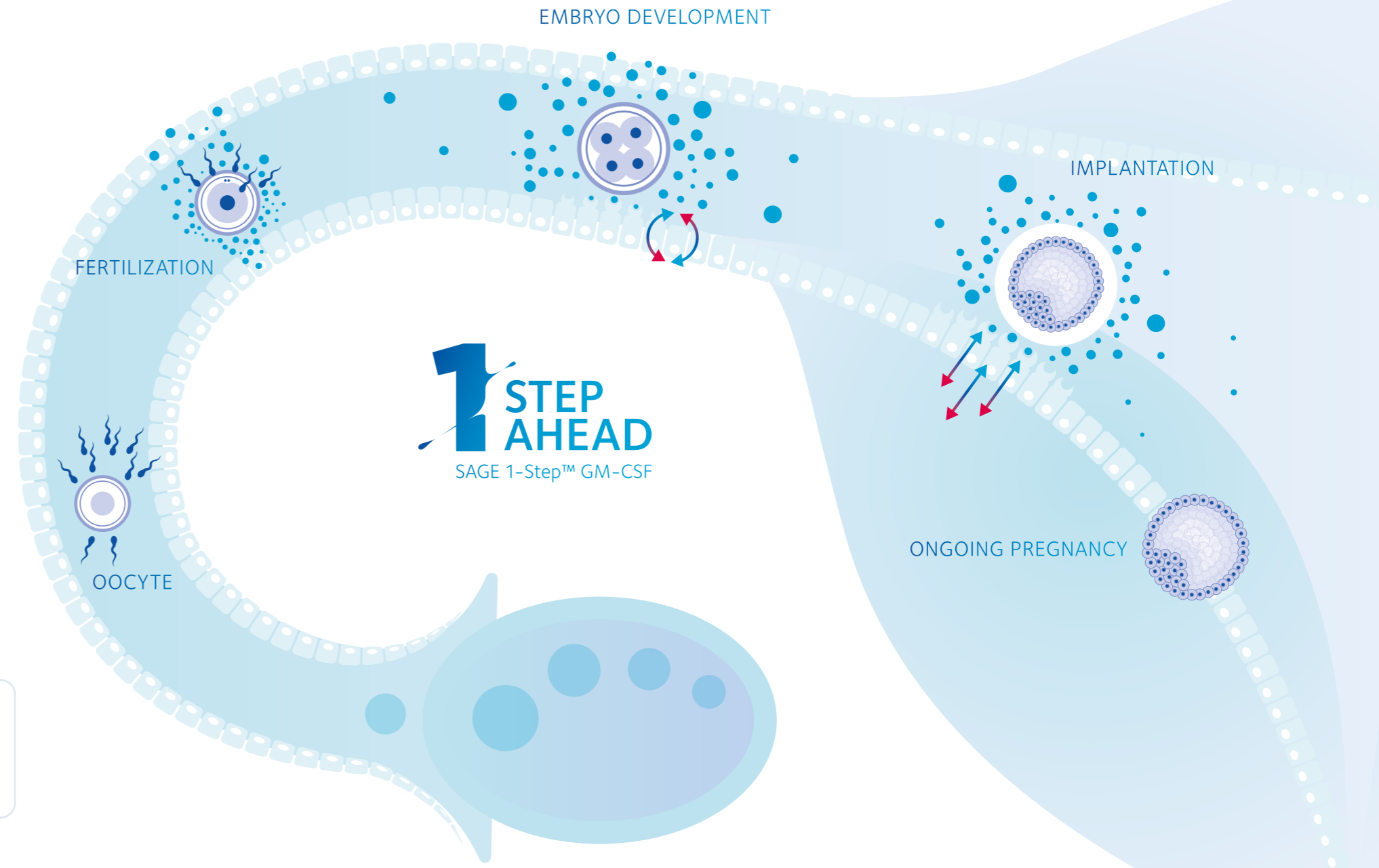
- 1 Conception**

After natural conception, the endometrium secretes the GM-CSF cytokine during the mid-luteal phase.³⁻⁶ This stimulates the conversion of circulating neutrophils to poly-morphonuclear myeloid-derived suppressor cells, which facilitate immune tolerance of the implanting fetal allograft.⁷
- 2 Development**

Acting as a signaling agent, the GM-CSF cytokine mediates communication between the embryo and maternal tissue, aiding local signaling and early embryo development, embryogenesis, and survival through specific receptor-mediated signaling.^{3,7}
- 3 Implantation**

The autocrine and paracrine signaling mediated by GM-CSF fine-tunes gene expression, protects embryos from cell stress, and promotes normal glucose uptake. This, in turn, enhances cell survival⁸ and facilitates on-time development and implantation.³

Collectively, the research shows GM-CSF's signaling *in vivo* plays a crucial role in facilitating successful implantation, embryo development, promoting enhanced immune response¹ and protecting the embryo from cell stress.³



1. Mor, G., Aldo, P. & Alvero, A. The unique immunological and microbial aspects of pregnancy. *Nat Rev Immunol* 17, 469–482 (2017). <https://doi.org/10.1038/nri.2017.64>

2. Weng J, Couture C, Girard S. Innate and Adaptive Immune Systems in Physiological and Pathological Pregnancy. *Biology* (Basel). 2023 Mar 3;12(3):402. doi: 10.3390/biology12030402. PMID: 36979094; PMCID: PMC10045867.

3. Robertson, S.A. (2018) GM-CSF in IVF Embryo Culture. *ART Scientific Edition* 4: 1–4.

4. Giacomini, G., Tabibzadeh, S. S., Satyaswaroop, P. G., Bonsi, L., Vitale, L., Bagnara, G. P., Strippoli, P., & Jasonni, V. M. (1995). Epithelial cells are the major source of biologically active granulocyte macrophage colony-stimulating factor in human endometrium. *Human Reproduction (Oxford, England)*, 10(12), 3259–3263. <https://doi.org/10.1093/oxfordjournals.humrep.a135899>

5. Zhao, Y., & Chegini, N. (1994). Human fallopian tube expresses granulocyte-macrophage colony stimulating factor (GM-CSF) and GM-CSF alpha and beta receptors and contain immunoreactive GM-CSF protein. *The Journal of Clinical Endocrinology and Metabolism*, 79(2), 662–665. <https://doi.org/10.1210/jcem.79.2.7519195>

6. Zhao, Y., & Chegini, N. (1999). The expression of granulocyte macrophage-colony stimulating factor (GM-CSF) and receptors in human endometrium. *American Journal of Reproductive Immunology* (New York, N.Y. : 1989), 42(5), 303–311. <https://doi.org/10.1111/j.1600-0897.1999.tb00106.x>

7. Li, C., Chen, C., Kang, X. et al. (2020) Decidua-derived granulocyte macrophage-colony stimulating factor induces polymorphonuclear myeloid-derived suppressor cells from circulating CD15+ neutrophils. *Hum Reprod* 35: 2677–2691.

8. O'Neill C. (2008). The potential roles for embryotrophic ligands in preimplantation embryo development. *Human reproduction update*, 14(3), 275–288. <https://doi.org/10.1093/humupd/dmn002>
regulation of reproductive function. Bull Exp Biol Med 143: 75–79.

Designed for success

Designed to personalize journeys and improve outcomes

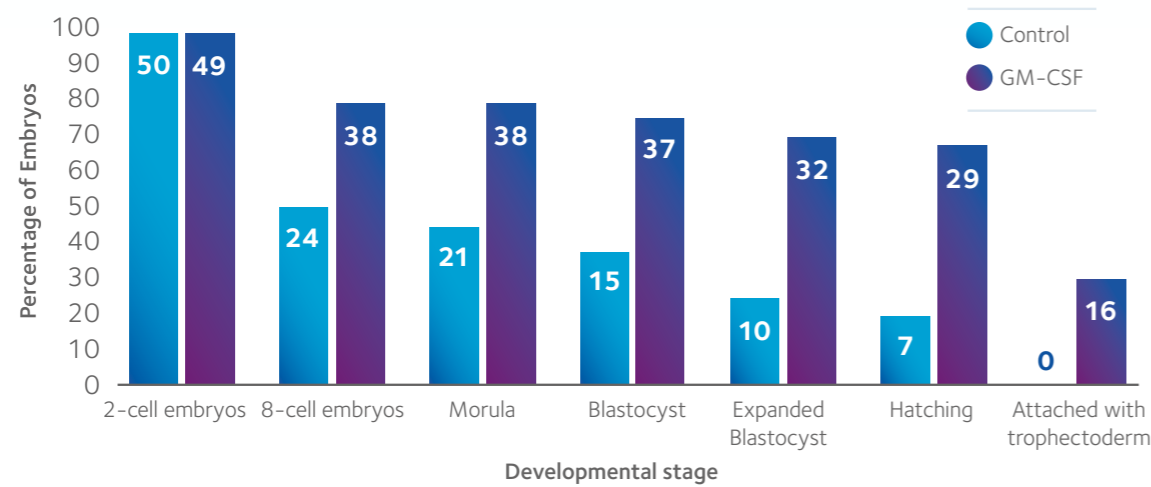
45+ YEARS OF RESEARCH DATA

GM-CSF and its role in reproduction have been researched since the 1970s, and the past 25 years of research have led to its inclusion in ART media. Multiple studies have revealed its impact on clinical outcomes, particularly for some subsets of women.

GM-CSF acts as a survival factor

When cultured in the presence of GM-CSF, there is a higher developmental percentage of embryos cultured to blastocysts compared to the control media.¹

The effect of rhGM-CSF on the development of embryos to blastocyst, hatching, and attachment stages.¹

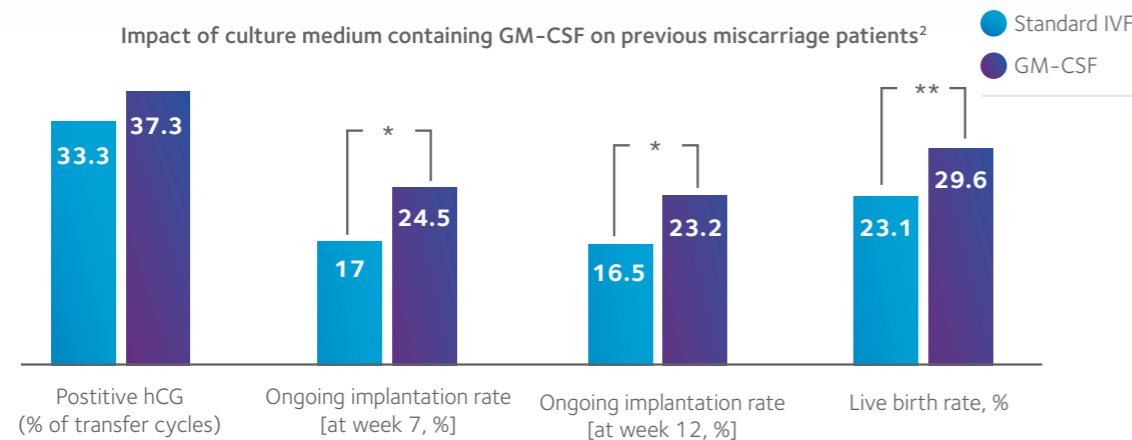


Data were analysed by Fisher's exact test.

Medium containing GM-CSF is an effective treatment option that improves outcomes for miscarriage patients

In women with previous miscarriage, GM-CSF can increase ongoing implantation rates

Impact of culture medium containing GM-CSF on previous miscarriage patients²

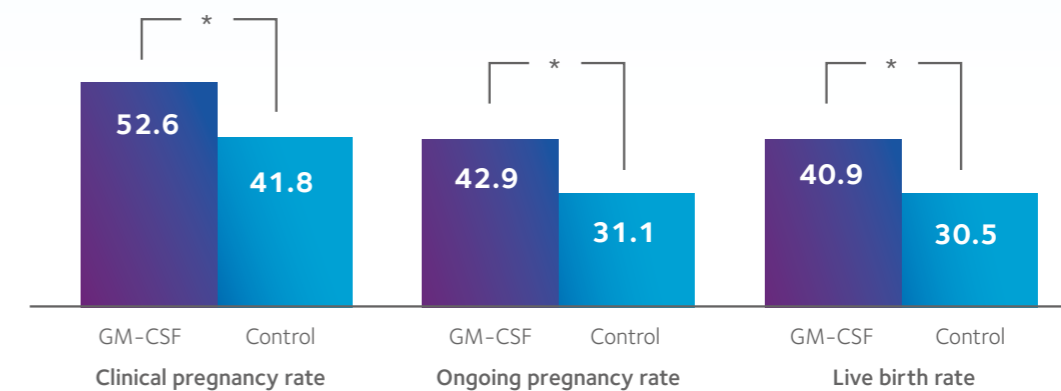


*P<0.004; **P<0.001 denote significant difference from control group.

Increased implantation rate for frozen embryo transfer with SAGE 1-Step™ Media

The use of SAGE 1-Step™ GM-CSF in post warming culture and transfer improved the live birth rate as a result of increased implantation rate in the frozen-thawed blastocyst-transfer cycle.³

Overall and embryo-transfer outcomes (%) GM-CSF-containing medium vs. Control medium

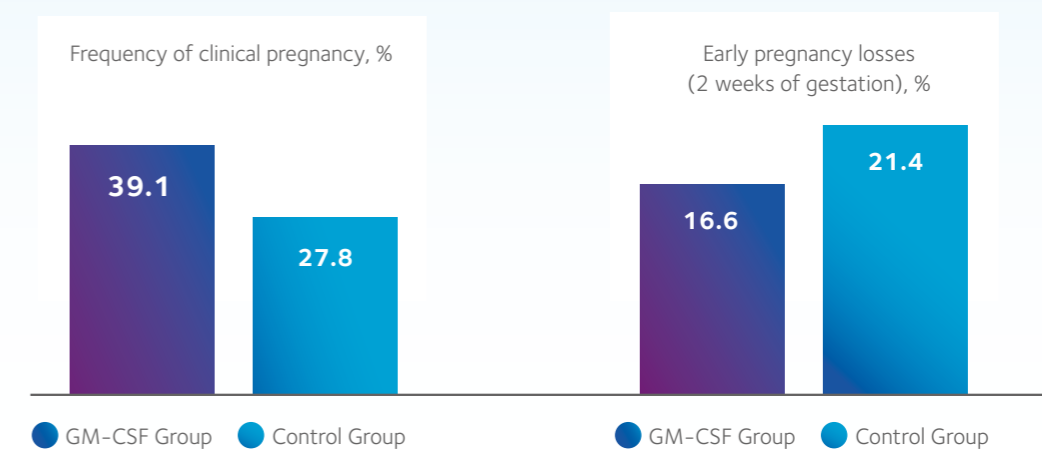


*P<0.03 denote significant difference from control group.

Positive effect on pregnancy outcome in women with RIF⁴

GM-CSF supplemented embryo culture is associated with increased frequency of clinical pregnancy and decreased early pregnancy loss – relevant for patients with preceding failed attempts.⁴

Positive effect on pregnancy outcome in women with RIF



1. Sjöblom, C., Wikland, M., & Robertson, S. A. (1999). Granulocyte-macrophage colony-stimulating factor promotes human blastocyst development in vitro. *Human Reproduction* (Oxford, England), 14(12), 3069–3076. <https://doi.org/10.1093/humrep/14.12.3069>

2. Ziebe, S., Loft, A., Povlsen, B. B., Erb, K., Agerholm, I., Aasted, M., Gabrielsen, A., Hnida, C., Zobel, D. P., Munding, B., Bendz, S. H., & Robertson, S. A. (2013). A randomized clinical trial to evaluate the effect of granulocyte-macrophage colony-stimulating factor (GM-CSF) in embryo culture medium for *in vitro* fertilization. *Fertility and Sterility*, 99(6), 1600–1609. <https://doi.org/10.1016/j.fertnstert.2012.12.043>

3. Okabe-Kinoshita, M., Kobayashi, T., Shioya, M. et al. (2022) Granulocyte-macrophage colony-stimulating factor-containing medium treatment after thawing improves blastocyst-transfer outcomes in the frozen-thawed blastocyst-transfer cycle. *J Assist Reprod Genet* 39: 1373- 1381

4. Tevkin, S., Lokshin, V., Shishimorova, M. et al. (2014) The frequency of clinical pregnancy and implantation rate after cultivation of embryos in a medium with granulocyte macrophage colony-stimulating factor (GM-CSF) in patients with preceding failed attempts of ART. *Gynecol Endocrinol* 30 (Suppl 1): 9-12.

SAGE 1-STEP™ GM-CSF MEDIA



Product Specifications

GM-CSF: 2 ng/mL
HSA: 5 mg/mL
pH: 7.2 – 7.4
Osmolality: 257-273 mOsm/Kg
26 weeks shelf life / 7 day open bottle usage

Components

Recombinant human GM-CSF
Sodium hyaluronate
HSA
Physiological salts
Energy substrates
EDTA
Gentamicin sulfate
Phenol red
Essential amino acids
Non-essential amino acids
Antioxidants

Product Code	Product Name	Volume	Article Description
77010003A	SAGE 1-Step™ GM-CSF	3 mL	With HSA and phenol red



To learn more about SAGE 1-Step GM-CSF media,
speak with your local CooperSurgical representative today.

