UPDATES IN

CONTROLLED OVARIAN STIMULATION

2026

Evidence Review · Emerging Protocols · New Standards

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Table of Contents

Eight advances reshaping how we stimulate, monitor and think about ovarian response in ART

01 **Historical Perspective**
From natural cycles to GnRH analogues

02 **Paradigm Shift: Vitrification**
Freeze-all liberates stimulation goals

03 **PPOS — Progestin-Primed COS**
Oral tablets replace injections

04 **Random-Start Stimulation**
Freedom from day 2–3 restriction

05 **DuoStim — Double Stimulation**
Two retrievals in one cycle

06 **Letrozole in IVF**
Aromatase inhibition as adjuvant

07 **LH in Ovarian Stimulation**
From contaminant to essential cofactor

08 **Key Performance Indicators**
Dynamic metrics for precision dosing

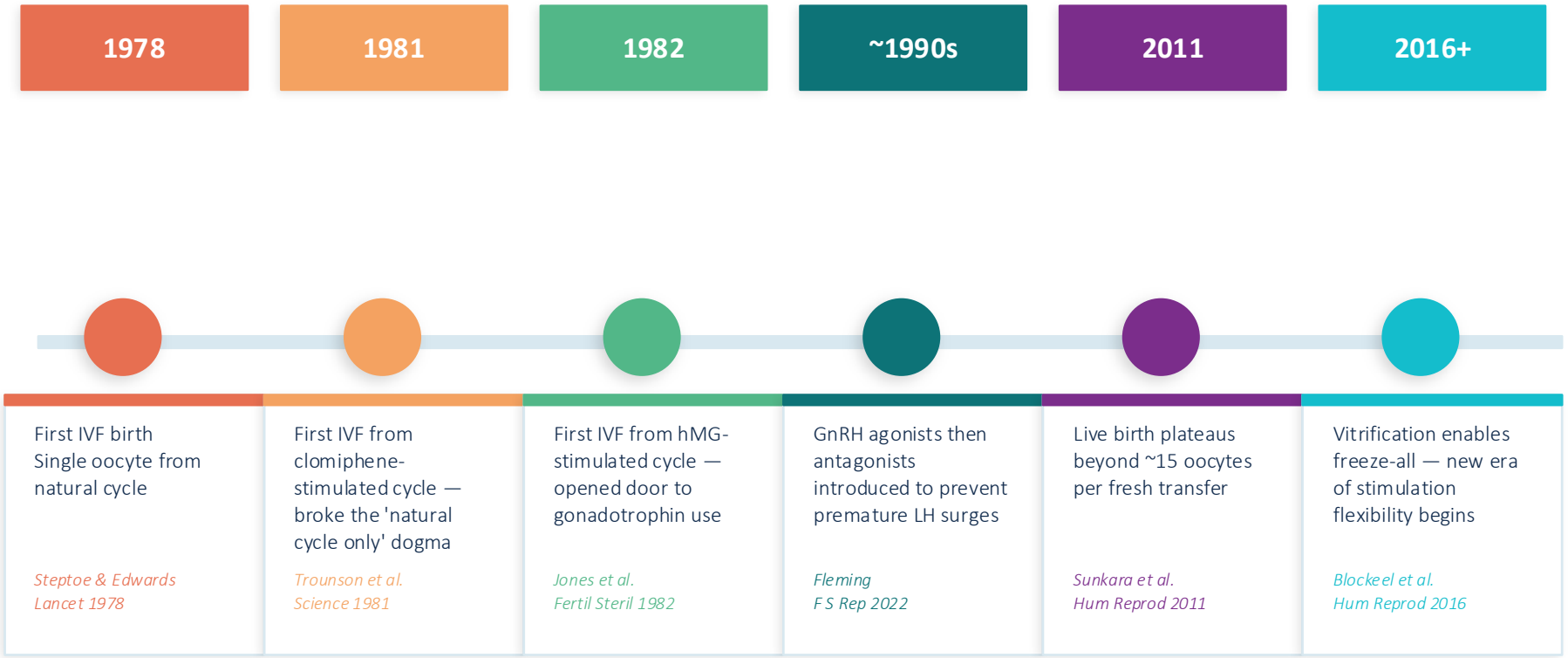
SECTION 01

Historical Perspective

1

Five decades of evolution — from single natural-cycle oocytes to modern multifollicular stimulation

A Brief History of Ovarian Stimulation for IVF



Steptoe & Edwards · Lancet · 1978 | Trounson et al. · Science · 1981 | Jones et al. · Fertil Steril · 1982 | Sunkara et al. · Hum Reprod · 2011 | Blockeel et al. · Hum Reprod · 2016

Conventional GnRH Antagonist Protocol

Standard stimulation designed for fresh embryo transfer — four key limitations now recognised

Day 2–3	Day 5–6	Day 8–12	Day 10–14	+36 h	+3–5 d
Start FSH	Add Antagonist	Monitor US + E_2	Trigger hCG/GnRH-a	Oocyte Retrieval	Fresh Transfer

OHSS Risk

Multifollicular growth + hCG trigger = compounding vascular risk

Eliminated by freeze-all + GnRH agonist trigger

Endometrial Disruption

Late-follicular P4 rise advances endometrium out of sync

Mandates cryotherapy in high-P4 cycles

Rigid Scheduling

Stimulation must start day 2–3 of each cycle

Constrains oncofertility, donor programmes, patient flexibility

Oocyte Yield Ceiling

Fresh-transfer LBR plateaus at 12–18 oocytes

Protocol optimised for one fresh transfer, not CLBR

Ata RBMO 2025 | Sunkara et al. Hum Reprod 2011 | Venetis et al. Hum Reprod Update 2013

Maximizing Oocyte Yield: The New Paradigm

Old goal	Aim for ~15 oocytes — beyond this, fresh LBR plateaus and OHSS risk increases
New goal	Cautiously MAXIMIZE oocyte yield — cumulative LBR keeps rising with each additional oocyte
Key enabler	GnRH agonist trigger + freeze-all eliminates OHSS risk, removing the ceiling on stimulation
Outcome shift	The ultimate measure of success is no longer LBR per fresh transfer — it is CLBR per stimulation cycle

CLBR

↑ Continuously

with each oocyte retrieved

SECTION 02

Vitrification & Freeze-All

2

How cryopreservation liberated ovarian stimulation from conventional constraints

Vitrification: Game-Changer for Ovarian Stimulation

=

Fresh & Frozen LBR now equivalent

↑∞

CLBR rises with every oocyte — no plateau

0

Clinically significant OHSS with GnRHa trigger + freeze-all

CLBR replaces LBR per ET

Cumulative live birth rate is the new gold standard — unlike fresh LBR, it increases continuously with each additional oocyte retrieved.
Law et al. · Reprod Biomed Online · 2021

Cycle Segmentation

Separating stimulation from transfer ('segment') allows optimal timing for both oocyte retrieval and endometrial preparation.
Devroey et al. · Hum Reprod · 2011

Progesterone Elevation Mitigated

Freeze-all bypasses the negative effect of late-follicular progesterone elevation on endometrial receptivity.
Racca et al. · Hum Reprod · 2021

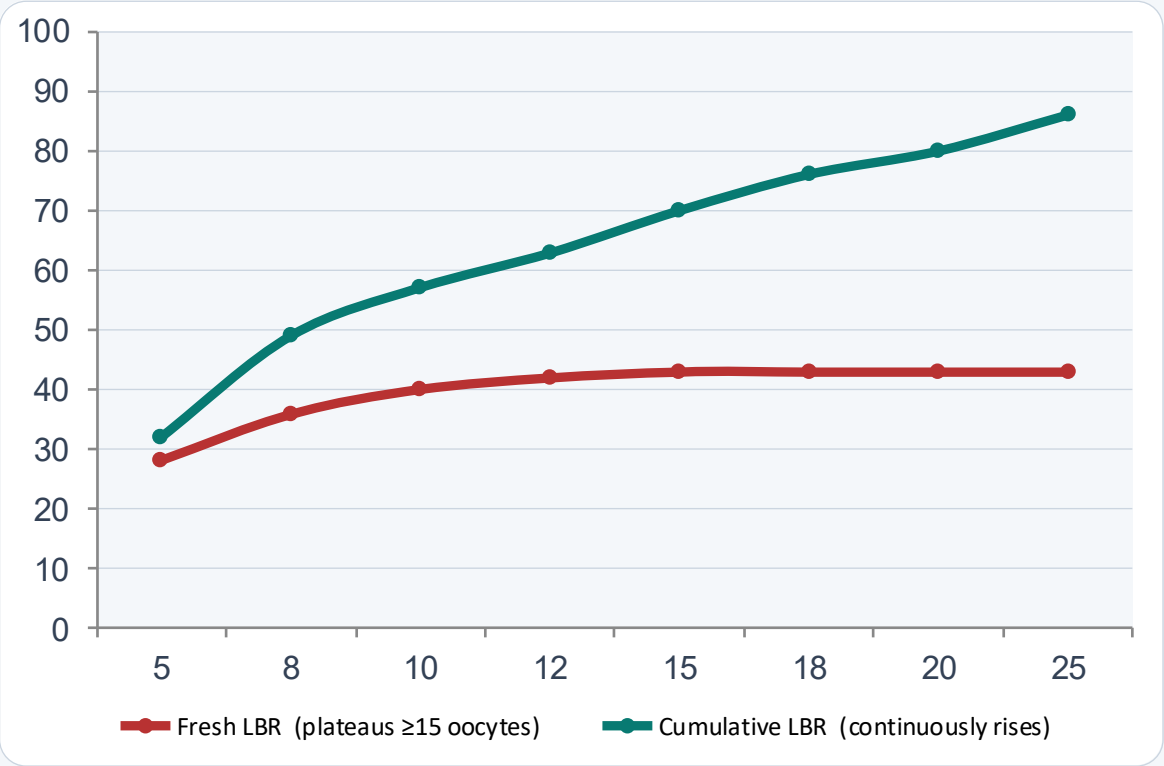
Fertility Preservation Enabled

Reliable vitrification expanded ART indications to include oncofertility, social egg-freezing, and oocyte banking programs.
de Ziegler & Sokteang · Fertil Steril · 2025

Devroey et al. · Hum Reprod · 2011 | Law et al. · Reprod Biomed Online · 2021 | Racca et al. · Hum Reprod · 2021 | de Ziegler & Sokteang · Fertil Steril · 2025

CLBR vs Fresh LBR — Redefining Stimulation Goals

Every additional oocyte adds cumulative value — the case for cautious maximisation over a 'safe range'



Fresh LBR Plateau

Peaks at 12–18 oocytes

Near-zero marginal gain beyond 15 oocytes for fresh transfer

CLBR Keeps Rising

No ceiling detected in cumulative analysis (Law et al. 2021)

Every additional oocyte contributes to eventual success

Strategic Shift

Goal: 'safe range' → cautious maximisation

GnRH agonist trigger + freeze-all remove both OHSS and P4 ceilings

Ata RBMO 2025 | Sunkara et al. Hum Reprod 2011 | Law et al. Reprod Biomed Online 2021

SECTION 03

Progestin-Primed COS

3

Oral progestins as an injection-free alternative to GnRH analogues

Progestin-Primed Ovarian Stimulation (PPOS)

Mechanism & Origin

Inspired by natural luteal-phase suppression of pituitary gonadotrophins by high progesterone.

First described: 10 mg/day oral medroxyprogesterone acetate (MPA) + gonadotrophins in 150 women undergoing freeze-all.

Kuang et al. · Fertil Steril · 2015

Any available progestin can be used — dydrogesterone, MPA, micronized progesterone, norethindrone.

Oral route replaces GnRH analogue injections — lower cost, fewer needles.

Key Evidence

Cumulus cells unaffected

MPA does not perturb gonadotropin-responsiveness or steroidogenesis.
Oktem et al. · Hum Reprod · 2024

Equivalent oocyte quality

Blastulation, euploidy, live birth per transfer & CLBR equivalent to GnRH analogue cycles.
Giles et al. · Fertil Steril · 2021

Similar stimulation parameters

Duration, gonadotrophin consumption, and oocyte yield are comparable.
Ata & Kalafat · Reprod Biomed Online · 2024

Fresh transfer excluded

The only absolute requirement — endometrial progestin exposure mandates freeze-all strategy.
Ata et al. · Hum Reprod Update · 2021

Kuang et al. · Fertil Steril · 2015 | Oktem et al. · Hum Reprod · 2024 | Giles et al. · Fertil Steril · 2021 | Ata & Kalafat · Reprod Biomed Online · 2024 | Ata et al. · Hum Reprod Update · 2021

PPOS vs GnRH Analogue — Head-to-Head

Equivalent outcomes with lower injection burden and cost (Ata et al. Hum Reprod Update 2021)

Parameter	GnRH Analogue Protocol	PPOS Protocol
Route of suppression	Daily subcutaneous injections	Oral tablets — no injections required
Cost	Higher (analogue + administration)	Significantly lower
Mechanism	GnRH receptor blockade / pituitary desensitisation	High progesterone → decreased GnRH pulse frequency
Oocyte yield	Standard reference	**[OK] Equivalent**
Euploidy / blastulation	Standard reference	**[OK] Equivalent (Giles et al. 2021)**
CLBR	Standard reference	**[OK] Equivalent**
Fresh transfer	**[OK] Possible**	**[X] Not possible — freeze-all required**
Patient convenience	Moderate — daily injections	**[+] High — oral administration only**

Ata RBMO 2025 | Ata et al. Hum Reprod Update 2021 | Giles et al. FS 2021

SECTION 04

Random-Start Stimulation

4

Freedom from the day 2–3 restriction — any cycle phase is valid

Random Start Stimulation: Any Phase Works

Oocyte yield and developmental potential are NOT affected by the day stimulation starts.

Ata et al. · Reprod Biomed Online · 2023

Early Follicular

Day 2–3

PROS

Classic; well-studied; synchronized follicular growth

CONS

Must wait for next cycle; scheduling rigid

Peri-ovulatory

Day ~13–15

PROS

Endogenous progesterone prevents LH surge — minimal/no exogenous suppression needed

CONS

Careful timing required vs pre-ovulatory follicle

Late Follicular

Day 8–12

PROS

Flexibility; can trigger pre-ovulatory follicle then stimulate new cohort

CONS

GnRH antagonist or progestin needed as backup

Luteal Phase

Day 15–25

PROS

Follicles most synchronous mid-luteal; benefits poor responders

CONS

2–3 days longer; must exclude existing pregnancy

Ata et al. · Reprod Biomed Online · 2023 | Baerwald et al. · Biol Reprod · 2003 | De Rijdt et al. · Reprod Biomed Online · 2024

Scientific Basis for Random-Start Stimulation

Follicular recruitment waves occur throughout the menstrual cycle — not only in the early follicular phase

Scientific Foundation

Follicular Wave Biology (McNatty et al. 1983)

Healthy antral follicles present throughout the entire menstrual cycle — not only in the early follicular phase. First demonstrated 1983, clinically ignored for two decades.

Multiple Recruitment Waves (Baerwald et al. 2003)

Multiple follicular waves occur across the cycle. Stimulation at any wave yields developmentally competent oocytes with equivalent potential.

Cycle Segmentation Removes Synchrony Requirement

In freeze-all cycles, follicular and endometrial growth no longer need synchronisation — enabling any-day-start protocols.

Clinical Confirmation (Ata et al. 2023)

Oocyte yield, blastulation, euploidy, LBR, and CLBR are unaffected by stimulation start day — all phases equivalent.

Early Follicular (Day 2–3)

Conventional start — best follicle cohort synchrony

Recommended when fresh transfer is planned

Standard reference for all outcome comparisons

Late Follicular / Peri-Ovulatory

Rising corpus luteum P4 suppresses LH — no analogue needed

Ultra-minimal option: long-acting FSH + trigger (2 injections)

Mid-Late Luteal Phase

Endogenous P4 suppresses LH — no injection needed

2–3 days longer; benefits low responders

Exclude pregnancy before starting

Ata RBMO 2025 | Baerwald et al. Biol Reprod 2003 | McNatty et al. 1983 | Ata et al. Reprod Biomed Online 2023

Random-Start Protocol Variants

Three valid starting phases — each with distinct clinical advantages and considerations

Peri-Ovulatory Start

ADVANTAGES

- Rising corpus luteum P4 prevents LH surge — no exogenous analogue needed
- Ultra-minimal option: long-acting FSH + trigger (2 injections only)
- Most injection-light protocol currently described

CONSIDERATIONS

– Must confirm dominant follicle has peaked or ruptured

– Stimulated cohort must develop before LH-sensitivity window

Late Follicular Start

ADVANTAGES

- Pre-ovulatory follicle triggered to clear path for stimulated cohort
- GnRH antagonist or PPOS added if LH rise risk present
- Flexible entry — anytime in late follicular phase

CONSIDERATIONS

– Careful sizing of dominant follicle required at start

– Stimulated cohort must be smaller than pre-ovulatory follicle at trigger

Mid-Late Luteal Phase

ADVANTAGES

- Endogenous P4 provides natural LH suppression — no injection needed
- Most synchronous follicle cohort among all three options
- Particularly beneficial in low/poor responders (Ata 2025)

CONSIDERATIONS

– 2–3 days longer total stimulation duration

– Must exclude early pregnancy before initiating

Ata RBMO 2025 | De Rijdt et al. Reprod Biomed Online 2024 | Semrl et al. 2024 | Lawrenz et al. 2024

Luteal Phase Stimulation: Details & Clinical Cautions

Duration

Only 2–3 days longer than follicular start cycles — a minor tradeoff for scheduling independence.
Ata et al. · Reprod Biomed Online · 2023

Follicle Synchrony

Follicles most synchronous mid-luteal phase; may improve cohort homogeneity, especially for poor responders.
Ata · RBMO · 2025

Key Risk: Pregnancy

Undetected existing pregnancy → inadvertent exposure → severe OHSS in high responders. Eligibility criteria advised.
Semrl et al. · Reprod Biomed Online · 2024

Patient Selection

Exclude young women with short unexplained infertility (higher pregnancy likelihood) from luteal starts.
Lawrenz et al. · Reprod Biomed Online · 2024

Progestin Optional

Endogenous progesterone may suffice; exogenous progestin can be omitted if levels remain adequate through triggering.
Ata · RBMO · 2025

OHSS Prevention

GnRH agonist trigger + freeze-all neutralizes OHSS risk regardless of stimulation start day — the cornerstone of safety.
Devroey et al. · Hum Reprod · 2011

Ata et al. · Reprod Biomed Online · 2023 | Semrl et al. · Reprod Biomed Online · 2024 | Lawrenz et al. · Reprod Biomed Online · 2024 | Devroey et al. · Hum Reprod · 2011

SECTION 05

DuoStim
Double Stimulation

5

Two complete stimulations in one cycle — maximising oocyte yield for poor responders

DuoStim — Double Stimulation in One Cycle

Shanghai Protocol (Kuang 2014) → simplified DuoStim (Vaiarelli & Ubaldi 2020)

Key Evidence (Kuang et al. 2014)

- 38 poor responders: luteal phase yielded 3.5 vs 1.7 oocytes vs follicular phase
- 30/38 proceeded directly to luteal stim the day after retrieval #1
- Proved follicular wave availability throughout the menstrual cycle

DuoStim vs Separate Cycles

- Similar euploidy rates between follicular & luteal phase oocytes
- Similar obstetric and perinatal outcomes (Vaiarelli et al. 2020)
- Time advantage confirmed; not superior to two separate stimulations (RCT: Cerrillo 2023)

Optimal Patient Profile

- Poor / diminished ovarian reserve (Bologna criteria)
- Urgent fertility preservation — oncology patients
- PGT-A cycles requiring multiple euploid blastocysts

Ata RBMO 2025 | Kuang et al. Reprod Biomed Online 2014 | Vaiarelli et al. Hum Reprod 2020 | Cerrillo et al. Reprod Biomed Online 2023

Does Ovarian Stimulation Affect Oocyte Quality?

Harvey et al. undertook an extensive assessment within the OS 2.0 series (Fertil Steril, 2025).

Follicular Fluid	OS alters some follicular fluid markers *Harvey et al. · Fertil Steril · 2025*	Mixed
Embryo Euploidy	Euploidy rate NOT affected by gonadotrophin dose; natural cycle vs OS shows no difference *Harvey et al. · Fertil Steril · 2025*	Reassuring
Endometrial Histology	Morphological differences vs natural cycle reported; but may NOT impact implantation rates *Harvey et al. · Fertil Steril · 2025*	Neutral
Endometrial Receptivity	Freeze-all + deferred transfer mitigates concern entirely when response is intense *de Ziegler & Sokteang · Fertil Steril · 2025*	Resolved
PPOS Oocyte Quality	MPA does not affect cumulus cell molecular function, steroidogenesis or oocyte developmental potential *Oktem et al. · Hum Reprod · 2024*	Reassuring

SECTION 06

Letrozole in IVF

6

New remedy or old mirage? Evidence for aromatase inhibition as adjuvant in ART

Aromatase Inhibitors (Letrozole) as Co-Treatment in ART

Bulow & Macklon · Fertil Steril · 2025

Role in Poor Responders

Letrozole added to OS protocols may improve live birth rates in poor responders. Systematic reviews support benefit through earlier follicular recruitment.
Bulow & Macklon · Fertil Steril · 2025

Androgen Amplification

Intraovarian androgen accumulation (via inhibited aromatization) amplifies FSH signalling — synergizes with exogenous gonadotrophins.
de Ziegler & Sokteang · Fertil Steril · 2025

Ovulation Induction

Already used for ~20 years in oligo-anovulation instead of clomiphene citrate — now extended to OS protocols for ART.
Bulow & Macklon · Fertil Steril · 2025

Breast Cancer Patients

Letrozole co-treatment reduces peak estradiol during stimulation — preferred option for fertility preservation in estrogen-sensitive cancers.
Bulow & Macklon · Fertil Steril · 2025

Letrozole as Adjuvant in Poor Responders

Meta-analysis: 20 studies, 11 RCTs, n = 2,596 women — first robust evidence for LBR improvement

+7%
LBR Increase
(95% CI: 1–13%)

+11%
LBR in Women
< 35 Years

FSH-
Gonadotropin
Consumption

11
RCTs in
Meta-Analysis

Key Findings — Bülow et al. Reprod Biomed Online 2022

+7% LBR vs gonadotropin alone (95% CI 1–13%) — first meta-analytic evidence of benefit

No significant difference in oocyte yield or cycle cancellation rate

Significant reduction in FSH consumption and stimulation duration

Larger benefit in younger poor responders (<35 yrs): +11% LBR (Kahraman & Tulek 2022)

RECOMMENDED PROTOCOL

LZ 5 mg/day simultaneously with FSH

Continue ≥5 days or until trigger day

Add GnRH antagonist co-treatment

Freeze-all with GnRH agonist trigger

Bülow et al. Reprod Biomed Online 2022 | Bülow & Macklon FS 2025 | Kahraman & Tulek Arch Gynecol Obstet 2022

Letrozole: Luteal Phase Support & OHSS Reduction

Novel evidence: LZ normalises the luteal phase and may reduce need for progesterone supplementation

Letrozole → Enhanced Luteal Phase Support

Late-follicular supraphysiological E_2 is the primary disruptor of corpus luteum function (Beckers et al. 2003)

LZ prevents E_2 surge → preserves corpus luteum function and natural P4 production

RCT: LZ → elevated midluteal LH, P4, and androgen levels (Bülow et al. FS 2022)

Extended duration of unsupported luteal phase with LZ co-treatment

Potential to reduce or eliminate exogenous progesterone supplementation — ongoing RCTs

30 x

Increase in midluteal P4 with LZ + GnRH agonist trigger vs controls

Dreyer Holt et al. J Clin Endocrinol Metab 2022

OHSS Risk Reduction

Supraphysiological E_2 restriction proposed to reduce OHSS severity

Systematic review (8 studies, n = 1,551): reduced moderate/severe OHSS

Not yet in ASRM 2024 guidelines due to result heterogeneity

EVIDENCE IN DEVELOPMENT

Active RCT evaluating LZ in OHSS reduction

Current best practice: freeze-all + GnRH agonist trigger

LZ luteal-phase benefit already evidence-supported

Bülow & Macklon FS 2025 | Dreyer Holt et al. J Clin Endocrinol Metab 2022 | ASRM OHSS Guidelines 2024

Letrozole in FET Cycles & Neonatal Safety

Promising evidence for endometrial preparation; reassuring safety data despite early concerns

LZ-Stimulated FET — Oligoanovulatory Women

LZ 5 mg/day (day 3–7) induces follicular growth → E_2 → ovulation → corpus luteum P4

Multiple cohort studies: higher LBR vs artificial cycle (AC-FET) in PCOS

Lower hypertensive disorders (HDP) and LGA neonates vs AC-FET

Two RCTs show similar LBR — cohort advantage not confirmed under controlled conditions

Why LZ Over Artificial Cycle?

AC-FET (no corpus luteum): associated with adverse obstetric outcomes in large registry studies

LZ-FET preserves natural luteal P4 — mechanistically similar to modified natural-cycle FET

Preferred over AC-FET in oligoanovulatory women — confirmatory RCTs ongoing

Neonatal Safety — Evidence Timeline

2005 — Biljan et al. — 150 neonates raised concerns (locomotor/cardiac). High risk-of-bias: flawed controls, spontaneous pregnancies.

2006 — Tulandi et al. — 911 children: no increase in major congenital malformations vs other fertility treatments. First large reassurance dataset.

2021 — Pundir et al. systematic review — 4,697 children after LZ-IUI: no increased malformation risk (Hum Reprod Update).

2022–24 — Bülow RCT follow-up: all children normal weight-for-GA; zero neonatal malformations at 1-month assessment.

Bülow & Macklon FS 2025 | Tulandi et al. FS 2006 | Pundir et al. Hum Reprod Update 2021

Letrozole in ART — Evidence by Patient Group

Current recommendations across indications (Bülow & Macklon, Fertil Steril 2025)

Patient Group	Indication	Key Outcome	Evidence Level	Recommendation
Anovulatory / PCOS	OI / IUI	LBR = CC; lower multiple pregnancy risk	Multiple RCTs	**[OK] First-line (ESHRE 2023)**
Poor Responders	Adjuvant FSH — IVF	LBR +7% (95% CI 1–13%)	11-RCT meta-analysis	**[OK] Supported (<35 yrs)**
Normal Responders	Adjuvant FSH — IVF	~2 more oocytes; LBR similar	Limited RCTs	**[?] Insufficient evidence**
High Responders	Adjuvant FSH — IVF	No LBR benefit; OHSS data pending	Limited data	**[RCT] Awaiting results**
Ovulatory women	FET prep	Similar LBR to natural cycle	Cohort studies	**[OK] Natural cycle preferred**
Oligoanovulatory	FET prep	Higher LBR vs AC-FET; lower HDP/LGA	Cohort + 2 RCTs	**[OK] Preferred over AC-FET**
Breast cancer	Fertility pres. IVF	Lower E_2 exposure; similar oocyte yield	Multiple studies	**[OK] Standard of care**

Bülow & Macklon FS 2025 | Bülow et al. Reprod Biomed Online 2022 | Teede et al. FS 2023

SECTION 07

LH in Ovarian Stimulation

7

From feared contaminant to required co-driver — the rehabilitation of luteinising hormone

The Essential Role of LH in Ovarian Stimulation

Four eras of evolving understanding — from feared contaminant to required co-driver

THE TWO-CELL MODEL > LH drives Theca cells > Androgens > Granulosa cells > Aromatase > Estradiol > Oocyte maturation & quality

1980s

LH = Contaminant

FSH:LH 1:1 in hMG. LH believed to compromise oocyte quality. Drove development of pure recombinant FSH preparations.

1990s–2000s

FSH-Only Era

Pure rFSH: follicular growth in hypothalamic amenorrhea but zero E_2 production. Oocytes unusable. LH role revealed.

2000s–2010s

LH Recognised

Evidence accumulates: LH drives theca-cell androgen production — essential for granulosa aromatisation. A cofactor, not a contaminant.

Today

LH Tactfully Desired

LH (as rLH, hMG, or via LZ) incorporated strategically. Critical in older patients, poor responders, and low-LH states.

SECTION 08

Key Performance Indicators

8

Dynamic metrics for comprehensive, individualised monitoring of follicular development

New Proposed KPIs for COS Monitoring

Beyond FORT and FOI — dynamic tracking from stimulation day 1 to retrieval (Sunkara et al. 2025)

Existing Metrics & Limitations

Ovarian Sensitivity Index (OSI)

>> Dosing algorithms vary between clinics — limits generalisability and cross-clinic comparison

FORT (Follicular Output Rate)

>> Omits follicles <16 mm; misses early recruitment stages contributing to oocyte yield

ORR (Oocyte Retrieval Rate)

>> Cannot distinguish growth efficacy, trigger quality, and retrieval technique

FOI (Follicle-to-Oocyte Index)

>> Static snapshot; misses growing vs atretic follicles; cannot guide in-cycle adjustment

New Proposed KPIs (Sunkara et al. 2025)

Early FORT

% follicles ≥10–11 mm on day 5/6 vs AFC at cycle start — enables early hypo/hyperresponse detection for in-cycle dose adjustment

Modified FORT

% follicles ≥12 mm at maturation trigger vs AFC at start — includes smaller follicles shown to yield mature oocytes

Advanced FOI

Total oocytes retrieved vs AFC (first 5 days) + Mature FOI: MII oocytes vs AFC — two-level assessment of retrieval competence

Modified ORR

Oocytes from follicles ≥12 mm AND ≥16 mm + Mature ORR for MII — distinguishes trigger efficacy from retrieval technique

Proposed New KPIs for Individualized OS Monitoring

Sunkara et al. · Fertil Steril · 2025 | Pirtea, Ayoubi & Ata · Fertil Steril · 2025

Early FORT

Day 5–6

Formula: ≥10–11mm follicles / AFC at start

Enables EARLY detection of hypo/hyperresponse → in-cycle gonadotrophin dose adjustment

Modified FORT

At Trigger

Formula: ≥12mm follicles / AFC at start

Captures smaller follicles' potential to yield mature oocytes — better than original FORT

Advanced FOI

At Retrieval

Formula: Total oocytes / AFC (first 5 days)
Sub-type: Mature FOI = MII / AFC

Holistic assessment of entire stimulation efficiency referenced to actual ovarian potential

Modified ORR

At Retrieval

Formula: Oocytes from ≥12mm and ≥16mm follicles
+ Mature ORR (MII oocytes)

Granular oocyte recovery analysis; distinguishes trigger efficacy from retrieval performance

The Future of Ovarian Stimulation

Oral Gonadotrophins

Development of oral gonadotrophins could further reduce injection burden and transform patient experience.

Remote Monitoring

Advancement of remote monitoring technologies — including at-home ultrasound devices — could drastically reduce clinic visits during stimulation.

AI & Machine Learning

AI-driven KPI thresholds and individualized protocol selection based on patient-specific data from growing datasets.

Automated Follicle Tracking

Reduces operator variability in follicle measurements, improving precision of new KPIs and stimulation monitoring.

In Vitro Maturation (IVM)

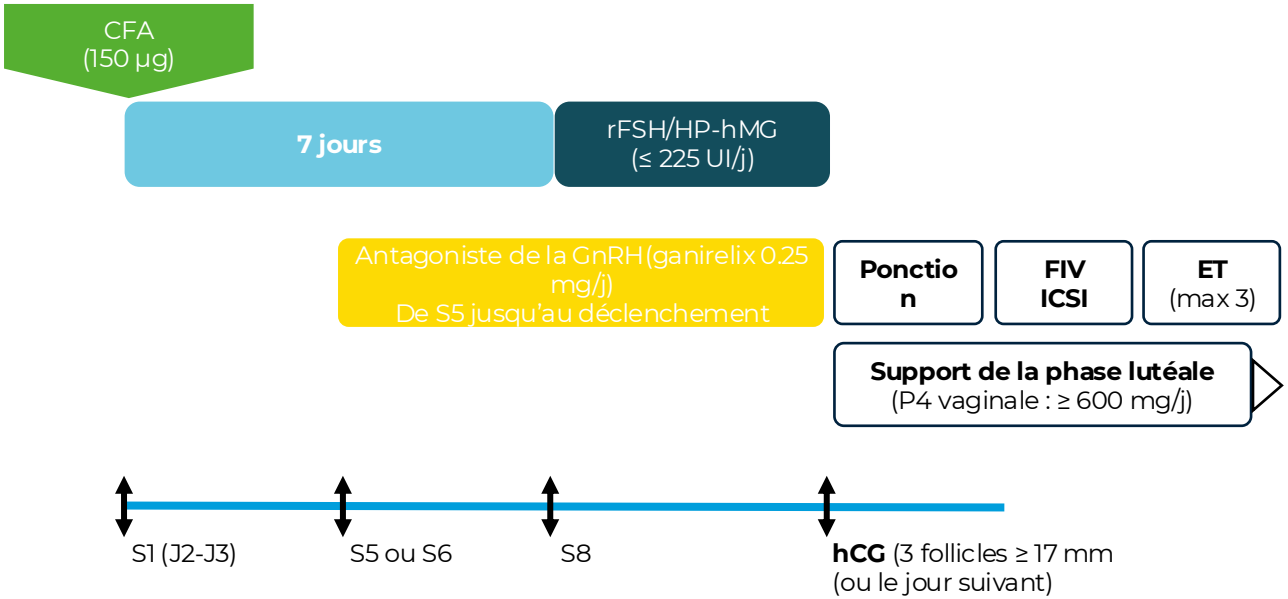
If IVM can achieve equivalent results to in-vivo maturation, ovarian stimulation could become obsolete — collecting immature oocytes from unstimulated cycles.

Personalized Protocols

Greater use of biomarkers (AMH, AFC, genetic) to tailor gonadotropin type, dose, and protocol — improving both safety and outcomes.

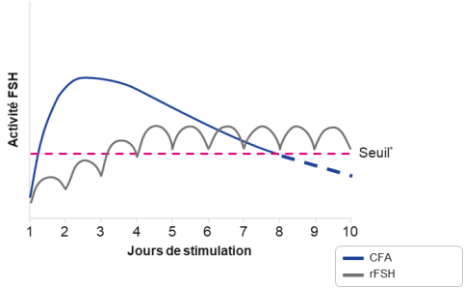
TRUST

Schéma de l'étude



CFA, corifollitropin alfa; ET, embryo transfer; GnRH, gonadotrophin-releasing hormone; hCG, human chorionic gonadotropin; hMG, human menopausal gonadotropin; ICSI, intracytoplasmic sperm injection; IU, international unit; IVF, in-vitro fertilization; max, maximum; mg, milligram; µg, microgram; mL, milliliter; mm, millimeter; rFSH, recombinant follicle-stimulating hormone.

Notre proposition



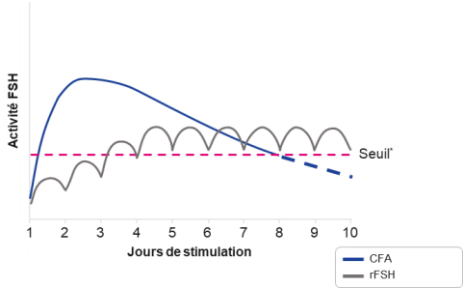
Déclenchement Agoniste GnRH

Daily FSH

PPOS

1 2 3 4 5 6 7 8 9 10 11 12 13 14

Notre proposition



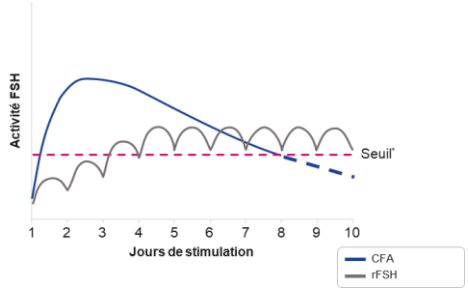
Déclenchement Agoniste GnRH

150 µg

PPOS

1 2 3 4 5 6 7 8 9 10 11 12 13 14

Notre proposition



Déclenchement Agoniste GnRH

150 µg

100 µg

PPOS

1 2 3 4 5 6 7 8 9 10 11 12 13 14

CONCLUSIONS & FUTURE DIRECTIONS

01 Freeze-All & CLBR

Vitrification shifted the goal to cumulative LBR. Cautious maximisation with agonist trigger is the standard aim.

02 PPOS — Simpler COS

Oral progestins replace injections with equivalent outcomes. Lower cost, higher convenience in planned freeze-all cycles.

03 Random Start Valid

Stimulation can begin any cycle day without compromising oocyte yield or quality. Day 2–3 restriction is obsolete.

04 Letrozole Emerging

Adjuvant LZ: +7% LBR in poor responders, improved luteal support, reduced FSH use. Standard care in oligoanovulatory FET.

05 LH is Essential

LH is required for oocyte quality via the two-cell model. Adequate LH activity must be ensured in all COS protocols.

06 KPIs Enable Precision

New metrics (Early FORT, Modified FORT, Advanced FOI, Modified ORR) track follicular dynamics for individualised dosing.

Future Horizons > Oral gonadotrophins • Remote monitoring & AI • IVM equivalent to stimulated cycles • Personalised KPI-driven dose algorithms

Ata RBMO 2025 | de Ziegler & Sokteang FS 2025 | Bülow & Macklon FS 2025 | Pirtea, Ayoubi & Ata FS 2025