

# The artificial endometrial preparation for frozen embryo transfer – the litmus test

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## 3 Main Messages

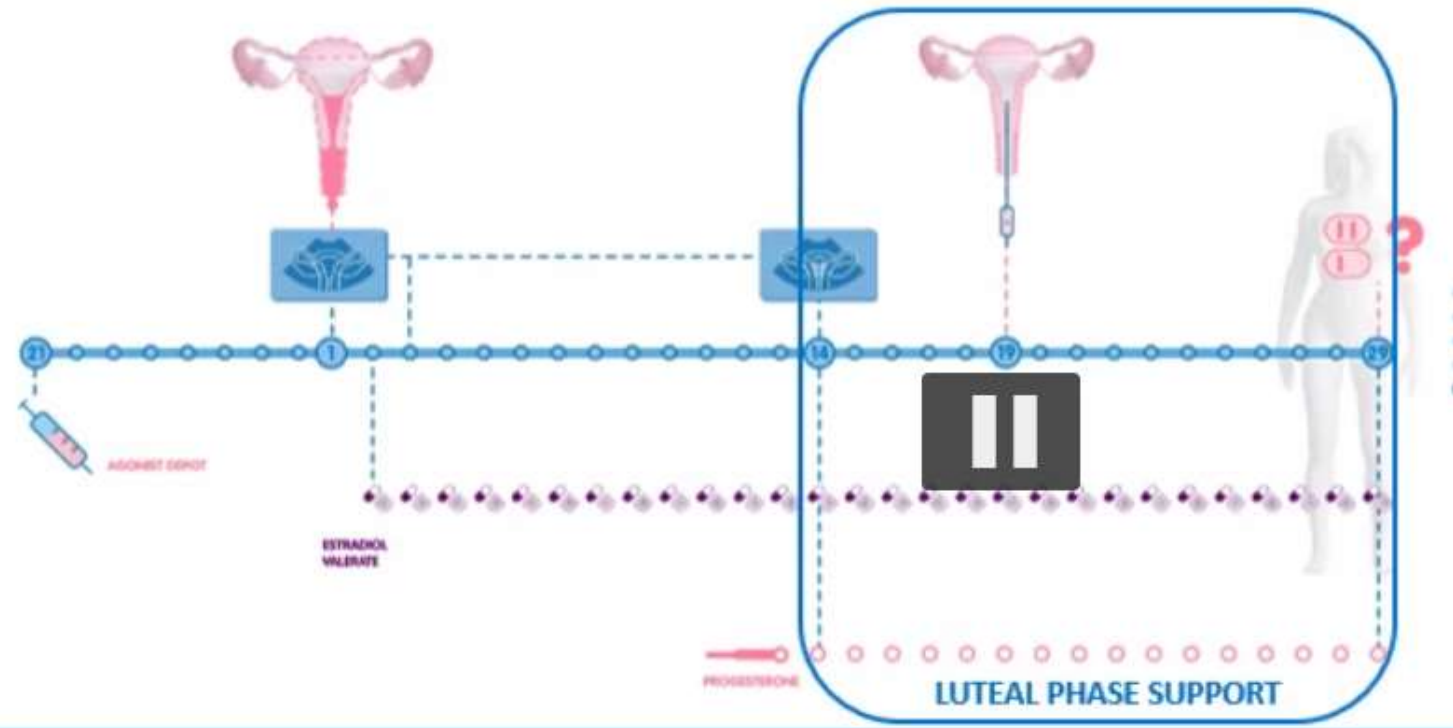
- Monitor luteal phase
- 25% -30% - inadequate progesterone levels
- How can we rescue the situation



# Artificial cycle / HRT

50% own eggs

95% donor cycles



PROGESTERONE : vaginal, oral, rectal, subcutaneous, intramuscular

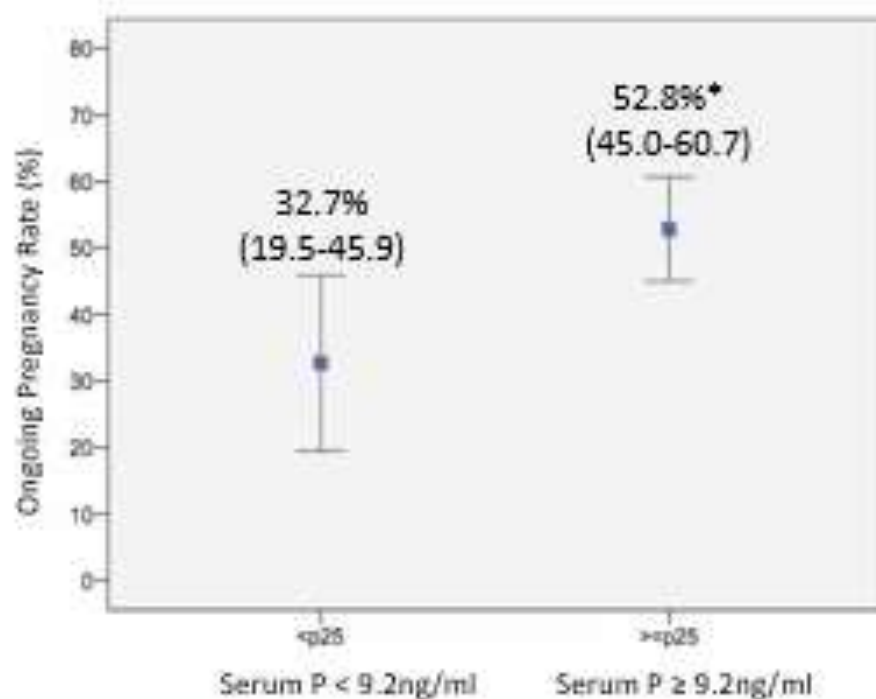
- Doses are different – not sure which is the best dose

- Natural or synthetic progesterone

- Most preferred route is vaginal ( studied )

- No monitoring of luteal phase has been done because
  - In a natural cycle progesterone is not constant.
  - HRT cycle is more constant but serum level of intramuscular and vaginal routes differ significantly and in addition serum levels may not match levels in endometrial tissue.
  - ( Paulsen et al JCCM 2014 ) showed that serum progesterone levels has not been shown to correlate with endometrial transformation and ability to establish pregnancy.
- But in the last few year things have changed
  - ( Young et al Hum Repro 2017 ) found that endometrial structure and function depends on serum progesterone both maturation and gene expression of the endometrium
  - There are a few retrospective studies also indicating that pregnancy outcome may depend on serum progesterone levels

## Low serum progesterone on the day of embryo transfer is associated with a diminished ongoing pregnancy rate in oocyte donation cycles after artificial endometrial preparation: a prospective study



\* $p=0.016$

RR (95% CI)= 0.62 (0.41-0.94)

### PROSPECTIVE study

- 244 patients (211 analysed)
- Oocyte donation
- HRT cycles
- 400mg/12h vaginal P
- Mean serum P: 12.7ng/ml

# Investigate Further

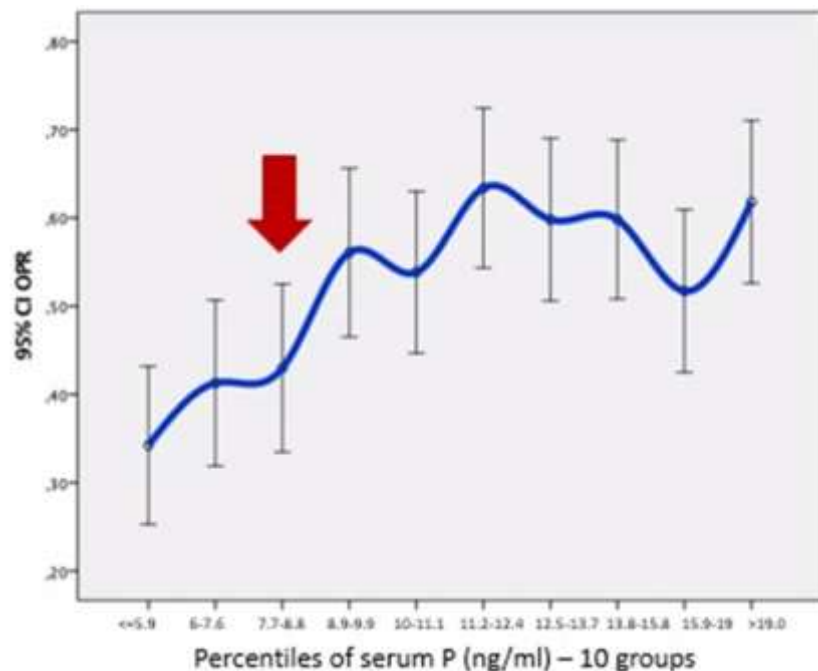
- Applicable to the general population
- Same effect mid to late luteal-phase
- Consistency
- Correctable



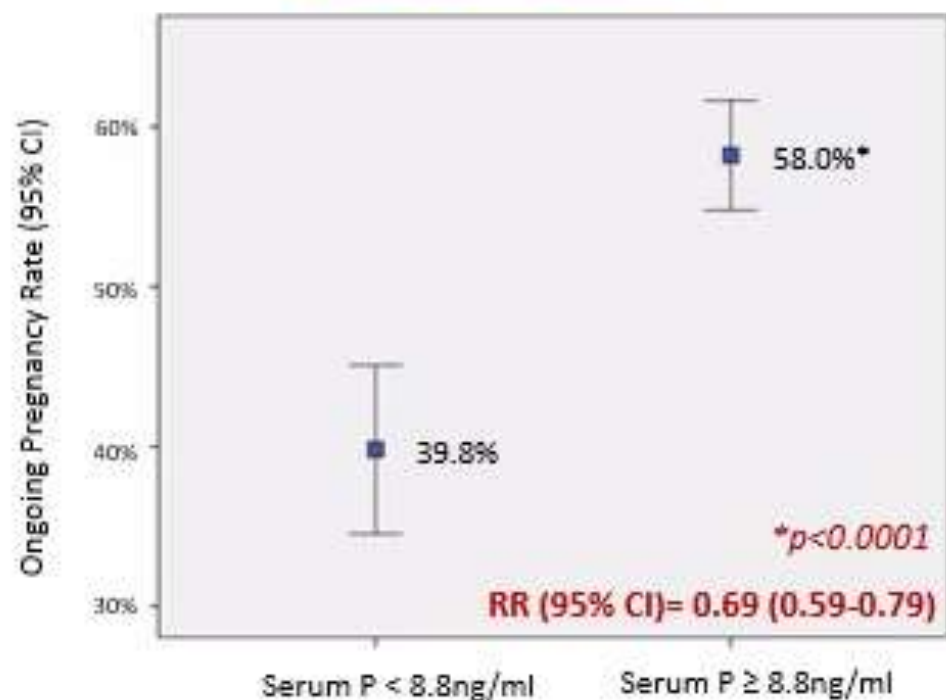
## LARGE PROSPECTIVE COHORT STUDY

- IVI RMA Valencia, Spain
- 1197 HRT cycles
- Own & donor eggs
- No restrictive inclusion criteria
- September 2017-November 2018
- ClinicalTrials.gov: NCT03272412

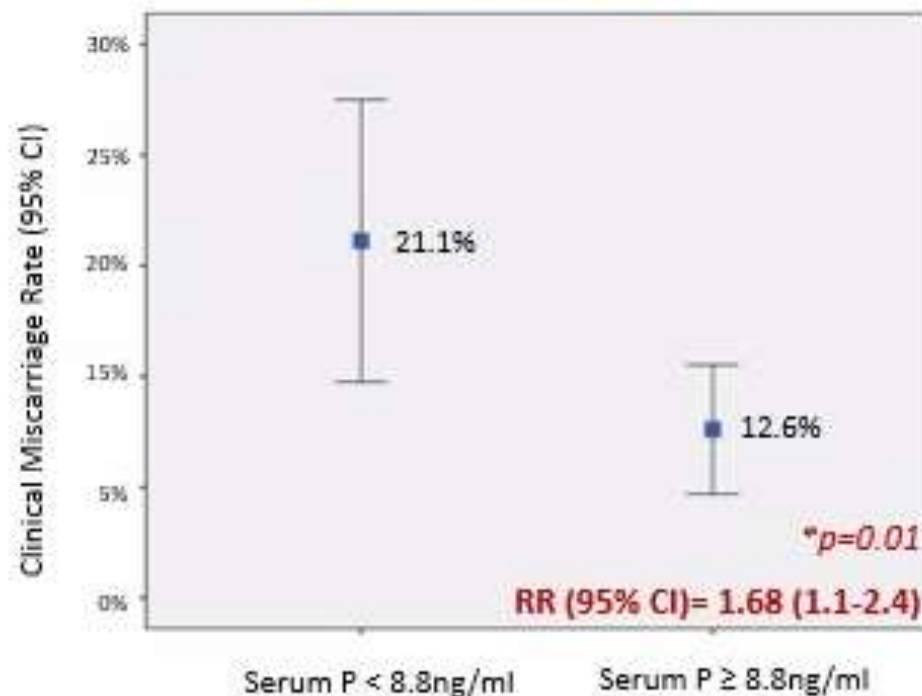
- 1127 patients
- Mean serum P: 12.1 ng/ml




### Ongoing Pregnancy



### Clinical Miscarriage

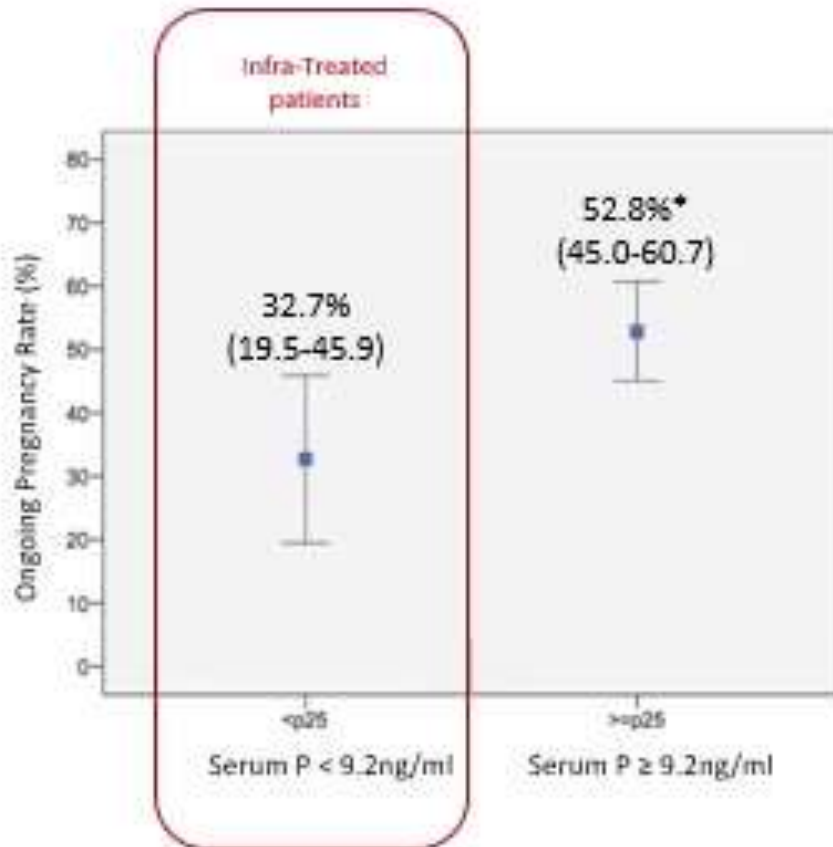


## SAME EFFECT ON MID or LATE LUTEAL-PHASE

- Progesterone was measured on Day 4, 7 and 11 after the transfer
  - Good consistency found throughout
  - In addition, in over 80% of cases patients receiving the same dose in another cycle were also consistent
  - ?? – Do we need 3-4 days to reach a steady level, in fact consistency was found already from day 1
- 

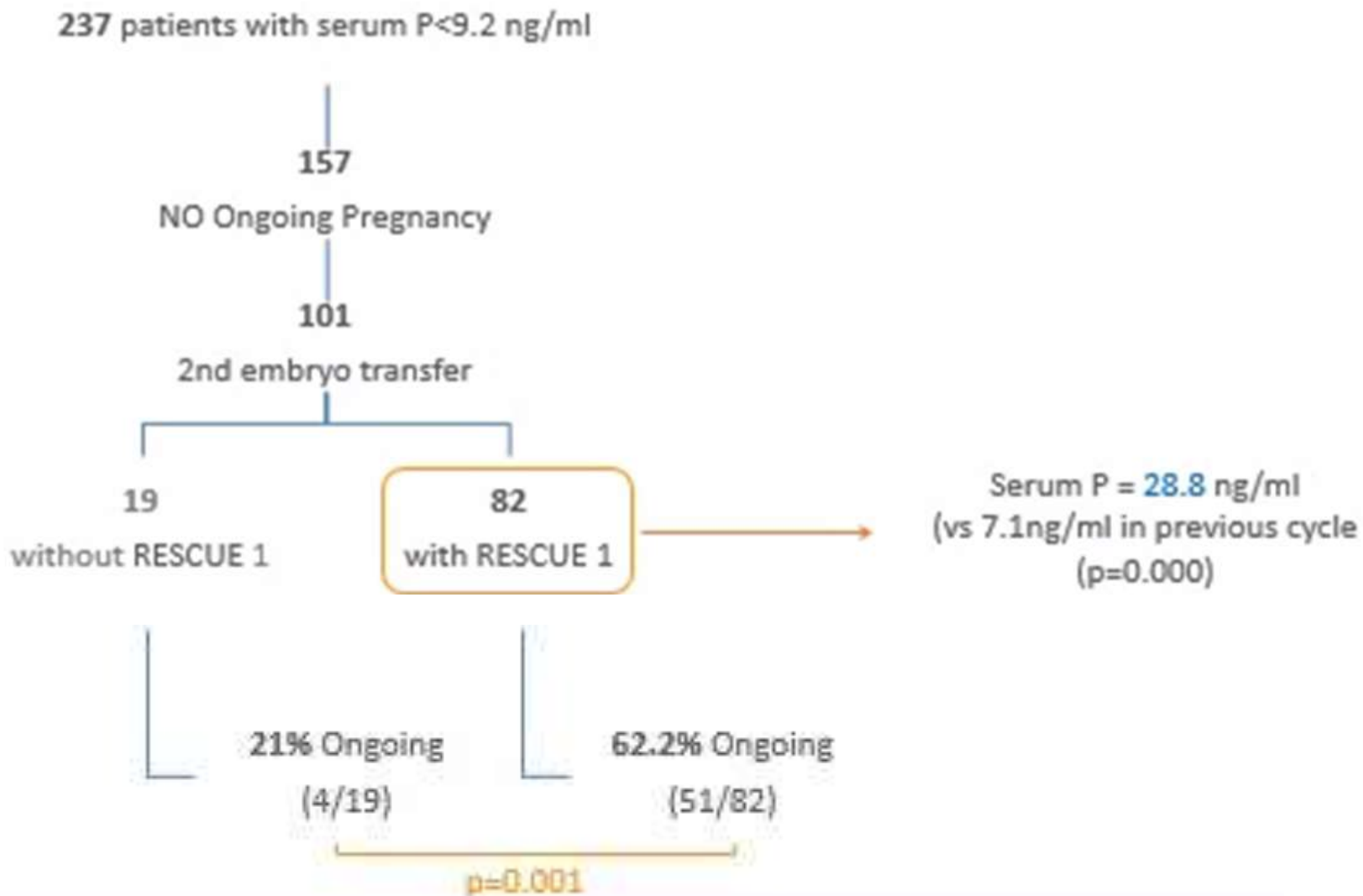


# IS IT CORRECTABLE ?



- Increase the progesterone levels:
  - Increase the vaginal dose of P
  - Add another route of administration – Subcut/IM
- They added subcutaneous progesterone

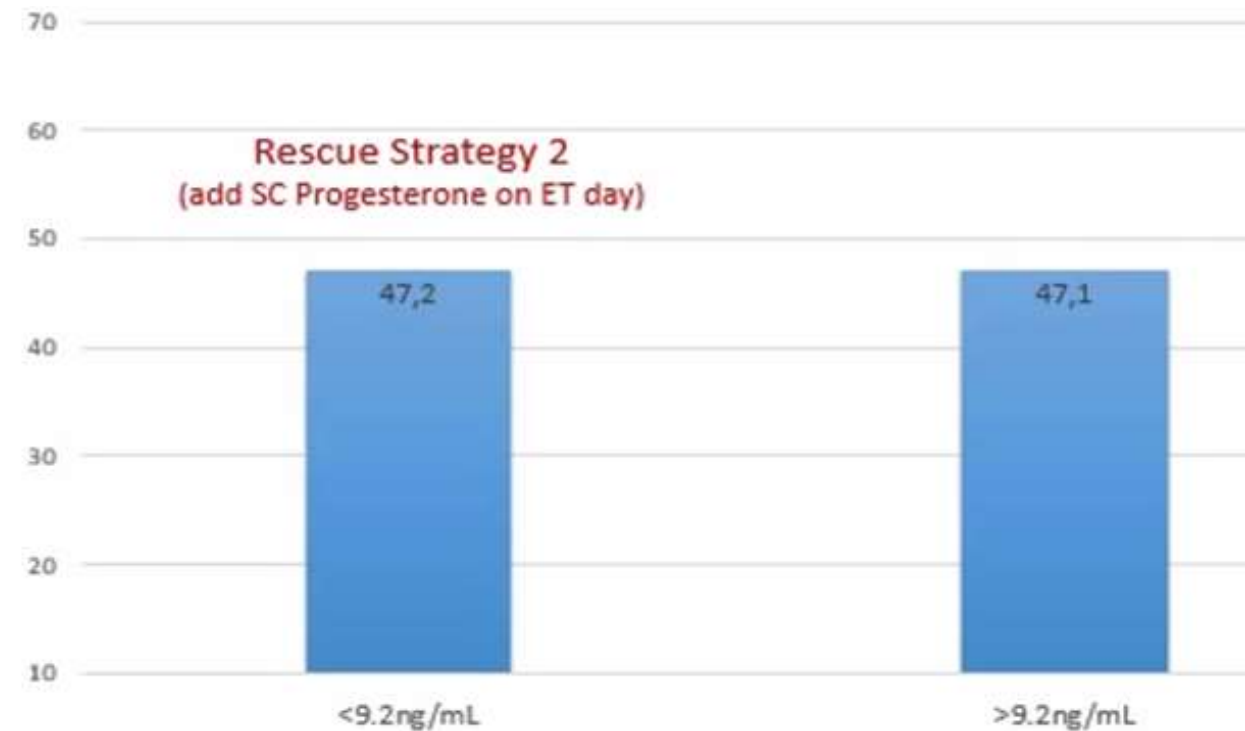
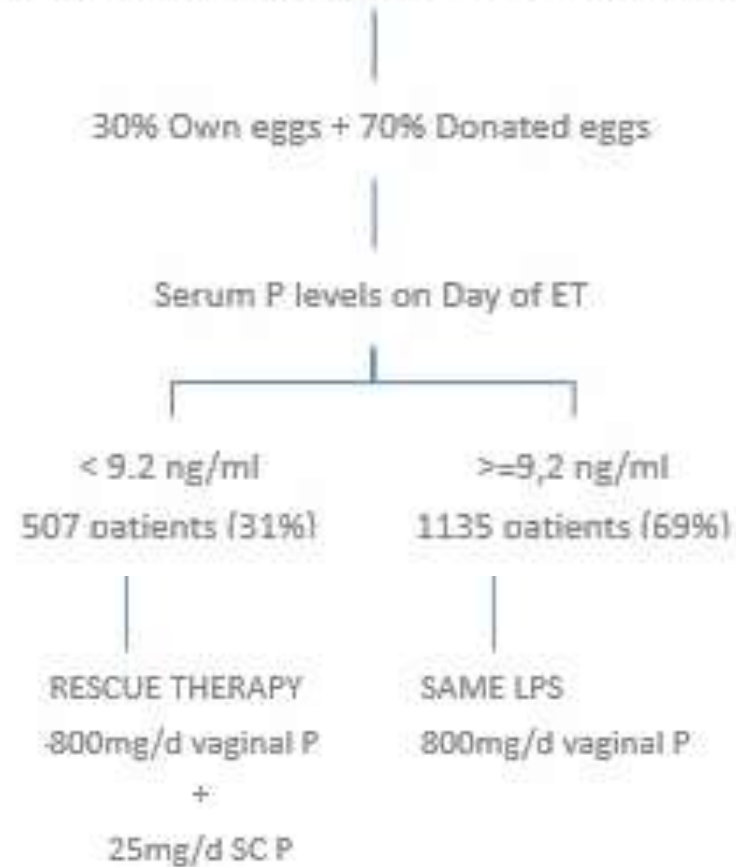
## Scenario 1



## Scenario 2 : Current HRT Cycle with Serum P < 9.2 ng/ml on Day of Transfer (added progesterone on the same day)

1642 artificial cycles for ET (December-March 2019)

HRT cycle: Estradiol valerianate + 400mg/12h natural micronized P



# Conclusion

## 3 out of 10 women

show inadequate levels of serum P when using micronized vaginal P in HRT cycles



Objective:  
Identify “infra” treated patients

## Individualize LPS

- Adding other ways of P administration (addition of SC P is effective)
- Increase dose of P
- Change type of P
- Natural Cycle

