

Materials and Methods

COS Protocols

COS was performed in the vast majority of patients using an antagonist protocol. The protocols have been adapted over the years to the improvements reported such as the use of letrozole (Oktay, et al., 2006), random start (Cakmak, et al., 2013) and agonist trigger (Oktay, et al., 2010). In conventional COS, gonadotropins were initiated on day 2-3 of the menstrual cycle using either recombinant follicle stimulating hormone (Gonal-F, Merck or Puregon, MSD), or hMG (Menopur, Ferring). The dose was individualized according to the patient's age, her BMI and estimated ovarian reserve. The GnRH antagonist (0.25 mg/daily, Orgalutran, MSD) was initiated s.c. on the fifth day of COS. In random-start group, stimulation was categorized as starting in late follicle phase (cycle day 6-13) or in luteal phase (after day 14) for comparison purposes.

Letrozole was introduced to COS in Sweden at the end of 2009. In COS with letrozole, a daily dose of 5 mg has been used (Oktay, et al., 2006). Initially, COS with letrozole was given to women with ER positive BC only. As complete information on tumor characteristics and receptor status could be missing at the time of referral, use of letrozole-based protocols has been extended to all women with BC at three of the centers. The last dose of letrozole was taken on the evening of trigger injection. In some cases, letrozole was re-initiated after egg retrieval for 3-5 days (Oktay, et al., 2005). Final oocyte maturation was induced with hCG (Otrivelle, Merck; Pregnyl, MSD) or GnRHa (Suprefact, Sanofi AB; Gonapeptyl, Ferring). In cycles with letrozole, the trigger injection was administered when at least 3 lead follicles had a mean diameter > 19 mm (Azim, et al., 2008), whereas a diameter of 17 mm was otherwise used (Huang and Rosenwaks, 2014).

Oocyte retrieval was performed with transvaginal ultrasound guidance 37 hours after administration of trigger. Oocytes were cryop-

reserved by slow freeze or vitrification according to the laboratory standard of each clinic at the time. Cryopreservation of embryos was performed at cleavage day-2-stage or as blastocysts, following the clinically established routines at each center. For some women, only a part of the oocytes was fertilized, so that they could preserve both embryos and oocytes according to their wish.

References

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