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P-477 Ovarian stimulation and PGT-A outcomes with random start letrozole protocol for fertility preservation in breast cancer patients

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Study question: Data on random start letrozole ovarian stimulation (RSL) in breast cancer patients is scant. We studied RSL outcomes from a single-center with fertility preservation expertise.

Summary answer: RSL appears to result in high oocyte and embryo/blastocyst yield, with an age-appropriate aneuploidy rate.

What is known already: With increasing utility of neoadjuvant chemotherapy regimens in breast cancer, young women have limited time to undergo fertility preservation (FP) by oocyte or embryo cryopreservation. Random start stimulation protocols were developed to complete an ovarian stimulation cycle in the shortest time possible before cancer patients started chemotherapy. In addition, letrozole protocols were developed to mitigate the potential risks of high estrogen levels during ovarian stimulation in breast cancer patients. Even though both random start and letrozole supplemented ovarian stimulation have been studied individually, there is limited data on combining both strategies in random start letrozole (RSL) protocols.

Study design, size, duration: We reviewed our records from 2014 to 2021. We included the first FP cycle of all breast cancer patients undergoing RSL ovarian stimulation for oocyte or embryo cryopreservation. Cancer stages were grouped as 0-4, 0 being ductal carcinoma in situ (DCIS). Twenty-eight cycles met the criteria. Main outcome measures were number of oocytes retrieved and embryos cryopreserved. Secondary outcome measures were fertilization, blastocyst, and euploidy rates for the embryo cryopreservation group.

Participants/materials, setting, methods: Ovarian stimulation began on cycle days 3-26 with letrozole 5 mg/day initiated simultaneously with rFSH. The rFSH dose was based on age and antral follicle counts (AFC). Oocyte maturation was triggered with leuprolide acetate, rhCG or both 35h prior to retrieval.

Main results and the role of chance: The mean age was 33.5±4.9 years (range 26-40) and BMI 22.3±2.9(18.4-30.3). The mean breast cancer stage at FP was 1.7±0.9 (0-4), with 42.3% being stage-I disease. 77% of cases were estrogen receptor positive. AMH was 2.7±2.4 (0.16-7.9) and AFC 18.5±8.9(4-42). Ovarian stimulation began on cycle-day 13.7±7.3(2-26). 15(54%) cycles were started in the follicular and 13(46%) in the luteal-phase. The mean total rFSH dose was 3880±1615.4IU(1275-8325) with a stimulation length of 11.8±2.4 days(8-19).

Mean oocytes retrieved were 16.4±6.9(1-36) with a maturity rate of 71.4±17.9%(35.7-94.4). From 13 patients, 10.4±4.7(1-22) oocytes were cryopreserved. Among the 15 patients proceeding to embryo cryopreservation, the fertilization rate was 96.9±6.8%(80-100), resulting in 7.1±4.4(1-15) embryos. 24 embryos were cryopreserved on day-3 and 82 as blastocysts. PGT-

A was performed in 72% of the cases, with euploidy rate of 37.7±24.4%(0-63.6). There was no difference in oocyte or embryo yield between follicular and luteal start patients. Likewise, fertilization rates and euploidy rates were similar. The comparative results are summarized in Table 1.

To date, two patients conceived utilizing cryopreserved embryos. Both pregnancies resulted in healthy term babies.

Limitations, reasons for caution: Though our report is one of the largest series of RSL, it can be strengthened with longer follow up that includes pregnancy outcomes in a greater proportion of patients.

Wider implications of the findings: This is the first detailed report of the RSL protocol utility with PGT-A results in a breast-cancer population. RSL appears to result in high oocyte-yield, fertilization, and blastocyst formation rates, with age-appropriate euploidy. Additionally, the outcomes appear to be similar between patients undergoing follicular and luteal phase start RSL.

Trial registration number: not applicable

P-477 Table 1

Outcome variables: mean±SD(range)	Follicular- phase start	Luteal- phase start	p- value
Oocytes retrieved	16.6±6.5(9-36)	16.2±8.6(1-33)	0.88
Maturity%	67.7±19.3(35.7-91.7)	77±4.9(50-94.4)	0.21
Fertilization%	96±7.6(80-100)	100±0.0	0.51
Embryos cryopreserved	7.1±3.5(4-13)	7±5.9(1-15)	0.96
Euploidy%	40.9±24.2(20-63.6)	50.1±40.9(0-100)	0.71