Treatment Recommendation: Fertility Preservation Options for Known BRCA+ Patients

Background
- Patients with known BRCA 1 or 2 mutation are at increased risk of breast and ovarian cancer
- Removal of the ovaries can reduce the risk of developing ovarian cancer
- Occult malignancies are found in about 3% of BRCA+ patients who have ovaries removed for risk reduction
- Incidence of ovarian cancer in BRCA+ increases with age as does the risk of finding these occult malignancies at oophorectomy
- Age 39 is a critical “cut off” point where this risk begins to significantly increase
- Patients and providers must balance the desire for fertility with cancer risk

Monitoring and patient selection for fertility preservation:
- All patients should be enrolled in the early cancer detection program
- No fertility intervention (without more extensive workup) unless BOTH
  - Ca125 is in normal range for age
  - There is nothing “suspicious” visible in the ovary by ultrasound (etc.) visualization

Fertility Preservation Options available for BRCA+ women under age 39:

Standard of Care*:
1. Embryo Banking (best option)**
2. Oocyte Banking (if no partner/sperm source) (*freezing of oocytes is currently considered experimental, but hundreds of live births from frozen oocytes have been reported world wide)
3. Both of these options involve stimulation of the ovaries with fertility drugs and ultrasound guided egg retrieval
4. There is no evidence to suggest that the elevated estradiol levels in the few days of stimulation increase the cancer risk for these patients

Experimental:
1. Ovarian Tissue Cryopreservation is an additional option that patients can exercise at that time of the removal of the ovaries for risk reduction but should not be used as a primary means of fertility preservation
2. Cryopreserved ovarian tissue can currently be used in only two ways:
   - Ovarian Transplant has resulted in human pregnancies, but is contraindicated in this group of patients due to the risk of ovarian malignancy.
   - Isolation of follicles with in vitro follicle maturation (IFM) and fertilization in vitro. To date, this technique has only been successful in rodents.

**NOTE: Preimplantation Genetic Diagnosis (PGD) should be offered to all patients who choose embryo banking as their fertility preservation method.
Oncofertility Consortium Research Protocols/Options for patients having risk reduction oophorectomy who will consent to enroll in a research protocol:

1. Inclusion Criteria
   - Age 39 or under
   - Ca125 is in normal range for age AND
   - Nothing “suspicious” visible in the ovary by ultrasound (etc.) visualization

2. 20% of cortical tissue from random areas of the ovary to pathology for examination (all of fallopian tube and any non-cortical tissue to pathology).

3. If patient desires fertility preservation and wishes to participate in research protocol:
   - 80% of the tissue remaining after pathology portion is removed is frozen for the patient own use.
   - 20% of the tissue remaining after pathology portion is removed goes into research pool.
   - If any cancer is found in the portion of the tissue provided to pathology, any patient tissue remaining in the lab will be returned to pathology (i.e. patient or research tissue but not oocytes).
   - Cost of cryopreservation of ovarian tissue including the first year of storage is provided free of charge.

4. If patient does NOT desire fertility preservation and wishes to participate in research protocol:
   - ALL of the tissue remaining after pathology portion is removed goes into research pool. Oocytes obtained from the tissue donated for research will not be fertilized.
   - If any cancer is found in the portion of the tissue provided to pathology, any patient tissue remaining in the lab will be returned to pathology (i.e. patient or research tissue but not oocytes).

NOTE: This document is specific to patients with a known BRCA mutation and should not be generalized to all women with breast cancer for whom BRCA status is not known. In newly diagnosed patients, fertility preservation should not necessarily be delayed in order to obtain the BRCA results. However, it is recommended that all reproductive age breast cancer patients have a consultation to discuss genetic testing.