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Positive Quality Intervention: Fertility and the Oncology Patient

Description: This document will aid in the guidance of fertility preservation with cancer patients of childbearing potential.

Background: Fertility preservation plays a pivotal role in the comprehensive care of individuals battling cancer. For adults, adolescents, and children alike, cancer treatment often entails therapies that may compromise fertility, such as chemotherapy, radiation, or surgery.[1,2] Preserving fertility options before initiating cancer treatment provides these patients with hope for future family planning, helping to alleviate distress and maintain quality of life amidst the challenges of cancer diagnosis and treatment. Recognizing the emotional and psychological significance of fertility preservation underscores its importance as an integral component of cancer care, fostering resilience and empowering patients to envision a future beyond cancer.[1-3]

PQI Process: At the time of diagnosis, all patients of reproductive age (and parents or guardians of children and young adolescents) should be offered fertility preservation counseling if they will undergo a gonadotoxic treatment, and this should be documented in a medical record.[1,4]

- Example of scripting: "The treatment you are about to receive can affect your future fertility. Have you had an appointment to discuss this with a fertility specialist?"
- Females[1-5]
    - *Preferred:* Oocyte (egg) or embryo cryopreservation, if the patient has started menses (postpubescent)
    - Ovarian/uterine transposition may be an option if patient is undergoing pelvic radiation therapy
    - Ovarian tissue cryopreservation is an acceptable fertility-preservation technique and is no longer considered experimental
        - Only method to preserve fertility for prepubescent females
        - This intervention can be done immediately and doesn't require any hormonal stimulation, so it's a good option for time sensitive situations
    - Note there is insufficient evidence regarding the effectiveness of ovarian suppression (gonadotropin-releasing hormone analogs such as leuprolide) as a fertility preservation method, and these agents should only be used in hopes of reducing the likelihood of chemotherapy-induced ovarian insufficiency and if other treatments are not feasible
- Males[1-5]
    - Sperm cryopreservation for postpubertal males before the start of the treatment is the most established method
    - Testicular sperm extraction (TESE), sperm collection from urine, and testicular tissue cryopreservation are still experimental

Patient-Centered Activities:

- Review the supplemental list for examples of gonadotoxic medications according to their package labeling (*Supplemental Information*)
- Refer the patient to your reproductive endocrinologist.
    - Counsel the patient to identify themselves as an oncofertility patient when reaching out to their local fertility clinic. This will ensure they are seen with urgency
- Be familiar with the fertility medication programs sponsored by manufacturers for cancer patients
    - Ferring Heartbeat
    - ReUnite Oncofertility

    - LiveStrong
- Some states have legislature around fertility treatment for cancer patients
    - For additional resources, visit About the Fertline - The Oncofertility Consortium (msu.edu)

References:

1. Kutluk Oktay B, Harvey BE, Partridge AH, et al. Fertility Preservation in Patients with Cancer: ASCO Clinical Practice Guideline Update. 2018 Apr 5;19(36). Available at: https://ascopubs.org/doi/10.1200/JCO.2018.78.1914 (11-10-23).
2. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Adolescent and Young Adult (AYA) Oncology. V.2.2024.
3. Lambertini M, Del Mastro L, Pescio MC, et al. BMC Medicine. 2016;14(1):1.
4. Loren AW, Mangu PB, Beck LN, Brennan L, Magdalinski AJ, Partridge AH, Quinn G, Wallace WH, Oktay K; American Society of Clinical Oncology. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2013 Jul 1;31(19):2500-10.
5. ASRM Practice Committee. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. Fertil Steril. 2019;112(6):1022-1033.

Supplemental Information:[3]

Degree of Risk (Females)	Type of Anti-Cancer Treatment
High risk (> 80% risk of permanent amenorrhea)	• HSC transplantation with cyclophosphamide/TBI or cyclophosphamide/busulfan • External beam radiation to a field that includes the ovaries • CMF, CEF, CAF, TAC x 6 cycles in women ≥ 40 years old
Intermediate risk (40-60% risk of permanent amenorrhea)	• BEACOPP • CMF, CEF, CAF, TAC x 6 cycles in women 30-39 years old • AC x 4 cycles in women ≥ 40 years old • AC or EC x 4 → Taxanes
Low risk (< 20% risk of permanent amenorrhea)	• Nonalkylating chemotherapy: ABVD in women ≥ 32 years old, CHOP x 4-6 cycles, COP • AC x 4 cycles in women ≤ 40 years old • CVP • AML therapy (anthracyclines/cytarabine) • ALL therapy (multi-agent) • CMF, CEF, CAF, TAC x 6 cycles in women ≤ 30 years old
Very low or no risk	• ABVD in women < 32 years old • Methotrexate • Fluorouracil • Vincristine • Tamoxifen
Unknown risk	• Monoclonal antibodies (trastuzumab, bevacizumab, cetuximab, etc.) • Tyrosine kinase inhibitors (erlotinib, imatinib, etc.)

Degree of Risk (Males)	Type of Anti-Cancer Treatment
High risk (prolonged azoospermia)	• Radiation > 2.5 Gy to testies • Chlorambucil 1.4 g/m^2 • Cyclophosphamide 19 g/m^2 • Procarbazine 4 g/m^2 • Melphalan 140 mg/m^2 • Cisplatin 500 mg/m^2 • BCNU 1 g/m^2 and CCNU 500 mg/m^2
Intermediate risk (likelihood of azoospermia especially when given with other sterilizing agents)	• Busulfan 600 mg/kg • Ifosfamide 42 g/m^2 • BCNU 300 mg/m^2

	• Nitrogen mustard • Actinomycin D
Low risk (only temporary reductions in sperm counts especially when not given with other sterilizing agents)	• Carboplatin 2 g/m^2 • Doxorubicin 770 mg/m^2 • Thiotepa 400 mg/m^2 • Cytosine arabinoside 1 g/m^2 • Vinblastine 50 g/m^2 • Vincristine 8 g/m^2
Very low or no risk (temporary reductions in sperm count but additive effects are possible)	• Amsacrine • Bleomycin • Dacarbazine • Daunorubicin • Epirubicin • Etoposide • Fludarabine • Fluorouracil • 6-mercaptopurine • Methotrexate • Mitoxantrone • Thioguanine • Prednisone • Interferon-a
Unknown risk	• Oxaliplatin • Irinotecan • Monoclonal antibodies (trastuzumab, bevacizumab, cetuximab, etc.) • Tyrosine kinase inhibitors (erlotinib, imatinib, etc.) • Taxanes

Note: This list of treatments is not exhaustive to all treatments available and their degree of risk.
Abbreviations: HSC: hematopoietic stem cell, TBI: total body irradiation, CMF: cyclophosphamide, methotrexate, fluorouracil, CEF: cyclophosphamide, epirubicin, fluorouracil, CAF: cyclophosphamide, doxorubicin, fluorouracil, TAC: docetaxel, doxorubicin, cyclophosphamide, BEACOPP: doxorubicin, bleomycin, vincristine, etoposide, cyclophosphamide, procarbazine, BCNU: carmustine, CCNU: lomustine, AC: doxorubicin, cyclophosphamide, EC: epirubicin, cyclophosphamide, ABVD: doxorubicin, bleomycin, vinblastine, dacarbazine, CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone, CVP: cyclophosphamide, vincristine, prednisone, AML: acute myeloid leukemia, ALL: acute lymphocytic leukemia.