

Breast cancer risk and screening in BRCA mutations and perhaps women with Fanconi Anemia

- Screening in patients with BRCA mutations begins between ages 25 and 30.
- Typically performed twice a year
- Often includes clinical breast exams and mammography alternating with MRI.
- Obtain education about breast self-examination by early 20s.
- Biopsy palpable breast masses immediately.

Breast cancer screening and Fanconi Anemia: some considerations

- FA patients have an elevated sensitivity to radiation exposure from underlying defects in DNA repair.
- Long-term risks of radiation exposure with mammography weighed against benefits with early detection
- Magnetic resonance imaging (MRI) very sensitive for detecting breast tumors
- MRI high false-positive rate

Breast cancer screening and Fanconi Anemia: Is MRI the best tool for screening for breast cancer in FA?

- MRI more sensitive for detecting tumors after menopause, when the breast tissue less dense
- MRI may be preferred over mammography in post-menopausal patients with FA as a way to minimize radiation exposure from mammograms
- This concept has not been studied in women with FA

Secondary cancer after hematopoietic stem cell transplantation in Fanconi Anemia



Fanconi anemia

Secondary cancer after HSCT

- Secondary cancers common after HSCT
- Squamous cell cancers more common in women with graft versus host disease
- Possibly related to radiation, HPV disease, mosaicism
- Potential role of HPV vaccination



NIH HPV vaccination study after stem cell transplant

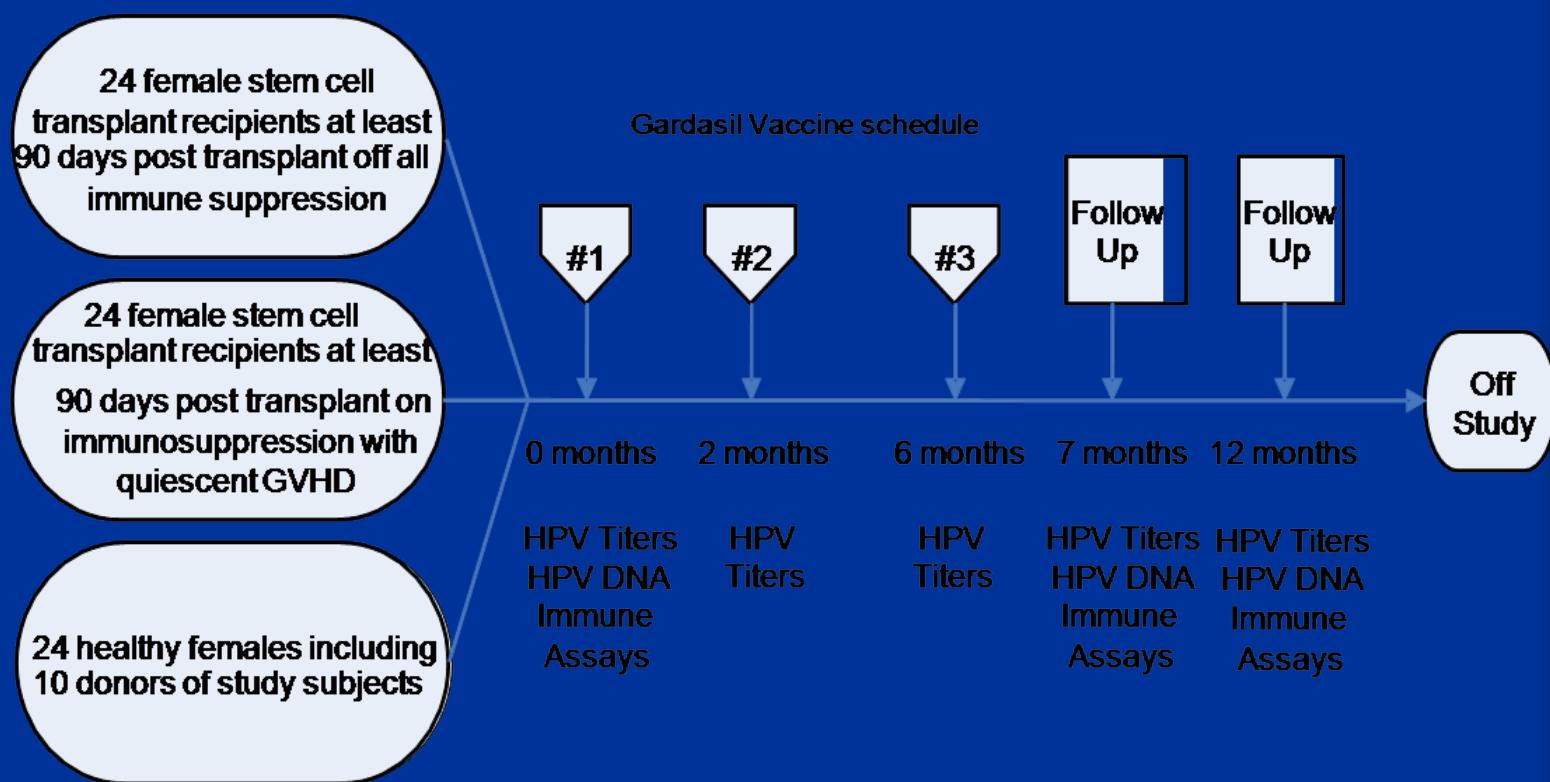
Background

- After transplant, immunity is altered
- Long-term one third of women post stem cell transplant found to have genital HPV disease

Hypothesis

- Quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine is a safe and effective way to reduce the rate of post-transplant HPV-related disease in females who have undergone stem cell transplantation.

Gardasil study visits



Other secondary cancers after stem cell transplant

Breast cancer surveillance should begin 8 years after stem cell transplant if total body radiation was performed

Fanconi anemia

Menopause health risks

- Premature menopause
- Post menopausal health risks
 - Osteoporosis
 - Cardiovascular disease
 - Breast cancer
- Consider these risks in FA patients
- Management of hot flashes



Risks and benefits for hormone replacement for menopausal symptoms: Lessons learned from the Women's Health Initiative

- Women's Health Initiative – Post-menopausal hormone replacement therapy study
 - Protection against bone loss
 - Increased risk of heart attack, stroke, and thromboembolic disease
 - Slightly increased risk of breast cancer

Menopausal hormone replacement and Fanconi Anemia: general considerations

- In general, women who experience premature menopause and do not use hormone therapy tend to have higher rates of illness and death compared with those who take hormones.
- Hormone therapy is recommended for young women with FA who undergo premature menopause.

Hormone replacement and Fanconi Anemia: cardiovascular risk

- Assess an individual patient's family history of cardiovascular disease
- Monitor lipid profiles, insulin resistance and blood pressure as part of a cardiovascular disease risk assessment.
- Pay attention to the effects of androgen therapy on lipids.
- Hormone replacement therapy may be contraindicated for patients who have cardiovascular disease risk factors.

Menopause, Fanconi Anemia, and Bone density

- Low bone density increases the risk of bone fractures
- Osteoporosis treatment options
 - Bisphosphonates – prevent bone resorption
 - Hormone replacement
 - Calcium
 - Vitamin D

Menopausal hormone replacement and Fanconi Anemia: general considerations

- Treatment of menopausal symptoms
 - Hot flashes
 - Vaginal dryness
 - Pain with intercourse
- Types of hormone therapy
 - Oral contraceptive pills
 - Post menopausal hormone therapy
 - Combination of estrogen and progestins



Genital squamous cancer screening and treatment in Fanconi anemia

- HPV vaccination, repeat after stem cell transplant
- Annual exam
 - Comprehensive by age 18
 - Includes cervical cytology
 - Inspect vulva (and vagina) for lesions
 - Any lesions should be treated aggressively with surgery
 - If cancer, see gynecologic oncologist immediately
 - Monitor more frequently after pre-cancer

Breast cancer screening in Fanconi Anemia

- Screening should begin by mid-20s
 - MRI breast versus mammography
 - Palpable breast lumps should be biopsied

Fertility issues in Fanconi anemia

- May be less fertile, especially after transplant
- AMH testing may predict POI
- Pregnancy well tolerated
- Pregnancy should be managed by maternal fetal medicine specialist
 - Perform prenatal diagnosis
 - Minimize complications during pregnancy
 - Time delivery

Reproductive options in Women with Fanconi Anemia

- Cryopreservation (preservation by freezing) of embryos possible reproductive option
 - Donor oocyte
 - Adoption
 - Surrogacy
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- Use contraception when pregnancy not desired



Management of menopause in Fanconi anemia

- Consider hormone replacement therapy – estrogen and progestin to women under age 50 with premature menopause
- Treat menopausal symptoms
- Monitor lipids, cardiovascular risk
 - Androgens may increase cardiovascular risk
- Monitor for osteoporosis