# Do Patients with Solid Organ Transplant (SOT) Require Special Needs?

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# Disclosures

- Michael Gold, MD: *No financial relationships or conflict of interest to disclose*

# Overall Objectives

- To summarize current knowledge of cervical cancer, SIL, and HPV infection in women who have undergone solid organ transplant

# Background

- Long recognized as a risk factor for development of new cancers
  - Standard incidence rate (SIR) of 2.0-6.6
- Attributed to ongoing use of immunosuppressive medications
- Historical studies failed to take into consideration cervical cancer screening or additional risk factors
- Newer studies demonstrate increased risk, especially among women on multiple classes of immunosuppressive medications

# Screening history among SOT recipients

- Courtney et al. *Nephrology Dialysis Transpl* 2009
  - 173 kidney transplant recipients over median follow-up 121 months
  - 425/1148 anticipated paps (annual)
    - 10% (18) had recommended number of screens
    - 32% (56) had no screens
- Alloub et al. *BMJ* 1989
  - 41% (20) had recommended screening
    - 14 no prior screening
    - 3 no screening in prior 10 years
- Origoni et al.  2011
  - SOT recipients underwent annual pap
  - No increase risk of SIL
- Inadequate screening after SOT may contribute to increased risk

# Human Immunodeficiency Virus (HIV)– and Non-HIV–Associated Immunosuppression and Risk of Cervical Neoplasia

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- Nested case-control study among women enrolled in KPNC
- Cases defined as new diagnosis of CIN 2+
- Source population 2.1 million women
  - Case group 20,146 women w/ CIN 2+
    - 50% CIN 3 & 3% cancer
  - Control group 100,144 (5:1) women w/o CIN 2+

# Silverberg et al. 2018

| | Cases | Controls | P-value |
|---|---|---|---|
| **HIV** | **36 (0.2%)** | **79 (0.1%)** | |
| **Prior SOT** | **51 (0.3%)** | **68 (0.1%)** | **<.001** |
| **Type** | 34 kidney, 8 liver, 7 lung, 2 heart | 56 kidney, 9 liver, 1 lung, 2 heart | |
| **Time since transplant** | 5.6 years | 6.1 years | |
| **Immunosuppressive Meds** | **1370 (6.8%)** | **6353 (6.3%)** | **.013** |
| **2 Classes** | **0.4%** | **0.3%** | **.004** |
| **3+ Classes** | **0.5%** | **0.2%** | **<.001** |

# Silverberg et al. 2018

- Adjusted risk model
  - HIV+ — RR 2.0 (1.3-2.0)
    - CD4+ 500 — RR 0.8 (0.4-1.7)
    - CD4+ 200-499 — RR 3.0 (1.6-5.5)
    - CD4+ <200 — RR 5.6 (2.1-14.7)
  - SOT — RR 3.3 (2.3-4.8)
    - 1 Immuno Class — RR 0.9 (0.9-1.0)
    - 2 Immuno Classes — RR 1.2 (1.0-1.5)
    - 3+ Immuno Classes — RR 1.7 (1.3-2.2)

- Increased risk of CIN 2+ among SOT recipients
- Risk of CIN 2+ increases with increasing number of Immunosuppressive medication classes

# Type of SOT

- Malouf et al. *J Heart Lung Transpl* 2004 - Lung Transplant
  - Cross Sectional Australian Study
    - LGSIL 42.2 / 1000 post transplant vs. 8.3 / 1000 in general registry population
    - HGSIL 30 / 1000 post transplant vs. 6.2 / 1000 in general registry population
- Maggie et al. *PLOS One* 2013 - Liver Transplant
  - 160 women followed for median 7.2 years
    - Overall SIR for cervical cancer 5.7 (95% CI 0.1-31.9)
    - 10 years after SOT, SIR for cervical cancer 22.6 (95% CI 0.5-123.8)
- Kidney Transplant
  - Halpert et al. *Obstet Gynecol* 1986 – OR for CIN 9.0 (3.4-20.2)
  - Kessler et al. *Transpl Int.* 2006 – SIR for Cervical Cancer 25.3 (9.3-55.0)
- Increased risk of CIN 2+ with Lung, Liver, and Kidney Transplant

# Interval from SOT to Cervical Cancer Diagnosis

- Kasiske et al. *Am J Transpl* 2004
  - Cumulative incidence of cervical cancer after SOT
    - 1 year 0.02% (rate ratio 1.0)
    - 2 years 0.09% (rate ratio 6.0)
    - 3 years 0.18% (rate ratio 5.7)
- Vajdic et al. *JAMA* 2006
  - Renal transplant registry (Australia & New Zealand)
  - Median time from transplant to cervical cancer 8.5 years (SD 4.7)
  - Incidence compared to general population
    - After renal transplant 13 observed vs. 5.21 expected
    - During dialysis 13 observed vs. 5.03 expected
    - 5 years prior to dialysis 11 observed vs. 6.87 expected
- Risks increases with time since SOT, but also increased among renal failure patients

# Immunosuppression among SOT Recipients

- Classes include
  - Corticosteroids — RR 1.1 (95% CI 0.99-1.1)
  - Antiproliferative agents — RR 2.4 (95% CI 1.9-3.1)
  - Calcineurin inhibitors (cyclosporine & tacrolimus) — RR 1.5 (95% CI 1.2-1.8)
  - TNF inhibitors — RR 1.3 (95% CI 0.9-1.9)
  - Folate antimetabolites — RR 1.4 (95% CI 1.1-1.9)
  - Cytotoxic agents — RR 1.3 (95% CI 1.1-1.6)

Silverberg et al. *Obstet Gynecol* 2018

# Summary

- Inadequate screening after SOT may contribute to increased risk
- Increased risk of CIN 2+ with Lung, Liver, and Kidney Transplant
- Risks increases with time since SOT, but also increased among renal failure patients
- Risk of CIN 2+ increases with increasing number of Immunosuppressive medication classes
  - Risk related to the type of immunosuppressive  med

# Thank You