CROI 2024 Update: Co-Occurring Conditions

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Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities
CROI Updates: Co-Occurring Conditions

• Updates in anal cancer screening strategies

• Review updates in metabolic complications of HIV
  o Use of semaglutide

• Updates in HBV vaccination
  o BEe-HIVe Arm A results
Anal Dysplasia Screening
Anal Cancer in PWH

- Incidence of anal cancer is high among PWH; particularly among MSM

- ANCHOR: Treating anal HSIL reduces incidence of anal cancer (57% reduction)

- HRA (high resolution anoscopy) is gold standard for HSIL detection….…..but availability is limited

- Need practical strategies to approach anal cancer screening in PWH
  - Prioritization of referrals by demographics, low CD4 nadir, cytology/high risk HPV (HR-HPV)
180 MSM LWH had anal cytology, anal HPV, and HRA collected on same day

<table>
<thead>
<tr>
<th></th>
<th>Median (±SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47 (±10.7)</td>
</tr>
<tr>
<td>CD4 nadir (cells/uL)</td>
<td>350 (±241)</td>
</tr>
<tr>
<td>Current CD4 (cells/uL)</td>
<td>800 (±272)</td>
</tr>
<tr>
<td>CD4/CD8</td>
<td>1.03 (±0.39)</td>
</tr>
<tr>
<td>HIV RNA (copies/mL)</td>
<td>&lt;37</td>
</tr>
</tbody>
</table>

**Results**

<table>
<thead>
<tr>
<th>Cytology</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>NILM</td>
<td>10%</td>
</tr>
<tr>
<td>ASC-US</td>
<td>14%</td>
</tr>
<tr>
<td>LSIL</td>
<td>69%</td>
</tr>
<tr>
<td>ASC-H</td>
<td>5%</td>
</tr>
<tr>
<td>HSIL</td>
<td>2%</td>
</tr>
</tbody>
</table>

**HR-HPV***

<table>
<thead>
<tr>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>75%</td>
</tr>
</tbody>
</table>

**HRA**

<table>
<thead>
<tr>
<th>HSIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>43%</td>
</tr>
</tbody>
</table>

*Of HR-HPV, 54% HPV-16
Results

Cavallari et al. CROI 2024
CD4 Nadir and anal cancer risk

- PWH with nadir CD4 <200 had highest anal cancer risk (aIRR 29 v nadir > 350)

- PWH with nadir CD4 > 350 with similar risk as compared to general population

- Age, MSM, and nadir CD4 count strongest association w/anal cancer risk in PWH

Figure 2. Risk factors for anal cancer in the multivariable model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Adjusted IRR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (time updated), years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30</td>
<td>4171</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-44</td>
<td>10188</td>
<td></td>
<td>0.116</td>
</tr>
<tr>
<td>45-59</td>
<td>6836</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>&gt;60</td>
<td>1736</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Transmission group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>4603</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>10561</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-MSM men</td>
<td>7767</td>
<td></td>
<td>0.081</td>
</tr>
<tr>
<td>Nadir CD4+ cell count</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;350</td>
<td>6533</td>
<td></td>
<td></td>
</tr>
<tr>
<td>200-350</td>
<td>6723</td>
<td></td>
<td>0.037</td>
</tr>
<tr>
<td>&lt;200</td>
<td>9675</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Calendar period of HIV diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;2015</td>
<td>4445</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009-2014</td>
<td>5612</td>
<td></td>
<td>0.173</td>
</tr>
<tr>
<td>2004-2008</td>
<td>4964</td>
<td></td>
<td>0.054</td>
</tr>
<tr>
<td>1998-2003</td>
<td>5323</td>
<td></td>
<td>0.151</td>
</tr>
<tr>
<td>&lt;1998</td>
<td>2587</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

IRR adjusted for calendar time, age (time-updated), risk group and nadir CD4+ cell count
Anal Self-Sampling for HR-HPV Detection

• Access to HRA, cytology limited in certain settings (such as sub-Saharan Africa)

• Evaluation of anal self-sampling (ASS) for HR-HPV detection as compared to anal swab by practitioner (ASP) in 188 MSM (67% with HIV) in Togo
  – Practitioner conducted anal exam and anal cytology post self-sampling

• Acceptability: 99% found ASS procedurally easy; 60% would prefer ASS to ASP (19% with no preference)

• Performance: 6% v 4% of ASS samples uninterpretable
Anal Self-Sampling for HR-HPV Detection

- Substantial agreement between methodologies for HR-HPV (89.7%, k = 0.66) and HPV16 (90.3%, k = 0.75)
- At least one HR-HPV detected in 83% of ASS and 77% of ASP samples
- HPV16 detected in 28% of ASS and 26% of ASP

High concordance between sampling methods; high acceptability, ease of ASS

ASS may help achieve anal cancer screening targets, especially in LMIC
In discussion of how to develop guidance for HRA referral, consider:
- HPV testing (HR-HPV types 16 and 18), inclusive of self-sampling
- Anal cytology in combination
- Nadir CD4, Age, MSM
Metabolic Complications
GLP-1 Receptor Agonists

• Mechanism: Promote insulin release and suppress hepatic glucose output

• Semaglutide
  o DM: 2% decrease in A1c, 6.4 kg weight loss, 26% decrease in MACE events
  o Without DM: 3-4 kg weight loss, 20% decrease in MACE events

• Semaglutide in PWH?
Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is common among people with HIV
- GLP-1 (semaglutide) associated with metabolic improvements including improved hepatic steatosis

Semaglutide for MASLD in HIV:
- **ACTG A5361 (SLIM LIVER)**: single arm, open label, phase IIb study of effects of semaglutide on hepatic steatosis
  - MRI proton density fat fraction (MRI-PDFF) quantified intrahepatic triglyceride content (IHTG)

49 PWH suppressed on ART w/ elevated minimum waist circumference, insulin resistance, and ≥ 5% IHTG on MRI-PDFF

Initiated on semaglutide, uptitrated over 24 weeks: 0.25 mg sc weekly → 0.5 mg → 1.0 mg)
  - MRI-PDFF performed again at week 24
Demographics:

- 37% cis-women, 6% transwomen, 57% cis-men
- 27% white non-Hispanic, 33% Black or African American, 39% Hispanic
- Median BMI 35 kg/m², Median waist circumference 114 cm
- Median CD4 701 (IQR 586,869)
- 82% on INSTI, 22% on NNRTI, 4% on PI

Overall clinically significant reductions in IHTG

- 1/3 of participants with complete MASLD resolution
- IHTG improvements correlated with weight loss (mean 7.8 kg loss over 24 weeks) along with waist circumference, fasting plasma glucose, A1c, and serum triglycerides
Semaglutide in HIV

• Effects of Semaglutide on Muscle Structure and Function in the SLIM Liver Study (Ditzenberger et al.)
  o Use of semaglutide associated with loss of psoas muscle volume (without change in physical function) but no change in muscle fat among SLIM Liver participants

• Impact of Semaglutide on Weight Change Among People with HIV: A Stratified Analysis by Baseline BMI (Crane et al.)
  o Among PWH, semaglutide a/w significant weight loss (6.5 kg, 5.7% of body weight)
  o Sensitivity analysis: weight loss was the same regardless of INSTI use
Takeaways

• Use of semaglutide in PWH:
  - Associated with significant weight loss
  - Can be used for successful treatment of MASLD
  - May impact muscle volume without impact in physical function (in short term)

• Needs:
  - Longer term data
  - Access to medication!
Hepatitis B Vaccination in PWH
HBV vaccine seroprotection rates (SPR) in persons with HIV (PWH) are lower (range 18-71%) than in adults without HIV (range 60-80%) with conventional HBV vaccine (HepB-alum)¹

ACTG 5379 (BEe-HIVe):

Arm B (vaccine naïve)²

- 100% of PWH receiving 3-dose series HepB-CpG (Heplisav-B) vaccine achieved seroprotection response (SPR, HBsAb ≥ 10 mIU/mL), 84% HBsAb ≥ 1000 mIU/mL
- 98.5% achieved SPR after two doses, though at lower titers (28% HBsAb ≥ 1000 mIU/mL)

Entry Criteria Arm A and B
- PWH and age 18-70 years
- On ART & HIV-1 RNA <1,000 copies/mL
- CD4 >100 cells/mm³
- Negative HBV surface Ab (sAb)
- No history of hepatitis B
- Not pregnant

Arm A (Vaccine Non-Responders)
- Serum Hep B sAb <10 mIU/mL
- HBV vaccination (>168 days prior)

Arm B (Vaccine Naïve)
- Hep B sAb negative (<45 days)

Arm A: HBV Vaccine Non-Responders
- HepB (CpG) 2 doses: 0, 4 weeks
- HepB (CpG) 3 doses: 0, 4, and 24 weeks
- HepB (Eng-B) 3 doses: 0, 4, and 24 weeks

Arm B: HBV Vaccine Naïve
- HepB (CpG) 3 doses: 0, 4, and 24 weeks

BEe-HIVe: Arm A (Vaccine Non-Responder) Results

**Primary SPR Proportion**

- **N = 174**
  - 2-Dose: 93.1%
  - 3-Dose: 80.6%

- **N = 169**
  - 2-Dose: 99.4%

- **N = 165**
  - 3-Dose: 80.6%

**HepB-CpG SPR Comparison to HepB-Alum**

- 2-Dose: HepB-CpG non-inferior
- 3-Dose: HepB-CpG superior

**SPR% difference**

- **HepB-alum superior <<>> HepB-CpG superior**
  - 12.5% (4.1%, 20.9%)
  - 18.4% (10.4%, 26.2%)
Distribution of Anti-HBs titers at respective endpoints

<table>
<thead>
<tr>
<th></th>
<th>HepB-alum (3-dose)</th>
<th>HepB-CpG (2-dose)</th>
<th>HepB-CpG (3-dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>165 80.6%</td>
<td>174 93.1%</td>
<td>169 99.4%</td>
</tr>
<tr>
<td>SPR%0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>35%</td>
<td>26%</td>
<td>78%</td>
</tr>
<tr>
<td></td>
<td>28%</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18%</td>
<td></td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td>3%</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-HBs titers (mIU/mL)</td>
<td>&gt;1000</td>
<td>100-1000</td>
<td>10-99</td>
</tr>
</tbody>
</table>

Percentage of participants
Takeaways

• PWH with non-response to conventional HBV vaccine achieved superior SPR as compared to 3 doses of HepB-alum

• Three doses of HepB-CpG achieved high proportion of SPR with HBsAb titers > 1000 mIU/mL (78%)
  o Do we need titers this high?
  o Underrepresentation of factors associated with poor response (low CD4 cell count, HIV viremia, HCV, older age)

• No unexpected safety issues or deaths
Co-Occurring Conditions: Take Home Points

• A triaged referral process including CD4 nadir, age, MSM, and HR-HPV (including self-testing) for anal cancer screening in PWH may help tailor population who will benefit most

• Semaglutide leads to significant weight loss and improvement of MASLD in PWH

• HepB-CpG (Heplisav-B) is superior to conventional HBV vaccination in PWH who are prior vaccine non-responders
Questions?

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