CROI Update: Prevention
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Julie Dombrowski, MD, MPH
Professor, University of Washington
Deputy Director, HIV/STI/HCV Program
Public Health – Seattle & King County

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Disclosures

I have conducted research with supplies donated by Hologic and Mayne Pharmaceuticals
Disclaimer

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Prevention

DOXY-PEP  HIV PREP
Doxy-PEP: Clinical trial result updates, impact of use in clinical practice, & preliminary AMR data
• Multicenter, 2 x 2 factorial randomized, open-label trial

• Primary efficacy endpoints:
  - Impact of Doxy-PEP on time to first episode of syphilis or chlamydia
  - Impact of 4CMenB vaccine on time to first episode of gonorrhea
Final Results of ANRS 174 DOXYVAC: A Randomized Trial to Prevent STI in MSM on PrEP

Time to first episode of syphilis or chlamydia

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Adjusted Hazard Ratio &amp; p-value</th>
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<tr>
<td>Doxy-PEP</td>
<td>0.67 (95% CI: 0.52 – 0.87), p=0.003</td>
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<tr>
<td>4CMenB</td>
<td>0.78 (95% CI: 0.60 – 1.01), p=0.061</td>
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High-level TCN-resistant GC
- 12.5% no doxy-PEP (N=40)
- 35.5% doxy-PEP (N=31)
- P-value for difference: 0.043
Doxy-PEP Effectiveness in Men Who Have Sex with Men (MSM) and Transgender Women (TGW) on HIV PrEP

Bacon O, et al. Abstract #1151

- San Francisco City Clinic, Pre- (11/2021 – 11/2022) & Post- (11/2022 – 11/2023) Doxy-PEP implementation
- Compared STI test positivity among doxy-PEP users vs. non-users
- Analysis: difference in differences

**Figure 1: Chlamydia Positivity**

- CT ↓ 90% (95% CI: 79-95%)

**Figure 2: Early Syphilis Positivity**

- Early syphilis ↓ 56% (95% CI: 8-79%)

- Value for difference of differences = 0.06
Doxy-PEP Effectiveness in Men Who Have Sex with Men (MSM) and Transgender Women (TGW) on HIV PrEP

Bacon O, et al. Abstract #126

- San Francisco City Clinic, Pre- (11/2021 – 11/2022) & Post- (11/2022 – 11/2023) Doxy-PEP implementation
- Compared STI test positivity among doxy-PEP users vs. non-users

Figure 3: Gonorrhea Positivity

Non-significant ↓ in GC
23% (95% CI: -2 to 42%)
Doxy-PEP Associated with Declines in Chlamydia and Syphilis in MSM and Trans Women in San Francisco
Sankaran M, et al. Abstract #127

• Population level: San Francisco citywide surveillance data
• Ecological analysis
• Before & after doxy-PEP guidelines, focus on “post-COVID” era
• Interrupted time series
• Estimated >3700 people on doxy-PEP, ~20% of MSM & TGW

Background: STI Trends in San Francisco
MSM and TGW, 2014-2023

[Graph showing trends in Chlamydia, Gonorrhea, and Early Syphilis with data points for 2014-Q1 to 2023-Q1, highlighting declines post-doxy-PEP]
Doxy-PEP Associated with Declines in Chlamydia and Syphilis in MSM and Trans Women in San Francisco
Sankaran M, et al. Abstract #127

50% decrease in chlamydia ($p<0.001$)*
51% decrease in early syphilis ($p<0.001$)

1.8% per month increase in gonorrhea ($p<0.001$)

*no change in CT cases among cisgender women in the same time period
Impact of Doxycycline as STI Postexposure Prophylaxis on the Gut Microbiome and Antimicrobial Resistance Gene Expression
Chu V, et al. Abstract #1154

- Doxy-PEP study collected rectal swabs at enrollment & 6 months
- DNA and RNA metagenomic sequencing of samples from participants with the highest reported doxy-PEP use vs. standard-of-care

Microbiome (not shown)
Bacterial diversity & total bacterial abundance did not differ between doxy-PEP and SOC or over time by arm

**Tetracycline ARG expression**

*Figure 2. Impact of doxy-PEP use on ARG class expression, normalized by reads per million sequenced and gene length (depth per million, dpm) in the doxy-PEP RNA-seq samples (n=55). Tetracycline ARG expression significantly increased between Day 0 and Month 6, while no difference was observed among non-tetracycline ARG classes.*
Doxy-PEP was associated with a dose-dependent increase in tetracycline antimicrobial resistance gene abundance.
Doxy-PEP Section Summary

- Doxy-PEP decreases STI rates in MSM and transgender women
  - Clear impact on chlamydia and syphilis in both clinical trial & practice data
  - Decreased gonorrhea risk in clinical trials but no clear impact in practice

- Scale-up occurred quickly in San Francisco (high interest in the intervention)

- Doxy-PEP use does not appear to impact gut bacterial diversity over 6 months, but is associated with a dose-dependent increase in tetracycline AMR genes in the gut
  - Clinical significance & impact of longer term use unknown
PrEP: Novel Formulations
**PrEP: What’s in the pipeline?**

- **Weekly oral medication**
- Novel oral nucleoside reverse transcriptase translocation inhibitor (NRTTI) – MK-8527
- Phase 1 study
- Safe & well-tolerated
- PK profile supports weekly (or less frequent dosing)

Mean MK-8527 concentration following a single dose
PrEP: What’s in the pipeline?

- Longer acting injectable
- Approved cabotegravir formulation + recombinant human hyaluronidase
- A new ultra-long-acting CAB formulation
- Phase 1 study
- IM version of ultra-long acting well-tolerated
- Dosing interval ≥ 4 months
PrEP: What’s in the pipeline?

- **Annual TAF implant**

First in-human Phase 1 Study: 48 weeks

31% removed early, median 19 weeks

Lower than planned drug release
Ecological study of association between PrEP coverage & new diagnoses

PrEP use: commercial data sets

PrEP coverage: # of PrEP users/100 persons with indications (CDC & AIDSVu data)
Thank you!
jdombrow@uw.edu
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