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Doxy-PEP Associated With Clearance of Mycoplasma genitalium Urogenital Infection

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BACKGROUND

- *Mycoplasma genitalium* (MG) causes 15-25% of nongonococcal urethritis cases in men.
- Rectal MG is prevalent in asymptomatic men who have sex with men (MSM), but its clinical significance is unclear.
- Sequential therapy with doxycycline followed by moxifloxacin is the recommended treatment for MG, but doxycycline is only 30-40% effective as MG monotherapy.
- In the ANRS 174 DOXYVAC trial, doxycycline post-exposure prophylaxis (doxy-PEP) reduced detection of MG at quarterly visits by 28% at any anatomic site.[1]

METHODS

- The DoxyPEP Study randomized MSM and transgender women (TGW) with HIV or on PrEP 2:1 to open-label doxy-PEP or standard of care (SOC; no doxy-PEP) to assess impact on bacterial STI incidence. 637 participants (ppts) were enrolled in San Francisco and Seattle from 2020-23.[2]
- Baseline MG prevalence, as well as incidence and clearance over ≤12 months were evaluated in a convenience sample of DoxyPEP trial ppts.
- Urine and rectal swabs, collected at enrollment and quarterly visits regardless of symptoms, were tested retrospectively with the Hologic Aptima MG test.
- In ppts with MG testing at ≥2 visits, time to MG incidence and clearance was compared between doxy-PEP and SOC groups using interval-censored survival analysis.

Table 1: Characteristics of Study Participants With ≥2 MG Specimens, Including 1 From Baseline

	N (%) or median (IQR)
N	585
Age (median)	37 (31-44)
Race	
White	369 (65.2%)
Black	36 (6.4%)
Asian/Pacific Islander	68 (12.0%)
Multiple races/other	93 (16.4%)
Hispanic/Latino ethnicity	171 (29.2%)
Living with HIV	179 (30.6%)
STIs diagnosed in 12 mo. pre-enrollment	
Gonorrhea	392 (67.0%)
Chlamydia	347 (59.3%)
Syphilis	111 (19.0%)
≥2 STIs	314 (53.7%)
N partners in 3 mo. pre-enrollment	9 (4-18)
Condomless insertive sex acts	5 (3-15)
Condomless receptive sex acts	8 (3-20)

Table 2: Incidence of Urogenital and Rectal MG by Study Arm in the DoxyPEP Study

	Urogenital		Rectal	
Incidence	**SOC**	**Doxy-PEP**	**SOC**	**Doxy-PEP**
Ppts with MG test at ≥2 visits	113	360	152	341
Incident events	1	3	25	52
Person-years of observation	91.2	350.0	96.9	305.3
Incidence rate (per 100 PY)	**1.10**	**0.86**	**25.8**	**17.0**
HR (95% CI), p value	Ref	0.76 (0.08, 7.32), p = 0.81	Ref	0.72 (0.44, 1.16), p = 0.17

Table 3: Clearance of Urogenital and Rectal MG by Study Arm in the DoxyPEP Study

	Urogenital		Rectal	
Clearance	**SOC**	**Doxy-PEP**	**SOC**	**Doxy-PEP**
Ppts with MG test at ≥2 visits	9	23	24	67
Clearance events	3	19	12	48
Person-years of observation	6.9	17.5	11.9	37.8
Clearance rate (per 100 PY)	**43.5**	**108.5**	**100.8**	**126.9**
HR (95% CI), p value	Ref	**3.48 (1.02, 11.89), p = 0.046**	Ref	1.48 (0.78, 2.81), p = 0.23

Doxy-PEP use was associated with urogenital MG clearance, but did not significantly affect rectal MG clearance. Estimated effects on MG incidence were similar to other studies but not significant.

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RESULTS

- 585 study ppts, 30.6% of whom have HIV, provided MG specimens at ≥2 study visits.
- Baseline urogenital MG prevalence was 7% in the SOC arm and 6% in the doxy-PEP arm, whereas rectal MG prevalence was 14% and 16%, respectively. Prevalence was similar by HIV status.
- **Among ppts without MG detected at enrollment (Table 2):**
  - Urogenital MG incidence rate was 1.10 per 100 person-years (100 PY) in the SOC arm and 0.86 in the doxy-PEP arm (HR 0.76, 95% CI 0.08, 7.32).
  - Rectal incidence rate was 25.8 and 17.0, respectively (HR 0.72, 95% CI 0.44, 1.16).
- **Among ppts with urogenital MG at enrollment (Table 3):**
  - Clearance rate in the SOC arm (43.5/100 PY) was lower than the doxy-PEP arm (108.5/100 PY, HR 3.48, 95% CI 1.02, 11.89, **p = 0.046).**
- **Among ppts with rectal MG at enrollment (Table 3):**
  - Clearance rate per 100 PY was 100.8 and 126.9, respectively (HR 1.48, 95% CI 0.78, 2.81).

CONCLUSIONS

- Urogenital MG prevalence was comparable to previous estimates in similar populations of MSM and TGW, whereas rectal MG prevalence was higher.[3, 4]
- There was a nonsignificant trend toward lower MG incidence among doxy-PEP recipients, with similar effect estimates as in the DOXYVAC trial.[1]
- The clearance rate of urogenital MG, but not rectal MG, was significantly higher in the doxy-PEP arm.
- The impact of doxy-PEP on MG incidence and clearance was modest and warrants further study with larger sample sizes and longer follow-up.

LIMITATIONS

- MG specimens were not collected at regular intervals for all DoxyPEP participants.
- There were few ppts with urogenital MG at baseline and few incident urogenital MG events.

PLAIN LANGUAGE SUMMARY

Among people with MG detected in the urine, those on doxy-PEP were more likely to clear MG than those who were not on doxy-PEP. Doxy-PEP did not prevent new MG infections.