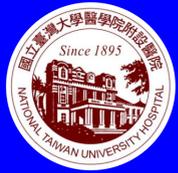


# Effectiveness and Tolerability of Single-Dose Azithromycin in Treatment of Early Syphilis in HIV-infected Patients in an Area of Low Prevalence of Macrolide-resistant *Treponema pallidum*

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**Objectives:** Effectiveness and tolerability of 2-g, single-dose azithromycin in treatment of early syphilis in HIV-infected patients are rarely evaluated in the era of HAART

**Methods:** Consecutive patients with early syphilis who received single-dose azithromycin under direct observation were prospectively observed between May 2012 and Sep. 2013. *Treponema pallidum* was detected from clinical specimens using PCR assays and genotypic resistance to macrolides was determined. Information on adverse effects (AEs) were solicited 24 and 48 hours after treatment. Tests for rapid plasma reagen (RPR) titer were performed at baseline and every 3 months after treatment. Primary outcome of interest was decline of RPR titer by 4-fold or greater at 6 months after treatment.

**Results:** During the study period, 205 HIV-infected patients (204 MSM) with a median RPR titer of 6 log<sub>2</sub> (range, 2-10 log<sub>2</sub>): 37 (18.0%) primary, 62 (30.2%) secondary, 7 (3.4%) both primary/secondary, and 108 (52.7%) early latent syphilis. 167 (81.5%) were receiving HAART, with a CD4 count of 528 cells/μl (range, 34-1455) and plasma HIV RNA load 1.3 log<sub>10</sub> copies/ml (1.3-6.0 log<sub>10</sub>). One of the 69 *T. pallidum* strains identified (1.4%) harbored macrolide resistance mutations (A2058G). Of 97 patients who had completed 6 months of longer follow-up, the serological response rate was 68.0% (n=66). The serologic response rate at 6 months in 91 HIV-infected patients who received 1-dose benzathine penicillin G (BPG) was 75.8% during the same study period. After taking azithromycin (n=205), 79.7% (n=161) developed any gastrointestinal AEs, 33.8% (n=69) central nervous system AEs, and 14.2% (n=29) Jarisch-Herxheimer reaction. No significant association was observed between effectiveness by 3 months or AEs and use of cART.

**Conclusions:** While gastrointestinal AEs were common, single-dose azithromycin demonstrated comparable effectiveness to BPG in treatment of early syphilis among HIV-infected patients in an area of low prevalence of macrolide-resistant *T. pallidum*.

## Introduction

1. Azithromycin has been demonstrated to be equivalent to 1-dose benzathine penicillin in treatment of early syphilis in HIV-negative patients.
2. Effectiveness and tolerability of 2-g, single-dose azithromycin in treatment of early syphilis are rarely evaluated in HIV-infected MSM in areas of low prevalence of macrolide-resistant *T. pallidum* (0.7% in Taiwan, 2009-2013)

## Methods

1. **Subjects:** HIV-infected patients with early syphilis (primary, secondary, early latent) and RPR titers ≥4
2. **Exclusion:** concurrent antibiotic therapy
3. **Study design:** prospective observation study
4. **Study site:** 6 hospitals around Taiwan
5. **Treatment:** 1-dose benzathine penicillin G or single 2-g dose of azithromycin administered directly observed
6. **Follow-up:** RPR titer every 3 months
7. **Primary endpoint:** RPR decline by 4-fold or greater at 6 months of treatment
8. **Treatment failure:** increase of RPR by 4-fold or greater after ever achieving serological response; no decline of RPR titers at 6 months; retreatment administered
9. **Tolerability and safety:** telephone inquiry 24 and 48 hours after treatment; hemogram and aminotransferases 1 week later

Figure 1. Study flow of the patients receiving azithromycin for early syphilis

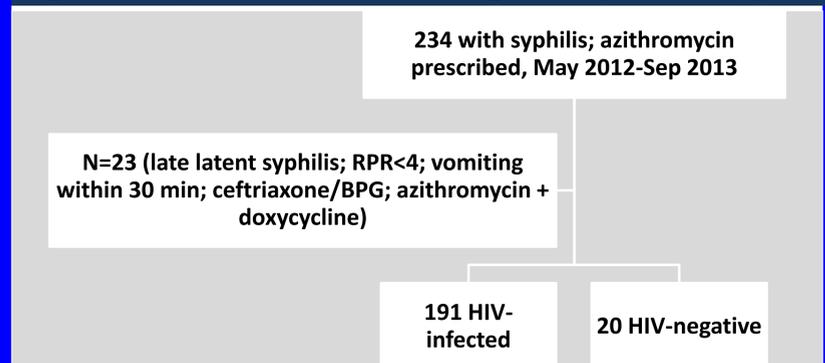


Table 1. Clinical characteristics of HIV-infected patients receiving azithromycin in treatment early syphilis

Characteristics	with HAART	No HAART	All patients
N=	167 (81.46)	38 (18.54)	205 (100)
MSM, n (%)	167 (100.0)	37 (97.4)	204 (99.5)
Age, median (range), years	34.6 (21.4-56.3)	27.2 (18.8-34.8)	32.3 (18-56)
CD4, median (range), cells/mm <sup>3</sup>	548 (34-1455)	443 (134-888)	528 (34-1455)
PVL, (range), log <sub>10</sub> copies/ml	1.3 (1.3-5.4)	4.6 (3.2-6.0)	1.3 (1.3-6.0)
RPR titer, median (range), log <sub>2</sub>	6 (2-10)	6 (2-9)	6 (2-10)
Primary syphilis, n (%)	30 (18.0)	7 (18.4)	37 (18.0)
Secondary syphilis	49 (29.3)	13 (34.2)	62 (30.2)
Primary, secondary	6 (3.6)	1 (2.6)	7 (3.4)
Early latent syphilis	91 (54.5)	17 (44.7)	108 (52.7)

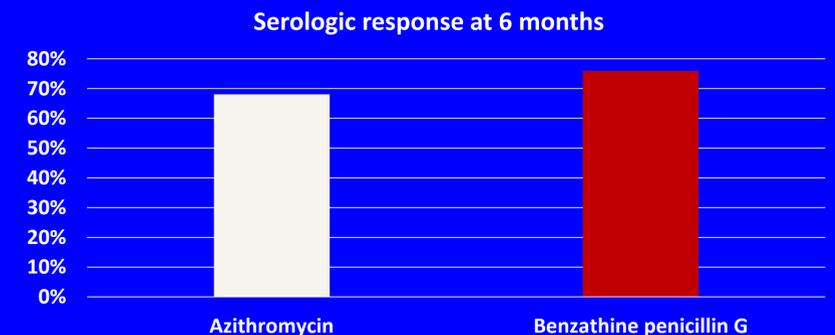
Table 2. Tolerability of HIV-infected patients receiving azithromycin in treatment early syphilis

Symptom	with HAART	No HAART	All patients
Diarrhea	90 (54.88)	23 (60.53)	113 (55.94)
Loose stool passage	13 (7.93)	3 (7.89)	16 (7.92)
Abdominal pain	28 (17.07)	9 (23.68)	37 (18.32)
Nausea	43 (26.22)	11 (28.95)	54 (26.73)
Vomiting	5 (3.05)	0	5 (2.48)
Abdominal bloating	36 (21.95)	7 (18.42)	43 (21.29)
Indigestion	2 (1.22)	2 (5.26)	4 (1.98)
Dizziness	32 (19.51)	8 (21.05)	40 (19.80)
Headache	6 (3.66)	2 (5.26)	8 (3.96)
Vertigo	4 (2.44)	2 (5.26)	6 (2.97)
Lassitude/somnolence	31 (18.90)**	0 (0.00)	31 (15.35)
Jarisch-Herxheimer reaction	24 (14.46)	5 (13.16)	29 (14.1%)

Figure 2. Trends of RPR titers after azithromycin treatment in 97 patients who had completed 6 months or longer follow-up



Figure 3. Serologic response to azithromycin (n=97) and 1-dose benzathine penicillin G (n=91) at 6 months of treatment



## Conclusions

1. 68.0% of the HIV-infected patients receiving azithromycin for early syphilis achieved a 4-fold or greater decline of RPR at 6 months of treatment.
2. Azithromycin is associated with significant gastrointestinal adverse effects (>80% for any gastrointestinal AE), but with a lower risk for Jarisch-Herxheimer reaction