Research news in clinical context

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TENOFOVIR ALAFENAMIDE (TAF) VS. TENOFOVIR DISOPROXIL FUMARATE (TDF) FOR HIV PRE-EXPOSURE PROPHYLAXIS (PREP): WEEK 96 DATA

The double-blind, multicentre, randomised phase III DISCOVER trial is comparing TAF (n=2694) versus TDF (n=2693), both in combination with emtricitabine (FTC), as daily PrEP for preventing HIV acquisition among at-risk men and transgender people who have sex with men. At week 96, TAF/FTC was non-inferior to TDF/FTC: 8 versus 15 HIV infections occurred in the two arms, respectively (incidence rate ratio 0.54; 95% CI 0.23 to 1.26). Adherence was high and did not differ between arms. Compared with TDF users, those on TAF showed better bone mineral density and renal biomarkers, but also more weight gain (median 1.7 kg vs 0.5 kg) and worse lipid profiles, whereas rates of adverse events were similar. Studies are needed to assess TAF/FTC as PrEP in other populations and in real-world settings.

Ogbuagu O, Ruane PJ, Podzamczak D, *et al.* Long-term safety and efficacy of emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis: week 96 results from a randomised, double-blind, placebo-controlled, phase three trial. *Lancet HIV* 2021;8:e397-e407. doi:10.1016/S2352-3018(21)00071-0

A COURSE OF DOXYCYCLINE IS SUPERIOR TO A SINGLE AZITHROMYCIN DOSE FOR TREATING ASYMPTOMATIC RECTAL CHLAMYDIA IN MSM

Rectal chlamydia is prevalent but usually asymptomatic in men who have sex with men (MSM) and regular screening is recommended. This double-blind trial randomly assigned 625 MSM with asymptomatic rectal chlamydia to receive doxycycline (100 mg

twice daily for 7 days) or azithromycin (1 g single dose). In the intention-to-treat analysis, proportions with microbiological cure (negative week-4 NAAT) were higher with doxycycline (97%) than azithromycin (76%); a risk difference of 20% ($p < 0.001$) was confirmed after adjusting for age, HIV status, use of HIV PrEP, douching before receptive anal sex and previous history of chlamydia diagnosis. Adverse events were more common among azithromycin recipients (34% vs 45%), with diarrhoea accounting for the difference (26% vs 40%; $p < 0.001$). Although limited to men and asymptomatic infection, the findings add weight to previous observational studies in support of recommending doxycycline as first-line treatment for rectal chlamydia.

Lau A, Kong FYS, Fairley CK, *et al.* Azithromycin or doxycycline for asymptomatic rectal *Chlamydia trachomatis*. *New Engl J Med* 2021;384(25):2418-2427. doi:10.1056/NEJMoa2031631

PUBLISHED IN STI—THE EDITOR'S CHOICE: SELF-PRESCRIBING OF ANTIBIOTIC STI PROPHYLAXIS IS COMMON AMONG PREP USERS

Investigators conducted an online community survey to study the prevalence and factors associated with self-prescribed antibiotic STI prophylaxis among HIV PrEP users in the UK. Among 1857 MSM, 9% reported use of STI prophylaxis. Self-prescribing was most common among those also reporting risky sexual behaviour or a recent STI diagnosis. In adjusted analyses, factors associated with self-prescribing comprised ≥ 5 condomless sex partners within 6 months, chemsex within past year and a chlamydia diagnosis within past year. Sexual health clinicians should consider asking attendees, especially HIV PrEP users, about the use of antibiotics as STI prophylaxis, to inform appropriate counselling, testing and management. Although antibiotic prophylaxis may decrease the risk of acquiring bacterial STIs, the practice is not routinely recommended and may contribute to antibiotic resistance, decreasing effectiveness of treatment.

O'Halloran C, Croxford S, Mohammed H, *et al.* Factors associated with reporting antibiotic use as STI prophylaxis among HIV PrEP users: findings from a cross-sectional online community survey, May–July 2019.

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NO IMPAIRMENT OF FERTILITY WITH USE OF AN INTRAUTERINE DEVICE

In the 1970s, the Dalkon Shield intrauterine device (IUD) was associated with cases of septic abortion, pelvic inflammatory disease and infertility. Concerns about a risk of upper genital tract infection and infertility lingered despite safer IUD models being brought to market. A multi-centre cohort study prospectively evaluated time to conception among 461 women following discontinuation of common birth control methods. Over up to 24 months, there was no difference between 275 IUD users and never-users in median time to conception and adjusted analysis confirmed the lack of an association (adjusted HR 1.25; 95% CI 0.99 to 1.58). Of note, serological evidence of past *Mycoplasma genitalium* infection was associated with reduced conception by 12 months and longer time to conception, regardless of birth control methods.

Peipert JF, Zhao Q, Schreiber CA, *et al.* Intrauterine device use, sexually transmitted infections, and fertility: a prospective cohort study. *Am J Obstet Gynecol* 2021;225:e1-e9. doi.org/10.1016/j.ajog.2021.03.011

A SMALL SUBSET OF HIV CONTROLLERS MAY BENEFIT FROM ANTIRETROVIRAL TREATMENT

Firm indications to start ART in HIV controllers (HIC) remain elusive. French investigators reviewed data from 301 HIC, classing them as either consistently undetectable (*u*-HIC) or blippers (*b*-HIC) based on the viral load history while untreated. Over a median follow-up of nearly 15 years, 83/228 (36%) *b*-HIC and 7/73 (9%) *u*-HIC started ART, mainly due to declining CD4 cell counts, increasing viral load and non-AIDS-defining events. Among *b*-HIC, treatment led to small but significant immunological improvements, with an increase in CD4:CD8 ratios and a decrease in circulating activated (CD38⁺, HLA-DR⁺) CD4 and CD8 lymphocytes. No such changes were observed in treated *u*-HIC. While *u*-HIC status is highly stable, treatment initiation may benefit a subset of *b*-HIC by reducing HIV-associated chronic inflammation.

Plaçais L, Boufassa F, Lécroux C, *et al.* Antiretroviral therapy for HIV controllers: reasons for initiation and outcomes in the French ANRS-CO21 CODEX cohort. *EclinicalMedicine* 2021;37:100963. doi.org/10.1016/j.eclinm.2021.100963

WHICH PNEUMOCOCCAL VACCINE FOR PREGNANT WOMEN WITH HIV?

Pneumococcus causes substantial morbidity in people with HIV and evidence is needed to guide vaccination practices. This Brazilian randomised, double-blind trial studied 346 ART-treated pregnant women (median CD4 count 548 cells/ μ L) who received the conjugate PCV-10 vaccine, the polysaccharide PPV-23 vaccine or placebo at gestational age 14 to <34 weeks. Grade ≥ 3 adverse events were similarly infrequent (2%–3%) in the three groups; grade 2 local and systemic events occurred in 14%, 7% and 3%, respectively. While most pregnancy outcomes did not differ across groups, preterm birth was surprisingly less common with PCV-10 (2%) versus PPV-23 (13%) or placebo (12%). Equal proportions of PCV-10 and PPV-23

recipients showed an antibody response (65% at week 4 post-vaccination) and antibody transfer was seen equally in their infants. Both pneumococcus vaccines are safe and efficacious in ART-treated pregnant women with HIV.

Weinberg A, Muresan P, Laimon L, *et al.* Safety, immunogenicity, and transplacental antibody transport of conjugated and polysaccharide pneumococcal vaccines administered to pregnant women with HIV: a multicentre randomised controlled trial. *Lancet HIV* 2021;8 (7):e408–e419. doi:10.1016/S2352-3018(20)30339-8

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