Immunization with RG1-VLP adjuvanted with human-applicable alum-MPL induced robust L2 antibodies (ELISA titers 2,500–12,500), which cross-neutralised mucosal high-risk HPV26/33/35/39/68/59/68/73/69/53/34, low-risk HPV6/11/32/40/44/70, and cutaneous HPV2/27/3/76 (titers 25–1,000), and a vigorous CTL response. *In vivo*, mice were efficiently protected against experimental vaginal challenge with mucosal high-risk PsV types HPV16/18/45/31/33/52/58/35/39/51/59/68/56/73/26/53/66/34 and low-risk HPV6/43/44. Enduring protection was demonstrated 1 year after vaccination.

RG1-VLP is a promising next-generation vaccine with broad efficacy against all relevant mucosal and also cutaneous HPV types.

001.6 PERSISTENT SIV-SERONEGATIVE MACAQUE MONKEYS GENERATE MULTI-CYTOKINE ANTI- SIV MUCOSAL IMMUNE RESPONSES FOLLOWING SERIAL LOW-DOSE SIV MUCOSAL CHALLENGE

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Background There are no systematic prospective human or simian studies on the effects of repeated sub-infectious doses of HIV/SIV on mucosal and systemic immunity. The capacity and mechanism of how these responses may impact acquisition and subsequent disease course are also unknown.

Methods To address this, we examined cynolmolgus macaques as part of a vaccine trial, for their ability to generate mucosal and systemic immune responses following repeated ultra low-dose mucosal SIVmac239 challenge. Animals were challenged intra-rectally weekly according to a 24-week dose-escalation. Blood was obtained weekly, and rectal biopsies were obtained 18 to 24w post SIV challenge and analysed by flow cytometry for anti-SIV T-cell responses. Intracellular cytokine responses (IFN-γ, IL-2, TNFα and CD107a) were measured.

Results Total CD4+ responses against two distinct antigenic targets correlated with apparent resistance to infection as measured by the number of challenges, total dose and infecting dose. Moreover, CD8+ responses were also predictive of susceptibility to infection. Both CD4 and CD8 T cell effectors were observed secreting IFN γ, TNF α, IL2 and CD107a in response to SIV gene products not present in the SIV vaccine that the animals received. Placebo-vaccinated animals did not have significantly fewer mucosal immune responses than vaccinees but they did have fewer blood responses suggesting that mucosal responses were generated by the SIV exposure while systemic responses were generated by the vaccine. Multiple sub-infectious SIV challenges did not induce humoral responses in the blood, as determined by western blot assay.

Conclusions Together, this data suggests that these mucosal immune responses are the predominantly the result of priming by repeated low dose SIV challenge. Such an effect alters subsequent susceptibility to infection which has implications for vaccine studies and for understanding the biology of transmission since it increases the resistance to infection of both vaccinees and placebo recipients unpredictably.

0.02 - Antimicrobial therapy for genital tract infections

002.1 A RANDOMISED, CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF NIFURATEL VAGINAL TABLETS ON BACTERIAL VAGINOSIS

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Background Bacterial vaginosis (BV) is a polymicrobial infection and the most common cause of vaginal discharge in women during their reproductive years. A randomised, evaluator-blinded, parallel group pivotal study was carried out to assess the efficacy and safety of the local treatment with nifuratel vaginal tablets in comparison with metronidazole vaginal suppositories in premenopausal, non-pregnant women suffering from BV.

Methods A total of 727 adult women in 38 German sites, with BV diagnosed by Amsel and Nugent criteria, were enrolled after providing their written informed consent. Patients received one course of vaginal treatment with metronidazole 100 mg once daily (o.d.) for six days or nifuratel 250 mg o.d. for ten days. The test of cure visit was performed on day 24 ± 3 after the beginning of the treatment. The efficacy was evaluated using the therapeutic cure rate defined as a combined endpoint including Amsel criteria, clinical signs and symptoms and Nugent score evaluated by a blinded central assessor. The non-inferiority of nifuratel compared to metronidazole at the pre-specified margin of Δ-15% was defined as the clinically acceptable difference between the two active treatments.

Results The therapeutic cure rate was achieved in the per protocol data set by the 53.7% of women: 54.5% in the nifuratel group and 52.9% in metronidazole treated patients (p = 0.0002). Concerning Nugent score (0–3), the two treatments had similar responder rates: 66.2% nifuratel vs. 66.8% metronidazole (p = 0.0006), same results were obtained in terms of Amsel criteria normalisation 78.9% nifuratel vs. 78.6% metronidazole (p = 0.0001). Nifuratel was slightly better to metronidazole curing vulvovaginal signs and symptoms: 81.2% vs. 78.6% (p < 0.0001).

Conclusion The study results suggest that nifuratel 250 mg vaginal tablet o.d. for 10 days may be recommended as first-line treatment in BV as well as the golden standard metronidazole since their efficacy is comparable.

002.2 SUSCEPTIBLITY OF BACTERIAL VAGINOSIS (BV)-ASSOCIATED BACTERIA AND LACTOBACILLI TO RIFAXIMIN, METRONIDAZOLE AND CLINDAMYCIN

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Objective Rifaximin is a semisynthetic rifamycin with poor oral bioavailability, used as an oral agent for the treatment of traveller's diarrhoea and hepatic encephalopathy. Rifaximin is in development as a topical agent for the treatment of bacterial vaginosis (BV). The objective of this study was to evaluate the antimicrobial susceptibility of vaginal isolates of facultative and anaerobic bacteria to rifaximin, clindamycin and metronidazole.

Methods A total of 411 unique BV-related bacteria and 100 isolates of lactobacilli recovered from the human vagina of US women during the years 2009–2012 were tested for antimicrobial susceptibility by the agar dilution CLSI reference method to calculate MICs.

Results Overall, 142 (35%) of the BV-associated vaginal isolates tested were resistant to metronidazole, 63 (15%) were resistant to clindamycin and 11 (2.6%) were resistant to rifaximin. Metronidazole resistance was observed most frequently among *Gardnerella vaginalis* (n = 100 isolates, 69% resistant), *Atopobium vaginae* (n = 62, 87% resistant) and *Mobiluncus* (n = 40, 42% resistant), whereas most were susceptible to both clindamycin (197/202; 98% susceptible) and rifaximin (191/202; 95% susceptible). Both rifaximin and metronidazole were effective against all strains of *Prevotella bivia*

(n = 34), *P timonensis* (n = 33), *Anaerococcus tetradius* (n = 21), *Finegoldia magna* (n = 20) and *Peptoniphilus lacrimalis* (n = 20), whereas clindamycin resistance was detected among 74%, 42%, 19%, 30% and 30% of these anaerobes isolates, respectively. More than 90% of *Prevotella amnii* (n = 33), *Peptoniphilus harei* (n = 23) and *Megasphaera*-like bacteria (n = 25) were susceptible to all three antibiotics. As expected, none of the *Lactobacillus* isolates were susceptible to metronidazole, whereas a majority were susceptible to both clindamycin and rifaximin *in vitro*.

Conclusion Rifaximin had MIC values for a range of microorganisms associated with BV which were superior or similar to the other two drugs approved for the treatment of this condition and deserves clinical evaluation as a new therapeutic agent for the treatment of BV.

002.3 TREATMENT OUTCOMES FOR PERSISTENT MYCOPLASMA GENITALIUM-ASSOCIATED NGU: EVIDENCE OF MOXIFLOXACIN TREATMENT FAILURES

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Background Recent treatment trials have demonstrated low efficacy of doxycycline against *Mycoplasma genitalium* (MG) and increasing resistance to azithromycin. Treatment with azithromycin is recommended for persistent NGU if not used for the initial episode. We evaluated microbiologic cure rates for men with NGU and persistent detection of MG.

Methods English-speaking men aged 16 years attending the STD clinic in Seattle, WA with NGU (urethral discharge or urethral symptoms plus ≥ 5 PMNs/HPF) were enrolled in a randomised trial of NGU therapy between January 2007 and July 2011. Urine was tested for MG by PCR. Men received 1g azithromycin plus placebo doxycycline or doxycycline (100mg bid x 7d) plus placebo azithromycin. Treatment failures after 3 weeks received 'reverse therapy' (active doxycycline if they first received active azithromycin and vice versa). Persistent failures after 6 weeks received moxifloxacin (400mg x 7d). After September 2010, microbiologic failures at 3 weeks received moxifloxacin.

Results Of 606 enrolled men, 65 were positive for MG at enrollment and returned after 3 weeks. Microbiologic failure (positive MG test) occurred in 23/38 (60.5%) who received azithromycin and 19/27 (70.4%) who received doxycycline (p = 0.41). Of the 37 men with microbiologic treatment failure who received 'reverse therapy' and returned after 6 weeks, 19 (51.4%) had persistent detection of MG, including 14/20 (70.0%) retreated with doxycycline and 5/17 (29.4%) retreated with azithromycin (p = 0.02). All 19 men were prescribed moxifloxacin; 16 returned at 9 weeks and 2 (12.5%) had microbiologic failure, despite clinical cure. Four men received moxifloxacin after initial failure; 1 had microbiologic failure at 6 weeks, was retreated with moxifloxacin and microbiologically cured at 9 weeks.

Conclusion One half of MG-positive men retreated with a second standard NGU treatment regimen experienced microbiologic treatment failure. Moxifloxacin treatment failure, while not common, did occur, suggesting antimicrobial susceptibility in MG merits careful monitoring.

002.4 PERSISTENT/RECURRENT CHLAMYDIAL INFECTION AMONG STD CLINIC PATIENTS TREATED WITH CDC-RECOMMENDED THERAPIES

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Background CDC guidelines recommend azithromycin or doxycycline as treatments for chlamydial infection. Recently, one randomised trial comparing these therapies suggested doxycycline was superior, while another found the two therapies were equivalent. We examined the risk of persistent/recurrent chlamydial infection among patients treated with doxycycline or azithromycin.

Methods We performed a secondary analysis of data from Project Aware, a randomised, controlled trial of a behavioural intervention. The trial enrolled patients aged ≥ 18 years without a prior HIV diagnosis in 9 U.S. STD clinics in 2010. At baseline, women with urogenital chlamydial infection and men with urethral and/or rectal chlamydial infections were treated with azithromycin or doxycycline, per clinic standard of care. Patients with a positive chlamydia test at 6-month follow-up were considered to have persistent/recurrent infection.

Results Of 5012 participants, 492 (9.8%) tested positive for *C. trachomatis* at baseline. Of these, 338 (69%) were treated with doxycycline or azithromycin without a second drug active against *C. trachomatis*; 92% (76 of 83) and 88% (225 of 255), respectively, were re-tested at 6 months. Comparing doxycycline and azithromycin, overall 7 (9.2%) and 26 (11.6%), respectively, had persistent/recurrent infection (RR = 0.80, 95% CI = 0.36–1.76). Among persons with urogenital infections, 6 (10.0%) of 60 and 18 (10.1%) of 179 (RR = 0.99, 95% CI = 0 0.41–2.39), respectively had persistent/recurrent infection. Among men with rectal infections, 2 (9.5%) of 21 and 8 (16.3%) of 49 who received doxycycline and azithromycin, respectively, had persistent/recurrent infection (RR = 0.58, 95% CI = 0.14–2.52). On multivariate analysis, persistent/recurrent infection was significantly associated with black (vs. white) race (aRR = 4.29, 95% CI = 1.14–16.16) and rectal (vs. urogenital) infection (aRR = 5.42, 95% CI = 0.99–29.55), but not treatment regimen.

Conclusion There were no differences in persistent/recurrent urogenital chlamydia infections at six months by treatment type. Treatment failure of rectal infections among men may be more common with azithromycin and merits additional study.

002.5 A PHASE II, DOSE RANGING STUDY TO EVALUATE THE EFFICACY AND SAFETY OF SINGLE-DOSE ORAL SOLITHROMYCIN (CEM-101) FOR TREATMENT OF PATIENTS WITH UNCOMPLICATED UROGENITAL GONORRHOEA

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Objectives Emerging resistance to available treatment creates an urgent need for new therapies for uncomplicated gonorrhoea. Solithromycin, a new 4th generation macrolide with 3 ribosomal targets, is highly active against most antibiotic-resistant strains of *Neisseria gonorrhoeae*. A Phase II, dose ranging study to evaluate the efficacy and safety of single-dose oral solithromycin for uncomplicated urogenital gonorrhoea was conducted.

Methods Consenting participants with suspected *Neisseria gonorrhoeae* infection were cultured at the urethra/cervix, rectum, and pharynx at enrollment and Day 7. The primary outcome was bacterial eradication (conversion from positive baseline *N. gonorrhoeae* urethral/cervical culture to negative) at Day 7. Secondary outcomes included eradication of rectal or pharyngeal gonorrhoea and the eradication of gonococcal and chlamydial nucleic acids. Initially, eligible patients received a single 1200 mg oral dose of solithromycin; following demonstration of bacteriologic efficacy, a second cohort was treated with a single 1000 mg dose.

Results Of 41 (19 M, 22 F) participants enrolled, 28 were treated with a 1200 mg dose and, to date, 13 with 1000 mg. Gonococcal eradication rates in 22 evaluable 1200 mg patients were 100% (22/22) for urethral/cervical, pharyngeal (5/5), and rectal (2/2) infections. Of