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### 631. Preliminary safety and pharmacokinetic profile of VIR-2482: a monoclonal antibody for the prevention of influenza A illness

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**Session:** P-24. Clinical Trials

***Background:*** VIR-2482 is a fully human immunoglobulin G1(IgG) monoclonal antibody (mAb) directed against a highly-conserved epitope in the influenza A hemagglutinin stem region and is in clinical development for the prevention of influenza A illness. The Fc region of VIR-2482 has been modified to provide an extended half-life.

***Methods:*** This is a randomized, placebo-controlled, Phase 1/2 study of VIR-2482 administered intramuscularly (IM) to healthy adult volunteers aged 18-64 years old who have not received a current influenza vaccine. The Phase 1 portion of the study will evaluate the safety, tolerability, pharmacokinetic (PK), and immunogenicity profile of VIR-2482 following single (Part A) or multiple doses (Part B). The Phase 2 study will evaluate the efficacy of VIR-2482 in the prevention of influenza A illness as well as safety, tolerability, and PK. Part A is ongoing and consists of four single dose cohorts (N=25/cohort) randomized (4:1) to a single dose of VIR-2482 or placebo at 60, 300, 1200, or 1800 mg. Safety, tolerability, PK and immunogenicity will be evaluated for at least 52 weeks post-dose.

***Results:*** In Part A, all 100 subjects received a single dose of VIR-2482 (N=80) or placebo (N=20). Preliminary blinded safety data for all cohorts and PK data for the 300 and 1200 mg cohorts are reported here. Dosing was well tolerated; 6% (6/100) of subjects experienced mild injection site reactions, which generally resolved within 48 hrs. Through 12 weeks post-dosing, the majority (124/126; 98.4%) of adverse events (AEs) were mild to moderate in nature, no serious AEs were reported, and no subjects discontinued due to an AE. Based on available data, exposure ($C_{max}$ and AUC) between 300 and 1200 mg of VIR-2482 increased in a dose proportional manner. The PK profile of VIR-2482 is consistent with a half-life extended IgG.

***Conclusion:*** Based on available data, VIR-2482 has been well tolerated following single IM doses of up to 1800 mg in healthy subjects. The preliminary PK profile of VIR-2482 enables once per season dosing. Overall, these data support initiation of a Phase 2 study to evaluate efficacy of VIR-2482 for the prevention of influenza A illness.

***Disclosures:*** Jennifer Sager, PharmD, Vir Biotechnology (Employee) David K. Hong, MD, Vir Biotechnology (Employee) Aurelio Bonavia, PhD, Vir Biotechnology (Employee) Lynn Connolly, MD, PhD, Vir Biotechnology (Employee) Deborah Cebrik, PhD, Vir Biotechnology (Independent Contractor) Marie Christine Fanget, MS, Vir Biotechnology (Employee) Erik Mogalian, PharmD, PhD, Vir Biotechnology (Employee)

### 632. A Randomized, Placebo-Controlled, Double-Blind, Clinical Trial Evaluating Two Dose Regimens of Rifaximin (550mg daily or twice-daily) for Chemoprophylaxis Against Travelers' Diarrhea Among Deployed U.S. and U.K. Military Personnel (PREVENT TD)

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**PREVENT-TD Study Team**

**Session:** P-24. Clinical Trials

***Background:*** Travelers' diarrhea (TD) is a leading threat to military readiness. Most trials of rifaximin chemoprophylaxis involve civilians or short-duration travel, whereas military travelers are exposed for longer periods at austere locations and are often physically taxed. We sought to assess efficacy of two regimens among military personnel deployed overseas.

***Methods:*** This was a multi-site, double-blind, placebo-controlled trial of deployed military, randomized to placebo, rifaximin 550 mg daily, or rifaximin 550 mg twice-daily, for up to 42 days (1:1:1; 6 randomizations/block). Diaries were reviewed with subjects on return. Primary endpoint was time to first unformed stool (TFUS) in a TD episode. Other endpoints were assessed by intention to treat (ITT) and subgroups included incidence of any loose stool, meeting criteria for TD, safety, efficacy, adherence and impact to activity endpoints.

***Results:*** 343 subjects were included in the ITT population. All UK travelers deployed to a single-site in Kenya; US travelers mostly deployed to various Asia-Pacific locations. Of 73 (21.2%) subjects reporting diarrhea, 42 (57.5%) met TD criteria. Among rifaximin-treated subjects, 15.9% (n=17) reported diarrhea in the twice-daily arm, 20.7% (n=25) in the daily arm, vs. 27.0% (n=31) of placebo recipients; p=.04 and 0.26 respectively. TD was reported by 10.3% (n=11) and 10.7% (n=13) in the daily and twice-daily arms, vs. 15.7% (n=18) among placebo recipients; p=0.24 vs. 0.26 respectively. Among UK personnel, a twice-daily regimen vs. placebo resulted in significantly fewer TD episodes (1.6% vs. 11.9%; p=0.03). Adverse events were similar between groups.

Table 1: Demographics, endpoints, and adverse events (Comparisons are across placebo vs. each dosing regimen. Intent-to-treat [ITT] population defined as subjects enrolled into the study, randomized, travelled and had follow-up. p-values calculated from chi-square or Fisher's exact test [categorical variables] and Wilcoxon-Mann-Whitney test [continuous variables]. Analyses performed on SAS v9.4. BID: twice-daily)

| | Rifaximin 550mg BID | Rifaximin 550mg daily | Placebo | Total | p-value twice-daily | p-value daily |
|---|---|---|---|---|---|---|
| **Total ITT population n (%)** | 107 (31.2) | 121 (35.3) | 115 (33.5) | 343 | NA | NA |
| **Gender n (%)** | | | | | 0.786 | 0.291 |
| Male | 97 (90.6) | 113 (93.4) | 103 (89.6) | 313 (91.2) | | |
| **Travel Duration (days)** | | | | | | |
| Median (IQR) | 45 (39-50) | 45 (38-50) | 45 (40-50) | 45 (38-50) | 0.955 | 0.592 |
| **Subject Group n (%)** | | | | | 0.926 | 0.749 |
| US | 44 (41.1) | 53 (43.8) | 48 (41.7) | 145 (42.3) | | |
| UK | 63 (58.9) | 68 (56.2) | 67 (58.3) | 198 (57.7) | | |
| **Region n (%)** | | | | | 0.659 | 0.901 |
| South America | 1 (0.9) | 1 (0.8) | 1 (0.9) | 3 (0.9) | | |
| Sub-Saharan Africa | 71 (66.4) | 73 (60.8) | 75 (65.2) | 219 (64.0) | | |
| South-East Asia | 22 (20.6) | 32 (26.7) | 28 (24.4) | 82 (24.0) | | |
| East-North Asia | 8 (7.5) | 11 (9.2) | 10 (8.7) | 29 (8.5) | | |
| Central America | 2 (1.9) | 0 (0) | 0 (0) | 2 (0.6) | | |
| South-Central Asia | 3 (2.8) | 3 (2.5) | 1 (0.9) | 7 (2.0) | | |
| **Subjects Reporting any diarrhea (Loose stools)** | 17 (15.9) | 25 (20.7) | 31 (27.0) | 73 (21.2) | 0.045 | 0.256 |
| **Subjects Meeting TD Criteria** | 11 (10.3) | 13 (10.7) | 18 (15.7) | 42 (12.2) | 0.235 | 0.264 |
| **Subjects Reporting any Diarrhea (Loose stools – by UK Subject Group)** | 4 (6.4) | 11 (16.2) | 15 (22.4) | 30 (15.2) | 0.0097 | 0.360 |
| **Subjects Meeting TD Criteria (by UK Subject Group)** | 1 (1.6) | 5 (7.4) | 8 (11.9) | 14 (7.1) | 0.034 | 0.366 |
| **Subjects Reporting any Diarrhea (Loose stools – by US Subject Group)** | 14 (29.6) | 14 (26.4) | 16 (33.3) | 43 (29.7) | 0.696 | 0.441 |
| **Subjects Meeting TD Criteria (by US Subject Group)** | 10 (22.7) | 8 (15.1) | 10 (20.8) | 28 (19.3) | 0.826 | 0.452 |
| **TFUS** | | | | | | |
| **Days: Median (IQR)** | 11.8 (5.3-50.6) | 21.3 (12.9-30.3) | 14.3 (5.9-34.9) | | 0.75 | 0.76 |
| **Adverse events** | | | | | 0.559 | 0.139 |
| None | 77 (72.0) | 90 (74.4) | 77 (67.0) | 244 (71.1) | | |
| Mild/Moderate | 30 (28.0) | 27 (74.4) | 37 (32.2) | 94 (27.4) | | |
| Severe | 0 (0) | 4 (3.3) | 1 (0.9) | 5 (1.5) | | |

***Conclusion:*** This is the first trial comparing two high-dose regimens of rifaximin prophylaxis in deployed personnel. Unlike prior reports, neither regimen was associated with an overall significant decrease in TD, potentially due to low overall TD incidence. However, the twice-daily regimen was associated with a numerically lower incidence of diarrheal stool, and in the UK subject group, there was a significant decrease of both TD and diarrheal stool. The impact of variability in regional TD risk, pathogen distribution and adherence in austere deployment environments on efficacy will be reviewed.

***Disclosures:*** **All Authors**: No reported disclosures

### 633. Bictegravir/Emtricitabine/Tenofovir Alafenamide (B/F/TAF) Efficacy in Participants with Pre-Existing Primary Integrase Inhibitor Resistance Through 48 Weeks of Phase 3 Clinical Trials

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