Results. ADR: Out of 513 Filipino PLHIV from an ADR surveillance study on one year of ARV treatment, 53 (10.3%) failed (HIV VL >1,000 copies/mL). Among these, 48 had clinically significant mutations. Table 1 shows NNRTI ADR frequencies. There was no significant ADR difference between first-generation and newer generation NNRTIs. TDR: 298 treatment-naïve Filipino PLHIV underwent baseline sequencing. All 298 had SBS: 266 had successful NGS. Table 1 shows SBS and NGS TDR NNRTI resistance at a 5% minor variant cutoff. There was no significant TDR difference between first-generation and newer generation NNRTIs.

Conclusion. ADR and TDR rates to the newer NNRTIs are similar to first-generation NNRTIs. High TDR to doravirine on NGS is concerning, but its clinical significance is unclear. Efavirenz had the lowest TDR and ADR and may be the most useful new-generation NNRTI. However, integrase strand transfer inhibitor-based regimens will likely be more durable.

Table 1. ADR and TDR NNRTI resistance in the Philippines.

| Antiretroviral | SBS ADR Resistance (%) among those with clinically significant mutations (%) | SBS TDR Resistance (%) among those with TDR N=48 and overall (%) | NGS TDR Resistance (%) among those with TDR N=48 and overall (%) |
|---------------|--------------------------------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|
| DOR           | 39 (1.3%) (73.6%) (7.6)                                                        | 3 (16.7%) (1.0)                                                  | 20 (44.5%) (7.5)                                                 |
| EFV           | 45 (93.8%) (84.8%) (8.8)                                                       | 6 (33.3%) (2.0)                                                  | 8 (17.8%) (3.0)                                                  |
| ETR           | 36 (75.0%) (68.0%) (7.0)                                                       | 2 (11.1%) (0.7)                                                  | 6 (13.5%) (2.3)                                                  |
| NVP           | 43 (95.3%) (84.9%) (8.8)                                                       | 9 (33.3%) (2.0)                                                  | 9 (20%) (3.4)                                                   |
| RPV           | 41 (85.4%) (77.3%) (8.0)                                                       | 9 (50%) (3.0)                                                   | 16 (35.6%) (6.0)                                                  |
| Any NNRTI     | 47 (97.9%) (88.7%) (9.2)                                                        | 10 (55.6%) (3.4)                                                 | 30 (66.7%) (11.3)                                                 |

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2508. Virologic Suppression in Patients Switched to BIC/TAF/FTC with Baseline NNRTI and/or INSTI Resistance
Kayla M. Natal, PharmD, AAPHIV®; Rahul Tilani, BA¹; Ijhad Slim, MD²; Saint Michael’s Medical Center, Montville, New Jersey; University of New England College of Osteopathic Medicine, Newark, New Jersey

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Background. BIC/TAF/FTC is the first fixed-dose combination tablet to contain both a second-generation INSTI and TAF and has therefore become a popular treatment option for HIV. Historically, patients with NRTI mutations were placed on four-drug, NRTI-retaining regimens or two-drug, NRTI-sparing regimens. Recently, data have emerged supporting the use of second-generation INSTIs with tenofovir/FTC in the setting of the M184V mutation alone. There is a paucity of data, however, evaluating the use of BIC/TAF/FTC in the setting of NRTI and/or INSTI mutations. This study assessed the role of BIC/TAF/FTC in patients with baseline NRTI and/or INSTI mutations.

Methods. This was an observational retrospective study conducted at an inner city HIV clinic. Patients were eligible if they were switched to BIC/TAF/FTC with confirmed adherence and had either the M184V mutation alone, M184V plus another NRTI mutation(s), an INSTI mutation alone, or both NRTI and INSTI mutation(s) at the time of ART switch. We evaluated virologic response (HIV RNA < 200 copies/mL) and duration of BIC/TAF/FTC therapy.

Results. There were 16 patients eligible for analysis. Among the patients, 69% were male and 31% were female. The majority of patients were Black (81%). The mean age was 63 years (SD ± 8.6). Thirty patients were virologically suppressed (HIV RNA < 200 copies/mL) at baseline. The mean CD4 count at baseline was 630.4 cells/mm³ (SD ± 297.1). Mutations at baseline were as follows: M184V alone (25%), M184V plus another NRTI mutation(s) (56.25%), INSTI mutation alone (12.5%), NRTI and INSTI mutation(s) (6.25%). BIC/TAF/FTC median duration of therapy was 10.5 months (range 6–14 months). The mean CD4 count of the patients switched to BIC/TAF/FTC was 687 cells/mm³ (SD ± 20.7). All patients switched to BIC/TAF/FTC achieved or maintained virologic suppression (HIV RNA < 200 copies/mL) with a mean HIV RNA of 26.25 copies/mL (SD ± 14.1). Fifteen of those switched to BIC/TAF/FTC had an undetectable HIV RNA level (HIV RNA < 50 copies/mL).

Conclusion. While a larger cohort and longer follow-up period is needed, BIC/TAF/FTC may maintain virologic suppression in patients with select baseline NRTI and/or INSTI mutations.

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2509. Pooled Resistance Analyses of Darunavir (DRV) Once Daily (QD) Regimens and Formulations Across 10 Clinical Studies of Treatment-Naïve (TN) and Treatment-Experienced (TE) Patients with Human Immunodeficiency Virus (HIV)-1 Infection
Background. DRV has demonstrated high efficacy and barrier to resistance development across diverse populations, from TN to heavily TE patients. We evaluated resistance data from 10 clinical studies of different DRV 800 mg QD–based antiretroviral regimens and formulations.

Methods. The analysis included patients from 10 phase 2/3 studies (48–192 weeks of duration) of ritonavir- and cobicistat-boosted DRV 800 mg QD–based regimens in TN and virologically failing or suppressed TE patients with HIV-1 (table). Three Phase 3 studies of the DRV/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) 800/150/200/10 mg single-tablet regimen (STR) Post-baseline resistance was evaluated in patients experiencing protocol-defined virologic failure (PDVF) definitions and criteria for resistance testing varied slightly among studies. Resistance-associated mutations (RAMs) were based on respective International Antiviral Society–USA mutation lists over time.

Results. Of the 3,635 patients evaluated, 250 met PDVF criteria and 205 had post-baseline genotypes/phenotypes. Overall, 4 (0.1%) patients developed (or had identified [switch studies]) ± DRV and/or primary protease inhibitor (PI) RAM (table), and only 1 (< 0.1%, ODIN) patient lost DRV phenotypic susceptibility; this TE patient had prior VF with lopinavir. Among those who used a nucleo(t)side reverse transcriptase inhibitor (NRTI) backbone (mostly emtricitabine [FTC] + tenofovir [TFV]), 12 (0.4%) patients had ≥1 NRTI RAM, including 10 with M184V associated with FTC resistance. This DRV RAM was observed in patients receiving D/C/F/TAF (n = 1,949), none had post-baseline DRV, primary PI, or TFV RAMs; only 2 (0.1%) patients developed an FTC RAM. Across a large, diverse population using DRV 800 mg QD–based regimens and formulations, resistance development remains rare; 0.1% of patients had ≥1 DRV and/or primary PI RAM post-baseline. Among 3 trials of the D/C/F/TAF STR, no patients developed a DRV or primary PI RAM. After > 10 years of investigating DRV 800 mg QD–based regimens in clinical trials, loss of phenotypic susceptibility to DRV has never been observed in TN or TE virologically suppressed patients and was only once observed in a TE patient with prior VF on multiple antiretrovirals, including a PI.

Table. Post-Baseline Resistance-Associated Mutations Across Studies

| Study (duration) | Population | Treatment (N) | PDI (post-BL resistance data) | Patients with ≥1 (emergent) RAM, in (%) |
|------------------|------------|---------------|--------------------------------|--------------------------------------|
| ARTEMIS (12 weeks) | TN | DRV+FTC/TFD (143) | 1 (0.7%) | 1 (0.7%) |
| GS-US-219-010 | TN | DRVobc+FTD/TFD (103) | 0 (0%) | 0 (0%) |
| GS-US-219-010 | TN and TE | DRV+obc+2 NRTIs (413) | 0 (0%) | 0 (0%) |
| ODIN (48 weeks) | TE | DRV+vs=32 NRTIs (94) | 0 (0%) | 0 (0%) |
| INROADS (45 days) | TN and TE (with transmitted resistance) | DRV+obc+EIR (54) | 0 (0%) | 0 (0%) |
| MONET (144 weeks) | Virologically suppressed | DRV+non-HIV+TV (127) | 0 (0%) | 0 (0%) |
| PROTEA (96 weeks) | Virologically suppressed | DRV+non-HIV+TV (18) | 0 (0%) | 0 (0%) |
| EMERALD (96 weeks) | Virologically suppressed | D/C/F/TAF (703) | 0 (0%) | 0 (0%) |
| AMBER (56 weeks) | Switch to D/C/F/TAF (52) | 0 (0%) | 0 (0%) |
| DIAMOND (48 weeks) | TN (newly diagnosed) | D/C/F/TAF (109) | 0 (0%) | 0 (0%) |
| Total (3,635) | 250 (205) | 4 (0.1%) | 2 (0.1%) |

Figure 1. Trends of Resistance Rates to Three-Class Drug (NRTI + PI + NNRTI) in the US and Canada

Figure 2. Resistance Rates to Four-Class Drug (NRTI + PI + NNRTI + INSTI)

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2510: Systematic Literature Review of Multiclass Resistance in Heavily Treated Exposed Persons with HIV

Josephine Mauskopf, PhD; Maria M. Fernandez, PhD, MBA; Jade Ghon, MD, PhD1;2; Paul Sax, MD; Julie Priest, MSPhD; Cindy Garris, MS; Andrew Clark, MD; IRTI Health Solutions, Research Triangle Park, North Carolina; 2; IRTI Health Solutions, Durham, North Carolina; 3; Assistance Publique – Hôpitaux de Paris, Service des Maladies Infectieuses et Tropicales, Groupe Hospitalier Paris Nord Val de Seine, site Bichat-Claude Bernard, Paris, France; 4; Université Paris Diderot, INSERM U137 TAME, PRES Sorbonne Paris Cité, Paris, Ile-de-France, France; 5; Brigham and Women’s Hospital, Harvard Medical School, Boston, Massachusetts; 6; VUH Healthcare, Durham, North Carolina

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Background. Because of progress in antiretroviral therapy (ART), fewer people with HIV experience virologic failure with multiclass resistance. We sought to estimate the prevalence of multiclass resistance since the introduction of INSTI-based regimens using a systematic literature review.

Methods. A systematic literature search using PubMed, Embase, and the Cochrane Library was conducted of articles published since 2008, the year when INSTI-based regimens for treatment-experienced people with HIV became widely used. Bibliographies of existing literature reviews, websites of European and International organizations reporting data on HIV and AIDS, and abstracts presented from 2016–2018 at conferences were searched to identify additional relevant studies. Using predefined criteria, two reviewers independently reviewed studies reporting multiclass (three-class or greater) resistance in persons with HIV infection who are treatment experienced and were either perinatally infected or infected as adults. Studies from Western Europe, Australia, Canada and the United States (US) using any type of resistance definitions and resistance tests were included.

Results. A total of 441 unique articles were identified, 343 were excluded during level 1 screening and 98 articles were included for full-text review. A total of 34 articles (11 US studies, 3 from Canada, 1 from Australia, and 19 from Western European countries) met the inclusion criteria and were included in data extraction analysis. Over the past decade, a modest decrease in the prevalence of three-class (NNRTI, NRTI, PI) resistance was observed in studies from the United States and Canada, ranging from 8.3% in 2009 to 6.7% in 2014 (Figure 1). Western European countries and Australia showed similar trends. The prevalence of 4-class resistance (including INSTIs) with virologic failure in the current treatment era is less, 2% (Figure 2).

Conclusion. The prevalence of multiclass resistance has decreased over the past decade, with three-class resistance continuing to decline and four-class resistance rate. Although the population with treatment failure and no viable options for a suppressive regimen is currently small, this group of people with HIV are in urgent need of novel treatment options.