A CME NEWSLETTER

ARV Therapies and Therapeutic Strategies

Reporting From

The XIX International AIDS Conference (AIDS 2012)

Jointly Sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC.

AIDS 2012*
July 22-27, 2012
Washington, D.C.

Faculty

Calvin J. Cohen, MD, MS
Research Director, CRI New England
Clinical Instructor, Harvard Medical School
Boston, Massachusetts

David Cooper, MD
Professor, University of New South Wales
Director of The National Centre in
Epidemiology & Clinical Research
Sydney, Australia

Joseph Eron, MD
Professor, University of North Carolina
School of Medicine
Chapel Hill, North Carolina

Graeme Moyle, MD, MB, BS
Associate Director of HIV Research
Chelsea & Westminster Hospital
London, United Kingdom

Jürgen Rockstroh, MD
Professor, University of Bonn
Bonn, Germany

Supported by an unrestricted educational grant from Merck & Co., Inc.

*This coverage is not sanctioned by the conference organizers and is not an official part of the conference proceedings.

Introduction

This newsletter is based on discussions held during the continuing medical education Internet symposium ARV Therapies and Therapeutic Strategies. This program provided an update on important presentations made during the XIX International AIDS Conference (AIDS 2012).

The faculty for this program consisted of: Course Director and Moderator Calvin J. Cohen, MD, MS from Harvard Medical School, Boston, Massachusetts, and faculty members David Cooper, MD from University of New South Wales, Sydney, Australia; Joseph Eron, MD from University of North Carolina School of Medicine, Chapel Hill, North Carolina; Graeme Moyle, MD, MB, BS, from Chelsea & Westminster Hospital, London, United Kingdom; and Jürgen Rockstroh, MD from University of Bonn, Bonn, Germany.

HIV Prevention

Partners PrEP Study

In a report presented at the Conference, investigators from the Partners PrEP Study – a trial of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC)/TDF pre-exposure prophylaxis (PrEP) provided to HIV-uninfected members of serodiscordant couples in two African countries – assessed the efficacy of PrEP among a subset of couples who had higher baseline risk characteristics. **[Abst. TUAC0102].**[1] Higher-risk couples had risk factors associated with HIV transmission, including age of HIV-uninfected partner, number of children together, circumcision status of the male HIV-uninfected partner, self-reported unprotected sex, and HIV RNA concentrations in the HIV-infected partner.

Among the 4,747 HIV-serodiscordant couples in the Partners PrEP Study, 1,085 (22.9%) were classified as higher-risk couples. The investigators found that the HIV incidence was 5.0/100 person-years (28 transmissions) among those assigned placebo, 1.3/100 person-years (7 transmissions) among those assigned TDF PrEP, and 1.1/100 person-years (6 transmissions) among those assigned FTC/TDF PrEP. These findings indicate an estimated PrEP HIV-protection efficacy of 72% for TDF PrEP and 78% for FTC/TDF PrEP. The investigators concluded that PrEP provided substantial protection against HIV acquisition for higher-risk HIV-serodiscordant couples, and that higher-risk HIV-serodiscordant couples could be a priority population for PrEP implementation.

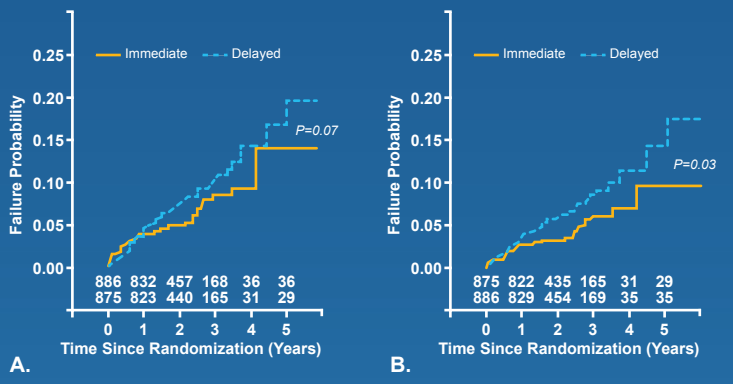
Management of Treatment-Naïve Patients

Early vs. Delayed Initiation of ARV Therapy

Researchers analyzed clinical outcomes during follow-up of HPTN 052 to determine optimal timing of ART initiation **[Abst. THLBB05].**[2] Participants in the study consisted of HIV-positive adults with CD4 cell counts 350-550 cells/mm^3 from Africa, Asia, and South America who were randomized to receive ART immediately or after CD4 counts fell below <250 cells/mm^3 or AIDS. The primary clinical events tracked were death, WHO Stage 4, tuberculosis, severe bacterial infection, and targeted serious non-AIDS events.

The investigators reported that compared with immediate ART, delayed ART was associated with shorter time to first primary clinical event, AIDS-defining disease, and tuberculosis (Figure 1). There was also a higher incidence of tuberculosis and all targeted clinical events. Sensitivity analysis excluding pre-specified secondary events (recurrent upper respiratory tract infections, unexplained weight loss [moderate and severe], unexplained chronic diarrhea, unexplained persistent fever, unexplained anemia, lipodystrophy and hypertension) showed a consistent result. Based on these findings, the research team concluded that in HIV-positive adults with CD4 cell counts 350-550 cells/mm^3, immediate ART significantly reduced the incidence of clinical events, notably tuberculosis, AIDS-defining events, and WHO Stage 2/3 clinical events.

Figure 1. Time to First Primary Event (A) and Time to First AIDS defining Disease (B)

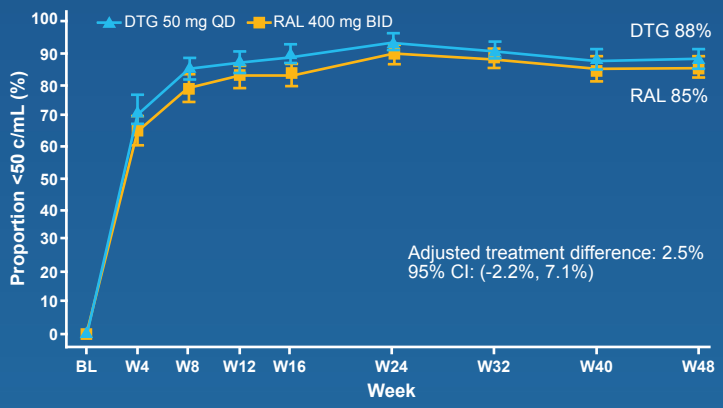


SPRING-2 Study

The integrase inhibitor dolutegravir (DTG) was studied in SPRING-2, a multicenter, double-dummy-blinded, phase III, non-inferiority study in which HIV-infected ART-naïve adults with HIV RNA ≥1,000 copies/mL and no evidence of viral resistance were randomized 1:1 to receive DTG 50 mg QD or raltegravir (RAL) 400 mg BID, in addition to investigator-selected backbone NRTIs of either TDF/FTC or abacavir (ABC)/lamivudine (3TC) **[Abst. THLBB04].**[3] The primary endpoint was proportion of subjects with HIV RNA <50 copies/mL through Week 48.

As reported at IAC, 822 subjects were randomized to either DTG (n=411) or RAL (n=411). The proportion of subjects meeting the primary endpoint was 88% for DTG and 85% for RAL (Figure 2); the difference met the 10% non-inferiority criteria. For subjects with HIV RNA >100,000 copies/mL, the response rate was 82% for DTG vs. 75% for RAL. Secondary analyses supported non-inferiority: HIV RNA <50 copies/mL per-protocol (DTG 90% vs. RAL 88%), treatment-related discontinuation=failure (93% vs. 92%) and virologic non-response (5% vs. 8%). Median CD4 increases were observed to be similar in both groups: 230 cells/mm^3 each. At virologic failure, there was no genotypic integrase or NRTI resistance in the DTG group vs. 1 subject and 4 subjects, respectively, in the RAL group.

Figure 2: SPRING-2 Outcomes at Week 48



Study 114: Cobicistat vs. Ritonavir as Pharmacoenhancer

Investigators reported on Study 114, an international, randomized, double-blind, double-dummy, active controlled trial designed to evaluate the efficacy and safety of cobicistat vs. ritonavir as pharmacoenhancers of atazanavir (ATV/co vs. ATV/r) in combination with FTC/TDF in treatment-naïve patients **[Abst. TUAB0103].**[4] The key eligibility criteria for the study were that patients had HIV RNA ≥5,000 copies/mL and an estimated glomerular filtration rate (eGFR) ≥70 mL/min. The primary endpoint was HIV RNA <50 copies/mL at week 48 by snapshot algorithm, and the noninferiority margin was 12%.

A total of 692 subjects were randomized and received at least 1 dose of study drug (344 in the ATV/co group and 348 in the ATV/r group). At week 48, virologic success was achieved in 85% (ATV/co) and 87% (ATV/r). Among subjects with baseline

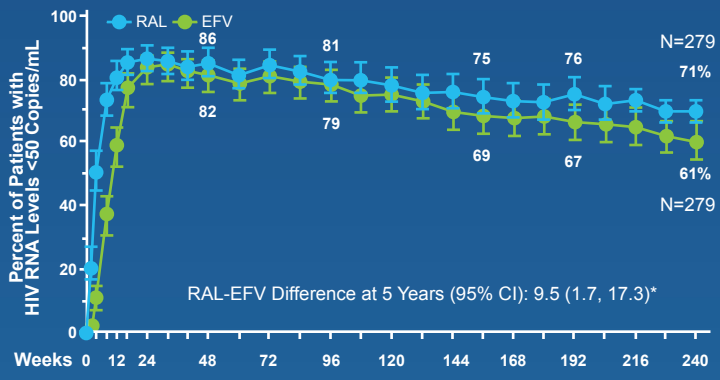
HIV RNA ≤100,000 copies/mL, the response rates were 84% for ATV/co and 88% for ATV/r; for those with a baseline HIV RNA >100,000 copies/mL, the response rates were the same for both groups (86% vs. 86%). Two subjects in the ATV/co and none in the ATV/r group developed resistance mutations to study drugs; both were M184V/I. Similar percentages of subjects in both groups (ATV/co vs. ATV/r) had serious AEs (11% vs. 7%), discontinued study drug due to any AEs (7% vs. 7%), or had bilirubin-related AEs (4% vs. 3%). Median increases in total bilirubin at week 48 in ATV/co and ATV/r group were 1.9 and 1.7 mg/dL. In summary, ATV/co was found to be noninferior to ATV/r in combination with FTC/TDF at week 48. Both regimens achieved high rates of virologic success. Safety and tolerability profiles of the two regimens were comparable.

STARTMRK: Raltegravir vs. Efavirenz at 5 Years

A presentation at the Conference discussed final results from STARTMRK, a 5-year, blinded, randomized trial that compared the long-term efficacy and safety of RAL- vs. efavirenz (EFV)-based therapy in treatment-naïve patients **[Abst. LBPE19].**[5] Participants in STARTMRK were previously untreated patients without baseline resistance to EFV, TDF, or FTC who received FTC/TDF plus either RAL (400 mg BID) or EFV (600 mg QHS). The primary efficacy outcome was the percentage of patients with HIV RNA levels <50 copies/mL, counting non-completers as failures. Changes from baseline CD4 count used an observed-failure approach to missing data.

The follow-up at 4 and 5 years indicated that RAL + FTC/TDF was superior to EFV/FTC/TDF in terms of better virologic and immunologic efficacy. The percentage of patients with HIV RNA levels <50 copies/mL was 71% in the RAL group and 61% in the EFV group (Figure 3). CD4 cell increments were significantly higher in RAL vs. EFV recipients, and generally consistent virologic and immunologic effects between treatment groups were maintained within the examined demographic subpopulations and prognostic subgroups at baseline. Over the course of the entire 5-year study, RAL-based therapy had a consistently favorable safety profile compared with EFV-based therapy, including fewer reported patients with drug-related adverse events or overall CNS side effects. The investigators concluded that RAL + FTC/TDF offers an efficacious and well-tolerated option for the initial therapy of treatment-naive HIV-patients regardless of baseline viral load and CD4 cell count.

Figure 3. STARTMRK Proportion (%) of Patients Achieving HIV RNA <50 copies/mL



*At 5 Years: *P*-value for non-inferiority <0.001; Met criteria superiority.

MERIT: Maraviroc vs. Efavirenz at 5 years

Results were presented for the Maraviroc versus Efavirenz Regimens as Initial Therapy (MERIT) study, a randomized, double-blind, multicenter study of treatment-naïve patients with R5 HIV and screening viral load >2,000 copies/mL **[Abst. TUPE026].**[6] Patients were assigned to treatment with maraviroc (MVC) 300 mg once QD, MVC 300 mg BID, or EFV 600 mg QD, each in combination with zidovudine (ZDV)/3TC 300 mg/150 mg BID for 96 weeks. Following an interim analysis at week 16, the MVC QD treatment arm was discontinued and the study continued with two arms. The study was unblinded after the last patient's week 96 visit, and patients could enter the nominal, 3-year, open-label phase.

Of the 917 patients randomized in the study, 311 and 303 patients who were treated with MVC BID and EFV QD, respectively, had confirmed R5 HIV and were included in the efficacy analysis. The proportion of patients achieving viral load <50 copies/mL peaked at approximately week 20 and decreased gradually to week 240 in both treatment groups. Viral load <50 and <400 copies/mL and CD4 count changes

were statistically similar between groups at weeks 48, 96 and 240. Overall AE incidence was 95% in the MVC BID group and 96% in EFV QD group. Serious AEs occurred in 21% of patients in the MVC BID group and 23% in the EFV QD group. Treatment related serious AEs were recorded for 3% of MVC-BID-treated patients and 4% of EFV QD-treated patients. In this report, MVC maintained similar long-term antiviral efficacy to EFV over 5 years in treatment-naïve patients with R5 HIV.

Treatment Experienced Patients

SPIRIT: Switch from a Boosted Protease Inhibitor to Rilpivirine

The Switching boosted PI to Rilpivirine In-combination with Truvada as a Single-Tablet Regimen (SPIRIT) study is a randomized, open-label, multicenter, international, 48-week study designed to evaluate the safety and efficacy of switching from ritonavir-boosted protease inhibitor (PI/r)-based HAART to a simplified regimen of the single table regimen (STR) FTC/rilpivirine (RPV)/TDF **[Abst. TUAB0104].**[7] In SPIRIT, 476 patients who were stable (HIV RNA <50 copies/mL) for ≥6 months on a PI/r + 2 NRTI regimen where randomized to either continued therapy with a PI/r + 2 NRTIs (n=159) or STR with FTC/RPV/TDF for 24 weeks (n=317).

The investigators reported that viral suppression at 24 weeks (the primary end point) from switching to FTC/RPV/TDF was non-inferior to remaining on a PI/r + 2 NRTIs regimen: 94% achieved viral suppression with FTC/RPV/TDF vs. 90% with a PI/r + 2 NRTIs. Changes in CD4 cell counts were +20 cells/mm^3 for FTC/RPV/TDF vs. +32 cells/mm^3 for PI/r + 2 NRTIs. Switching to FTC/RPV/TDF STR also resulted in a greater improvement in 10-year Framingham Risk Score at Week 24 compared to PI/r + 2 NRTIs. It was also found that at week 24, participants who switched to FTC/RPV/TDF reported higher satisfaction with their treatment regimen by HIV-TSQ than those who stayed on PI/r + 2 NRTIs.

SPIRAL Study Results

The SPIRAL study was a 48-week, multicenter, open-label, randomized trial in which HIV-infected adults with <50 copies/mL of HIV RNA for at least the previous 6 months on PI/r -based therapy were randomized (1:1) to switch from PI/r to RAL or to continue on PI/r-based therapy. Investigators analyzed the efficacy and safety of ABC/3TC vs. FTC/TDF combined with either RAL or PI/r **[Abst. TUPE093].**[8] There were 143 (73%) patients who took FTC/TDF and 54 (27%) who took ABC/3TC. In the RAL group, there were 3 (11%) treatment failures with ABC/3TC and 8 (11%) with FTC/TDF. In the PI/r group, there were 4 (14%) treatment failures with ABC/3TC and 12 (17%) with FTC/TDF. The investigators concluded that ABC/3TC may display similar efficacy and safety as FTC/TDF when combined with RAL in virologically suppressed HIV-infected adults treated with PI/r in whom the PI component is replaced by RAL.

Inflammatory Marker Changes with NRTI Switches

Investigators conducted a randomized comparison to better clarify the cardiovascular disease risk associated with ABC use **[Abst. THPE093].**[9] For this study, 27 HIV-infected patients taking fixed-dose ABC/3TC-based ART with HIV RNA <48 copies/mL were randomized to remain on their current regimen (n=13), or switched to FTC/TDF (n=14). Plasma biomarkers reflecting inflammation (high-sensitivity C-reactive protein [hsCRP], interleukin-6 [IL-6], and D-dimer) and endothelial dysfunction (soluble inter-cellular adhesion molecule [sICAM-1], serum thrombomodulin [sTM], von Willebrand Factor [VWF], and asymmetric dimethylarginine [ADMA]) were measured at baseline and at 1 and 6 months.

The research team reported 6-month improvements in the inflammatory markers for the TDF vs. ABC group were statistically significant for hsCRP and the inflammatory rank composite. There was no suggestion of a treatment effect on the panel of vascular biomarkers. Therefore, this randomized, proof-of-concept study suggested that switching from ABC/3TC- to FTC/TDF-based ART, in the context of viral suppression, may reduce inflammation.

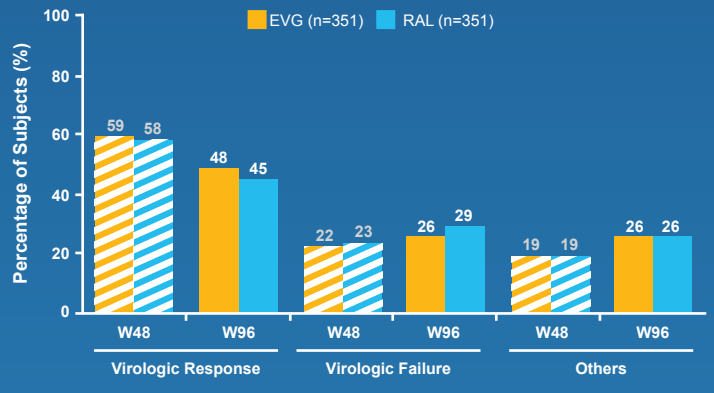
Study 145: Elvitegravir vs. Raltegravir

Once-daily elvitegravir (EVG) was found to be noninferior in efficacy compared with twice-daily RAL in combination with a PI/r and a second agent in a phase 3 study of

treatment-experienced patients (GS-US-183-0145) at week 48. The investigators presented 96-week results at the Conference **[Abst. TUAB0105].**[10] This study was a randomized, double-blinded, active-controlled, 96-week noninferiority trial. Key eligibility criteria were HIV RNA ≥1,000 copies/mL, any CD4 cell count, and resistance to and/or 6 months' experience with at least two classes of antiretroviral drugs. The primary endpoint was achievement and maintenance of HIV RNA <50 copies/mL through week 48.

It was reported that at week 96, 48% in the EVG and 45% in the RAL group were suppressed (Figure 4). Mean increases in CD4 cell count were similar in EVG and RAL groups (205 cells/mm^3 vs. 198 cells/mm^3). Similar percentages in EVG and RAL groups reported serious AEs, grade 3 or 4 AEs, or discontinued study drug due to AEs. Grade 3 or 4 AST and ALT elevations (>5x ULN) were less common on EVG vs. RAL (2.3 vs. 5.9%; 1.7 vs. 5.3%). The investigators concluded that at week 96, once-daily EVG in combination with a fully active PI/r and another second agent in treatment-experienced patients continued to be noninferior to twice-daily RAL in efficacy with excellent tolerability, and that these data support the long-term use of EVG in treatment-experienced patients.

Figure 4. Study 145: HIV RNA <50 copies/mL at Weeks 48 and 96



Adverse Events and Metabolics

A number of studies presented at IAC addressed the important question concerning effects of ARVs on lipid and other levels. Among these were the following:

- **CASTLE Lipodystrophy Substudy.** Investigators evaluated the incidence of the combination of elevated waist circumference (WC) and hypertriglyceridemia and changes in visceral adipose tissue (VAT) in treatment-naïve HIV infected subjects enrolled in CASTLE **[Abst. MOPE081].**[11] New onset of hypertriglyceridemic waist (HTW) phenotype for combined genders increased by 10% on ATV/r and 18% on LPV/r over 96 weeks. Significant differences in changes in VAT, subcutaneous adipose tissue (SAT) and limb fat were noted between ATV/r and LPV/r among subjects with the lowest baseline BMI (<22) and lowest baseline CD4 cell counts (<50 cells/mm^3). In patients taking LPV/r, a gain in fat, in particular VAT, was often associated with a notable increase in TG levels and may increase the risk of cardiovascular diseases.
- **SPRING-2 Renal Safety.** Investigators reported that the creatinine median change from baseline was 0.14 mg/dL for DTG compared with 0.06 mg/dL for RAL. For urine albumin/creatinine, the median change from baseline (mg/mmol CR) was 0.0 for both DTG and RAL **[Abst. THLBB04].**[12]
- **Study 114: Creatinine and eGFR.** At week 48, investigators reported median increases in serum creatinine for ATV/co were 0.13 mg/dL and for ATV/r were 0.09 mg/dL, while median increases in eGFR for ATV/co were -12.9 mL/min and for ATV/r were -9.1 mL/min **[Abst. TUAB0103].** Median increases in total cholesterol were 4 mg/dL for ATV/co and 10 mg/dL for ATV/r; increases in LDL were 5 mg/dL for ATV/co and 8 for ATV/r; increases in triglycerides were 16 mg/dL for ATV/co and 24 mg/dL for ATV/r.
- **SPIRIT: Changes from Baseline in eGFR.** At week 24, the creatinine clearance by Cockcroft-Gault was 108.9 mL/min for PI/r + 2 NRTIs vs. 105.4 mL/min for FTC/RPV/TDF. The investigators also reported that switching to FTC/RPV/TDF resulted in a greater improvement in 10-year Framingham Risk Score at week 24 compared to PI/r + 2 NRTIs **[Abst. TUAB0104].**

- **Study A4001078 Renal Function.** At week 96, median change from baseline in creatinine clearance was -5.5 mL/min for MVC + ATV/r vs. -18 mL/min for TDF/FTC + ATV/r **[Abst. TUAB0102].**
- **Change in Lipids by NRTI Backbone in SPIRAL.** It was also reported that at 48 weeks in SPIRAL, the proportion of patients showing triglycerides >200 mg/dL, total cholesterol >240 mg/dL, or LDL cholesterol >160 mg/dL was not different between ABC/3TC and FTC/TDF groups **[Abst. TUPE093].** However, the proportion of patients showing HDL cholesterol <40 mg/dL at 48 weeks was significantly lower with ABC/3TC relative to that with FTC/TDF.
- **ACTG5224s: Inflammatory Markers and AIDS or non-AIDS Events.** Substudy A5224s measured inflammatory biomarkers of subjects from baseline and at weeks 24 or 96 **[Abst. THLBB06].**[13] The investigators reported that higher baseline IL-6, soluble tumor necrosis factor receptor I (sTNF-RI), soluble tumor necrosis factor receptor II (sTNF-RII), and soluble intercellular adhesion molecule-1 (sICAM-1) were significantly associated with increased risk of AIDS-defining events. Adjustment for baseline HIV RNA did not change results, while adjusting for CD4 count left sTNF-RI and sICAM-1 significantly associated with increased AIDS-defining events risk. Time-updated values of these biomarkers were also associated with increased risk of AIDS-defining events, even after adjusting for ART assignment, baseline and changes in CD4 and HIV RNA. For non-AIDS events, only baseline hsCRP was significantly associated with increased risk; after adjustment for baseline CD4 count, IL-6 became significantly associated with higher risk. Analyses of time-updated biomarker values showed TNF-α to be significantly associated with increased risk of non-AIDS-defining events, even after adjustment for ART, baseline and changes in CD4 and HIV RNA.

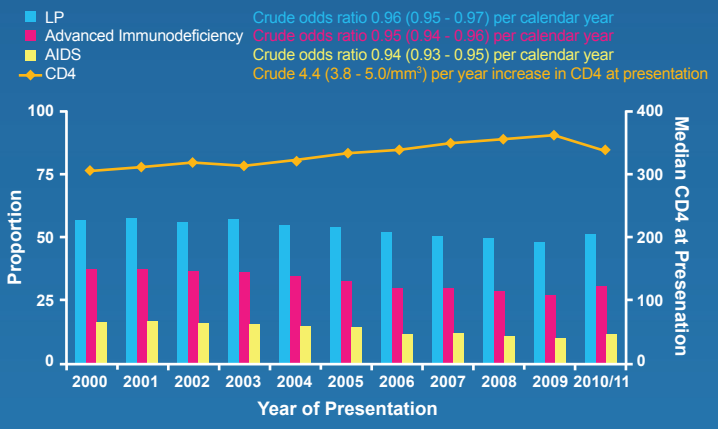
Management Issues

Late Presentation in the COHERE Cohort

A presentation at IAC discussed a study that investigated trends in the percentage of individuals presenting late for care and identified factors associated with late presentation. The Collaboration of Observational HIV Epidemiological Research Europe (COHERE) study included 33 cohorts from across Europe that consisted of patients who presented for care for the first time after January 1, 2000 **[Abst. THAB0303].**[14] Late presentation was defined as a person presenting for care with a CD4 count <350 cells/mm^3 or an AIDS defining event. Logistic regression was used to identify factors associated with late presentation.

Of the 90,786 individuals included in the analysis, there were 47,384 (52.2%) who were classified as late presenters, including 28,869 (60.9%) who presented with advanced disease (a CD4 count <200 cells/mm^3 or an AIDS defining event). The odds of presenting late decreased minimally over time (Figure 5). Individuals who were older, whose mode of transmission was not MSM (particularly heterosexual males), and those originating from Africa or other regions other than Europe were more likely to present late for care.

Figure 5. Late Presentation in the COHERE Cohort



Hepatic Decompensation: HIV/HCV-co-infected vs. HCV monoinfected Patients

Investigators compared the incidence of hepatic decompensation between ART-treated HIV/HCV-coinfected

A CME NEWSLETTER

ARV Therapies and Therapeutic Strategies

Reporting From

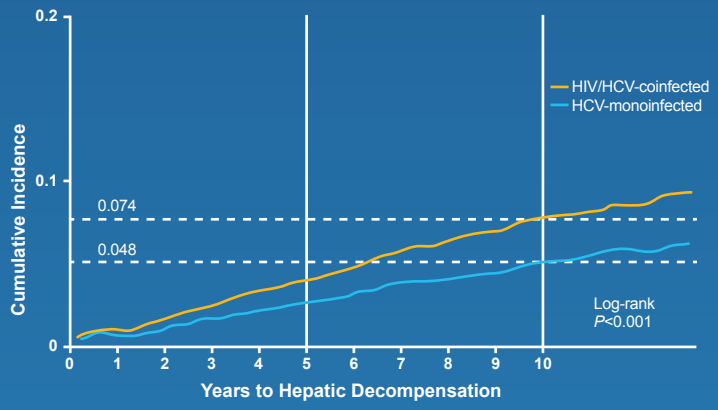
The XIX International AIDS Conference (AIDS 2012)

Jointly Sponsored by the Postgraduate Institute for Medicine and ViralEd, LLC.

and HCV-monoinfected patients and evaluated determinants of decompensation among coinfected patients on combination ART **[Abst. WEAB0102].**[15] This effort was a cohort study of 4,286 ART-treated HIV/HCV-coinfected and 6,639 HCV-monoinfected patients in the Veterans Aging Cohort Study Virtual Cohort (1997-2010). All patients in the study had HCV viremia and were HCV treatment-naïve. Coinfected patients received ART for at least one year and had an HIV RNA level >500 copies/mL within 180 days prior to starting ART. Hepatic decompensation events – defined by a diagnosis of ascites, spontaneous bacterial peritonitis, variceal hemorrhage, or hepatocellular carcinoma – and death were evaluated. Cox regression was used to determine the adjusted hazard ratio (aHR) of hepatic decompensation associated with ART-treated coinfection and evaluate baseline risk factors for decompensation in coinfected patients on ART.

The researchers reported that compared with HCV-monoinfected patients, ART-treated HIV/HCV-coinfected patients had a higher cumulative incidence and risk of hepatic decompensation and hepatocellular carcinoma (Figure 6). After decompensation, mortality was higher in coinfected patients. Non-black race, advanced liver fibrosis, and baseline hemoglobin <10 g/dL were associated with decompensation among co-infected patients.

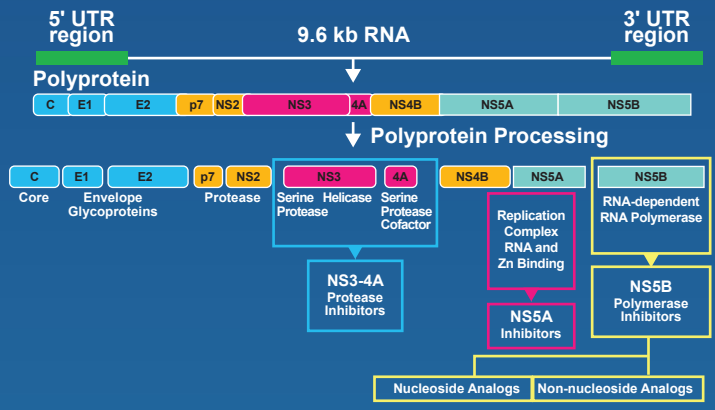
Figure 6. Hepatic Decompensation: HIV/HCV Co-infected vs. HCV Monoinfected Patients



HCV Drugs in Development: Final Comments by Dr. Rockstroh

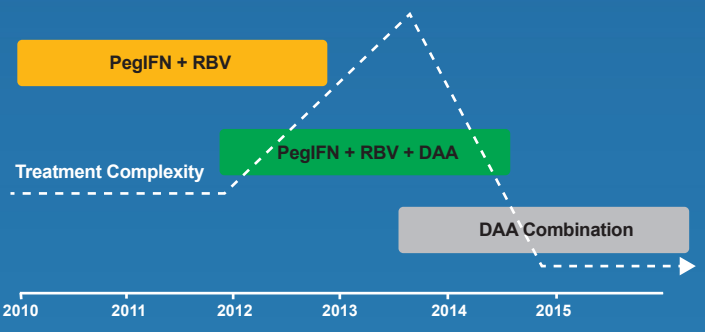
While HCV protease inhibitors (PIs) have recently been approved, several other drugs are currently in development that have other antiviral targets (Figure 7). Triple therapy with an HCV PI + pegylated interferon (PegIFN) + ribavirin (RBV) is complex; although it has increased cure rates to >70%, it can cause drug-drug interactions, more toxicity, and other management issues. Consequently, clinicians who treat the millions of patients with HCV infection are looking forward to future treatments that will include less toxic, interferon-free regimens. We can envision that by 2014, we will have better tolerated, easier to use, and potentially shorter treatment duration medications for HCV patients, which impacts when we decide who we want to treat now.

Figure 7. Direct-acting Antiviral Agent Targets



As noted in Dr. Gregory Dore's presentation **[Abst. THSS0202],**[16] we are moving through different phases of HCV treatment. With interferon-based therapy, which he envisioned to last until 2014, clinicians primarily treat liver diseases: we target more advanced fibrosis stages in patients who cannot wait for easier-to-use options. In the future (as shown on Figure 8), we expect to have better agents, which will result in simplified, interferon-free therapy.

Figure 8. Direct-Acting Antiretroviral Agents: Development Timeline



References

[1] Kahle E, et al. PrEP has high efficacy for HIV-1 prevention among higher-risk HIV-1 serodiscordant couples: a subgroup analysis from the Partners PrEP Study. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. TUAC0102.

[2] Grinsztein B, et al. Effect of early versus delayed initiation of antiretroviral therapy (ART) on clinical outcomes in the HPTN 052 randomized clinical trial. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. THLBB05.

[3] Raffi F, et al. Once-daily dolutegravir (DTG; S/GSK1349572) is non-inferior to raltegravir (RAL) in antiretroviral-naive adults: 48 week results from SPRING-2 (ING113086). XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. THLBB04.

[4] Galant J, et al. Cobicistat versus ritonavir as pharmacoenhancers in combination with atazanavir plus tenofovir disoproxil fumarate/emtricitabine: phase 3 randomized, double blind, active-controlled trial, week 48 results. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. TUAB0103.

[5] Rockstroh J, et al. Long-term safety and efficacy of raltegravir (RAL)-based versus efavirenz (EFV)-based combination therapy in treatment-naïve HIV-1 infected patients: final 5-year double-blind results from STARTMRK. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. LBPE19.

[6] Cooper DA, et al. 5-year efficacy and safety of maraviroc versus efavirenz, each in combination with zidovudine/lamivudine, in treatment-naïve HIV-1-infected patients: open-label extension of the randomized, double-blind MERIT study. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. TUPE026.

[7] Palella F, et al. SPIRIT study: switching to emtricitabine/rilpivirine/tenofovir df (FTC/RPV/TDF) single-tablet regimen (STR) from a ritonavir-boosted protease inhibitor and two nucleoside reverse transcriptase inhibitors (NRTIS) maintains HIV suppression and improves seru. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. TUAB0104.

[8] Martinez E, et al. Abacavir/lamivudine versus tenofovir/emtricitabine with either raltegravir or protease inhibitors in virologically suppressed patients: a sub-analysis of SPIRAL study. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. TUPE093.

[9] Alozie O, et al. Switching from abacavir/lamivudine to tenofovirDF/emtricitabine reduces biomarkers of inflammation. XIX International AIDS Conference, Washington, DC, July 22-27, 2012 Abst. THPE093.

[10] Elion R, et al. Efficacy and safety results from a randomized, double blind, active controlled trial of elvitegravir (once-daily) versus raltegravir (twice-daily) in treatment-experienced HIV-positive patients: long term 96-week data. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. TUAB0105.

[11] Moyle G, et al. The incidence of the hypertriglyceridemic waist phenotype in a randomized prospective comparison between atazanavir/ritonavir (ATV/r) and lopinavir/ritonavir (LPV/r) each in combination with tenofovir DF/emtricitabine (TDF/FTC) in antiretroviral naive HIV. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. MOPE081.

[12] Raffi F, et al. Once-daily dolutegravir (DTG; S/GSK1349572) is non-inferior to raltegravir (RAL) in antiretroviral-naive adults: 48 week results from SPRING-2 (ING113086). XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. THLBB04.

[13] McComsey GA, et al. Associations of inflammatory markers with AIDS and non-AIDS clinical events after initiation of antiretroviral therapy (ART): AIDS Clinical Trials Group A5224s, a substudy of ACTG A5202. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. THLBB06.

[14] Lundgren J, et al. Characteristics of individuals presenting late for care across Europe: results from the Collaboration of Observational HIV Epidemiological Research Europe (COHERE). XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. THAB0303.

[15] Lo Re V, et al. Increased risk of hepatic decompensation and hepatocellular carcinoma in HIV/HCV-co-infected patients compared to HCV-mono-infected patients despite combination antiretroviral therapy. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. WEAB0102.

[16] Dore G. Access to HCV treatment for people with HIV/HCV. XIX International AIDS Conference, Washington, DC, July 22-27, 2012. Abst. THSS0202.