CME NEWSLETTER

ARV Therapies and Therapeutic Strategies

Reporting From the

13th European AIDS Conference (EACS) and the 49th Annual Meeting of the Infectious Diseases Society of America (IDSA)

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

EACS 2011
October 12-15, 2011
Belgrade, Serbia
IDSA
October 20-23, 2011
Boston, Massachusetts

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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 13th European AIDS Conference (EACS), held on October 12-15, 2011 in Belgrade, Serbia, and the 49th Annual Meeting of the Infectious Disease Society of America (IDSA), held October 20-23, 2011 in Boston, Massachusetts.**

The faculty panel and contributors for the program consisted of director and moderator John Bartlett, MD from the Johns Hopkins University School of Medicine in Baltimore, Maryland, and panelists/contributors José Arribas, MD from Hospital de La Paz in Madrid, Spain, Calvin Cohen, MD from Harvard Medical School, Boston, Massachusetts, Edwin DeJesus, MD from the Orlando Immunology Center, Orlando, Florida, Jürgen Rockstroh, MD from the University of Bonn, Bonn, Germany and Paul Sax, MD from Harvard Medical School, Boston, Massachusetts.

Treatment-Naïve Patients

Dr. Sax addressed treatment of antiretroviral (ARV)-naïve patients, discussing guidelines released around the time of the two meetings. He first discussed the European AIDS Clinical Society (EACS) guidelines,[1] which has some subtle differences from other major guidelines, including those from the U.S. Department of Health and Human Services (DHHS).[2]

Regarding when to start ARV therapy, the EACS guidelines recommend ARV therapy for all patients with a CD4 count <350 cells/mm^3, but state that ARV therapy is to be considered in patients with a CD4 count of 350-500 cells/mm^3 and deferred in patients with CD4 cell counts >500 cells/mm^3 who have no symptoms. These are the most conservative guidelines regarding when to start and other guidelines recommend that ARV therapy be started in patients with CD4 counts of 350-500 cells/mm^3 and considered in patients with CD4 cell counts >500 cells/mm^3. Further, the EACS recommendation is interesting because there is indirect evidence suggesting that starting therapy at high CD4 cell counts is beneficial, although there is no proof of this from randomized trials, and there are no data showing that deferral of therapy is beneficial.

The EACS guidelines also include conditions that can influence the decision to treat that are not included in the DHHS guidelines. For example, the EACS guidelines recommend starting ARV therapy in patients with human papillomavirus (HPV)-associated cancers and other cancers. Dr. Sax noted that the data on the effectiveness of HIV therapy in controlling HPV are not very strong. Also, while there are significant data showing the importance of treating the infected partner in serodiscordant couples, the EACS guidelines do not recommend therapy, although they say it should be considered and actively discussed.

The EACS guidelines also differ from DHHS guidelines with regard to what is recommended as initial therapy. While raltegravir (RAL), atazanavir/ritonavir (ATV/r), darunavir/ritonavir (DRV/r) and efavirenz (EFV) are all recommended, just as they are in the DHHS guidelines, the EACS guidelines tend to be more inclusive, and they include ARVs not generally recommended or preferred by the DHHS guidelines, including nevirapine (NVP) and lopinavir/ritonavir (LPV/r). The EACS guidelines are more inclusive regarding the nucleos(t)ide reverse transcriptase inhibitor (NRTI) backbone as well. In addition to tenofovir/emtricitabine (TDF/FTC), the only combination recommended by the DHHS

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guidelines, the EACS guidelines recommend abacavir/lamivudine (ABC/3TC) as an initial regimen, although with caveats about patients with high viral load and cardiovascular disease. Some of these differences may reflect an attempt by the EACS committee to accommodate countries in which access to some drugs is difficult.

The updated EACS guidelines also contained a section on co-morbidities, emphasizing the importance of managing diabetes, screening for cancer, and monitoring cardiovascular complications and bone mineral density. The US guidelines also discuss how the selection of therapeutic regimen should be influenced by potential effects on co-morbidities.

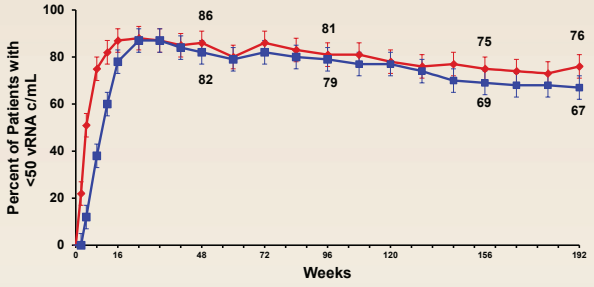
The DHHS guidelines were also updated immediately before the IDSA meeting. Probably the most important change is that rilpivirine (RPV) is now listed as an alternative non-nucleoside reverse transcriptase inhibitor (NNRTI) for initial therapy. In addition, ABC/3TC-containing regimens with DRV/r or RAL were made alternative choices as well. NVP-containing regimens were demoted into the acceptable category, but didanosine (ddI) + 3TC and unboosted fosamprenavir (FPV) were removed entirely from consideration as initial regimen strategies. Zidovudine (AZT)-containing regimens are now considered acceptable at best. Long-term AZT therapy is associated with toxicity, and there is currently no reason to use it. Dr. Sax said it is frustrating that it continues to be included in the DHHS and perinatal guidelines.

The first study discussed by Dr. Sax was the Lubumbashi trial conducted in the Republic of the Congo, which compared LPV/r vs. NVP as first line therapy.[3] There was also a comparison between AZT/3TC and TDF/FTC. It should be noted that the patient population included people with much more advanced disease than those found in most trials conducted in the developed world. For example, in more than half of patients, baseline CD4 cell counts were <200 cells/mm^3 and HIV RNA levels were >100,000 copies/mL. There were also high levels of hepatitis – especially hepatitis B.

The results in terms of percentage of patients with viral load (VL) <50 copies/mL in the LPV/r and NVP groups looked similar, but the groups were actually quite different. Specifically, the proportion of patients who had virologic failure was significantly higher in the patients who had NVP-based therapy (19/209) versus LPV/r (7/216; *P*=0.0144). NVP patients also exhibited more resistance. So, even though neither of these regimens is preferred or recommended as first line therapy in developed countries, the results confirm some themes we have seen before on initial protease inhibitor (PI) versus NNRTI treatment.

Dr. Sax then discussed results of the STARTMRK study, which is more relevant to current practice in developed countries. STARTMRK is a randomized, blinded comparison between RAL and EFV as initial therapy in patients also receiving TDF/FTC.[4,5] After 192 weeks of follow-up, the proportion of patients with VL <50 copies/mL favored RAL (Figure 1). Although the primary endpoint of the trial was 48 weeks, the result at 192 weeks is important because there has never been a comparator that has been shown to be significantly better than EFV.

Figure 1. STARTMRK: Proportion of Patients with <50 RNA copies/mL Over Time (Primary NC=F Approach)



Number of Contributing Patients

Raltegravir group	281	281	280	281	281	277	281	281
Efavirenz group	282	281	281	282	282	281	282	282

Discussion: It is unclear why this difference surfaced at 192 weeks, however, the two most likely reasons are: (1) That the incidence of toxicity was much higher in the EFV arm compared to the RAL arm; however, many of these patients did not discontinue the study. This suggests that EFV patients continuing in the study are having side effects, raising the question of whether there is a problem with adherence in these patients. (2) The study was not designed for statistical analysis of superiority at 4 years. Even though it is still randomized and blinded, the extended duration needs to be calculated into the equation when performing statistical analysis, because the investigators need to calculate the number of patients who are going to discontinue per year.

Looking at different definitions of treatment failure – either non-completer equals failure, treatment discontinuation equals failure, or just observed failure on treatment (virological failures) – the RAL group was consistently superior to the EFV group at week 192. These results raise the level of evidence in favor of RAL somewhat more, keeping in mind that week 192 was not the primary endpoint.

Discussion: Dr. Cohen said that these findings support the view that EFV, while virologically unsurpassed, may present problems with cumulative long-term toxicity. These findings suggest that some patients are experiencing something that led them to

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interrupt therapy in a consistent way. We are not thinking that EFV is somehow virologically inadequate, but if patients miss doses because they do not feel right, the result is viremia.

The metabolic profile of RAL/TDF/FTC was also favorable, as reflected by significantly smaller increases in total- and LDL-cholesterol levels as well as triglycerides and glucose levels. The total-cholesterol:HDL-cholesterol ratio declined in the RAL group (-0.17 change from baseline) and increased in the EFV group (+0.02 change from baseline), but the difference was not statistically significant (*P*=0.177).

Dr. Sax then discussed a post-hoc analysis of two trials of RPV vs. EFV as initial therapy, the ECHO and THRIVE studies.[6] This analysis examined the predictors of response in these studies, which Dr. Cohen noted showed that RPV was as effective as EFV in patients with low viral loads (and even superior at 48 weeks), but that RPV underperformed in patients with high viral loads. This new multivariate analysis looked at all factors that could have predicted virologic failure or success, with all toxicities and administrative drop-outs eliminated. The predictors of response for the two drugs were similar, but not identical. The most important factor for response to RPV was adherence, but adherence was the second-leading factor for EFV, supporting previous observations that there may be more forgiveness for missed doses of EFV. The second strongest predictor of RPV response was RPV exposure, which differs from adherence in that it takes into account the fact that food aids the absorption of RPV.

Discussion: Dr. Bartlett asked the panel to discuss the difference between a snack and a meal on the absorption of RPV. Dr. Cohen noted that there have been four conditions tested, and any solid food of >400 kcal supported the same absorption. However, when the food was liquid nutrition in the form of a caloric drink, absorption was not better than fasting. We know that a standard meal would be enough if it is solid food, rather than a protein shake, for example.

The next study discussed was PROGRESS, which compared the NRTI-sparing strategy of LPV/r + RAL versus the standard LPV/r + TDF/FTC.[7] Patients enrolled into this study at a relatively early stage of disease, so they had relatively high CD4 cell counts and relatively low HIV RNA levels. The results at 96 weeks were similar across the 2 arms, although the patients in the LPV/r + RAL arm had faster virologic suppression. The bone mineral density did not drop in the LPV/r + RAL arm as it did in the comparator arm and in most other studies. Another interesting observation in this relatively small study (~100 patients per arm) was that one patient had resistance to PIs despite receiving boosted PI therapy. Dr. Cohen noted this finding shows that resistance is not impossible in patients receiving boosted PI regimens, despite these regimens having a high genetic barrier to resistance mutations.

The final study discussed by Dr. Sax was a large Italian cohort analysis that can help physicians clarify what to tell their patients regarding expected time to virologic suppression.[8] Patients in this study were predominantly started on boosted PI/NNRTI regimens that did not include RAL, which is the fastest to virologic suppression. The results showed that the time to virologic suppression depended on the initial viral load and provided hard numbers that can assist in counseling patients about how long it is expected to take before their viral load drops below 50 copies/mL. Dr. Cohen noted that these findings remind us that a cut-off of 24 weeks to assess treatment success or failure is premature for some patients with high viral loads at baseline.

Antiretroviral-Experienced Patients

Dr. Cohen discussed recent studies in ARV-experienced patients, starting with the SWIFT trial, in which patients were virologically suppressed on 3TC/ABC and a boosted PI for at least 3 months.[9] They were then randomized to stay on 3TC/ABC or substitute TDF/FTC. The PI used by most patients was either LPV or ATV/r, with a smaller number on boosted fosamprenavir (FPV/r). The virologic results were similar across the two groups, although there were more virologic failures in the 3TC/ABC group (11 vs. 3; *P*=0.034).

The more interesting part of this update focused on the implications of lipid changes. Ten-year risk of coronary heart disease was assessed by Framingham risk score at baseline and 48 weeks. The results showed that the percentage of patients in the lowest risk category (<10% risk) was stable in the 3TC/ABC group but increased from 63.0% to 71.0% in the TDF/FTC group. Analysis of movement among the risk categories showed that those who were at higher risk at baseline had favorable movement in both arms but that there was more in the TDF/FTC arm. Those with moderate risk at baseline also had more favorable movement in the TDF/FTC arm compared with the 3TC/ABC arm. Those in the lowest risk category at baseline mostly stayed in that category.

Dr. Sax said that because both TDF/FTC and 3TC/ABC are more modern NRTI-based regimens and have less mitochondrial toxicity, they may be considered the same in terms of lipid issues, but it is now more clear that, in general, lipid profiles favor TDF/FTC. This is the case in prospective randomized trials of initial therapy and in trials of switch therapy and meta-analyses. The analysis done for the SWIFT study is especially useful

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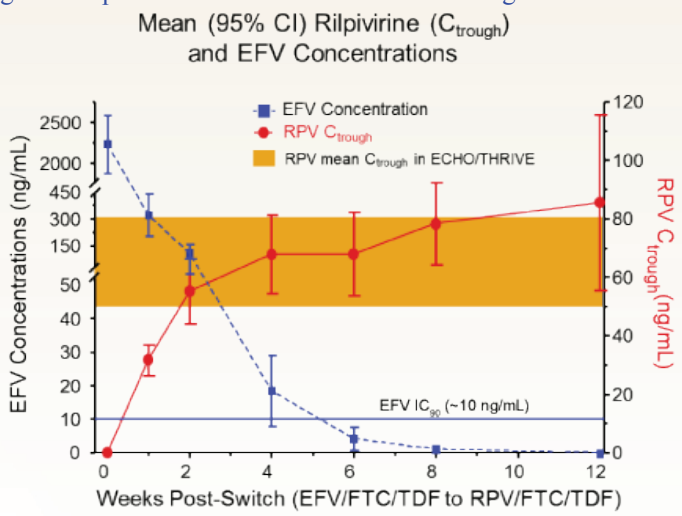
because it puts the lipid changes into the clinical context of 10-year risk of coronary heart disease, allowing physicians to see the benefit of using a treatment that has a favorable impact on lipids. It should be noted, however, that other safety measurements may favor ABC/3TC, especially renal safety.

Next, Dr. Cohen discussed a study with patients who experienced some toxicity on EFV and wanted to switch but preferred to continue taking a single tablet.[10] Patients who were stable on EFV/FTC/TDF for at least 3 months entered a single arm, open-label study in which they switched from the EFV-based triple therapy to an RPV-based triple therapy (FTC/RPV/TDF) – both of which involved a single tablet. There was concern about whether switching from EFV to RPV would be effective because EFV induces an enzyme that metabolizes RPV, possibly causing underexposure to RPV. The primary endpoint was at week 12 because the EFV induction effect would be over by then and any problem with RPV would be evident.

The patients were predominantly male with good CD4 cell counts. The results revealed no problems with the switch to RPV, and 100% of the 49 participants maintained virologic suppression through week 12. The lower confidence limit was 93%, suggesting a rather robust finding, even though there were only 49 patients.

Pharmacokinetic data from this study showed that EFV exposure remained above its IC_{90} for about 4 weeks after discontinuation. The C_{trough} for RPV achieved the therapeutic levels established in the ECHO and THRIVE studies within 2 weeks, even though EFV was still present (Figure 2). Fortunately, the continued presence of EFV was sufficient to maintain virologic suppression during those 2 weeks, probably explaining why there were no virologic failures.

Figure 2. Rilpivirine Pharmacokinetics after Switching from Efavirenz



Dr. Sax said that other explanations are possible, however. For example, after cessation of therapy in someone who has achieved long-term virologic suppression, it takes some time before clinically significant virologic rebound is observed. In addition, patients were still receiving TDF and FTC, which have very long intracellular half-lives, and continue to exert an antiviral effect. Dr. DeJesus noted that the results of this study should also be interpreted cautiously because the patients were highly selected among a cohort of patients who normally have very good adherence. They had to go from taking one pill without food at nighttime to taking a different pill with food. Patients in the community, if not selected as carefully, may not achieve the same level of success because of problems with adhering to such a change in treatment regimen.

Dr. Cohen then presented the results from a pilot study of switch therapy in 20 patients who were virologically suppressed on a NVP-containing regimen.[11] Ten of them were also on a boosted PI, 9 were on two NRTIs, and one patient was on one NRTI with NVP. They had VLs <40 copies/mL for a median of 55 months while on these NVP-containing regimens. The tested regimen was to stay on NVP twice a day, stop the other drugs and start RAL twice a day. So, patients were only taking NVP and RAL without an NRTI or a third drug, which is a regimen that most clinicians would be nervous about. All patients were RAL-naïve. Nadir CD4 cell counts were on the lower end, at a median of 190 cells/mm^3, suggesting that these patients, historically, were not the easiest to treat. During the study, each of the 20 patients maintained virologic suppression.

This was a small, controversial pilot study, possibly suggesting a treatment option for some patients. For example, if a patient has an elevated creatinine, cannot tolerate ABC, or has failed on a ritonavir-based regimen, then there are very few options. One option would be to add 3TC or FTC, but the results of this study suggest that this regimen may be another choice for patients who have no other options. It should be noted, however, that a similar study using RAL and etravirine (ETR) did not work as well. Inclusion of 3TC or FTC is a good idea in most cases. Even though there are no large clinical trials of these NRTI-sparing regimens, they may have usefulness in very specific patients, so expert panel recommendations based on these limited data would be helpful.

Dr. Cohen then presented updated results of the VIKING trial, which enrolled patients with RAL resistance.[12] It was reported previously that dolutegravir (DTG), once daily, was active in some patients with RAL-resistant virus. Higher DTG dose leads to higher exposure, and theoretically better coverage of these

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resistant mutants. A second cohort was done of viremic patients with 3-class ARV resistance including integrase resistance. Patients were either currently on RAL and viremic, or historically on RAL and viremic. Most had been on RAL for about 2 years and had >100-fold resistance to RAL. Most also had CD4 cell counts <200 cells/mm^3 and phenotyic sensitivity scores (PSS) of zero. The treatment regimen involved a lead-in of 11 days of DTG plus the current background regimen and stopping RAL if patients were on it. On day 12, they started a new regimen in one of two cohorts. Cohort 1 received DTG 50 mg once daily, and cohort 2 received DTG 50 mg twice daily. Cohort 2 also had to have a second fully active drug to give DTG a chance to work.

As expected, DTG alone led to very little viral suppression. But patients who had one or two other active drugs did well, with the majority having a viral load of <50 copies/mL at week 24. The most important predictor of response was the phenotype of the background regimen that was added at day 11. Furthermore, high CD4 cell counts remained predictive. This study was reassuring because it showed that DTG can be effective for the small but important subset of patients who develop resistance to RAL if it is used in the right active combination. DTG was also well-tolerated, even at higher doses. It is now being studied in phase III trials and appears very promising for resistant patients.

The last study presented by Dr. Cohen was an analysis of an observational database looking at the impact of patients receiving simple regimens, such as regimens with a single tablet, in the clinical setting outside of clinical trials.[13] The study used an anonymous, multi-state Medicaid database and incorporated adherence data based on pharmacy refill records. It asked a simple question: after the co-formulated EFV/TDF/FTC tablet became available, what difference did it make in terms of outcomes at 5 years, versus a multi-tablet regimen?

The data included 7,783 people – half were female, half were male – reflecting Medicaid enrollment. About 10% were older than 55 years. The co-morbidity index showed that it was a fairly healthy cohort. Although it was not a randomized trial, the two groups were well-matched for predictors of hospitalization. Most of the multi-tablet regimens were PI-based.

The analysis showed that there was significantly better refill adherence to a single tablet regimen (STR). It also showed that the multi-tablet regimen (MTR) was associated with more hospitalizations, higher inpatient and outpatient medical costs, and higher pharmacy costs. These results indicate that there are some patients who are more likely to adhere to a STR than a MTR, and that lack of adherence can be associated with hospitalization, probably due to viremia.

Discussion: Dr. DeJesus asked if pregnant women or women of child-bearing age were excluded from the analysis, because they would not be on an EFV regimen. Dr. Cohen responded that they are currently performing that analysis and suggested that the predictive value of adherence is likely to hold in that analysis. Dr. Sax noted that similar findings have been observed in difficult-to-treat patients, such as homeless people. He also noted a caveat that there is often selection bias as providers choose to use EFV-sparing regimens in difficult-to-treat populations because they want to avoid EFV resistance. Dr. Cohen noted that even after controlling for that issue, they still saw better outcomes in patients receiving the STR.

Hepatitis Co-Infection and other Co-Morbidities

Dr. DeJesus discussed presentations from the EACS and IDSA meetings that addressed treatment of HIV patients who have hepatitis C virus (HCV) co-infection or other co-morbidities. The first presentation was an update on the EACS guidelines for the management of HCV co-infected patients.[1] The new guidelines provide guidance for managing patients who are chronically infected with HIV but get acutely infected with HCV. They recommend measuring viral load at 4 weeks. If the HCV viral load has declined by >2 $\log_{10}$ copies/mL, clinicians should continue to follow the patient without treatment. If the patient then has undetectable HCV RNA levels after 12 weeks, continue serial HCV RNA measurements through 48 weeks to confirm resolution of the acute HCV infection. In this case, the patient does not receive treatment for HCV infection. However, if the patient does not become undetectable at week 12, or has <2 $\log_{10}$ reduction in HCV RNA levels at week 4, then treatment is recommended.

What is new in these guidelines is that after 4 weeks of therapy with pegylated interferon (PegIFN) and ribavirin (RBV), they recommend measuring HCV viral load again. If the patient has achieved a rapid virologic response (RVR – undetectable viral load at 4 weeks), then treatment can be safely limited to 24 weeks. If they do not achieve an RVR, then a treatment duration of 48 weeks should be considered. There are few data to support that approach, but Dr. DeJesus agrees with the recommendation. He said that the guidelines still recommend both PegIFN and RBV for acute HCV in co-infected patients.

Dr. DeJesus noted that acute HCV co-infection is a hidden epidemic in the HIV-infected population, in part because patients who have achieved successful suppression of HIV viral load may have the mistaken impression that they can have unprotected sex with other virally suppressed HIV-positive individuals. This view overlooks the risk of other sexually transmitted viruses, such as HCV.

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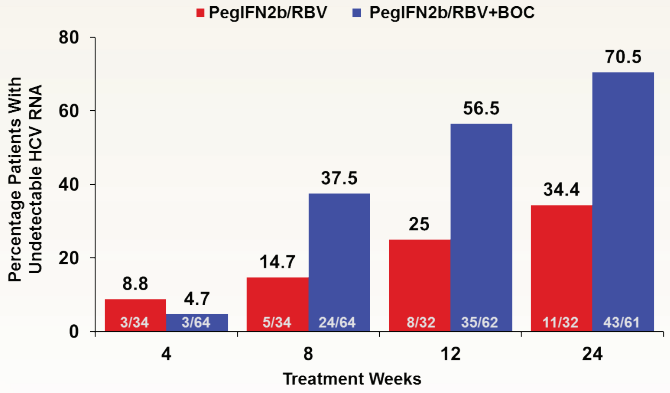
Dr. DeJesus then presented data from the IDSA meeting on a small, early-phase trial addressing the use of boceprevir (BOC) + PegIFN/RBV in HIV patients with chronic HCV co-infection.[14] HIV-positive patients (N=98) with HIV VL <50 copies/mL were treated with PegIFN alfa-2b plus weight-based RBV during a 4-week lead-in period. Those who achieved at least 1 $\log_{10}$ reduction in HCV RNA at the end of the lead-in period were randomized (2:1) to receive additional BOC (800 mg three times daily) or placebo, with all patients continuing to receive PegIFN/RBV. Patients who did not achieve a decline of at least 2 $\log_{10}$ in HCV RNA at week 12, or still had detectable HCV RNA at week 24 were discontinued.

Patients using a diverse range of ARV agents were enrolled, even though drug-drug interaction studies between BOC and many of those drugs had not been finalized when the study began. Allowed drugs included boosted PIs ATV/r, LPV/r and DRV/r, the NRTIs ABC, 3TC, FTC and TDF, integrase inhibitors, and CCR5 antagonists. Disallowed drugs included EFV, which is known to potently decrease BOC levels. During the treatment phase, 3 of 34 (9%) patients in the placebo arm discontinued due to adverse events (AEs) compared to 9 of 64 (14%) in the BOC arm. However, 11 of 34 (32%) in the placebo arm discontinued due to treatment failure, compared to only 3 of 63 (5%) in the BOC arm.

The percentage of patients who had undetectable HCV RNA increased in both arms through weeks 8, 12 and 24, but the rates were substantially higher in the BOC arm (70.5% vs. 34.4% at week 24) (Figure 3). These results suggest that the HIV PIs did not have much of an effect on BOC activity. With regard to HIV, 4 patients (2 in each arm) had viral breakthrough, which is interesting, because interferon has ARV activity.

Figure 3. Virologic Response Over Time (Percentage of HCV RNA Undetectable)



Clinicians are advised to assess patients carefully before considering this type of therapy. If the patient does not have many risk factors for progression or has an IL28B variant associated with poor response, then it may not be necessary to rush into treatment. Some patients may not respond to BOC and at this time, we do not know how resistance mutations to BOC will influence future treatment options. Dr. DeJesus said that he uses liver biopsies and IL28B analyses to assess HIV/HCV co-infected patients. Based on the results, if the patient cannot wait for the new drugs to be approved, he treats them with the best option currently available.

The next study discussed was an evaluation of response to PegIFN/RBV therapy for HCV in patients receiving methadone maintenance therapy (MMT), compared with patients not receiving MMT.[15] Patients in the two groups had similar baseline characteristics, including similar percentages with IL28B CC genotype, cirrhosis and similar average body-mass index. Rates of sustained virologic response (SVR) were similar in the two groups across all HCV genotypes. These results indicate that clinicians should not alter treatment for patients who are on a methadone maintenance program or consider that they are not going to respond as well as others.

Next, Dr. DeJesus discussed updates to the EACS algorithm for treatment of patients with hepatitis B virus (HBV) co-infection.[1] The revised algorithm simplified treatment decisions based on available data about the patient. For example, in HIV-positive patients who are HBV surface antigen-positive and have cirrhosis, treatment is recommended. Treatment is also recommended for patients without cirrhosis but who have elevated HBV DNA levels (>2000 IU) or elevated ALT levels, so a biopsy may not be necessary in many patients.

Dr. DeJesus discussed data from EuroSIDA on the prevalence of anti-hepatitis D antibodies.[16] Among the 16,597 patients in EuroSIDA, 1,319 were infected with hepatitis B. The EuroSIDA investigators analyzed available blood samples from 422 of those 1,319 patients. They found that almost 15% of those patients were co-infected with hepatitis D virus (HDV), a defective virus that needs hepatitis B surface antigen to replicate. Of those patients with available samples, 31 of 38 (82%) had HDV viremia. That finding is significant because active hepatitis D in a co-infected individual can potentially accelerate the progression of hepatitis B, even when the levels of HBV DNA tend to be lower. The acceleration is highly dependent on the HBV genotype. These results suggest that clinicians should check for HDV in HBV surface antigen-positive patients, especially those who obtained the infection by blood-borne transmission, such as injecting drug users.

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Next discussed were data from the Organ Procurement and Transplant Network (OPTN) on trends in liver transplant among hepatitis B and C patients.[17] Between January 2000 and December 2010, there were 65,891 transplants; 61,752 were unique, and 4,139 were patients who were re-transplanted. Interestingly, from 2000 to 2006 there was an increase of 39% in liver transplants, but from 2006 to 2010 there was a decline of 2%. When we look retrospectively, this change occurred when clinicians began treating HCV with PegIFN/RBV. These findings suggest that treatment had a positive impact on patient outcomes as well as the health care system.

Dr. DeJesus described an update to the EACS guidelines related to cancer screening.[1] The guidelines recommend screening for anal cancer, breast cancer, cervical cancer, colorectal cancer, hepatocellular carcinoma and prostate cancer. They describe the patients who need it and the procedure that should be used, as well as the evidence supporting the recommendation. They vary somewhat from the American Cancer Society recommendations, but are similar in most respects. Cancer screening guidelines are controversial in the United States, and will likely be controversial in Europe as well, because we do not know if we are benefitting some people with these procedures.

Another presentation at IDSA evaluated compliance with the American Cancer Society screening guidelines, comparing HIV patients managed by infectious disease providers versus HIV-negative patients managed by internists.[18] This study retrospectively compared 78 HIV patients who had good treatment compliance and follow-up with HIV-negative, matched controls. Even though 56% of the 78 HIV-positive patients also had a primary care doctor, the rate of colonoscopy screening in HIV-infected patients was much lower than the rate of colonoscopy screening for HIV-negative patients. It is disturbing that HIV patients who are being followed closely are not being screened for colorectal cancer. These findings suggest that there is still work to be done to improve screening rates, especially in HIV-positive individuals.

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