

## Perspective

# Advances in the Treatment of Hepatitis C Virus Infection

*Since 2007, the annual age-adjusted mortality rate in hepatitis C virus (HCV) infection in the United States has been greater than that in HIV disease, reflecting the continuing decline in HIV-related mortality and the continuing increase in HCV-related mortality. The approval of 2 new direct-acting antivirals within the past year, as well as the promise offered by numerous other direct-acting agents in development, provides hope that we will be able to markedly improve our ability to cure HCV disease. The addition of a protease inhibitor (PI) to what has been the standard HCV therapy of peginterferon alfa and ribavirin dramatically improves sustained virologic response rates in treatment-naive patients with genotype 1 infection. Similar results have been observed in some treatment-experienced patients in whom prior peginterferon alfa/ribavirin therapy has failed. The use of these new agents has also permitted response-guided therapy, wherein early sustained virologic response to treatment allows for a shortened treatment duration. However, these new PIs add cost and adverse effects to HCV therapy. Boceprevir is associated with increased risk of anemia and dysgeusia, and telaprevir is associated with increased risk of anemia and skin and gastrointestinal adverse effects. Early studies indicate that the addition of PIs results in high response rates in patients with HCV/HIV coinfection. Other studies suggest that combinations of PIs and other direct-acting antivirals may ultimately permit cure when used in interferon-sparing regimens. This article summarizes a presentation by David L. Thomas, MD, MPH, at the IAS–USA live continuing medical education course held in New York City in October 2011.*

Since 2007, the annual age-adjusted mortality rate in HIV disease in the United States has been surpassed by that of hepatitis C virus (HCV) disease, reflecting the continuing decline in HIV-related mortality and the continuing increase in HCV-related mortality.<sup>1</sup> The prevalence of HCV-related cirrhosis is projected to continue to increase until it reaches a peak around 2020, reflecting what is commonly a 20- to 40-year period between HCV acquisition and the later-stage manifestations of cirrhosis, end-stage liver disease, and liver cancer. These projections assumed no changes in our ability to treat HCV infection.

The rate of sustained virologic response (SVR; ie, absence of HCV RNA in blood for 6 months after the end of treatment) with what has been the standard treatment of peginterferon alfa plus ribavirin is approximately 40% in patients with HCV genotype 1

infection, the predominant type of infection in the United States. The rate is less than 30% in HIV/HCV-coinfected patients with HCV genotype 1. However, the past year has brought the approval of 2 new drugs for treating HCV infection—the HCV protease inhibitors boceprevir and telaprevir—and numerous new drugs are in advanced stages of development. It is hoped that these new weapons will allow us to improve the projections for HCV disease outcomes.

## Treatment Outcomes With Telaprevir and Boceprevir

### Treatment-Naive Patients

In the trial supporting approval of telaprevir, more than 1000 treatment-naive patients with HCV genotype 1 infection were randomly assigned to receive telaprevir for 8 weeks or 12 weeks plus concurrent standard peginterferon alfa/ribavirin therapy for up to 48 weeks, or peginterferon alfa/ribavirin alone for 48 weeks.<sup>2</sup> Patients receiv-

ing telaprevir who achieved a virologic response that was sustained between weeks 8 and 12 were further randomly assigned to stop peginterferon alfa/ribavirin after week 24 or continue for the full 48 weeks. Overall, cure (ie, SVR) was achieved in 69% of patients receiving 8 weeks of telaprevir and 75% of those receiving 12 weeks of telaprevir, compared with 44% of those receiving peginterferon alfa/ribavirin alone. In black patients, who are known to have lower rates of response to peginterferon alfa/ribavirin, SVR rates were 25% with standard therapy, versus 58% and 62% with 8 weeks and 12 weeks of telaprevir, respectively. Among nonblack patients, SVR rates were 48% with peginterferon alfa/ribavirin, compared with 73% and 79% with the addition of telaprevir for 8 weeks and 12 weeks, respectively.

Patients who stopped therapy at 24 weeks after an early response to telaprevir-containing therapy had outcomes similar to those who continued to receive peginterferon alfa/ribavirin for the full 48-week course. The 12-week course of telaprevir was approved in 2011 by the US Food and Drug Administration (FDA) for use in combination with peginterferon alfa/ribavirin, as was the shortened treatment duration in patients with early sustained response to treatment.

With regard to the ability to abbreviate therapy based on early response to treatment, Sherman and colleagues performed a study in treatment-naive, genotype 1–infected patients.<sup>3</sup> Patients who achieved early rapid virologic response (eRVR; defined as undetectable HCV RNA at week 4 and week 12) with telaprevir plus peginterferon alfa/ribavirin therapy were randomly assigned to continue receiving peginterferon alfa/ribavirin for the full 48 weeks or to stop treatment after a total of 24 weeks. The overall SVR rate was 72%, with 65% of the total of 540 patients achieving eRVR. SVR rates were 92% among those stopping treatment after 24 weeks and 88% among those receiving 48 weeks

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of treatment. Among those who did not achieve eRVR, the SVR rate was 64%.

In the pivotal boceprevir trial, approximately 1100 treatment-naive patients with genotype 1 infection received a lead-in of peginterferon alfa/ribavirin for 4 weeks.<sup>4</sup> This was followed by either continuation of peginterferon alfa/ribavirin treatment for 44 weeks (total of 48 weeks); addition of boceprevir for 44 weeks (fixed-duration group); or addition of boceprevir for 24 weeks followed by treatment discontinuation if virus was undetectable from 8 weeks to 24 weeks or treatment continuation with peginterferon alfa/ribavirin alone for 20 weeks if virus was detectable (response-guided therapy group). Overall, SVR rates were 63% in the response-guided therapy boceprevir group and 66% in the fixed-duration boceprevir group, compared with 38% in the peginterferon alfa/ribavirin treatment group. SVR rates were improved with the addition of boceprevir in black patients (42% in the response-guided therapy group and 53% in the fixed-duration group vs 23% in the standard treatment group) and nonblack patients (67% and 69% vs 41%, respectively). Boceprevir was approved by the FDA in 2011 for use in combination with peginterferon alfa/ribavirin, including a shortened response-guided course of therapy in treatment-naive patients.

### Treatment-Experienced Patients

Telaprevir and boceprevir have each been shown to achieve cure in a substantial proportion of HCV-infected patients in whom prior peginterferon alfa/ribavirin therapy had failed. In a study of more than 600 treatment-experienced patients, Zeuzem and colleagues found SVR rates of 64% with the combination of 12 weeks of telaprevir plus 48 weeks of peginterferon alfa/ribavirin; 66% with a 4-week lead-in regimen of peginterferon alfa/ribavirin followed by 12 weeks of telaprevir and 44 weeks of peginterferon alfa/ribavirin; and 17% with retreatment with 48 weeks of peginterferon alfa/ribavirin.<sup>5</sup> Among patients with relapse (ie, those who relapsed after

having undetectable virus at the end of prior treatment) SVR rates were 83%, 88%, and 24%, respectively. Among those who had shown a partial virologic response to prior treatment, SVR rates were 59%, 54%, and 15%, respectively. For those with no virologic response to prior treatment (null responders), SVR rates were 29%, 33%, and 5%, respectively.

In a trial in approximately 400 treatment-experienced patients conducted by Bacon and colleagues, overall SVR rates were 66% in patients receiving boceprevir and 48 weeks of peginterferon alfa/ribavirin, 59% in those receiving boceprevir with response-guided therapy, and 21% in those receiving standard peginterferon alfa/ribavirin.<sup>6</sup> SVR rates were 75%, 69%, and 29%, respectively, among patients who had relapsed after prior therapy and 52%, 40%, and 7%, respectively, among those who had partial response to prior treatment.

### Increased Toxic Effects With Addition of Telaprevir or Boceprevir

Jacobson and colleagues reported that adverse events occurred more frequently in telaprevir-containing study arms

than in the peginterferon alfa/ribavirin alone arm. Adverse effects included pruritus (45%-50% with telaprevir vs 36% with peginterferon alfa/ribavirin), nausea (40%-43% vs 31%), rash (35%-37% vs 24%), anemia (37%-39% vs 19%), and diarrhea (28%-32% vs 22%). In the boceprevir trial conducted by Poordad and colleagues, anemia (49% in the boceprevir group vs 29% in standard treatment group) and dysgeusia (37%-43% vs 18%, respectively) were more common in boceprevir-containing study arms.

### Resistance to HCV Protease Inhibitors

Because neither interferon alfa nor ribavirin is a direct-acting antiviral agent, viral resistance is a new phenomenon in HCV treatment. Resistance to the protease inhibitors (PIs) telaprevir and boceprevir is detected in approximately 50% of patients in whom therapy containing these agents fails.<sup>7,8</sup> To date, there is no evidence that resistant variants have greater replicative fitness or pathogenicity than wild-type virus. As has been observed with HIV, there is a return to predominance of wild-type virus generally within 18 months of stopping HCV PI treatment.<sup>9</sup> However, unlike HIV,

**Table 1.** Sustained Virologic Response Rates According to Patient and Disease Characteristics in Treatment-Naive Patients Receiving Telaprevir or Boceprevir plus Peginterferon Alfa/Ribavirin Compared with Peginterferon Alfa/Ribavirin Alone

	Sustained Virologic Response Rate (%)			
	TPV 12 and Peg/RBV 24-48	Peg/RBV 48	BOC 44 and Peg/RBV 24-48	Peg/RBV 48
Viral load (IU/mL)				
< 800,000	78	70	85	64
≥ 800,000	74	36	63	33
Race				
White	75	46	68	40
Black	62	25	53	23
Fibrosis stage				
0-2	77	47	67	38
3-4	62	33	52	38
Body mass index (kg/m <sup>2</sup> )				
< 25	83	44	67	47
25-30	67	45	65	33
> 30	71	41	66	33

TPV 12 indicates patients receiving telaprevir for 12 weeks; Peg/RBV 24-48, peginterferon alfa and ribavirin for 24 to 48 weeks; Peg/RBV 48, peginterferon alfa and ribavirin for 48 weeks; BOC 44, boceprevir for 44 weeks. Adapted from Jacobson et al<sup>2</sup> and Poordad et al.<sup>4</sup>

there is no biologic basis for archiving of PI-resistant variants in the body.

The long-term consequences of selecting for HCV PI resistance are unclear at this time. Investigations are currently underway on whether emergence of resistance will result in poorer response to subsequent treatment containing a PI. There are no convincing data thus far that baseline resistance to HCV PIs affects response to treatment. Thus, although there is a commercially available assay for testing for HCV resistance, for now there is no indication for testing to guide immediate treatment decisions. However, it may be prudent to document resistant variants in case the information becomes useful in the future.

### More Potent Therapy Reduces Predictive Value of Some Risk Factors for Poor Response

More potent anti-HCV therapy reduces the value of some of the traditional factors predictive of poor response to peginterferon alfa/ribavirin therapy. This is a good thing, however, because the loss of predictive value is the result of higher cure rates in subgroups of patients with traditionally greater risk of poor response. Most notable is the diminished effect of higher HCV viral load in predicting poorer treatment outcome with peginterferon alfa/ribavirin (see Table 1). For example, in the pivotal telaprevir trial, SVR rates were similar among telaprevir-receiving patients with baseline HCV RNA viral load 800,000 IU/mL or higher and those with viral load less than 800,000 IU/mL (74% and 78%, respectively).<sup>2</sup> The SVR rate in those with elevated viral load receiving telaprevir represents a striking improvement over the response rate among patients with high viral load receiving peginterferon alfa/ribavirin alone (36%). In the pivotal boceprevir trial, the SVR rate among boceprevir recipients with elevated baseline viral load was 63%, compared with 33% among patients with elevated baseline viral load receiving peginterferon alfa/ribavirin alone.<sup>4</sup>

As noted previously, black race is also a risk factor for poorer response

to peginterferon alfa/ribavirin. The difference in the frequency of the unfavorable interleukin-28B genotype explains about half of the difference in treatment response between black and nonblack patients. Although there was still a difference in SVR rates between black patients and white patients receiving telaprevir (62% and 75%, respectively), the SVR rate in black patients represents a striking improvement over that achieved with peginterferon alfa/ribavirin alone (25%).<sup>2</sup> Similarly, black patients receiving boceprevir had a lower SVR rate than white patients, but the high cure rate in black patients receiving boceprevir compared with those receiving peginterferon alfa/ribavirin alone is another striking improvement—53% versus 23%, respectively.<sup>4</sup> Some of the differences observed between the telaprevir and boceprevir studies, with regard to response rates in patient subgroups, likely reflect the fact that the post hoc analyses were performed in different patient populations.

### Comparison of Telaprevir- and Boceprevir-Containing Regimens

Table 2 provides an overview of characteristics of HCV treatment with telaprevir- and boceprevir-containing regimens. A 4-week lead-in period with peginterferon alfa/ribavirin is recommended before adding boceprevir and no lead-in is recommended for patients receiving telaprevir,<sup>8,10</sup> reflecting the way the drugs were developed in phase II and, especially, phase III studies. Boceprevir is administered for 24 weeks or 44 weeks in treatment-naïve patients and for 32 weeks or 44 weeks in treatment-experienced patients, depending on early virologic response, whereas telaprevir is administered for 12 weeks in both treatment-naïve and treatment-experienced patients.

Response-guided therapy is not recommended in patients with cirrhosis or in HIV-coinfected patients. Response-guided therapy in HIV-seronegative, noncirrhotic, treatment-naïve patients is permitted based on an HCV RNA-negative response during weeks 8 to

24 with boceprevir treatment and at weeks 4 and 12 with telaprevir treatment. Based on clinical trial data, it is estimated that 44% of treatment-naïve patients receiving boceprevir and 58% to 65% of treatment-naïve patients receiving telaprevir are eligible for response-guided therapy. The total duration of anti-HCV treatment in treatment-naïve patients, depending on presence or absence of early virologic response, is 28 weeks or 48 weeks for boceprevir, and 24 weeks or 48 weeks for telaprevir.

Response-guided therapy in treatment-experienced patients is not recommended for patients receiving boceprevir who were null responders to prior treatment or for patients receiving telaprevir who were partial or null responders. For treatment-experienced patients receiving boceprevir, total anti-HCV treatment duration is 36 weeks (for those with eRVR) or 48 weeks. Total treatment duration is 24 weeks or 48 weeks for patients receiving telaprevir. Anti-HCV therapy with boceprevir should be stopped due to futility if HCV RNA level is greater than 100 IU/mL at week 12 or if there is detectable HCV RNA at week 24. The recommended stopping rule for telaprevir-containing therapy is a viral load of greater than 1000 IU/mL at week 4 or 12, or detectable virus at week 24.

As noted previously, there are added adverse effects with the addition of either of the PIs to peginterferon alfa/ribavirin. There is an increased risk of anemia with boceprevir compared with peginterferon alfa/ribavirin therapy alone, and telaprevir is associated with increased risk of anemia and skin and gastrointestinal side effects. Pill burdens differ between the two treatments, with boceprevir requiring four 200 mg pills every 8 hours and telaprevir requiring two 375 mg pills every 8 hours. There is also a difference in food requirements: boceprevir needs to be taken with some food, whereas each dose of telaprevir needs to be taken with a meal containing at least 20 g of fat.

The addition of a new agent to HCV treatment regimens increases cost as well as cure rates. A 48-week course of

Table 2. Selected Characteristics of Boceprevir and Telaprevir

	Boceprevir	Telaprevir
4-week peginterferon alfa/ribavirin lead-in	Yes	No
PI duration		
HCV treatment-naive	24 weeks or 44 weeks	12 weeks
HCV treatment-experienced	32 weeks or 44 weeks	12 weeks
Criterion for RGT*	RNA-negative at weeks 8-24	RNA-negative at week 4 and week 12
RGT-eligible, treatment-naive patients	~44%	~58%-65%
RGT-eligible, treatment-experienced patients	Relapsers and partial responders (null responders not eligible)	Relapsers (partial and null responders not eligible)
Total duration of treatment in treatment-experienced patients	36 weeks (with eRVR) or 48 weeks	24 weeks or 48 weeks
Stopping rule for futility	HCV RNA > 100 IU/mL at week 12 Detectable virus at week 24	HCV RNA > 1000 IU/mL at week 4 or week 12 Detectable virus at week 24
Added adverse effects	Anemia, dysgeusia	Anemia, rash, pruritus, nausea, diarrhea
Dosage	Four 200 mg pills every 8 hours	Two 375 mg pills every 8 hours
Food requirement	Must be taken with some food	Must be taken with meal containing $\geq$ 20 g of fat

\*RGT indicates response-guided therapy; PI, protease inhibitor; eRVR, early rapid virologic response. RGT is not recommended in patients with cirrhosis or HIV coinfection.

peginterferon alfa/ribavirin costs approximately \$38,000. Full courses of telaprevir (12 weeks) and boceprevir (up to 44 weeks) cost approximately \$50,000.

### Ongoing Studies of HCV PIs

Patients with HCV infection in whom PI treatment has yet to be fully evaluated are those with more advanced disease (eg, patients with decompensated cirrhosis and transplant patients), those with HBV coinfection, and those with HIV coinfection. In addition, safety and efficacy of these drugs have not been established in patients with HCV genotype 2 or 3 infection. Genotype 2 infection is responsive to peginterferon alfa/ribavirin in most patients, and there is some indication that cure rates are improved with the addition of a PI. Genotype 3 infection is more difficult to treat in many cases, and there is some evidence indicating that

response rates are not improved with the addition of a PI.

### Studies in HIV Coinfection

In a small study by Sulkowski and colleagues, patients with HCV/HIV coinfection received a full 48-week course of anti-HCV therapy with telaprevir plus peginterferon alfa/ribavirin or peginterferon alfa/ribavirin alone with or without antiretroviral therapy.<sup>11</sup> The group receiving peginterferon alfa/ribavirin without antiretroviral therapy included patients with high CD4+ cell counts who did not meet current guidelines for initiation of antiretroviral therapy. Patients who received antiretroviral therapy took efavirenz/tenofovir/emtricitabine, or ritonavir-boosted atazanavir with tenofovir/emtricitabine or tenofovir/lamivudine. Patients who received the efavirenz-containing regimen received an additional telaprevir pill with each dose to compensate for

lowered blood levels due to pharmacokinetic interaction with efavirenz. As shown in Figure 1, the telaprevir-containing regimen markedly improved week 4 and week 12 virologic responses in patients receiving and not receiving antiretroviral therapy. These promising findings need to be confirmed in larger studies.

A phase II trial of boceprevir with peginterferon alfa/ribavirin in HIV/HCV-coinfected patients is ongoing. A total of 99 coinfecting patients with stable HIV disease are being treated with a lead-in of 4 weeks of peginterferon alfa plus weight-based ribavirin, then randomly assigned to add boceprevir (800 mg every 7-9 hours) or placebo for an additional 44 weeks. Subjects were allowed into the study if they were on raltegravir or ritonavir-boosted PIs. Baseline HCV RNA level was above 800,000 IU/mL for 88% of subjects; 82% were white, and 5% had cirrhosis.<sup>12</sup>

The proportion of patients with undetectable HCV RNA at week 8 was higher in the group receiving boceprevir (24 of 64 [37.5%] with undetectable HCV RNA) than in the group receiving placebo (5 of 34 [14.7%]). At week 24, HCV RNA was undetectable in 43 of 61 patients (70.5%) in the boceprevir arm and undetectable in 11 of 32 (34.4%) in the placebo arm. Treatment was discontinued in 3 (9%) and 9 (14%) of the patients in the placebo and boceprevir arms, respectively, because of adverse events.

Updates on the trials described above were presented at the 19th Conference on Retroviruses and Opportunistic Infections in March 2012. In the telaprevir trial in HIV/HCV-coinfected patients, 28 of 38 patients (74%) receiving telaprevir plus peginterferon alfa/ribavirin had undetectable levels of HCV RNA at week 24 (end of treatment), compared with 12 of 22 patients (55%) in the peginterferon alfa/ribavirin-only control group.<sup>15</sup> Twelve weeks after stopping therapy, all 28 of the 38 (74%) who had undetectable levels of HCV RNA at the end of telaprevir treatment had sustained virologic response. In the control group, 10 of 22 patients (45%) had sustained virologic response.

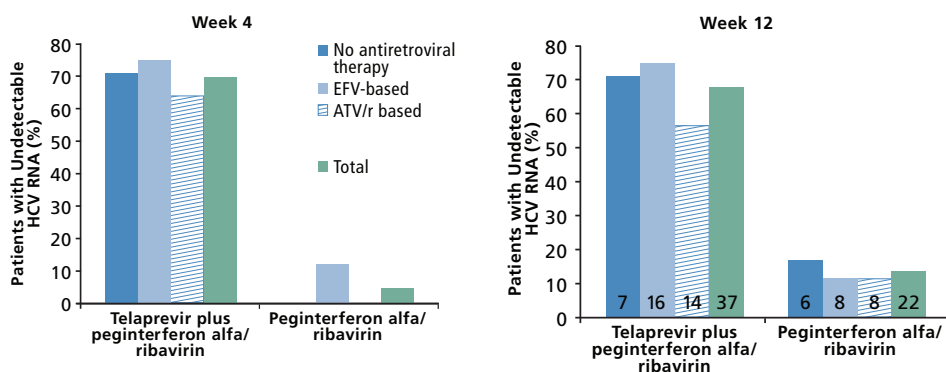


Figure 1. Hepatitis C virus (HCV) virologic responses to telaprevir-containing therapy at week 4 (left) and week 12 (right) in patients with HCV/HIV coinfection, according to antiretroviral regimen. Numerals in bars show total number of patients in treatment group. EFV indicates efavirenz/tenofovir/emtricitabine; ATV/r, ritonavir-boosted atazanavir with tenofovir/emtricitabine or tenofovir/lamivudine. Adapted from Sulkowski et al.<sup>11</sup>

In the boceprevir trial, 39 of 61 coinfecting patients (63.9%) receiving boceprevir plus peginterferon alfa/ribavirin had undetectable HCV RNA at week 48 (end of treatment), compared with 10 of 34 (29.4%) receiving peginterferon/alfa alone.<sup>14</sup> Twelve weeks after stopping therapy, 37 of 61 patients (60.7%) who had received boceprevir had sustained virologic response, compared with 9 of 34 (26.5%) in the peginterferon alfa/ribavirin-only group.

These results in coinfecting patients are notable because in both studies, virologic response was substantially better than with interferon alfa/ribavirin alone. Virologic response rates were also nearly as high as those in monoinfecting patients.

### Potential for Cure Without Interferon Alfa

Peginterferon alfa therapy is associated with considerable toxicity, and there is intense interest in developing treatments that would spare patients from the rigors of such therapy. An example of studies assessing this possibility was reported by Lok and colleagues.<sup>15</sup> Patients who were prior null responders to peginterferon alfa/ribavirin therapy received a combination of an HCV PI and an HCV nonstructural protein 5A (NS5A) inhibitor (which is active at different steps of the viral replication process than PIs), with or without peginterferon alfa/ribavirin.

Four of 11 patients receiving the PI and NS5A inhibitors without peginterferon alfa/ribavirin had viral loads that fell below the limit of quantitation at week 12 and remained undetectable after stopping therapy, showing in principle that cure is achievable without interferon alfa therapy. Six of the 11 patients exhibited viral breakthrough. It is also noteworthy that all 10 patients receiving the 2 direct-acting antivirals in combination with peginterferon alfa/ribavirin had undetectable virus at week 12, a remarkable outcome of treatment in prior null responders. There is considerable excitement over what might be achieved with multi-drug combinations of the numerous investigational direct-acting agents.

Although formal guidelines for treatment of HIV/HCV-coinfecting persons are being planned, at this time treatment should be prioritized for those with advanced liver fibrosis (cirrhosis and bridging fibrosis). When possible, coinfecting patients should be enrolled in clinical trials to expand the available information on optimal HCV treatments in that setting.

### Summary

The current era in HCV treatment is reminiscent of the transformation of HIV treatment that occurred in the mid-1990s. With the new HCV treatments, cure and complications occur more frequently. We can make smart

applications of the treatments available to us right now in some patients, and we await tomorrow's treatments for other patients. As with the first wave of HIV medications in the potent antiretroviral era, the new HCV drugs offer huge advantages but also present substantial challenges.

Presented by Dr Thomas in October 2011. First draft prepared from transcripts by Matthew Stenger. Reviewed and edited by Dr Thomas in February 2012.

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## Cases on the Web



### NEW Preexposure Prophylaxis for HIV Infection

Jason R. Faulhaber, MD

CME Credit Available: 1.5 AMA PRA Category 1 Credits™  
Level: Advanced

There may finally be a viable breakthrough in the prevention of new HIV infections, as data from recent studies have demonstrated. These studies evaluated the use of preexposure prophylaxis (PrEP) as oral medication or topical microbicide to reduce the risk of HIV acquisition. Dr Jason Faulhaber describes the role of health care practitioners in altering the future of HIV transmission.

### NEW Osteomalacia and Osteoporosis in the HIV-infected Patient

Michael Yin, MD, MS, and Emily Stein, MD, MS

CME Credit Available: 1.5 AMA PRA Category 1 Credits™  
Level: Advanced

The incidence of age-related comorbidities affecting bone mineral density has increased among HIV-infected individuals. HIV primary care practitioners will need to learn about the effects of antiretroviral drugs on vitamin D levels, bone metabolism, and the diagnosis and management of osteomalacia and osteoporosis. Dr Michael Yin and Dr Emily Stein describe the differences between these disease processes and the challenge of treating them.

### HIV and Pain

Greer A. Burkholder, MD

CME Credit Available: 2.5 AMA PRA Category 1 Credits™  
Level: Advanced

Patients with HIV infection now have near-normal life expectancies, but 40% to 55% still report pain. Various comorbid conditions, including cardiovascular disease, frailty, and non–AIDS-defining malignancies, are prevalent in the HIV-infected population,

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which also has high rates of substance abuse. Dr Jessica Merlin and Dr Rodney Tucker present an approach to the treatment of pain, an underdiagnosed and undertreated condition in HIV-infected patients.

### Quality Measures in HIV Care

Kathleen Clanon, MD, and Steven Bromer, MD

CME Credit Available: 1.75 AMA PRA Category 1 Credits™  
Level: Advanced

Choosing a set of quality of care measures and a strategy for using them is an investment in time and resources—the resulting information can be either a powerful tool for improving care or a useless paper exercise. Dr Kathleen Clanon and Dr Steven Bromer provide guidelines and advice on selecting performance measures, determining data collection methods, and using and leveraging the eventual results to improve care.

### Initiation of Antiretroviral Therapy in Treatment-Naive HIV-Infected Patients

Greer A. Burkholder, MD

CME Credit Available: 1.75 AMA PRA Category 1 Credits™

What impact does the timing of antiretroviral therapy (ART) initiation have on the prognosis of HIV-infected patients? Dr Greer Burkholder discusses the influence of CD4+ cell count, plasma HIV RNA level, AIDS-related and non–AIDS-related comorbidities, pregnancy, and patient willingness to take lifelong medications. Because of the evolving nature of guidelines and evidence regarding timing of ART, HIV practitioners need to update their knowledge on this topic regularly.

## COMING SOON

Look for these new *Cases on the Web* activities in coming months.

- **Drug Interactions with Medications for Treating Hepatitis C Virus (HCV) Infection**—Boceprevir and telaprevir have led to increased successful response rates in treating HCV infection. The use of these agents, however, is associated with drug interactions with primary care medications and many HIV antiretroviral drugs.
- **Sexually Transmitted Infections in the HIV-Infected Patient**—The presence of sexually transmitted infections may facilitate onward transmission and acquisition of HIV infections. Coinfection has an impact on individual health and on the health of partners and the community.

## CME CREDIT

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