ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Management of Anorectal Symptoms Associated with Telaprevir

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G&H How frequently do telaprevir-treated patients experience anorectal burning, itching, or other discomfort?

PJP Based on my clinical experience with telaprevir (Incivek, Vertex), I would say that anorectal symptoms occur 25–30% of the time. The package insert for telaprevir cites a similar figure, reporting anorectal symptoms in 29% of telaprevir-treated patients compared to only 7% of patients treated with peginterferon and ribavirin. Overall, approximately one fourth of patients seem to experience some type of anorectal symptoms when treated with telaprevir.

G&H How common are anorectal symptoms compared to other side effects associated with telaprevir? Are anorectal symptoms associated with other hepatitis C virus medications?

PJP The most common side effects with telaprevir treatment are rash and anemia, occurring in 56% and 36% of patients, respectively. Compared to rash and anemia, anorectal symptoms are less prevalent (and less severe).

In the absence of telaprevir, anorectal symptoms are rare but can still occur. Anorectal symptoms were reported by 7% of the patients in the control arm of the telaprevir trials (who were treated with peginterferon and ribavirin alone), although my feeling is that these symptoms were not anorectal burning, per se, but more likely loose stools, diarrhea, or maybe hemorrhoids. Anorectal symptoms have not been reported with boceprevir (Victrelis, Merck). Also, anorectal symptoms are not being reported with the new hepatitis C virus (HCV) drugs that are currently in development; researchers have observed photosensitivity, rash, and other skin-related side effects with these new drugs but not anorectal symptoms. Thus, I think anorectal symptoms may be specific to telaprevir.

G&H How severe are telaprevir-associated anorectal symptoms?

PJP My colleagues and I recently analyzed data from the first 103 patients treated with telaprevir at our center. Although a number of patients discontinued treatment due to adverse events or severe adverse events, none of these discontinuations were due to anorectal symptoms. Anorectal symptoms did occur, but they were never severe enough to stop a patient from completing therapy. Similarly, the telaprevir package insert reports that less than 1% of all treatment discontinuations are due to anorectal symptoms.

G&H What management strategies are available for patients who experience anorectal burning, itching, or other discomfort?

PJP The usual therapies for these symptoms include a topical steroid cream, a hemorrhoidal ointment or cream, or a steroid suppository. I also recommend that patients keep the area dry and clean; patients should try not to get sweaty, they should change clothes when needed, and they should maintain excellent hygiene to keep the area clean. In addition, patients should try to avoid constipation or diarrhea, so I typically recommend a fiber supplement. Finally, I sometimes use a treatment called a rectal rocket, which is a combination of a caine product and a topical steroid in a suppository; this therapy seems to work very well. Any steroid-containing suppository would be equally effective.

While these management strategies are typically effective, a final recourse is to alter the patient's diet and increase the fat content consumed with the telaprevir dosing. One theory suggests that anorectal symptoms occur because the fat content in the patient's diet is inadequate, resulting in diminished absorption of the drug; as a result, the active drug is excreted in the patient's stool, which is what causes anorectal symptoms. This theory has not been studied or validated, but it has been proposed as a possible explanation.

G&H Does the occurrence of anorectal symptoms with telaprevir influence your choice of HCV therapy?

PJP Concern about anorectal symptoms is not really a consideration when selecting a treatment regimen for HCV-infected patients. However, anemia is a pressing concern with both boceprevir and telaprevir and sometimes affects my decision regarding which protease inhibitor to use. Originally, I chose to use telaprevir because the treatment regimen was easier: Telaprevir is only administered for 12 weeks (vs 24–44 weeks for boceprevir), and no lead-in period is required with the telaprevir regimen. However, my colleagues and I found that many telaprevir-treated patients develop anemia quite quickly, and there was a rapid learning curve as we determined the best strategies for managing this side effect. Boceprevir also causes anemia, but it does so more slowly; in this regard, a boceprevir-based regimen seems to be slightly gentler on the patient. At the end of the day, however, my choice of therapy is usually driven by efficacy and the promise of a sustained virologic response for the particular patient I am treating.

G&H What data are available regarding the side effects associated with telaprevir and boceprevir?

PJP The data in the package inserts for both telaprevir and boceprevir come from the phase II and phase III studies that were performed prior to the approval of these drugs. In addition, hepatologists now have more than 1 year of clinical experience with these drugs. To date, my colleagues and I have treated approximately 150 patients with protease inhibitors—most of whom were treated with telaprevir—and we recently compiled data on the first 103 telaprevir-treated patients for an abstract that was presented at this year's meeting of the American Association for the Study of Liver Diseases. For this abstract, we assessed adverse events, treatment discontinuations, and side effects among the patients treated at our center.

While some of our data confirm the results of the published phase III trials of telaprevir, our patient population was generally sicker than the patient population enrolled in these trials. For example, advanced fibrosis or cirrhosis was present in 68% of the patients treated at our center, compared to only 10–15% of patients enrolled in the phase III studies of telaprevir. Although patients with cirrhosis had a higher incidence of anemia, they did not have a higher occurrence of anorectal symptoms in our study.

G&H Have clinicians begun to publish data based on their real-life experiences with boceprevir and telaprevir?

PJP Many clinicians are in the process of compiling such data, but none of these studies have been published to date. There is a large, ongoing French study—called the CUPIC study—in which researchers are compiling data on cirrhotic patients who are being treated at multiple centers throughout France; data from this study have been presented at meetings but have not yet been published. Presentations by CUPIC researchers have addressed treatment discontinuation, side effects, hospitalizations, and response rates, but these presentations have not mentioned anorectal burning as a major problem. However, the published results of the CUPIC study may include more robust analyses with additional details.

G&H Are further studies needed in this area?

PJP I do not think we need randomized clinical trials to assess the side effects associated with protease inhibitors at this moment. Given the growing clinical experience with both boceprevir and telaprevir, I think we will soon see publications based on real-life experience that will show us how to appropriately manage the side effects associated with these drugs. A number of research groups are compiling such data now; some of these data have been presented at meetings, and these studies will probably be published in the next 6–12 months.

Suggested Reading

Cunningham M, Foster GR. Efficacy and safety of telaprevir in patients with genotype 1 hepatitis C infection. *Therap Adv Gastroenterol*. 2012;5:139-151.

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Sherman KE, Flamm SL, Afdhal NH, et al; ILLUMINATE Study Team. Response-guided telaprevir combination treatment for hepatitis C virus infection. *N Engl J Med*. 2011;365:1014-1024.