An interferon-free combination of three drugs plus ribavirin achieved a sustained virologic response (SVR12) in 96% of previously untreated patients with genotype 1 hepatitis C infection, AbbVie reported in a recent press release.

The results are the first in a sequence of six announcements of the results of phase III studies due to take place over the next few months, prior to presentation of the full results at scientific meetings in 2014.

AbbVie plans to file for registration of the combination in the United States and the European Union in the second quarter of 2014, and hopes to have the first interferon-free combination for the treatment of genotype 1 hepatitis C infection available for prescription by early 2015.

The regimen consists of a fixed-dose combination tablet containing the NS5A inhibitor ABT-267 and ABT-450 boosted by ritonavir, dosed once daily, and a second tablet, the non-nucleoside polymerase inhibitor ABT-333, dosed twice daily. The combination is being tested with and without ribavirin to determine whether it is possible to cure hepatitis C infection without ribavirin, which can cause anemia.

The SAPPHIRE 1 study released recently represents an easier-to-treat population of patients without cirrhosis. The study recruited 631 participants with genotype 1a or 1b hepatitis C and randomized them to receive either ABT-450 boosted by ritonavir, ABT-333 and ABT-267, or a placebo, for 12 weeks. Participants in the placebo group received the active treatment after 12 weeks.

The headline results showed that 96% of the study population achieved SVR12, and only 1.7% of participants experienced virologic relapse after completing treatment. There was little difference in virologic response by sub-genotype: 95% of genotype 1a and 98% of genotype 1b patients achieved SVR12. Treatment discontinuations due to adverse events were rare (0.6%) and the main side effects reported by patients were nausea, headache and fatigue.

Further phase III studies will report on the efficacy of the combination in treatment-experienced patients, and also determine whether there are differences between genotypes 1a and 1b and between treatment-naive and treatment-experienced patients in their need for ribavirin. The Turquoise study is comparing 12- and 24-week ribavirin-containing regimens in genotype 1 patients, including those with cirrhosis.

AbbVie is also conducting phase II studies of a once-daily two-drug combination, of ABT-450/r and ABT-267, and reported the first results from these studies at The Liver Meeting 2013, held in November.
Fixed-dose sofosbuvir/ledipasvir with or without ribavirin cures most genotype 1 hepatitis C patients, LONESTAR study shows

By Liz Highleyman
aidsmap

At least 95% of newly treated people with genotype 1 hepatitis C and prior non-responders achieved sustained virological response using a fixed-dose combination of sofosbuvir plus ledipasvir, with or without ribavirin, according to findings from the LONESTAR study presented at The Liver Meeting 2013, the 64th annual meeting of the American Association for the Study of Liver Diseases (AASLD) in Washington, DC. While response rates were high overall, the two relapers in the trial were not taking ribavirin.

The advent of direct-acting antiviral agents has revolutionized treatment of chronic hepatitis C. While these agents were initially tested as add-ons to interferon-based therapy, many people with hepatitis C virus (HCV) and their care providers are awaiting all-oral regimens that dispense with pegylated interferon and its difficult side-effects.

Eric Lawitz of the Texas Liver Institute reported results from the phase 2 LONESTAR study, which evaluated a fixed-dose combination pill containing Gilead Sciences’ HCV polymerase inhibitor sofosbuvir (formerly GS-7977) plus the NS5A inhibitor ledipasvir (formerly GS-5885), taken with or without ribavirin for 8 or 12 weeks.

LONESTAR enrolled two cohorts at a single center in the United States. Cohort 1 included 60 treatment-naive individuals (people who had not taken treatment before) who did not have liver cirrhosis. Cohort 2 included 40 people, about half with cirrhosis, who did not achieve a cure with the current standard of care: triple therapy with the approved HCV protease inhibitors boceprevir (Victrelis) or telaprevir (Incivek) plus pegylated interferon/ribavirin.

Overall, two-thirds of participants were men, 9% were black and the mean age was 50 years. Most (87%) had hard-to-treat HCV genotype 1a and only 15% had the favorable IL28B CC gene variant associated with interferon responsiveness. In Cohort 2, 55% had cirrhosis at study entry. Just over half (55%) had previously been treated with boceprevir while 45% had used telaprevir. All experienced prior virological failure; people who stopped previous therapy due to adverse events were excluded.

Participants in Cohort 1 were randomly assigned (1:1:1) to receive the once-daily fixed-dose tablet containing 400mg sofosbuvir and 90mg ledipasvir either with or without 1000-1200mg/day weight-based ribavirin for 8 weeks, or without ribavirin for 12 weeks. Treatment-experienced patients were randomised to receive sofosbuvir/ledipasvir either with or without ribavirin for 12 weeks.

All participants completed therapy except for one who withdrew consent. In Cohort 1, 95% of treatment-naive patients treated with sofosbuvir/ledipasvir for either 8 or 12 weeks achieved sustained virological response, or continued undetectable HCV RNA at 12 weeks post-treatment (SVR12). The SVR12 rate was 100% in the 8-week sofosbuvir/ledipasvir plus ribavirin arm.

In Cohort 2, SVR12 rates were 95% for sofosbuvir/ledipasvir and 100% for sofosbuvir/ledipasvir plus ribavirin given for 12 weeks. All patients without cirrhosis achieved sustained response, as did all but one of the people with cirrhosis (91%).

Continued on page 14
New drug may help with diarrhea

By Patrick Clay, PHARMD
Positively Aware

Diarrhea is not the problem it once was for people on HIV therapy, but it’s still a significant concern, especially when it can impact ART (antiretroviral therapy) adherence. But even today’s simplified once-daily combination pills still sometimes caused moderate to severe diarrhea in patients during the clinical trials.

What are HIV patients and their providers to do?

Historically, though never tested in HIV patients, over-the-counter and prescription anti-diarrheals were used. Thankfully, for the majority of patients, this is enough. For the others for whom it didn’t work or side effects (dry mouth, intermittent constipation-diarrhea) were too much, more radical approaches had to be considered.

Enter a new option. On New Year’s Eve 2012, a new drug was approved to treat diarrhea in HIV patients taking ART. The drug is crofelemer or Fulyzaq (pronounced FUL-ih-zack). Below is a summary of what we learned about the drug learned while conducting the ADVENT study (http://clinicaltrials.gov/ct2/show?term=crofelemer&rank=1) and importantly, as presented at this year's ICAAC conference, who will most likely respond well to Fulyzaq.

What is it?
First off, it is a botanical. The bark of the Amazon River delta-based Croton lechleri tree is purified and Fulyzaq is obtained. Tribal shamans traditionally have and continue to use the sap from this tree (also known as “dragon’s blood” because of its red color) for various gastrointestinal issues among other maladies.

How does it work?
Very simplistically, diarrhea is essentially more water in the gut than needed to “move things along.” Water gets into the gut using channels in the intestine. These channels have gates. Some of the gates are controlled by chloride. Fulyzaq is believed to work by blocking two of these chloride gates. Both gates are located on the luminal enterocytes of the intestinal epithelium [absorbent cells on the inside of the intestinal lining]. In other words, inside the gut.

Where does it work?
Because Fulyzaq isn’t really absorbed, it works directly on the gut from the inside. Because it doesn’t get into the bloodstream, and the drug-interaction poster at ICAAC (A-1577) confirms this, there is no concern about drug interactions. Those patients taking ritonavir-boosted PI or even Atripla regimens had no detrimental changes in any of their drug levels, viral load, or CD4 counts. (So finally, there is a drug that doesn’t make life more complicated for patients and providers alike!)

How is it taken?
The 125 mg enteric coated capsules are taken with or without food twice a day.

Who is most likely to benefit from Fulyzaq?
Data presented at ICAAC (Poster H-1264) showed that the drug appears to have the greatest success in patients with the following four characteristics of their bowel movements: two or more per day (six times more likely to respond), more than two years of loose stools (approximately 2.5 times more likely to respond), use of anti-diarrheal previously (up to 27 times more likely to respond), used an anti-diarrheal within the last four weeks without benefit (six times more likely to respond), and basically “pourable poop.” Yes, that was how we asked the question during the study—“If your poop was in a bucket, could you pour it?” (two times more likely to respond). As far as making life more complicated for patients, earlier this year it was shown at the IAPAC conference (Poster 140) that Fulyzaq patients’ adherence was either maintained or improved after it was added to their ART therapy (iapac.org/AdherenceConference/assets/ADH8_Poster_Abstracts.pdf).

In summary
Importantly, any infectious cause must be ruled out first! Fulyzaq is an option to consider for those with loose stools daily after the non-prescription agents do not satisfy the goals for the patient. It is well tolerated, doesn’t cause drug interactions, and is easily incorporated into existing medication plans. The product website contains full prescribing, as well as patient assistance program information (fulyzaq.com).

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Simeprevir, sofosbuvir produces high sustained response rates for hard-to-treat patients in COSMOS trial

By Liz Highleyman

A 12-week all-oral combination of simeprevir plus sofosbuvir led to sustained virological response in 93% of genotype 1 prior null responders with mild-to-moderate liver fibrosis, working as well as a longer course of treatment or triple therapy including ribavirin, according to late-breaking findings from the COSMOS trial presented at The Liver Meeting 2013.

The study also showed that 100% of treatment-naive patients and null responders with advanced fibrosis or cirrhosis achieved early sustained response at 4 weeks post-treatment using the same dual regimen.

The advent of next-generation direct-acting antivirals (DAAs) has been described as a revolution in the treatment of chronic hepatitis C virus (HCV) infection. While the first of these new agents will initially be approved as add-ons to interferon-based therapy, people with hepatitis C and their clinicians are eagerly awaiting interferon-free regimens.

Multiple DAAs developed by several major drug companies have performed well in all-oral regimens in trials to date, but their effectiveness varies based on a bewildering array of factors including HCV subtype (1b vs 1a), host IL28B gene pattern ('CC' vs non-'CC'), prior treatment status (untreated, relapser, prior partial or null responder) and extent of liver damage (absent, mild or moderate fibrosis vs advanced fibrosis or cirrhosis).

Ira Jacobson of Weill Cornell Medical College presented findings from the phase 2a COSMOS trial, evaluating oral regimens containing Janssen/Medivir's HCV protease inhibitor simeprevir (formerly TMC435) and Gilead Science's nucleotide polymerase inhibitor sofosbuvir (formerly GS-7977), taken with or without ribavirin.

This open-label study enrolled two cohorts of patients with genotype 1 chronic hepatitis C:
- Cohort 1: 80 prior interferon null responders with absent-to-moderate fibrosis (Metavir stage F0-F2);
- Cohort 2: 87 treatment-naive individuals and prior null responders with advanced fibrosis or compensated cirrhosis (F3-F4).

About 60% of participants in Cohort 1 were men, 29% were black and the median age was 56 years. Just over three-quarters had harder-to-treat HCV subtype 1a, and half of these had the Q80K resistance mutation at baseline. Only 6% had the favorable IL28B 'CC' gene variant associated with good interferon responsiveness – typical of null responders. About 40% had stage F0-F1 fibrosis while 60% had F2.

In Cohort 2, two-thirds were men, 9% were black and the median age was 58 years. Again 78% had subtype 1a, 40% with the Q80K mutation. Participants were about evenly divided between treatment-naïves and null responders, and 21% had the favorable 'CC' variant. Just over half had advanced fibrosis, the rest cirrhosis.

Participants were randomly assigned to receive a dual regimen of 150mg once-daily simeprevir plus 400mg once-daily sofosbuvir, or else a triple regimen of these two drugs plus 1000-1200mg weight-based ribavirin taken twice-daily. In addition, they were randomised to receive these regimens for either 12 or 24 weeks.

Jacobson presented results from a planned interim analysis. Cohort 1 started earlier and had long enough follow-up to determine sustained virological response at 12 weeks after completing treatment (SVR12), which is considered a cure. Cohort 2 started later and had 4-week post-treatment follow-up results (SVR4), which is too soon to declare them cured as relapses could still occur.

All participants treated for 12 weeks completed therapy in both cohorts. In Cohort 1, about 87% treated for 24 weeks finished therapy. Two people in the dual therapy arm and three in the triple therapy arm stopped early, one in each arm due to adverse events. More than 90% of Cohort 2 participants treated for 24 weeks were still in treatment or follow-up; again one in each arm discontinued due to adverse events.

All Cohort 1 participants who completed therapy had undetectable HCV RNA at the end of treatment and no viral breakthroughs occurred. Amongst those treated for 12 weeks, 93% taking simeprevir/sofosbuvir and 96% taking simeprevir/sofosbuvir/ribavirin achieved SVR12. There was one relapse in each regimen arm. Amongst those treated for 24 weeks,

Continued on page 5
SVR12 rates were 93% and 79%, respectively. There was one relapser and four people with ‘non-virological failure’ in the ribavirin arm.

In Cohort 2, all 14 participants who completed therapy had undetectable end-of-treatment viral load with no breakthroughs. One hundred per cent of both treatment-naive patients and null responders taking simeprevir/sofosbuvir who had adequate follow-up (seven of each) achieved SVR4, as did 100% of naive participants and 93% of null responders (all but one) treated with simeprevir/sofosbuvir/ribavirin. In both cohorts, 100% of people with HCV subtype 1b or with subtype 1a but lacking the Q80K mutation achieved SVR12 or SVR4. Three relapsers in Cohort 1 and one in Cohort 2 had subtype 1a with the mutation (SVR12 of 89% and SVR4 of 91%, respectively).

The researchers looked at the effect of adding ribavirin to the 12-week course of therapy for difficult-to-treat subgroups in both cohorts combined. Amongst people with unfavorable IL28B status, 96% taking either the ribavirin-sparing or the ribavirin-containing regimen achieved SVR4. Amongst prior null responders the SVR4 rate was 95% using either regimen. Amongst people with cirrhosis, SVR4 rates were 100% without and 91% with ribavirin.

Treatment was generally safe and well tolerated. Amongst people treated for 12 weeks in both cohorts combined, there were no serious adverse events, grade 3-4 laboratory abnormalities or discontinuations due to adverse events with either regimen. Amongst people treated for 24 weeks, serious adverse events were rare (3 to 4%) and there were two discontinuations due to adverse events in both regimen arms.

The most common side effects were fatigue, headache, nausea and insomnia, which occurred with similar frequency in both the ribavirin-sparing and ribavirin-containing arms. Anemia and elevated bilirubin, however, were more common amongst ribavirin recipients.

Based on these findings the researchers concluded that treatment with simeprevir plus sofosbuvir, with or without ribavirin, resulted in high SVR12 rates (79 to 96%) in HCV genotype 1 null responders with stage F0-F2 fibrosis, as well as high SVR4 rates (96 to 100%) in treatment-naive and null responder patients with stage F3 fibrosis or F4 cirrhosis. Addition of ribavirin to simeprevir and sofosbuvir "may not be needed to achieve high rates of SVR in this patient population," they added. “12 weeks of treatment may confer similar SVR rates compared with 24 weeks of treatment.”

Given last month’s recommendation for approval of both simeprevir and sofosbuvir by a US Food and Drug Administration advisory committee, Jacobson was asked about the prospect of using these drugs together off-label as an interferon-free regimen, especially for patients with advanced disease who need treatment now but cannot tolerate ribavirin.

"It's difficult to provide definitive guidance," Jacobson replied. "But all of us want to help our patients, and it's not difficult to imagine extrapolating from these data."

Reference


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Sofosbuvir taken before or after liver transplant reduces hepatitis C recurrence in nearly two-thirds of patients

By Liz Highleyman
aidsmap

An interferon-free combination of sofosbuvir plus ribavirin administered before liver transplantation prevented hepatitis C recurrence in nearly two-thirds of patients, while the same regimen led to early viral clearance in three-quarters of those treated after transplantation, according to studies presented recently at The Liver Meeting 2013.

Over years or decades chronic hepatitis C virus (HCV) infection can cause advanced liver disease including cirrhosis and liver cancer, and hepatitis C is a leading indication for liver transplantation. Hepatitis C patients awaiting liver transplants are in dire need of treatment but often cannot tolerate interferon-based therapy. Left untreated, HCV almost always infects the new liver soon after transplantation, which can lead to cirrhosis, graft failure and death.

Sofosbuvir + ribavirin pre-transplant
Michael Curry of Beth Israel Deaconess Medical Center in Boston presented findings from a study of sofosbuvir and ribavirin to prevent HCV recurrence following liver transplantation. Sofosbuvir (formerly GS-7977) is a once-daily oral nucleotide polymerase inhibitor with a high barrier to resistance.

This open-label phase 2 study enrolled 61 people at 16 sites, mostly in the US. Most participants (80%) were men, 90% were white and the median age was 59 years. A majority (73%) had HCV genotype 1 (including 39% with harder-to-treat subtype 1a), 13% had genotype 2, 12% had genotype 3 and one had genotype 4. Three-quarters had previously been treated for hepatitis C and 22% had the favorable IL28B CC gene variant associated with interferon responsiveness.

Participants had well-compensated liver disease and were listed for transplantation due to hepatocellular carcinoma, a type of liver cancer. The median MELD score was 8 and most had Child-Pugh scores of 5 (43%), 6 (30%) or 7 (23%). People with hepatitis B or HIV co-infection, decompensated cirrhosis or kidney impairment were excluded.

Participants received 400mg once-daily sofosbuvir plus 1000-1200mg/day weight-based ribavirin while awaiting transplants. The original protocol called for treatment lasting 24 weeks but this was later extended to 48 weeks. The last dose was taken on the day of transplantation. They received standard immunosuppressive therapy (tacrolimus, mycophenolate mofetil or prednisone) to prevent rejection of the new liver.

The primary study endpoint was post-transplant virological response, or continued undetectable HCV RNA among people who received sofosbuvir/ribavirin for more than 12 weeks and had undetectable viral load at the time of transplantation.

A total of 41 of participants underwent transplantation with undetectable HCV RNA while three people did so while viral load was still detectable. Ten discontinued treatment, four finished treatment but were still awaiting transplants and one was still on therapy while waiting.

HCV viral load declined rapidly after starting sofosbuvir/ribavirin. Most patients who received treatment for any duration (93%) or for at least 12 weeks (91%) had HCV RNA below the lower limit of quantitation (LLOQ) at the time of transplantation. Among those with undetectable HCV at transplantation, 64% maintained viral suppression at 12 weeks post-transplant.

People who did not experience HCV recurrence had undetectable viral load for a median of 95 days before transplantation compared with just 5.5 days for those who did have a recurrence. Only 1 patient had a recurrence after having undetectable HCV for 30 days or more.

In a multivariate analysis, longer duration of undetectable HCV RNA prior to transplantation was the only factor that significantly predicted HCV non-recurrence. HCV genotype 1b and IL28B CC status were of borderline significance in a univariate analysis but not the multivariate analysis.

Sofosbuvir/ribavirin was generally safe and well tolerated in this difficult-to-treat population. There were 11 serious adverse events – none of which were
considered related to sofosbuvir – and two discon-
tinuations due to adverse events (3%), as well as
seven cases of grade 4 laboratory abnormalities.
Three people died before transplantation and five
afterwards. The most common side-effects were
fatigue (38%), anemia (23%) and headache (23%).

"Sofosbuvir + ribavirin treatment prior to transplan-
tation prevented HCV recurrence in the majority
(64%) of patients who were HCV RNA <LLOQ at
transplant," the researchers concluded. "The num-
ber of consecutive days with HCV RNA
[undetectable] prior to transplant appears to be the
strongest predictor of post-transplant virological
response."

These results, Curry said, are a "vast improve-
ment" over current treatment. But it is not yet pos-
sible to answer an audience question about wheth-
er it might be advisable to delay transplantation in
order to take sofosbuvir for longer prior to trans-
plantation.

Sofosbuvir + ribavirin post-transplant
The second study, by Michael Charlton of the
Mayo Clinic and colleagues, looked at sofosbuvir
plus ribavirin for treatment of established HCV re-
currence after liver transplantation.

This open-label phase 2 study included 40 partici-
pants in France, Germany, New Zealand, Spain
and the US. Again, about 80% were men, most
were white and the median age was 59 years.
More than 80% had HCV genotype 1 (including
55% with 1a), 15% had genotype 3, one had geno-
type 4 and none had genotype 2. Most (88%) were
treatment-experienced and one-third had the IL28B
CC variant.

Participants had undergone liver or combined liver
and kidney transplants between six months and 12
years (median four years) prior and did not experi-
ence organ rejection or have signs of decompensa-
tion. Forty per cent had cirrhosis in the engrafted
liver while 23% had bridging fibrosis (Metavir stage
F3) and 35% had mild-to-moderate fibrosis (stage
F1-F2).

Participants were treated with 400mg once-daily
sofosbuvir for 24 weeks. They also started with a
low 400mg dose of ribavirin which was gradually
increased based on tolerability (determined by he-
moglobin levels).

HCV again declined rapidly after starting therapy. At
week 4 and at the end of treatment all participants
had undetectable viral load. Four weeks after com-
pleting treatment 77% had early sustained virological
response (SVR4). This is a promising result, but too
early to determine a cure as relapse has been seen
after this point in other sofosbuvir studies.

No baseline factors were found to predict which pa-
tients would relapse, including HCV genotype, IL28B
status, prior treatment or extent of fibrosis. Charlton
noted that the average ribavirin dose was "almost
identical" for responders and non-responders

There were six serious adverse events (15%) and two
(5%) that led to treatment discontinuation. There were
no deaths, cases of graft loss or episodes of rejection.
The most common side-effects were fatigue (28%),
headache (25%), joint pain (23%) and diarrhea
(23%). There were 11 grade 4 laboratory abnormali-
ties (28%); 15% developed anemia and several re-
quired erythropoietin, blood transfusions or ribavirin
dose reduction.

No interactions were reported between sofosbuvir
and any immunosuppressant agents including tacroli-
mus (used by 70%), mycophenolate mofetil (35%),
prednisone (28%) or cyclosporin (25%), though four
people did increase their tacrolimus does while on
sofosbuvir.

Based on these findings, the investigators concluded,
"Sofosbuvir + ribavirin is a potential all-oral therapy
for treatment of HCV infection following liver trans-
plantation."

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Daclatasvir and asunaprevir cures 85% of genotype 1b hepatitis C patients in Japanese study

By Liz Highleyman

An interferon- and ribavirin-free oral regimen of daclatasvir plus asunaprevir taken for 24 weeks led to sustained virological response (SVR12) in 85% of Japanese patients with hepatitis C virus subtype 1b, according to findings presented recently at The Liver Meeting 2013.

The development of direct-acting antivirals has brought about a revolution in the treatment of chronic hepatitis C virus (HCV) infection. While the first of these new agents were initially approved as add-ons to interferon-based therapy, people with hepatitis C and their care providers are eagerly awaiting all-oral regimens that avoid the difficult side-effects of interferon.

Kazuaki Chayama of Hiroshima University presented results from a phase 3 trial testing an interferon-free regimen of Bristol-Myers Squibb's HCV NS5A replication complex inhibitor daclatasvir (formerly BMS-790052) plus the NS3 protease inhibitor asunaprevir (formerly BMS-650032) for patients who were either non-responders to prior interferon-based therapy or ineligible for or intolerant of interferon.

The study enrolled 222 people with chronic hepatitis C subtype 1b, the predominant type in Japan. In contrast with most US and European studies, two-thirds of participants were women and the average age was a bit older at 63 years; 40% were over age 65. Half had the favorable IL28B CC gene variant associated with interferon responsiveness and 10% had liver cirrhosis.

The population included 22% prior null responders, 16% prior partial responders, 45% deemed ineligible to take interferon (for reasons such as pre-existing depression, anemia, other co-morbidities or advanced age) and 16% who were interferon intolerant (previously discontinued interferon before 12 weeks due to toxicities).

All participants in this open-label study received 60mg once-daily daclatasvir plus 100mg twice-daily asunaprevir for 24 weeks. They were followed-up for an additional 24 weeks after finishing treatment to determine sustained virological response (SVR24), or continued undetectable HCV RNA, which is considered a cure.

The overall SVR24 rate was 85% in a modified intent-to-treat analysis, broken down to 87% for people who were interferon ineligible or intolerant and 81% for prior non-responders.

HCV viral load declined rapidly after starting therapy, with 84% of people who were interferon ineligible/intolerant and 61% of prior non-responders showing rapid virological response at week 4; 96 and 87%, respectively, had undetectable HCV RNA at the end of therapy. However, 11 people who were interferon ineligible/intolerant and six prior non-responders (8%) relapsed during post-treatment follow-up.

High sustained response rates were obtained regardless of IL28B status (85% for favorable CC, 85% for intermediate CT and 83% for least favorable TT). Other baseline factors did not significantly affect response rates. Interestingly, people with cirrhosis did at least as well as people who did not have cirrhosis (91 and 84%, respectively) and people aged 65 and older fared slightly better than younger participants (90 vs 81%).

Daclatasvir plus asunaprevir was generally safe and well-tolerated. Overall, 6% of participants experienced serious adverse events, 7% developed grade 3-4 laboratory abnormalities and 5% discontinued due to adverse events, with all these outcomes being a bit more common among people who were interferon ineligible/intolerant compared to prior non-responders.

The most common adverse events were upper respiratory infections (30%), elevated ALT or AST liver enzyme levels (16 and 13%), headache (16%), fever (12%) and diarrhea (10%); anemia was rare (3%). All but one of the 11 people who discontinued treatment early due to side effects did so for elevated ALT or AST, which returned to normal after stopping treatment.

"[The] all-oral combination of daclatasvir and asunaprevir achieved high rates of SVR24 in Japanese patients without treatment options and in patients with no prior response to interferon-based therapy", the researchers concluded. "This all-oral, interferon-free, ribavirin-free regimen was well tolerated with
Sofosbuvir plus ribavirin produces sustained response in 76% of genotype 1 HIV/HCV co-infected people

By Liz Highleyman

An interferon-free regimen of sofosbuvir plus ribavirin taken for 24 weeks cured hepatitis C infection in three quarters of previously untreated HIV-positive people co-infected with hepatitis C virus (HCV) genotype 1, while 12 weeks of treatment cured 88 and 67% of those with genotypes 2 or 3, according to findings from the phase 3 PHOTON-1 study presented recently at The Liver Meeting 2013.

People co-infected with HIV and HCV experience more rapid liver disease progression and do not respond as well to interferon-based hepatitis C treatment as people with HCV alone. Direct-acting antivirals have the potential to dramatically improve response rates for co-infected individuals, but this population may be more prone to adverse events and faces the issue of drug-drug interactions with antiretroviral therapy (ART).

Mark Sulkowski of Johns Hopkins Medical Center and colleagues conducted a study to evaluate the safety and efficacy of Gilead Sciences’ sofosbuvir (formerly GS-7977) administered with ribavirin to co-infected patients.

Sofosbuvir is a potent nucleotide HCV NS5B polymerase inhibitor with activity against HCV genotypes 1 through to 6 and a high genetic barrier to resistance. Unlike some HCV protease inhibitors, it does not affect CYP3A4 liver enzyme metabolism and has demonstrated no significant interactions with many widely used antiretroviral drugs.

Last month, a US Food and Drug Administration advisory committee recommended approval of sofosbuvir both as an add-on to pegylated interferon/ribavirin for people with HCV genotype 1 and as part of a dual regimen with ribavirin for people with genotypes 2 or 3. This all-oral regimen was previously found to produce a sustained virological response rate (SVR, considered a cure) as high as 97% for HIV-negative genotype 2 patients. However, sofosbuvir’s initial indication is not expected to include HIV/HCV co-infection.

The open-label PHOTON-1 trial enrolled 114 co-infected US patients with HCV genotype 1 who had not been previously treated for hepatitis C. They received 400mg once-daily sofosbuvir plus 1000 to 1200mg weight-based ribavirin for 24 weeks and were followed for 12 weeks after completion of therapy to determine SVR12.

The study also included 109 people with genotypes 2 or 3. Treatment-naive patients – 26 with genotype 2 and 42 with genotype 3 – received the same regimen for 12 weeks and were again followed for 12 weeks post-treatment. The remainder are treatment experienced and received sofosbuvir plus ribavirin for 24 weeks; the latter group is still in treatment or follow-up and not included in Sulkowski's report.

Across all genotypes, most participants (81%) were men and the mean age was about 49 years. One-third of genotype 1 patients, 23% of genotype 2 patients and only 5% of genotype 3 patients were black, a population that responds less well to interferon-based therapy; 27, 39 and 36%, respectively, had the favorable IL28B CC gene variant associated with good interferon response. Most genotype 1 patients had harder-to-treat HCV subtype 1a. In the genotype 1 and 2 groups, 4% had compensated cirrhosis, rising to 14% in the genotype 3 group. Participants had well-controlled HIV disease. More than 90% were on antiretroviral treatment and the mean CD4 cell count was above 600 cells/mm3.

Approximately one third used ART regimens containing efavirenz (Sustiva), followed by the boosted HIV protease inhibitors atazanavir (Reyataz) or darunavir (Prezista) and the integrase inhibitor raltegravir (Isentress), all in combination with tenofovir/emtricitabine (the drugs in Truvada).

About 90% of participants across all genotype groups completed treatment. Rapid virological response rates at week 4 after starting therapy were 96% for genotype 1 and 2 patients, and 100% for those with genotype 3. At the end of treatment, 100, 96 and 98%, respectively, had undetectable HCV viral load.

After finishing therapy, however, a number of people experienced treatment failure, resulting in SVR12 rates of 76% for genotype 1, 88% for genotype 2 and 67% for genotype 3 – substantially high-
Once-daily raltegravir effective as maintenance therapy

By Liz Highleyman
aidsmap

Almost all HIV-positive people with undetectable viral load who switched to once-daily raltegravir (Isentress) maintained viral suppression, French researchers reported at the 14th European AIDS Conference in Brussels during October. In an effort to facilitate once-daily dosing, Merck is working on a new tablet that appears less affected by food than the current formulation.

Raltegravir is a highly effective component of combination antiretroviral therapy (ART) and is one of the best-tolerated HIV medications, but its standard twice-daily dosing schedule makes it less convenient than once-daily options.

Fabienne Caby of Hôpital Pitié-Salpêtrière and colleagues evaluated whether once-daily raltegravir is able to maintain virological control when people switch from a fully suppressive combination regimen. Although pharmacokinetic data suggest that once-daily raltegravir may provide adequate drug levels, the randomized Phase 3 QDMRK trial showed that 800mg once-daily raltegravir failed to meet the criteria for non-inferiority to 400mg twice-daily raltegravir for people starting ART for the first time, with 83 vs 89% achieving undetectable viral load. This was largely driven by poorer efficacy among people with high baseline viral levels (74 vs 84%, respectively). But raltegravir may be able to keep HIV under control if viral load is already suppressed.

This observational study enrolled 71 people at 2 centers in Paris who had undetectable viral load (<50 copies/ml) for at least six months. A majority (66%) were men, the mean age was 46 years and the median CD4 cell count was 588 cells/mm3. At the time they switched, participants had been on ART for 14 years on average and had used five antiretroviral 'lines.'

Participants received treatment optimization that included introduction of 800mg once-daily raltegravir. Nearly one quarter switched from 400mg twice-daily raltegravir (taken for an average of eight months), whilst the rest switched from other drugs and were integrase inhibitor-naïve. This was not a randomized trial and patients were not assigned to a regimen. In addition to once-daily raltegravir, 56% used tenofovir/emtricitabine (the drugs in Truvada) and 18% used abacavir/lamivudine (the drugs in Kivexa). Others were on non-standard regimens including 10% taking etravirine (Intelen), 10% taking boosted or unboosted atazanavir (Reyataz), three people taking nevirapine (Viramune) and one taking efavirenz (Sustiva).

The most common reason for switching was abnormal blood lipid levels (20%), followed by liver toxicity or elevated bilirubin (15%), lipodystrophy (13%), neuropsychiatric symptoms (10%), prevention of drug interactions (8%), gastrointestinal symptoms (7%) and treatment simplification (6%).

At 24 weeks after switching, 99% of participants still had undetectable viral load, falling to 96% at 48 weeks. The median CD4 count remained stable at 24 weeks (589 cells/mm3) and rose to 631 cells/mm3 at 48 weeks.

One person experienced virological failure at week 24 (defined as any HIV RNA measurement >400 copies/ml or two measurements >50 copies/ml), joined by two more participants at week 48. In two of these cases, virological failure was associated with emergence of raltegravir resistance mutations. All three of these people received raltegravir with two NRTIs and had a prior history of virological failure on NRTI-containing regimens; two had pre-existing NRTI resistance mutations.

Among participants with pharmacokinetic data, 17% (including two of the patients with virological failure) had raltegravir minimum concentrations below 50 ng/ml, considered the cut-off for adequate potency.

"In this study, switching to raltegravir [once-daily] maintains virological suppression over 48 weeks as long as raltegravir is associated with a fully active backbone," the researchers concluded, emphasizing that this requires clinicians to determine a patient's entire antiretroviral history and previous genotypic resistance test results.

New raltegravir formulation
Rajesh Krishna and colleagues from Merck conducted a study looking at the pharmacokinetics and effect of food on a new 600mg tablet formulation of raltegravir, part of an assessment of the feasibility of once-daily dosing using a higher dose.

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Dolutegravir matches or surpasses other regimens for first-line HIV treatment

By Liz Highleyman

The recently approved HIV integrase inhibitor dolutegravir (Tivicay) provides at least equivalent antiviral efficacy and better tolerability compared with approved antiretroviral drugs for treatment-naive people, according to data reported at the 14th European AIDS Conference in Brussels during October and in a recent edition of Lancet Infectious Diseases.

Bonaventura Clotet of Hospital Universitari Germans Trias i Pujol, Barcelona, presented a subgroup analysis from the FLAMINGO trial comparing dolutegravir versus ritonavir-boosted darunavir (Prezista) in people new to antiretroviral therapy (ART).

This multicenter, open-label, non-inferiority study enrolled 484 treatment-naive adults with HIV. Most participants (85%) were men, a majority were white, 23% were black and the median age was 34 years. At baseline, the median CD4 cell count was 395 cells/mm3 and one quarter had high viral load (HIV RNA >100,000 copies/ml).

Participants were randomly assigned to receive 50mg dolutegravir or 800/100mg darunavir/ritonavir, both once daily. In addition, they received investigator-selected NRTIs, with 67% using tenofovir/emtricitabine (Truvada) and 33% using abacavir/lamivudine (Kivexa).

Results from the primary analysis, presented in September at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), showed that 90% of people taking dolutegravir and 83% taking darunavir/ritonavir achieved undetectable viral load in a ‘snapshot’ analysis, with dolutegravir meeting the criteria for statistical superiority. CD4 cell gains were the same in both arms at 210 cells/mm3. Fewer people in the dolutegravir arm discontinued due to adverse events (1 vs 4%) and serious drug-related adverse events were rare (one vs none).

Clotet’s late-breaker presentation at EACS focused on pre-specified subgroups. Dolutegravir’s advantage was particularly notable amongst people with high viral load, with a 48-week response rate of 93%, compared to 70% in the darunavir/ritonavir arm. The difference was smaller amongst people with lower viral load, 88 vs 87%, respectively.

The larger difference in the high viral load strata was mainly driven by lower likelihood of virological non-response (7 vs 18%) and fewer drop-outs due to adverse events (0 vs 7%) in the dolutegravir arm. Response rates for people with CD4 counts above and below 350 cells/mm3 were similar to those seen in the primary analysis as a whole (88 vs 80% for <350; 91 vs 84% for >350). Response rates were comparable for younger and older patients, Clotet said (90 vs 81% for <50; 89 vs 92% for >50 years). Rates for men (91 vs 85%) and for white patients (91 vs 84%) were similar to the overall primary analysis. Rates were lower for women (84 vs 73%) and black patients (85 vs 77%), but with the same pattern of differences favoring dolutegravir. There were no differences according to NRTIs used (90 vs 85% with Kivexa; 90 vs 81% with Truvada).

Overall, side-effects in the subgroups were similar to those observed in the analysis as a whole, with most subgroups reporting more adverse events in the darunavir/ritonavir arm. There were no significant differences in adverse events leading to withdrawal by subgroup. Dolutegravir recipients experienced smaller rises in LDL (‘bad’) cholesterol. Some people taking dolutegravir had small increases in serum creatinine, attributed to the drug’s effect on a transporter protein.

Based on these findings the researchers concluded, “Dolutegravir provide a potent and well-tolerated new option for first-line HIV treatment.”

Dolutegravir vs other regimens

Approval of dolutegravir was based in part on favorable first-line therapy results from two randomized controlled trials: SINGLE trial, which tested dolutegravir plus abacavir/lamivudine against Atripla (efavirenz/tenofovir/emtricitabine single tablet regimen), and SPRING-2, comparing dolutegravir against raltegravir (Isentress), the first approved integrase inhibitor.

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The extended 96-week analysis from SPRING-2, published in the November 2013 issue of Lancet Infectious Diseases, showed that 50mg once-daily dolutegravir had non-inferior efficacy and similar tolerability compared to 400mg twice-daily raltegravir, both taken with either tenofovir/emtricitabine or abacavir/lamivudine.

At 96 weeks, 81% of dolutegravir recipients and 76% of raltegravir recipients had viral load below 50 copies/ml, not a significant difference. Median CD4 cell increases were similar (276 and 264 cells/mm³). Virological non-response was less common in the dolutegravir group (5 vs 10%, respectively). None of the dolutegravir recipients who experienced virological failure had new integrase or NRTI resistance mutations.

Just 2% of participants in each treatment arm discontinued due to adverse events, with none in the dolutegravir group and one in the raltegravir group doing so between weeks 48 and 96; no drug-related serious adverse events occurred during this period.

As presented in a poster at last week’s EACS meeting, ViiV Healthcare/GlaxoSmithKline researchers performed a systematic review and ‘network meta-analysis’ to indirectly compare dolutegravir against current preferred first-line regimens.

It is not practical to compare new therapies against every possible competitor, especially older regimens used by fewer people. The researchers therefore used results from the two trials that directly compared dolutegravir against efavirenz or raltegravir, along with data from 46 randomised controlled trials comparing the latter two drugs against other agents, to estimate dolutegravir’s comparative efficacy. They ran the analyses both adjusted and non-adjusted for which NRTI ‘backbone’ was used.

They found that dolutegravir was significantly more likely to lead to viral suppression than the boosted protease inhibitors atazanavir (Reyataz), darunavir (this analysis did not include FLAMINGO) or lopinavir/ritonavir (Kaletra), as well as the NNRTI rifampicine (Edurant, also in Eviplera). Efficacy was similar to that of the other integrase inhibitors, raltegravir and elvitegravir (part of the Stribild co-formulation). Dolutegravir was also associated with higher CD4 cell gains than most comparators.

"Overall, meta-analysis estimates show dolutegravir is comparable to or more effective than all guideline-recommended third-agent options for first-line treatment of HIV-1-infected patients," the researchers concluded.

The future of dolutegravir

In an editorial accompanying the SPRING-2 report in The Lancet Infectious Diseases, Mark Boyd and David Cooper from the Kirby Institute of the University of New South Wales speculated about how dolutegravir might alter standard antiretroviral treatment and provide more options in resource-limited settings. Possibilities might include NRTI-sparing regimens, ART without pharmacokinetic boosting and even dolutegravir monotherapy, they suggested.

In the shorter term, ViiV announced last week that it has requested US regulatory approval of a new single-tablet regimen containing dolutegravir, abacavir and lamivudine. A European regulatory application has also been submitted, according to the company. This combination, taken as separate pills, worked well in the aforementioned trials. If approved, the new co-formulation will offer the first once-pill, once-daily regimen that does not contain tenofovir/emtricitabine (as does Gilead’s trio of Atripla, Complera/Eviplera and Stribild), which could be particularly beneficial for people with, or at risk for, kidney disease or osteoporosis.

References


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Study explores difficulties of certain therapies for those over 65

A note from Alan Franciscus, editor in chief, HCV Advocate:
The study below is interesting because it explores the difficulties that people 65 years and older experience with pegylated interferon plus ribavirin therapy — more side effects and lower efficacy. If someone is considering treatment this information should definitely be factored into the treatment decision process when considering if it is safe (or not) to wait for newer medications that have less side effects and higher cure rates.

Efficacy and safety of peginterferon plus ribavirin for patients aged ≥ 65 years with chronic hepatitis C: A systematic review and meta-analysis.


Source
Shanghai Public Health Clinical Center Affiliated to Fudan University, No. 2901, Gaolang Rd, Jinshan District, 201508 Shanghai, PR China.

ABSTRACT
Methods:
Studies up to August 30, 2012 of the efficacy and safety of peginterferon plus ribavirin therapy in CHC patients aged≥65 years were systematically identified in PubMed, Ovid, Web of Knowledge and Cochrane Library databases. A meta-analysis was performed using both fixed- and random-effects models based on heterogeneity across studies.

Results:
The overall sustained virological response (SVR) in CHC patients aged≥65 years was significantly lower than in patients aged<65 years on both intention-to-treat (ITT; 42.0% vs. 60.1%, respectively; P<0.00001) and per-protocol (PP; 54.4% vs. 67.4%, respectively; P=0.002) analyses, including treatment-naïve patients. Subgroup analysis showed that patients≥65 years with either hepatitis C virus (HCV) genotype 1/4 or 2/3 had lower SVR rates than younger patients. No statistically significant differences were observed between the two groups in terms of rapid virological response (RVR) and early virological response (EVR) rates (both P≥0.05). However, the end-of-treatment virological response (ETR) rate was lower in patients≥65 years, who also had a significantly higher risk of relapse than those aged<65 years (39.8% vs. 26.9%, respectively; P<0.00001). The discontinuation rate in the older patients was also significantly higher than in the younger patients (25.5% vs. 14.8%, respectively; P<0.00001). Ribavirin dose reduction in the older patients treated with peginterferon plus ribavirin was also significantly higher than in younger patients (44.5% vs. 32.8%, respectively; P<0.00001).

Conclusion:
Peginterferon plus ribavirin therapy was effective for older patients with CHC, particularly those with HCV genotype 2/3. Response-guided therapy can be used for older patients with genotype 1/4, but such patients had poorer treatment adherence, leading to poorer treatment efficacy.

Men’s Support Group

2014 Dinners will take place Jan. 6, Feb. 3, March 3, April 8, May 5, June 10, July 7, August 4, September 8, October 6, November 3 and December 1

All meetings will start at 6:30 p.m.

Meeting location will be determined on a month-to-month basis so check your email and HACA’s website, www.HACAcare.org

No social worker will be in attendance
RSVP to Brenda, 703-352-7641 or admin@hacacares.org

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Response rates for all arms remained the same at 24 weeks post-treatment (SVR24). These results compared favorably to historical SVR24 rates of about 70% for people without cirrhosis and 44% for people with cirrhosis in pivotal trials of boceprevir or telaprevir plus pegylated interferon/ribavirin.

The 95% response rates reflected three people who did not achieve SVR12/24. One patient in Cohort 1 who received sofosbuvir/ledipasvir alone for 8 weeks and one in Cohort 2 who received sofosbuvir/ledipasvir for 12 weeks experienced viral relapse, while one person in Cohort 1 who received sofosbuvir/ledipasvir for 12 weeks was lost to follow-up after reaching SVR8. Both relapsers had HCV genotype 1a. No one who took ribavirin relapsed.

Seven of the nine people with NS5A resistance mutations and all 28 people with NS3/4A (protease) resistance mutations at baseline nevertheless achieved sustained response. One patient had evidence of the S282T mutation and multiple NS5A resistance mutations at the time of relapse at week 8. This individual was retreated with sofosbuvir/ledipasvir plus ribavirin for 24 weeks and went on to achieve SVR12.

Sofosbuvir/ledipasvir was generally safe and well-tolerated with or without ribavirin. Two people receiving sofosbuvir/ledipasvir alone and two receiving ribavirin experienced serious adverse events, but no one discontinued treatment for this reason. Grade 3 to 4 adverse events (0 vs 14%) and grade 3 to 4 laboratory abnormalities (7 vs 14%) were more common among those taking ribavirin. Anemia was seen only in the ribavirin arms (19%).

Asked whether ribavirin is still important, Lawitz said these results confirm that "for a large proportion of patients we can remove ribavirin without impacting SVR," and "outside clinical trials, anything we can do to improve compliance is a benefit".

The phase 3 ION trials are currently underway, testing sofosbuvir/ledipasvir with or without ribavirin for 8, 12 or 24 weeks in treatment-naive patients with genotype 1 and prior non-responders, Lawitz noted.

Results from the phase 2 ELECTRON trial, also reported at the Liver Meeting, showed that Gilead’s non-nucleoside polymerase inhibitor GS-9669 as a third agent instead of ribavirin also led to SVR12 rates of 100% for difficult-to-treat genotype 1 patients.

Reference
Lawitz E et al. Once daily sofosbuvir/ledipasvir fixed dose combination with or without ribavirin resulted in ≥95% sustained virologic response in patients with HCV genotype 1, including patients with cirrhosis: the LONESTAR trial. 64th Annual Meeting of the American Association for the Study of Liver Diseases, Washington, DC, abstract 215, 2013.

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low rates of discontinuation, representing a clinically meaningful improvement in both safety and efficacy compared to current standard of care."

Based on these findings, Bristol-Myers Squibb announced during the conference that it has submitted this first interferon- and ribavirin-free regimen for regulatory approval in Japan, where an estimated 1.2 million people are living with hepatitis C.

While these are good results for people with HCV 1b, studies have shown that the dual regimen of daclatasvir/asunaprevir is not as effective against subtype 1a. (Asunaprevir is also not active against HCV genotypes 2 or 3.) However, as also reported at the Liver Meeting, adding a third agent – the non-nucleoside NS5B polymerase inhibitor BMS-791325 – raised sustained response rates to 91% for people with HCV 1a and 100% for 1b. Bristol-Myers Squibb is working on a fixed-dose combination pill containing these three drugs.

Reference
Chayama K et al. All-oral combination of daclatasvir plus asunaprevir in interferon ineligible naive/intolerant and nonresponder Japanese patients chronically infected with HCV genotype 1b: results from a phase 3 trial. 64th Annual Meeting of the American Association for the Study of Liver Diseases, Washington, DC, abstract 211, 2013.

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HCV/HIV Today

er than cure rates seen in historical studies of pegylated interferon plus ribavirin.

Relapse rates were 22% for genotype 1 and 29% for genotype 3 patients, but no one with genotype 2 relapsed. This finding supports the growing awareness that genotypes 2 and 3 should not be classified together as “easier to treat,” as in fact genotype 3 is more difficult.

Most relapses occurred within four weeks after finishing treatment. The two individuals who experienced HCV viral breakthrough while on treatment (one each in the genotype 1 and 2 groups) were found to be non-adherent. No resistance mutations (including S282T) were detected in people with virological failure.

Black race – but not IL28B status – and failure to complete therapy were the only factors that independently predicted non-response. Cirrhosis and HCV subtype 1b (contrary to most studies) were also associated with lower response, but numbers were small and differences did not reach statistical significance.

Sofosbuvir plus ribavirin was generally safe and well tolerated. Across all genotypes, serious adverse events (7% in both the 12- and 24-week treatment arms) and grade 3 and 4 laboratory abnormalities (10 and 13%) were uncommon; 4 and 3%, respectively, discontinued treatment early due to adverse events. The most common side-effects were fatigue, insomnia, headache and nausea, which occurred with similar frequency in the 12- and 24-week arms. Anemia was reported in 10 and 19%, respectively, and elevated bilirubin was seen among people taking atazanavir.

Looking at HIV disease progression, two patients had HIV viral breakthrough and both were found to be non-adherent to ART. Absolute CD4 counts fell (a known effect of ribavirin) but CD4 percentages remained stable.

"The interferon-free regimen of sofosbuvir + ribavirin resulted in high SVR12 rates in HCV treatment-naive, HIV-infected patients with genotype 1, 2 and 3 co-infection," the researchers concluded. "SVR12 rates were similar to those observed in patients with HCV mono-infection."

Reference
Sulkowski MS et al. All-oral therapy with sofosbuvir plus ribavirin for the treatment of HCV genotype 1, 2, and 3 infection in patients co-infected with HIV (PHOTON-1). 64th Annual Meeting of the American Association for the Study of Liver Diseases, Washington, DC, abstract 212, 2013.

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This open-label, single-dose study enrolled 36 healthy HIV-negative volunteers. Participants were randomly assigned to take either three of the marketed 400mg raltegravir oral compressed tablets or two of the reformulated 600mg tablets, in either case receiving a total dose of 1200mg.

The new formulation was found to be generally safe and well tolerated, with no clinical or laboratory serious adverse events reported and no discontinuations for this reason.

Taken while fasting, 1200mg doses of the new tablet and the old tablet led to similar drug exposure levels. The researchers noted that a recently concluded multiple-dose study found that steady-state 24-hour concentrations were virtually the same, 82 nM using the old tablet and 83 nM using the new version.

The reformulated tablet was less affected by food, however. A low-fat meal reduced the 'area under the curve' (AUC) or overall drug exposure by 71% using the old tablet versus 40% using the new tablet. Administration with a high-fat meal, in contrast, increased AUC by 26% using the old tablet but by only 3% using the new formulation.

The clinical significance of changes in drug exposure with meals is being further investigated, they said.

In a press release issued to coincide with the conference, Merck indicated that it plans to initiate a phase 3 clinical trial of once-daily raltegravir in early 2014.

References

Hemophilia Association of the Capital Area
2014 Calendar of Events

January
11-12 NBC4 Health and Fitness Expo, Washington, DC
13 Board Meeting, Location TBD—7 pm
15 Deadline for Qualley Scholarship
16 KUWYH Dinner, Persistent Pain, Buca di Bepo, Washington DC – 6:30 pm
19-20 Richmond Days; Visits to Assembly Members, Richmond, VA
25 KUWYH Dinner: Deciding if you are Camp Ready, Location/Time TBD

February
1 Board of Directors Planning Meeting
3 Men’s Dinner, Location TBD – 6:30 pm
6 KUWYH Dinner, Nutrition & Weight, Royal Restaurant, Alexandria, VA 6:30 pm.
20 KUWYH Dinner, Inhibitors, Maggiano’s Restaurant, Chevy Chase, MD – 6:30 pm.
Program given in English. Spanish interpreter will be present.
(Parking to be covered by HACA.)
22 New Family Luncheon, PF Changs/Fairfax, Noon- 2 pm
26-28 NHF Washington Days

March
3 Men’s Dinner, Location TBD – 6:30 pm
13 KUWYH Dinner, Spanish Language: Self Advocacy, Virginia, Location/Time TBD
27-28 Region 3 HTC Annual Meeting, Alexandria, VA
27-29 HFA Symposium

April
4-5 Adult Retreat – Location TBD
7 Board Meeting, 7:00 pm – Location TBD
8 Men’s Dinner, Location TBD – 6:30 pm)
12-13 Teen Retreat – Location TBD (in conjunction with HFM and VHF)
17 World Hemophilia Day
17 KUWYH Lunch, Transition Children to Independence, Washington, DC,
Location/Time TBD

All events are free to HACA members. To join or register for an event, contact us at
703-352-7641 or admin@hacacares.org