A newsletter from **EUGENE GASTROENTEROLOGY CONSULTANTS, P.C.**, the largest and most experienced digestive specialty group in Lane County.

for your digestion

October 2011 Vol. I, Ed. III

New agents for Hepatitis C: **triple** therapy/**twice** as good/**one** big bill

By William Wu, M.D. Eugene Gastroenterology Consultants, P.C.

Hepatitis C is a silent epidemic, infecting nearly 4 million Americans. Chronic Hepatitis C (CHC) often follows a progressive course, which may lead to cirrhosis, hepatocellular carcinoma and liver failure, resulting in death or the need for transplantation. As CHC treatment options expand, choosing the right treatment becomes more complicated.

With the recent approval of two protease inhibitors (telaprevir = Incivek; boceprevir = Victrelis) and accompanying marketing frenzy, deciding on the correct treatment regimen has become profoundly more difficult. The following will provide a foundation to help you understand these two new drugs.

About Chronic Hepatitis C

It is important to review some basic information about CHC to facilitate discussion on current treatment recommendations.

- **Chronic Hep C is a common and typically asymptomatic disease.**
- **The disease process will not influence the longevity nor the well-being of patients 80–85% of the time. Therefore, not all patients with CHC should be considered for treatment, only those at higher risk of progression to cirrhosis and complications.**
- **Response to treatment is determined by a number of factors, with genotype being paramount. Genotypes 1 and 4 are the least responsive to therapy, whereas genotypes 2 and 3 require shorter treatment intervals and demonstrate higher response rates.**

Drug interactions and side effects

With the introduction of telaprevir (Incivek) and boceprevir (Victrelis) to the U.S. market in May, it is important to discuss the role of these viral replication inhibitors. Telaprevir and boceprevir are to be used with pegylated interferon and ribavirin. Protease inhibitors should never be used as monotherapy in the treatment of CHC.

Therefore, overall side effects for this new "triple therapy" will include all the commonly known side effects of dual therapy, in addition to side effects and risks specific to these protease inhibitors: severe rash (including Stevens-Johnson syndrome), nausea, vomiting, cytopenias (beyond those typically encountered with dual therapy), anorectal discomfort including pruritis ani, dysgeusia, mucositis, profound drug-drug interactions, and development of resistance. This latter complication is of particular concern because both protease inhibitors are to be taken on a three-times-a-day schedule (with food). For this reason, patients who are selected for triple therapy should be deemed reliable, consistent and fully committed to the treatment regimen. Otherwise, non-compliance will likely lead to drug resistance.

Improvements in treatment

The goal of treatment is a sustained virological response (SVR), which is the absence of detectible Hep C virus 24 weeks after treatment. The excitement generated by these two drugs comes from significant treatment success (see chart on back page summarizing dual and triple therapy). As you can see, adding a protease inhibitor to dual therapy significantly increases SVR in nearly all categories (naïve, relapsers, partial responders and null responders). To date, there are no head-to-head studies, so we cannot comment on which may be superior. Telaprevir and boceprevir are probably equivalent, with the SVRs more likely related to the different study protocols than to actual drug effect.

Cost is a factor

Unfortunately, these new agents will triple or quadruple the cost of treatment. Currently, pegylated interferon plus ribavirin cost approximately $600 per week (with treatment for genotype 1 requiring 48 weeks). Telaprevir (Incivek) will cost $49,200 for 12 weeks of treatment in addition to the baseline costs of Peg/Riba ($28,800), totaling nearly $80,000 for a single-course treatment.

Perhaps offsetting the profound cost increases, to some extent, will be a new paradigm of Response Guided Therapy (RGT) that would adjust treatment

CONTINUED ON BACK

We invite your comments and suggestions for topics in future editions. Also, if you would rather receive this newsletter electronically or not at all, email newsletter@eugenegi.com.

Kimberly catching rainbow trout on the Deschutes with fly fishing guide Dan Anthon.

Meet Kimberly Hanson, A.N.P.

A natural detective, Kimberly Hanson enjoys collecting data as much as she loves the outdoors. A patient-focused problem solver and an adventurous traveler, Kimberly came to EGC seven years ago from Alaska, where she was the only medical provider in a village of 350 that was accessible only by air. Kimberly is EGC's resident Hepatitis C expert. In this role, she is responsible for selecting patients and monitoring the treatment of Hepatitic C. In addition to providing general gastroenterology care, she has supervised Interferon/Ribavirin dual therapy in more than 200 patients with Hepatitis C. The most rewarding part of her job, she says, is successfully treating patients so they can live happy, healthy lives.

EUGENE GASTROENTEROLOGY CONSULTANTS, P.C. • 541-868-9500 • www.EugeneGI.com
3355 RiverBend Drive, Suite 500, Springfield, OR 97477 • Northwest Specialty Clinics Bldg, 5th floor

CONTINUED FROM FRONT

duration based on clinical response. That is, triple therapy may be foreshortened due to favorable response, or stopped altogether in those who do not respond. Despite this exorbitant expense, it's wise to remember the old adage: "The most expensive treatment is the one that doesn't work."

While triple therapy will certainly become the new standard of care for Hepatitis C, enthusiasm needs to be tempered by the recognition of specific caveats regarding side effects, development of drug resistance, extensive and profound drug-drug interactions and extremely high cost. Given this complexity, Eugene Gastroenterology Consultants would be happy to assist you in deciding which chronic Hepatitis C patients warrant treatment. We can also guide them through the maze of treatment options.

Response to Treatment

Sustained Virological Response (SVR)

	Dual Therapy (Interferon/ Ribavirin)	Triple Therapy with Telaprevir (Incivek)	Triple Therapy with Boceprevir (Victrelis)
Not previously treated			
Genotype 1 (non-black) (black)	40 – 50% 23%[B]	69 – 75%[A] Not studied	67 – 68%[B] 42 – 53%[B]
Genotypes 2 and 3	75 – 80%	Not indicated *(FDA approved only for genotype 1)*	Not indicated
Previously treated Genotype 1 patients only			
Relapser	20[C] – 24%[D]	69[C] – 88%[D]	69 – 75%[E]
Partial Responder	15[D] – 40%[C]	54[D] – 62%[C]	40 – 52%[E]
Null Responder	5[D] – 9%[C]	31[D] – 39%[C]	Not studied
Treatment Cost	$600/week	$49,200/12 wks	$1,100/week
24 week regimen	$14,400	$63,600@	$43,200#
48 week regimen	$28,800	$78,000&	$77,200*

[A] NEJM 2011; 364:2405-16
[B] NEJM 2011; 364:1195-1206
[C] NEJM 2011; 362:1292-303
[D] NEJM 2011; 364:2417-28
[E] NEJM 2011; 364:1207-17

@ Telapravir + Peg/Riba x 12 wks, then 12 wks of Peg/Riba alone
# Peg/Riba x 4 wks, then Boceprevir + Peg/Riba x 24 wks
& Telaprevir + Peg/Riba x 12 wks, then 36 wks of Peg/Riba alone
* Peg/Riba x 4 wks, then Boceprevir + Peg/Riba x 44 wks

Chronic Hepatitis C Definitions

During treatment:

Rapid Virological Response (RVR) – HCV RNA negative after 4 weeks of treatment

Early Virological Response (EVR) – HCV RNA positive at 4 weeks, but negative at 12 weeks

After completion of treatment:

Sustained Virological Response (SVR) – HCV RNA negative 24 weeks after completion of therapy; this is the goal of treatment

Relapse – HCV RNA negative at end-of-treatment, but subsequent return of detectible RNA

Partial response – HCV negative or 100-fold decrease in HCV RNA by week 12 of treatment, but HCV positive at end of treatment

Null response – absence of at least 100-fold decrease in HCV RNA by week 12 of treatment

Our Registration Department serves as the first point of contact for patients who come to EGC. Meet (left to right) Angela Williamson, Jenn Mills, Terri Martin and Suzy Vandehey.

Eugene Gastroenterology Consultants, P.C.
3355 RiverBend Drive, Suite 500
Springfield, OR 97477