



Summary of Recently Published Studies on Treatments for Hepatitis C

Working Document

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Introduction

This working document was produced to supplement [Treatment for Hepatitis C Virus Infection in Adults](#) by Roger Chou, MD, Daniel Hartung, PharmD, MPH, Basmah Rahman, MPH, Ngoc Wasson, MPH, Erika Cottrell, PhD, and Rongwei Fu, PhD, published by Agency for Healthcare Research and Quality in November 2012. Chou et al., was based on research published through August 2012 on antiviral agents approved by the FDA prior to this time. This document summarizes studies published since August 2012 and includes information on several more recent antiviral agents.

To prepare this document, a search of the Medline and Cochrane Collaboration databases was performed for the period August 2012 through August 2014 using search terms for hepatitis C and terms for either randomized controlled trials or controlled clinical trials. Non-human studies and non-English-language citations were excluded. The search included no restrictions on the treatments used in the studies.

The search produced a total of 2,112 citations. The titles and abstracts of all citations were screened for possible relevance, based on whether the study examined the treatment of hepatitis C with any antiviral agent or combination of agents. Studies that examined treatment with regimens containing only interferon and/or ribavirin were excluded. Studies were included if they contained data about efficacy and/or harms of the treatments. The screening was not performed in duplicate.

Following the screening of the titles and abstracts, a total of 101 citations were judged possibly relevant. All were retrieved and reviewed in full text, and 39 then judged to include non-duplicated data on the efficacy or harms of one or more antiviral agents. These studies examined a total of 19 different therapeutic agents. The results were compiled only for those agents examined in at least two studies, which included a total of 36 of the relevant studies. Of the studies that examined treatment efficacy, all used sustained virologic response at either 12 or 24 weeks as the primary outcome measure. The scope of these studies is briefly summarized below.

Telaprevir and **boceprevir** are protease inhibitors that were approved for use in the United States in 2011. Of a total of eight studies, two were comparisons of regimens containing telaprevir to regimens containing boceprevir, and the remaining six examined regimens containing telaprevir (but not boceprevir). These studies enrolled a total of 3749 participants. All but one study examined combination regimens in which telaprevir or boceprevir were combined with interferon and ribavirin. One study was a randomized trial comparing a triple drug combination containing telaprevir to a triple drug combination containing boceprevir. These studies provide evidence that both telaprevir and boceprevir improve response rates when added to the combination of interferon and ribavirin. The studies also provide information about treatment-related harms, including renal impairment, anemia, and skin reactions (including rare cases of severe skin reactions).

Sofosbuvir is an oral nucleotide analogue inhibitor of the HCV-specific NS5B polymerase that was approved for use in the United States in 2013. Seven studies of sofosbuvir were identified. These studies enrolled a total of 2,009 patients. Three studies focused exclusively on patients diagnosed with HCV genotype 1, and four focused exclusively on patients diagnosed with HCV genotypes 2 and 3. All studies of HCV genotype 1 patients, two of which were RCTs, examined the combination of sofosbuvir and the NS5A replication complex inhibitor **ledipasvir**, with and without ribavirin. Three of the four studies in HCV genotype 2 and 3 patients compared the combination of sofosbuvir and ribavirin; one study also included interferon. The fourth study examined the combination of sofosbuvir and **daclatasvir**. These studies provide evidence that most patients, even those who previously failed interferon-based treatment regimens, can achieve sustained virologic response when treated with sofosbuvir-based treatment regimens. All studies also provide information about rates of common side effects associated with sofosbuvir regimens, the most common of which were headache, fatigue, and nausea. In 2013, the FDA approved the combination of sofosbuvir and ribavirin for the treatment of Hepatitis C genotypes 2 and 3. It also approved the combination of sofosbuvir, ribavirin, and interferon for the treatment of genotypes 1 and 4. On October 10, 2014, the FDA approved the combination of sofosbuvir and ledipasvir for the treatment of genotype 1 patients.

Daclatasvir is a NS5A replication complex inhibitor that has not yet been approved by the FDA for clinical use in the United States. Seven studies of daclatasvir that included 541 participants were identified. The studies examined the use of daclatasvir in combination with **asunaprevir** (a protease inhibitor not yet approved by the FDA), sofosbuvir, or interferon/ribavirin. Clinical trials have shown that the combination of daclatasvir and asunaprevir is highly efficacious for achieving a virologic response among people with genotype 1b but may be less efficacious among people with other genotypes. Adverse effects include hepatic abnormalities, fatigue, headaches, and nausea. The combination of daclatasvir and asunaprevir has been proposed as a fixed drug combination for treating hepatitis C.

Paritaprevir (ABT-450) is a protease inhibitor that has not yet been approved by the FDA for clinical use in the United States. Five studies of paritaprevir were identified. These studies enrolled a total of 2,190 patients. All studies examined the combination regimen of paritaprevir and the protease inhibitor **ritonavir**. Two of these were placebo controlled studies of paritaprevir and ritonavir in combination with **dasabuvir**, **ombitasvir**, and ribavirin. Dasabuvir is a nonnucleoside polymerase inhibitor, and ombitasvir is a NS5A replication complex inhibitor. One of these two studies was a four-arm trial of paritaprevir and ritonavir in combination with dasabuvir, ribavirin, and ombitasvir. One study evaluated paritaprevir, ritonavir, ombitasvir, daclatasvir with or without ribavirin. These studies provide evidence that the combination regimen of paritaprevir and ritonavir improve response rates when combined with: ombitasvir, daclatasvir, and ribavirin; dasabuvir and ribavirin; or ombitasvir, dasabuvir, and ribavirin. The studies also provide information about adverse events, with four studies reporting serious adverse events, three studies reporting grade 3/4 adverse events, and three studies reporting grade 3/4 laboratory abnormalities.

Faldaprevir (a protease inhibitor) and/or **deleobuvir** (a NS5B polymerase inhibitor) were examined in a total of five studies. Both have been withdrawn from further development by the manufacturers because of poor efficacy. Information from these studies was not compiled.



In conclusion, since August 2012, there has been a large body of clinical research on many antiviral agents with potential usefulness for treating hepatitis C. This research has led to several agents moving through the regulatory approval process. Two agents (sofosbuvir and ledipasvir) have recently received FDA approval as components of multi-drug regimens.

Included Studies

1. Afdhal, N, Kr Reddy, Dr Nelson, E Lawitz, Sc Gordon, E Schiff, R Nahass, *et al.* "Ledipasvir and Sofosbuvir for Previously Treated Hcv Genotype 1 Infection." Clinical Trial, Phase III; Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't, *The New England journal of medicine* 370, no. 16 (2014): 1483-93. doi:10.1056/NEJMoa1316366, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/291/CN-00989291/frame.html>.
2. Asselah, T. "Sofosbuvir-Based Interferon-Free Therapy for Patients with Hcv Infection." Journal: Note, *Journal of hepatology* 59, no. 6 (2013): 1342-5. doi:10.1016/j.jhep.2013.07.023, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/172/CN-00915172/frame.html>.
3. Belperio, P. S., E. W. Hwang, I. C. Thomas, L. A. Mole, R. C. Cheung, and L. I. Backus. "Early Virologic Responses and Hematologic Safety of Direct-Acting Antiviral Therapies in Veterans with Chronic Hepatitis C." [In eng]. *Clin Gastroenterol Hepatol* 11, no. 8 (Aug 2013): 1021-7.
4. Buti, M., K. Agarwal, Y. Horsmans, W. Sievert, E. Janczewska, S. Zeuzem, L. Nyberg, *et al.* "Telaprevir Twice Daily Is Noninferior to Telaprevir Every 8 Hours for Patients with Chronic Hepatitis C." [In eng]. *Gastroenterology* 146, no. 3 (Mar 2014): 744-53 e3.
5. Colombo, M., I. Fernandez, D. Abdurakhmanov, P. A. Ferreira, S. I. Strasser, P. Urbanek, C. Moreno, *et al.* "Safety and on-Treatment Efficacy of Telaprevir: The Early Access Programme for Patients with Advanced Hepatitis C." [In eng]. *Gut* 63, no. 7 (Jul 2014): 1150-8.
6. De Meyer, S., A. Ghys, G. R. Foster, M. Beumont, B. Van Baelen, T. I. Lin, I. Dierynck, H. Ceulemans, and G. Picchio. "Analysis of Genotype 2 and 3 Hepatitis C Virus Variants in Patients Treated with Telaprevir Demonstrates a Consistent Resistance Profile across Genotypes." [In eng]. *J Viral Hepat* 20, no. 6 (Jun 2013): 395-403.
7. Dusheiko, G, N Afdhal, Eg Giannini, Pj Chen, K-H Han, M Rodriguez-Torres, S Rugina, *et al.* "Results of Enable 2, a Phase 3, Multicenter Study of Eltrombopag and Peginterferon Alfa-2b Treatment in Patients with Hepatitis C and Thrombocytopenia." *Journal of hepatology* 56, no. Suppl 2 (2012): S27. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/666/CN-00844666/frame.html>.
8. Everson, G. T., K. D. Sims, M. Rodriguez-Torres, C. Hezode, E. Lawitz, M. Bourliere, V. Loustaud-Ratti, *et al.* "Efficacy of an Interferon- and Ribavirin-Free Regimen of Daclatasvir, Asunaprevir, and Bms-791325 in Treatment-Naive Patients with Hcv Genotype 1 Infection." [In eng]. *Gastroenterology* 146, no. 2 (Feb 2014): 420-9.
9. Feld, Jj, Kv Kowdley, E Coakley, S Sigal, Dr Nelson, D Crawford, O Weiland, *et al.* "Treatment of Hcv with Abt-450/R-Ombitasvir and Dasabuvir with Ribavirin." Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't, *The New England journal of medicine* 370, no. 17 (2014): 1594-603. doi:10.1056/NEJMoa1315722, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/779/CN-00988779/frame.html>.
10. Ferenci, P., D. Bernstein, J. Lalezari, D. Cohen, Y. Luo, C. Cooper, E. Tam, *et al.* "Abt-450/R-Ombitasvir and Dasabuvir with or without Ribavirin for Hcv." [In eng]. *N Engl J Med* 370, no. 21 (May 22 2014): 1983-92.

11. Gane, Ej, P Pockros, S Zeuzem, P Marcellin, A Shikhman, C Bernaards, Es Yetzer, *et al.* "Interferon-Free Treatment with a Combination of Mericitabine and Danoprevir/R with or without Ribavirin in Treatment-Naive Hcv Genotype 1-Infected Patients." *Journal of hepatology* 56, no. Suppl 2 (2012): S555-s56. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/727/CN-00844727/frame.html>.
12. Gane, Ej, Ca Stedman, Rh Hyland, X Ding, E Svarovskaia, Gm Subramanian, Wt Symonds, Jg McHutchison, and Ps Pang. "Efficacy of Nucleotide Polymerase Inhibitor Sofosbuvir Plus the Ns5a Inhibitor Ledipasvir or the Ns5b Non-Nucleoside Inhibitor Gs-9669 against Hcv Genotype 1 Infection." *Journal: Article, Gastroenterology* 146, no. 3 (2014): 736-43.e1. doi:<http://dx.doi.org/10.1053/j.gastro.2013.11.007>, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/325/CN-00982325/frame.html>.
13. Jacobson, I. M., S. C. Gordon, K. V. Kowdley, E. M. Yoshida, M. Rodriguez-Torres, M. S. Sulkowski, M. L. Schiffman, *et al.* "Sofosbuvir for Hepatitis C Genotype 2 or 3 in Patients without Treatment Options." [In eng]. *N Engl J Med* 368, no. 20 (May 16 2013): 1867-77.
14. Kowdley, K. V., S. C. Gordon, K. R. Reddy, L. Rossaro, D. E. Bernstein, E. Lawitz, M. L. Schiffman, *et al.* "Ledipasvir and Sofosbuvir for 8 or 12 Weeks for Chronic Hcv without Cirrhosis." [In eng]. *N Engl J Med* 370, no. 20 (May 15 2014): 1879-88.
15. Kowdley, K. V., E. Lawitz, F. Poordad, D. E. Cohen, D. R. Nelson, S. Zeuzem, G. T. Everson, *et al.* "Phase 2b Trial of Interferon-Free Therapy for Hepatitis C Virus Genotype 1." [In eng]. *N Engl J Med* 370, no. 3 (Jan 16 2014): 222-32.
16. Larrey, D, Aw Lohse, C Trepo, J-P Bronowicki, K Arasteh, M Bourliere, Jl Calleja, *et al.* "Antiviral Effect, Safety, and Pharmacokinetics of Five-Day Oral Administration of Deleobuvir (Bi 207127), an Investigational Hepatitis C Virus Rna Polymerase Inhibitor, in Patients with Chronic Hepatitis C." *Journal: Article, Antimicrobial agents and chemotherapy* 57, no. 10 (2013): 4727-35. doi:10.1128/AAC.00565-13, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/367/CN-00916367/frame.html>.
17. Lawitz, E, Ff Poordad, Ps Pang, Rh Hyland, X Ding, H Mo, Wt Symonds, Jg McHutchison, and Fe Membreño. "Sofosbuvir and Ledipasvir Fixed-Dose Combination with and without Ribavirin in Treatment-Naive and Previously Treated Patients with Genotype 1 Hepatitis C Virus Infection (Lonestar): An Open-Label, Randomised, Phase 2 Trial." *Clinical Trial, Phase II; Randomized Controlled Trial; Research Support, Non-U.S. Gov't, Lancet* 383, no. 9916 (2014): 515-23. doi:10.1016/S0140-6736(13)62121-2, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/401/CN-00978401/frame.html>.
18. Lenz, O, B Fevery, L Vijgen, J Verbeeck, M Peeters, M Beumont-Mauviel, S Zeuzem, and G Picchio. "Tmc435 in Patients Infected with Hcv Genotype 1 Who Have Failed Previous Pegylated Interferon/Ribavirin Treatment: Virologic Analyses of the Aspire Trial." *Journal of hepatology* 56, no. Suppl 2 (2012): S5. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/664/CN-00844664/frame.html>.
19. Lok, A, D Gardiner, C Hezode, E Lawitz, M Bourliere, and G Everson. "Confirmation That Quadruple Therapy with Daclatasvir (Ns5a Inhibitor), Asunaprevir (Ns3 Inhibitor) and Peginterferon/Ribavirin Results in High Rate of Svr4 in Hcv Genotype 1 Null Responders." *Journal of hepatology* 56, no. Suppl 2 (2012): S557. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/728/CN-00844728/frame.html>.
20. Lok, As, Df Gardiner, C Hezode, Ej Lawitz, M Bourliere, Gt Everson, P Marcellin, *et al.* "Randomized Trial of Daclatasvir and Asunaprevir with or without Pegifn/Rbv for Hepatitis C Virus Genotype 1 Null Responders." *Journal: Article, Journal of hepatology* 60, no. 3 (2014): 490-9. doi:<http://dx.doi.org/10.1016/j.jhep.2013.10.019>, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/766/CN-00982766/frame.html>.
21. Lok, As, Df Gardiner, E Lawitz, C Martorell, Gt Everson, R Ghalib, R Reindollar, *et al.* "Preliminary Study of Two Antiviral Agents for Hepatitis C Genotype 1." *Clinical Trial, Phase II; Randomized Controlled Trial; Research Support, Non-U.S. Gov't, New England journal of medicine* 366, no. 3 (2012): 216-24.

doi:10.1056/NEJMoa1104430, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/120/CN-00804120/frame.html>.

22. Mauss, S., D. Hueppe, and U. Alshuth. "Renal Impairment Is Frequent in Chronic Hepatitis C Patients under Triple Therapy with Telaprevir or Boceprevir." [In eng]. *Hepatology* 59, no. 1 (Jan 2014): 46-8.
23. Nelson, Dr, E Lawitz, V Bain, N Gitlin, T Hawkins, and P Marotta. "High Svr12 with 16 Weeks of Tegobuvir and Gs-9256 with Peginterferon-Alfa 2a and Ribavirin in Treatment-Naïve Genotype 1 Hcv Patients." *Journal of hepatology* 56, no. Suppl 2 (2012): S6-s7.
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/665/CN-00844665/frame.html>.
24. Pol, S, Rh Ghalib, Vk Rustgi, C Martorell, Gt Everson, Ha Tatum, C Hézode, et al. "Daclatasvir for Previously Untreated Chronic Hepatitis C Genotype-1 Infection: A Randomised, Parallel-Group, Double-Blind, Placebo-Controlled, Dose-Finding, Phase 2a Trial." Clinical Trial, Phase II; Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't, *Lancet infectious diseases* 12, no. 9 (2012): 671-7.
doi:10.1016/S1473-3099(12)70138-X, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/932/CN-00879932/frame.html>.
25. Poordad, F., E. Lawitz, K. V. Kowdley, D. E. Cohen, T. Podsadecki, S. Siggelkow, M. Heckaman, et al. "Exploratory Study of Oral Combination Antiviral Therapy for Hepatitis C." [In eng]. *N Engl J Med* 368, no. 1 (Jan 3 2013): 45-53.
26. Saibara, T, N Enomoto, S Kaneko, K Chayama, M Sata, M Imaiari, S Onishi, and K Okita. "Clinical Efficacy of Combination Therapy with Me3738 and Pegylated Interferon-Alpha-2a in Patients with Hepatitis C Virus Genotype 1." Journal: Article, *Hepatology research* 44, no. 4 (2014): 410-9.
doi:<http://dx.doi.org/10.1111/hepr.12139>,
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/500/CN-00984500/frame.html>.
27. Soriano, V, E Gane, P Angus, F Stickel, J Bronowicki, S Roberts, M Manns, et al. "The Efficacy and Safety of the Interferon-Free Combination of Bi201335 and Bi207127 in Genotype 1 Hcv Patients with Cirrhosis - Interim Analysis from Sound-C2." *Journal of hepatology* 56, no. Suppl 2 (2012): S559-s60.
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/731/CN-00844731/frame.html>.
28. Sulkowski, M. S., D. F. Gardiner, M. Rodriguez-Torres, K. R. Reddy, T. Hassanein, I. Jacobson, E. Lawitz, et al. "Daclatasvir Plus Sofosbuvir for Previously Treated or Untreated Chronic Hcv Infection." [In eng]. *N Engl J Med* 370, no. 3 (Jan 16 2014): 211-21.
29. Sulkowski, Ms, T Asselah, J Lalezari, P Ferenci, H Fainboim, B Leggett, F Bessone, et al. "Faldaprevir Combined with Pegylated Interferon Alfa-2a and Ribavirin in Treatment-Naïve Patients with Chronic Genotype1 Hcv: Silen-C1 Trial." *Hepatology* 57, no. 6 (2013): 2143-54.
doi:<http://dx.doi.org/10.1002/hep.26276>,
<http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/677/CN-00905677/frame.html>.
30. Sulkowski, Ms, M Bourlière, Jp Bronowicki, T Asselah, Jm Pawlotsky, Sd Shafran, S Pol, et al. "Faldaprevir Combined with Peginterferon Alfa-2a and Ribavirin in Chronic Hepatitis C Virus Genotype-1 Patients with Prior Nonresponse: Silen-C2 Trial." Clinical Trial, Phase II; Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't, *Hepatology (Baltimore, Md.)* 57, no. 6 (2013): 2155-63.
doi:10.1002/hep.26386, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/020/CN-00877020/frame.html>.
31. Sulkowski, Ms, Ke Sherman, V Soriano, J Rockstroh, Dt Dieterich, and P-M Girard. "Telaprevir in Combination with Peginterferon Alfa-2a/Ribavirin in Hcv/Hiv Co-Infected Patients: Svr24 Final Study Results." *Hepatology (Baltimore, Md.)* 56, (2012): 219a. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/265/CN-00861265/frame.html>.

32. Sullivan, Gj, M Rodrigues-Torres, E Lawitz, F Poordad, M Kapoor, and A Campbell. "Abt-267 Combined with Pegylated Interferon Alpha-2a/Ribavirin in Genotype 1 (Gt1) Hcv-Infected Treatment-Naive Subjects: 12 Week Antiviral and Safety Analysis." *Journal of hepatology* 56, no. Suppl 2 (2012): S480. <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/712/CN-00844712/frame.html>.
33. Suzuki, Y., K. Ikeda, F. Suzuki, J. Toyota, Y. Karino, K. Chayama, Y. Kawakami, *et al.* "Dual Oral Therapy with Daclatasvir and Asunaprevir for Patients with Hcv Genotype 1b Infection and Limited Treatment Options." [In eng]. *J Hepatol* 58, no. 4 (Apr 2013): 655-62.
34. Torii, H., H. Sueki, H. Kumada, Y. Sakurai, K. Aoki, I. Yamada, and M. Ohtsuki. "Dermatological Side-Effects of Telaprevir-Based Triple Therapy for Chronic Hepatitis C in Phase Iii Trials in Japan." [In eng]. *J Dermatol* 40, no. 8 (Aug 2013): 587-95.
35. Toyota, J., I. Ozeki, Y. Karino, Y. Asahina, N. Izumi, S. Takahashi, Y. Kawakami, *et al.* "Virological Response and Safety of 24-Week Telaprevir Alone in Japanese Patients Infected with Hepatitis C Virus Subtype 1b." [In eng]. *J Viral Hepat* 20, no. 3 (Mar 2013): 167-73.
36. Zeuzem, S, T Asselah, P Angus, J-P Zarski, D Larrey, B Mullhaupt, E Gane, *et al.* "Faldaprevir (Bi 201335), Deleobuvir (Bi 207127) and Ribavirin Oral Therapy for Treatment-Naive Hcv Genotype 1: Sound-C1 Final Results." *Journal: Article, Antiviral therapy* 18, no. 8 (2013): 1015-9. doi:<http://dx.doi.org/10.3851/IMP2567>, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/998/CN-00977998/frame.html>.
37. Zeuzem, S, Gm Dusheiko, R Salupere, A Mangia, R Flisiak, Rh Hyland, A Illeperuma, *et al.* "Sofosbuvir and Ribavirin in Hcv Genotypes 2 and 3." *Clinical Trial, Phase III; Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't, The New England journal of medicine* 370, no. 21 (2014): 1993-2001. doi:10.1056/NEJMoa1316145, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/148/CN-00993148/frame.html>.
38. Zeuzem, S, Im Jacobson, T Baykal, Rt Marinho, F Poordad, M Bourlière, Ms Sulkowski, *et al.* "Retreatment of Hcv with Abt-450/R-Ombitasvir and Dasabuvir with Ribavirin." *Clinical Trial, Phase III; Multicenter Study; Randomized Controlled Trial; Research Support, Non-U.S. Gov't, The New England journal of medicine* 370, no. 17 (2014): 1604-14. doi:10.1056/NEJMoa1401561, <http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/778/CN-00988778/frame.html>.
39. Zeuzem, S., V. Soriano, T. Asselah, J. P. Bronowicki, A. W. Lohse, B. Mullhaupt, M. Schuchmann, *et al.* "Faldaprevir and Deleobuvir for Hcv Genotype 1 Infection." [In eng]. *N Engl J Med* 369, no. 7 (Aug 15 2013): 630-9.