Sofosbuvir (Sovaldi®) is the first polymerase inhibitor approved as a component of antiviral therapy for treating patients infected with hepatitis C virus (HCV). Advantages of sofosbuvir include oral administration, shorter treatment durations, and higher sustained virologic response (SVR) rates compared to traditional therapies. The standard therapy for HCV infection, interferon + ribavirin, has an SVR rate of 85% in treatment-naive patients, and 55-60% in patients with prior treatments. In patients unable to take interferon containing therapies, sofosbuvir + ribavirin therapies resulted in an SVR rate of 78%. When sofosbuvir is used in combination with ribavirin and interferon the reported SVR rate was 90% in treatment-naive patients. Overviews of the NEUTRINO and POSITRON trials are provided in Table 1 (page 6).

NEUTRINO Trial:  
In a single-group, open-label study, the SVR rate was evaluated in patients receiving sofosbuvir + peginterferon + ribavirin. Oral sofosbuvir 400 mg and oral ribavirin (1000 mg daily for patients less than 75 kg and 1200 mg daily for patients 75 kg or over) were administered daily. Peginterferon 180 mcg was administered subcutaneously once weekly. For patients without cirrhosis, the SVR was 92%. Patients with cirrhosis had lower rates of SVR (80%) after 12 weeks. The rates of SVR did not differ significantly according to race, ethnicity, or HCV genotype. Limitations of this study included the absence of a control group, patients with predominantly HCV genotype 1 (89%), and the addition of sofosbuvir to combination therapy already established as effective.

POSITRON Trial:  
The rates of SVR were compared in patients taking either sofosbuvir + ribavirin or placebo in a randomized, double-blinded trial. Patients who had previously discontinued interferon therapy due to side effects, who had concurrent medical conditions precluding treatment with an interferon-containing regimen, or who had decided against interferon-based regimens were included. Prior treatment failures with interferon regimens were not considered a reason for exclusion. Sofosbuvir 400 mg was administered daily in combination with ribavirin 1000 mg per day for patients with a body weight of less than 75 kg and 1200 mg per day for patients a body weight of 75 kg or more. HCV genotype 3 infection was associated with a significantly lower SVR rate compared to HCV genotype 2 (93% for genotype 2, 63% for genotype 3). Patients with cirrhosis also had lower SVR rates compared to those without cirrhosis (81% without cirrhosis, 61% with cirrhosis). Limitations were the exclusion of several HCV genotypes and use of placebo as a comparative therapy.

Adverse Effects:  
Relatively few patients (2%) discontinued treatment during the NEUTRINO and POSITRON trials. Reasons for discontinuation included fatigue, insomnia, and anemia. Other common adverse events, such as nausea, diarrhea, and rash, occurred in similar numbers between patients receiving treatment and patients receiving placebo in the POSITRON trial. Decreased hemoglobin concentration was reported in 7% of patients taking sofosbuvir + ribavirin in comparison to placebo. Compared to the POSITRON trial, adverse events were more pronounced in the NEUTRINO trial where peginterferon was added to the sofosbuvir + ribavirin combination. Furthermore, effects on lymphocyte, neutrophil, platelet, and white cell counts were only observed in patients also receiving peginterferon.

Dosing and Administration:  
The recommended dose of sofosbuvir is 400 mg once daily by mouth. Sofosbuvir should be taken in combination with ribavirin or in combination with peginterferon and ribavirin for the treatment of HCV genotype 1, 2, 3 or 4 infections. The treatment regimen and duration are dependent on viral genotype and patient-specific factors. The recommended regimens and treat-
What is Lyme disease?
Lyme disease is caused by the bacterium *Borrelia burgdorferi* and is spread to people through infected ticks. Lyme disease is most commonly carried by deer ticks (see picture in lower right). When a tick bites you, it can spread the germ that causes Lyme disease to your body. However, a tick must stay attached for at least a day to infect you.

Who gets Lyme disease?
The Centers for Disease Control and Prevention estimates that 300,000 new cases occur each year. Where you work, live, play, or vacation may affect your chances of getting Lyme disease.

Risk factors include:
- **Spending time in grassy or wooded areas.** Deer ticks are most common in the heavily wooded Northeast and Midwest regions of the United States.
- **Having skin exposed.** Bare skin is an easy place for ticks to attach
- **Not removing a tick right away.** Ticks need 36 to 48 hours to spread the bacteria.

What are the symptoms of Lyme disease?
- **Rash.** A small red bump from a tick bite is common, but a bull’s eye pattern is a hallmark sign of Lyme disease (see photo).
- **Flu-like symptoms**
  - Headache
  - Fatigue
  - Fever
  - Body aches and pains
If Lyme disease goes untreated, other areas of your body may be affected, including your joints, heart, or nervous system.

How can I prevent Lyme disease?
There is no vaccine to prevent Lyme disease, but there are steps you can take to reduce your risk of getting Lyme disease.

![Image of Lyme disease symptoms](http://pmtwww.uptodate.com/contents/image?imageKey=PI/58798&topicKey=PI%2F4011&source=outline_link)

Bull’s Eye Rash, hallmark sign of Lyme disease. Note the tick bite in the middle of the rash.

<table>
<thead>
<tr>
<th>Wear long sleeves and pants.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ticks are found in tall grass and shrubs and can attach to people or pets passing by. They cannot jump or fly.</td>
</tr>
<tr>
<td>Use tick repellant. Use repellants containing 20-30% DEET.</td>
</tr>
<tr>
<td>Wear light-colored clothing. Light-colored clothing makes it easier to see ticks.</td>
</tr>
<tr>
<td>Check yourself, your children, and your pets. Ticks may be difficult to see because they are about the size of the head of a pin. Remove any attached ticks promptly.</td>
</tr>
</tbody>
</table>

What should I do if I get bitten by a tick?
1. Use tweezers to grasp the tick as close to the skin as possible.
2. Pull the tick straight out slowly and carefully.
3. Wash the area with soap and water.

How is Lyme disease treated?
Lyme disease is effectively treated with antibiotics. You may be prescribed antibiotics for 14 to 21 days or longer.

By Kristine Percival, PharmD Candidate

**REFERENCES:**
Commonly used heartburn medications like Prilosec®, Nexium®, Pepcid®, Zantac®, and others are associated with vitamin B12 deficiency when taken routinely for two years or longer. Medications used to treat heartburn are readily available over-the-counter and carry health risks when taken for two years or more. Two types of heartburn medication are associated with an increased risk of vitamin B12 deficiency; proton pump inhibitors (PPIs) and histamine receptor 2 blockers (H-2 blockers). A recent article published in the Journal of the American Medical Association found higher rates of vitamin B12 deficiency in people taking medications used to treat heartburn for two years or longer. A list of medications found to increase the risk of vitamin B12 deficiency is provided in Table 1.

Vitamin B12 is necessary for maintaining your health. The body’s ability to transport oxygen, transmit signals through the nervous system, and regulate cell activity depends on vitamin B12. Taking heartburn medications can reduce the absorption of vitamin B12.

**SYMPTOMS OF B12 DEFICIENCY**

Vitamin B12 deficiency from heartburn medications develops slowly, and it may take several years for symptoms become noticeable.

- Fatigue
- Weight loss
- Tingling or numbness of fingers and/or toes
- Difficulty walking properly (staggering)
- Forgetfulness

Over-the-counter medications used for heartburn are associated with health risks when taken incorrectly. Always take your medication as directed. See your health care provider if you still have heartburn symptoms after two weeks of using heartburn medications.

**By Stephen Trautman, PharmD Candidate**

### HOW TO REDUCE YOUR RISK OF B12 DEFICIENCY

- Do not take heartburn medications (PPIs or H-2 blockers) for longer than 14 days unless directed to by a physician.
- See your health care provider if heartburn persists beyond 14 days of treatment with a PPI or H-2 blocker.
- Factors that may lead to an increase in heartburn symptoms include smoking, alcohol use, and caffeine use.
- Heartburn may be reduced by eating smaller meals, decreasing the intake of dietary fat, and eating at least 3 hours before going to bed or lying down.

### REFERENCES:


### Table 1: Medications Commonly Used for Heartburn

<table>
<thead>
<tr>
<th>Type</th>
<th>Brand Name</th>
<th>Generic Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proton Pump Inhibitors (PPIs)</td>
<td>Prilosec®, Pracid®, Nexium®, Protonix®, Dexilant®, Aciphex®</td>
<td>Omeprazole, Lnasoprazole, Esomeprazole, Pantoprazole, Dxlansoprazole, Rabeprazole</td>
</tr>
<tr>
<td>Histamine Receptor 2 Blockers (H-2 Blockers)</td>
<td>Tagamen®, Pepcid®, Axid®, Zantac®</td>
<td>Cimetidine, Famotidine, Nizatidine, Ranitidine</td>
</tr>
</tbody>
</table>
For adults and children ages 12 and older, Nasacort Allergy® 24HR should be sprayed two times into each nostril once daily, yielding a dose of 220 mcg per day.\(^4\)\(^5\) For children ages 6-12, the starting dose is 110 mcg per day, delivered as one spray in each nostril once daily. The dose may be increased to two sprays in each nostril once daily (220 mcg/day) in children 6-12 years if symptoms are not adequately controlled. For children ages 2-6, the maximum dose is 110 mcg per day given as one spray in each nostril once daily. Nasacort Allergy® 24 HR is most effective when it is used on a consistent basis, but it should not be used more than once daily.\(^4\)\(^5\)

Intranasal corticosteroids are generally well tolerated. Nasal irritation and epistaxis are the most commonly reported adverse effects.\(^4\)\(^5\) Rare but possible side effects include *Candida albicans* infections, nasal ulceration, and septal perforation.\(^4\)\(^5\) Proper administration technique can minimize local side effects.\(^2\)

There is concern about reduced growth in children who use corticosteroids, but the studies are conflicting. One study in children with asthma found a significant reduction in growth in children who used orally inhaled budesonide 200 mcg twice daily over a mean of 4.3 years.\(^6\) On the other hand, studies with intranasal fluticasone propionate, mometasone furoate, and budesonide failed to show an effect on growth.\(^7\)\(^9\) Routine monitoring of growth in pediatric patients may be warranted.

**REFERENCES:**


The risk of Alzheimer’s disease (AD) may be affected by health and lifestyle factors. Physical health, diet, mental activity, and other diseases are AD risk factors that can be improved. Current studies are looking at how these health and lifestyle factors may slow or prevent AD. The table below summarizes the effects of these factors on AD risk.

Physical fitness may help prevent AD. Staying active has been associated with a 50% reduced risk of getting AD later in life. The Alzheimer’s Association recommends at least 30 minutes of aerobic exercise at least four days a week. Weight training and balance workouts are also suggested.

Diet also plays an important role in the risk of AD. A diet high in saturated fats and refined sugars is associated with an increased risk of AD. On the other hand, a diet high in fruits, vegetables, beans, whole grains, and poly-unsaturated fats is associated with a decreased risk of AD. The Mediterranean diet focuses on these nutritious foods and may help reduce the risk of AD.

Dietary supplements may help improve brain function. Folic acid, vitamins B6, B12, and D, and omega-3 fatty acids are associated with lower risk of AD. Antioxidants, such as resveratrol, coenzyme Q, and vitamins E and A, might also help slow or prevent mental decline. However, too much vitamin E may be harmful, so it should be obtained through the diet if possible. Too much iron and copper has been linked to mental problems. Aluminum may also increase risk of AD, so it may be wise to avoid aluminum-containing food or products.

Mental activity may affect your risk of AD. Stay mentally and socially active and seek a learning atmosphere to decrease the risk of AD. Try reading, writing, listening to or playing music, playing strategy games, and learning new things. Higher education and difficult tasks at work may also reduce risk of mental decline.

Certain chronic diseases appear to increase the risk of AD. High blood pressure, high cholesterol, diabetes, and obesity raise the risk of heart disease. Studies show that up to 80% of AD patients also have heart disease. Depression may also increase the risk of getting AD later in life. Preventing or controlling these diseases is advised to lower the risk of mental decline and AD.

Other lifestyle factors may affect your risk of getting AD. Use of tobacco products and moderate to high alcohol intake have been associated with increased risk of AD. Head trauma may also lead to mental decline. People should protect their heads by wearing seatbelts and helmets and fall-proofing their homes. Caffeine is thought to improve brain function, but more studies are needed to confirm this.

Regrettably, certain AD risk factors cannot be changed. Old age, family history of AD, and genetic factors all increase the risk of AD. Luckily, there are many risk factors that can be improved to lower the risk of getting AD. The health and lifestyle factors noted above may slow or prevent mental decline and AD. Start these changes today to lower your risk of developing AD in the future.

By Melissa Briery, PharmD Candidate

### References on Page 7

<table>
<thead>
<tr>
<th>Health and Lifestyle Factors</th>
<th>Increases Risk of AD</th>
<th>Decreases Risk of AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Fitness</td>
<td>Physical inactivity</td>
<td>Aerobic exercise, 30 minutes a day for at least 4 days a week</td>
</tr>
<tr>
<td>Diet</td>
<td>High intake of saturated fats and refined sugars</td>
<td>High intake of fruits, vegetables, beans, whole grains, and poly-unsaturated fats</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Caffeine</td>
</tr>
<tr>
<td>Supplements</td>
<td>Low vitamin and antioxidant intake</td>
<td>Folic acid, omega-3 fatty acids, and vitamins B6, B12, and D</td>
</tr>
<tr>
<td></td>
<td>Too much intake of iron and copper</td>
<td>Antioxidants, such as resveratrol, coenzyme Q, vitamin E, and vitamin A</td>
</tr>
<tr>
<td></td>
<td>Aluminum-containing food and/or products</td>
<td></td>
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<tr>
<td>Mental Activity</td>
<td>Social isolation</td>
<td>Stay mentally and socially engaged</td>
</tr>
<tr>
<td></td>
<td>Mental inactivity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low education</td>
<td></td>
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<tr>
<td>Chronic Diseases</td>
<td>High blood pressure, high cholesterol, diabetes, obesity, and depression</td>
<td>Prevent and medically control these disease states</td>
</tr>
<tr>
<td>Other factors</td>
<td>Use of tobacco products</td>
<td>Avoidance of tobacco products</td>
</tr>
<tr>
<td></td>
<td>Moderate to high alcohol intake</td>
<td>Low alcohol intake</td>
</tr>
<tr>
<td></td>
<td>Head trauma</td>
<td>Wear seatbelts and helmets, fall-proof the home</td>
</tr>
</tbody>
</table>
Sofosbuvir (cont. from page 1)

<table>
<thead>
<tr>
<th>Table 1: NEUTRINO and POSITRON Trials</th>
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<tbody>
<tr>
<td>Trial</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>NEUTRINO</td>
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<tr>
<td>POSITRON</td>
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</table>

<table>
<thead>
<tr>
<th>Table 2: Recommended Sofosbuvir Regimens and Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV Genotype</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>Patients with genotype 1 or 4</td>
</tr>
<tr>
<td>Patients with genotype 2</td>
</tr>
<tr>
<td>Patients with genotype 3</td>
</tr>
</tbody>
</table>

Treatment durations for sofosbuvir combination therapy is provided in Table 2 (above).

Conclusion:
The NEUTRINO and POSITRON trials demonstrated the efficacy of sofosbuvir when used as combination therapy for treatment-naive patients, and patients without treatment options for HCV infection. The rates of SVR with standard therapy, peginterferon + ribavirin for 24 weeks, are similar to that of sofosbuvir treatment regimens. Sofosbuvir in combination with ribavirin appears to have fewer side effects than interferon-based regimens. In both the NEUTRINO and POSITRON trials, sofosbuvir was used in combination therapy. Therefore, it is not clear whether the adverse effects reported in these trials are directly related to sofosbuvir. Primary advantages of sofosbuvir are oral administration, once daily dosing, and shorter treatment durations. Post-marketing surveillance will be critical in determining the long-term benefits of sofosbuvir treatment regimens in addition to other adverse effects.

By Stephen Trautman, PharmD Candidate

REFERENCES:
Alzheimer’s Disease References (cont. from page 5)


