Ebola Virus: An Overview

September 30, 2014:
The first case of travel-associated Ebola was diagnosed in the United States.

What is Ebola?
- Ebola is a virus that impairs the human body’s normal response to fight off infections.
- The virus disrupts the body’s blood supply system causing internal and external bleeding.
- The virus is also known as the Ebola hemorrhagic fever.
- Ebola affects humans as well as animals.

How is Ebola Transmitted?
- Physical contact with the blood or body fluids of a symptomatic human infected with Ebola.
- Contact with an animal or raw meat of an animal infected with Ebola.
- The virus is not spread through air, water, or food.

What are the Symptoms?
Watch for symptoms up to 21 days after exposure to Ebola.
- Fever
- Diarrhea
- Headache
- Abdominal pain
- Muscle pain
- Vomiting
- Weakness
- Bleeding or bruising

Prevention Tips
- Practice Proper Hand Hygiene.
- Avoid:
  - Geographic locations with Ebola outbreaks.
  - Hospitals treating Ebola patients.
  - Blood and body fluids of infected patients.
  - Undercooked meat or contact with animals that may be infected with Ebola.

Treatment
- No vaccination is available.
- No medications are approved that fight the Ebola infection.
- Supportive care and management of symptoms is the current standard of care.
  - Hydration, electrolyte replacement, oxygen support, etc.
- Ebola can be fatal; the average risk of death is 50%
- After recovery from an Ebola infection, a person develops antibodies that are protective against reinfection for at least 10 years.

By Cara Laslovich, PharmD Candidate

REFERENCES:

DIS News
College of Health Professions and Biomedical Sciences
Drug Information Service

PATIENT INFORMATION:
Ebola Virus: An Overview

October 2014
Volume 18, Issue 10

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We welcome any comments and suggestions for future newsletter topics.

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http://www.cdc.gov/vhf/ebola/resources/index.html
http://www.africabusinessreview.net/business-news/ebola-virus-typical-path-through-a-human-being
Sivextro® (tedizolid) is an oxazolidinone antibiotic that was approved by the FDA in June 2014 for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults. Although the mechanism and efficacy of tedizolid is similar to linezolid, its pharmacokinetics allow for a more convenient once-daily dosing.

Tedizolid was approved to treat adults with ABSSSI caused by Gram-positive microbes. Susceptible microorganisms include the following:

- *S. aureus*
- *MRSA*
- *MSSA*
- *S. pyogenes*
- *S. agalactiae*
- *S. constellatus*
- *S. faecalis*

Oral tedizolid was non-inferior to oral linezolid in adults with ABSSSI. The phase 3, randomized, double-blind, non-inferiority trial compared tedizolid 200 mg daily for 6 days to linezolid 600 mg twice daily for 10 days in 667 patients. Response rates at 48-72 hours after starting treatment were similar in both groups (79.5% vs. 79.4%; treatment difference 0.1%, 95% CI −6.1% to 6.2%). Because the lower limit of the confidence interval was above the predetermined −10% margin for non-inferiority, the authors concluded that once daily oral tedizolid was non-inferior to twice daily oral linezolid for the treatment of ABSSSI.

Intravenous tedizolid was also found to be non-inferior to intravenous linezolid in patients with ABSSSI. This phase 3, double-blind, non-inferiority study compared tedizolid 200 mg once daily for 6 days to linezolid 600 mg twice daily for 10 days in 666 patients. The primary endpoint was ≥20% reduction in lesion area at 48-72 hours compared to baseline with a non-inferiority margin of -10%.

At 48-72 hours, the response rates were 85% in the tedizolid group and 83% in the linezolid group (treatment difference 2.6%, 95% CI −3.0% to 8.2%). The authors concluded that once-daily IV tedizolid was non-inferior to twice-daily IV linezolid for the treatment of ABSSSI.

Both studies were limited by the differences in clinical practice among the study sites and the lack of well-defined end points for ABSSSI studies. Since patients with previous treatment failure at the same site were ineligible for both studies, the results cannot be generalized to patients with recurrent infection.

Tedizolid phosphate is a prodrug and is converted to tedizolid by phosphatase enzymes. Tedizolid exhibits its main bacteriostatic activity by binding to the 50S subunit of the bacterial ribosome, which inhibits protein synthesis. Tedizolid is also thought to have interactions with additional target sites on the 23S binding region of the bacterial ribosome which may add to its efficacy.

**Dosage and Administration (adult)**

- **Intravenous:** 200 mg IV infusion over 1 hour once daily for 6 days
- **Oral:** 200 mg by mouth once daily for 6 days

**Adverse Effects**

- Nausea (8%)
- Headache (6%)
- Diarrhea (4%)
- Vomiting (3%)
- Dizziness (2%)

Uncommon (<2%): Anemia, palpitations, tachycardia, blurred vision, visual impairment, *Clostridium difficile* colitis, oral candidiasis, decreased white blood cell count, increased hepatic transaminases, hypoesthesia, paresthesia, insomnia, pruritus, urticaria, dermatitis, flushing, hypertension

By Taryn Moore, PharmD Candidate

**REFERENCES:**


Orbactiv™ (oritavancin)

Orbactiv™ (oritavancin) is a new alternative antibiotic to vancomycin for treatment of infections caused by methicillin-resistant Staphylococcus aureus (MRSA). Only oritavancin received FDA approval on August 6, 2014 for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible gram-positive bacteria. Only one intravenous dose of oritavancin is required to treat an infection due to its long terminal half-life of about 245 hours. The single dose administration helps reduce healthcare costs and improve safety by reducing the risk of infusion reactions, eliminating the need for therapeutic drug level monitoring, and improving compliance.

Two phase 3, double-blind, randomized, controlled trials evaluating oritavancin for ABSSSI have been performed (SOLO I and II), but only SOLO I has been published at this time. Oritavancin was non-inferior to vancomycin in both SOLO I and SOLO II. The prescribing information for oritavancin contains pooled data from both clinical trials.

SOLO I Trial

This trial was designed to evaluate the efficacy and safety of a single IV dose of oritavancin compared to 7-10 days of IV vancomycin. Four hundred and seventy-five patient received a single 1200 mg dose of oritavancin, and 479 patients received twice-daily vancomycin (1 g or 15 mg/kg). There were no significant differences between the oritavancin and vancomycin groups in any of the efficacy endpoints. Oritavancin and vancomycin at 48 to 72 hours had similar rates of shrinking or lack of growth in the baseline lesion, absence of fever, and no rescue antibiotic use (80.1% [n=402] for oritavancin and 82.9% [n=416] for vancomycin). Without further details, SOLO II cannot be completely evaluated.

Safety was evaluated for 60 days in both the SOLO I and II trials to account for oritavancin’s long terminal half-life. Headache (7.1%), nausea (9.9%), vomiting (4.6%), limb and subcutaneous abscesses (3.8%), and diarrhea (3.7%) were the most commonly reported adverse effects reported in the SOLO trials. Cellulitis (0.4%) and osteomyelitis (0.3%) were most commonly associated with discontinuation of oritavancin.

SOLO II Trial

FDA approval documents for oritavancin contain limited information from the SOLO II trial. The SOLO II trial was conducted similarly to the SOLO I trial. There was no significant difference found between oritavancin and vancomycin at 48 to 72 hours for shrinking or lack of growth in the baseline lesion, absence of fever, and no rescue antibiotic use (80.1% [n=402] for oritavancin and 82.9% [n=416] for vancomycin). Without further details, SOLO II cannot be completely evaluated.

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Warnings and Precautions

- Administration of IV unfractionated heparin sodium during the first 48 hours after administration of oritavancin
- Known hypersensitivity to oritavancin

Contraindications

- Administration of IV unfractionated heparin sodium during the first 48 hours after administration of oritavancin
- Known hypersensitivity to oritavancin

Dosing and Administration

- Adults: a single 1200 mg dose administered intravenously over three hours
- Children: Oritavancin has not yet been studied in children <18 years of age
- No dosage adjustment is necessary for hepatic or renal impairment. However, oritavancin use in severe renal and hepatic impairment has not been studied.

In clinical trials, oritavancin was an effective alternative to vancomycin for ABSSSI caused by susceptible gram-positive bacteria, including MRSA. Treating ABSSSI with oritavancin requires only a single dose instead of multiple infusions for vancomycin for 7 to 10 days. The single dose administration does not require therapeutic drug level monitoring, reduces the risks associated with multiple infusions, and has the potential to reduce healthcare costs. Oritavancin’s safety is similar to vancomycin, even two months after administration. More research is needed to evaluate oritavancin for the treatment of other infections such as osteomyelitis, prosthetic joint infections, and bacteremia.

By Stephen Hummel, PharmD Candidate

REFERENCES:

Medicated adhesive patches commonly cause skin irritation. Usually this reaction is not severe enough for people to stop using their medication. If you experience irritation from the use of a medicated patch, there are many easy ways to avoid this side effect.

- If irritation occurs that cannot be tolerated, talk to your healthcare provider about the need to use a patch. If the medication is available in a different form, you may be able to stop using a patch.

**If you believe you are having an allergic reaction, contact a healthcare provider immediately.**

**Signs of an allergic reaction:**
- Irritation/redness spreading past the borders of the patch
- Significant itching
- A rash beginning more than one day after removing the patch
- Irritation lasting longer than 48 hours

**Tips to Avoid Irritation**
- There are many types of transdermal patches. Ask a healthcare provider for instructions on how and where your specific patch should be applied and how often it should be changed.
- Rotate the site of application every time you change your patch and try to avoid using the same exact spot multiple times.
- Apply the patch to clean dry skin, avoiding application immediately following the use of soap or lotions.
- Bathing can weaken the skin’s natural barriers causing skin to become dry and vulnerable. Try to limit bathing to 5-10 minutes. If possible, shower in the evening and apply the patch the next morning.
- Remove adhesive left on the skin with mild soap or oil-based products (petroleum jelly or olive oil). Avoid using non-medical adhesive removers, rubbing alcohol, and products that contain acetone.
- Avoid using calamine lotion to soothe irritation because it can dry out the skin.
- Use mild cleansers and lotions only. Apply lotions to moist skin after bathing. Brands which carry mild products include:
  - Cetaphil®
  - Aquaphor®
  - CeraVe™
  - Eucerin®
  - Vaseline®
  - Vanicream™

- If you have persistent irritation, your healthcare provider may prescribe a steroid cream. Avoid putting this cream on the area of skin where you plan to apply your patch.

**By Cassidy Lloyd, PharmD Candidate**

**REFERENCES:**


**PHOTOS:**

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The use of Aromatase Inhibitors & Testosterone Replacement in Men

The off-label use of aromatase inhibitors in men on testosterone replacement therapy is becoming more popular. The long-term safety of aromatase inhibitors in men is not well understood as the majority of studies on this drug class have been completed in post-menopausal women with breast cancer. Short-term, off-label use of aromatase inhibitors became attractive to body builders, both with and without the concomitant use of anabolic steroids, as a means of achieving supra-physiological levels of circulating androgens otherwise unattainable without the development of estrogen-related side effects.\(^1\)\(^2\)  

In patients using testosterone replacement therapy alone, estradiol levels are commonly above the normal limits.\(^3\)\(^4\) Aromatase inhibitors decrease the conversion of testosterone to estradiol through inhibition of aromatase and subsequent inhibition of negative estrogen feedback.\(^5\) This suppression increases levels of LH and FSH which increase testosterone levels in males up to 50% above baseline.\(^6\)\(^7\) Unlike in women, the suppression of the conversion of testosterone to estradiol is incomplete in males (20–30% in males versus 80–90% in post-menopausal females).\(^4\)\(^5\) This incomplete suppression may be beneficial as excessively low levels of estradiol in males may be detrimental, and maintenance of the ratio between estradiol and testosterone could also contribute to negating adverse effects of testosterone replacement therapy.\(^1\)\(^4\)\(^5\)

High circulating levels of estradiol are responsible for the estrogen-related side effects of testosterone. High levels of estradiol in males can cause gynecomastia, bloating/water retention, and fat accumulation, predominately in the abdomen. In addition to changes in body composition, use of aromatase inhibitors may affect carbohydrate and lipid metabolism, bone density, and cognition.\(^6\) The pros and cons of aromatase inhibitor use in men are outlined in the table below.

Third generation, selective, non-steroidal aromatase inhibitors should be used in men due to risk of adverse effects with the earlier, non-selective agents. Of the aromatase inhibitors, anastrazole (Arimidex\(^6\)) may be a better option than letrozole (Femara\(^6\)).\(^1\)\(^7\) Anastrozole 1 mg daily has been evaluated in the majority of studies on aromatase inhibitor use in men. Anastrozole is more selective, while letrozole is more potent, may cause excessively low levels of estradiol, and more commonly causes adverse effects.\(^7\) A dosing regimen of anastrozole 1 mg twice weekly has been evaluated and was equally efficacious at reducing estradiol levels as anastrozole 1 mg daily.\(^7\)

By Cassidy Lloyd, PharmD Candidate

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<th>Outcome</th>
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<td>Gynecomastia(^8)</td>
<td>Aromatase inhibitors are effective at decreasing gynecomastia, weight gain, and water retention associated with testosterone replacement</td>
<td>Moderate—Good history of the use of aromatase inhibitors for gynecomastia; case reports dominate published evidence</td>
<td>The addition of anastrozole can be beneficial in negating the adverse effects of testosterone replacement therapy</td>
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| Mood, Libido, Cognition\(^3\)\(^9\) | • No effect on mood has been studied  
• Increased estradiol levels (>5 ng/dL) are positively associated with increased libido  
• Increased spatial memory when added to testosterone replacement therapy | Moderate—Small, randomized, controlled trials with anastrozole and testosterone replacement therapy evaluated libido and cognition | Monitor estradiol levels to assure excessive suppression is avoided |
| Bone Mineral Density\(^6\)\(^10\)\(^11\) | Decreased bone mineral density and increased risk of fracture due to decreased serum estradiol levels | Conflicting study results in men on anastrozole without testosterone replacement therapy | Use with caution and monitor bone mineral density |
| Arthralgias/Myalgias\(^2\) | Increased incidence of arthralgias and myalgias due to decreased serum estradiol levels | Studies limited to post-menopausal women | Caution when used in men predisposed to arthralgia/myalgia |
| Cardiovascular\(^6\) | Worsening lipid profiles | Studies limited to post-menopausal women | Monitor lipid profile |
| Prostate\(^4\) | Increased prostate-specific antigen (PSA) levels | Conflicting study results | Monitor PSA levels |
PATIENT INFORMATION:

Enterovirus D68

What is Enterovirus D68?
Enterovirus D68 (EV-D68) is a virus that causes mild to severe respiratory illness. Infants, children, and adolescents are primarily affected due to their lack of immunity from previous exposure. Individuals with asthma are more likely to be infected and develop severe illness.

How common is EV-D68?
The prevalence of EV-D68 infections in the United States varies annually, with most infections occurring in the summer and fall seasons. The virus is relatively uncommon, but has recently been widespread for unknown reasons, with infections occurring in 42 states and the District of Columbia so far this year. Five hundred people with severe respiratory illness had confirmed cases of EV-D68 infection in August and September of 2014, with almost all cases occurring in children. Five of these cases were reported in Montana. More cases will be continue to be confirmed as more individuals are tested.

How is EV-D68 spread?
The virus is found in the saliva, nasal mucus, and sputum of infected individuals and can be spread through coughing, sneezing, and contact with contaminated surfaces.

What are the symptoms of EV-D68?
Mild symptoms:
- Fever
- Runny nose
- Sneezing
- Cough
- Muscle aches

Serious symptoms:
- Wheezing
- Difficulty breathing
- Sudden unexplained limb weakness

While most EV-D68 symptoms are minor and cold-like, several severe cases of respiratory illness have occurred, most commonly in children with asthma or a history of wheezing. As of October 2014, EV-D68 infection has been confirmed in 4 individuals who have died, although the exact causes of death are unknown.

Cases of EV-D68 have also recently been confirmed in 4 children hospitalized for sudden neurologic illness. Although the virus is not known to be the cause, individuals 21 years old or younger with sudden limb weakness occurring after August 1, 2014 are currently being tested for infection.

How is EV-D68 treated?
There are currently no antiviral medications available to treat EV-D68 infections. However, over-the-counter medications can be used to help alleviate minor symptoms. If severe symptoms occur, such as difficulty breathing, hospitalization may be necessary.

What can I do to protect myself from EV-D68 infection?
You can reduce the likelihood of spreading any infection by doing the following:
* Wash hands frequently with soap and water or hand sanitizer
* Do not touch your eyes, mouth, or nose without washing your hands
* Avoid close contact with people who are sick
* Regularly disinfect frequently touched surfaces
* Cover coughs and sneezes with your sleeve or tissue instead of your hands
* Do not go to school or work if you are sick

By Andrea Friend, PharmD Candidate

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