Case Vignette:

History of Present Illness: A 32-year-old man is admitted to the intensive care unit (ICU) with shortness of breath, dyspnea, fever, and acute renal dysfunction. He also reports a 2-month history of fatigue and weight loss and a recent history of sore throat and altered taste.

Medical History: GERD (gastroesophageal reflux disease); asthma

Social History: Admits alcohol use (average 1 or 2 drinks per day), tobacco use (1 pack/day), and marijuana use (1 or 2 blunts per week). Sexually active with 15 lifetime partners (male and female partners). Admits inconsistent condom use

Current Medications: Omeprazole 20 mg orally twice daily; fluticasone/salmeterol 500/50 mg inhaler 1 puff twice daily; albuterol 90 mcg inhaler 1 or 2 puffs every 6 hours as needed for shortness of breath

Allergies: Penicillin

Vital Signs: Blood pressure 110/62 mm Hg; heart rate 120 beats/minute; temperature 39°C; respiratory rate 25 breaths/minute; O_2 sat 94%; weight 62 kg; height 74 inches (188 cm)

Laboratory Values: WBC (white blood cell count) 4.7 x 10^3 cells/mm^3 (SI 4.7 x 10^9/L); hemoglobin 11.7 mg/dL (SI 117g/L); hematocrit 34.5% (SI 0.345); platelet count 75,000/mm^3 (SI 75 x10^9/L); BUN (blood urea nitrogen) 50 mg/dL (SI 17.85 micromoles/L); SCr 3.5 mg/dL (SI 309.4 micromoles/L)

Human immunodeficiency virus type 1/type 2 (HIV-1-/-2) antibody reactive; western blot pending; blood and sputum cultures pending

Procedure Data: Chest radiograph: Diffuse bilateral alveolar infiltrates

Other Data: N/A

Question 1

The physician would like to initiate the patient on therapy for esophageal candidiasis. Which is the most appropriate antimicrobial regimen for this indication?

1. Amphotericin B
2. Caspofungin
3. Fluconazole
4. Voriconazole

Answer: 3. Fluconazole

Rationale: Fluconazole is the preferred treatment for esophageal candidiasis because of its superior efficacy, good absorption, and good tolerability. Other agents, including caspofungin, amphotericin B, or voriconazole, can be considered in patients with a history of refractory candidiasis.

Citations:

1. Pappas PG, Kauffman CA, Andes D, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009;48:503.

2. Kaplan JE, Benson C, Holmes KK, et al. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm Rep 2009;58:1.

Question 2

The patient is admitted to the ICU in respiratory distress, where an arterial blood gas reveals an oxygen partial pressure of 62 mm Hg and his physicians suspect *Pneumocystis jiroveci* pneumonia. Which regimen would you recommend for management of his suspected *Pneumocystis* pneumonia?

1. Sulfamethoxazole/trimethoprim 300 mg (as trimethoprim) intravenously every 12 hours
2. Sulfamethoxazole/trimethoprim 300 mg (as trimethoprim) intravenously every 12 hours and prednisone 40 mg orally twice daily
3. Sulfamethoxazole/trimethoprim 300 mg (as trimethoprim) intravenously every 8 hours
4. Sulfamethoxazole/trimethoprim 300 mg (as trimethoprim) intravenously every 8 hours and prednisone 40 mg orally twice daily

Answer: 2. Sulfamethoxazole/trimethoprim 300 mg (as trimethoprim) intravenously every 12 hours and prednisone 40 mg orally twice daily

Rationale: Sulfamethoxazole/trimethoprim is the treatment of choice for *Pneumocystis* pneumonia with a dose adjustment of 15–20 mg/kg/day as trimethoprim divided every 6–8 hours. However, for a creatinine clearance (CrCl) of 15–30 mL/minute, the dose should be adjusted as half of the normal dose. This patient's CrCl is 26 mL/minute; therefore, he would require dose adjustment to 10 mg/kg/day divided every 12 hours. In addition, because his oxygen partial pressure is less than 70 mm Hg, he qualifies for prednisone therapy at a dose of 40 mg twice daily x 5 days, followed by 40 mg daily x 5 days and then 20 mg daily for 11 days.

Citations:

1. Kaplan JE, Benson C, Holmes KK, et al. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm Rep 2009;58:1.

2. The National Institutes of Health-University of California Expert Panel for Corticosteroids as Adjunctive Therapy for *Pneumocystis* Pneumonia. Consensus statement on the use of corticosteroids as adjunctive therapy for *Pneumocystis* pneumonia in the acquired immunodeficiency syndrome. N Engl J Med 1990;323:1500.

Question 3

The patient's western blot returns, confirming the diagnosis of HIV-1. He also has a CD4 and HIV RNA viral load drawn, which are 125 cells/microliter and 75,000 copies/mL, respectively. His physician would like to initiate antiretroviral therapy. Which additional testing would you recommend to help select an appropriate regimen?

1. Genotype
2. Tropism
3. Genotype and HLA-B*5701
4. Genotype, Tropism , and HLA-B*5701

Answer: 3. Genotype and HLA-B*5701

Rationale: Genotypic testing for antiretroviral resistance should be done before initiating therapy. The DHHS (Department of Health and Human Services) guidelines recommend tenofovir/emtricitabine as the backbone nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) for all first-line regimens in treatment-naive patients. If a reason not to use tenofovir exists (resistance, renal failure), an alternative NRTI backbone should be considered, specifically abacavir/lamivudine. Before prescribing abacavir, however, HLA-B*5701 screening should be completed to determine the likelihood of patient having a hypersensitivity response. Because this patient is currently in acute renal failure, an alternative NRTI backbone should be considered. A tropism assay is needed only if maraviroc use is being considered. Because maraviroc is not a component of a first-line regimen, it is not currently a treatment consideration, and tropism does not need to be completed.

Citation: Guidelines for Use of Antiretroviral agents in HIV-1 Infected Adults and Adolescents. Available at www.aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/11/what-to-start. Accessed January 7, 2014.

Question 4

The patient is initiated on sulfamethoxazole/trimethoprim with prednisone for his pneumonia and abacavir, lamivudine, darunavir, and ritonavir for his HIV. After 1 week of therapy, he has begun to improve clinically, so he is transferred to the step-down unit. He has been transitioned to oral therapy to prepare for discharge and develops a diffuse maculopapular rash, which his physician suspects is an allergic reaction to sulfamethoxazole/trimethoprim. Which antimicrobial regimen would you recommend to complete his *Pneumocystis* therapy?

1. Atovaquone 750 mg orally twice daily
2. Clindamycin 450 mg orally four times daily and primaquine base 15 mg orally daily
3. Dapsone 100 mg orally once daily
4. Pentamidine 250 mg intravenously daily

Answer: 2. Clindamycin 450 mg orally four times daily and primaquine base 15 mg orally daily

Rationale: Moderate to severe disease is best treated with sulfamethoxazole/trimethoprim as the first-line agent, and alternatives include pentamidine, clindamycin/primaquine, and trimetrexate. For mild to moderate disease, acceptable treatment options include atovaquone, dapsone with trimethoprim, and clindamycin with primaquine. This patient would be considered to have moderate-severe disease, which is improving and likely does not require continued intravenous therapy; thus, pentamidine (option 4) would not be appropriate. Dapsone is effective only when given in conjunction with trimethoprim; therefore, option 3 would not be appropriate. In general, atovaquone is recommended only for mild-moderate disease. Because clindamycin with primaquine can be given orally and is as effective as sulfamethoxazole/trimethoprim, it would be the preferred alternative regimen in this case.

Citations:

1. Kaplan JE, Benson C, Holmes KK, et al. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm Rep 2009;58:1.

2. Noskin GA, Murphy RL, Black JR, et al. Salvage therapy with clindamycin/primaquine for *Pneumocystis carinii* pneumonia. Clin Infect Dis 1992;14:183.

Question 5

The patient is discharged home, and after 6 weeks, he continues on abacavir, lamivudine, darunavir, and ritonavir as well as on his previous home medications and citalopram 20 mg daily for depression. In a follow-up with his primary care provider, he presents with recurrent oral candidiasis and weight gain in his face and abdomen, which is accompanied by abdominal striae. Which drug interaction may account for these symptoms?

1. Darunavir/ritonavir and omeprazole
2. Darunavir/ritonavir and fluticasone/salmeterol
3. Darunavir/ritonavir and citalopram
4. Tenofovir/emtricitabine and fluticasone/salmeterol

Answer: 2. Darunavir/ritonavir and fluticasone/salmeterol

Rationale: The patient has signs and symptoms consistent with Cushing syndrome, which can result from excess glucocorticoid. Because both darunavir and ritonavir are potent inhibitors of CYP3A4, the enzyme responsible for corticosteroid metabolism. There is potential for inhaled or intranasal corticosteroids to be absorbed systemically with increased levels when given with any protease inhibitor such as ritonavir or darunavir. Recommendations are to use a lower-potency corticosteroid, when possible, for these patients.

Citations:

1. Guidelines for Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Available at www.aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/11/what-to-start. Accessed January 7, 2014.

2. Clevenbergh P, Corcostegui M, Gerard D, et al. Iatrogenic Cushing's syndrome in an HIV-infected patient treated with inhaled corticosteroids (fluticasone propionate) and low dose ritonavir enhanced PI containing regimen. J Infect 2002;44:194-5.