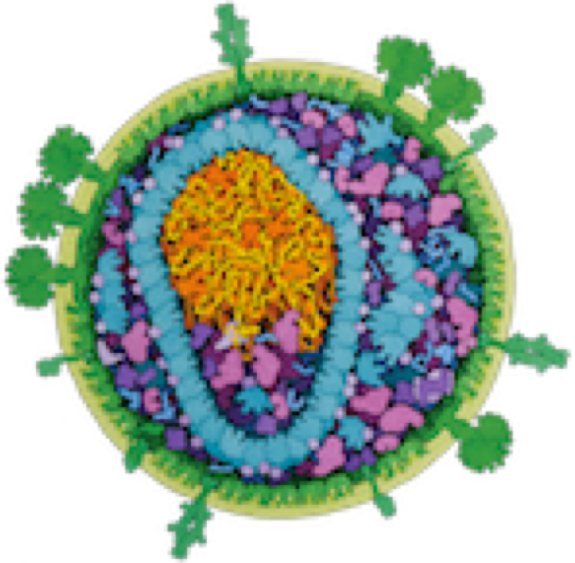

CROI

Conference on Retroviruses and Opportunistic Infections

CROI-Quiz 2019

Pre-Assessment Questions

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Frage 1 / 20

The composition and function of the microbiome has been implicated in many human diseases, including HIV infection. Which statement is true with respect to the microbiome?

A. Different body sites on the same individual would have less beta-diversity than would the same body site in 2 different individuals.

B. Compositionally similar microbiomes have similar functional profiles.

C. Increased HIV susceptibility is associated with vaginal microbiota dominated by Lactobacillus crispatus.

D. Sex behaviors are a minor contributor to gut microbiome variation and a large contributor to vaginal microbiome composition.

E. Mass spectrometry based proteomic analysis can provide data on microbiome composition, diversity, and function, and 16S rRNA sequencing only provides data on composition and diversity.

Antwort 1/ 20

Correct answer is E. 16S rRNA does not provide any functional information, and is typically restricted to genus level classifications and diversity measurements; ‘omics techniques such as proteomics can provide functional data.
Microbiome diversity is much greater between body sites, even on the same individual, than would be found on different individuals on the same body sites.
Functional potential, gene content, transcript expression, or proteome content can vary substantially between samples with similar bacterial composition.
Vaginal microbiomes that are Lactobacillus sp. depleted tend to have higher level of genital inflammation and have been linked to increased HIV acquisition risk in women. Sex behaviors are a major contributor to gut microbiome variation in the gut and the vagina.

Frage 2/20

The primary outcome measure in many HIV prevention trials is the HIV incidence rate in the experimental arm relative to the HIV incidence rate in the control arm, known as the rate ratio (or relative risk). What does the statistical precision of this measure depend on?

A. The total follow-up (person-years of observation)

B. The total number of HIV infection endpoints

C. The number of HIV infection endpoints in each trial arm

D. The total follow-up and the total number of HIV infection endpoints

Antwort 2/ 20

Correct answer is C. This is a statistical property of the measure. The precision is not determined by the amount of follow-up, only the number of observed HIV infection endpoints. The distribution of endpoints between the trial arms is also important; the more unequal they are, the less the precision.

Frage 3/20

A trial is evaluating the effectiveness of a long-acting antiretroviral therapy (ART) compared with oral tenofovir disoproxil fumarate (TDF)/emtricitabine for the prevention of HIV infection for a large-scale rollout. The primary outcome of the study is time to HIV infection that will be summarized as an incidence rate and compared by arms using an incidence rate ratio.

For the primary analysis, the investigator plans to censor follow-up time for individuals who leave the study early at the time of last known HIV serostatus.

Which is an appropriate sensitivity analysis for this primary analysis?

A. An analysis that includes only individuals who remained on treatment per protocol

B. An analysis that uses inverse probability of censoring weighting

C. An analysis restricted to individuals reporting sexual activity during the study

D. An analysis that treats death on study as failure (individuals with HIV infection)

Antwort 3/ 20

Correct answer is B. An inverse probability of censoring weighting will provide an alternative way of handling censoring in the analysis and will provide an alternate estimate for the primary question of interest: the relative rate of HIV infection between the 2 treatment strategies in a large-scale roll out program. This analysis approach may in fact be more appropriate as a primary analysis since it will be more robust in the event that the relationship between the probability of leaving the study early is associated with measured risk factors. Options A and C might be appropriate secondary or subgroup analyses, but they do not address the primary objective of the study. Option A is focused more on assessing the efficacy of the treatment options when taken as prescribed. Of note, this analysis will be subject to an additional selection bias that would need to be accounted for in analysis. Option C is focusing on a different study population. Rather than a full-scale rollout, it is addressing the more targeted question of treatment effectiveness in a sexually active population. It is not clear what question the imputation of death as an infection is trying to answer.

Frage 4/20

Chronic hepatitis E virus (HEV) infection is a problem in immunosuppressed patients such as transplant recipients or patients with HIV infection. Which is true about chronic hepatitis E?

A. It is limited to the European HEV infections (genotype 3)

B. It should be diagnosed by HEV polymerase chain reaction (PCR) testing, not by serology

C. It should always be treated with ribavirin

D. It is associated with extrahepatic manifestations in the majority of cases

Antwort 4/ 20

Correct answer is B. Only PCR is adequate to diagnose chronic ongoing HEV infection in immunosuppressed patients. Serology might provide a false negative test result. Chronic HEV infections have been described from Europe, Asia and the USA. There are different treatment options, e.g. reduction of immunosuppression, if possible. Extrahepatic manifestations occur only in a minority.

Frage 5/20

There is a 61-year-old patient with HIV/hepatitis C virus (HCV) coinfection, HCV genotype 1a. Additional test results are as follows:

HCV RNA level: 1.1 million IU/mL
Cirrhosis by Fibroscan: 22 kPa; and aspartate aminotransferase (AST) to platelet ratio index (APRI): 2.1
Child-Pugh-Turcotte (CPT) class: B
Model for End-stage Liver Disease (MELD) score: 13.

His prior therapy with teleprevir, peginterferon-alpha, and ribavirin failed in 2011. His HIV infection is well-controlled (CD4+ cell count 419/mL; undetectable HIV RNA) and he is taking dolutegravir, tenofovir alafenamide (TAF), and emtricitabine.

What would you do next for his HCV infection?

A. Treat him now with sofosbuvir/velpatasvir/voxilaprevir for 12 weeks
B. Delay treatment and send him to a liver transplant program
C. Perform resistance-associated substitution testing and tailor therapy based on results
D. Treat now with sofosbuvir/velpatasvir for 12 weeks

Antwort 5 / 20

Correct answer is B. This is the recommendation from American Association for the Study of Liver Diseases/Infectious Diseases Society of America (AASLD/IDSA) 2018 guidelines.
Sofosbuvir/velpatasvir/voxilaprevir contains a protease inhibitor and can cause fulminant liver failure if used in decompensated cirrhosis. RAS testing is not indicated for genotype 1 infection in individuals in whom you are not considering either sofosbuvir/velpatasvir or sofosbuvir/ledipasvir. Sofosbuvir/velpatasvir is not recommended for an individual with decompensated cirrhosis; sofosbuvir/velpatasvir/ribavirin is, however.

Frage 6/20

The patient is a 54 year-old woman with chronic HCV infection, genotype 3, and compensated cirrhosis, who was treated with 12 weeks of glecaprevir/pibrentasvir but had virologic relapse. Cirrhosis is compensated. Her CPT class is A and MELD score is 8.

What is the most appropriate next step?

A. Treat her now with sofosbuvir/velpatasvir/voxilaprevir for 12 weeks

B. Delay treatment and send her to a liver transplant program

C. Perform resistance associated substitution testing and tailor therapy based on results

D. Treat now with sofosbuvir/velpatasvir for 12 weeks

Antwort 6 / 20

Correct answer is A, based on observational prospective study showing sustained viral response (SVR) at 12 weeks of 93%. B is not correct because the patient has compensated cirrhosis and has a low MELD score. Resistance associated substitution testing is not indicated based on AASLD/IDSA recommendations and findings that baseline resistance associated substitution did not affect SVR rate with sofosbuvir/velpatasvir/voxilaprevir. Treating with just one new drug (sofosbuvir) is not a good strategy so sofosbuvir/velpatasvir is not right answer.

Frage 7/20

Which is an approved pharmacologic treatment for nonalcoholic steatohepatitis (NASH)?

A. Statin
B. Vitamin E
C. Omega 3
D. Metformin

Antwort 7 / 20

Correct answer is B. Vitamin E is approved for NASH treatment.

Frage 8/20

Which antiretroviral is listed as a preferred antiretroviral on the US Department of Health and Human Services (DHHS) guidelines for the Use of Antiretroviral Drugs in Pregnant Women with HIV?

A. TAF
B. Elvitegravir/cobicistat
C. Rilpvirine
D. Raltegravir
E. Lopinavir/ritonavir

Antwort 8/ 20

Correct answer is D. The DHHS guidelines list raltegravir as a preferred antiretroviral drug.

Frage 9/20

Which statement is false about why pregnant women should be included in HIV research?

A. Pregnant women should have fair access to direct benefits of study participation, such as access to therapies unavailable outside the research setting

B. Many drugs require dosing adjustments in pregnancy

C. It is important to characterize and quantify risks to fetuses

D. It is important to characterize and quantify health risks and benefits to pregnant women

E. Robust pregnancy-specific human data are usually required before a drug can be used in pregnant populations

Antwort 9/ 20

Correct answer is E. The standard practice has been to use drugs in pregnant women for years before robust pregnancy-specific safety, efficacy, and pharmacokinetic data are available. The average time it takes for fetal safety determination of drugs is 27 years post-approval; for HIV drugs, pregnancy-specific pharmacokinetic data are available an average of 6 years post-approval, even as these drugs are widely used. The US Food and Drug Administration has indicated that approval for use of drugs in the adult population is inclusive of pregnant women absent specific contraindications, and that prescription of medications in that absence does not constitute “offlabel use” even where pregnancy-specific data are not available.

Frage 10/20

When is the time of greatest risk for development of neural tube birth defect in a woman receiving antiretroviral drugs?

A. When using a drug any time during pregnancy

B. When starting a drug during the second or third trimester of pregnancy

C. When starting a drug after recognition of pregnancy during first trimester

D. When using a drug at time of conception

Antwort 10 / 20

Correct answer is D, in a woman who is using the drug at the time of conception. The beginning of week 3 through 8 post-fertilization is the period of embryogenesis, the period of major organ development, which is the most sensitive period for teratogen exposure. The neural tube closure is complete in humans by 28 days post-fertilization, and exposure to a teratogen during this period can disrupt neural tube closure and result in a neural tube defect such as anencephaly or meningomyelocele. This is generally 6 weeks after a pregnant woman's last menstrual period and 2 weeks after a woman first recognizes she has missed her menses and may be pregnant, thus is prior to recognition of pregnancy in the vast majority of women. Hence the greatest risk for development a neural tube defect with drug exposure is not in women first starting a drug during pregnancy but in those who conceive while receiving

Frage 11/20

HIV drug resistance testing generates HIV nucleotide sequence data that can be useful for selecting a treatment regimen. In addition to their use in medical-decision making, these nucleotide sequence data can be useful for which purpose?

A. Determining the immune status of a patient
B. Detecting when HIV is spreading quickly
C. Determining the identity of an individual
D. Identifying where a person is located

Antwort 11 / 20

Correct answer is B. Nucleotide sequence data generated through drug resistance testing can be used to conduct molecular analysis to identify groups of sequences that are very similar. If groups of sequences are very similar, it is an indication that HIV is spreading quickly and prevention efforts should be implemented to respond and interrupt transmission.

Frage 12 /20

Which statement is true about HCV?

A. A preventative vaccine is available

B. Treatment (with peginterferon-alpha or direct acting antiviral agents) that results in viral clearance also results in protective immunity that prevents patients from getting HCV infection again

C. The incidence of HCV infection is declining in the United States following the introduction of direct acting antiviral agents in 2014

D. Treatment of HCV infection resulting in clearance reduces, but does not eliminate, the risk of liver disease progression, including hepatocellular carcinoma in patients with cirrhosis

Antwort 12/ 20

Correct answer is D. No vaccine to prevent HCV infection is available and HCV incidence is rising in the
Score Report: CROI 2019 Postactivity Knowledge Assessment: Clinical Seite 8 von 13
https://www.proprofs.com/quiz-school/quizreport.php?title=croi-2019-postactivity-kn...
22.03.2019
United States. Treatment that clears infection does not provide protective immunity and patients at ongoing risk of infection must be counseled on this and screened for infection with HCV RNA testing. Treatment dramatically reduces the risk of liver disease progression but should be initiated before cirrhosis ensues because patients with advanced liver disease at the time of treatment remain at elevated risk of liver cancer and failure even with cure.

Frage 13/20

Which medication is now recommended by the World Health Organization (WHO) in their 2018 guidelines as a "Group A" medication that should be used to treat a majority of people with rifampin-resistant tuberculosis?

A. Kanamycin
B. Clofazimine
C. Bedaquiline
D. Delamanid

Antwort 13 / 20

Correct answer is C. Bedaquiline is a drug that was first conditionally approved for the treatment of rifampinresistant
tuberculosis (RR-TB) in 2012 by the US Food and Drug Administration and it was conditionally recommended by the WHO for some people with rifampin-resistant tuberculosis in 2013. Although the phase III trial of bedaquiline is currently ongoing, a number of observational studies have shown that bedaquiline use is associated with a decreased mortality rate. For this reason, WHO recommended bedaquiline as a "Group A" medication for the treatment of most people with RR-TB in their 2018 guidelines. Kanamycin is no longer recommended for the treatment of RR-TB, clofazimine is classified as a "Group B" drug, and delemanid is classified as a "Group C" drug in these guidelines.

Frage 14/20

Clinically relevant drug interactions can occur in patients treated for HIV and for tuberculosis (TB) infection. Which antiretroviral cannot be given with rifampicin-based TB therapy due to the magnitude of the interaction?

A. Raltegravir
B. Dolutegravir
C. Bictegravir
D. Efavirenz

Antwort 14 / 20

Feedback
Correct answer is C. Based on a clinical drug interaction study in which bictegravir, in the fixed-dose combination of bictegravir/emtricitabine /TAF, was given twice daily with rifampicin the magnitude of the interaction (a >60% decrease in bictegravir exposure) precludes the coadministration of these drugs. In contrast, dolutegravir given twice daily gave good outcome in a clinical pharmacokinetic study (the Inspiring study). Raltegravir once daily should not be used with rifampicin and if this combination is unavoidable twice daily raltegravir should be used (possibly with a dose increase). Efavirenz can be administered with rifampicin without a dose adjustment.

Frage 15/20

The prevalence of obesity has risen over the past 2 decades among persons with HIV infection in the United States. To which factor have studies not attributed this rise?

A. Secular trends of rising body mass index in the general population

B. Access to social support services, mental health treatment, and smoking cessation with linkage to HIV care

C. The initiation of ART at higher CD4+ T cell levels

D. Changes in the recommended first-line antiretroviral regimens

Antwort 15 / 20

Correct answer is C. Although earlier linkage to care and treatment initiation has resulted in persons with HIV infection starting ART at higher CD4+ T cell levels, prior studies have shown a lower CD4+ T cell count to be associated with weight gain. The increasing prevalence of obesity among persons with HIV infection has been linked to greater obesity in the general population, lower food insecurity and increased access to food support, concomitant treatment for depression and tobacco use, and the increased use of integrase strand transfer inhibitors in first-line treatment regimens.

Frage 16/20

Which of the following has been consistently linked to poor brain health (eg, worse cognitive performance, brain injury from imaging studies) in aging study participants with HIV infection who have suppressed of plasma HIV RNA?

A. Duration of HIV infection
B. Current CD4+ cell count
C. Plasma measures of inflammation
D. Being on more than three antiretroviral medications

Antwort 16 / 20

Correct answer is C. Plasma measures of inflammation have been consistently linked to poor brain health in these individuals.

Frage 17/20

Among study participants with HIV infection on ART with suppressed plasma HIV RNA who have symptomatic cognitive impairment, what is the typical course of illness?

A. A fluctuating but relatively stable course

B. Slow insidious decline over years with progression to dementia

C. Improvement with resolution of symptoms over months to years

Antwort 17 / 20

Correct answer is A. A fluctuating but relatively stable course is the typical course.

Frage 18/20

Regarding cerebrovascular disease in the setting of HIV infection, which statement is not supported by current published reports?

A. The burden of white matter lesions on brain magnetic resonance imaging (MRI) is linked to typical cerebrovascular disease risk factors, such as hypertension and smoking

B. In the setting of HIV infection, white matter lesions on brain imaging are found only among individuals who report past or current methamphetamine use

C. The amount of white matter lesion burden seen on brain MRI inversely correlates to performance on cognitive testing

D. In an autopsy series, up to 50% of people who died with HIV had moderate to severe cerebral atherosclerosis

Antwort 18 / 20

Correct answer is B. Current published reports do not support the idea that in the setting of HIV infection, white matter lesions on brain imaging are found only among individuals who report past or current methamphetamine use.

Frage 19/20

Which statement regarding Alzheimer's disease in aging patients with HIV infection is supported by existing published evidence?

A. Activation of microglia due to HIV infection is protective against Alzheimer’s disease

B. Cerebrospinal fluid Alzheimer’s disease markers (eg, amyloid, tau, and phosphorylated tau) are consistently able to distinguish HIV-associated neurocognitive disorder (HAND) from Alzheimer’s disease in study participants with HIV infection

C. Central atrophy on brain imaging differentiates HAND from Alzheimer’s disease

D. The pattern of neuropsychological testing performance can be similar in HAND and Alzheimer’s disease

Antwort 19 / 20

Correct answer is D. The pattern of neuropsychological testing performance can be similar in HAND and Alzheimer’s disease.

Frage 20/20

DHHS guidelines for ART recommend a 2-drug regimen of dolutegravir and lamivudine in which of the following situations?

A. Initial regimen for most people with HIV infection
B. Initial regimen in certain clinical situations
C. Simplifying treatment for persons with suppressed HIV
D. Patients with viral suppression and a history of treatment failure

Antwort 20 / 20

Correct answer is B. Dolutegravir and lamivudine is one of three 2-drug ART options (others are darunavir/ritonavir, lamivudine darunavir/ritonavir, and raltegravir) for initial therapy in certain clinical situations, namely where abacavir, TDF, or TAF cannot be used or are not optimal. A is incorrect as longer-term data are needed before this regimen is recommended for most individuals, C because data in suppressed switch is limited, and D because of lack of data and theoretical failure risk.