What's New in HIV, Hepatitis C, and Hepatitis B?

Brian R. Wood, MD
Associate Professor of Medicine
University of Washington & AIDS Education and Training Center

September 6, 2019

AETC AIDS Education & Training Center Program
National Coordinating Resource Center

Disclosures

No financial disclosures or conflicts of interest.

Outline

- Resources for Continuing Education
- What's New and What's Coming?
  - HIV
  - Hepatitis C (HCV)
  - Hepatitis B (HBV)

Resources for HIV & HCV CME/CNE

https://idea.medicine.uw.edu

the IDEA platform

utilized by three national infectious disease curriculums

National HIV Curriculum

Provides ongoing, up-to-date information needed to meet the core competency knowledge for prevention, screening, diagnosis, and ongoing treatment and care of HIV.

www.hiv.uw.edu

National STD Curriculum

Addresses the epidemiology, pathogenesis, clinical manifestations, diagnosis, management, and prevention of STDs.

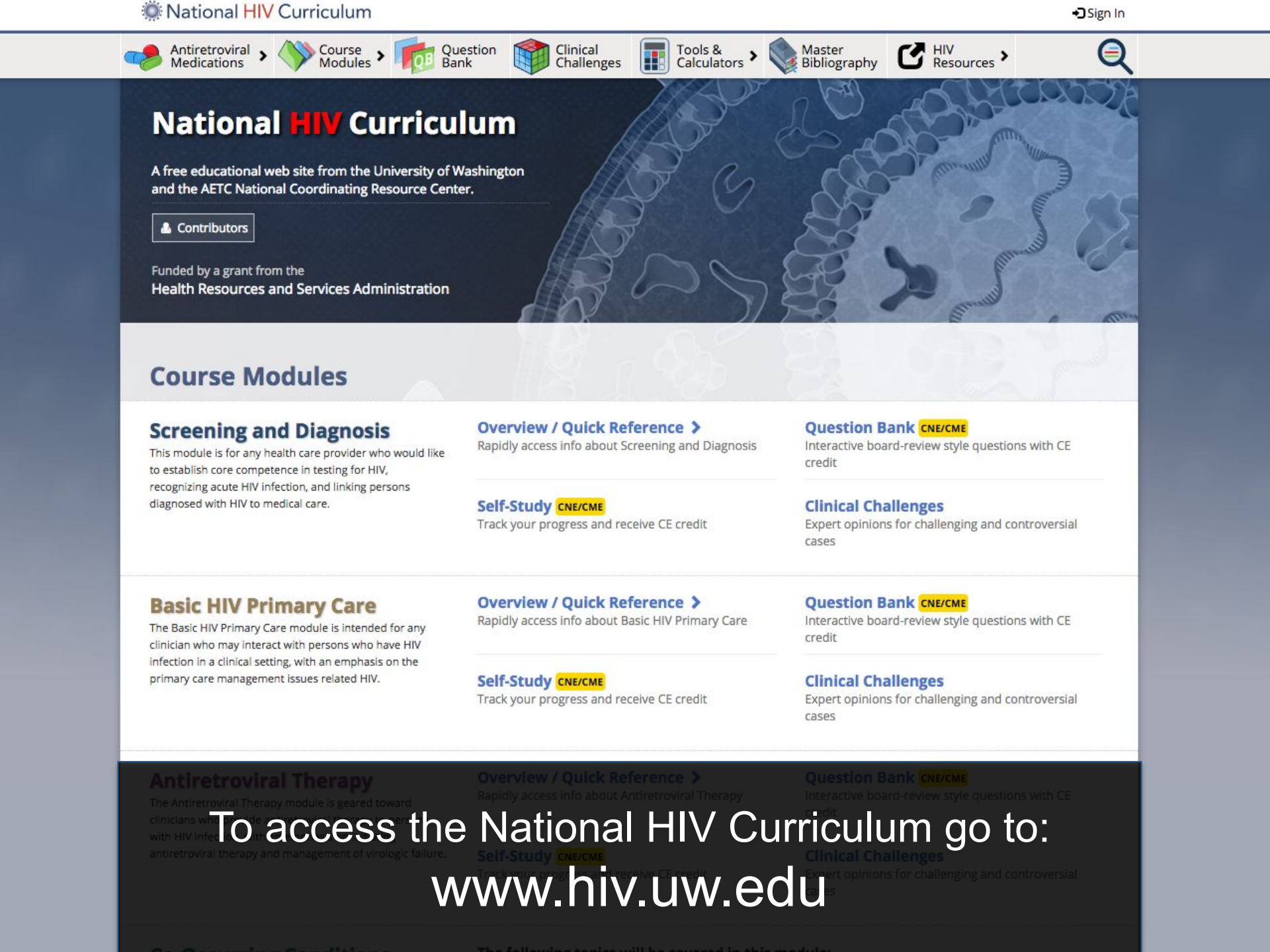
www.std.uw.edu

Hepatitis C Online

A comprehensive resource that addresses the diagnosis, monitoring, and management of hepatitis C virus infection.

www.hepatitisc.uw.edu

www.hiv.uw.edu www.std.uw.edu www.hepatitisc.uw.edu



To access the National HIV Curriculum go to:

www.hiv.uw.edu

Hepatitis C Online

Sign In

HCV Medications › | Course Modules › | Tools & Calculators › | Master Bibliography

HCV Medications

Medication Summaries

Clinical Studies

Slide Decks

Learn about medications to treat HCV »

Course Modules

Screening and Diagnosis of Hepatitis C Infection

For any clinician who may encounter persons with hepatitis C virus infection and would like to establish core competence in testing for hepatitis C, counseling patients on preventing hepatitis C transmission, and diagnosing acute hepatitis C infection.

Overview / Quick Reference ›
Rapidly access info about Screening and Diagnosis of Hepatitis C Infection

Self-Study CNE/CME
Track your progress and receive CE credit

Evaluation, Staging, and Monitoring of Chronic Hepatitis C

Intended for clinicians involved in long-term management of persons with chronic hepatitis C infection. Content includes initial evaluation, natural history, preventing liver damage, staging of liver fibrosis, evaluation of cirrhosis, [illegible] extrahepatic manifestations.

Overview / Quick Reference ›
Rapidly access info about Evaluation, Staging, and Monitoring of Chronic Hepatitis C

Self-Study CNE/CME
Track your progress and receive CE credit

To access the National Hepatitis C Curriculum go to:

www.hepatitisc.uw.edu

National HIV Curriculum

What's New in HIV Treatment & Prevention?

What's New in HIV Treatment?
KEY POINTS

- Start ART as soon as possible (send genotype resistance assay, but don't wait for results)
- All first-line regimens are now integrase inhibitor based
- **A suppressed VL means HIV will not be transmitted!**
- Several two-drug (dual) ART options have been approved
- The future of HIV treatment is long-acting ARV's

Start ART as Soon as Possible (Even Same Day as Diagnosis or First Visit)

HHS Antiretroviral Therapy Guidelines: 2018
When to Start ART

Antiretroviral Therapy is Recommended for:	
All persons living with HIV, regardless of CD4 count, to reduce morbidity and mortality	**AI**
All persons living with HIV to prevent transmission	**AI**
On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.	
Conditions that increase the urgency of ART: pregnancy; opportunistic infection; CD4 count <200; HIV-associated dementia, malignancy, or nephropathy; HBV/HCV; acute HIV	

Source: HHS Antiretroviral Therapy Guidelines. 2018. aidsinfo.nih.gov

Rapid Initiation of ART
Rapid Start in SF (Part of "Getting to Zero")

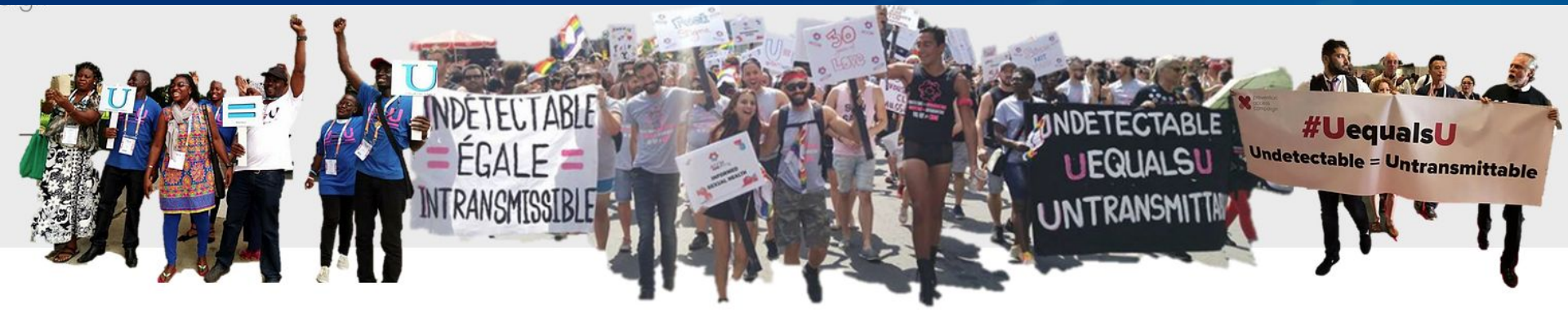
Median Time to Care, ART, and Virologic Suppression

Metric	2013	2014	2015	2016	%△ 2013-2016
New HIV diagnoses	399	329	295	265	
Met rapid definition (%)	23 (6)	45 (14)	50 (17)	80 (30)	
Diagnosis to care (days)	8	7	7	5	-38%
1st visit to ART (days)	27	17	6	1	-96%
Diagnosis to VL <200 (days)	134	92	77	61	-54%

- Rapid ART: visit within 5 days of HIV diagnosis and ART within 1 day of visit
- Visit includes: meeting with SW, benefits counselor, care provider, counselor & pharmacist
- Diagnosis to VL <200 decreased significantly in all groups (gender, race/ethnicity, age, housing)

Bacon O et al. CROI 2018. Abstract 93.

HIV Treatment is Prevention;
Undetectable = Untransmittable (U=U)



Undetectable = Untransmittable

Source: Prevention Access Campaign, www.preventionaccess.org

HIV Treatment is Prevention
Summary of Data to Date

Study	Methodology	Approx. # CLS Acts	# Linked Transmiss.	HIV Transmission Risk
HPTN 052	ART early versus delayed	-	Zero	93-96% risk reduction
Partner 1	888 serodifferent couples (548 MF couples, 350 MM couples); 1,238 CYFU	58,000	Zero	95% CI 0.0-0.3/100 CYFU (0.0-0.84 for MM couples)
*Partner 2	783 serodifferent couples (all MM); 1,596 CYFU	77,000	Zero	95% CI 0.0-0.23/100 CYFU
Opposites Attract	343 serodifferent couples (all MM); 591 CYFU	17,000	Zero	95% CI 0.0-0.62/100 CYFU

*New data in 2018
MM = male-male, MF = male-female, CLS = condomless sex acts, CYFU = couple years of follow up

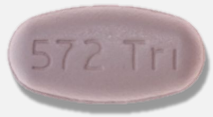
Sources: Cohen 2011, Cohen 2016, Roger 2016, Bavinton 2017, Rodger 2018

Key Points About “U=U”

- **Powerful message that can reduce stigma**
- Important to continue STI prevention counseling
- “Undetectable” in the studies was <200 or <400 copies/mL
- Applies to women living with HIV who become pregnant, sexual transmission among M-F and M-M sexual partners, ?persons who inject drugs (PWID), ?occupational PEP

All First-Line Regimens are Integrase Inhibitor Based

DHHS Guidelines 2018
Recommended Initial Regimens for Most People With HIV

Components (Integrase with 2 NRTI's)	Trade Name	Pill
Dolutegravir-Abacavir-Lamivudine[+]	*Triumeq*	
Dolutegravir + TAF-Emtricitabine[#*]	*Tivicay + Descovy*	
Bictegravir-TAF-Emtricitabine[#]	*Biktarvy*	
Raltegravir + TAF-Emtricitabine[#*]	*Isentress + Descovy*	

[+]Only if HLA-B*5701 negative; caution if history of ischemic CV disease
[#]TAF ok with creatinine clearance as low as 30 mL/min
*Options with TAF shown; TDF is also reasonable per HHS guidelines; IAS-USA guidelines favor TAF

Source: HHS Antiretroviral Therapy Guidelines. 2018. aidsinfo.nih.gov

DHHS Guidelines 2018
Recommended Initial Regimens In Certain Clinical Situations

Components
Other Integrase Inhibitor plus 2 NRTI's
Elvitegravir/Cobicistat/Emtricitabine/TAF (*Genvoya*)
Elvitegravir/Cobicistat/Emtricitabine/TDF (*Stribild*)
Boosted PI plus 2 NRTI's
Darunavir (with a booster[+]) plus 2 NRTI's*
Atazanavir (with a booster[+]) plus 2 NRTI's*
NNRTI with 2 NRTI's
Efavirenz-TDF-Emtricitabine (*Atripla*)
Rilpivirine-TAF-Emtricitabine (*Odefsey*) or Rilpivirine/TDF/Emtricitabine (*Complera*)
Doravirine-TDF-Lamivudine (*Delstrigo*)

[+]Booster can be a combined tablet with cobicistat or a separate ritonavir tablet
[*]NRTI combinations: TAF-emtricitabine, TDF-emtricitabine, or abacavir-lamivudine

Dual ART for Initial or Maintenance Antiretroviral Therapy
Key Trials

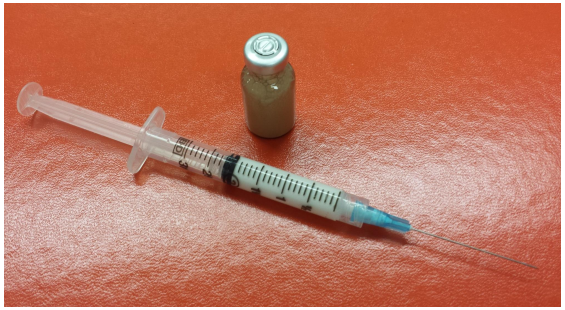
- **Initial ART**
  - **Dolutegravir/lamivudine** (PADDLE, ACTG 5353, GEMINI)
  - Boosted darunavir + lamivudine (ANDES)
  - Boosted darunavir + rilpivirine (PREZENT)

- **Maintenance ART**
  - Long-acting IM cabotegravir + rilpivirine (ATLAS, ATLAS-2M, FLAIR)
  - Boosted darunavir + dolutegravir (DUALIS)
  - **Dolutegravir/rilpivirine** (SWORD1&2)
  - Dolutegravir/lamivudine (LAMIDOL, ASPIRE, TANGO)
  - Boosted darunavir + lamivudine (DUAL GESIDA)

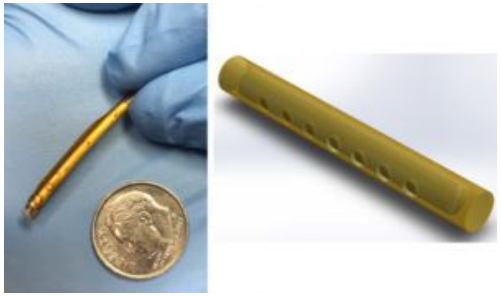
Source: clinicaltrials.gov

Other Trends in ARV Development

- Long-acting agents are coming soon!
  - *IM cabotegravir + rilpivirine-LA
  - Oral eFdA/MK-8591 (*Islatravir*)
- Novel formulations & delivery systems
  - Implants, injectables, etc.
- **Concerns**:
  - Side effects and need for oral lead-in
  - Resistance and need for oral tail
  - Burden on staff if clinic-administered



IM cabotegravir
(Image courtesy of Dr. Landovitz, UCLA)



TAF implant
(betablog.org)

How Will Generic ART Change Things?

- **Examples**:
  - Lamivudine/TDF (*Cimduo*)
    Efavirenz/lamivudine/TDF (*Symfi, Symfi Lo*)
- **Questions**:
  - Will these be widely manufactured?
  - How much lower will the cost be?
  - For whom is TDF considered acceptable and safe?
  - Will insurance make the decision or will practitioners?

Current ART Controversies

- Does dolutegravir increase risk of fetal neural tube defects?
  - Observational study in Botswana found a safety signal (3/1000 with DTG vs 1/1000 with non-DTG)
- Do INSTI's, especially dolutegravir, lead to more weight gain than other ARV's?
  - Confirmed in multiple studies
  - Is this toxicity? Faster return to health? What to do about it?
- Other questions
  - Does abacavir increase risk of ischemic cardiovascular events?
  - Is TAF ok with severe renal impairment?

Sources: Zash et al. IAS 2019, Mexico City, July 2019. Wood BR, CID 2019.

Key Points About OI Prophylaxis & HIV Treatment Monitoring

- Pneumocystis (PCP/PJP) prophylaxis is still important when CD4 count <200 cells/mL
- Guidelines agree that MAC prophylaxis no longer necessary even if CD4 count <50 cells/mL
- After starting ART, continue to follow viral load monthly until undetectable, then every 3-6 months
- Once CD4 count is above 250 cell/mL, stop checking, as long as HIV RNA remains suppressed

Sources: DHHS Guidelines, aidsinfo.nih.gov; IAS-USA Guidelines, iasusa.org

Update on HIV Pre-Exposure Prophylaxis (PrEP) & Post-Exposure Prophylaxis (PEP)

HIV Pre-Exposure Prophylaxis (PrEP)
KEY POINTS

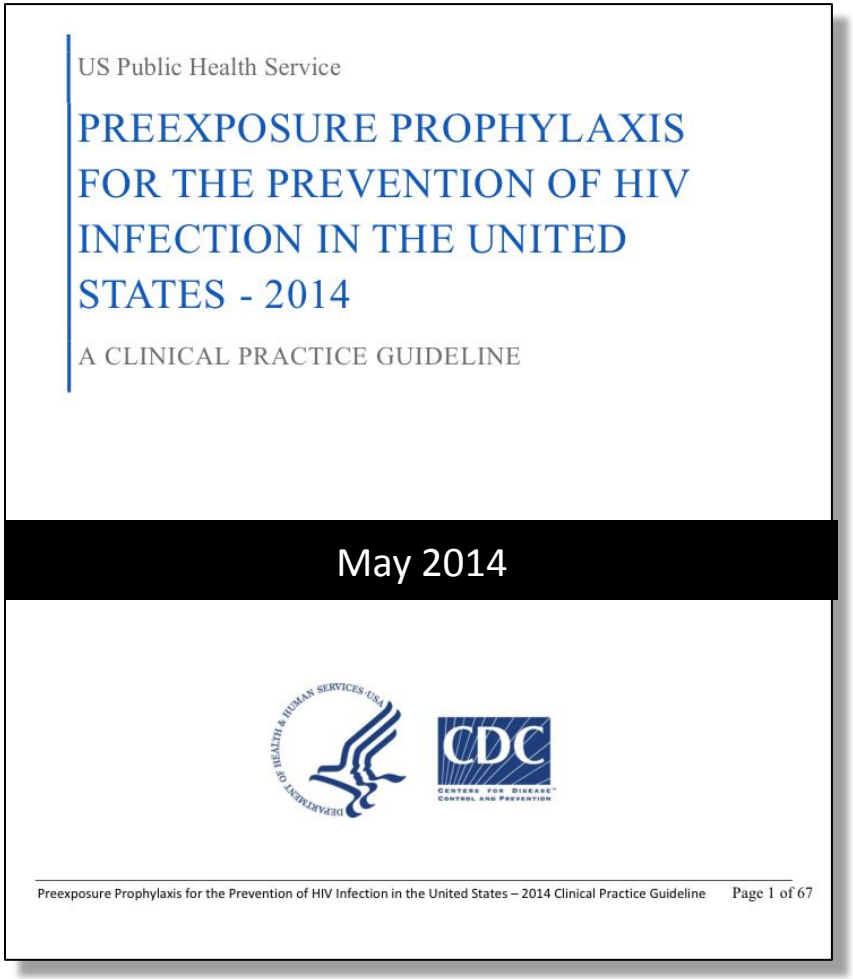
- Currently FTC/TDF (*Truvada*) is only approved PrEP drug
- **FTC/TAF (*Descovy*) may be approved for PrEP soon!**
- Other delivery systems, including long acting, are coming
- Intermittent (pericoital or “on-demand”) dosing for cisgender men who have sex with men (MSM) remains controversial
- Biggest PrEP challenges: awareness, access, adherence

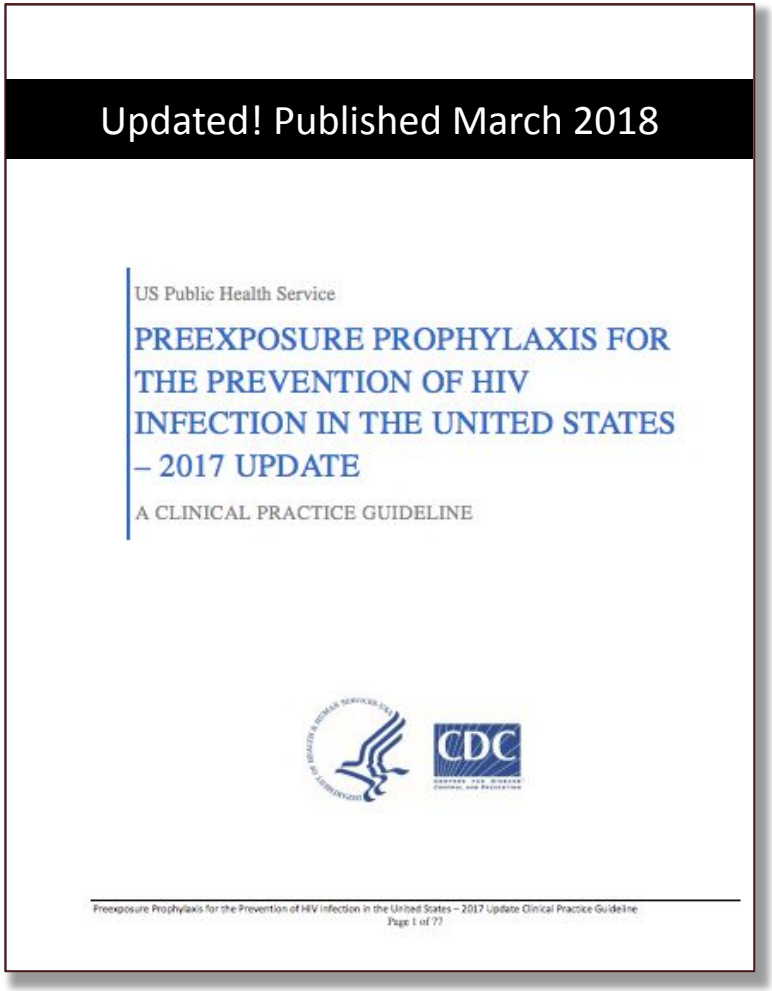
Key Considerations with HIV PrEP

- HIV PrEP with TDF/FTC is >80-90% effective
- Failures with good adherence are quite rare
- Side effects are generally mild and transient
- Important to screen for HIV before starting
- Individuals continue to have high risk of STI's after starting HIV PrEP – regular screening is important
- TDF/FTC not recommended with any renal insufficiency, but data for TAF/FTC are promising (and NDA submitted)

Sources: PrEP Guidelines, aidsinfo.nih.gov or cdc.gov

CDC released official PrEP guidelines in 2014, and updated them in 2017





http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf
https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

"On-Demand" PrEP for Cisgender MSM

- IPERGAY
  - 2 emtricitabine-tenofovir DF (*Truvada*) tabs before sex then 2 in 48 hours after
  - Compared to placebo
  - Trial stopped; **86% reduction** in HIV incidence
- PREVENIR
  - Open-label; men opt for daily or on-demand dosing
  - About half chose each option
  - At mean follow-up 7 months, **zero HIV transmissions**

Sources:
IPERGAY: Molina JM, et al. N Engl J Med 2015;373:2237-46.
PREVENIR: Molina JM, et al. IAS Conference, Amsterdam, July 2018.

Controversy Around "On-Demand" PrEP for Cigender MSM

- Not recommended in CDC PrEP Guidelines
- Used in Europe and considered an alternative per IAS-USA
- Issues: how to monitor labs, adherence, and refills?

*Other unanswered PrEP questions:

- Should we be offering generic TDF/3TC as HIV PrEP? CDC guidelines say no, but could improve access

- What is the role of PrEP for a serodifferent couple when the partner with HIV has an undetectable viral load?

- Also, doxycycline shown to be effective for chlamydia and syphilis PrEP and PEP, but should we be offering it?

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

HIV PrEP in the Future

Pill

Gel

Vaginal film

Vaginal ring

Injectable

- Tenofovir-containing pills are not feasible for everyone. There is an encouraging pipeline of new PrEP prevention products that will deliver additional options.
- However, we would be naïve to imagine that any one of these will work or be workable for every person.
- What is wanted = prevention ***options***.

PrEP Coverage in Washington

- Washington State PrEP DAP (also lists PrEP providers and PrEP navigators)

www.doh.wa.gov/YouandYourFamily/IllnessandDisease/HIVAIDS/HIVCareClientServices/PrEPDAP

- Gilead Medication Assistance Program

www.gilead.com/responsibility/us-patient-iaccess/truvada%20for%20prep%20medication%20assistance%20program

- Project Inform (flow sheet with additional resources)

http://www.projectinform.org/pdf/PrEP_Flow_Chart.pdf

HIV Post-Exposure Prophylaxis (PEP)

- No dramatic changes
- Same strategy – 3-drug ART within 72 hours of exposure
- Preferred regimen TDF/FTC (*Truvada*) + raltegravir *or* dolutegravir
- Follow up labs at 6 and 16 weeks
- Some outstanding questions: *is PEP indicated if source has undetectable viral load? Is TAF/FTC as effective as TDF/FTC?*

Source: CDC guidelines; aidsinfo.nih/gov

What's New in HCV Treatment?

Who Should Be Treated for HCV?

- Treatment is recommended for all individuals with HCV (unless very limited life expectancy) because it:
  - Reduces liver-related complications (ESLD, HCC, decompensation events) and all-cause mortality
  - Improves symptoms, liver inflammation, and liver fibrosis
  - Eliminates the risk of transmission to others!
  - Now generally requires only 2-3 months of oral therapy with >90% chance of SVR (cure) for most individuals!

Source: hcvguidelines.org

Who Should be Treated for HCV More Urgently?

- Advanced stage of fibrosis
  - Especially stage 3 or compensated stage 4 fibrosis
  - If decompensated, need co-management with a specialist
- Symptomatic or systemic complications (cryoglobulinemia, porphyria, lichen planus, arthritis, fatigue, etc)
- HIV or HBV co-infection; other causes of liver disease
- High risk of transmitting to others

Source: hcvguidelines.org

What Evaluation Is Needed Before Treating HCV?

1) Need to know treatment-naïve or experienced?

2) Labs:

- Hepatitis C RNA (viral load) and ?genotype
- Baseline CMP (consider CBC, INR)
- Hepatitis B serology panel
- Very rarely need a resistance test at baseline

3) Assessment of fibrosis stage

Assessment of Fibrosis Stage

Liver biopsy

- Also provides assessment of other causes of liver disease (NASH, iron, autoimmune hepatitis, etc)
- Subject to observer variability, sampling error

or…

Non-invasive markers

- Elastography (Fibroscan)
- Direct biomarkers (Fibrosure, Fibrotest)
- Indirect markers (APRI, FIB-4)
- *Usually combine 2 of the above

Source: hcvguidelines.org

Another Pre-Treatment Consideration: Risk of Hepatitis B Reactivation

- FDA warning (October 2016)
- 24 cases of hep B reactivation during hep C DAA therapy
  - 2 deaths; 1 liver transplant
- Check hep B serology panel prior to treatment
  - If surface Ag+ start hep B treatment first
  - If only core Ab+ monitor AST/ALT monthly during hep C tx

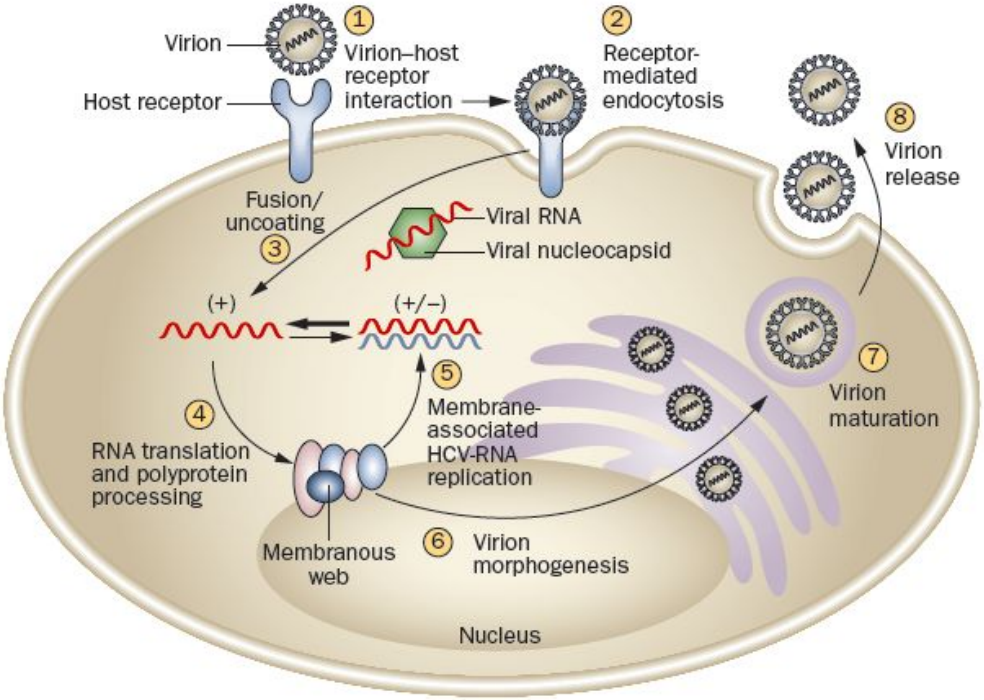
Source: hcvguidelines.org, fda.gov

TREATMENT OF CHRONIC HEPATITIS C

Guidelines for Treatment-Naïve Individuals (hcvguidelines.org)

DAA: Directly Acting Antiviral

- "**PREVIR**": protease inhibitors (e.g. glecaprevir, grazoprevir, voxilaprevir)
- "**BUVIR**": polymerase inhibitors (e.g. sofosbuvir)
- "**ASVIR**": NS5A inhibitors (e.g. ledipasvir, elbasvir, velpatasvir, pibrentasvir)



Adapted from talk by Dr. Kristen Marks (April 2018, IAS-USA Webinar)

HCV Treatment Recommendations, Updated Sept. 2017
Treatment Naïve Genotype 1a Chronic HCV

Treatment Regimen	Duration- No Cirrhosis	Duration- Compensated Cirrhosis
Sofosbuvir/velpatasvir (*Epclusa*) 1 tab daily	**12 weeks**	**12 weeks**
Sofosbuvir/ledipasvir (*Harvoni*) 1 tab daily	*12 weeks	12 weeks
Glecaprevir/pibrentasvir (*Mavyret*) 3 tabs daily	**8 weeks**	**12 weeks**
Elbasvir/grazoprevir (*Zepatier*) 1 tab daily	No NS5A resistance: 12 weeks NS5A resistance: not recommended	No NS5A resistance: 12 weeks NS5A resistance: not recommended

*8 weeks may be sufficient if HCV RNA <6 million, no HIV infection, and not African American

Source: AASLD/IDSA/IAS-USA (www.hcvguidelines.org).

HCV Treatment Recommendations, Updated Sept. 2017
Treatment Naïve Genotype 1b Chronic HCV

Treatment Regimen	Duration- No Cirrhosis	Duration- Compensated Cirrhosis
Ledipasvir/velpatasvir (*Epclusa*)	**12 weeks**	**12 weeks**
Ledipasvir/sofosbuvir (*Harvoni*)	*12 weeks	12 weeks
Glecaprevir/pibrentasvir (*Mavyret*)	**8 weeks**	**12 weeks**
Elbasvir/grazoprevir (*Zepatier*)	12 weeks	12 weeks

*8 weeks may be sufficient if HCV RNA <6 million, no HIV infection, and not African American

Source: AASLD/IDSA/IAS-USA (www.hcvguidelines.org).

HCV Treatment Recommendations, Updated December 2014
Treatment Naïve Genotype 2 Chronic HCV

Treatment Regimen	Duration- No cirrhosis	Duration- Compensated Cirrhosis
Sofosbuvir/velpatasvir (*Epclusa*)	**12 weeks**	**12 weeks**
Glecaprevir/pibrentasvir (*Mavyret*)	**8 weeks**	**12 weeks**

Source: AASLD/IDSA/IAS-USA (www.hcvguidelines.org).

HCV Treatment Recommendations, Updated December 2014
Treatment Naïve Genotype 3 Chronic HCV

Treatment Regimen	Treatment Duration- No Cirrhosis	Treatment Duration- Cirrhosis
Sofosbuvir/velpatasvir (*Epclusa*)	**12 weeks**	**12 weeks***
Glecaprevir/pibrentasvir (*Mavyret*)	**8 weeks**	**12 weeks**

*Consider resistance testing at baseline and if Y93H mutation present, consider adding ribavirin or using sofosbuvir/velpatasvir/voxilaprevir x 12 weeks

Source: AASLD/IDSA/IAS-USA (www.hcvguidelines.org).

Choosing Between the Regimen Options

- A lot depends on the payer
- Factors may indicate need for one regimen over another:
  - Decompensated cirrhosis: avoid PI's (so avoid G/P, use a sofosbuvir-based option) *treat with help of a transplant center
  - Stage 4/5 CKD: avoid sofosbuvir (G/P ok)
  - Some drug-drug interactions (DDI's) may be a factor

Source: AASLD/IDSA/IAS-USA (www.hcvguidelines.org).

Drug-Drug Interactions

- A comprehensive assessment of all prescribed & OTC meds is recommended prior to initiating treatment
  - Good resource: http://www.hep-druginteractions.org/
- Examples:
  - Ledipasvir & velpatasvir interact with PPI's
  - HCV PI's interact with rifampin, some statins, some anti-epileptics, etc.
  - There are some interactions with HIV ART (that are surmountable)

Monitoring During and After Hep C Treatment

- Hep C RNA (viral load) at two time points: end of treatment and 12-24 weeks post treatment
  - Optional at 4 weeks of treatment (mostly to assess adherence)
  - Optional 12 months after treatment (consider if cirrhosis or HIV+)
  - Repeat if concern for reinfection at later timepoint
- CMP at 4 weeks
  - Then q4 weeks if concern or if hep B surface Ag+ or isolated core Ab+
- Ongoing surveillance for HCC if cirrhosis present pre-treatment

Source: AASLD/IDSA/IAS-USA (www.hcvguidelines.org).

Medication Access and Patient Assistance

- www.MySupportPath.com, 1-855-7MyPath
- Patient assistance programs for uninsured through drug companies
- Patient Access Network (PAN) Foundation for high deductibles
- HepEducation project (Seattle)

What's New in HBV Treatment & Prevention?

HBV Treatment Options

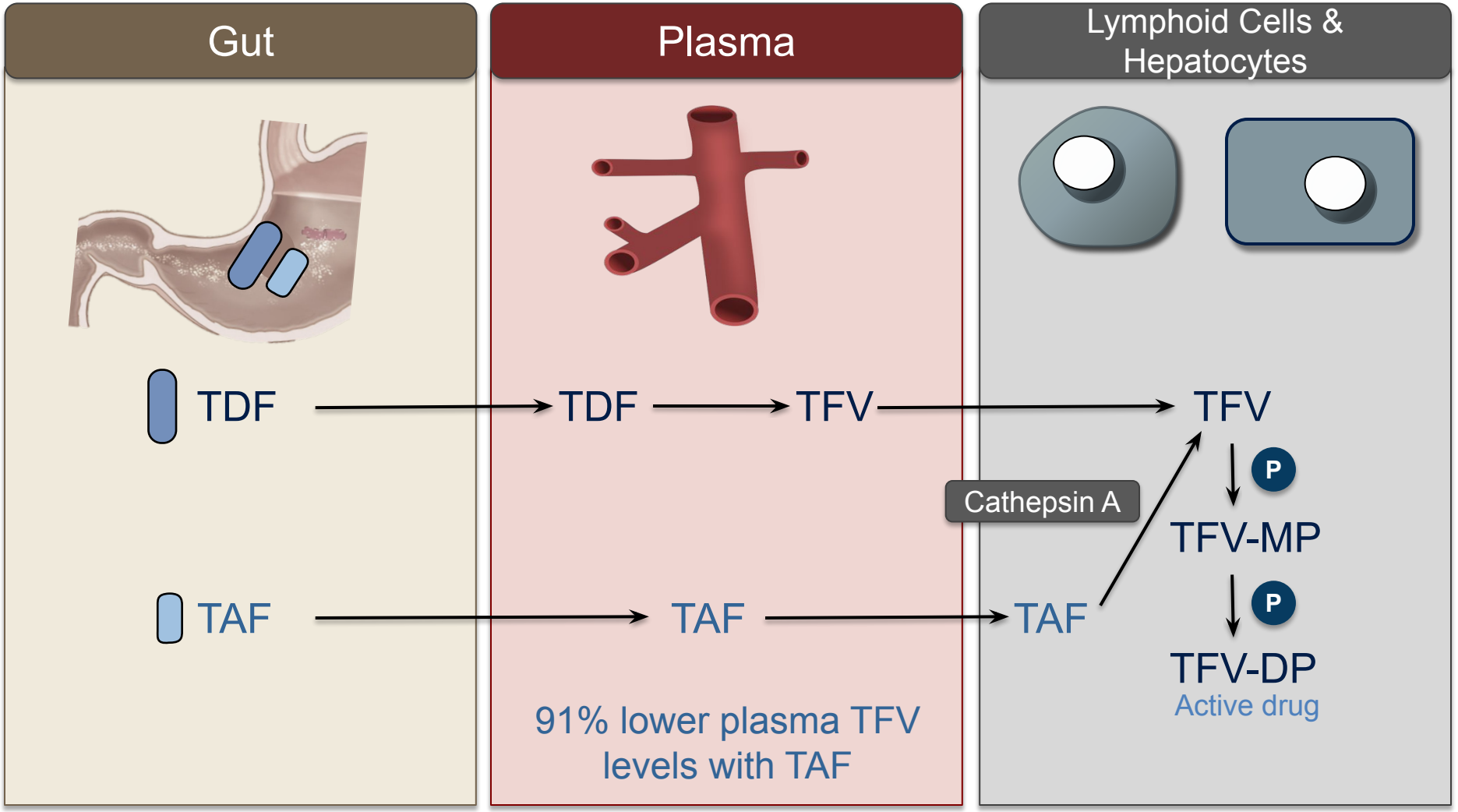
- Interferon (rarely used)
- Nucleos(t)ides (current standard):
  - **Tenofovir alafenamide (TAF)**
  - Tenofovir disoproxil fumarate (TDF)
  - **Entecavir (ETV)**
  - Lamivudine (3TC) (only in combination)

Drugs in phase I/II development

siRNAs
ARB-1467
ARB-1740
RG6004 (HBV LNA)
ARO-HBV
Entry Inhibitor
Myrcludex B
Capsid Inhibitors
NVR 3-778
JNJ-56136379
ABI-H0731
AB-423
HBsAg Inhibitors
REP 2139
REP 2165

Source: Kim WR, Advances in Hepatology, Vol 14, July 2018.

Tenofovir DF (TDF) versus Tenofovir alafenamide (TAF)



TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Slide courtesy of Dr. David Spach

Indications for Hepatitis B Treatment
No Cirrhosis

HBeAg	HBV DNA	ALT	Treatment Strategy
+	>20,000 IU	≤2x ULN	• Treatment generally not recommended; may consider if older or family history of HCC, otherwise monitor DNA and ALT
+	>20,000 IU	>2x ULN	• Treat if no spontaneous clearance of eAg after 3-6 months, or immediately if severe hepatitis • ETV, TAF, or TDF preferred • Continue for at least 12 months after eAg seroconversion
-	>2,000 IU	>2x ULN or 1-2x ULN with liver biopsy or other tests showing moderate/severe inflammation or fibrosis (≥F2)	• Treat with ETV, TAF, or TDF • Continue until SAg loss • Generally several years or indefinite
-	≤2,000 IU	≤ULN	• Monitor

Source: Management of Hepatitis B, UpToDate.

Indications for Hepatitis B Treatment
Cirrhosis

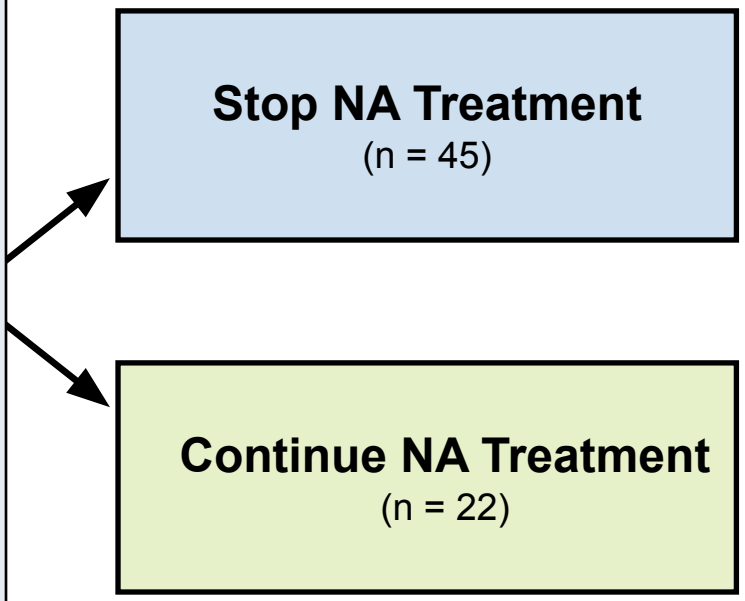
HBeAg	HBV DNA	ALT	Treatment Strategy
+/-	Detectable	Any	• Treat immediately if decompensated • If compensated, treat if HBV DNA >2,000 IU, or ALT elevated • ETV, TAF, or TDF indefinitely
+/-	Undetectable	Any	• Observe and monitor HBV DNA and ALT if compensated, refer for transplant eval if decompensated

Source: Management of Hepatitis B, UpToDate.

Hepatitis B
The STOP Study

The STOP Study: Design

- **Background**: Randomized, controlled, open-label, phase IV trial
- **Inclusion Criteria:**
  - Chronic HBV (sAg+ >6 months)
  - Received nucleos(t)ide analog (NA) treatment >12 months
  - If eAg positive at start of NA treatment, undetectable HBV DNA for 12 months
  - If eAg negative at start of NA treatment, undetectable HBV DNA for 36 months
  - No decompensated cirrhosis
  - No HIV or HCV coinfection
- **Primary Endpoint:**
  - Response at end of follow up (72 weeks)
  - Sustained HBV DNA <2,000, sAg loss



Hepatitis B
The STOP Study

Results of the The STOP Study		
	Stop (n = 45)	**Continue** (n = 22)
HBV DNA <2,000 at week 48	24%	95%
HBV sAg loss at week 48	2%	5%
Retreated by week 72	38%	-
Clinical relapse (HBV DNA >2,000 and ALT >1.5x ULN) by week 72	13%	-
Virologic relapse (HBV DNA >2,000 and ALT <1.5x ULN) by week 72	27%	-

Conclusion: 72 weeks after stopping NA therapy, a majority of participants had a relapse; no benefit was found to stopping NA treatment

Source: Liem KS et al, The Liver Meeting, Nov 2018.

Newest HBV Vaccine: Heplisav®

- FDA approved 11/2017 for adults 18+ years
- Only 2-dose adjuvanted Hep B vaccine for adults
- Adjuvant is a phosphorothioate oligonucleotide that targets TLR-9 to enhance antibody response

Table 2: Comparisc

			Seroprotection rates (SPR)		
Study	**Age range**	**Sample size**	**Heplisav-B (95% CI)**	**Engerix-B (95% CI)**	**Difference in SPRs (95% CI)**
Study 1	18 to 55	Heplisav-B (N=1511) Engerix-B (N=521)	95% (93.9, 96.1)	81.3% (77.8, 84.6)	13.7% (104, 17.5)
Study 2	40 to 70	Heplisav-B (N=1121) Engerix-B (N=353)	90.1% (88.2, 91.8)	70.5% (65.6, 75.2)	19.6% (14.7, 24.8)
Study 3	18 to 70	Heplisav-B (N=5592) Engerix-B (N=2782)	90.0% (87.4, 92.2)	65.1% (59.6, 70.3)	24.9% (19.3, 30.7)

Sources: Halperin SA et al. Vaccine 2012. Heyward WL et al. Vaccine 2013. Jackson S et al. Vaccine 2017. Janssen J et al. Vaccine 2015

Concern for Acute MI Risk

- One of the randomized controlled trials showed increased risk of acute MI
  - 0.3% (n=19) with Heplisav-B vs 0.1% (n=3) with Engerix-B
  - All had CV risk factors but more in the Heplisav group at CV risk factors

- Conclusions from FDA
  - Acute MI incidence was expected based on CV risk factors
  - No temporal association with vaccine administration
  - Recommended ongoing surveillance post-marketing

Source: https://www.fda.gov/vaccines-blood-biologics/vaccines/heplisav-b

ACIP Recommendations for HBV Immunization

- Recombivax®: 3 dose series (0, 1, 6 months) 10 µg/mL IM **(AII)**

OR

- Engerix®: 3 dose series (0, 1, 6 months) 20 µg in 1.0 mL IM **(AII)**

OR

- Heplisav®: 2-dose series (0, 1 month) 20 µg in 0.5 mL IM **(CIII)**

Assess anti-HB sAb 1-2 months after completion of series

Source: https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hepb.html

Questions?
bwood2@uw.edu