Elimination of HCV from an HIV clinic
IAS & Summer 2015 Update

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IAS Update
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Disclosure Statement for Arthur Kim

Grant/research support to institution: Gilead, Abbvie
(Updated 8/6/15)

I will discuss the following off-label use in this presentation:

Off-label use of sofosbuvir + simeprevir, ledipasvir/sofosbuvir, paritaprevir/ritonavir/ombitasvir + dasabuvir, daclatasvir

Unapproved direct-acting agents and combinations

Funding: National Institutes of Health
(National Institute of Allergy and Infectious Diseases, National Institute of Drug Abuse)
Definitions

**Eradication**: permanent reduction to zero of worldwide incidence of infection

  Example: Smallpox

**Elimination**: reduction to zero of incidence of disease or infection in a defined geographical area, requiring presence of continued control measures

  Examples: measles, polio

**Control**: reduction in the incidence, prevalence, morbidity or mortality of an infectious disease to acceptable level
A tale of two viruses

**HIV**
- Sex > Blood
- Targets immune cells
- Years to clinical illness
- High levels of viremia
- Frequently mutates
- 1 cure after BMT

**HCV**
- Blood > Sex
- Targets hepatocytes
- Decades to clinical illness
- High levels of viremia
- Frequently mutates
- HCV >90% curable

Liver deaths remain important cause of mortality in HIV infected patients
HIV / HCV co-infection is double trouble

Compared to HIV-negative individuals, those with HIV suffer from:

1. Susceptibility to mucosal transmission, higher rates of persistence
2. Accelerated rate of fibrosis, higher rates of cirrhosis
3. Higher rates of decompensation & higher liver-related mortality

To reduce the burden of HIV/HCV co-infection we must screen, test, and treat!
A perfect storm for sexual HCV transmission: HIV+MSM

Bloody practices
Semen exposure
Other STDs
Sildenafil
Internet

Higher levels of virus in plasma and semen
Immune deficiency, especially at GI mucosa

Sex
Drugs
HIV

Crystal methamphetamine
Rules of 3: risk after needlestick

- HBV: 30%
- HCV: 3% (~1-2%)
- HIV: 0.3%
Likelihood of HCV infection: duration of IDU

Depending on context: much higher in areas of world without services for PWID

Global access to opiate agonist therapy varies per region / country

Global availability of opioid substitution therapy

Although heroin addiction is a global problem, much of the world remains without a form of substitution therapy.
Opioid agonist / substitution therapy associated with decreased risk of death among HIV+ PWID

British Columbia HIV+ PWID
- ART alone: Decreases risk of death 54%
- OAT alone: Decreases risk of death 66%
- ART+OAT: Decreases risk of death 84%

Nosyk et al. IAS 2015
HIV/HCV Co-infection Outbreak in the U.S.

Community Outbreak of HIV Infection Linked to Injection Drug Use of Oxytherone — Indiana, 2015

On April 28, 2015, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

On January 23, 2015, the Indiana State Department of Health (ISDH) began an ongoing investigation of an outbreak of human immunodeficiency virus (HIV) infection, after Indiana health department officials reported 13 confirmed HIV cases among a rural county in southeastern Indiana. Historically, fewer than five cases of HIV infection have been reported annually in the county. The majority of cases were in residents of the same community and were linked to 13 injecting drug users injecting the prescription opioid oxymorphone (a powerful and semi-synthetic opioid analgesic). As of April 21, ISDH had diagnosed HIV infection in 135 persons (128 with confirmed HIV infection and seven with preliminarily positive results) from eight HIV cases that were pending confirmatory testing in a community of 4,200 persons (3).

The age range of the 135 patients is 18–57 years (median = 35 years; mode = 23 years; 74 [54.3%] are male). A total number of pregnant women was diagnosed with HIV infection and started on antiretroviral therapy during pregnancy. As of April 21, no infants had tested positive for HIV. Of the 135 persons with diagnosed HIV infection, 108 (80.0%) had received at least one injection drug use (IDU) and 23 (17.0%) have been interviewed to determine IDU status. Among the 108 who have reported IDU, all reported disusing and injecting oxymorphone as their drug of choice, some reported injecting oxymorphone and heroin, methamphetamine and heroin, or methamphetamine alone. Ten (7.4%) female patients have been identified as commercial sex workers. Combination of hepatitis C virus has been diagnosed in 114 (84.4%) patients.

Need for HCV prevention and vaccine!

135 cases as of report

Investigation triggered by HIV surveillance

Injection of oxymorphone

Multigenerational use of injection drugs

84.4% (114/135) diagnosed with HCV infection
Which is the closest to your screening practice for incident HCV in your HIV clinic?

A. I don’t screen very often for HCV
B. I rely mostly on changes in LFTs to catch incident HCV
C. I apply yearly anti-HCV screening to the highest risk individuals (HIV+MSM or heterosexual with multiple partners)
D. I screen all with anti-HCV yearly
How well do we screen for incident HCV among HIV-infected?

- Study at 7 U.S. HIV clinics
- Nearly all patients screened at enrollment
- Only half ever screened again
- Repeat screening poor even when ALT is elevated
- Site of care more predictive than reported risk behaviors
- MGH’s rate 1 year ago of HCV Ab in last year: 20%

Freiman et al. CID, 2015
Case

49 y/o African-American woman with HIV/HCV co-infection
Infected via husband who died of AIDS-related complications
Insulin-dependent diabetes developed 5 years earlier
Hypertension: metoprolol, lisinopril, amlodipine
PCOS: ethinyl estradiol / progestin
Other meds: ASA 81 mg
BMI: 31, no significant EtOH use

HIV: Suppressed on TDF/FTC + ritonavir + atazanavir
HCV: 1b infection, 12 years ago, bx 1/6 fibrosis, attempted PEG-IFN / RBV, complicated by anemia, requiring transfusion, managed by dose reduction + erythropoietin.
Case

49 y/o African-American woman with HIV/HCV co-infection
HIV Prior regimens: AZT/3TC, AZT/3TC/indinavir, TDF/FTC/EFV, now suppressed on TDF/FTC + ritonavir + atazanavir

HCV: 1b infection, 12 years ago biopsy 1/6 fibrosis

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>63 U/L</td>
</tr>
<tr>
<td>AST</td>
<td>71 U/L</td>
</tr>
<tr>
<td>TBili</td>
<td>2.2 mg/dL</td>
</tr>
<tr>
<td>INR</td>
<td>1.1</td>
</tr>
<tr>
<td>Platelets</td>
<td>152,000</td>
</tr>
<tr>
<td>eGFR</td>
<td>62 ml/min/1.73m²</td>
</tr>
</tbody>
</table>

What would inform a decision to treatment?
How do you decide to (re-)stage the degree of liver fibrosis for this patient?

1. No further staging - labs sufficient
2. Routine ultrasound
3. FibroTest
4. Transient elastography
5. MR elastography
6. Liver biopsy
7. Other
Fibrosis regression (reduction in kPa on Fibroscan) in HIV/HCV co-infected patients

Casado et al. IAS 2015
Potential Therapeutic Targets in the HCV Replication Cycle

- **HCV NS proteins**
  - NS2
  - NS3
  - NS4B
  - NS5A
  - NS5B

- **HCV RNA**
  - Fusion and uncoating
  - RNA replication
  - Transport and release
  - Viral assembly

- **NS3/4A protease inhibitors**
- **NS5A inhibitors**
- **NS5B polymerase inhibitors**

*Courtesy Ray Chung*
Possible combinations of HCV treatments then are applied to different viral genotypes.
Antiviral HCV treatments
(FDA-approved as of July 24, 2015)

**Monotherapies**

- IFN-2a
- IFN-2b
- PEG-IFN 2a
- PEG-IFN 2b

**Combination Therapies**

- IFN-2a + Ribavirin
- IFN-2b + Ribavirin
- PEG-IFN 2a + Ribavirin
- PEG-IFN 2b + Ribavirin

**PEG-IFN + ribavirin plus either:**

- Boceprevir (GT1)
- Telaprevir (GT1)
- Simeprevir (GT1)

**In combination with other agents:**

- Sofosbuvir

- Paritaprevir + ritonavir + ombitasvir (FDC) + dasabuvir (GT1)
- Paritaprevir + ritonavir + ombitasvir (FDC) + dasabuvir (GT4)
- Simeprevir + Sofosbuvir (GT1)
- Daclatasvir + Sofosbuvir (GT3)
- Ledipasvir + Sofosbuvir (FDC, GT1)
Preliminary Study of Two Antiviral Agents for Hepatitis C Genotype 1

Lok et al. NEJM 2012
HCV versus HIV/HCV, genotype 1 in Clinical Trials
Not head to head comparison


Antiviral Drugs Advisory Committee Meeting, FDA review, 10/24/13
Lawitz et al. NEJM 2013 versus Torres - Rodriguez et al., IDSA 2013
**Recommended regimens for HIV/HCV-coinfected individuals.**

HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications (see Initial Treatment of HCV Infection and Retreatment of Persons in Whom Prior Therapy Has Failed sections).

**Rating:** Class I, Level B

- Overall studies in the DAA era show similar efficacy in HIV coinfection compared to monoinfection, when accounting for genotype/treatment experience/fibrosis
  - Some subgroups lacking data

- Management of drug-drug interactions
  - Maximize DAA efficacy and minimize toxicity
  - Ensure HIV-1 suppression
>90% cure rates for GT1

- SAPPHIRE-1: Feld et al. NEJM 2014; SAPPHIRE-2 Zeuzem et al. NEJM 2014

SAPPHIRE/TURQUOISE are 12 week arms only. ION studies are RBV-sparing arms only.

ION-1 and 2: RBV addition did not enhance SVR

Cirrhotics (TURQUOISE)
24 weeks 95.9% SVR

Tx-Exp (ION-2)
24 wks LDV/SOF 108/109 SVR
Audience response

49 y/o African-American woman with HIV/HCV co-infection

Which of these is most problematic with

1. Insulin
2. Metoprolol
3. Lisinopril
4. Amlodipine
5. Ethinyl estradiol / progestin
6. ASA 81 mg
7. TDF/FTC
8. Ritonavir + Atazanavir
ARS Answer

49 y/o African-American woman with HIV/HCV co-infection

Which of these is most problematic with

1. Insulin
2. Metoprolol
3. Lisinopril
4. Amlodipine - levels rise, may need dose reduction
5. Ethinyl estradiol / progestin - elevated LFTs - avoid
6. ASA 81 mg
7. TDF/FTC
8. Ritonavir + Atazanavir - elevated bilirubin
Turquoise-1: 3D regimen for HIV/HCV Coinfected patients, GT1 n=63

3D: coformulated ABT-450/r*/ombitasvir, 150 mg/100 mg/25 mg QD; dasabuvir, 250 mg BID

RBV: 1000 or 1200 mg daily according to body weight in 2 divided doses (<75 kg and ≥75 kg, respectively)

*Ritonavir is dropped from the atazanavir-inclusive ART regimen during the period of co-administration with the 3-DAA regimen

Sulkowski et al. JAMA 2015
**Turquoise-1: 3D regimen for HIV/HCV Coinfected patients, GT1 n=63**

**TURQUOISE-I:**
Baseline Demographics and Disease Characteristics

<table>
<thead>
<tr>
<th></th>
<th>12-Week Arm (N = 31)</th>
<th>24-Week Arm (N = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>29 (94)</td>
<td>29 (91)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>7 (23)</td>
<td>8 (25)</td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>50.9 ± 6.0</td>
<td>50.9 ± 8.3</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
<td>6 (19)</td>
<td>6 (19)</td>
</tr>
<tr>
<td>IL28B non-CC genotype, n (%)</td>
<td>26 (84)</td>
<td>25 (78)</td>
</tr>
<tr>
<td>HCV genotype 1a, n (%)</td>
<td>27 (87)</td>
<td>29 (91)</td>
</tr>
<tr>
<td>HCV RNA (log₁₀ IU/mL), mean ± SD</td>
<td>6.54 ± 0.57</td>
<td>6.60 ± 0.78</td>
</tr>
<tr>
<td>Prior pegIFN/RBV experience, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naïve</td>
<td>20 (65)</td>
<td>22 (69)</td>
</tr>
<tr>
<td>Relapse</td>
<td>1 (3)</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Partial response</td>
<td>5 (16)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Null response</td>
<td>5 (16)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>CD4+ T-cell count/mm³, mean ± SD</td>
<td>633 ± 236</td>
<td>625 ± 296</td>
</tr>
<tr>
<td>Atazanavir HIV-1 ART regimen</td>
<td>16 (52)</td>
<td>12 (38)</td>
</tr>
<tr>
<td>Raltegravir HIV-1 ART regimen</td>
<td>15 (49)</td>
<td>20 (63)</td>
</tr>
</tbody>
</table>

Sulkowski et al. JAMA 2015
TURQUOISE-1 3D+RBV x 12 or 24 wks in HIV/HCV SVR 12: Treatment naive + PR experienced

Mean age 58
~24% Black
19% cirrhosis

n=63
r/ATV (n=28)
RAL (n=35)

No discontinuations
1 withdrew consent
1 breakthrough in nonresponder/cirrhotic
5 >moderate AEs

High CD4 (median 600s)

5 had “blips” HIV-1 RNA > 40 copies/mL, all re-suppressed without change or intensification
A5329 opening shortly includes RAL and rDRV (QD -> BID)

Sulkowski et al. JAMA 2015
3D Abbvie Regimens for HIV/HCV coinfection compatible with HIV protease inhibitors

**Figure 2. Effect of 3D Regimen on $C_{\text{max}}$, $AUC_t$, and $C_{\text{trough}}$ of HIV Protease Inhibitors**

- **DRV** Ctrough lower
- **ATV** Ctrough higher
- **LPV** Ctrough higher
- **PTV** levels higher with r/ATV QPM and r/LPV
- **OBV** & **DSV** levels relatively unaffected
- Well-tolerated, no new safety concerns
- Recommended no dose adjustment of 3D. Due to higher RTV dose, avoid with r/LPV

Khatri et al. ICAAC September 2014, Washington DC Abstract #038
Audience response

49 y/o African-American woman with HIV/HCV co-infection

Which of these is most problematic with

1. Insulin
2. Metoprolol
3. Lisinopril
4. Amlodipine
5. Ethinyl estradiol / progestin
6. ASA 81 mg
7. TDF/FTC
8. Ritonavir + Atazanavir
ledipasvir + sofosbuvir (FDC) ION-4 for HIV/HCV

- Phase 3, multicenter, open-label study (NCT02073656)
- HCV GT 1 or 4 patients in US, Canada, and New Zealand
- Broad inclusion criteria
  - HCV treatment-naïve or treatment-experienced
  - 20% with compensated cirrhosis
  - Platelets $\geq 50,000/mm^3$; hemoglobin $\geq 10$ mg/dL, CrCl $\geq 60$ mL/min
  - HIV-1 positive, HIV RNA $< 50$ copies/mL; CD4 cell count $> 100$ cells/mm$^3$
- ART regimens included emtricitabine and tenofovir disoproxil fumarate plus efavirenz, raltegravir, or rilpivirine
ledipasvir + sofosbuvir (FDC) ION-4 for HIV/HCV

Naggie et al. NEJM 2015
ledipasvir + sofosbuvir (FDC) ION-4 for HIV/HCV
**Tenofovir Exposures**

Slide Courtesy of Gilead Sciences

- **TFV exposures are higher when TDF is coadministered with LDV/SOF compared to without LDV/SOF**
- **Compared to the range of TFV exposures with available safety data**
  - For EFV or RPV: TFV exposures fall within the range\(^1\)
  - For RTV-boosted PIs: TFV exposures partially exceed the range\(^2\)

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1. Data on File, Gilead Sciences.
5. Chittick GE, et al. AAC. 2006; 50(4):1304-10 (SQV+RTV)
6. Zhu. 9th IWCPHT. 2008. #023 (ATV+RTV & LPV/r)

\(^1\) HIV-infected subjects in CASTLE study

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**TFV AUC\(_{tau}\) (ng·h/ml)**

- **NNRTIs**
  - Without LDV/SOF\(^1,2\)
  - With LDV/SOF\(^3\)
- **RTV-Boosted PIs**
  - Without LDV/SOF\(^4-9\)
  - With LDV/SOF\(^10\)

Range of TFV exposures with available safety data

- EFV
- RPV
- ATR
- CPA
- FPV
- SQV
- LPV/r
- ATV
- DRV
- ATV
- DRV

\(N = 30\)

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*Slide Courtesy of Gilead Sciences*
ledipasvir + sofosbuvir (FDC) ION-4 for HIV/HCV

4 patients (1%) had change in creatinine ≥ 0.4 mg/dL
- 2 completed treatment with no ART change
- 1 had dose reduction of TDF, 1 discontinued TDF

Naggie et al. CROI 2015
HCV Interactions Summary

**LDV/SOF**: Key interactions -
- monitor for potential tenofovir toxicity
  - Particularly with HIV protease inhibitors
  - Care with eGFR < 60 mL/min/1.73 m², high-risk patients
  - Monitor urine protein, serum BUN/Cr, electrolytes including phosphorus

**3D regimen**: Key interactions -
- AVOID with efavirenz, rilpivirine, lopinavir/ritonavir
- Ensure proper ritonavir dosing
- ACTG 5329 will examine compatibility with boosted darunavir

### Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg):
- Because ledipasvir increases tenofovir levels, concomitant use mandates consideration of creatinine clearance (CrCl) rate and should be avoided in those with CrCl below 60 mL/min. Because potentiation of this effect is expected when tenofovir is used with ritonavir-boosted HIV protease inhibitors, ledipasvir should be avoided with this combination (pending further data) unless antiretroviral regimen cannot be changed and the urgency of treatment is high.

**Rating**: Class IIa, Level C

For combinations expected to increase tenofovir levels, baseline and ongoing assessment for tenofovir nephrotoxicity is recommended.

**Daily fixed-dose combination of paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) plus twice-daily dosed dasabuvir (250 mg) (hereafter paritaprevir/ritonavir/ombitasvir plus dasabuvir):**
- Paritaprevir/ritonavir/ombitasvir plus dasabuvir should be used with antiretroviral drugs with which it does not have substantial interactions: raltegravir (and probably dolutegravir), enfuvirtide, tenofovir, emtricitabine, lamivudine, and atazanavir.

**Rating**: Class IIa, Level C
<table>
<thead>
<tr>
<th>ARV Interaction Score Card</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Simeprevir</strong>¹</td>
</tr>
<tr>
<td><strong>ATV/r</strong></td>
</tr>
<tr>
<td><strong>DRV/r</strong></td>
</tr>
<tr>
<td><strong>LPV/r</strong></td>
</tr>
<tr>
<td><strong>TPV/r</strong></td>
</tr>
<tr>
<td><strong>EFV</strong></td>
</tr>
<tr>
<td><strong>RPV</strong></td>
</tr>
<tr>
<td><strong>ETR</strong></td>
</tr>
<tr>
<td><strong>RAL</strong></td>
</tr>
<tr>
<td><strong>EVG/cobi</strong></td>
</tr>
<tr>
<td><strong>DTG</strong></td>
</tr>
<tr>
<td><strong>MVC</strong></td>
</tr>
<tr>
<td><strong>TDF</strong></td>
</tr>
</tbody>
</table>

¹Only problematic when administered with TDF, TFV levels increased, ²Decrease DCV dose to 30mg QD with ATV, increase DCV dose to 90mg QD with EFV and ETR, ³3D + EFV led to premature study discontinuation due to toxicities
¹⁰Ouwerkerk-Mahadaven IDWeek 2012, ¹¹Kirby AASLD 2012, ¹²Harvoni package insert, ¹³German Int WkshpClin Pharm HIV and Hep C Therapy 2014, ¹⁵German CROI 2015,
HCV Drug-Drug Interactions

• Requires close attention - develop a systematic approach
  • www.hep-druginteractions.org — University of Liverpool
  • www.hcvdruginfo.ca
  • www.aidsinfo.nih.gov

• HIV antiretrovirals
  – Do NOT interrupt therapy
  – Determine need and feasibility for ART switch
    – Factors include prior HIV genotypic testing and ARV history
      – Consult HIV specialist
    – With present cautions and contraindications, majority of patients may require consideration of ARV change, except use of DCV/SOF
  – HIV suppression remains goal, without compromising future options
    – Monitor adherence, side effects closely during switch
ALLY-2: Study Design

- Primary endpoint: SVR12 in treatment-naive patients with GT 1 treated for 12 weeks
- Standard DCV dose is 60 mg
  - Dose-adjusted for concomitant ARV therapy: 30 mg with ritonavir-boosted PIs, 90 mg with NNRTIs except RPV

* HCV RNA <LLOQ (TD or TND) at posttreatment Week 12, assessed using the Roche HCV COBAS TaqMan Test v2.0 (LLOQ 25 IU/mL).
### ALLY-2: Demographics, HCV Disease Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Naive 12 Week N = 101</th>
<th>Experienced 12 Week N = 52</th>
<th>Naive 8 Week N = 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median years (range)</td>
<td>52 (24–71)</td>
<td>57 (43–66)</td>
<td>50 (28–75)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>92 (91)</td>
<td>43 (83)</td>
<td>42 (84)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>66 (65)</td>
<td>31 (60)</td>
<td>28 (56)</td>
</tr>
<tr>
<td>Black</td>
<td>30 (30)</td>
<td>20 (38)</td>
<td>19 (38)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (5)</td>
<td>1 (2)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>HCV GT, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>71 (70)</td>
<td>33 (63)</td>
<td>35 (70)</td>
</tr>
<tr>
<td>1b</td>
<td>12 (12)</td>
<td>11 (21)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>2</td>
<td>11 (11)</td>
<td>2 (4)</td>
<td>6 (12)</td>
</tr>
<tr>
<td>3</td>
<td>6 (6)</td>
<td>4 (8)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>4</td>
<td>1 (1)</td>
<td>2 (4)</td>
<td>0</td>
</tr>
<tr>
<td>HCV RNA, mean log_{10} IU/mL (SD)</td>
<td>6.50 (0.76)</td>
<td>6.52 (0.79)</td>
<td>6.40 (0.71)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)*</td>
<td>9 (9)</td>
<td>15 (29)</td>
<td>5 (10)</td>
</tr>
</tbody>
</table>
## ALLY-2: HIV Disease Characteristics and Treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Naive 12 Week N = 101</th>
<th>Experienced 12 Week N = 52</th>
<th>Naive 8 Week N = 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV RNA &lt; 50 copies/mL, n/N (%)</td>
<td>94/100 (94)</td>
<td>47/49 (96)</td>
<td>45/48 (94)</td>
</tr>
<tr>
<td>CD4 cells/mm², median (range)</td>
<td>520 (122–1147)</td>
<td>636 (262–1470)</td>
<td>575 (157–1430)</td>
</tr>
<tr>
<td>Receiving HIV treatment, n (%)</td>
<td>100 (99)</td>
<td>51 (98)</td>
<td>48 (96)</td>
</tr>
<tr>
<td>PI regimens*</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Darunavir/r</td>
<td>19 (19)</td>
<td>11 (21)</td>
<td>21 (42)</td>
</tr>
<tr>
<td>Atazanavir/r</td>
<td>19 (19)</td>
<td>12 (23)</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Lopinavir/r</td>
<td>9 (9)</td>
<td>0</td>
<td>3 (6)</td>
</tr>
<tr>
<td>NNRTI regimens</td>
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</tr>
<tr>
<td>Efavirenz</td>
<td>18 (18)</td>
<td>8 (16)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>5 (5)</td>
<td>3 (6)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>5 (5)</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Other regimens</td>
<td></td>
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</tr>
<tr>
<td>Raltegravir</td>
<td>22 (22)</td>
<td>10 (20)</td>
<td>8 (16)</td>
</tr>
<tr>
<td>Dolutegravir</td>
<td>3 (3)</td>
<td>4 (8)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Nucleosides only</td>
<td>0</td>
<td>2 (4)</td>
<td>0</td>
</tr>
<tr>
<td>DCV SOF</td>
<td></td>
<td></td>
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</tbody>
</table>
Daclatasvir + Sofosbuvir ALLY-2 study for HIV/HCV 8/12 weeks for naïve, 12 for experienced

GT 1 (N = 168)
- 12-Week Naïve: 96%
- 12-Week Experienced: 98%
- 8-Week Naïve: 76%

All Patients (N = 203)
- 12-Week Naïve: 97%
- 12-Week Experienced: 98%
- 8-Week Naïve: 76%

Follow-up Wk 12 data missing (n = 1)
- Detectable at EOT (n = 1)
- Relapse (n = 1)

Relapse (n = 10)
- Follow-up Wk 12 data missing (n = 2)

DCV 60 mg standard dose, 30 mg with boosted PIs, 90 mg with NNRTIs except rilpivirine

Wyles et al. NEJM 2015
ALLY-2 Safety and Tolerability, HIV Outcomes

- A total of 4/203 patients suffered serious AE
- 1 patient in 8 week group died of cardiac arrest post-treatment week 4

- HIV outcomes
  - 10 patients had HIV RNA > 50 copies/mL at end of treatment
    - 2 patients lost to f/u
    - 8 patients repeated testing with 7 HIV RNA < LLOQ (<40 copies/mL) - no change in cART
  - 2 patients with HIV RNA > 400 copies/mL
    - 1 lost to follow-up (incarceration)
    - 1 HIV failure confirmed in post-treatment f/u
Recommended regimens for HIV/HCV-coinfected individuals.

Daily daclatasvir (refer above for dose) and sofosbuvir (400 mg), with or without RBV (refer to Initial Treatment of HCV Infection and Retreatment of Persons in Whom Prior Therapy Has Failed sections for duration) is recommended when antiretroviral regimen changes cannot be made to accommodate alternative HCV direct-acting antivirals.

Rating: Class I, Level B

- **Daclatasvir** is compatible with almost all commonly used antiretrovirals
  - sofosbuvir may not be used with tipranavir
  - Adjustment for rATV (30 mg), EFV/ETR (90 mg)
- **Daclatasvir + sofosbuvir** achieved excellent SVR rates in HIV/HCV
  - 97% overall SVR for 12 weeks of DCV/SOF
  - Smaller numbers in certain subgroups
  - Extension of therapy for cirrhosis
Background of the Hepatitis C Guidance

New direct-acting oral agents capable of curing hepatitis C virus (HCV) infection have been approved for use in the United States. This initial cohort of agents were approved in 2011, and many more oral drugs are expected to be approved in the next few years. As new information is presented at scientific conferences and published in peer-reviewed journals, health care practitioners have expressed a need for a credible source of unbiased guidance on how best to treat their patients with HCV infection. To provide healthcare professionals with timely guidance, the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) in collaboration with the International Antiviral Society–USA (IAS-USA) have developed a web-based process for the rapid formulation and dissemination of evidence-based, expert-developed recommendations for hepatitis C management.

New sections will be added, and the recommendations will be updated on a regular basis as new information becomes available. An ongoing summary of “recent changes” will also be available for readers who want to be directed to updates and changes.

About Hepatitis C

An estimated 3 million to 4 million persons in the United States are chronically infected with HCV, and approximately half are unaware of their status. These individuals may ultimately progress to advanced liver disease and/or hepatocellular cancer. However, those outcomes can be prevented by treatment, which is rapidly
A plan to eliminate HCV in your HIV clinic

1. **Prevent** (harm reduction)
2. **Diagnose** (yearly testing for at risk HIV+)
3. **Stage to determine fibrosis degree** (F3/F4 at risk for complications)
4. **Address drug-drug interactions**
5. **Treat** to prevent transmission & liver-related complications

**Eradication** will be difficult, but **Elimination** or **Control** may be possible

- thanks to Susanna Naggie (ION-4), David Wyles (ALLY-2), natap.org