A Practical Guide to Hepatitis C Management

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TV Safe JY-Sept. 30, 2014
What is hepatitis C?

- RNA virus.
- Parenteral transmission.

1989: HCV is cloned and sequenced.
1991: Anti-HCV ELISA is introduced.
1991: FDA approves the first drug for HCV.
2011: FDA approves “triple therapy” for GT1.

Up to 70-80% patients can be cured.

How common is hepatitis C?

- Incidence, 1990: ~ 180,000 new cases/ year.
- Incidence, 2013: ~ 17,000 new cases / year.
- 3.2-5 million HCV-infected in U.S.
- Prevalence:
  - General population 1%
  - IVDUs 80-90%
  - Incarcerated 15%
  - HIV-infected ~ 30%
What are the consequences of HCV infection?

- Symptoms:
  - Fatigue.
  - Joint pain.
- Chronic liver disease.
- Glomerulonephritis.
- Cryoglobulinemia.
- Non-Hodgkin lymphoma.
What are the consequences of HCV infection?

- Symptoms:
  - Fatigue.
  - Joint pain.
  - Chronic liver disease.
  - Glomerulonephritis.
  - Cryoglobulinemia.
  - Non-Hodgkin lymphoma.
How common is HCV-induced cirrhosis and what are its consequences?

- Increasing prevalence of cirrhosis in HCV-infected individuals.
  - 9.0% in 1996.
  - 18.5% in 2006.
- Cirrhosis develops in 20%.
- Increasing prevalence of liver cancer in HCV-infected individuals.
  - 0.1% in 1996.
  - 1.3% in 2006.
- ~15,000 deaths each year.


Why do we treat?
Why do we treat?

Is treatment effective?

Important dates in the history of hepatitis C

Sustained virologic response = SVR = cure!

PegIFN + RBV + protease inhibitor


-100%

-75%

-50%

-25%

Interferon α2b

IFN + Ribavirin

PegIFN + RBV

PegIFN + RBV in HIV-HCV
Why do we treat? Is treatment effective? Is treatment cost effective?

↓ liver-related mortality.
↓ all-cause mortality.
↓ incidence of liver cancer.

van der Meer AJ et al. JAMA. 2012;308:2584-93
Why do we treat?

Is treatment effective?

Is treatment cost effective?

Screening followed by treatment

$47,000 per Quality-adjusted life-year saved


The USPSTF recommends:

- Screening for HCV infection in persons at high risk for infection.

- One-time screening for HCV infection in adults born between 1945 and 1965.

Screening for Hepatitis C Virus Infection in Adults: U.S. Preventive Services Task Force Recommendation Statement

Ann Intern Med 2013; Sep 3;159(5):349-57
Why do we try to assess the severity of chronic hepatitis C?

- Estimate prognosis.
- Guide to aggressiveness of therapy.
Hepatitis C:
Assessing severity

Standard labs and scans
- AST / ALT
- T.bili, Albumin, INR
- Platelet count
- Ultrasound

Liver biopsy
- Grade (inflammation)
- Stage (fibrosis)

Normal liver
Hepatitis C: Assessing severity

- Standard labs and scans
  - AST / ALT
  - T.bili, Albumin, INR
  - Platelet count
  - Ultrasound

- Liver biopsy
  - Grade (inflammation)
  - Stage (fibrosis)

- Liver fibrosis markers
  - Hepascore®
  - FibroSURE®

- Fibroelastography
  - FibroScan®

Who do we treat?
**Who do we treat?**

“Triggers” for treating hepatitis C

- Liver:
  - HCV mono-infected: ≥ stage 2 fibrosis.
  - HIV-HCV coinfected: all patients?
- Kidney disease.
- Cryoglobulinemia: skin, joints.
- Non-Hodgkin lymphoma.
- Symptoms: e.g. fatigue.
- Fear of the future.

**Who do we not treat?**

Points to consider:

- Symptoms.
- Patient age.
- Co-morbidity.
- Motivation; anticipated compliance.
- Severity of underlying liver disease.

Not every patient should be treated.
Who would you treat?

Patient #1: Cirrhosis on biopsy. No ascites. No varices.
- Albumin 3.5 g/dL
- T.bili 1.5 mg/dL
- INR 1.2
- Platelets = 150,000/mm³
Who would you treat?

Patient #1:
Cirrhosis on biopsy.
No ascites. No varices.
- Albumin 3.5 g/dL
- T.bili 1.5 mg/dL
- INR 1.2
- Platelets = 150,000/mm³

Patient #2:
History of ascites last year.
Ascites is controlled on diuretics.
- Albumin 3.0 g/dL
- T.bili 1.8 mg/dL
- INR 1.3
- Platelets = 120,000/mm³

Patient #3:
Asymptomatic.
CT scan: nodular liver; large spleen.
- Albumin 3.2 g/dL
- T.bili 1.5 mg/dL
- INR 1.3
- Platelets = 50,000/mm³
Who would you treat?

Patient #3:
Asymptomatic.
CT scan: nodular liver; large spleen.
- Albumin 3.2 g/dL
- T.bili 1.5 mg/dL
- INR 1.3
- Platelets = 50,000/mm³

Patient #4:
Small esophageal varices.
CT scan: small nodular liver.
- Albumin 3.5 g/dL
- T.bili 1.2 mg/dL
- INR 1.1
- Platelets = 80,000/mm³

Hepatitis C:
Distribution of genotypes in U.S.

- Genotype 1: 50%
- Genotypes 2 and 3: 22%
- Genotype 1: Low Viral Load: 24%
- Genotype 1: High Viral Load: 4% (Others)

Batt LM et al.
How do you treat genotypes 2 & 3?

Peg-IFN α-2a 180 μg/wk + Ribavirin 800-1200 mg/day

Peg-IFN α-2b 1.5 μg/kg/wk + Ribavirin 800-1400 mg/day

Weeks 0 4 8 12 16 24 28 36 48

STOP

Week 24: Stop all meds.

SVR = up to 82%


How do you treat genotypes 2 & 3?

Peg-IFN α-2a 180 μg/wk + Ribavirin 800-1200 mg/day

Peg-IFN α-2b 1.5 μg/kg/wk + Ribavirin 800-1400 mg/day

Weeks 0 4 8 12 16 24 28 36 48

STOP

Week 24: Stop all meds.

SVR = up to 82%
What about the boxed warning?

- Alpha interferons may cause or aggravate:
  - Neuropsychiatric
  - Autoimmune
  - Ischemic
  - Infectious disorders.

- Ribavirin may cause:
  - Birth defects.
  - Death of the fetus.
  - Must avoid pregnancy in:
    - Female patients.
    - Female partners of male patients.

- Ribavirin-induced anemia:
  - Can worsen cardiac disease.

Is there guidance for dose reduction?
Is there guidance for dose reduction?

**Peg-IFN α-2a**

<table>
<thead>
<tr>
<th>Laboratory Parameters</th>
<th>Reduce Peginterferon Dose (see note 1), if needed</th>
<th>Reduce Ribavirin Dose (see note 2, if needed)</th>
<th>Discontinue Therapy if</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANC &lt;500 cells/mm³</td>
<td>ANC &lt;500 cells/mm³</td>
<td>Discontinue treatment until ANC values return to more than 1000 cells/mm³. Reduce to 135 mcg and monitor ANC.</td>
<td></td>
</tr>
<tr>
<td>Platelet &lt;50,000 cells/mm³</td>
<td>Platelet &lt;50,000 cells/mm³</td>
<td>Reduce to 90 mcg.</td>
<td></td>
</tr>
<tr>
<td>Platelet &lt;25,000 cells/mm³</td>
<td>Platelet &lt;25,000 cells/mm³</td>
<td>Discontinue treatment.</td>
<td></td>
</tr>
</tbody>
</table>

**Peg-IFN α-2b**

- **Renal insufficiency**
  - CrCl < 50 mL/min or HD:
    - Reduce dose to 135 mcg/week.

- **Ribavirin**
  - Do not use in patients with CrCl < 50 mL/min.

- **Peg-IFN α-2b**
  - CrCl 30-50 mL/min:
    - Reduce dose by 25%.
  - CrCl 10-29 mL/min or HD:
    - Reduce dose by 50%.
How do you avoid dose reduction or drug discontinuation?

- Drink lots of fluids.
- Small frequent meals.
- Moderate low impact exercise.
- Relaxation techniques.
- Good sleep habits.


How do you avoid dose reduction or drug discontinuation?

- Treatment of cytopenias.
  - GCSF (e.g. Neupogen®).
  - Erythropoietin (e.g. Epogen®, Procrit®).
- Attention to patient’s emotional well-being.
  - Counseling.
  - Treatment of irritability.
    - gabapentin (Neurontin®).
    - bupropion (Wellbutrin®)
  - Treatment of depression.
    - citalopram (Celexa®).
    - venlafaxine (Effexor®).
How do you treat genotype 1?

Peg-IFN + RBV

SVR

40-45%
How do you treat genotype 1?

Peg-IFN + RBV  
40-45%

Peg-IFN + RBV + Protease Inhibitor  
63-75%


Protease inhibitors for HCV GT1: Before you start treating...

- Boceprevir (Virectin®).
- Telaprevir (Incivek®).
  - Approved for use in genotype 1.
  - Must not be used as monotherapy.
  - Must only be prescribed with both PegIFN and RBV.
  - Must not be used in pregnant patients.
  - Are not used as re-treatment after failure of a regimen utilizing another protease inhibitor.
Protease inhibitors for HCV GT1: Downsides of therapy

Boceprevir (Victrelis®).
Telaprevir (Incivek®).

• Add a new drug → get a new side effect.

Protease inhibitors for HCV GT1: Common adverse drug reactions

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Boceprevir + PegIFN + RBV</th>
<th>Telaprevir + PegIFN + RBV</th>
<th>PegIFN + RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>58%</td>
<td>56%</td>
<td>50-59%</td>
</tr>
<tr>
<td>Rash</td>
<td>17%</td>
<td>56%</td>
<td>18-34%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>--</td>
<td>47%</td>
<td>28</td>
</tr>
<tr>
<td>Nausea</td>
<td>46%</td>
<td>39%</td>
<td>28-42%</td>
</tr>
<tr>
<td>Anemia</td>
<td>50%</td>
<td>36%</td>
<td>17-30%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>25%</td>
<td>26%</td>
<td>17-22%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>20%</td>
<td>13%</td>
<td>8-13%</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>44%</td>
<td>10%</td>
<td>3-10%</td>
</tr>
<tr>
<td>Anal or rectal discomfort / pruritus</td>
<td>44%</td>
<td>17%</td>
<td>4%</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>--</td>
<td>12%</td>
<td>3%</td>
</tr>
</tbody>
</table>
Protease inhibitors for HCV GT1: Downsides of therapy

Boceprevir (Victrelis®).

Telaprevir (Incivek®).
- Pill burden.
- Complex drug-drug interactions.
- Risk of drug resistance mutations.
- Expense.
- ~ 8-12% of patients discontinue treatment.

Protease inhibitors for HCV GT1: Before you start treating...

- Boceprevir (Victrelis®) and Telaprevir (Incivek®):
- Be aware of drug-drug interactions.

[Diagram showing drug interactions and effects]
**Boceprevir and telaprevir are contraindicated with these drugs**

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drugs within class</th>
<th>Potential complication</th>
</tr>
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<tbody>
<tr>
<td>Alpha-1-adrenoceptor antagonists</td>
<td>alfuzosin</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Ergot derivatives</td>
<td>dihydroergotamine, ergonovine, ergotamine</td>
<td>Vasospasm, ischemia</td>
</tr>
<tr>
<td>GI motility agent</td>
<td>cisapride</td>
<td>Arrhythmia</td>
</tr>
<tr>
<td>HMG-CoA reductase inhibitors</td>
<td>atorvastatin, lovastatin, simvastatin</td>
<td>Myopathy, rhabdomyolysis</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>droperidone</td>
<td>Hyperkalemia</td>
</tr>
<tr>
<td>PDE5 enzyme inhibitors</td>
<td>sildenafil / Revatio tadalafil / Adcirca</td>
<td>Hypotension, syncope, prolonged erection</td>
</tr>
<tr>
<td>Neuroleptic</td>
<td>pimozide</td>
<td>Arrhythmia</td>
</tr>
<tr>
<td>Sedative/hypnotics</td>
<td>triazolam, oral midazolam</td>
<td>Increased sedation, respiratory depression</td>
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**Boceprevir and telaprevir are contraindicated with these drugs**

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<td>Anticonvulsants</td>
<td>carbamazepine, phenobarbital, phenytoin</td>
<td>Decreased efficacy of protease inhibitor</td>
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<td>Antimycobacterial drugs</td>
<td>rifampin</td>
<td>Decreased efficacy of protease inhibitor</td>
</tr>
<tr>
<td>Herbal products</td>
<td>St. John' wort (hypericum perforatum)</td>
<td>Decreased efficacy of protease inhibitor</td>
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Use of ART with DAA in HIV-HCV coinfectected patients with GT1

Patients not on ART → Boceprevir or Telaprevir

Patients receiving RAL + 2 NRTIs → Boceprevir or Telaprevir

Patients receiving ATV / r + 2 NRTIs → Use Telaprevir at standard dose. Do not use Boceprevir.

Patients receiving EFV + 2 NRTIs → Use Telaprevir at increased dose of 1125 mg every 7-9 hours. Do not use Boceprevir.


Use of ART with DAA in HIV-HCV coinfectected patients with GT1

NNRTIs: • Rilpivirine • Etravirine → Use Telaprevir

How do you treat genotype 1?

Boceprevir
Treatment-naïve patients

- **HCV RNA Week 8 neg.**
  - **Week 24 neg.**
    - PR 4 weeks
    - Boceprevir + PR x 24 weeks
  - **Week 24 pos.**
    - PR 4 weeks
    - Boceprevir + PR x 32 weeks

- **HCV RNA Week 8 neg.**
  - PR 4 weeks
  - Boceprevir + PR x 24 weeks

- **Patients with cirrhosis:**
  - PR x 4 weeks
  - PRB x 44 weeks

- **28 week RGT**
- **40 week RGT**
- **PR 12 weeks**

Week 12:
Stop all meds if HCV RNA > 100 IU/mL

Week 24:
Stop all meds if HCV RNA detectable
### Boceprevir

#### Previous treatment failures

<table>
<thead>
<tr>
<th>HCV RNA</th>
<th>Week 8 neg.</th>
<th>Week 24 neg.</th>
<th>PR x 4 weeks</th>
<th>PR + Boceprevir x 32 weeks</th>
<th>48 week RGT</th>
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<th>HCV RNA</th>
<th>Week 8 pos.</th>
<th>Week 24 neg.</th>
<th>PR x 4 weeks</th>
<th>PR + Boceprevir x 32 weeks</th>
<th>PR x 12 weeks</th>
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#### SVR:
- Prior relapsers = 72%
- Prior partial responders = 52%


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### Telaprevir

#### Treatment-naïve patients & relapsers

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<tr>
<th>HCV RNA</th>
<th>Week 4 neg.</th>
<th>Week 12 neg.</th>
<th>PR + telaprevir 12 weeks</th>
<th>PR x 12 weeks</th>
<th>24 week RGT</th>
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<th>HCV RNA</th>
<th>Week 4 pos.</th>
<th>Week 12 pos.</th>
<th>PR + telaprevir 12 weeks</th>
<th>PR x 36 weeks</th>
<th>48 week RGT</th>
</tr>
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#### Patients with cirrhosis:
- PRT x 12 weeks.
- PR x 35 weeks.

---

#### Week 4:
- Stop all meds if HCV RNA > 1000 IU/mL

#### Week 12:
- Stop all meds if HCV RNA > 1000 IU/mL

#### Week 24:
- Stop all meds if HCV RNA Detectable
Telaprevir
Treatment-naïve patients

SVR
- Naïve patients, SVR = 75%
- Prior relapers, SVR = 83%
- In cirrhotics, SVR = 62%
- In African-American patients, SVR = 62%

HCV RNA
Week 4 neg.
Week 12 neg.
- PR + telaprevir
  12 weeks
- PR x 12 weeks

HCV RNA
Week 4 pos.
Week 12 pos.
- PR + telaprevir
  12 weeks
- PR x 36 weeks

Weeks
0  4  8  12  16  24  28  36  48
STOP  STOP  STOP

Week 4:
Stop all meds if HCV RNA > 1000 IU/mL

Week 12:
Stop all meds if HCV RNA > 1000 IU/mL

Week 24:
Stop all meds if HCV RNA detectable

Telaprevir
Prior partial & null responders

HCV RNA
Week 4 neg.
- PR + telaprevir
  12 weeks
- PR x 36 weeks

HCV RNA
Week 4 pos.
- PR + telaprevir
  12 weeks
- PR x 36 weeks

Weeks
0  4  8  12  16  24  28  36  48
STOP  STOP  STOP

Week 4:
Stop all meds if HCV RNA > 1000 IU/mL

Week 12:
Stop all meds if HCV RNA > 1000 IU/mL

Week 24:
Stop all meds if HCV RNA detectable
Telaprevir
Prior partial & null response

SVR
- Prior partial responders, SVR = 34%
- Prior null responders, SVR = 14%

Weeks 0 4 8 12 16 24 28 36 48

Week 4: Stop all meds if HCV RNA > 1000 IU/mL
Week 12: Stop all meds if HCV RNA > 1000 IU/mL
Week 24: Stop all meds if HCV RNA detectable

The NYS DOC Experience:
HCV Pilot Project with Telaprevir

- Initiated October 2011
- 50 patients treated with Telaprevir based regimens
  - 51 patients enrolled
  - 1 patient refused treatment after being enrolled
- Extensive educational initiatives to train health care staff
  - MD’s, NP’s, PA’s, nurses, pharmacists, social workers
- Extensive use of telemedicine to monitor and supervise treatment: IFD follow up mandatory
- DOT only with dedicated medication lines
- Maximum of 5 patients per facility were on treatment with PI’s at any given time (limit was not mandatory)
The NYS DOC Experience: HCV Pilot Project with Telaprevir

- Discontinuation of treatment: 2 / 50
  - Completion Rate = 96%.
  - Thrombocytopenia
  - Psychiatric decompensation
- SVR: 44/48 (92%) Failed Rx: 4 (1 patient prior to week 12).
  - eRVR 34/48
  - No eRVR 10/48
  - Stage 1-3 eRVR 31/41 (76%)
  - Stage 4 eRVR 3/9 (33%)
- Treatment failure: 4
  - Stage 1-3: 2
  - Stage 4: 2

Data & slides supplied by Dr. Harish Moorjani

The NYS DOC Experience: HCV Pilot Project with Telaprevir

- Hgb <12: 72%
- Hgb 8-10: 16%
- Hgb <8: 4%
- Procrit use not allowed
- Aggressive ribavirin dose reduction instituted
- Ribavirin dose reduction 68%
- Transfusions: none (0%)

Data & slides supplied by Dr. Harish Moorjani
Boceprevir, telaprevir and anemia: 
The importance of RBV dose reduction

- Manufacturer's recommendations:
  - If Hgb > 10 g/dL: continue at current dose.
  - If Hgb < 10 g/dL: reduce dose to 600 mg/D.
  - If Hgb < 8.5 g/dL: discontinue RBV.
- If patient has stable cardiac disease:
  - > 2 g/dL decrease in Hgb → reduce dose to 600 mg/D.
  - Hgb < 12 g/dL after week at reduced doses → discontinue RBV.
- RBV dose reductions do not decrease SVR rates.

Telaprevir and rash

**Mild**
Localized.
Rx:
Apply moisturizers.
Avoid alcohol-based lotions.
Topical steroid cremes.
Oral anti-histamines.

**Moderate.**
< 50% BSA
May have skin peeling.
Rx:
Same as for "mild".

**Severe**
Generalized rash (> 50% BSA)
May have vesicles, bullae ulcerations (other than SJS).
Rx:
STOP Telaprevir
May continue PegIFN/RBV.
Consider Derm. consult.
HIV-HCV Coinfection: Boceprevir-based Triple Rx for GT1

Sułkowski M, et al. 19th CROI; Seattle, WA; March 5-8, 2012. Abst. 47.

Use of ART with DAA in HIV-HCV coinfected patients with GT1

DHHS Guidelines March 27, 2012

Patients not on ART → Boceprevir or Telaprevir
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Patients receiving ATV / r + 2 NRTIs → Use Telaprevir at standard dose. Do not use Boceprevir.
Patients receiving EFV + 2 NRTIs → Use Telaprevir at increased dose of 1125 mg every 7-9 hours. Do not use Boceprevir.

What are the new therapies for HCV?

Should we “warehouse”?
Sofosbuvir and genotypes 2 & 3

Sofosbuvir = uridine nucleotide NS5B polymerase inhibitor

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Treatment group</th>
<th>SVR12 Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>FISSION</td>
<td>Genotype 2/3 treatment naïve</td>
<td>Sofosbuvir + RBV x 12 weeks or Peg-IFN + RBV x 24 weeks</td>
<td>67% (107/253) -- 67% (162/243)</td>
</tr>
<tr>
<td>POSITRON</td>
<td>Genotype 2/3 IFN intolerant, ineligible or unwilling</td>
<td>Sofosbuvir + RBV x 12 weeks or Placebo x 12 weeks</td>
<td>78% (161/207) -- 0% (0/71)</td>
</tr>
<tr>
<td>FUSION</td>
<td>Genotype 2/3 treatment experienced</td>
<td>Sofosbuvir + RBV x 12 weeks or Sofosbuvir + RBV x 16 weeks</td>
<td>50% (50/100) -- 73% (69/95)</td>
</tr>
</tbody>
</table>

Gane E et al, EASL, 2013

Sofosbuvir + RBV in GT1
**Sofosbuvir + RBV in GT1**

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<th>Population</th>
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<th>SVR12 Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEUTRTINO</td>
<td>Genotype 1/4/5/6 treatment naïve</td>
<td>Sofosbuvir + RBV + Peg-IFN x 12 weeks</td>
<td>90% (295/327)</td>
</tr>
<tr>
<td>ELECTRON</td>
<td>GT1 naïve</td>
<td>Sofosbuvir + RBV x 12 weeks</td>
<td>84% (21/25)</td>
</tr>
<tr>
<td>ELECTRON</td>
<td>GT1 prior null</td>
<td>Sofosbuvir + RBV x 12 weeks</td>
<td>10% (1/10)</td>
</tr>
<tr>
<td>ELECTRON</td>
<td>GT1 naïve</td>
<td>Sofosbuvir + RBV + Ledipasvir x 12 weeks</td>
<td>100% (25/25)</td>
</tr>
<tr>
<td>ELECTRON</td>
<td>GT1 prior null</td>
<td>Sofosbuvir + RBV + Ledipasvir x 12 weeks</td>
<td>100% (10/10)</td>
</tr>
<tr>
<td>ELECTRON</td>
<td>GT1 naïve</td>
<td>Sofosbuvir + RBV + GS 9669 x 12 weeks</td>
<td>92% (23/25)</td>
</tr>
<tr>
<td>ELECTRON</td>
<td>GT1 prior null</td>
<td>Sofosbuvir + RBV + GS 9669 x 12 weeks</td>
<td>100% (10/10)</td>
</tr>
<tr>
<td>COSMOS</td>
<td>GT1 prior null</td>
<td>Sofosbuvir + RBV + Simeprevir x 12 weeks</td>
<td>96% (26/27)</td>
</tr>
</tbody>
</table>

**Daclatasvir in GT1**

<table>
<thead>
<tr>
<th>Population</th>
<th>Treatment group</th>
<th>SVR12 Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>GT1 naïve</td>
<td>Daclatasvir + Asunaprevir + BMS-791325 x 12 weeks</td>
<td>94% (15/16)</td>
</tr>
<tr>
<td>GT1 prior failure of triple therapy</td>
<td>Daclatasvir + Sofosbuvir x 24 weeks</td>
<td>100% (21/21)</td>
</tr>
</tbody>
</table>

Daclatasvir = NS5A replication complex inhibitor  
Asunaprevir = protease inhibitor  
BMS-791325 = non-nucleoside NS5B polymerase inhibitor  
Sofosbuvir = uridine nucleotide NS5B polymerase inhibitor  

References:  
Everson GT et al, EASL 2013.  
Sukowski IMS et al, EASL 2013.
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