Janssen Symposium at 2014 ADDS

Managing the Treatment-Experienced Hepatitis C Patient in a New Era

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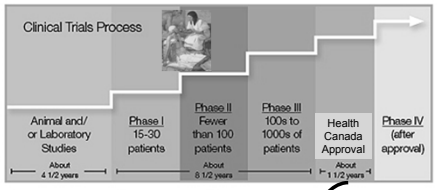
The New AASLD Guidelines and what they mean to Canadian HCV treaters

The "Normal" Clinical Trial Pathway for Therapeutics: From Discovery to Prescription



Timelines typically year to years

Provincial Formulary

Clinical Use and Long and Happy Patent Life

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Friday, June 6, 2014 (11:45am to 12:45pm)

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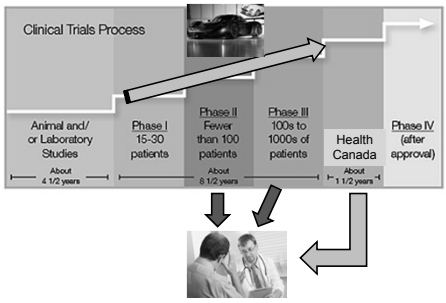
Disclosures

Gilead
Janssen
Boehringer - Ingelheim
Bristol-Myers-Squibb
Abbvie
Idenix
Vertex
Merck
Roche
GlycoReg Immune
*Discussion of off label use of medications

The Changing Paradigm for HCV Therapeutics: A new dynamism in therapy



HCV Therapy: Expert panels changing and adapting treatment recommendations in "Real Time" in the absence of "classical" Phase III Trial evidence

HEPATOLOGY
Official Journal of the American Association for the Study of Liver Diseases

Preparing for the Uncertain Yet Inevitable: Off-Label Combinations of Antiviral Agents in Hepatitis C Virus

Andrew Aronsohn,[1,2] Nancy Reau,[1] and Donald Jensen[1]

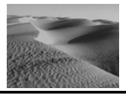
Hepatology May 2014

American Association for the Study of Liver Diseases
AASLD

IDSA
Infectious Diseases Society of America

Recommendations for Testing, Managing, and Treating Hepatitis C

AASLD, IDSA, IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Accessed April 24, 2014.



HCV Testing and Linkage to Care

- HCV testing is recommended at least once for persons born between 1945 and 1965 = "baby boomers" (1975 in Canada)
- **Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures, and conditions associated with an increased risk of HCV infection:**
  - 1. *Risk behaviors*
    - Injection-drug use (current or ever, including those who injected once)
    - Intranasal illicit drug use
  - 2. *Risk exposures*
    - Long-term hemodialysis (ever)
    - Getting a tattoo in an unregulated setting
    - Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-infected blood
    - Children born to HCV-infected women
    - Prior recipients of transfusions or organ transplants, including persons who:
      - were notified that they received blood from a donor who later tested positive for HCV infection
      - received a transfusion of blood or blood components, or underwent an organ transplant before July 1992
      - received clotting factor concentrates produced before 1987
    - Were ever incarcerated
  - 3. *Other medical conditions*
    - HIV infection
    - Unexplained chronic liver disease

AASLD: New Recommendations for the Treatment of HCV

Messages from the *Cosmos*

AASLD: Application of Phase II Clinical Trial data to make "off-label" treatment recommendations and decisions

SIM / SOF

AASLD: Naïve G1 Patient Therapy

IFN Eligible
Recommended: SOF (400 mg/d) + PEG/RBV x 12 weeks
(SVR = 89%; cirrhosis 80%; no cirrhosis 92%)

IFN Ineligible
Recommended: SOF (400 mg/d) + SMV (150 mg/d) ± RBV (WBD) x 12 weeks (Sim/Sof)
(COSMOS Phase II data: SVR 93-100%)

Alternatives
(i) IFN Eligible: SMV (150 mg/d) x 12 weeks + PEG/RBV x 24 weeks (G1b or G1a without Q80K) (SVR 84%)

(ii) IFN Ineligible: SOF (400 mg/d) + RBV x 24 weeks (SVR ~72%)

Defining "Intolerance" to IFN

1. Autoimmune hepatitis and other autoimmune disorders
2. Hypersensitivity to PEG or any of its components
3. Decompensated hepatic disease
4. Major uncontrolled depressive illness
5. Baseline neutrophil count below 1500/μL, or a baseline platelet count below 90,000/μL or baseline hemoglobin below 10 g/dL
6. History of preexisting cardiac disease

AASLD: Naïve G1 patient: **Not** Recommended

(i) TVR + PEG/RBV x 24 or 48 weeks (RGT)

(ii) BOC + PEG/RBV x 28 or 48 weeks (RGT)

(iii) PEG/RBV x 48 weeks

(iv) Monotherapy with PEG, RBV, or a DAA

- Do not treat decompensated cirrhosis with PEG or SMV

AASLD: Naïve G2 Patient Therapy

Recommended

SOF (400 mg/d) + RBV (WBD) x 12 weeks
(SVR ~ 94 %)

Alternative
None

NOT Recommended
- PEG/RBV x 24 week
- Monotherapy with PEG, RBV, or a DAA
- Any regimen with TVR, BOC, or SMV

AASLD: Naïve G3 Patient Therapy

Recommended (based on data from 105 pts)

SOF (400 mg/d) + RBV (WBD) x 24 weeks
(SVR ~ 93%; similar with or without cirrhosis)

Alternative (based on data from 39 pts)
SOF (400 mg/d) + PEG/RBV x 12 weeks
(SVR ~ 97%; Phase II)

NOT Recommended
- PEG/RBV x 24-48 weeks
- Monotherapy with PEG, RBV, or a DAA
- Any regimen with TVR, BOC, or SMV

AASLD: Naïve G4 Patient Therapy

Recommended (based on small numbers of pts treated)

IFN Eligible: SOF + PEG/RBV x 12 weeks (SVR ~ 96%)

IFN Ineligible: SOF + RBV x 24 weeks (SVR~ 100%)

Alternative
SMV (150 mg/d) x 12 weeks + PEG/RBV x 24-48 weeks

NOT Recommended
- PEG/RBV x 48 weeks
- Monotherapy with PEG, RBV, or a DAA
- Any regimen with TVR or BOC

AASLD: Naïve G5/6 Patient Therapy

Recommended (based on small numbers of pts treated)

SOF (400 mg/d) + PEG/RBV x 12 weeks (SVR ~ 100%)

Alternative
PEG/RBV x 48 weeks

NOT Recommended
- Monotherapy with PEG, RBV, or a DAA
- Any regimen with TVR or BOC

What is happening in the EU?

OLYSIO (Simeprevir) should only be co-administered with other direct acting antiviral medicinal products if the benefits are considered to outweigh the risks based upon available data.

OLYSIO with sofosbuvir (ie Sim/Sof) should only be used in patients who are intolerant to or ineligible for interferon therapy, and are in urgent need of treatment.

Ribavirin could be added based on a clinical assessment of each individual patient (see sections 4.4, 4.8 and 5.1). The recommended treatment duration is 12 weeks. A longer treatment duration (up to 24 weeks) of OLYSIO with sofosbuvir (with or without ribavirin) could be considered based on an individual basis (see sections 4.4, 4.8 and 5.1).

Impact of AASLD (and EU) Guidelines in Canada?