HCV treatment in Australia: a new role for GPs

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Disclosures

- I have received honoraria for presentations and/or consultancies from:
  - AbbVie
  - BMS
  - Gilead
  - Janssen
  - MSD
  - Roche

HCV: a new role for GPs

- Why treat HCV?
- Evolution of HCV Therapy
  - The bad old days of interferon
  - The new wonder drugs
- Assessing your patient
  - HCV genotype
  - Assessment of liver disease
- Where to get help

HCV is common (Aust ~230,000)

Gower E. et al. J Hepatol 2014;61:S45–S57

The health burden is growing

Sievert W. et al. J Gastroenterol Hepatol 2014; 29 (S1):1-9

HCV is expensive

Sievert W. et al. J Gastroenterol Hepatol 2014; 29 (S1):1-9
Curing HCV improves outcomes

- Liver-related death or transplant
  - Without cure vs. With cure (p < 0.001)
- Hepatocellular carcinoma
  - Without cure vs. With cure (p < 0.001)
- Liver failure
  - Without cure vs. With cure (p < 0.001)
- All-cause mortality
  - Without cure vs. With cure (p < 0.001)

Van der Meer A, JAMA 2012 (530 patients with Ishak 4-6, median follow up 8.4 years, death in 13/192 with SVR, 100 non-SVR)

But barriers to treatment exist

- Tested for HCV
- Referred to specialist
- Offered treatment
- Received treatment
- Willing to undergo treatment
- Liver failure
- All-cause mortality
- Liver-related death or transplant

Aust: all diagnosis, no treatment...

Diagnosis rate (%), Treatment rate (%)

2013 estimates

Barriers in Australia (Care cascade)

Kirby Institute 2015

Some terminology

- HCV antibody (Ab) indicates exposure to HCV
- HCV PCR detects RNA and indicates current infection
- Pegylated interferon (pegIFN) is an old HCV treatment
- Direct-acting antivirals (DAAs) are the new treatments
- Sustained virological response (SVR) indicates that HCV RNA is not detectable after treatment finishes
- SVR12 means no HCV 12 weeks after finishing = CURE

The evolution of HCV treatment

- Interferon (sIFN)
- PegIFN + RBV
- PegIFN + RBV + SPC + TVR
- IFN-free, all-oral DAA


Liver biopsy optional, retreatment possible
2006: HCV treatment with pegIFN
- Pegylated interferon (pegIFN) sub cut injection weekly
- Ribavirin tablets twice daily
- Treatment for up to 48 weeks!!!
- Lots of side effects

2006: pegIFN + RBV results

2006: treatment was complicated . . .

2006: GP’s role in HCV treatment
Hepatitis Treatment Centre of Excellence

2016: a new DAA dawn
Where the DAAs act

- Cellular infection
- Replication
- Assembly & secretion

How to remember the names . . .

- NS3
- NS4B
- NS5A
- NS5B
- Protease inhibitors
- NS4A
- NS5A
- Polymerase inhibitors
- Nuc
- Non-nuc

Three important questions

- Does my patient have hepatitis C?
  - HCV antibody (Ab) indicates exposure to HCV
  - Up to 45% of people will clear HCV without treatment
  - If HCV PCR is positive, the person still has HCV

- Which HCV genotype is present?
  - Single blood test
  - Can be requested by GPs (covered by MBS)
  - Australia has mainly GT 1 or GT 3

- Does my patient have cirrhosis?
  - Tricky . . .

HCV genotypes in Australia

Data from >10,000 patients at VIDRL in Melbourne
Victorian Infectious Diseases Reference Laboratory (data on file)

GT: genotype

How long is treatment?

- Treatment for most people with HCV being treated in primary care is for:
  - 12 weeks

- If the person has cirrhosis, treatment may be for 24 weeks

nb: people with cirrhosis should be referred to a liver specialist

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>GT 1</th>
<th>GT 2</th>
<th>GT 3</th>
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<tr>
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</tr>
<tr>
<td>GT 3</td>
<td>95</td>
<td>95</td>
<td>96</td>
</tr>
</tbody>
</table>

DAA regimens* on the PBS

- LDV/SOF
- DCV
- SOF
- RBV
- AbbVie 3D
- Viekira Pak
- Sovaldi

SVR12 (%)

* These results are from separate clinical trials and not from head-to-head comparisons.
Which treatment?

- Several options
- Mainly determined by HCV genotype
- Occasionally by drug-drug interactions
- Sometimes determined by patient or doctor preference
- GPs should focus on patients with:
  - Genotype 1 or 3
  - No cirrhosis
  - Fewer co-morbidities & normal renal function

Genotype 1

- Genotype 1a
  - Ledipasvir/sofosbuvir (Harvoni®)
    - Single pill daily
    - Few adverse effects
    - Few significant drug-drug interactions
    - SVR rate of up to 98% (similar success rate for Genotype 1b)
- Genotype 1b
  - Ombitasvir/paritaprevir/rit + dasabuvir (Viekira Pak ®)
    - 3 morning pills and 1 evening pill (daily pack)
    - Few adverse effects
    - More drug-drug interactions (ritonavir boosting)
    - SVR rate of almost 100%

Genotype 3

- Genotype 3
  - Sofosbuvir (Sovaldi ®) in combination with
    - Daclatasvir (Daklinza ®)
    - Daily pill (60mg)
    - Few adverse effects
    - Few drug-drug interactions
    - SVR rate of ~95% with sofosbuvir in genotype 3

- Genotype 2 is treated with Sofosbuvir + ribavirin
- Genotypes 4,5 and 6 only pegIFN + ribavirin + SOF (PBS)

Drug-drug interactions

- Need to check HCV treatment compatible with patient's other medications
- Important contra-indicated medications:
  - Amiodarone
  - Carbamazepine
  - Phenytoin
- Beware:
  - Statins
  - High dose PPIs

www.hep-druginteractions.org

How to assess cirrhosis

- Pre-test probability
  - Older patients, longer Hx of HCV, alcohol, GT 3
- Clinical signs
  - Spider naevi, leukonychia, splenomegaly, jaundice
- Investigations
  - Low platelets, low albumin, raised bilirubin
  - APRI (AST to Platelet Ratio Index)
  - FibroScan® (where available)
Linking with a specialist

- Linking with Specialist Care
- Who can prescribe these new treatments?
  - States and territories may have specific requirements about prescriber eligibility for the new medicines in their jurisdiction.
  - For the PBS subsidy, where state or territory requirements allow, gastroenterologists, hepatologists, or infectious disease physicians experienced in the treatment of chronic hepatitis C infection are eligible to prescribe the new medicines.
  - All other medical practitioners, including general practitioners (GPs), are also eligible to prescribe under the PBS, provided that is done in consultation with one of the specified specialists experienced in the treatment of chronic hepatitis C infection. For example, a GP must consult with one of the specified specialists by phone, mail, email or videoconference in order to meet the prescriber eligibility requirements.

Referral for ‘specialist consultation’

New strategies & models of care

- Elimination strategies
- Treatment as Prevention (TAP) study
- Nurse-led models of care
- Treatment in prisons
- Treatment in primary care
- Treatment in NSP/OST settings
Summary

- **DAAs** are the new standard of care for HCV
- All-oral DAA therapy for HCV is now available for anyone in Australia with HCV via PBS
- Very well tolerated and highly effective (95+\%)
- Some limitations and barriers to treatment still exist
- New models of care are needed to provide treatment to everyone with HCV
- GPs will be integral to eliminating HCV

Thank you

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- Google images