Eliminating Hepatitis C from New Zealand

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Disclosures

- I have the following financial relationships to disclose within the past 12 months:
  - Advisory board committees or speaking for Gilead Sciences, Abbvie
Hepatitis C in NZ

- Estimated 50000 in NZ with Hepatitis C
  - Approximately 50% diagnosed
- “The silent epidemic”
- This virus can be cured
Who is at risk for Hepatitis C in New Zealand?

- **Factor concentrates pre-1987** (Jackson, 2000) - 89%
- **Active injecting drug user** (Robinson, 1995) - 75%
- **Prison inmates (female)** (Brunton, 2000) - 30%
- **Blood transfusion pre-1992** (Brullen, 2000) - 6%
- **Haemodialysis** (Marshall, 1999) - 3%
- **STD clinic** (McKenna, 1992) - 2.5%
- **Caucasian blood donors** (Bullen, 1999) - 0.9%
- **Maori/Pl blood donors** (Woodfield, 2000) - 0.49%
- **New Zealand population** (ESR Report, 2000) - 1.2%
Decreasing Incidence of HCV in Australia/NZ
Related to falling incidence in Injecting Drug Use

Dore et al. HCV Projections Working Group 2007
Characteristics of the local HCV Population Age and Gender

- Christchurch Community Clinic

Brunton C (unpublished)
Characteristics of the local HCV Population
Age and size of population

- 50,000 infected, median age of 47 years

Most have been infected for 20-30 years at time of diagnosis
Characteristics of the local HCV Population
Proportion with Cirrhosis

- HCV Pilots in Bay of Plenty and Wellington
  - 788 Fibroscans performed in community

16% have established cirrhosis
25% have at least severe fibrosis
The total number of HCV infections is expected to decline in New Zealand while the disease burden is expected to increase.

In fact, national estimates show an increase in HCC cases and HCC deaths.
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Current liver cancer (HCC) rates are increasing by 10% per year in New Zealand.
Incidence of Liver Failure from HCV is rising more rapidly than projected in 2000 ESR Report

Patients with decompensated HCV cirrhosis referred for Liver Transplant

Number of HCCs per annum

- HCV
Global: HCV is now the leading cause of liver-related morbidity and mortality

Global Burden of Disease 2013
estimated age-sex-specific all-cause mortality

Deaths due to HCV more than doubled between 1990–2013;
Liver cancer deaths due to HCV increased 300%

Cowie BC, et al. EASL 2015; Poster #P1256;

WHAD, 28 July, 2015
HCV-infected adults are at increased risk of premature death

Premature death (<65 years) and median age at death among all deaths, NYC (2000–2011)

- 25% died prematurely
  - No HCV or HIV: 78 yrs
  - HCV mono-infected: 60 yrs
  - HCV/HIV co-infected: 52 yrs

Current treatment options cannot meet the unmet medical need in New Zealand patients with HCV

1. Poor tolerability
   - Side-effects of interferon
   - Not suitable for elderly, or advanced disease

2. Complex dosing regimen
   - Large number of pills
   - Frequent monitoring
   - Interfere with commonly prescribed drugs

3. Limited Efficacy

WHAD, 28 July, 2015
Treatment Rate by Year In New Zealand

Numbers started on treatment

PHARMAC data on file
ACS, CCST data on file

WHAD, 28 July, 2015
Targets in the HCV Life Cycle for Direct Acting Antiviral Agents

Receptor binding and endocytosis

Fusion and uncoating

Transport and release

Virion assembly

Translation and polyprotein processing

(+) RNA

Membranous web

ER lumen

LD

NS5A inhibitors

NS3 Protease Inhibitors

Non-Nuc NS5B inhibitors

NUC NS5B inhibitors

RNA replication
Proof of Concept HCV Studies

Inform-1 Study
- Dual HCV oral antivirals can suppress Hepatitis C and prevent resistance

Gane, Roberts, Stedman et al. Lancet 2010

ELECTRON Study
- Proof of concept that HCV can be cured in interferon-free regimen of sofosbuvir + ribavirin

Fixed Dose Combination

♦ **Ledipasvir**
  – Picomolar potency against HCV GT 1a and 1b\(^1\)
  – Effective against NS5B RAV S282T\(^2\)
  – Once daily, oral, 90 mg

♦ **Sofosbuvir**
  – Potent antiviral activity against HCV GT 1–6
  – High barrier to resistance
  – Once-daily, oral, 400-mg tablet approved for use with other agents to treat HCV infection

♦ **Ledipasvir/Sofosbuvir FDC**
  – Once-daily, oral, fixed-dose (400/90 mg) combination tablet
  – No food effect

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Ledipasvir/Sofosbuvir in HCV Genotype 1

Phase 3 Trials: ION-1, ION-2, ION-3

97% (1886/1952) overall SVR rate

Error bars represent 95% confidence intervals.
Hepatitis C Genotype 1: Ledipasvir/Sofosbuvir “Harvoni”

One pill
Once daily
8-12 weeks
97% cure
Hepatitis C Genotype 1: Sofosbuvir/Ledipasvir Single Tablet Regimen

One pill
Once daily
8-12 weeks
97% cure

>$27000 NZ per month
Sofosbuvir/Ribavirin in Genotypes 2 & 3 HCV: VALENCE Study

Zeuzem S, et al. AASLD 2013 Poster 1085
1. EARLY INHIBITION
- NS3/4A protease inhibitor

- Translation and polyprotein processing

2. MID-LIFECYCLE INHIBITION
- non-nucleoside NS5B polymerase inhibitor

- RNA replication

3. MID-/LATE LIFECYCLE INHIBITION
- NS5A inhibitor

- Ombitasvir (OBV)

- Dasabuvir (DSV)

- HCV Receptor binding and endocytosis
- Fusion and uncoating
- Transport and release
- (-) RNA
- (+) RNA
- ER
- GOLGI

Abbvie “Viekira Pak”

- **12 week all oral regimen**

  - Coformulated paritaprevir /ritonavir (PTV/r) 150 mg/100 mg plus Ombitasvir (OBV) 25 mg (QD)

  - ± Ribavirin (RBV) weight-based dose (BID)

  - Dasabuvir (DSV) 250 mg (BID)

- **Ritonavir boosting**
  - Allows twice daily dosing
  - Drug-drug interactions

- [http://hep-druginteractions.org](http://hep-druginteractions.org)
Abbvie Viekira Pak in HCV Genotype 1 patients with cirrhosis:

- 380 patients with GT1 HCV.
- All patients with established cirrhosis

New therapies open up new horizons……
What would it take to reduce the health burden associated with chronic hepatitis C?

- **Reduce morbidity and mortality**
  - Funding of new oral therapies for all cirrhotics
  - Capacity to treat 2%/year
  - Fibroscan access - to identify cirrhotics

- **Eliminate HCV infection**
  - Funding of new oral therapies for everyone
  - Capacity to treat 10%/year
  - Identify the 30,000 New Zealanders who are undiagnosed
  - Treat those who are transmitting HCV (PWID, prisoners) i.e. “treatment as prevention”
Impact of Different Scenarios

Total viremic infections peaked in 2010, but HCV related healthcare costs will continue to increase past 2035 – under current Tx paradigm

- In 2015, estimated annual healthcare costs of $25 million NZD
- By 2035, annual healthcare costs will increase 71% to $42 million NZD per year
- Total cumulative healthcare costs during 2015-2035 are estimated at $700 million NZD
- Annual healthcare costs peak in 2038 at $43 million NZD
Increasing the number of cured HCV individuals will lead to a reduction in HCV-related healthcare costs.

### Percent Reduction in Healthcare Costs in 2015-2035 (Million NZD)

<table>
<thead>
<tr>
<th></th>
<th>Percent Reduction</th>
<th>Reduction in Liver Related Deaths in 2015-2035</th>
<th>Lives lost due to delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase SVR</td>
<td>10% ($73)</td>
<td>655</td>
<td></td>
</tr>
<tr>
<td>Elimination (no delay)</td>
<td>53% ($375)</td>
<td>2,980</td>
<td></td>
</tr>
<tr>
<td>Elimination (1 year delay)</td>
<td>49% ($342)</td>
<td>2,715</td>
<td>265</td>
</tr>
<tr>
<td>Elimination (2 years delay)</td>
<td>44% ($311)</td>
<td>2,450</td>
<td>530</td>
</tr>
</tbody>
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### Total Healthcare Costs

The chart illustrates the total healthcare costs over the years 2015 to 2035 for different scenarios:
- **Base**: Baseline healthcare costs.
- **SVR Only**: Costs with SVR only.
- **Elimination**: Costs with elimination of HCV.
  - **No delay**: No delay in achieving elimination.
  - **1 year delay**: One-year delay in achieving elimination.
  - **2 year delay**: Two-year delay in achieving elimination.

The graph shows a significant reduction in total healthcare costs over time for each scenario, especially for the elimination scenarios with or without delay.
Hepatitis C: Conclusions

- **HCV disease burden will increase over time** even though the total number of HCV infections is expected to decline
- **Hepatitis C is curable with short duration all-oral regimens**
  - major shift away from interferon-based therapy
  - Drug costs and availability are limiting implementation of new therapy
- **The increase in HCV related disease burden can be mitigated through higher cure rate therapies**
  - Delaying access to treatment results in loss of lives
- **There is potential for Hepatitis C elimination in NZ**