The burden of Hepatitis C in Lithuania and the gaps in screening and treatment. Development of Lithuanian National Hepatitis C strategy

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Population of Lithuania (LT)
Estimated anti-HCV (+) prevalence in LT population

- Current population of Lithuania - 2,836,076
- Lithuania population is equivalent to 0.04% of the total world population
- 70% of the population is urban (1,980,389 people in 2017)
- The median age in Lithuania is 43.2 years

- Anti-HCV (+) prevalence in Lithuania was 2.78%:
  - Study enrolled 1528 adults from the 5 biggest cities of LT and it’s rural regions
  - Anti-HCV (+) more prevalent among males: 4.02% males vs. 1.49% females, p=.003
  - Vilnius & Kaunas regions have higher infection rates than smaller rural regions (2.92% & 3.01% vs. 2.24%, 0.74% and 1.35%)

Chronic HCV infection in Lithuania

• Estimated prevalence of HCV infection 2-3% (2.78%): ≈ 50,000
  • Only ≈ 20-30% of infected are identified

• Estimated number of patients with chronic HCV infection on follow-up:
  ≈ 10,000 - 15,000

• ≈ 1000 newly diagnosed chronic HCV infection cases per year mostly working-age people

• 30 – 40 newly diagnosed acute HCV infection cases per year
Prevalence of HCV genotypes in Lithuania

- Genotype 1 - 65% (~90% of all - G1b)
- Genotype 2 - 8.7% (~80% of all - G2a/c)
- Genotype 3 - 26.3% (~80% of all - G3a)

Prevalence of hepatitis C among IDUs in Lithuanian regional Low Threshold Centers

The prevalence of anti-HCV (+) among IDU is 72–82%, most probable resulted from sharing of infecting paraphernalia.
Access to HCV virology tests and other examination for patients with CHC

• From 2008 **HCV-RNA** testing before, during and after treatment and on follow up reimbursed 100%

• From 2008 **HCV genotyping** reimbursed 100%

• **Liver biopsy** prior treatment start is mandatory, should be performed in one of the main centers for infectious diseases or gastroenterology in 5 biggest cities of Lithuania

• **Fibroscan** equipment is available in 4 centers of 3 hospitals in Lithuania (Vilnius, Kaunas and Klaipėda); transient elastography is not mandatory before treatment
Treatment of chronic HCV infection in Lithuania

• In 2014 total of 890 patients with CHC treated with antivirals (PegIFN, RBV with or without TVR, BOC)

• Total of 60% of all treated had G1 HCV infection (534 pts)

• From 2014 Lithuanian State Sick Fund (VLK) allocated annually ~ 4 million EUR for the treatment of patients with G1 HCV infection and advanced fibrosis - stage F3-F4
Hepatitis C treatment milestones in Lithuania

• **1996** – Standard Interferon alfa-2b (*Realdiron®*)
• **2000** – Standard Interferon alfa-2b + Ribavirin
• **2006** – Pegylated Interferon alfa 2a/b + Ribavirin
• **2014** – Pegylated Interferon alfa 2a/b + Ribavirin and **Telaprevir** for **G1** CHC with fibrosis stage F3/F4
• **2015** – Pegylated Interferon alfa 2a/b + Ribavirin and **Boceprevir** for **G1** CHC with fibrosis stage F3/F4
### 2012–2015 budgetary costs of medicinal products for infectious diseases and chronic hepatitis (mln EUR)

<table>
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<tr>
<th>Year</th>
<th>Lėtinis virusinis B hepatitas ir lėtinis virusinis C hepatitas</th>
<th>Kvėpavimo takų ligos</th>
<th>Žmogaus imunodeficito viruso sukelta liga</th>
<th>Tuberkuliozė</th>
<th>Kitos infekcinės ligos</th>
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<td>2012 m.</td>
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<tr>
<td>2014 m.</td>
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<td>1.73</td>
<td>2.67</td>
<td>0.10</td>
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</table>
Hepatitis C treatment milestones in Lithuania

• Since 29 Oct 2015 – Interferon-free therapy with Ombitasvir/Paritaprevir/ritonavir and Dasabuvir +/- Ribavirin (3D) for G1 CHC T-naïve and T-experienced patients with fibrosis stage F3/F4 (100% reimbursement)

• Since 13 Jul 2016 – Interferon-free therapy with Ombitasvir/Paritaprevir/ritonavir and Dasabuvir +/- Ribavirin (3D) for G1 CHC T-naïve and T-experienced patients with fibrosis stage ≥ F2 (100% reimbursement)

2015 - treated 550 CHC patients – budgetary costs 8,713,240 Eur

2016 - treated 936 CHC patients – budgetary costs 13,803,160 Eur
Restrictions for reimbursement of interferon-free direct-acting antiviral therapies for HCV infection in Europe

Minimum fibrosis stage required for reimbursement of HCV DAAs for treatment of HCV infection in Europe

Alison D. Marshall, et al. EASL abstract 2017
Restrictions for reimbursement of interferon-free direct-acting antiviral therapies for HCV infection in Lithuania

- Reimbursement of HCV DAA with **GT 1 and fibrosis stage ≥F2** (METAVIR):
  - Yes - ombitasvir/paritaprevir/ritonavir + dasabuvir + ribavirin
  - No - sofosbuvir + ribavirin
  - No - sofosbuvir/ledipasvir + ribavirin
  - No - sofosbuvir/velpatasvir + ribavirin
  - No - elbasvir-grazoprevir + ribavirin
  - No - sofosbuvir + daclatasvir + ribavirin
  - No - sofosbuvir + simeprevir + ribavirin

- No listed drug or alcohol use restriction
- Requirement for a specialist to prescribe HCV DAAs
- No additional restrictions for HIV/HCV co-infected persons

- **No reimbursement of HCV DAA with GT 2, 3, 4**
Viral hepatitis B and C epidemiological surveillance and control programme for 2001 – 2005
(Lithuanian Ministry of Health, 2001)

OBJECTIVES

Middle objectives:
• By 2003, 70% reduce the incidence of HBV carriers in 2-3 years age group
• By 2003, introduce into clinical practice molecular diagnostic methods of HBV and HCV infection (HBV DNA, HCV RNA, HCV genotyping)
• By 2005, improve the screening of HCV and HBV infection with wider application of immunological testing methods for the selection of patients

Long term objectives:
• By 2005, 80% reduce the frequency of HBV carrier in up to 5 years age group
• By 2005, stabilize the incidence of hepatitis C
• By 2010, 50% reduce the incidence of hepatitis B
• Until 2006, improve patient selection for anti-viral therapy, optimize the therapeutic strategy and tactics (duration of treatment and optimal doses of medications), increase the effectiveness of treatment, stable remission rate, reduce disease progression to liver cirrhosis and primary liver cancer risk
Due to viral hepatitis situation in Lithuania

(14 Jun 2013 Letter of Vice minister of Health)
Project of National Hepatitis C Control 2017 - 2030 year strategy

(Submitted to Lithuanian Ministry of Health 28 Aug, 2016)
Hepatitis C infection control strategy in Lithuania for 2017 - 2030: vision and goals

Vision of the strategy formulated in line with the WHO:

„Achieve that viral hepatitis C would be eliminated from the list of the most important diseases“

Without fundamentally changing the current diagnostic methods and without having to install modern and efficient medical aid, 2015-2025 years, disease-induced complications number will double compared to the 2005-2010 period:

• deaths from liver cirrhosis
• liver cancer
• liver failure
• liver transplants
Unresolved problems in the field of HCV infection:

National strategy

• There is no **national strategy** or plan exclusively for viral hepatitis prevention and control in Lithuania

• No single government department/section responsible exclusively for viral hepatitis and other co-ordination with the disease-related activities

• The government has financed and participated in the events devoted to the World Hepatitis Day 2012, but did not support any other activities for the public understanding of viral hepatitis promotion from January 2011

The government should cooperates with the health care providers and patient organization and implement hepatitis C prevention and control program
Unresolved problems in the field of HCV infection: 
**Surveillance, reporting, registry**

- Lithuania has an active surveillance system of acute A, B, C, D and E hepatitis types with the mandatory reporting of new cases, but for chronic hepatitis this not works

No inspection programs for risk populations:
- IDU; residents born in 1945-1965; HIV infected; homosexuals; prisoners; immigrants

- There is no monitoring/registration systems of infected people implemented

- The government does not publicly announce existing data on chronic hepatitis incidence and prevalence

**National surveillance system for CHC with the mandatory reporting of new chronic hepatitis cases and hepatitis registry should be implemented**
Unresolved problems in the field of HCV infection:
Screening and prevention

- **Hepatitis C screening program** is not integrated along with other screening programs

- There remains many HCV undetected patients

- New HCV infection still occurs (mostly by IDU, MSM)

- No educational program for patients on how to prevent reinfection

- Periodic epidemiological analysis of hepatitis C risk groups are not carried out

**Universal hepatitis C screening program should be implemented**
Unresolved problems in the field of HCV infection: Treatment, post-treatment monitoring

• No hepatitis C centralized monitoring system before, on and after treatment:
  • Virological response, treatment adherence and compliance, time from diagnosis to start of treatment, incidence of cirrhosis, HCC

• Treatment protocols and guidelines are updated too slowly, their effectiveness is not assessed

• Treatment is appointed to limited populations

• No individual monitoring and treatment plan for patients, whose treatment was ineffective

Well organized treatment programs supported by government with affordable DAAs with SVR rate > 90% should be implemented; every CHC patient should be treated
Challengers in Hepatitis C strategies

Epidemics of hepatitis C represent a growing public health concern in most countries of Eastern Europe as well as in Lithuania, and it is urgent need of **National Hepatitis Program**

- Patient identification by risk assessment or by age (surveillance system) is not in place in Lithuania and should be implemented
- Strategy should emphasize efforts to increase awareness and testing for HCV
- Strategy should prevent stigmatization
- Active prevention measures are necessary especially in health care settings
Challengers in access to treatment for hepatitis C

The term “standard of care” refers to evidence-based, internationally recognized treatment regimens that are most successful in clearing the HCV from patients

• Introduction of newer treatments “usually slow”
  • convince government to pay for treatment
  • long negotiate affordable prices

• The cost of IFN-free medications for CHC are unaffordable for all other patients, who are not included in to the group for reimbursement – the access to treatment should be improved, as every CHC patient should be treated

• Well organized treatment programs supported by government with affordable DAAs with SVR rate > 90% should be implemented
Conference “Baltic Countries National Strategies towards the elimination of Hepatitis C”
14th February 2017

• Number of participants: 41 from 3 Baltic countries

• WHO priorities and 5 strategic directions for elimination of viral hepatitis were discussed

• Romalda Baranauskiene Welcome on behalf of Lithuania MoH
  • “We should find the best solutions for treatment for our people. Lithuania is facing problems: on one hand we must have and deliver the best possible treatment; on the other hand - the budget issue-how to tailor it to fit our compensation scheme. The target should be to improve diagnostics and treatment, exchange good practises of other countries”.

• Decided to form a group among conference participants: Baltic Coalition. Write a paper about the conference and to remind to take an action to act. Coalition paper included the opinions of experts from all 3 Baltic countries. The paper already was sent to Lithuanian Ministries of Health.
The key conclusion of the meeting by all External Experts

• There is a need for National Hepatitis C Control Strategy Program. It could be achieved in close collaboration and active negotiation among multiple stakeholders: HCPs, Governmental institutions, Patient Organizations. All Baltic States should stand as one and work together towards initiating and implementing the changes.

• The Experts are urging for “Call for action”: Prepare a resolution on behalf of meeting attendees and submit the document to Ministries of Health and other institutions, responsible for local HCV infection health policies.