

Viral Hepatitis Prevention Board

A new era for screening and treatment of hepatitis C: a public health challenge

**SPLIT, CROATIA
14 and 15 November 2013**

Objectives

- To give an overview of the developments in hepatitis C therapy and their potential for controlling the disease
- To review country examples of screening and treatment strategies and their impact on the public health
- To identify barriers to the identification and treatment of patients with hepatitis C, and to discuss equal access to treatment and the perspectives of different stakeholders (hepatologists, patients, public health experts)
- To examine the impact of the increasing number of patients seeking care on existing public health resources (financial and human)
- To provide an overview of the status of the development of hepatitis C vaccines

Context

- Large number of chronic HCV infections (170 million globally, 6.1 million in EU, up to 4.4 million in USA; 10 million infected IDUs, globally; 4-5 million co-infected with HIV); and high mortality (0.5 million; 17,000 in USA) – and considerable under-reporting. Most HCV+ people: unaware, undiagnosed and untreated
- Prevalence varies – relatively low (0.4-4.0%) in developed world but high in some other countries (e.g. Egypt)
- Incidence: steady overall in Europe but falling in North/West, rising in South/East; rising in some countries (e.g. Australia, USA and Uzbekistan); rural spread a problem (Canada and USA)
- Routes of transmission: IDU, but globally most infections due to suboptimal infection control
- Epidemic of HCV-related chronic liver disease including HCC expected to peak around 2032

Clinical aspects

- HCV – a silent killer
- Chronic HCV infection can lead to no clinical disease, mild disease, or severe liver disease including hepatocellular carcinoma and death
- Important cause of liver cancer, with rapidly rising rates
- Disease is often diagnosed late, with consequential high costs of treatment and increased admissions to hospital
- Liver biopsy can be replaced by non-invasive methods (such as Fibroscan)

Therapeutic issues

- Diagnosis of HCV without offering treatment to those who need it is not in line with principles of screening but can offer patients power to decide
- Strategies for treatment – treat to prevent transmission and disease, treat all HCV+ or select patients?
- Careful selection of patients needed together with monitoring (and associated tests, e.g. for viral load)
- Treatment regimens are complex, with different approaches for naïve subjects, relapsers, and partial and non-responders, for different viral genotype and degree of fibrosis
- Toxicity still an issue with current regimens but expected to be significantly lower with next generation of drugs
- PegIFN/ribavirin may remain the standard of care in countries with limited resources

Therapeutic issues

- Treatment rates still very low, with constraints of eligibility, non-compliance and drop out; competence and capacity
- Recognition of treatment as prevention
- Many patients refuse treatment – reasons include side effects, work/family implications, and wanting to await arrival of newer treatments
- Few specialists and not all gastroenterologists or infectious disease experts willing or able to treat hepatitis C; some treating physicians withdrawing because of increasing complexities of treatment
- Need for education of physicians, nurses and patients
- EASL project for centralized European database

Changing therapeutic landscape

- Steady improvements in SVR with combination therapy - modelling indicates impact of treatment in terms of predicted deaths averted (up to 400,000 in USA as a result of screening the 1945-65 birth cohort if all infected subjects are treated)
- Introduction of direct acting agents improving benefits of treatment; new treatments recently licensed – better cure rates but still serious side effects
- Success rates with current therapies vary with genotype (up to 90% for GT2 but progressively lower for GT3, 1b and 1a)
- New safe, highly effective therapies will be available within weeks; algorithms for new treatment being developed
- Many more antiviral agents in pipeline (different classes with different mechanisms of action) – rapid progress, revolutionizing treatment and breaking down barriers to treatment
- All-oral, IFN-free treatment regimens can dramatic increase in number of patients treated (including IDUs) is imminent, but issues of cost

Treatment – price and costs

- Price of treatment a contentious issue – likely to be high (around US\$ 80,000) for the next few years – and will be a major barrier in many countries
- Reimbursement covered by the State or private health insurance in some countries; lack in other countries means that new treatments will be unavailable
- Support must be provided to countries to scale up HCV testing and treatment
- Comparison of prices a useful approach for countries before negotiations on purchases - other approaches include national procurement, tiered-pricing or rebates
- Urgent need to explore innovative funding mechanisms to ensure equitable access, including analyses of success factors that enabled the creation of some existing models (e.g. Global Fund to Fight AIDS, Tuberculosis and Malaria, the GAVI Alliance, UNITAID)

Treatment guidelines

- EASL due to update Clinical Practice Guidelines in January 2014
- WHO to issue guidelines on screening, care and treatment of hepatitis C virus infection in April 2014
- Other national and international guidelines exist or are imminent: ECDC/EMCDDA, EU HepScreen 2014, American Association for the Study of Liver Disease, Infectious Diseases Society of America, EU Hep Frame (due 2015), treatment guidelines in the Netherlands (including protease inhibitors and uniquely containing management of side effects), and Swedish guidelines (the 2011 edition is being replaced in 2014)
- All guidelines will need updating imminently in the light of introduction of interferon-free protocols

Testing/screening

- Clear benefits of screening and treating
- What testing protocol to follow – immunoassay followed by nucleic acid tests (NAT) or simultaneous testing?
- Debate on the introduction of rapid low-cost tests for monitoring response to therapy and the importance of follow-up of viral load throughout treatment course
- Do all countries have resources for testing?
- US birth cohort approach (with cost covered by health insurance) unique, well accepted (with legislative mandate in some states) and beginning to produce results; questions regarding follow-up and monitoring - potential for expanding approach to other countries
- Cost-effectiveness is equivalent to that of other screening programmes

Testing/screening

- Guidance for testing IDUs clear, but most other guidance is exhortational rather than directive – need for “real” guidance; a list of high-risk groups does not constitute a screening programme
- Cost of testing insignificant compared with that of treatment
- Need for better performance data on screening initiatives
- Cost-effectiveness of testing insensitive to testing costs and prevalence, and more sensitive to treatment costs and low rates of treatment take up
- New technologies for testing can expand access to treatment – examples include rapid point of access testing (affordability in developing countries?) and use of dry blood spot sampling established; could be extended to newborns

Country experiences

- Croatia – political will (Parliament's resolution on viral hepatitis) exists, consensus conference held and the costs of protease inhibitors reimbursed
- Netherlands – higher rates of HCV infection in first-generation migrants from endemic countries, multiple genotypes circulating, national viral hepatitis programme, national guidelines and clinical trials underway
- Sweden – guidelines include treatment of infection with different genotypes and treatment of children; for many patients treatment is being deferred until the arrival of new treatments

Country experiences

- Balkan and Mediterranean countries – changing epidemiology; major population infected comprises migrants; societal factors include legacy of war, civil unrest, and displacement; lack of recognition of viral hepatitis as a public health problem; stakeholders include WHO and EU; 2012 summit conference issued a call for action covering among other things surveillance, case detection, counselling and testing, and access to treatment
- France and Germany – governments can afford to pay for treatment, but disparities within Europe about willingness and ability to pay
- Many countries report substantial prevalence rates in migrants

Prevention

- Recognition of treatment as prevention

Vaccines

- Candidate vaccines exist and small clinical trials have begun
- But little prospect of success or commercial interest
- Obstacles to development include: very high viral mutation rate and genetic diversity of HCV; neutralizing antibodies ineffective; humoral responses; and lack of animal model

Barriers to treatment

- Barriers seen at all steps of care and at all levels: health system, providers, patients and pharmaceutical industry
- Underserved populations – little or no access to testing, assessment or treatment
- Solutions – from decriminalization of drug use to public awareness and education (including physicians), and provision of need-adapted care systems
- Brain-storming workshops at meeting identified barriers, some solutions and potential actors

Matters for consideration

- How to raise awareness about hepatitis C as a global health problem and create and maintain greater political will and commitment? Experience from HIV/AIDS: value of cost-effectiveness data for shaping policy on expanding access to care and treatment (create investment cases?)
- How to generate more and better data, including burden of disease and health economic studies (cost-effectiveness of treatment and screening)?
- Other experiences from HIV/AIDS – treatment as prevention, expanding access
- How to tackle infections related to health care? - action plans (France and Scotland) referred to blood supply issues

Matters for consideration - contd

- Injecting drug users: successful national action plan but other actions could include decriminalizing injecting drug use
- How to develop screening recommendations that destigmatize hepatitis C
- How to overcome (urgently) major barriers at all levels: lack of awareness, poor knowledge and inadequate education? Need for accurate information and for consensus within the medical community
- Data on severe disease outcomes not available
- Need to improve interventions to prevent transmission particularly among PWID
- Explore further the potential of combined interventions – harm reduction and antiviral treatment – for IDUs

Matters for consideration - contd

- What policy should be adopted for those diagnosed with HCV infection but without access to treatment?
- How can we apply the new treatments to lower the barriers to treatment? The complexity of treatment provides uncertainties for care providers (and patients) and postponement or deferral of treatment (a phenomenon reported in several countries)
- Need for education and training, sharing of best practices, monitoring and evaluation, networks and partnerships between public health experts and policy-makers, clinicians, funders, doctors and patients
- Some high-level of support and interest (e.g. ECDC, DG Sanco, EU's Seventh Framework Programme for Research (€6 billion, including allocations for viral hepatitis and Balkan and Mediterranean countries); how to raise priority in other relevant agencies or bodies?

Matters for consideration – cont'd

- How will guidelines be updated? – at present they are rapidly becoming obsolescent
- What are factors of success? – some have been identified, e.g. good data, patient representation, contributions from the pharmaceutical industry, increasing access (project ECHO)
- Need for more work on nosocomial infections and improvements in infection control
- New drugs hold great promise for improving benefits and reducing adverse effects of current treatment
- Stigmatization is a real problem and its drivers need to be better understood; health care workers, especially in primary health care, need training to counter it
- Recognition of HCV as a carcinogenic virus might help destigmatize HCV infection

In conclusion

- Other key messages: a tsunami of cases expected, HCV is about to become a global public health emergency, urgent need globally for testing campaigns linked to action (e.g. treatment, prevention and adherence to infection control procedures), issues of access must be resolved, and urgent need for public health measures
- Need for clear, simple messages
- The goal of elimination of hepatitis C (through increased treatment and prevention) appears to be feasible in the long-term – but only with political will, infrastructure and health system capacity-building