October - November 2012

FSRC
focus scientific research center

HEPATITIS BULLETIN

FSRC EDITORIAL

Dr. Arun Gowda
Director - FSRC, phamax AG,
Bangalore, India
arun.gowda@fs-researchcenter.com

Dear Reader,

It is my pleasure to make my debut editorial with the third edition of FSRC hepatitis bulletin. Our continued focus and work in Egypt, the country with the highest prevalence rates of HCV in the world, shows us how significant an impact the disease has on the country's economy and the healthcare infrastructure. What becomes apparent to us with the findings is that the realization of enormity of the situation needs to trickle down to the masses as well as the policy makers to bring about a change. We believe that no organization or individual will succeed in this initiative alone and the need is for a collaboration of stakeholders at multiple levels and activities.

Continuing our efforts to increase the awareness of hepatitis, we bring a guest article from Dr. Gerd Bodlaj on "Chronic Hepatitis C – the Austrian experience". He is sharing his experience on the epidemiological impact and management of HCV in Austria.

Among other topics in this edition is coverage on the New Anti-Viral Therapies Sessions – Abstract and Posters presented during the '19th International Symposium on Hepatitis C Virus and Related Viruses' held in Venice, Italy.

The HCV Codex in this edition throws light on the Global Prevalence of HCV. Finally, we bring news from around the world impacting the HCV space.

We hope you enjoy this bulletin and are looking forward to your feedback.

Stay healthy,

Arun

ABOUT FSRC

Our Belief

We believe that unbiased and credible scientific information and recommendations allow healthcare stakeholders to make improved decisions for the enhancement of healthcare.

How we do it?

A dedicated group of in-house physicians, in collaboration with academic institutes and scientific experts, research and analyze the subject extensively to distil relevant knowledge.

What we do?

We develop unique scientific solutions addressing the needs of the healthcare system.

Our vision is to bring various groups within the healthcare ecosystem such as clinical leaders, patient organizations, nongovernment organizations (NGOs), governments, and pharmaceutical companies together under one platform to discuss, debate, and jointly develop strategies to overcome various healthcare access issues in emerging markets. In recent years, we have developed a network of various stakeholders across emerging and developed markets. During the course of our work and interactions with stakeholders, we have witnessed different aspects of access issues from a healthcare standpoint. We have extensively analyzed various data and information clearly indicating the existence of a significant gap between what needs to be done and what is actually being done from a healthcare delivery aspect.

Our belief is if we provide the "right information to the right people in the healthcare ecosystem," then

FSRC TEAM

Behsad Zomorodi
Founder and CEO,
phamax AG, Basel,
Switzerland
behsad.zomorodi@
phamax.ch

Anand Patil
Managing Partner,
phamax AG,
Bangalore, India
anand.patil@
phamax.ch

a majority of the access issues could be resolved. Validated, unbiased, credible scientific information and recommendations undoubtedly allow healthcare stakeholders to formulate robust health care plans. This in turn empowers healthcare personnel in arriving at improved decisions for enhanced healthcare management.

FSRC has completed various projects in Middle Eastern and Northern and sub-Saharan African countries, and we are currently completing projects in Egypt, Morocco, Cameroon, and CIS countries to assess the socioeconomic burden of HCV in these countries. The key goal of all these projects is to devise an action plan for local organizations (government and nongovernment organizations) to manage the disease more effectively and improve healthcare access for HCV patients.

In Egypt, which has the world's highest HCV prevalence, FSRC is currently conducting a study to estimate the economic impact of failing to treat hepatitis C at an early stage. This report will be potentially utilized in managing hepatitis C more effectively in the future.

In CIS countries, we are collaborating with multiple stakeholders to ascertain the burden of hepatitis C. This study is being conducted under the guidance of local governments.

As a team, we constantly strive toward identifying and recommending the best healthcare practices in those areas where effective and comprehensive healthcare policies are not in place. Through this strategy, we hope to contribute to the larger goal of providing effective healthcare to everyone.

Dr. Vijay Panickar
Senior Scientific Advisor
vijay.panickar@fs-researchcenter.com

Dr. Jyoti Rao
Scientific Advisor
Jyoti.rao@fs-researchcenter.com

Dr. Seema Samanth
Scientific associate
seema.samanth@fs-researchcenter.com

CHRONIC HEPATITIS C – THE AUSTRIAN EXPERIENCE

Dr. Gerd Bodlaj

Associate Professor of Medicine, 2nd Department of Medicine, St. Vincent Hospital, Stumpergasse 13, 1060 Vienna, Austria

Tel.: +43-1-599 88 – 6121

FAX: +43-1-599 88 – 4043

e-mail: gerd.bodlaj@bhs.at

Epidemiology

Chronic hepatitis C (CHC) is a major public health problem due to late complications, such as liver failure and hepatocellular carcinoma.[1] The prevalence of CHC has been estimated to be 3% worldwide with large geographical differences.[2] In Austria, the prevalence of CHC is considered to be low like in most western European countries. With about 8 million inhabitants in Austria and an estimated prevalence of slightly below 0.5%, we have to face up to 40,000 patients. Most of them got infected many years ago in the seventies and eighties, during plasma donation or when they received infected blood or blood products.[3,4] Since the beginning of the nineties, all blood products in Austria are checked for hepatitis. Today, the main sources of infection in our country are considered to be intravenous drug abuse with needle sharing and tattoos or piercings under unhygienic conditions. In about 40% of newly diagnosed patients, the mode of infection is unknown. The genotype (GT) distribution of the hepatitis C virus shows strong variations worldwide. In a retrospective analysis of 1239 patients in Upper Austria, GT 1 was the most common GT with 80.4%, followed by GT 3 (12.3%), GT 2 (4.5%) and GT 4 (2.7%).

GT 5 and 6 are extremely rare in our region. Interestingly, patients with GT 1 were older at the time of diagnosis (48.2 years) than patients with GT 2 (43.4 years), GT 3 (37.7 years) and GT 4 (39.7 years).[4] A possible reason for this finding could be that the majority of older patients got infected during plasma donation decades ago and GT 1 was the most common GT with this route of transmission. In contrast, GT 2 and 3 are considered to be frequently transmitted by intravenous drug abuse and those patients are mostly of younger age. In addition, males were significantly younger at the time of diagnosis than females (45.0 vs. 49.3 years, $P < 0.001$).[4]

Current treatment of chronic hepatitis C

The current standard therapy is the combination of pegylated interferon-(PegIFN-α) once weekly and ribavirin daily. The dosage of ribavirin and the duration of treatment depend on viral GT and viral kinetics:

- Patients with GT 1 and 4: PegIFN-α+ ribavirin (1000 – 1200mg/d) for 24 – 72 weeks.
- Patients with GT 2 and 3: PegIFN-α+ ribavirin (800 mg/d) for 16 – 24 weeks.

In patients with GT 1, two new drugs, boceprevir or telaprevir, can be combined with the standard therapy to a triple therapy and help to increase the success rates from 45 – 50% to 70 – 75%. However, these new direct acting antivirals (DAA) can cause severe drug interactions and side effects, and therefore, strict patient selection and close clinical and laboratory monitoring are necessary. In addition, drugs must be administered every 7 – 9 hours.[5-8]

Who should be treated with triple therapy?

1. Therapy naïve patients that are not negative on PCR after 4 weeks of standard therapy.
2. Patients with relapse on previous standard therapy with PegIFN-α and ribavirin. They have a success rate of up to 90%.
3. Patients with compensated cirrhosis (Child A) and non-response on previous standard therapy. They might have the greatest benefit, however, response rates are poor (14% for telaprevir, no data for boceprevir).
4. Patients without cirrhosis that had a partial response or a non-response on previous standard therapy (dependent on urgency).

Who should not be treated with triple therapy?

1. Patients with GT 2 – 6.
2. Patients after liver transplantation because of severe drug interactions.
3. Patients with decompensated cirrhosis.
4. Patients with only mild liver fibrosis can possibly wait for newly developed drugs.[5-8]

References:

1. *El-Serag HB. Hepatocellular carcinoma and hepatitis C in the United States. Hepatology 2002; 36: S74-S83.*
2. *Heintges T, Wands JR. Hepatitis C virus: epidemiology and transmission. Hepatology 1997; 26: 521-6.*
3. *Mühlberger N, Schwarzer R, Lettmeier B, Sroczynski G, Zeuzem S, Siebert U. HCV-related burden of disease in Europe: a systematic assessment of incidence, prevalence, morbidity, and mortality. BMC Public Health 2009; 9: 34.*
4. *Maieron A, Metz-Gercek S, Hackl F, et al. Chronic hepatitis C in Austria, 1992-2006: genotype distribution and demographic factors. Euro Surveill 2010; 15: 19492.*
5. *Bacon BR, Gordon SC, Lawitz E, et al. Boceprevir for previously treated chronic HCV genotype 1 infection. N Engl J Med 2011; 364: 1207-17.*
6. *Poordad F, McCone J, Bacon BR, et al. Boceprevir for untreated chronic HCV genotype 1 infection. N Engl J Med 2011; 364: 1195-206.*
7. *Zeuzem S, Andreone P, Pol S, et al. Telaprevir for retreatment of HCV infection. N Engl J Med 2011; 364: 2417-28.*
8. *Jacobson IM, McHutchinson JG, Dusheiko G, et al. Telaprevir for previously untreated chronic hepatitis C virus infection. N Engl J Med 2011; 364: 2405-16.*

19TH INTERNATIONAL SYMPOSIUM ON HEPATITS C VIRUS AND RELATED VIRUSES

Date: Friday, 5 - Tuesday, 9 October 2012
Venue: Palazzo del Cinema, Lido - Venice, Italy
Event Website: http://hcv2012.org

Industry presentations in the new anti-viral therapies section

- **MSD LECTURE -** The impact of antiviral therapy on the natural history of Hepatitis C, *Massimo Colombo, Università degli Studi di Milano, Milan, Italy*
- **GILEAD LECTURE** - Genetics, HCV and treatment response: unravelling the future waves of HCV therapies, *John McHutchison, Gilead Sciences, Foster City, USA*
- **ROCHE LECTURE** - Clinical research of combinations of multiple classesof direct antiviral agents in an Interferon-free regimen, *Savino Bruno, AO Fatebenefratelli Oftalmico, Milan, Italy*

Main Sponsors

Roche

MSD

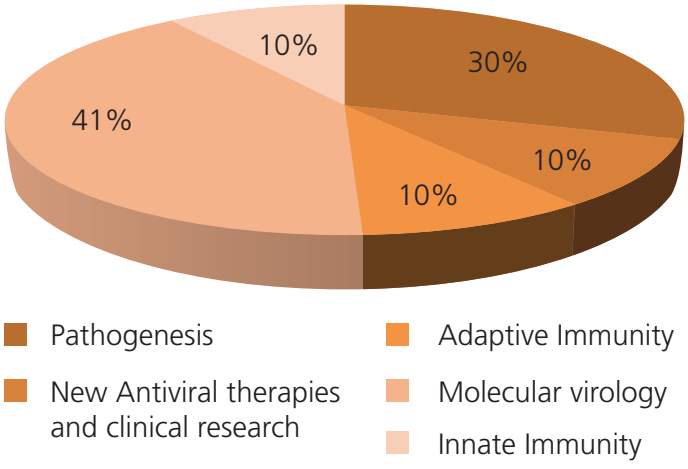
Idenix PHARMACEUTICALS

GILEAD

NOVARTIS VACCINES AND DIAGNOSTICS

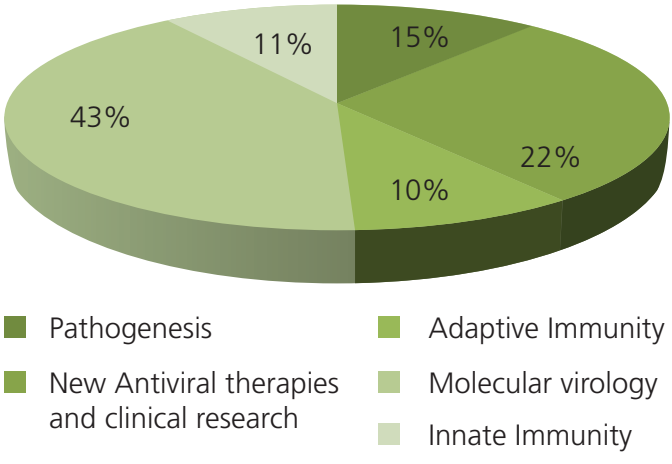
DIA.PRO Diagnostic BioProbes s.r.l

Abstracts Presented at the conference



- At the conference, maximum oral presentations were made on molecular virology (41%), followed by pathogenesis (30%).
- Oral presentations on new antiviral therapies and clinical research, adaptive and innate immunity were made in equal number (10%)
- At the conference, maximum posters were made on molecular virology (43%), followed by new antiviral therapies and clinical research (22%).
- Abstracts were also presented on pathogenesis (15%), innate (11%) and adaptive (10%) immunity

Posters Presented at the conference



New Anti-viral therapy sessions

- Independent evolution of multi-dominant viral genome species observed in a single HCV carrier, *Ando Tomomi, Shinjyuku-Ku, Tokyo, Japan*

  The study demonstrated that considering each full-length species in patient serum is important for understanding HCV pathogenesis, and for discovering resistance mutations for developing anti-viral drugs. Existence of some virus species having different characters in one patient could have effects on HCV life cycle.

- A microRNA-based multivariate signature predicts sustained virological response in patients with chronic Hepatitis C, *Emilie Estrabaud, Inserm U773- Crb3, Paris, France*

  The authors identified a highly accurate signature of sustained virological response (SVR) (HCV genotype 1, IFI35 and mir-99a) with a positive predictive value, sensibility and specificity of respectively 86, 4%, 80, 0% and 80, 4%.

- Analysis of HCV resistance to Silibinin in vitro and in vivo reveals a novel antiviral mechanism targeting nonstructural protein 4B, Katharina *Esser-Nobis, Heidelberg, Germany*

  Legalon-SIL® (SIL) mainly acts by an entirely novel mode of action targeting NS4B, thereby affecting the structure of viral replication sites.

- Epigenetic remodeling and histone methylation by the G9amethyl transferase mediate Ribavirin effects on Inteferon responses, *Massimo Levrero, Università Di Roma La Sapienza, Rome, Italy*

  The positive Ribavirin (RBV) effect on interferon (IFN) responses might be related to its ability to switch-off pre-activated Interferon-Stimulated Genes (ISGs) by remodelling chromatin to restore an epigenetic environment favourable to full activation by exogenous IFN treatment.

- HCV NS5A inhibitors alter membranous web formation and reduce PI4P induction in cells expressing HCV non-structural proteins, *Carola Berger, Heidelberg, Germany*

  BMS-553 might affect the interaction between NS5A and PI4KIIIα or impair kinase activity, leading to the malformation of HCV replication compartments and thus to an inhibition of HCV replication.

- New drug-like cyclophilin inhibitors unrelated to cyclosporine potently inhibit HCV replication and revert HCV-induced mitochondrial dysfunctions, *Abdel Hakim Ahmed-Belkacem, INSERM U955, Créteil, France*

  The authors have generated a new family of potent "drug-like" cyclophilin inhibitors unrelated to cyclosporine A, with potent anti-HCV activity in vitro, promising pharmacologic properties and an inhibitory effect on HCV-induced mitochondrial dysfunction that may play a role in the prevention of HCV-induced hepatocellular carcinoma.

Posters on new antiviral treatment and clinical research	
Novel molecule/agent	• **Cannabinoid receptor 1 antagonists:** novel antiviral agents against Hepatitis C virus • Rational design of potent small-**molecules inhibitors of human cyclophilins** and HCV replication • Novel **allosteric inhibitors of the NS3 protease** from the Hepatitis C virus • The **anthocyanidin delphinidin** is a new inhibitor of Hepatitis C virus entry • The pharmacological properties of **IDX19368**, a novel nucleotide prodrug, highlight its potential for use in a low-dose DAA regimen for HCV • The antiviral effect of **interferon α** on Hepatitis C virus replication is impaired by Sorafenib • Antiviral activity of **glycyrrhizin** against Hepatitis C virus in vitro • Therapeutic potential of **Brazilian natural compounds** on Hepatitis C virus infection • **Naturally occurring Hepatitis C virus (HCV) protease inhibitor resistance**-associated mutations in naïve daa patients from São Paulo, Brazil • Development of a **prophylactic vaccine** for Hepatitis C virus using a novel E2 core domain • Multiple antiviral effects of the **polysaccharide DL2014** on the Hepatitis C virus life cycle • Novel **iminosugar derivatives** exhibit potent antiviral activity against Hepatitis C virus • New **IL28B single nucleotide polymorphism** compensates rs8099917 in the response to therapy for chronic Hepatitis C
Preclinical and clinical research	• Potent anti-HCV activities found in preclinical anti-malarial drugs is promptly exerted through oxidative stress • Preclinical characterization of the Hepatitis C virus NS5B polymerase non-nucleoside inhibitor BI 207127 • Phenotypic characterization of HCV genotype • 1 protease sequences derived from patients treated with telaprevir-based regimens in phase 3 studies • Optimizing ribavirin dose is critical for sustained viral response in patients with thalassemia major treated for chronic Hepatitis C • Standard of care, PegIFN plus Ribavirin anti-HCV therapy in HCV patients with and without mixed Cryoglobulinemia: results of a prospective, controlled
Manage-ment	• Optimizing ribavirin dose is critical for sustained viral response in patients with thalassemia major treated for chronic Hepatitis C • Standard of care, PegIFN plus Ribavirin anti-HCV therapy in HCV patients with

Management	and without mixed Cryoglobulinemia: results of a prospective, controlled • Selection of HCV-1 patients with chronic hepatitis who might benefit from current standard of therapy with peg-interferon and ribavirin
Mechanism of action	• Effects of PI4KIIIß inhibition on Hepatitis C virus and human cells • Monoclonal antibodies that target the HCV envelope proteins prevent in vivo infection of an escape variant isolated from a liver transplant patient • Antiviral activity and modulation of autophagy in the ex vivo model of human liver slices cultures infected with human Hepatitis C • Marked synergy of entry inhibitors and alisporivir on the inhibition of Hepatitis C virus infection • Identification of a new mechanism of non-nucleoside inhibition of HCV RNA-dependent RNA polymerase by the Flavonoid quercetagetin • Turmeric curcumin inhibits entry of all Hepatitis C virus genotypes into human liver cells • Application of RNAi gene silencing platform for the development of novel antiviral compounds targeting Hepatitis C virus • Evaluation of the Liver Fibrosis Index (LF Index) calculated by using real-time tissue elastography for the noninvasive assessment of liver fibrosis • Molecular basis for natural resistance to non-nucleoside inhibitors of HCV NS5B • Quasispecies analysis of HBV strains isolated from chronic Hepatitis B patients treated with Peg-interferon+Tenofovir therapy • Semisynthetic derivatives of glycopeptide antibiotics inhibit Hepatitis C virus replication through membrane binding and altering the lipid metabolism • Quadruple combinations of direct acting antivirals prevent the emergence of drug ressistant variants and rapidly clear hepatoma cells from their replication • Serum level of Hepatitis B surface antigen indicates fibrosis severity in treatment-naïve Hepatitis B E antigen-positive patients • How to distinguish HBeAg negative chronic hepatitis B, with high risk of reactivation, from inactive carriers: is there a place for HBsAg quantifications? • A serum protein signature predict response to pegylated interferon and ribavirin in chronic Hepatitis C • Ethanol facilitates HCV replication via up regulation of GW182 and HSP90 in human hepatoma cells • A serum protein signature detect early fibrosis in chronic Hepatitis C

Save your dates: 20th HCV 2013

Hosted by:

Sunday 6th October - Thursday 10th October 2013

Melbourne Convention and Exhibition Centre, AUSTRALIA

www.hcv2013.org

Important Dates

Registration Opens:

Monday, 4 February 2013

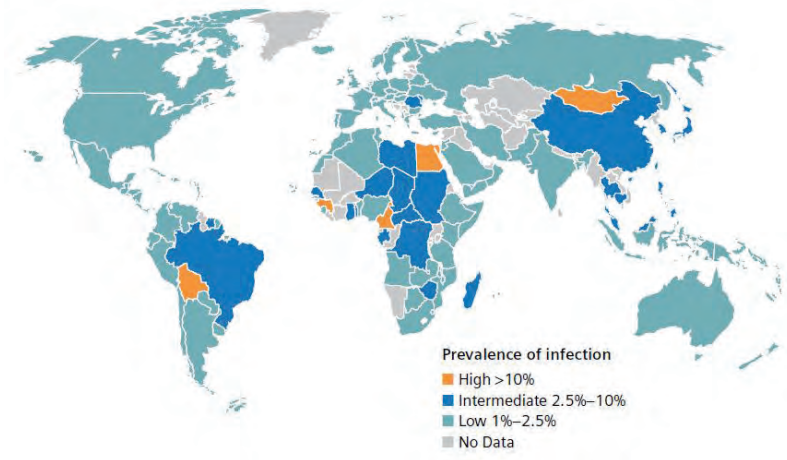
Abstract and award submission:

Friday 31 May 2013

HCV CODEX

In order to further FSRC's stated aim to gather and disseminate up-to-date, factual scientific information (especially for under-represented diseases in the emerging world) we are proud to present the Codex series. This will highlight in a serialized format, the most salient aspects of a chosen ailment, including but not restricted to: overview, epidemiology, clinical features, diagnosis and treatment.

Global prevalence of HCV



Reference:4

HCV remains a large health care burden to the world. Incidence rates across the world fluctuate and are difficult to calculate given the asymptomatic and often latent nature of the disease prior to clinical presentation. Prevalence rates across the world have changed as well with more countries being aware of transfusion-related hepatitis C and more and more evidence supporting intravenous drug use as the leading risk factor of spread of the virus.[1]

Most descriptions of global HCV epidemiology rely heavily upon HCV seroprevalence studies. These studies are typically cross-sectional in design and are done in select populations—e.g., blood donors or patients with chronic liver disease which may not be representative of the community or region in which they reside. Population-based studies representative of an entire community are more useful, but this kind of study is not feasible in most parts of the world.[2]

For several years, WHO has reported data on the worldwide prevalence of HCV infection, based on both published studies and submitted data. Although HCV is endemic worldwide, there is a large degree of geographic variability in its distribution. Countries with the highest reported prevalence rates are located in Africa and Asia; areas with lower prevalence include the industrialised nations in North America, Northern and Western Europe, and Australia. There is a wide range of prevalence estimates among developing countries, and generally less data available to validate assumptions about the burden of disease than in the developed world.[3]

Geographical distribution

HCV infections are common worldwide. An estimated 170 million people worldwide have chronic HCV infection, affecting 2-3 per cent of the world population.[5] It is estimated that there are about 4 million carriers in Europe alone.[6] Persistent HCV infection is a leading cause of serious liver disease, including cirrhosis and HCC.[7]

Estimated HCV burden worldwide

HCV infection	Estimated worldwide
Total Infected	~250–300 million
Chronic Infections	170–200 million
Newly Infected / Year	3–4 million
Deaths / Year	1.6%–2.5% of the carrier population

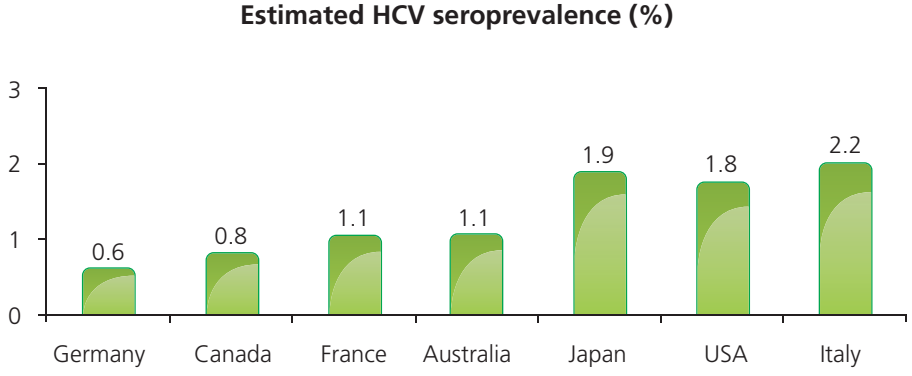
Reference: 8

Hepatitis C estimated prevalence and number infected by WHO Region

WHO region	Total Population (Millions)	Hepatitis C prevalence (Millions)	Infected Population (Millions)	Number of countries by WHO Region where data is not available
Africa	602	5.3	31.9	12
America	785	1.7	13.1	7
Eastern Mediterranean	466	4.6	21.3	7
Europe	858	1.03	8.9	19
South-East Africa	1500	2.15	32.3	3
Western Pacific	1600	3.9	62.2	11
Total	5811	3.1	169.7	57

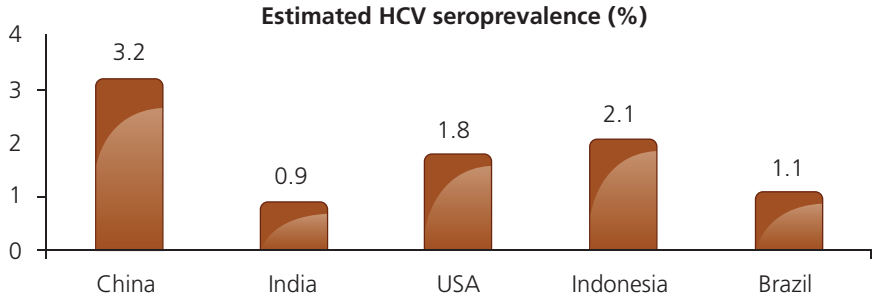
Reference: 8

HCV prevalence rates in some of the developed countries



Reference: 9, 10, 11, 12, 13, 14, 15

Reported HCV infection prevalence in the five most populous nations in the world



Reference: 16, 17, 18, 19, 20, 21

Reference:

1. *Sy T, Jamal MM. Epidemiology of hepatitis C virus (HCV) infection. Int J Med Sci. 2006;3(2):41-6. Epub 2006 Apr 1.*
2. *Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. Lancet Infect Dis. 2005 Sep;5(9):558-67.*
3. *Population Reference Bureau. 2004 world population datasheet.http://www.prb.org/pdf04/04WorldDataSheet_Eng.pdf (accessed July 25, 2005).*
4. *WHO. International travel and health. Maps. http://www.who.int/ith/maps/hepatitisc2007.jpg. Accessed September 2008*
5. *WHO. Global surveillance and control of hepatitis C. Report of a WHO Consultation organized in collaboration with the Viral Hepatitis Prevention Board, Antwerp, Belgium. J Viral Hepat1999;6:35–47*
6. *Viral Hepatitis Prevention Board. Hepatitis A, B & C: defining workers at risk. Viral Hepatitis, 1995, 3.*
7. *Huang RH, Hu KQ.A practical approach to managing patients with HCV infection. Int J Med Sci. 2006;3(2):63-8.*
8. *WHO. Hepatitis C fact sheet N 164. 2000. http::://www.who.int/mediacentre/factsheets/fs164/en/. Accessed August 2008.*
9. *Palitzsch KD, Hottentrager B, Schlottmann K, et al. Prevalence of antibodies against hepatitis C virus in the adult German population. Eur J Gastroenterol Hepatol 1999; 11: 1215–20.*
10. *Zou S, Tepper M, El Saadany S. Prediction of hepatitis C burden in Canada. Can J Gastroenterol 2000; 14: 575–80*
11. *Desenclos JC. Epidemiology of hepatitis C. Revue du Praticien 2000; 50: 1066–70.*
12. *Law MG, Dore GJ, Bath N, et al. Modelling hepatitis C virus incidence, prevalence, and long-term sequelae in Australia, 2001. Int J Epidemiol 2003; 32: 717–724.*
13. *Australian census, 2001, total population. http://www.abs.gov.au/ ausstats /abs%40census.nsf / ddc9b4f92657325cca256c3e000bdbaf/ 7dd97c937216e32fca256bbe008371f0! Open Document #Census Counts (accessed July 25, 2005).*
14. *Ohshima S, Komatsu M, Nakane K, et al. Iatrogenic GB virus C/hepatitis G virus infection in an area endemic for hepatitis C virus. J Hosp Infect 2000; 44: 179–85.*
15. *Puro V, Petrosillo N, Ippolito G, Aloisi MS, Boumis E, Rava L. Occupational hepatitis C virus infection in Italian health care workers. Am J Public Health 1995; 85: 1272–75.*
16. *Alter MJ, Kruszon-Moran D, Nainan OV, et al. The prevalence of hepatitis C virus infection in the United States, 1988 through 1994.N Engl J Med 1999; 341: 556–62.*
17. *Xia GL, Liu CB, Cao HL, et al. Prevalence of hepatitis B and C virus infections in the general Chinese population: results from a nationwide cross-sectional seroepidemiologic study of hepatitis A, B, C, D, and E virus infections in China, 1992. International Hepatology Communications 1996; 5: 62–73.*
18. *Chowdhury A, Santra A, Chaudhuri S, et al. Hepatitis C virus infection in the general population: a community-based study in West Bengal, India. Hepatology 2003; 37: 802–09*
19. *Sulaiman HA, Julitasari, Sie A, et al. Prevalence of hepatitis B and C viruses in healthy Indonesian blood donors. Trans R Soc Trop Med Hyg 1995; 89: 167–70.*
20. *Brandao AB, Costa FS. Risk factors for hepatitis C virus infection among blood donors in southern Brazil: a case-control study. BMC Gastroenterol 2002; 2: 18.*
21. *Khattak MF, Salamat N, Bhatti FA, Qureshi TZ. Seroprevalence of hepatitis B, C and HIV in blood donors in northern Pakistan. J Pak Med Assoc 2002; 52: 398–402.*

Hepatitis news

Abbott initiated phase III hepatitis C registrational programme following promising results from its phase II b clinical trial, known as Aviator, *November 16*

The phase III clinical trials are designed to evaluate safety and efficacy of a 12-week regimen of three direct acting antivirals (DAA), with and without ribavirin, for the treatment of HCV in genotype 1 (GT1) non-cirrhotic, treatment-naïve and treatment-experienced patients.

Abbott says interferon-free hep C regimens will be studied in broad patient populations across multiple countries.

The phase III programme, which is currently open for enrollment, will include more than 2,000 patients with HCV genotype 1, with trial sites in 29 countries. The DAAs in the studies include ABT-450/r (protease inhibitor and ritonavir), ABT-267 (NS5A inhibitor) and ABT-333 (non-nucleoside polymerase inhibitor). Treatment duration will be 12 weeks in non-cirrhotic patients, and 12 or 24 weeks in cirrhotic patients.

http://pharmabiz.com/NewsDetails.aspx?aid=72158&sid=2

Inovio's hepatitis B vaccine killer T cells show potential to clear HBV in liver, *November 15*

Inovio Pharmaceuticals announced that its synthetic hepatitis B (HBV) therapeutic vaccine has generated strong T cell responses that eliminated targeted liver cells in mice. This data points to the DNA vaccine's potential to clear HBV infection and thereby prevent liver cancer in humans; an encouraging development given that nearly one-third of the world's population is infected with hepatitis B, with 400 million at risk of developing liver cancer.

http://pharmabiz.com/NewsDetails.aspx?aid=72139&sid=2

Scientists determine how hepatitis B&D enter liver cells, *November 13*

In an eLife study, published today, scientists have filled a major gap in our understanding of hepatitis B and D: they've identified the receptor that allows hepatitis B and hepatitis D viruses to enter human liver cells. The study could help in the development of new therapies and treatments for a disease that is carried by more than two billion people around the world.

In identifying the receptor (Sodium taurocholate cotransporting polypeptide or NTCP), Wenhui Li and co-workers from the National Institute of Biological Sciences in Beijing, Peking University, and Peking Union Medical College have overcome enormous technical challenges.

http://news.bioscholar.com/2012/11/scientists-determine-hepatitis-bd-enter-liver-cells.html

Gilead Stocks Climbs on Study Results of Hepatitis C Combination, *November 13*

Gilead Sciences (world's biggest maker of HIV medicines) rose to its highest stock price in 20 years after a combination of its experimental hepatitis C therapies cleared the virus in all of the patients in a trial.

Gilead gained 14 percent to $73.93 at the close in New York, the largest single-day increase since October 2008 and the highest price since the company first offered stock in 1992.

http://www.bloomberg.com/news/2012-11-12/gilead-climbs-on-study-results-of-hepatitis-c-combo.html

Bristol-Myers Hepatitis C Combo Therapy Shows Promise, *November 12*

Results from a 16-patient trial presented today at the American Association for the Study of Liver Diseases in Boston showed that combining three of the company's experimental medicines, daclatasvir, asunaprevir and BMS-791325, cleared the hepatitis C virus in 94 percent of patients. Bristol-Myers plans to take the therapy into final-stage trials in 2014.

http://www.businessweek.com/news/2012-11-12/bristol-myers-hepatitis-c-combo-therapy-shows-promise

Investigational Hepatitis C Dual DAA Regimen of Daclatasvir and Asunaprevir Achieved SVR12 in 78%, *November 11*

Bristol-Myers Squibb Company announced new Phase II data demonstrating that the dual regimen of the investigational NS5A replication complex inhibitor daclatasvir (DCV) and the investigational NS3 protease inhibitor asunaprevir (ASV), without interferon or ribavirin, achieved high rates of sustained virologic response 12 weeks post-treatment (SVR12) in patients with genotype 1b (GT1b) hepatitis C virus (HCV) who were prior null responders to alfa interferon and ribavirin (alfa/RBV).

In this study, the DCV/ASV Dual regimen achieved SVR12 in 78% (14/18) and 65% (13/20) of GT1b patients when asunaprevir was dosed twice daily (Group A1) or once daily (Group A2), respectively.

http://www.dailyfinance.com/2012/11/11/investigational-hepatitis-c-dual-daa-regimen-of-da/

Merck Hepatitis C Drug Shows Promise, Merck now plans to explore interferon free regimen, *November 10*

A regimen containing an experimental MK-5172 suppressed the hepatitis C virus in most patients in a phase II study, and appears to be more potent than the company's Victrelis treatment.

330 patients were given various dose levels of MK-5172 in combination with ribavirin

and interferon for 12 weeks. The study found that 96% of patients who received the 100-milligram dose of MK-5172 had sustained virologic response 12 weeks after treatment ended.

Merck now plans to conduct new studies of its drug, MK-5172, as part of a potential all-oral hepatitis C regimen that eliminates interferon. Merck plans to conduct phase 2 studies of MK-5172 in combination with another experimental oral drug, MK-8742 with or without ribavirin.

Merck is among a pack of drug companies including Gilead Sciences and Abbott Laboratories, racing to tap what's expected to be a multibillion-dollar market for all-oral regimens.

http://online.wsj.com/article/SB10001424127887324894104578110710296702092.html

Gilead Announces 100% Sustained Virologic Response Rate (SVR4) for an Interferon-Free Regimen of Sofosbuvir (GS-7977), GS-5885 and Ribavirin in Treatment-Na ïve Genotype 1 Hepatitis C Infected Patients, *November 10*

Gilead Sciences announced interim data from the ongoing Phase II ELECTRON study examining a 12-week course of therapy with the investigational nucleotide sofosbuvir (formerly referred to as GS-7977), the NS5A inhibitor GS-5885 and ribavirin in patients with genotype 1 chronic hepatitis C virus (HCV) infection.

Among treatment-naïve patients receiving this combination, 100% (n=25/25) remained HCV RNA undetectable four weeks after completing therapy (SVR4). Study result was presented at the 63rd annual meeting of the American Association for the Study of Liver Diseases (The Liver Meeting 2012, November 13th) in Boston.

"These results indicate that adding GS-5885 to sofosbuvir-based regimens may enhance SVR rates, potentially offering HCV genotype 1 infected patients a convenient 12-week course of oral therapy," said Professor Edward Gane, principal investigator of the ELECTRON study.

http://www.gilead.com/pr_1757156

Boehringer Ingelheim to start late-stage hepatitis C drug trial, *November 10*

Boehringer Ingelheim said on Saturday it plans to initiate a late-stage clinical trial of its experimental hepatitis C treatment following promising results from earlier studies.

The company announced final data from a mid-stage trial of its treatment regimen which showed that 69% of patients in the study were free of the virus 12 and 24 weeks following the end of treatment.

http://in.reuters.com/article/2012/11/10/us-liver-boehringer-idINBRE8A90B820121110

Hepatitis hits more than 1,000 refugees in South Sudan: UNHCR, *November 09*

An outbreak of hepatitis E has infected at least 1,050 Sudanese refugees in South Sudan, killing 26 and threatening to spread further among people still arriving in crowded camps, the United Nations said on Friday.

About 175,000 people have already fled to South Sudan to escape fighting in Sudan's South Kordofan and Blue Nile states, the U.N. High Commissioner for Refugees said. Thousands more are expected to cross in coming weeks after the rainy season ends, it added.

http://in.reuters.com/article/2012/11/09/us-sudan-south-health-idINBRE8A80NB20121109

Roche's patent for Hepatitis C drug revoked, *November 04*

The patent on pegylated interferon alfa-2a (Pegasys) was revoked by the Intellectual Property Appellate Board (IPAB) in India on November 2, 2012. The patent was challenged by Sankalp Rehabilitation Trust (India)

The trust hopes that the absence of a patent barrier would spur generic competition to bring down the price of the much-needed pegylated interferon alfa-2a (Pegasys), bringing relief to people suffering from the disease. The Trust provides treatment to, and rehabilitation support, for injecting drug users (IDUs).

http://www.thehindu.com/health/policy-and-issues/roches-patent-for-hepatitis-c-drug-revoked/article4062590.ece

Vertex Joins Glaxo, J&J in Testing Hepatitis C Combos, *November 04*

Vertex Pharmaceuticals (maker of the hepatitis C drug Incivek) to test one of its experimental therapies for the disease with other drugs from Johnson & Johnson (JNJ) and GlaxoSmithKline (GSK).

The drug, VX-135, will be tested with J&J's simeprevir and Glaxo's GSK2336805 in separate 12-week trials to determine whether the combinations help rid patients of the virus. The companies will split development costs with Vertex.

http://www.bloomberg.com/news/2012-11-01/vertex-joins-glaxo-j-j-in-testing-hepatitis-c-combos.html

BioCryst drops hep C drug on safety issues, *October 31*

BioCryst Pharmaceuticals said it would withdraw an application to test its experimental hepatitis C drug in humans after the U.S. Food and Drug Administration expressed concern about its safety.

The FDA had concerns about the preclinical toxicity profile of the drug candidate, BCX5191, the company said.

The drug belongs to a new class of hepatitis C treatments, known as nucs, that is widely expected to be a game-changer in hepatitis C management but has been plagued by safety concerns.

In the past few months, the FDA has placed multiple nucs on clinical holds, citing safety issues, including Bristol-Myers Squibb Co's BMS-986094 and Idenix Pharmaceuticals Inc's IDX19368 and IDX184.

http://in.reuters.com/article/2012/10/30/us-biocryst-hepatitisc-idINBRE89T1SW20121030

Abbott hepatitis C drugs bring high cure rates in trial, *October 15*

Abbott on Monday announced initial data from a Phase IIb study suggesting that an interferon-free combination regimen of oral drugs resulted in a sustained virologic response (SVR) after 12 weeks in 97% to 99% of treatment-naïve patients with genotype 1 hepatitis C. In addition, 93% of null responders achieved a SVR.

For the AVIATOR study, researchers assigned 571 non-cirrhotic treatment-naïve patients and prior peg-interferon/ribavirin null responders to receive various combinations of the protease inhibitor ABT-450, the NS5A inhibitor ABT-267, and the polymerase inhibitor ABT-333, with or without ribavirin, for eight, 12 or 24 weeks. Of these, 438 patients were treatment-naive and 133 were prior null responders.

Abbott noted that the 12-week regimen of the three direct acting antivirals plus ribavirin had the highest SVR rates at 12 weeks.

http://www.firstwordpharma.com/node/1024906

http://in.reuters.com/article/2012/11/10/health-liver-abbott-hepatitisc-idINDEE8A904Y20121110

Contact us at: info@fs-researchcenter.com

CORPORATE HEADQUARTERS
phamax AG
Passage 6,
4104 Oberwil (BL), Switzerland
Phone : +41-61821 5687
Fax : +41-61821 5836

INDIA OFFICE
phamax Analytic Resources Pvt. Ltd.
KMJ Ascend No.19, 1st Cross, 17th C
Main, 5th Block, Koramangala
Bangalore - 560 095, India
Phone : +91-80 6745 1111
Fax : +91-80 6745 1122

ASIAPAC OFFICE
No.02-10
60 Havelock Road
River Place, Singapore 169658
Phone : +65 9457 6167
Fax : +65 6525 9414