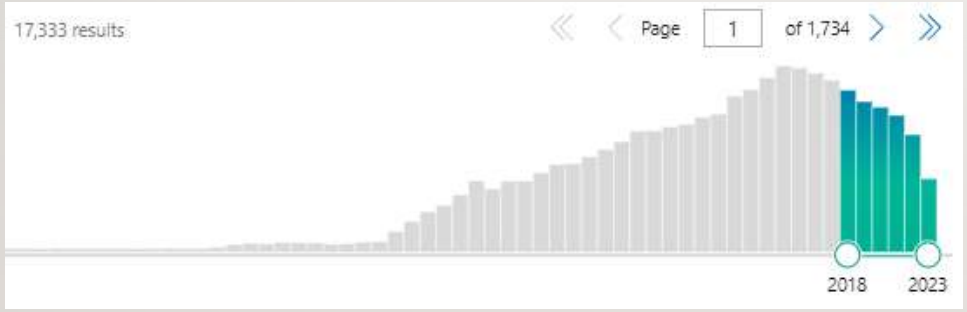
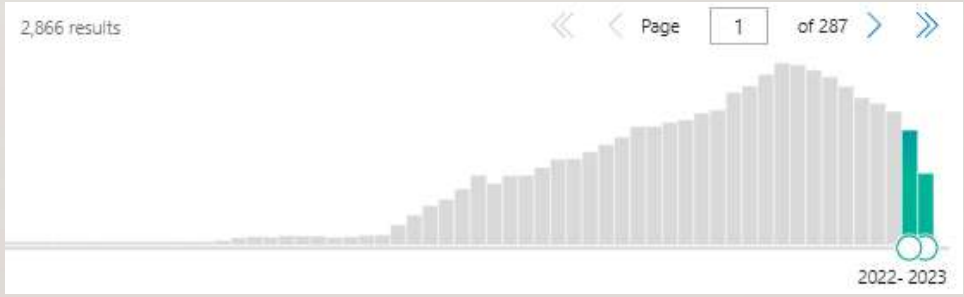
HEPATİT C'DE GÜNCEL YAYINLAR

DR. ÖĞR. ÜYESİ AYŞİN KILINÇ TOKER
ENFEKSİYON HASTALIKLARI VE KLİNİK MİKROBİYOLOJİ
SAĞLIK BİLİMLERİ ÜNİVERSİTESİ
KAYSERİ TIP FAKÜLTESİ

HEPATİT C'DE GÜNCEL YAYINLAR





Clinical Infectious Diseases
SUPPLEMENT ARTICLE

Direct-Acting Antiviral Therapy for Treatment of Acute and Recent Hepatitis C Virus Infection: A Narrative Review

Marianne Martinello,[1,2] Susanna Naggie,[3,4] Juergen Kurt Rockstroh,[5] and Gail V. Matthews[1,6]

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Following the discovery of hepatitis C virus (HCV) in 1989, 3 decades of basic, translational, and clinical research culminated in the development of direct-acting antiviral (DAA) therapy—curative oral treatment for HCV infection. The availability of DAA therapy revolutionized HCV clinical management, including acute (duration of infection <6 mo) and recent (duration of infection <12 mo) infection. Several DAA regimens, including the contemporary pan-genotypic combinations of sofosbuvir-velpatasvir and glecaprevir-pibrentasvir, have been shown to be safe and effective among people with acute and recent HCV infection, highlighting their potential in an HCV controlled human infection model. This article describes the natural history and management of acute and recent HCV infection in the era of DAA therapy and outlines a strategy for use of DAA therapies in the setting of an HCV controlled human infection model.

World Journal of Hepatology

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World J Hepatol 2022 June 27; 14(6): 1053-1073

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ISSN 1948-5182 (online)

REVIEW

Impact of direct-acting antiviral regimens on hepatic and extrahepatic manifestations of hepatitis C virus infection

Iman Ibrahim Salama, Hala M Raslan, Ghada A Abdel-Latif, Somaia I Salama, Samia M Sami, Fatma A Shaaban, Aida M Abdelmohsen, Walaa A Fouad

Journal of Clinical Medicine

MDPI

Article

Pan-Genotypic Direct-Acting Antiviral Agents for Undetermined or Mixed-Genotype Hepatitis C Infection: A Real-World Multi-Center Effectiveness Analysis

Hsu-Heng Yen [1,2,3,4,5], Yang-Yuan Chen [1,6,7], Jun-Hung Lai [8], Hung-Ming Chen [9], Chih-Ta Yao [10], Siou-Ping Huang [1], I-Ling Liu [1], Ya-Huei Zeng [1], Fang-Chi Yang [1], Fu-Yuan Siao [11,12,13,†], Mei-Wen Chen [14,†] and Pei-Yuan Su [1,*,†]

Review Article

Efficacy and Safety of Glecaprevir/Pibrentasvir in Patients with Chronic HCV Infection

Xiaoqing Liu and Peng Hu*

Department of Infectious Diseases, Institute for Viral Hepatitis, The Key Laboratory of Molecular Biology for Infectious Diseases, Chinese Ministry of Education, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

viruses

MDPI

Article

Four Weeks Treatment with Glecaprevir/Pibrentasvir + Ribavirin—A Randomized Controlled Clinical Trial

Lone W. Madsen [1,2,3,*], Peer B. Christensen [1,3], Janne F. Hansen [1], Birgit T. Røge [4], Dorte K. Holm [5], Sandra Dröse [1,3] and Anne Øvrehus [1,3]

[1] Department of Infectious Diseases, Odense University Hospital, 5000 Odense, Denmark; peer.christensen@rsyd.dk (P.B.C.); janne.fuglsang.hansen@rsyd.dk (J.F.H.); sandra.droese@rsyd.dk (S.D.); anne.oevrehus@rsyd.dk (A.Ø.)
[2] OPEN, Odense Patient Data Explorative Network, Odense University Hospital, 5000 Odense, Denmark
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[4] Unit for Infectious Diseases, Department of Medicine, Sygehus Lillebælt, 6000 Kolding, Denmark; birgit.thorup.roege@rsyd.dk
[5] Department of Clinical Immunology, Odense University Hospital, 5000 Odense, Denmark; dorte.holm@rsyd.dk
* Correspondence: lone.wulff.madsen@rsyd.dk; Tel.: +45-65411816

Abstract: Enhancing treatment uptake for hepatitis C to achieve the elimination goals set by the World Health Organization could be achieved by reducing the treatment duration. The aim of this study was to compare the sustained virological response at week 12 (SVR12) after four weeks of glecaprevir/pibrentasvir (GLE/PIB) + ribavirin compared to eight weeks of GLE/PIB and to estimate predictors for SVR12 with four weeks of treatment through a multicenter open label randomized controlled trial. Patients were randomized 2:1 (4 weeks:8 weeks) and stratified by genotype 3 and were treatment naïve of all genotypes and without significant liver fibrosis. A total of 27 patients were analyzed for predictors for SVR12, including 15 from the first pilot phase of the study. In the 'modified intention to treat' group, 100% (7/7) achieved cure after eight weeks and for patients treated for four weeks the SVR12 was 58.3% (7/12). However, patients with a baseline viral load <2 mill IU/mL had 93% SVR12. The study closed prematurely due to the low number of included patients due to the COVID-19 pandemic. Our results suggest that viral load should be taken into account when considering trials of short course treatment.

Keywords: chronic hepatitis C; HCV; DAA; glecaprevir; pibrentasvir; ribavirin; predictors; genotype; viral load

Citation: Madsen, L.W.; Christensen, P.B.; Hansen, J.F.; Røge, B.T.; Holm, D.K.; Dröse, S.; Øvrehus, A. Four Weeks Treatment with Glecaprevir/Pibrentasvir + Ribavirin—A Randomized Controlled Clinical Trial. *Viruses* **2022**, *14*, 614. https://doi.org/10.3390/v14030614

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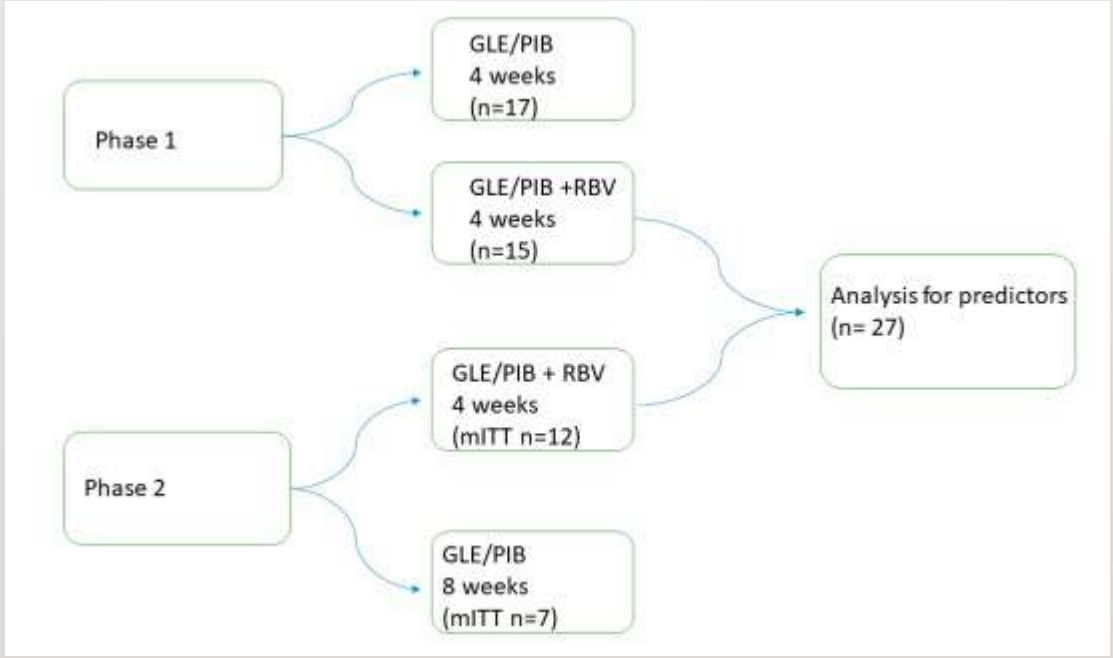
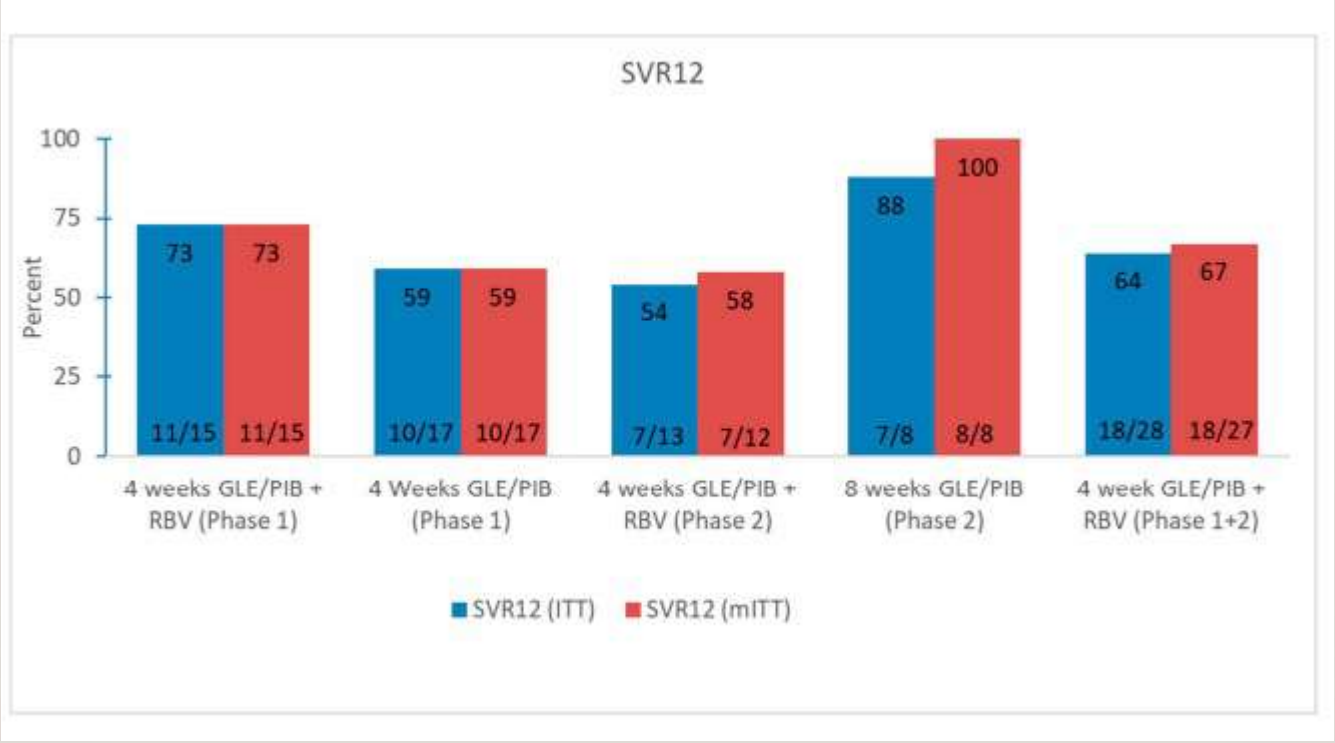

Phase 1
GLE/PIB
4 weeks
(n=17)
GLE/PIB +RBV
4 weeks
(n=15)
Phase 2
GLE/PIB + RBV
4 weeks
(mITT n=12)
GLE/PIB
8 weeks
(mITT n=7)
Analysis for predictors
(n= 27)


SVR12
Percent
100
75
50
25
0
73
73
11/15
11/15
59
59
10/17
10/17
54
58
7/13
7/12
88
100
7/8
8/8
64
67
18/28
18/27
4 weeks GLE/PIB + RBV (Phase 1)
4 Weeks GLE/PIB (Phase 1)
4 weeks GLE/PIB + RBV (Phase 2)
8 weeks GLE/PIB (Phase 2)
4 week GLE/PIB + RBV (Phase 1+2)
SVR12 (ITT)
SVR12 (mITT)


viruses

MDPI

Article

Four Weeks Treatment with Glecaprevir/Pibrentasvir + Ribavirin—A Randomized Controlled Clinical Trial

Lone W. Madsen [1,2,3,*], Fees B. Christensen [1,3], Janne F. Hansen [1], Birgit T. Rege [4], Dorte K. Holm [5], Sandra Dnise [1,3] and Anne Øvrehus [2,3]

- Çalışmanın genel sonuçlarının analizinde, dört hafta boyunca GLE/PIB + ribavirin ile tedavi edilen hastalarda %67'lik bir SVR12 oranı bulunmuş

- Tedavi için en güçlü belirleyiciler başlangıç viral yük ve genotip 3 olarak saptanmış

- Dört haftalık tedavideki düşük genel iyileşme oranına rağmen, başlangıç HCV RNA'sı < 2.000.000 IU/mL olan hastalar arasında %93'lük bir SVR12 gözlenmiş

ANNALS OF MEDICINE
2022, VOL. 54, NO. 1, 108–120
https://doi.org/10.1080/07853890.2021.2012589

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ORIGINAL ARTICLE

Drug-induced liver injury by glecaprevir/pibrentasvir treatment for chronic hepatitis C infection: a systematic review and meta-analysis

Hsuan-Yu Hung[a], Wei-Liang Hung[b], Chia-Lung Shih[c] and Chung-Yu Chen[d,e,f]

[a]Department of Pharmacy, Ditmanson medical foundation Chia-Yi Christian Hospital, Chiayi City, Taiwan; [b]Division of Nephrology, Department of Medicine, Zouying Branch of Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan; [c]Clinical Medicine Research Center, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chia-Yi, Taiwan; [d]Master Program in Clinical Pharmacy, School of Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan; [e]Department of Pharmacy, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; [f]Department of Medical Research, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

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ORIGINAL ARTICLE

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Drug-induced liver injury by glecaprevir/pibrentasvir treatment for chronic hepatitis C infection: a systematic review and meta-analysis

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- FDA tarafından yayınlanan, GLE/PIB ile tedavi edilen orta ila şiddetli karaciğer yetmezliği olan hastalarda karaciğer fonksiyonlarında kötüleşme ve karaciğer yetmezliği riski hakkında bir güvenlik duyurusu mevcut

- DEA'lar genel olarak non-sirotik veya hafif derecede (Child-Pugh A) siroz olan hastalarda güvenli ve etkili olarak kullanılıyor

ANNALS OF MEDICINE
2022, VOL. 54, NO. 1, 108–120
https://doi.org/10.1080/07853890.2021.2012589

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ORIGINAL ARTICLE

OPEN ACCESS Check for updates

Drug-induced liver injury by glecaprevir/pibrentasvir treatment for chronic hepatitis C infection: a systematic review and meta-analysis

Hsuan-Yu Hung[a], Wei-Liang Hung[b], Chia-Lung Shih[c] and Chung-Yu Chen[d,e,f]

[a]Department of Pharmacy, Ditmanson medical foundation Chia-Yi Christian Hospital, Chiayi City, Taiwan; [b]Division of Nephrology, Department of Medicine, Zouying Branch of Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan; [c]Clinical Medicine Research Center, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chia-Yi, Taiwan; [d]Master Program in Clinical Pharmacy, School of Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan; [e]Department of Pharmacy, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; [f]Department of Medical Research, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

- DEA ile HCV enfeksiyonlarında iyileşme oranları daha yüksek olsa da ilaca bağlı karaciğer hasarı (DILI) nadir vakalarda saptanmıştır

- DILI'de en sık görülen laboratuvar anormallikleri total bilirubin, ALT, AST değerlerinde artışıdır, ancak bu anormallikler minimum düzeydedir

- Çoğu vakada, tedavinin kesilmesinden sonra semptomların ve karaciğer fonksiyon değerlerinin düzeldiği gözlemlenmiştir

viruses

Review

Current Hepatitis C Vaccine Candidates Based on the Induction of Neutralizing Antibodies

Elsa Gomez-Escobar †, Philippe Roingeard * and Elodie Beaumont *

Inserm U1259 MAVIVH, Université de Tours and CHRU de Tours, 37000 Tours, France;
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* Correspondence: roingeard@med.univ-tours.fr (P.R.); elodie.beaumont@univ-tours.fr (E.B.)
† Current address: Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM), Montréal, QC H2X 0A9, Canada.

Abstract: The introduction of direct-acting antivirals (DAAs) has revolutionized hepatitis C treatment. Short courses of treatment with these drugs are highly beneficial to patients, eliminating hepatitis C virus (HCV) without adverse effects. However, this outstanding success is tempered by the continuing difficulty of eradicating the virus worldwide. Thus, access to an effective vaccine HCV is strongly needed to reduce the burden of the disease and contribute to the viral hepatitis. The recent failure of a T-cell vaccine based on the use of viral HCV non-structural protein sequences to prevent chronic hepatitis C in that the induction of neutralizing antibodies (NAbs) will be To induce NAbs, vaccines must contain the main target glycoproteins (E1 and E2). In this review, we sum that are targeted by NAbs and how these under development.

npj | vaccines

ARTICLE OPEN

Two-co… displ…

www.nature.com/npjvaccines

…cine consisting of virus-like particles … virus envelope protein 2 oligomers

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…rigo Velázquez-Moctezuma, Andreas Soerensen, Thomas Jørgensen, …Thor Theander, Morten A. Nielsen, Ali Salanti, Jens Bukh and

…that induce broadly neutralizing antibodies (bNAbs) is hindered by …pe glycoprotein vaccine candidates, most notably soluble E2 (sE2). …g self-assembling virus-like particles (cVLPs; component 2). Immunization …es was tested in cultured-virus …Abs (p = …

The challenge of the age of hepatitis C virus elimination: why is HCV vaccination necessary?

Hepatitis C virus is a common cause of chronic liver disease, that may lead to cirrhosis, hepatocellular cancer and liver transplantation. The advent of highly efficacious direct-acting antivirals and their success in the treatment of hepatitis C virus infection, generated soon an optimism. Thus, the World Health Organization has adopted a global strategy of reducing the incidence of new hepatitis B and C virus infection by 90 % by 2030. However, it turned out, that this goal is not achievable by drug treatment alone without a vaccination, because of the high number of infected persons, low rate of screening and poor access to treatment in several countries, and even the cost of the therapy. The paper discusses the virological and imunological feaures of the HCV infection, and the possibility of an effective vaccination against hepatitis C virus. In addition, we overview the types of potential vaccines and the models for the assessment of vaccine efficacy. The controlled human infection model using healthy volunters, became a real possibility, due to the availability of direct-acting antiviral treatment for hepatitis C. On the ground of the newest results of vaccine researches, we are confident to achive the goal of eliminating hepatitis C virus in the near future.

Keywords: hepatitis C virus, direct-acting antivirals (DAA), HCV vaccination, vaccines, controlled human infection model

Pár A. [The challenge of the age of hepatitis C virus elimination: why is HCV vaccination necessary?] Orv Hetil. 2023; 164(9): 322–331.

AASLD

…patitis C virus viral vector vaccine …ils and neutralizing antibodies in mice

…Donnison[1] | Joey McGregor[2,3] | Senthil Chinnakannan[1] | …ire Hutchings[1] | Rob J. Center[2,3] | Pantelis Poumbourios[2,4] | Paul Klenerman[1] | Heidi E. Drummer[2,3,4] | Eleanor Barnes[1,5]

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ARTICLE OPEN

Hepatitis C virus E1 and modified E2 delivered from an mRNA vaccine induces protective immunity

Tapas Patra, Keith Meyer[1], Yuki Haga[1], Erin K. Reagan, Drew Weissman[2] and Ranjit Ray[1,3]

Hepatitis C virus (HCV) is characterized by a high number of chronic cases due to an impairment of protective innate and adaptive immune responses. Here, we examined the contribution of the individual ectodomains of E1, E2, or a modified E2 with reduced CD81 binding and an inserted N-linked glycosylation site in combination as vaccine antigen mRNA-lipid nanoparticles (LNPs). The induction of a protective immune response to surrogate recombinant vaccinia virus (rVV) expressing homologous HCV glycoprotein(s) challenge infection in a BALB/c mouse model was observed. Vaccination with a mRNA-LNP expressing soluble E1 (sE1) significantly reduced rvvHCV titer in the mouse ovary. However, the addition of sE2 mRNA-LNP for immunization impaired the efficacy of the sE1 construct. Further analysis showed that Th1 related cytokine responses to the sE1 mRNA-LNP were significantly altered in the presence of sE2 following co-immunization. Evaluation of immunogenicity revealed that the use of modified $sE2_{\Delta AIDV}$ nucleoside mRNA-LNP vaccine results in an improved cellular immune response, IgG2a isotype switching, enhanced total IgG, and an increase in the neutralizing antibody response against HCV pseudotype virus. HCV cross genotype specific reactivity to peptides representing conserved E2 specific linear epitopes were enhanced in modified E2 vaccinated animal sera. In the absence of a suitable immunocompetent small animal model for HCV infection, protection from surrogate HCV vaccinia challenge infection model was observed in the immunized mice as compared to sE1 alone or an unmodified sE2 mRNA-LNP vaccine. Inclusion of sE1 with modified $sE2_{\Delta AIDV}$ as mRNA-LNP vaccine candidate appeared to be beneficial for protection.

npj Vaccines (2023)8:42; https://doi.org/10.1038/s41541-023-00635-9

PLOS ONE

RESEARCH ARTICLE

Design of a novel multi-epitope vaccine candidate against hepatitis C virus using structural and nonstructural proteins: An immunoinformatics approach

Esmaeil Behmard[1], Hussein T. Abdulabbas[2], Saade Abdalkareem Jasim[3], Sohrab Najafipour[4], Abdolmajid Ghasemian[5]*, Akbar Farjadian[6], Ebrahim Barzegari[6], Amin Kouhpayeh[7]*, Parvin Abdolmaleki[8]*

Abstract

Hepatitis C virus (HCV) infects the liver and causes chronic infection. Several mutations in the viral genome have been associated with drug resistance development. Currently, there is no approved vaccine against the HCV. The employment of computational biology is the primary and crucial step for vaccine design or antiviral therapy which can substantially reduce the duration and cost of studies. Therefore, in this study, we designed a multi-epitope vaccine using various immunoinformatics tools to elicit the efficient human immune responses against the HCV. Initially, various potential (antigenic, immunogenic, non-toxic and non-allergenic) epitope segments were extracted from viral structural and non-structural protein sequences using multiple screening methods. The selected epitopes were linked to each other properly. Then, toll-like receptors (TLRs) 3 and 4 agonists (50S ribosomal protein L7/L12 and human β-defensin 2, respectively) were added to the N-terminus of the final vaccine sequences to increase its immunogenicity. The 3D structure of the vaccine was modeled. Molecular dynamics simulations studies verified the high stability of final two vaccines and in complex with TLR3 and TLR4. These constructs were also antigenic, non-allergenic, nontoxic and immunogenic. Although the designed vaccine traits were promising as a potential candidate against the HCV infection, experimental studies and clinical trials are required to verify the protective traits and safety of the designed vaccine.

- İnsan çalışmalarında şu ana kadar yalnızca iki aşı adayı ilerleme kaydedebildi

Clinical Trial > Vaccine. 2010 Aug 31;28(38):6367-73. doi: 10.1016/j.vaccine.2010.06.084. Epub 2010 Jul 7.

Safety and immunogenicity of HCV E1E2 vaccine adjuvanted with MF59 administered to healthy adults

Sharon E Frey [1], Michael Houghton, Stephen Coates, Sergio Abrignani, David Chien, Domenico Rosa, Piero Pileri, Ranjit Ray, Adrian M Di Bisceglie, Paola Rinella, Heather Hill, Mark C Wolff, Viola Schultze, Jang H Han, Bruce Scharschmidt, Robert B Belshe

Affiliations + expand

PMID: 20619382 PMCID: PMC2923449 DOI: 10.1016/j.vaccine.2010.06.084

Free PMC article

Abstract

Background: Hepatitis C virus (HCV) causes chronic liver disease that often leads to cirrhosis and hepatocellular carcinoma. In animal studies, chimpanzees were protected against chronic infection following experimental challenge with either homologous or heterologous HCV genotype 1a strains which predominate in the USA and Canada. We describe the first in humans clinical trial of this prophylactic HCV vaccine.

Methods: HCV E1E2 adjuvanted with MF59C.1 (an oil-in-water emulsion) was given at 3 different dosages on day 0 and weeks 4, 24 and 48 in a phase 1, placebo-controlled, dose escalation trial to healthy HCV-negative adults.

Results: There was no significant difference in the proportion of subjects reporting adverse events across the groups. Following vaccination subjects developed antibodies detectable by ELISA, CD81 neutralization and VSV/HCV pseudotype neutralization. There were no significant differences between vaccine groups in the number of responders and geometric mean titers for each of the three assays. All subjects developed lymphocyte proliferation responses to E1E2 and an inverse response to increasing amounts of antigen was noted.

Conclusions: The vaccine was safe and generally well-tolerated at each of the 3 dosage levels and induced antibody and lymphoproliferative responses. A larger study to further evaluate safety and immunogenicity is warranted.

Clinical Trial > N Engl J Med. 2021 Feb 11;384(6):541-549. doi: 10.1056/NEJMoa2023345.

Randomized Trial of a Vaccine Regimen to Prevent Chronic HCV Infection

Kimberly Page [1], Michael T Melia [1], Rebecca T Veenhuis [1], Matthew Winter [1], Kimberly E Rousseau [1], Guido Massaccesi [1], William O Osburn [1], Michael Forman [1], Elaine Thomas [1], Karla Thornton [1], Katherine Wagner [1], Ventzislav Vassilev [1], Lan Lin [1], Paula J Lum [1], Linda C Giudice [1], Ellen Stein [1], Alice Asher [1], Soju Chang [1], Richard Gorman [1], Marc G Ghany [1], T Jake Liang [1], Michael R Wierzbicki [1], Elisa Scarselli [1], Alfredo Nicosia [1], Antonella Folgori [1], Stefania Capone [1], Andrea L Cox [1]

Affiliations + expand

PMID: 33567193 PMCID: PMC8367093 DOI: 10.1056/NEJMoa2023345

Free PMC article

Abstract

Background: A safe and effective vaccine to prevent chronic hepatitis C virus (HCV) infection is a critical component of efforts to eliminate the disease.

Methods: In this phase 1-2 randomized, double-blind, placebo-controlled trial, we evaluated a recombinant chimpanzee adenovirus 3 vector priming vaccination followed by a recombinant modified vaccinia Ankara boost; both vaccines encode HCV nonstructural proteins. Adults who were considered to be at risk for HCV infection on the basis of a history of recent injection drug use were randomly assigned (in a 1:1 ratio) to receive vaccine or placebo on days 0 and 56. Vaccine-related serious adverse events, severe local or systemic adverse events, and laboratory adverse events were the primary safety end points. The primary efficacy end point was chronic HCV infection, defined as persistent viremia for 6 months.

Results: A total of 548 participants underwent randomization, with 274 assigned to each group. There was no significant difference in the incidence of chronic HCV infection between the groups. In the per-protocol population, chronic HCV infection developed in 14 participants in each group (hazard ratio [vaccine vs. placebo], 1.53; 95% confidence interval [CI], 0.66 to 3.55; vaccine efficacy, -53%; 95% CI, -255 to 34). In the modified intention-to-treat population, chronic HCV infection developed in 19 participants in the vaccine group and 17 in placebo group (hazard ratio, 1.66; 95% CI, 0.79 to 3.50; vaccine efficacy, -66%; 95% CI, -250 to 21). The geometric mean peak HCV RNA level after infection differed between the vaccine group and the placebo group (152.51×10^2 IU per milliliter and 1804.93×10^3 IU per milliliter, respectively). T-cell responses to HCV were detected in 78% of the participants in the vaccine group. The percentages of participants with serious adverse events were similar in the two groups.

Conclusions: In this trial, the HCV vaccine regimen did not cause serious adverse events, produced HCV-specific T-cell responses, and lowered the peak HCV RNA level, but it did not prevent chronic HCV infection. (Funded by the National Institute of Allergy and Infectious Diseases; ClinicalTrials.gov number, NCT01436357.).

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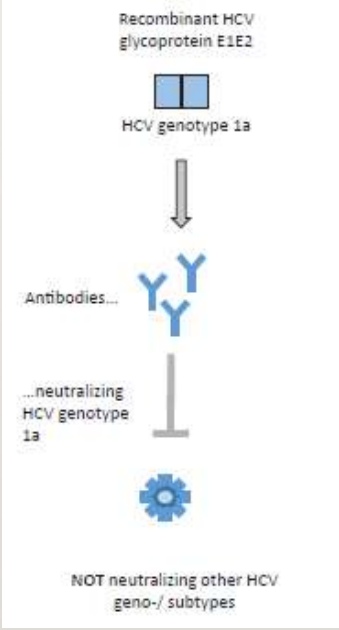

- Faz 1 güvenlik ve immünojenite çalışmasında aşı iyi tolere edilmiş
- Antikor ve lenfoproliferatif yanıtları indüklediği görülmüş
- Ancak çoğu gönüllüde nötralizasyon sağlayacak antikorlar üretemediği için verimlilik çalışması yapılmamış

Clinical Trial > N Engl J Med. 2021 Feb 11;384(6):541-549. doi: 10.1056/NEJMoa2023345.

Randomized Trial of a Vaccine Regimen to Prevent Chronic HCV Infection

Kimberly Page [1], Michael T Melia [1], Rebecca T Veenhuis [1], Matthew Winter [1], Kimberly E Rousseau [1], Guido Massaccesi [1], William O Osburn [1], Michael Forman [1], Elaine Thomas [1], Karla Thornton [1], Katherine Wagner [1], Ventzislav Vassilev [1], Lan Lin [1], Paula J Lum [1], Linda C Giudice [1], Ellen Stein [1], Alice Asher [1], Soju Chang [1], Richard Gorman [1], Marc G Ghany [1], T Jake Liang [1], Michael R Wierzbicki [1], Elisa Scarselli [1], Alfredo Nicosia [1], Antonella Folgori [1], Stefania Capone [1], Andrea L Cox [1]

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Free PMC article

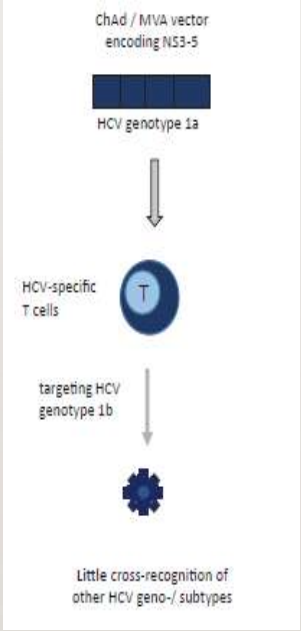
Abstract

Background: A safe and effective vaccine to prevent chronic hepatitis C virus (HCV) infection is a critical component of efforts to eliminate the disease.

Methods: In this phase 1-2 randomized, double-blind, placebo-controlled trial, we evaluated a recombinant chimpanzee adenovirus 3 vector priming vaccination followed by a recombinant modified vaccinia Ankara boost; both vaccines encode HCV nonstructural proteins. Adults who were considered to be at risk for HCV infection on the basis of a history of recent injection drug use were randomly assigned (in a 1:1 ratio) to receive vaccine or placebo on days 0 and 56. Vaccine-related serious adverse events, severe local or systemic adverse events, and laboratory adverse events were the primary safety end points. The primary efficacy end point was chronic HCV infection, defined as persistent viremia for 6 months.

Results: A total of 548 participants underwent randomization, with 274 assigned to each group. There was no significant difference in the incidence of chronic HCV infection between the groups. In the per-protocol population, chronic HCV infection developed in 14 participants in each group (hazard ratio [vaccine vs. placebo], 1.53; 95% confidence interval [CI], 0.66 to 3.55; vaccine efficacy, -53%; 95% CI, -255 to 34). In the modified intention-to-treat population, chronic HCV infection developed in 19 participants in the vaccine group and 17 in placebo group (hazard ratio, 1.66; 95% CI, 0.79 to 3.50; vaccine efficacy, -66%; 95% CI, -250 to 21). The geometric mean peak HCV RNA level after infection differed between the vaccine group and the placebo group (152.51×10^3 IU per milliliter and 1804.93×10^3 IU per milliliter, respectively). T-cell responses to HCV were detected in 78% of the participants in the vaccine group. The percentages of participants with serious adverse events were similar in the two groups.

Conclusions: In this trial, the HCV vaccine regimen did not cause serious adverse events, produced HCV-specific T-cell responses, and lowered the peak HCV RNA level, but it did not prevent chronic HCV infection. (Funded by the National Institute of Allergy and Infectious Diseases; ClinicalTrials.gov number, NCT01436357.).



- Her ikisi de HCV genotip 1b'nin yapısal olmayan proteinlerini kodlayan, primer olarak bir şempanze adenovirüs vektörü (ChAd3) ve boost olarak MVA vektöründen oluşur

- Faz 2'de HCV'ye özgü güçlü ve çok işlevli CD4+ ve CD8+ T hücre yanıtlarını uyarmasına rağmen, kronik HCV enfeksiyonunu önlemede başarısız olmuş

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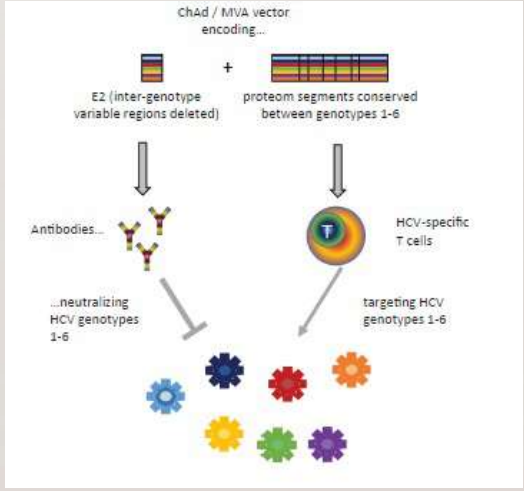
ORIGINAL ARTICLE

A pan-genotype hepatitis C virus viral vector vaccine generates T cells and neutralizing antibodies in mice

Timothy Donnison[1] | Joey McGregor[2,3] | Senthil Chinnakannan[1] | Claire Hutchings[1] | Rob J. Center[2,3] | Pantelis Poumbourios[2,4] | Paul Klenerman[1] | Heidi E. Drummer[2,3,4] | Eleanor Barnes[1,5]

- HCV'ye karşı başarılı bir profilaktik aşıya giden yolda ilk önemli adım olarak tanımlanmış
- Farelerde yapılan çalışmada güçlü nötralizan antikorların yanı sıra CD4+ ve CD8+ T hücre tepkisini belirgin şekilde indüklemiş



viruses

MDPI

Review

Hepatitis C Elimination: Opportunities and Challenges in 2023

Gadeer Taha [1], Levy Ezra [2] and Naim Abu-Freha [3,4,*]

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Abstract: Hepatitis C Virus (HCV) infection is a leading etiology of liver cirrhosis and its associated complications, namely, decompensated cirrhosis. As such, hepatitis C potentially necessitates liver transplantation and may result in death. Recently, HCV treatment has evolved. Current HCV treatment is effective in curing HCV; some of the agents are pan-genotypic. Numerous countries have adopted an initiative to eliminate HCV. Achieving elimination poses many challenges; it requires improved availability and accessibility of pan-genotypic therapy. Barriers exist at the level of the collective healthcare system and at the level of the individual healthcare providers and patients. Therefore, organized national and local efforts are needed. Surmounting these barriers calls for interventions concerning screening, linkage to care, and treatment delivery. Pertinent barriers include inadequate availability of screening, ill-equipped laboratory testing before treatment, and insufficient access to treatment. Interventions should seek to decentralize laboratory testing and treatment provision, increase funding for resources and personnel, and spread awareness. Special consideration should be allocated to at-risk populations, such as intravenous drug users, refugees, and prisoners. Computerized medical filing and telemedicine have the potential to refine HCV management by enhancing detection, availability, accessibility, and cost-effectiveness.

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Editorials

Challenges for hepatitis C in Mexico: a public health perspective towards 2030

JGIM

REVIEWS

Integrating Management of Hepatitis C Infection into Primary Care: the Key to Hepatitis C Elimination Efforts

Allison E. Wang, MD[1], Eric Hsieh, MD, FACP[1], Barbara J. Turner, MD, MSED, MA, MACP[1], and Norah Terrault, MD, MPH[1,2]

[1]Department of Internal Medicine, University of Southern California, Los Angeles, CA, USA; [2]Division of Gastrointestinal and Liver Diseases, Department of Medicine, University of Southern California, Los Angeles, CA, USA.

Morbidity and Mortality Weekly Report

Hepatitis C Virus Clearance Cascade — United States, 2013–2022

Carolyn Wester, MD[1]; Ademola Osinubi, MS[1]; Harvey W. Kaufman, MD[2]; Hasan Symum, PhD[3]; William A. Meyer III, PhD[2]; Xiaohua Huang, MS[2]; William W. Thompson, PhD[1]

DÜNYA SAĞLIK ÖRGÜTÜ (WHO) HCV GİRİŞİMİ

- DSÖ, yeni hepatit enfeksiyonlarını azaltmak, test ve tedaviye erişimi artırmak, sürveyans ve izlemeyi iyileştirmek için hedefler belirlemektedir
- Hedef, 2030 yılına kadar kronik HCV insidansında %90 azalma ve HCV mortalitesinde %65 azalmadır
- Birçok ülke bu hedefi benimseyerek HCV eliminasyon programlarını oluşturmuştur

viruses

MDPI

Review

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- Eliminasyonun sağlanması birçok zorluğu beraberinde getirir;
  - Pan-genotipik tedavinin daha iyi kullanılabilirliği ve erişilebilirliği
  - Kolektif sağlık sistemi ve hastalar düzeyinde organize ulusal ve yerel çalışmalar
  - Taramaların yeterli olması, tedavi öncesi laboratuvar testlerinin erişilebilir olması
  - Kaynak ve personel finansmanının artırılması ve farkındalığın yaygınlaşması
  - Damar içi uyuşturucu kullanıcıları, mülteciler ve mahkumlar gibi risk altındaki gruplara önem verilmesi

Narrative Review | Published: 28 April 2022

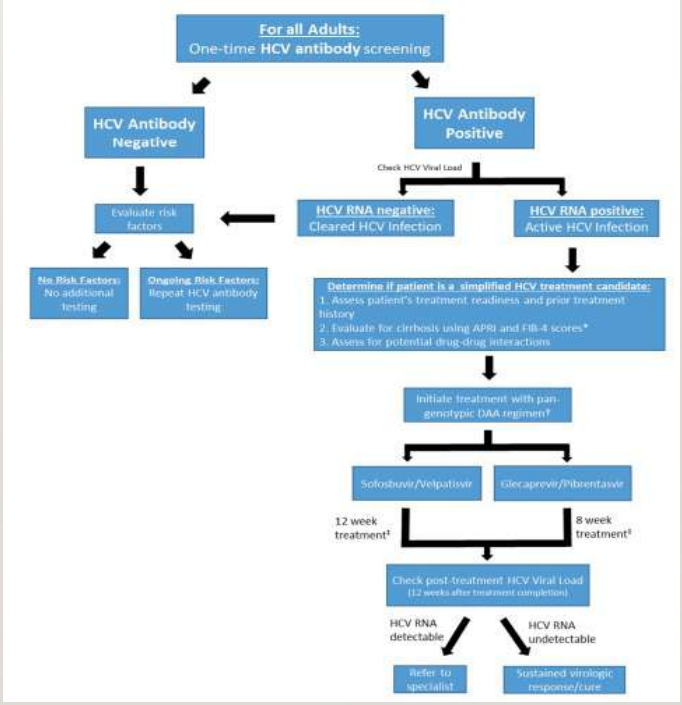
Integrating Management of Hepatitis C Infection into Primary Care: the Key to Hepatitis C Elimination Efforts

Allison E. Wang MD, Eric Hsieh MD, FACP, Barbara J. Turner MD, MSED, MA, MACP & Norah Terrault MD, MPH

Journal of General Internal Medicine **37**, 3435–3443 (2022) | Cite this article

HEPATİT C ENFEKSİYONU YÖNETİMİNİN BİRİNCİ BASAMAK HİZMETLERİNE ENTEGRE EDİLMESİ: HEPATİT C'Yİ ORTADAN KALDIRMA ÇABALARININ ANAHTARI

- Birinci basamak sağlık hizmeti sağlayıcılarının katılımı, kronik HCV'yi teşhis etme ve tedavi etme kapasitesini büyük ölçüde artırır



Carson JM et al. *Journal of the International AIDS Society* 2023, **26**:e26168
http://onlinelibrary.wiley.com/doi/10.1002/jia2.26168/full | https://doi.org/10.1002/jia2.26168

JIAS
JOURNAL OF THE INTERNATIONAL AIDS SOCIETY

RESEARCH ARTICLE

Sexual and drug use risk behaviour trajectories among people treated for recent HCV infection: the REACT study

Joanne M. Carson[1,§], Sebastiano Barbieri[2], Evan Cunningham[1], Eric Mao[1], Marc van der Valk[3,4], Jürgen K. Rockstroh[5], Margaret Hellard[6,7], Arthur Kim[8], Sanjay Bhagani[9], Jordan J. Feld[10], Ed Gane[11], Maria C. Thurnheer[12], Julie Bruneau[13], Elise Tu[1], Gregory J. Dore[1], Gail V. Matthews[1], Marianne Martinello[1] and the REACT study group[1]

[§]**Corresponding author**: Joanne M. Carson, The Kirby Institute, UNSW Sydney, Wallace Wurth Building, Sydney, NSW 2052, Australia. Tel: +61 2 9385 8370. (jcarson@kirby.unsw.edu.au)

Clinical trial registration: clinicaltrials.gov Identifier NCT02625909

YAKIN ZAMANDA HCV ENFEKSİYONU NEDENİYLE TEDAVİ GÖRMÜŞ KİŞİLER ARASINDA RİSKLİ CİNSEL DAVRANIŞ VE UYUŞTURUCU KULLANIM TUTUMLARI: REACT ÇALIŞMASI

- Yakın zamanda HCV tedavisi gören katılımcılar, davranışlarını değerlendirmek amacıyla 2 yıl boyunca 3 aylık aralıklarla takip edilmiş
- 212 katılımcı, 1252 gözlem
  - %84 MSM
  - %69 HIV
  - %26 IV uyuşturucu kullanımı

Australia
Canada
Germany
Netherlands
New Zealand
Switzerland
United Kingdom
United States

- IV ilaç ve uyarıcı kullanımına yönelik davranışsal gidişat değişmemiş
- Tedavi sonrasında hastaların bir kısmında; Kondomsuz homoseksüel ve heteroseksüel ilişki azalırken, önemli bir kısmında (%61) bu davranışların yükseldiği bulunmuş
- IV ilaç kullanıcılarında yüksek HCV yeniden enfeksiyon insidansı gözlenmiş

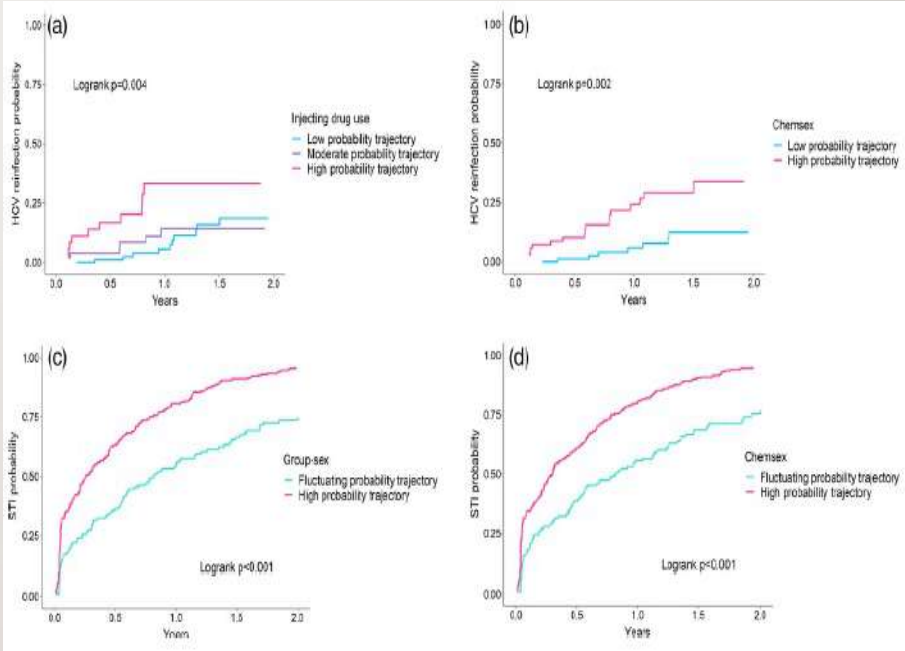


Figure 3. Cumulative hazards curves for behavioural trajectories. Cumulative hazard of HCV reinfection for (A) injecting drug use and (B) chemsex behavioural trajectories, and, of sexually transmitted infections for (C) group-sex and (D) chemsex behavioural trajectories.

- HCV tanısı konulduğunda kısa sürede kişileri tedaviye almak, bulaşmayı azaltmak ve eliminasyonu sağlamak için kritik öneme sahip olacaktır

- Tedaviyi takiben sınırlı riskli davranış değişikliği nedeniyle, düzenli yeniden enfeksiyon gözetimi ve yeniden tedaviye hızlı erişim, damar içi madde kullanan kişiler arasında HCV vakalarında kalıcı düşüşler sağlamak için kritik öneme sahip olacaktır

Clinical Infectious Diseases

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Hepatitis C Guidance 2023 Update: American Association for the Study of Liver Diseases– Infectious Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection

Debika Bhattacharya,[1,©] Andrew Aronsohn,[2] Jennifer Price,[3] and Vincent Lo Re III[4]; the American Association for the Study of Liver Diseases–Infectious Diseases Society of America HCV Guidance Panel[a]

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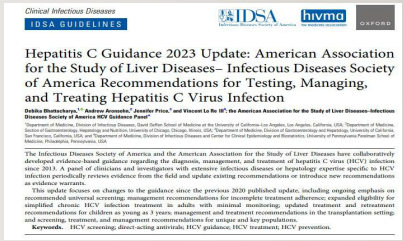
This update focuses on changes to the guidance since the previous 2020 published update, including ongoing emphasis on recommended universal screening; management recommendations for incomplete treatment adherence; expanded eligibility for simplified chronic HCV infection treatment in adults with minimal monitoring; updated treatment and retreatment recommendations for children as young as 3 years; management and treatment recommendations in the transplantation setting; and screening, treatment, and management recommendations for unique and key populations.

Keywords. HCV screening; direct-acting antivirals; HCV guidance; HCV treatment; HCV prevention.

KILAVUZDAKİ ÖNEMLİ NOKTALAR



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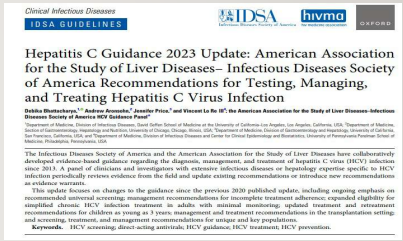
- ≥18 yaş tüm yetişkinlere en az bir kez HCV taraması yapılması önerilir
- Tüm hamileler için her hamilelik sırasında HCV taraması yapılması önerilir
- HIV ile enfekte kişilere de HCV tedavisi önerilmekte
- Solid organ alıcılarında DEA tedavisinin güvenliği ve etkinliği vurgulanmakta

BAŞLANGIÇ TEDAVİ REJİMİ



- 8 haftalık glecaprevir (300 mg)/pibrentasvir (120 mg) veya 12 haftalık sofosbuvir (400 mg)/velpatasvir (100 mg)

- Burada önemli bir değişiklik sofosbuvir/velpatasvir/voxilaprevir'in genotip 3 ve/veya kompanse sirozlu kişilerde alternatif rejim olarak kullanılabileceği önerisidir

Table 1. Recommendations for Initial Treatment of Hepatitis C Virus–Infected Adults

Regimen	Genotype	Classification	Duration	Rating	Caveats and Other Considerations
Treatment-naive without cirrhosis or with compensated cirrhosis Glecaprevir/pibrentasvir	1–6	Recommended	8 wk	I, A[a]	
Sofosbuvir/velpatasvir	1–6	Recommended	12 wk	I, A[b]	For genotype 3 infection with compensated cirrhosis, NS5A RAS testing is recommended. If baseline NS5A RAS Y93H is present, add weight-based ribavirin or choose another recommended regimen.
Ledipasvir/sofosbuvir	1, 4, 5, 6	Recommended	12 wk	I, A[c]	Not recommended for genotype 6e infection if subtype is known.
	1 without cirrhosis	Recommended	8 wk	I, B	Applicable to patients without cirrhosis who are not living with human immunodeficiency virus and whose HCV RNA is <6 million IU/mL.
Elbasvir/grazoprevir	1b, 4	Recommended	12 wk	I, A[d]	
	1a	Alternative	12 wk	I, A	For genotype 1a infection, NS5A RAS testing is recommended. If baseline RASs are present (ie, substitutions at amino acid positions 28, 30, 31, or 93), another recommended regimen should be used.
Sofosbuvir/velpatasvir + weight-based ribavirin	3	Alternative	12 wk	IIa, A	Applicable to genotype 3 infection with compensated cirrhosis and baseline NS5a Y93 RAS.
Sofosbuvir/velpatasvir/ voxilaprevir		Alternative	12 wk	IIa, B	Applicable to genotype 3 infection with compensated cirrhosis and baseline NS5a Y93 RAS.
Treatment-naive with decompensated cirrhosis					
Sofosbuvir/velpatasvir + weight-based ribavirin	1–6	Recommended	12 wk	I, A[a]	Low initial dose of ribavirin (600 mg) is recommended for patients with CTP class C cirrhosis; increase as tolerated.
Sofosbuvir/velpatasvir	1–6	Recommended	24 wk	I, A[e]	Applicable to patients who are ribavirin ineligible.
Ledipasvir/sofosbuvir + weight-based ribavirin	1, 4, 5, 6	Recommended	12 wk	I, A[f]	Low initial dose of ribavirin (600 mg) is recommended for patients with CTP class C cirrhosis; increase as tolerated.
Ledipasvir/sofosbuvir	1, 4, 5, 6	Recommended	24 wk	I, A[f]	Applicable to patients who are ribavirin ineligible.

Recommendations are listed by recommended vs alternative and by genotypic activity, evidence level, and alphabetically.

Abbreviations: CTP, Child–Turcotte–Pugh score; HCV, hepatitis C virus; NS5A, hepatitis C virus nonstructural protein 5A; RAS, resistance-associated substitution.

[a]The level of evidence rating is I, B for persons with compensated cirrhosis.

[b]The level of evidence rating is I, B for persons with genotype 5 or 6 infection.

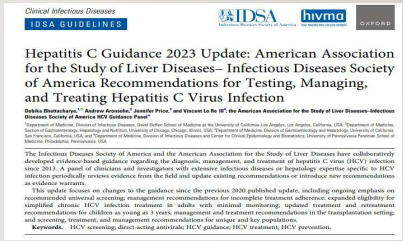
[c]The level of evidence rating is IIa, B for persons with genotype 5 or 6 infection and those with genotype 4 infection and compensated cirrhosis.

[d]The level of evidence rating is IIa, B for persons with genotype 4 infection and compensated cirrhosis.

[e]Only available data for genotype 6 infection are in persons with compensated cirrhosis.

[f]Only available data for genotypes 5 or 6 infection are in a small number of persons with compensated cirrhosis.

DOZ ATLAMA ÖNERİLERİ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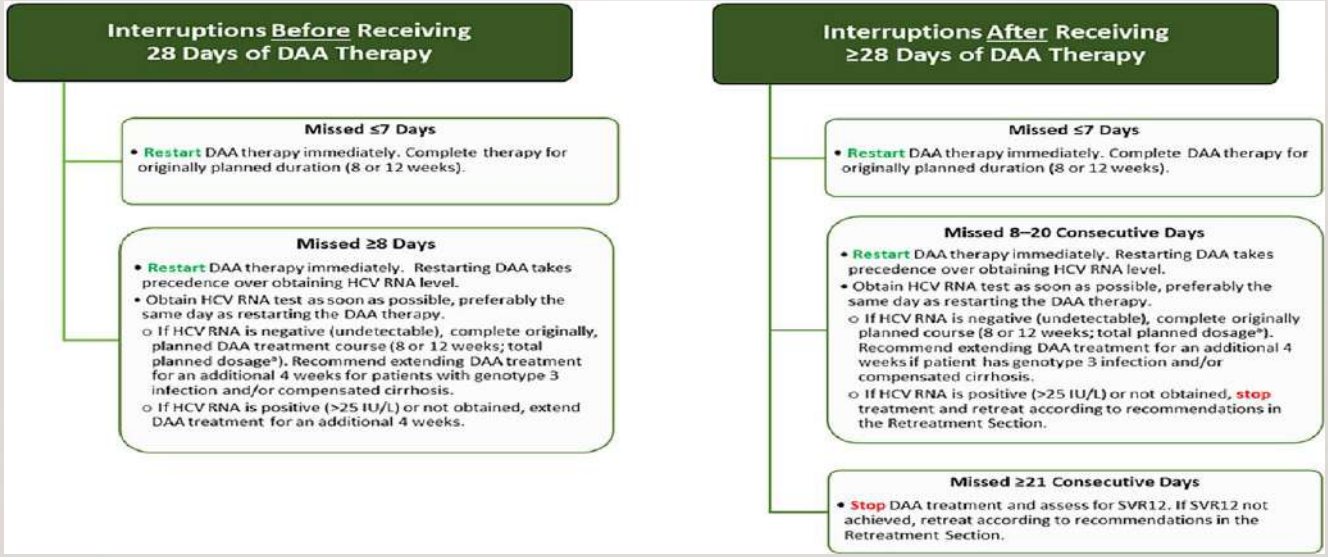

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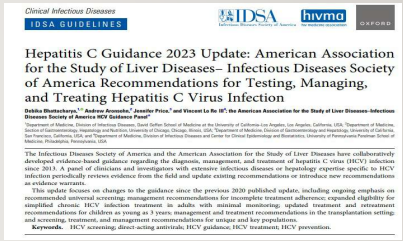
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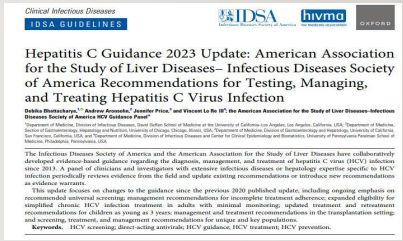
TEDAVİNİN İLK 28 GÜNÜNDE

- ≤7 gün ise aynen devam edilir
- ≥7 gün ise HCV RNA bakılır
  - Negatif ise planlanan tedavi süresi uygulanır (Genotip 3 ve/veya kompanze sirozda 4 hafta uzatılır)
  - Pozitif ise tedavi süresi 4 hafta uzatılır

TEDAVİNİN 28. GÜNÜNDEN SONRA

- ≤7 gün ise aynen devam edilir
- Ard arda 8-20 gün ise HCV RNA bakılır
  - Negatif ise planlanan tedavi süresi uygulanır (Genotip 3 ve/veya kompanze sirozda 4 hafta uzatılır)
  - Pozitif ise tedaviyi stoplanır, yeniden tedavi başlama kriterleri değerlendirilir

ÇOCUKLARDA TEDAVİ



Clinical Infectious Diseases

IDSA GUIDELINES

Hepatitis C Guidance 2023 Update: American Association for the Study of Liver Diseases– Infectious Diseases Society of America Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection

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The Infectious Diseases Society of America and the American Association for the Study of Liver Diseases have collaboratively developed evidence-based guidance regarding the diagnosis, management, and treatment of hepatitis C virus (HCV) infection since 2013. A panel of clinicians and investigators with extensive infectious diseases or hepatology expertise specific to HCV infection periodically reviews evidence from the field and update existing recommendations or introduce new recommendations as evidence warrants.

This update focuses on changes to the guidance since the previous 2020 published update, including ongoing emphasis on recommended universal screening; management recommendations for incomplete treatment adherence; expanded eligibility for simplified chronic HCV infection treatment in adults with minimal monitoring; updated treatment and retreatment recommendations for children as young as 3 years; management and treatment recommendations in the transplantation setting; and screening, treatment, and management recommendations for unique and key populations.

Keywords. HCV screening; direct-acting antivirals; HCV guidance; HCV treatment; HCV prevention.

- ≥3 yaş olan tüm HCV ile enfekte çocukların ve ergenlerin onaylanmış bir DEA rejim ile tedavi edilmesi önerilmektedir

Table 3. Recommendations for Initial Treatment of Hepatitis C Virus–Infected Pediatric Patients Without Cirrhosis or With Compensated Cirrhosis

Regimen	Genotype	Classification	Duration	Rating
Glecaprevir/pibrentasvir	1–6	Recommended	8 wk	I, B
Sofosbuvir/velpatasvir	1–6	Recommended	12 wk	I, B
Ledipasvir/sofosbuvir	1, 4, 5, 6	Recommended	12 wk	I, B

Recommendations are listed by genotypic activity, evidence level, and alphabetically.

SOLİD ORGAN NAKLİ SONRASI HCV YÖNETİMİ

- Klinik çalışmalar ve gerçek yaşam verileri solid organ nakli alıcılarında HCV DEA tedavisinin güvenliğini ve etkinliğini desteklemekte
- Mevcut veriler ile birçok transplantasyon merkezi HCV pozitif donörlerden alınan solid organları kullanmaya başladı
- Nonviremik kişiye HCV-viremik donörden solid organ nakli yapıldığı takdirde HCV tedavisinin mümkün olduğu kadar erken dönemde başlanması önerilmekte

Table 5. Recommendations for Hepatitis C Virus Treatment Posttransplantation

Regimen	Genotypes	Classification	Duration	Rating	Caveats and Other Considerations
Recurrent HCV post liver transplant without cirrhosis					
Glecaprevir/ pibrentasvir	1–6	Recommended	12 wk	I, B	
Sofosbuvir/ velpatasvir	1–6	Recommended	12 wk	I, B	
Ledipasvir/ sofosbuvir	1, 4, 5, 6	Recommended	12 wk	I, B	
Recurrent HCV post liver transplant with compensated cirrhosis					
Sofosbuvir/ velpatasvir	1–6	Recommended	12 wk	I, B	
Glecaprevir/ pibrentasvir	1–6	Recommended	12 wk	I, C	
Ledipasvir/ sofosbuvir	1, 4, 5, 6	Recommended	12 wk	I, A	
Recurrent HCV post kidney transplant without cirrhosis or with compensated cirrhosis					
Glecaprevir/ pibrentasvir	1–6	Recommended	12 wk	I, A[a] IIa, C[b]	
Sofosbuvir/ velpatasvir	1–6	Recommended	12 wk	IIa, C	
Ledipasvir/ sofosbuvir	1, 4, 5, 6	Recommended	12 wk	I, A	
Elbasvir/ grazoprevir	1, 4	Alternative	12 wk	I, B	Limited to patients without baseline NS5A RASs for elbasvir.
HCV-uninfected recipients of liver grafts from HCV-viremic donors					
Glecaprevir/ pibrentasvir	1–6	Recommended	12 wk	I, C	Timing: initiate treatment within the first 2 wk posttransplant, preferably within the first week.
Sofosbuvir/ velpatasvir	1–6	Recommended	12 wk	I, C	Timing: initiate treatment within the first 2 wk posttransplant, preferably within the first week.
HCV-uninfected recipients of non-liver solid organs from HCV-viremic donors					
Glecaprevir/ pibrentasvir	1–6	Recommended	8 wk[c]	I, C	Timing: initiate treatment prior to HCV RNA results, immediately pretransplant or day 0 posttransplant, if possible. Otherwise, begin on day 0 to within the first week posttransplant when clinically stable.
Sofosbuvir/ velpatasvir	1–6	Recommended	12 wk	I, C	Timing: initiate treatment prior to HCV RNA results, immediately pretransplant or day 0 posttransplant, if possible. Otherwise, begin on day 0 to within the first week posttransplant when clinically stable.

Recommendations are listed by genotypic activity, evidence level, and alphabetically.
Abbreviations: HCV, hepatitis C virus; NS5A, hepatitis C virus nonstructural protein 5A; RAS, resistance associated substitution.
[a]Rating is based on evidence for persons without cirrhosis.
[b]Rating is based on evidence for persons with compensated cirrhosis.
[c]If treatment initiation is delayed beyond the first week after transplant, treatment should be extended to 12 weeks.

- TEŞEKKÜRLER…….