

抗丙肝病毒药物靶标计量分析及趋势研究

[立刻下载](#)**Quantitative analysis and developing trend research on anti- HCV drug targets**

田军;郝博济;

摘要:

本文借助Thomson Reuters Pharma信息平台,以不同靶标药物在各研发阶段的数量分布为主要参考指标,辅以相关文献和典型药物资料,对抗丙肝病毒药物的研发现状进行了统计、分析和研究,并对其可能的发展趋势和方向做出了预测和判断。得出以下主要结论:(1)干扰素 α 是目前治疗丙型肝炎病毒(HCV)感染的主要药物,但在新药研发中的地位有所下降;(2)NS3蛋白酶和NS5B聚合酶是目前抗HCV新药开发研究最热的靶标,已上市的两种NS3蛋白酶抑制剂均取得了巨大成功,但数据也反映出这两类药物相对较高的研发难度;(3)NS5A蛋白靶标是抗HCV新药开发的新兴方向,未有药物上市,但临床研究取得了良好的预期效果,并得到专业分析机构的青睐。

关键词: 肝炎病毒;;干扰素类;;抗病毒药;;NS3蛋白酶;;NS5B聚合酶

基金项目: 天津市科技支撑计划重大项目(11ZXPTJH00200)和(11SYSYJH00100)

通讯作者: 田军;

Email:

参考文献:

- [1]MCGIVERN DR,LEMON SM.Virus-specific mechanisms of carcinogenesis in hepatitis C virus associated liver cancer[J].Oncogene,2011,30(17):1969-1983.
- [2]ALY HUSSEIN H,SHIMOTOHNO K,HIJKATA M,et al.Invitro models for analysis of the hepatitis C virus life cycle[J].Microbiol Immunol,2012,56(1):1-9.
- [3]HELBIG KJ,BEARD MR.The interferon signaling pathway genes as biomarkers of hepatitis C virus disease progression and response to treatment[J].Biomark Med,2012,6(2):141-150.
- [4]BOLEWSKA B,CZAJKA A,MOCZKO J,et al.Interferon alpha,gamma,omega before and during treatment of chronic hepatitis C with pegylated interferon alpha and ribavirin [J].Przegl Epidemiol,2007,61(4):755-763.
- [5]KAPPOS L,HARTUNG HP.10 years of interferon beta-1b(Beta feron)therapy[J].J Neurol,2005,252 Suppl 3:iii1-iii2.
- [6]MORAN MS.Method for treating hepatitis C virus with omega interferon:US,07727519[P].2010-01-01.
- [7]SCHULTZ B,YANG H,DELANEY WE 4th.Biochemical evaluation of HCV NS3 protease inhibitors

扩展功能**● 本文信息**[PDF\(221K\)](#)**参考文献****● 服务与反馈****引用本文****● 本文关键词相关文章**[肝炎病毒](#)[干扰素类](#)[抗病毒药](#)[NS3蛋白酶](#)[NS5B聚合酶](#)**● 本文作者相关文章**[田军](#)[郝博济](#)**● 中国知网**[田军](#)[郝博济](#)

- [J].Curr Protoc Phar-macol,2011,Chapter 13Unit:13B.7.
- [8]TSANTRIZOS YS.TMC-435,an NS3/4A protease inhibitor forthe treatment of HCV infection [J].Curr Opin Investig Drugs,2009,10(8):871-881.
- [9]WATKINS WJ,RAY AS,CHONG LS.HCV NS5B polymeraseinhibitors[J].Curr Opin Drug Discovery Dev,2010,13(4):441-465.
- [10]POWDRILL MH,BERNATCHEZ JA,GOTTE M.Inhibitors ofthe hepatitis C virus RNA-dependent RNA polymerase NS5B[J].Viruses-Basel,2010,2(10):2169-2195.
- [11]SOFIA MJ,CHANG WS,FURMAN PA,et al.Nucleoside,nucleotide, and non-nucleoside inhibitors of hepatitis C virusNS5B RNA-dependent RNA-polymerase[J].J Med Chem,2012,55(6):2481-2531.
- [12]BRILLANTI S,MAZZELLA G,RODA E.Ribavirin for chronichepatitis C:and the mystery goes on [J].Dig Liver Dis,2011,43(6):425-430.
- [13]TSUBOTA A,FUJISE K,NAMIKI Y,et al.Peginterferon andribavirin treatment for hepatitis C virus infection[J].World JGastroenterol,2011,17(4):419-432.
- [14]LALEZARI J,LAWITZ E,RODRIGUEZ-TORRES M,et al.Once daily PSI-7977 plus PEGIFN/RBV in a phase 2B trial:rapid virologic suppression in treatment-naive patients with HCVGT2/GT3[J].J Hepatol,2011,54:S28.
- [15]GUEDJ J,DAHARI H,SHUDO E,et al.Hepatitis C viralkinetics with the nucleoside polymerase inhibitor mericitabine(RG7128)[J].Hepatology,2012,55(4):1030-1037.
- [16]PATEL R,THOMPSON P,SHOWALTER R,et al.In vitrocombination studies of ANA598 with anti-HCV agents demon-strate enhanced anti-viral activity[J].Antiviral Res,2010,86(1):A41-A42.
- [17]MORIYAMA M,KATO N,OTSUKA M,et al.Interferon-betais activated by hepatitis C virus NS5B and inhibited by NS4A,NS4B, and NS5A[J].Hepatology International,2007,1(2):302-310.
- [18]RODRIGUEZ A,OLIVA C,GONZALEZ M.A comparative QM/MM study of the reaction mechanism of the hepatitis C virusNS3/NS4A protease with the three main natural substrates NS5A/5B,NS4B/5A and NS4A/4B[J].Phys Chem Chem Phys,2010,12(28):8001-8015.
- [19]SILLANPAA M,MELEN K,PORKKA P,et al.Hepatitis Cvirus core,NS3,NS4B and NS5A are the major immunogenicproteins in humoral immunity in chronic HCV infection[J].Virol J,2009,6:84.
- [20]WANG C,HUANG H,VALERA L,et al.Hepatitis C virusRNA elimination and development of resistance in replicon cellstreated with BMS-790052[J].Antimicrob Agents Chemother,2012,56(3):1350-1358.
- [21]REVIRIEGO C.Daclatasvit dihydrochloride treatment of hepa-titis C virus HCV NS5A inhibitor [J].Drugs Future,2011,36(10):735-739.
- [22]MARTINEZMIR I,ESTAN L,RUBIO E,et al.Antihistaminicand anticholinergic activities of mequitazine in comparison withclemizole[J].J Pharm Pharmacol,1988,40(9):655-656.
- [23]EINAV S,SOBOL HD,GEHRIG E,et al.The hepatitis C virus(HCV)NS4B RNA binding inhibitor clemizole is highlysynergistic with HCV protease inhibitors[J].J Infect Dis,2010,202(1):65-74.
- [24]ANGUS AG,PATER AH.Immunotherapeutic potential ofneutralizing antibodies targeting conserved regions of the HCVenvelope glycoprotein E2[J].Future Microbiology,2011,6(3):279-294.
- [25]GORDON FD,CHUNG RT,CURRY MP,et al.Monoclonalantibody MBL-HCV1 suppresses return of HCV following livertransplantation[J].Hepatology,2011,54 Suppl:1434A.
- [26]BELON CA,FRICK DN.Hepatitis C virus NS3 helicaseinhibitors,in hepatitis C:antiviral drug discovery and develop-ment[M].Caister Academic Press,2011:237-256.
- [27]FRICK DN.The hepatitis C virus NS3 protein:A model RNAhelicase and potential drug target [J].Current Issues Mol Biol,2007,9(1):1-20.