GILEAD
Creating Possible

DETER RFP:

Chronic Hepatitis Delta Treatment Research

Chronic hepatitis delta virus (HDV) infection carries a significant disease burden, accounting for up to 60 million infected individuals worldwide[1]. HDV poses a significant public health threat, as it increases risk of cirrhosis, decompensated cirrhosis, liver transplant, HCC and mortality[2,3,4]. Prior to 2020, the unmet medical need for HDV treatment was significant, with the only treatment option being off-label use of Peg-IFNα, which had low efficacy and poor tolerability[5].

In 2020, bulevirtide (BLV) 2 mg was conditionally approved by the European Medicines Agency (EMA) as a treatment option for chronic HDV infection in HDV-RNA positive adult patients with compensated liver disease[6]. This first-in-class entry inhibitor acts by blocking the entry of both HBV and HDV into liver cells by inhibiting the NTCP receptor[7].

In the primary data analysis of the phase 3 MYR301 trial, treatment with BLV 2mg daily through 48 weeks was found to be safe and efficacious, with 45% (22/49) of patients achieving the primary endpoint of combined response (≥2 $\log_{10}$ IU/mL decline from baseline in HDV RNA or undetectable HDV RNA combined with ALT normalization) compared with 2% (1/51) of patients who did not receive treatment[8]. A subsequent analysis at week 96 demonstrated that responses were sustained on BLV treatment, with 55% (27/49) of patients in the BLV 2 mg arm achieving a combined response[9].

Subsequently in 2023, full approval for BLV as a treatment option for HDV was granted by the EMA[6]. The European Association for the Study of the Liver (EASL) guidelines recommend all patients living with chronic HDV and compensated liver disease to be considered for treatment with BLV 2 mg[10].

While the emergence of BLV offers hope for improved treatment of HDV, the need for robust real-world research is important to inform and guide clinical practice. Real world data of on-label bulevirtide use in diverse patient populations with heterogeneous disease severities, co-morbidities, and treatment histories can supplement findings from clinical trials. Additionally, long-term data on viral suppression, durability of response, the impact on non-invasive tests, and various disease biomarkers of interest are still limited. Furthermore, potential drug-drug interactions and the safety profile in specific subgroups, like HIV or HCV coinfected patients, remain to be comprehensively investigated. Therefore, real-world studies with larger, diverse cohorts, and longer follow-up periods are crucial to address these important data gaps beyond the confines of clinical trials.

To understand and address data gaps related to BLV treatment in HDV, Gilead is launching the **DETER** (chronic hepatitis **DE**lta **T**reatment **R**esearch) request for proposal (RFP) program. Applications should include large scale, long-term, real world research projects that demonstrate clear objectives, include defined timelines, offer a comprehensive operational plan, propose data that has relevance to the medical community and policymakers, and include plans for the data to be submitted timely to relevant congresses and journals. Through this program, Gilead may only provide funding for research activities. Gilead will not provide study drug nor funding for drug.

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Application Criteria

Gilead will evaluate and support select programs which will:

1. Determine the real-world safety and efficacy of bulevirtide for the treatment of chronic HDV on virologic, biochemical, NIT measures, and/or histological outcomes
2. Assess impact of treatment on long term clinical outcomes, including cirrhosis, decompensation, HCC, liver transplantation, and mortality
3. Investigate the use of bulevirtide in the real world with respects to patient adherence and persistence
4. If possible, stratify efficacy and safety outcomes by special populations such as in individuals living with HIV or HCV

- Both investigator-sponsored research study proposals and collaborative research study proposals (developed in conjunction with Gilead) will be considered
- The proposed budget should be appropriately proportional with the study's scope, with minimal infrastructural/equipment costs
- The proposed study design should be feasibly executed within a reasonable timeframe proportional to the study's follow-up duration
- Research proposals should include a comprehensive publication plan to present study results in scientific forums, and to publish results in peer reviewed journals
- The total budget should include overhead costs and applicable taxes; overhead costs should not exceed 30% of the total budget
- Grant awards shall be for research purposes only. Requests that include routine medical care or other costs associated with routine medical care will not be considered
- Funding for or contribution of study drugs will not be provided
- LOIs will only be reviewed from countries where BLV is available & has regulatory approval
- There must be no more than one sponsor for contract negotiations and/or Institutional Review Board (IRB) review

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Application Process

To apply for consideration for funding under the DETER RFP Program, you will need to submit a Letter of Intent (LOI) that is no longer than two pages, contains a concise overview of the proposed project and includes the total estimated budget. Applicants should submit the LOI application in the Gilead OPTICS portal.

Gilead will evaluate and rank all letters of intent (LOIs) received on a rolling basis until funds are exhausted. **It is recommended to submit earlier than later to ensure that funding is available for your proposal.**

- Monday, March 4th, 2024 at 00:00 GMT: Submission window opens
- Friday, Sept. 27th, 2024 at 23:59 GMT: Submission window closes

Questions about the RFP or the application process can be submitted to your local Gilead Medical Scientist or DETER@gilead.com. A review of the LOIs will result in invitations for selected LOI applicants to submit a full application with detailed budget.

Gilead's approval of awards will depend on the availability of funds and receipt of meritorious and complete proposals. Awards shall be granted solely on the merit of the research and alignment with the criteria of this program.

No Guarantee of Funding

Gilead reserves the right to approve or decline any application at its sole discretion. Submission of an LOI or a full application does not guarantee funding.

No Inducement or Reward

Gilead approval of awards does not take into account the past, present, or future volume or value of any business or referrals between the parties. Awards are not being given, directly or indirectly, as an inducement or reward with respect to the past or potential future purchase, utilization, recommendation or formulary placement of any Gilead product. Furthermore, except for the use of the Gilead product in an approved award/research, the awardee is not required to purchase, order, recommend or prescribe to any patients any products manufactured by or available through Gilead.

About Gilead Sciences

References

1. Miao Z, Zhang S, Ou X, et al. Estimating the Global Prevalence, Disease Progression, and Clinical Outcome of Hepatitis Delta Virus Infection. J Infect Dis. 2020;221(10):1677-1687. doi:10.1093/infdis/jiz633.
2. Romeo R, Petruzziello A, Pecheur EI, et al. Hepatitis delta virus and hepatocellular carcinoma: an update. Epidemiol Infect. 2018;146(13):1612-1618. doi:10.1017/S0950268818001942.
3. Fattovich G, Giustina G, Christensen E, et al. Influence of hepatitis delta virus infection on morbidity and mortality in compensated cirrhosis type B. The European Concerted Action on Viral Hepatitis (Eurohep). Gut. 2000;46(3):420-426. doi:10.1136/gut.46.3.420.
4. Höner Zu Siederdissen C, Cornberg M. Management of HBV and HBV/HDV-Associated Liver Cirrhosis. Visc Med. 2016;32(2):86-94. doi:10.1159/000445518.
5. Deterding K, Wedemeyer H. Beyond Pegylated Interferon-Alpha: New Treatments for Hepatitis Delta. AIDS Rev. 2019;21(3):126-134. doi:10.24875/AIDSRev.19000080
6. European Medicines Agency. Hepcludex. https://www.ema.europa.eu/en/medicines/human/EPAR/hepcludex
7. Watashi K, Wakita T. Hepatitis B Virus and Hepatitis D Virus Entry, Species Specificity, and Tissue Tropism. Cold Spring Harb Perspect Med. 2015 Aug 3;5(8):a021378. doi:10.1101/cshperspect.a021378.
8. Wedemeyer H, Aleman S, Brunetto MR, et al. A Phase 3, Randomized Trial of Bulevirtide in Chronic Hepatitis D. N Engl J Med. 2023;389(1):22-32. doi:10.1056/NEJMoa2213429
9. Wedemeyer H, Aleman S, Brunetto MR, et al. Efficacy and safety at 96 weeks of bulevirtide 2 mg or 10 mg monotherapy for chronic hepatitis D (CHD): results from an interim analysis of a phase 3 randomized study. EASL 2023. Oral #OS-068
10. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on hepatitis delta virus. J Hepatol. 2023;79(2):433-460. doi:10.1016/j.jhep.2023.05.001

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