

Disclosures:

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LB18

USE OF DAILY INTERFERON ALFACON-1 (INFERGEN®, C1FN) PLUS RIBAVIRIN (RBV) IN PATIENTS INFECTED WITH HEPATITIS C (HCV) WHO ARE NONRESPONDERS TO PREVIOUS PEGYLATED INTERFERON PLUS RBV THERAPY: 24-WEEK DATA FROM THE DIRECT TRIAL Bruce Bacon¹, Arie Regev², Reem Ghalib³, Giuseppe Morelli⁴, Kenneth Rothstein⁵, Tarek Hassanein⁶, Mitchell Shiffman⁷, Brian Murphy⁸, Yi Xu⁸; ¹Saint Louis University Liver Center, St. Louis University School of Medicine, St. Louis, MO; ²University of Miami, Miami, FL; ³Liver Institute at Methodist Hospital, Dallas, TX; ⁴University of Florida, Gainesville, FL; ⁵Albert Einstein Center for Liver Disease, Philadelphia, PA; ⁶University of California San Diego, San Diego, CA; ⁷Virginia Commonwealth University, Richmond, VA; ⁸Valeant Pharmaceuticals International, Costa Mesa, CA

Background: The DIRECT Trial (Daily-Dose Consensus Interferon and Ribavirin: Efficacy of Combined Therapy) is a Phase 3 open-label multi-center US-based study enrolling patients who are previous non-responders to PEG-IFN/RBV therapy. Daily use of C1FN, which in vitro has been shown to be more effective than IFN alfa-2a and IFN alfa-2b, allows constant pharmacologic pressure on HCV and when combined with RBV, may be an effective treatment for the nonresponder patient. **Methods:** In the first phase of the DIRECT Trial, 343 genotype 1 patients were randomized to receive C1FN 9 µg/day plus RBV (1.0- 1.2 g/day) or C1FN 15 µg/day plus RBV. Patients had to have < 2 log decline in viral load (VL) while undergoing at least 12 weeks of previous PEG-IFN/RBV therapy and had to have a minimum of 90 days between the end of PEG-IFN/RBV therapy and the start of C1FN/RBV (washout period). Interim results include 12 and 24-week VL, and incidence of hematologic adverse events. No adjunctive growth factors were used. Patients had a negative VL if virus was undetectable by both bDNA and TMA assays. **Results:** Patient demographics included a mean age of 50 yrs, 70% male, 67% high viral load, mean weight of 89kg, 20% African Americans, 65% Caucasians and 77% with evidence of bridging fibrosis or cirrhosis on biopsy. Clinical outcomes data are listed in Chart 1. Mean washout period was 485 days for the C1FN 9 µg cohort and 535 days for the 15 µg group. **Conclusions:** Use of daily C1FN plus RBV in patients with advanced liver disease who were nonresponders to PEG-IFN based therapy achieved viral clearance in a dose-dependent manner, with highest clearance among the C1FN 15 µg group, which was further improved when patients receive ≥ 80% of the ideal C1FN dose. Based on this interim data, viral clearance could be enhanced by maximizing C1FN/RBV exposure through the use of adjunctive therapy with growth factors. Further study of these interventions is warranted, including assessing the impact of washout period on viral clearance.

Disclosures:

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Chart 1. Clinical Outcome

	C1FN 9 µg	C1FN 15 µg
% wk 12 EVR (2 log drop or viral load negative)	46%	54%
% wk 24 negative	14%	20%
% wk 24 negative with ≥ 80% C1FN dose	16%	30%
% grade 3 & 4 neutropenia	21%	27%
% grade 3 & 4 anemia	25%	28%

LB19

SIX MONTH MAINTENANCE THERAPY WITH 10 MG CLEVDINE MAINTAINS THE VIRAL SUPPRESSION AND BIOCHEMICAL IMPROVEMENT ACHIEVED WITH SIX MONTHS THERAPY WITH 30 MG Young Hwa Chung¹, Kwan Sik Lee², Ju Hyun Kim³, Soo Hyung Ryu⁴, Seung Woon Paik⁵, Soon Ho Um⁶, Byung Hoon Han⁷, Mong Cho⁸, Kwan Soo Byun⁶, Byung Ik Kim⁵, Joong-Won Park⁹, Heon Ju Lee¹⁰, Joon-Yeol Han¹¹, Seong Gyu Hwang¹², Haak Cheoul Kim¹³, Kwon Yoo¹⁴, Young Suk Lee¹⁷, Youn Jae Lee¹⁶, Young Soo Kim¹⁵, Jin Mo Yang¹⁸, Chae Yoon Chon², Se Hyun Cho¹¹, Sung Kyu Choi¹⁹, Hyo-Suk Lee²⁰, Byung Chul Yoo⁵; ¹Asan Medical Center, Seoul, South Korea; ²Yonsei University Hospital, Seoul, South Korea; ³Gachon Medical School, Incheon, South Korea; ⁴Inje University Seoul Paik Hospital, Seoul, South Korea; ⁵Samsung Medical Center, Seoul, South Korea; ⁶Korea University Hospital, Seoul, South Korea; ⁷Kosin Medical School, Busan, South Korea; ⁸Pusan National University Hospital, Busan, South Korea; ⁹National Cancer Center, Goyang-si, Gyeonggi-do, South Korea; ¹⁰Yongnam University Medical Center, Daegu, South Korea; ¹¹The Catholic University of Korea, Seoul, South Korea; ¹²Pochon CHA University Bundang CHA Hospital, Seongnam-si, Gyeonggi-do, South Korea; ¹³Wonkwang University Hospital, Iksan-si, Jeollabuk-do, South Korea; ¹⁴Ewha Womans University Mokdong Hospital, Seoul, South Korea; ¹⁵Inha University Hospital, Incheon, South Korea; ¹⁶Inje University Busan Paik Hospital, Busan, South Korea; ¹⁷The Catholic University of Korea, Bucheon-si, Gyeonggi-do, South Korea; ¹⁸The Catholic University of Korea, Suwon-si, Gyeonggi-do, South Korea; ¹⁹Chonnam National University Hospital, Gwangju, South Korea; ²⁰Seoul National University Hospital, Seoul, South Korea

Background: In the pivotal phase III clinical trials, clevidine 30 mg once daily for 6 months showed potent antiviral activity along with a marked post-treatment antiviral effect. E-max modeling has shown that the 30 mg dose achieved >90% of maximum predicted effect compared to approximately 77% at the 10 mg dose. **Objective:** To evaluate the effect of 6 months maintenance therapy with 10 mg clevidine once daily in treatment-naïve patients following 6 months therapy at 30 mg once daily. **Method:** Safety, antiviral activity, biochemical improvement and serologic response were monitored in patients receiving clevidine 30 mg for 24 weeks followed by clevidine 10 mg for an additional 24 weeks as a maintenance therapy with a 12-week follow-up period. Preliminary results from the 54 naïve patients (39 HBeAg(+), 15 HBeAg(-)) who have completed the study are presented here. **Results:** The table below summarizes the results of this study. **Conclusion:** Clevidine 30 mg once daily therapy was well tolerated and demonstrated significant viral suppression and biochemical improvement. While a maintenance dose of 10 mg once daily is not recommended due to the potential for resistance selection, it was able to sustain the antiviral and biochemical responses achieved with 30 mg.

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	HBeAg Positive			HBeAg Negative		
	Wk 24	Wk 48	Wk 60	Wk 24	Wk 48	Wk 60
% Patients with HBV DNA <300 c/ml	53	68	31	100	100	92
% ALT Normalization	82	89	89	67	100	85
% HBeAg loss	8	16	17	-	-	-