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A PHASE 1 STUDY OF LEDIPASVIR/SOFOSBUVIR IN PREGNANT WOMEN WITH HEPATITIS C VIRUS

Catherine A. Chappell1, Elizabeth E. Krans1, Katherine Bunge1, Ingrid Macio1, Debra Bogen1, Kimberly K. Scarsi2, Leslie A. Meyn1, Sharon L. Hillier1
1Magee–Womens Research Institute, Pittsburgh, PA, USA, 2University of Nebraska Medical Center, Omaha, NE, USA

Background:
Hepatitis C virus (HCV) infection is increasing among pregnant women in the United States, increasing the risk of perinatal transmission. Pregnancy is a window of opportunity for health care interventions, including HCV treatment that could improve maternal health and prevent perinatal HCV transmission. There are no published data on the safety or efficacy of HCV direct-acting antivirals in pregnancy. Therefore, the primary objective of this pilot study was to define the safety of and virologic response to ledipasvir 90mg-sofosbuvir 200mg (LDV/SOF) therapy in pregnancy.

Methods:
In this open-label, phase 1 study, HIV-negative pregnant women with chronic genotype 1 HCV infection were enrolled between 23-24 weeks of gestation and began a 12-week course of LDV/SOF. Participants had to take at least 73 (87%) planned doses to be evaluable. Viral load testing was performed at 7 visits: screening, enrollment, 13-21 days and 5-6 weeks after LDV/SOF initiation, 1-7 days and 12 weeks after LDV/SOF completion, and at delivery. Maternal adverse events, delivery outcomes and the sustained virologic response 12 weeks after therapy (SVR12), defined as undetectable HCV viral load, are reported.

Results:
Of 28 pregnant women with chronic HCV who screened, 20 were excluded because of genotype 2 or 3 infection (n=10), ongoing illicit drug use (n=4), declining study participation (n=3), intensions to delivery off-site (n=2), and an APRI score of >1 (n=1). Eight women were enrolled, all of whom were white, with a median age of 32 (range 25-38) years. Seven of the women were HCV infected due to intravenous drug use, 4 of whom were receiving opioid pharmacotherapy, and one was perinatally infected. Of 7 evaluable patients, the median HCV viral load at enrollment was 518,173 (range 103,457-3,757,923) copies/mL. All had a rapid response to therapy and all achieved SVR12 (Table). All adverse events related to LDV/SOF were ≤ grade 2. All seven participants delivered at term with undetectable HCV viral loads at delivery. One-year follow-up of infants is ongoing.

Conclusion:
In this first study of HCV treatment in pregnant women, response to LDV/SOF was similar to the viral response observed in nonpregnant individuals without any safety concerns identified. Larger studies are needed before this strategy can be recommended. A substantial proportion of women screened out due to genotypes 2 or 3 infection, highlighting the importance of further research to expand HCV treatment options in pregnancy.