1551

PHARMACOKINETICS OF GLECAPREVIR/PIBRENTASVIR IN CHILDREN WITH CHRONIC HCV INFECTION: INTERIM ANALYSIS OF PART 2 OF THE DORA STUDY

Dr. Maureen M. Jonas[1], Hoi Kei Lon[2], Susan Rhee[2], Dr. Susan M. Gilmour[3], Regino P Gonzalez-Peralta[4], Daniel H. Leung[5], Dr. Simon C. Ling[6], Steven Lobritto[7], Michael R Narkewicz[8], Vishakha Sabharwal[9], Antonio Del Valle-Segarra[10], Jessica W. Wen[11], Sandra Sinisi Lovell[2], Ariel Porcalla[2], Rakesh Tripathi[2] and Etienne M. Sokal[12], (1)Division of Gastroenterology, Hepatology, and Nutrition, Boston Children's Hospital and Department of Pediatrics, Harvard Medical School, Boston MA, USA, (2)Abbvie, (3)Stollery Children's Hospital, Alberta, Canada, (4)Pediatric Gastroenterology, Hepatology and Liver Transplant, Adventhealth for Children, Orlando, Florida, USA, (5)Pediatric Gastroenterology, Hepatology and Nutrition, Texas Children's Hospital, (6)Division of Gastroenterology, Hepatology & Nutrition, the Hospital for Sick Children, and Department of Paediatrics, University of Toronto, Toronto, Ontario, Canada, (7)Morgan Stanley Children's Hospital of NY, Columbia University Irving Medical Center, New York, USA, (8)Digestive Health Institute, Children's Hospital Colorado, Section of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics University of Colorado School of Medicine, Aurora, Colorado, USA, (9)Division of Pediatrics Infectious Diseases, Department of Pediatrics Boston University Medical Center, Boston, Massachusetts, USA, (10)San Jorge Children's Hospital, San Juan, Puerto Rico, (11)Children's Hospital of Philadelphia, Philadelphia, PA, (12)Cliniques Universitaires Saint-Luc, Université Catholique De Louvain, Brussels, Belgium

Abstract Text

Background: The pangenotypic regimen of glecaprevir and pibrentasvir (G/P) (GLE; identified by AbbVie and Enanta) is the first approved pangenotypic treatment for adults and adolescents with chronic hepatitis C virus (HCV) infection, and has yielded high cure rates in these populations in Phase 2 and 3 studies. A highly effective pangenotypic regimen with improved tolerability for children 3–11 years of age remains an unmet need.

Methods: DORA (NCT03067129) is an ongoing phase 2/3, non-randomized, open-label, multicenter study evaluating the pharmacokinetics (PK), safety and efficacy of G/P in pediatric patients with chronic HCV infection. For Intensive PK (IPK) analysis after dose adjustment, the pediatric population was divided into 3 cohorts: cohort 1 (9–11 years, ≥ 30 to < 45 kg, N = 10); cohort 2 (6–8 years, ≥ 20 to < 30 kg, N = 9); and cohort 3 (3–5 years, 12 to < 20 kg, N = 10). Pediatric dosage of G/P was determined as 250 mg GLE + 100 mg PIB for cohort 1, 200 mg + 80 mg for cohort 2, and 150 mg + 60 mg for cohort 3. We present an IPK analysis of treatment-naïve patients aged 3-11 years, who received a novel pediatric pellet formulation.

Results: Part 2 enrolled 48 pediatric patients. 40% (19/48) of patients were male; 77% (37/48) were white. Median (range) age and median (range) weight were 7 (3–11) years and 24 (13–44) kg, respectively. Median (range) HCV RNA level was 6 (3–7) log10 IU/mL. All patients were non-cirrhotic and received G/P for 8 weeks. The primary PK endpoint, steady-state AUC values for GLE and PIB, was evaluated. One patient received double doses the day of the week 2 study visit and was thus excluded from the IPK analysis. The predicted PK exposures (AUC_{24}) of GLE and PIB for the cohorts are shown in **Table.** Compared to the target GLE and PIB steady-state exposures in adults (4800 and 1430 hr*ng/mL, respectively), the target AUC/predicted AUC ratio for both GLE and PIB is between 1.00 to 1.31. Efficacy evaluation is ongoing, and to date 45/46 patients (98%) achieved SVR4 without any on-treatment virologic failures. One GT3 patient experienced relapse by post-treatment week 4. The safety profile of GLE/PIB demonstrated in these younger cohorts to date is comparable to those in adolescents and adults.

Conclusion: IPK exposures of GLE and PIB in pediatric patients treated with the new pellet formulation were comparable to exposures in adults and adolescents. Pediatric patients with chronic HCV infection treated with G/P achieved high rates of SVR4, with only one virologic relapse, and comparable safety profile to that in adults and adolescents.

Table: Steady State Pharmacokinetics of GLE and PIB in HCV-Infected Pediatric Patients

	Glecaprevir		Pibrentasvir	
	Pop-PK AUC* (hr*ng/mL)	AUC/Target AUC ratio	Pop-PK AUC* (hr*ng/mL)	AUC/Target AUC ratio
Cohort 1 (9-11 years)	5190	1.08	1440	1.00
Cohort 2 (6-8 years)	5770	1.20	1460	1.02
Cohort 3 (3-5 years)	6310	1.31	1430	1.00

*Pop-PK AUC shows the predicted PK exposures of GLE and PIB based on all the currently available PK information collected in the study (including data from other study weeks)

Disclosures

Maureen M. Jonas – BMS: Grant/Research Support; Echosens: Grant/Research Support; Merck: Grant/Research Support; Roche: Grant/Research Support; AbbVie: Grant/Research Support; Gilead: Grant/Research Support; Gilead: Consulting

Hoi Kei Lon – AbbVie: Stock Shareholder; AbbVie: Employment

Susan Rhee – AbbVie: Stock Shareholder; AbbVie: Employment

Susan M. Gilmour – AbbVie: Grant/Research Support

Regino P Gonzalez-Peralta – AbbVie: Grant/Research Support; Gilead: Grant/Research Support; Alexion: Advisory Committee or Review Panel; Kadmon: Advisory Committee or Review Panel; Gilead: Advisory Committee or Review Panel; Merck: Grant/Research Support; Roche: Advisory Committee or Review Panel

Daniel H. Leung – AbbVie: Grant/Research Support; BMS: Grant/Research Support; Gilead: Grant/Research Support; Roche: Grant/Research Support; Merck: Consulting

Simon C. Ling – AbbVie: Grant/Research Support; Gilead: Grant/Research Support

Steven Lobritto – AbbVie: Grant/Research Support; Kadmon: Advisory Committee or Review Panel

Michael R Narkewicz – Vertex: Consulting; AbbVie: Grant/Research Support; Gilead: Grant/Research Support

Vishakha Sabharwal – AbbVie: Grant/Research Support

Antonio Del Valle-Segarra – AbbVie: Grant/Research Support

Jessica W. Wen – Gilead: Consulting; Gilead: Grant/Research Support; AbbVie: Grant/Research Support; Alexion: Grant/Research Support

Sandra Sinisi Lovell – AbbVie: Stock Shareholder; AbbVie: Employment

Ariel Porcalla – AbbVie: Stock Shareholder; AbbVie: Employment

Rakesh Tripathi – AbbVie: Stock Shareholder; AbbVie: Employment

Etienne M. Sokal – AbbVie: Consulting; Takeda: Grant/Research Support; Gilead: Grant/Research Support; Promethera Biosciences: Management Position; AbbVie: Grant/Research Support