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Impact of baseline NS5A polymorphisms on sustained virologic response in patients infected with HCV treated with Daclatasvir-based regimens

Fiona McPhee
Bristol-Myers Squibb Co., USA

The most prevalent hepatitis C virus (HCV) genotype (GT) globally is GT-1 (46%) with GT-1b being the most common subtype (22%). In Europe, GT-1b accounts for approximately 50% of all HCV cases. Daclatasvir (DCV)-based regimens are approved in many countries globally, including Europe, United States and Asia, for the treatment of HCV. In patients infected with HCV, response rates to DCV-based regimens can depend on the regimen, GT and pre-treatment non-structural 5A (NS5A) resistance-associated polymorphisms (RAPs) to DCV. The effects of NS5A RAPs at L31 or Y93H on sustained virologic response (SVR) to treatment with DCV+asunaprevir (ASV; NS3 protease inhibitor) for 24 weeks or treatment with DCV+sofosbuvir (SOF; NS5B inhibitor) for 12 weeks were explored using pooled data from clinical studies in HCV GT-1b-infected patients. SVR with versus without baseline NS5A RAPs was compared by age (<65 vs. ≥65 years), cirrhosis status and baseline viral load. Baseline NS5A sequences were available for 1224 GT-1b patients treated with DCV+ASV and 28 GT-1b patients treated with DCV+SOF. NS5A RAPs at L31 or Y93H were observed pretreatment in 4% or 11% of patients, respectively. The overall SVR rate in DCV+ASV-treated patients without NS5A RAPs at L31 or Y93H was 95% compared to 40% with these RAPs. SVR rates in DCV+ASV treated patients without RAPs was high irrespective of cirrhosis, age or baseline viral load. The overall SVR rate in DCV+SOF-treated patients was 100%.

Biography

Fiona McPhee has completed her DPhil in Organic Chemistry from Oxford University and Postdoctoral studies on coxsackieviruses at the Max-Planck Institute, Germany and on HIV at the University of San Francisco, USA. She is the Discovery Head for Clinical Virology at Bristol-Myers Squibb where her current research focus includes HBV and HCV drug resistance. She has published more than 80 papers in peer-reviewed journals, over 80 communications at international scientific meetings and has 7 patents.

fiona.mcphee@bms.com

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