

ALLY 3+ Trial Investigating Daklinza (daclatasvir) in Combination with Sofosbuvir and Ribavirin Demonstrates High Cure Rates in Chronic Hepatitis C Genotype 3 Patients with Advanced Fibrosis or Cirrhosis

Daclatasvir+sofosbuvir+ribavirin regimen achieves SVR12 rates of 88% and 92% overall for 12 or 16 weeks of therapy respectively in GT-3 patients with advanced fibrosis or cirrhosis

MONTREAL, Nov. 16, 2015 /CNW/ - Bristol Myers-Squibb today announced late-breaking data from the Phase 3 ALLY-3+ Trial investigating a regimen of *Daklinza*[™] (daclatasvir, DCV) in combination with sofosbuvir (SOF) and ribavirin (RBV) in genotype 3 hepatitis C (HCV) patients with advanced fibrosis or cirrhosis, for treatment durations of 12 and 16 weeks. This patient population is one of the most difficult to treat, among whom sustained virologic response (SVR) rates, or cure, have proved harder to achieve with existing therapies.

The results show that SVR12 rates in cirrhotic patients only were 83 per cent and 89 per cent in the 12- and 16-week arms, respectively. Results will be presented at The Liver Meeting[®] 2015, the Annual Meeting of The American Association for the Study of Liver Diseases (AASLD), in San Francisco, CA, November 13 – 17.

Daklinza is a potent, pan-genotypic NS5A replication complex inhibitor (in vitro) that has been approved for use in combination with sofosbuvir (marketed in Canada by Gilead Sciences Canada Inc. as SOVALDI[™]) as a convenient, all-oral, once-daily regimen for the treatment of adult patients with hepatitis C genotypes 1 and 2 with compensated liver disease including cirrhosis. *Daklinza* has also received a Notice of Compliance with conditions (NOC/c) from Health Canada for the treatment of genotype 3 patients with compensated liver disease including cirrhosis. In Canada, genotypes 3 accounts for 20 per cent of hepatitis C infections.

Daklinza is contraindicated in combination with medicinal products that strongly induce CYP3A and P-glycoprotein transporter, as this may lead to lower exposure and loss of efficacy of *Daklinza*. *Daklinza* must not be administered as a monotherapy.

"Patients with genotype 3 hepatitis C infection make up about one in five cases of hepatitis C infection in Canada," said Dr Alnoor Ramji, Clinical Associate Professor of Medicine, Gastroenterology and Hepatology at the University Of British Columbia. "High cure rates for these patients have remained elusive, so this data is very encouraging. These cure rates significantly improve upon what we have seen in the past in patients with advanced fibrosis or cirrhosis and offer more hope for a high unmet medical need."

In the ALLY-3+ study, the daclatasvir+sofosbuvir+ribavirin combination regimen had no discontinuations due to adverse events (AEs) or treatment-related serious AEs. The eight frequent AEs were insomnia (30%), fatigue (26%) and headache (24%). Additionally, relapse

occurred in four patients (two in the 16-week and two in the 12-week arm). There was one death (12-week arm; not treatment-related). There were no virologic breakthroughs.

"Our continued scientific exploration of the potential for *Daklinza* used in combination with other direct-acting antivirals for HCV patients has yielded these encouraging results," said Douglas Manion, M.D., Head of Specialty Development, Bristol-Myers Squibb. "We remain committed to delivering therapeutic options to HCV patients with unmet needs around the globe, including those with more complicated disease and other difficult-to-treat groups such as genotype 3 patients with more advanced liver disease who still need help to achieve cure."

ALLY 3+ Study Design

This open-label, phase 3b study in HCV genotype 3-infected treatment-naive or -experienced patients with advanced fibrosis or compensated cirrhosis randomized patients 1:1 to receive 12 weeks versus 16 weeks of *Daklinza* (60 mg QD) + SOF (400 mg QD) + RBV (weight-based), stratified by advanced fibrosis or cirrhosis status.

Fifty patients were treated (12 weeks: 24 patients; 16 weeks: 26 patients). The majority of patients were male (80%), white (98%), and treatment-experienced (74%; 10% prior relapse on SOF+RBV); 72 per cent had cirrhosis and 52 per cent had HCV RNA ≥ 6 million IU/mL. Baseline characteristics were comparable between arms.

The primary endpoint was to estimate SVR12 in treatment-naive or – experienced subjects with compensated advanced fibrosis/cirrhosis (F3-F4) treated for 12 weeks and for 16 weeks.