Sofosbuvir/Velpatasvir/Voxilaprevir for 12 Weeks as a Salvage Regimen in NS5A Inhibitor-Experienced Patients with Genotype 1-6 Infection: The Phase 3 POLARIS-1 Study


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Abstract

Introduction: NS5A inhibitors are potent direct acting antiviral agents (DAAs) which are key components of HCV treatment regimens. In combination with other DAAs, NS5A inhibitors provide HCV treatments which cure over 90% of patients. For patients who have failed a regimen with an NS5A inhibitor, there is concern about long-lasting NS5A resistance-associated substitutions and currently no approved retreatment option. Sofosbuvir (SOF) and velpatasvir (VEL) are pangenotypic inhibitors of the HCV NS5B and NS5A proteins, respectively, and voxilaprevir (VOX, GS-9857) is a pangenotypic HCV NS3/4A protease inhibitor. This Phase 3 study evaluates treatment with a SOF/VEL/VOX fixed dose combination (FDC) for 12 weeks in patients who previously received an NS5A inhibitor.

Methods: Patients at 108 sites in North America, Europe, Australia and New Zealand were enrolled. Eligible patients received at least 4 weeks of a prior NS5A inhibitor-containing regimen which was not discontinued due to an adverse event or unsuccessful due to non-compliance. Those with HCV genotype (GT) 1 were randomized 1:1 to receive SOF/VEL/VOX (400mg/100mg/100mg) or matching placebo daily for 12 weeks, stratified by the presence or absence of cirrhosis. Patients of all other GTs were assigned to receive SOF/VEL/VOX for 12 weeks. Those patients assigned to receive placebo will be offered deferred treatment with SOF/VEL/VOX for 12 weeks. The primary endpoint evaluates the superiority of the sustained virologic response 12 weeks after treatment (SVR12) to a pre-specified performance goal of 65%.

Results: Of 415 patients treated, 77% were male, 78% were white, 18% had the IL28B CC genotype, 41% had compensated cirrhosis, 57% were from the US and 73% had GT 1 HCV infection. The majority of patients had DAA experience with an NS5A inhibitor given in combination with an NS5B inhibitor, and the most common prior treatment regimen was ledipasvir/SOF (66%). Treatment with SOF/VEL/VOX has been well tolerated; at the time of abstract submission, two patients have discontinued therapy due to adverse events not related to study drug, one due to chest pain, confusion, dizziness and blurred vision and another due to grade 4 elevations in transaminases, present prior to initiation of therapy. No serious adverse events attributed to study medication have been reported. Complete safety and SVR12 data for all patients will be presented.

Conclusions: The single tablet regimen of SOF/VEL/VOX for 12 weeks has the potential to be a safe, well tolerated and effective treatment for patients who previously failed an NS5A inhibitor-containing DAA regimen, a group that currently has no retreatment option.