Table 262.4. Clinical trial data with sofosbuvir plus daclatasvir.

Study (reference)	Number and type of patients	Duration of treatment	Outcome SVR12
BMSAI444-040 (Sulkowski *et al.*, 2014a)	211; naive, experienced, and PI failure; F4 = 15%	12 or 24 weeks	GT-1, naive, 12 weeks = **98%** GT-1, PI failure, 24 weeks =**98%** GT-2, naive, 24 weeks = **92%** GT-3, naive, 24 weeks = **89%**
ALLY-1 (Poordad *et al.*, 2016)	98; naive and experienced; GT-1; F4 = 100%	12 weeks	Child-Pugh A = **92%** Child-Pugh B = **94%** Child-Pugh C = **56%** Posttransplant = **95%**
ALLY-2 (Wyles *et al.*, 2015)	203; naive and experienced; VIH-VHC; GT-1, -2, -3; F4 = 93%	8 or 12 weeks	12 weeks, naive = **97%** 8 weeks, naive **= 76%** 12 weeks, experienced **= 98%**
ALLY-3 (Nelson *et al.*, 2015)	152; naive and experienced; GT-3; F4 = 21%	12 weeks	Naive = **90%** Naive, F4 = **57%** Experienced = **86%** Experienced, F4 = **69%**
ALLY-3+ (Leroy *et al.*, 2016)	49; naive, experienced, and decompensated cirrhosis (14); GT-3; F4 = 72%	12 or 16 weeks plus RBV	12 weeks = **88%** 16 weeks = **92%**
HEPATHER, ANRS CO-22 (Pol *et al.*, 2015a)	409; naive and experienced; GT-1; F4 = 78%	12 or 24 weeks	12 weeks = **85%** 12 weeks, RBV = **100%** 24 weeks = **93%** 24 weeks, RBV = **98%**
UK decompensated cirrhosis (Foster *et al.*, 2015b)	159; naive and experienced; GT-1, -3	12 weeks	GT-1, RBV = **82%** GT-3, RBV = **70%**
French ATU cohort (Hezode *et al.*, 2015)	284; naive, experienced, and DAA failure; GT-3; F4 = 79%	12 or 24 weeks	12 weeks, RBV = **100%** 12 weeks = **81%** 24 weeks, RBV = **81%** 24 weeks = **89%**

Abbreviations: SVR12: sustained virological response 12 weeks after cessation of therapy (a sign of cure); naive: treatment-naive patients; PI: protease inhibitor; F4: Fibroscan showing cirrhosis; GT: genotype; experienced: patients who underwent prior treatment that failed; VIH–VHC: patients with coinfection; RBV ribavirin; DAA: direct antiviral agents.

12 weeks, overall and genotype 1 SVR rates were 98.1% and 97.7%, respectively. This study showed clearly that, at least in co-infected patients, shortening treatment duration to 8 weeks was deleterious in term of efficacy.

Other studies

Comparable results were obtained among liver transplant patients with recurrences of severe HCV infection. The combination of sofosbuvir and daclatasvir with or without ribavirin for 24 weeks achieved an SVR between 91% and 100% (Fontana *et al.*, 2016; Leroy *et al.*, 2015).

Cohort studies

In the French HEPATHER cohort, 409 genotype 1 patients (79% with cirrhosis and 9% with decompensated cirrhosis) were treated with sofosbuvir and daclatasvir without ribavirin (n = 317) or with ribavirin (n = 92) for 12 (20%) or 24 (80%) weeks (Pol *et al.*, 2015a). SVR was achieved in all patients without cirrhosis whatever duration or use of ribavirin. In cirrhotic patients, SVR rates increased from 76% to 94% in patients treated without ribavirin when treatment duration was increased from 12 to 24 weeks. In a multivariate analysis in cirrhotic patients, increasing the treatment duration to 24 weeks appeared to be the most important predictive factors of response. Similar results were found in the French HIV–HCV co-infected cohort in which the SVR rate was 93% for the 64 cirrhotic patients treated with sofosbuvir and daclatasvir for 24 weeks (Sogni *et al.*, 2015).

In the UK cohort, 50 genotype 1 patients with advanced cirrhosis (mainly Child-Pugh B) were treated with sofosbuvir and daclatasvir with (n = 45) or without (n = 5) ribavirin for 12 weeks. SVR rates were 82% with and 60% without ribavirin (Foster *et al.*, 2015b).

The French CUPILT cohort enrolled 130 patients with recurrent HCV infection who were treated sofosbuvir plus daclatasvir with (42%) or without (58%) ribavirin for 12 weeks (11%) or 24 weeks (89%) (Coilly *et al.*, 2015). Among the 99 genotype 1 patients, the SVR rate was 97%.

In summary, sofosbuvir plus daclatasvir for 12 weeks in genotype 1 patients without cirrhosis and for 24 weeks in patients with cirrhosis was highly effective with no significant adverse events.