Supplementary Material*

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Table 1. Summary of clinical trial outcomes by oral DAA regimen

Study, Author, Year, Country	Target population	Study design	DAA Regimen	Summary of results	ROB
C-WORTHY **NCT 01717326** **Lawitz** **Lancet 2015**	HCV 1 Treatment naïve or experienced (null responder) With and without cirrhosis	RCT Open label Phase 2 Multicenter Total (N=471) Lawitz= 253 Sulkowski= 218	Treatment naive with cirrhosis GZP/EBV12w GZP/EBV + RBV 12w GZP/EBV 18w GZP/EBV + RBV 18w Treatment experienced w/without cirrhosis GZP/EBV 12w GZP/ EBV + RBV 12w GZP/EBV 18w GZP/EBV + RBV 18w	GZP/EBV for 12 weeks achieved high SVR rates in GT1 infected treatment naïve patients with cirrhosis (>90%) and treatment experienced patients without cirrhosis (>94%). The addition of RBV or extension of treatment did not significantly increase SVR rates but it did increase the risk of AEs.	Moderate (Merck)
Sulkowski **Lancet 2015**	HCV 1, Treatment naive Without cirrhosis. With and without HIV coinfection		Monoinfected GZP/EBV +RBV 8w GZP/EBV +RBV 12w GZP/ EBV 12w HIV Coinfected GZP/ EBV +RBV 12w GZP/ EBV 12w	GZP/EBV for 12 weeks achieved higher SVR rates than an 8 week regimen in monoinfected patients (93% vs 80%). In HIV co-infected patients without cirrhosis, the addition of RBV yielded higher SVR rates (97 vs 87%). Treatment was in general safe and did not interfere with permissible antiretrovirals.	Low (Merck)
C-EDGE **NCT 02105467** **Zeuzem** **Annals 2015**	HCV 1, 4, & 6 Treatment naïve With and without cirrhosis HCV 1-4-6* Treatment naïve	RCT Phase 3 Total (N= 639) Zeuzem= 421	GZP/EBV 12w Placebo + Deferred treatment GZP/EBV 12w	GZP/EBV for 12 weeks achieved high SVR rates (>92%) across multiple HCV genotypes in treatment naïve patients, with and without cirrhosis. Treatment was well tolerated. GZP/EBV for 12 weeks achieved high SVR rates (96%) across multiple HCV genotypes in HIV co-infected, treatment naïve, patients with and without cirrhosis. Treatment was well tolerated.	Moderate (Merck) Moderate (Merck)
Rockstroh **Lancet 2015**	With and without cirrhosis. With and without HIV coinfection	Rockstroh Open label Single arm (N= 218)			
C-EDGE TE **NCT02105701** **Kwo** **Gastroenterol ogy 2016**	HCV 1, 4, & 6 Treatment experienced With and without cirrhosis With and without HIV infection	RCT Phase 3 Open label Total N=420	GZP/EBV 12w GZP/EBV +RBV 12w GZP/ EBV 16w GZP/EBV +RBV 16w	GZP/EBV for 12 or 16 weeks achieved similar SVR (92.4%) across multiple HCV genotypes in treatment experienced, HIV uninfected and co-infected patients with and without cirrhosis. The addition of ribavirin and prolongation of therapy to 16 weeks increased SVR to 98.1% but was associated with increased rates of anemia, fatigue and nausea.	Low (Merck)
C-SURFER **NCT 02092350** **Roth** **Lancet 2015**	HCV 1 Treatment naïve CKD stage 4-5	RCT Phase 3 (N= 226) Multi Center US	GZP/EBV 12w Placebo + Deferred treatment	GZP/EBV for 12 weeks achieved high SVR rates among HCV1 infected, treatment naïve patients with CKD stage 4 and 5. Treatment was well tolerated.	Low (Merck)
Pearl 1 **NCT 01685203** **Lawitz** **Gastroenterol ogy 2015**	HCV 1b Treatment naïve or experienced With and without cirrhosis	RCT Phase 2b Open label Total N=270 HCV1b=181	Without cirrhosis TN: PTV/r/OBV + RBV 12w TE: PTV/r/OBV + RBV 12w With cirrhosis TN: PTV/r/OBV + RBV 24w TE: PTV/r/OBV + RBV 24w	PTV/r/OBV/DAV + RBV achieved high SVR rates in HCV 1b infection with or without cirrhosis including treatment naïve (98% and 95%) and treatment experienced (96% and 90%) patients. Treatment was well tolerated.	Moderate (AbbVie)

Hezode Lancet 2015	HCV 4 Treatment naïve or experienced Without cirrhosis	HCV4 (N=135) Multicenter	TN: PTV/r/OBV 12 w TN : PTV/r/OBV + RBV 12 w TE: PTV/r/OBV + RBV 12 w	PTV/r/OBV +DAV without RBV yielded high SVR rates (>91%) but increased to 100% when RBV was added both in treatment naïve and treatment experienced patients with HCV4 infection without cirrhosis. Treatment was well tolerated.	Low (AbbVie)
Pearl II **NCT 01674725** **Andreone Gastroenterology 2014**	HCV 1b Treatment experienced Without cirrhosis	RCT Phase 3 (N= 186) Multicenter	PTV/r/OBV + DAV + RBV 12 w PTV/r/OBV + DAV + Plac 12 w	PTV/r/OBV +DAV for 12 weeks yielded high SVR rates in HCV 1b treatment experienced patients without cirrhosis. The addition of RBV did not improve the outcome (100 vs 97%) but increased the incidence of AEs	Low (AbbVie)
Pearl III **NCT 01767116** **Ferenci NEJM 2014**	HCV 1b Treatment naïve Without cirrhosis	RCT Phase 3 (N= 419) Multicenter	PTV/r/OBV+ DAV + RBV 12 w PTV/r/OBV + DAV +Plac 12 w	PTV/r/OBV + DAV for 12 weeks yielded high SVR rates in treatment naïve patients with HCV1b infection without cirrhosis. The addition of RBV did not improve the outcome (99 vs 99%) but increased the incidence of AEs	Low (AbbVie)
Pearl IV **NCT 01833533** **Ferenci 2014**	HCV 1a Treatment naïve Without cirrhosis	RCT Phase 3 (N= 305) Multicenter	PTV/r/OBV + DAV + RBV 12 w PTV/r/OBV + DAV + Plac 12 w	PTV/r/OBV + DAV for 12 weeks yielded high SVR rates in treatment naïve patients with HCV1a infection without cirrhosis. The addition of RBV increased SVR rates from 90 to 97% but also increased the incidence of AEs especially anemia (42% vs 4%)	Low (AbbVie)
Sapphire I **NCT 01716585** **Feld NEJM 2014**	HCV 1 Treatment naïve Without cirrhosis	RCT Phase 3 plus open label (N=631) Multicenter	PTV/r/OBV+ DAV + RBV 12 w Placebo 12 w + Deferred treatment	PTV/r/OBV + DAV + RBV for 12 weeks yielded high SVR rates in treatment naïve patients with HCV 1a and 1b infection without cirrhosis. (96, 95 and 98%) Treatment was well tolerated.	Low (AbbVie)
Sapphire II **NCT 01715415** **Zeuzem NEJM 2014**	HCV 1 Treatment experienced Without cirrhosis	RCT Phase 3 Open label (N=394) Multicenter	PTV/r/OBV+ DAV + RBV 12 w Placebo 12 w + Deferred treatment	PTV/r/OBV + DAV + RBV for 12 weeks yielded high SVR rates (>96%) in treatment experienced 1a and 1b infected patients, without cirrhosis (96 and 97%). Treatment was well tolerated.	Low (AbbVie)
TURQUOISE I **NCT 01717326** **Sulkowski JAMA 2015**	HCV 1 With HCV/HIV coinfection	RCT Phase 2 (N= 63) Multicenter US	PTV/r/OBV+ DAV + RBV 12 w PTV/r/OBV+ DAV + RBV 24w	PTV/r/OBV+ DAV + RBV for 12 weeks yielded high SVR rates in patients co-infected with HCV and HIV (94%). Extending treatment from 12 to 24 weeks did not improve outcomes. Treatment was in general safe and did not interfere with antiretrovirals	Low (AbbVie)
TURQUOISE II **NCT 01704755** **Poordad NEJM 2014**	HCV 1 Treatment naïve and experienced With cirrhosis	RCT Phase 3 (N= 380) Multicenter	PTV/r/OBV + DAV + RBV 12w PTV/r/OBV +DAV + RBV 24w	PTV/r/OBV + DAV + RBV yielded high SVR rates in patients with HCV 1a and 1b infection. Extending treatment from 12 to 24 weeks increased SVR rates in HCV1a (87% vs 94%) but not in HCV1b (99% vs 100%) infection and was associated with increased AEs (most notably fatigue and dyspnea)	Moderate (AbbVie)
CORAL-1 **NCT 01782495** **Kwo NEJM 2014**	HCV 1 Post Liver transplant 12 months prior	RCT Phase 2 (N= 34) Multicenter	PTV/r/OBV + DAV + RBV 24 w	PTV/r/OBV/DAV + RBV for 24 weeks yielded high SVR rates in patients with recurrent HCV1 infection post liver-transplant.	Moderate (AbbVie)
RUBY-1 **NCT 02207088** **Pockros Gastroenterology 2016**	HCV 1 Treatment naïve CKD stage 4-5 Without cirrhosis	RCT Phase 3 (N= 20) Multicenter US	HCV 1a PTV/r/OBV +DAV + RBV 12 w HCV 1b PTV/r/OBV+ DAV 12 w	PTV/r/OBV + DAV+/- RBV for 12 weeks was efficacious in patients with HCV1 infection and stage 4 or 5 CKD, including those on hemodialysis (SVR 90%). RBV was interrupted in 9 of 14 patients and 4 received erythropoietin.	Moderate (AbbVie)
OPTIMIST 1 **NCT 02114177** **Kwo Hepatology 2016**	HCV 1 Treatment naïve and experienced Without cirrhosis	RCT Phase 3 Open label (N= 310) Multicenter US-Canada	SIM + SOF 8 w SIM + SOF 12 w	SIM + SOF for 12 weeks achieved higher SVR rates than 8 weeks (97 vs 83%) in treatment naïve and experienced HCV1 infected patients without cirrhosis. Treatment was well tolerated.	Low (Janssen Pharmaceuticals)

OPTIMIST 2 **NCT 02114151** **Lawitz** **Hepatology 2016**	HCV 1 Treatment naïve and experienced With cirrhosis	Open label single arm (N= 103) Multicenter US-Canada	SIM + SOF 12 w	SIM + SOF for 12 weeks achieved relatively low SVR rates in HCV1 infected treatment naïve (88%) and treatment experienced (79%) patients with cirrhosis.	Moderate (Janssen Pharmaceuticals)
Cosmos **NCT 01466790** **Lawitz** **Lancet 2014**	HCV 1 Treatment naïve and experienced With and without cirrhosis	RCT Phase 2 (N= 168) Multicenter US	SIM + SOF 12 w SIM + SOF + RBV 12 w SIM + SOF 24 w SIM + SOF + RBV 24 w	SIM + SOF for 12 weeks achieved high SVR rates in HCV1a (95%) and HCV1b (100%) treatment naïve and treatment experienced HCV 1 infected patients..	Moderate (Janssen Pharmaceuticals)
OSIRIS **NCT 02278419** **El-Raziky** **J Viral Hep 2016**	HCV 4 Treatment Naïve and Experienced	RCT Open label Phase 2 (N=63) Multicenter Egypt	Non cirrhotic SIM + SOF 8 weeks SIM + SOF 12 weeks Cirrhotic SIM + SOF	SIM + SOF for 12 weeks was associated with high SVR rates (100%) in HCV 4 regardless of treatment experience or cirrhosis status. SIM + SOF for 8 weeks was associated with lower SVR rates in HCV 4 (75%). Treatment was well tolerated	Moderate (Janssen Pharmaceuticals)
AI444040 **NCT 01359644** **Sulkowski** **NEJM 2015**	HCV 1, 2 and 3 Treatment naïve and experienced Without cirrhosis	RCT Open label (N=211) Multicenter US	HCV1-N: DCV + SOF 23w HCV1-N: – DCV + SOF 24w HCV1-N: DCV + SOF+ RBV 24w HCV1 -TE: –DCV+ SOF 24w HCV1 -TE: –DCV + SOF + RBV 24w HCV 2/3–N: –DCV +SOF 24w HCV 2/3–N: -DCV +SOF+RBV 24w	DCV + SOF for 24 weeks yielded high SVRs in patients with HCV1 treatment naïve or treatment experienced and HCV2 or 3 without cirrhosis (up to 100%). The addition of RBV does not improve the outcomes but increases the risk of AEs.	Moderate (Bristol-Myers Squibb & Gilead)
ALLY-1 **NCT02032875** **Poordad** **Hepatology 2016**	HCV 1-4 and 6 Pre and Post Liver transplant	Open label Single arm (N= 113) Multi Center US	Advanced Cirrhosis DCV+ SOF + RBV 12 w Post-Transplant DCV + SOF + RBV 12 w	DCV + SOF+ RBV for 12 weeks achieved high SVR rates across multiple HCV genotypes among patients with post-liver transplantation HCV recurrence or advanced cirrhosis and was well tolerated	Moderate (Bristol Myers Squibb)
ALLY-2 **NCT 02032888** **Wyles** **NEJM**	HCV 1-4 and HIV co-infection Treatment naïve and experienced	Open label RCT (N= 203) Multicenter US	TN: DCV + SOF 8w TN: DCV + SOF 12w TE: DCV + SOF 12w	DCV + SOF for 12 weeks achieved higher SVR rates across multiple HCV genotypes among treatment naïve (97%) and treatment experienced (98%) patients with HIV co-infection compared to 8 weeks of treatment (76%).	Moderate (Bristol Myers Squibb)
ALLY-3 **NCT 02032901** **Nelson** **Hepatology 2015**	HCV 3 Treatment naïve and experienced With and without cirrhosis	Open label Single arm (N= 152) Multicenter	TN : DCV + SOF 12 w TE: DCV + SOF 12 w	DCV + SOF for 12 weeks achieved high SVR rates in among treatment naïve (90%) or treatment experienced (86%) patients with cirrhosis. Treatment was well tolerated.	Moderate (Gilead)
ALLY 3 Plus **NCT 02319031** **Leroy** **Hepatology 2016**	HCV 3 Treatment naïve and experienced With advanced fibrosis including cirrhosis	RCT Phase 3 Open label (N= 50) Multicenter	DCV+ SOF + RBV 12 w DCV + SOF + RBV 16 w	DCV + SOF + RBV for 12 weeks achieved high SVR rates in patients with HCV3 infection in previously treated (88%) with cirrhosis (83%) and advanced fibrosis (100%). Increased length of treatment did not improve outcomes. Treatment was well tolerated.	Moderate (Bristol Myers Squibb)
LONESTAR **NCT 01726517** **Lawitz** **Lancet 2014**	HCV 1 Treatment naïve and experienced With and without cirrhosis	RCT Phase 2 (N= 100) Single center US	TN: LDV/SOF 8 w TN: LDV/SOF + RBV 8 w TN: LDV/SOF 12 w TE: LDV/SOF 12 w TE: LDV/SOF + RBV 12 w	LDV/SOF with or without RBV yielded high SVR rates (>95%) in treatment naïve and experienced patients with HCV1 infection.	Low (Gilead)
ION-1 **NCT 01701401** **Afdhal,** **NEJM 2014**	HCV1 Treatment naïve With and without cirrhosis	RCT Phase 3 Open label (N=865) Multicenter	LDV/SOF 12 w LDV/SOF + RBV 12 w LDV/SOF 24 w LDV/SOF + RBV 24 w	LDV/SOF with or without RBV yielded high SVR rates (>97%) in patients with HCV1 (a and b) infection with and without cirrhosis. The addition of RBV and the extension of the treatment duration increased the risk of AEs	Moderate (Gilead)

ION-2 **NCT 01768286** **Afdhal,** **NEJM 2014**	HCV 1 Treatment experienced With and without cirrhosis	RCT Phase 3 Open label (N= 440) Multicenter US	LDV/SOF 12 w LDV/SOF + RBV 12 w LDV/SOF 24 w LDV/SOF + RBV 24 w	LDV/SOF with or without RBV, yielded high SVRs (>94%) in treatment experienced patients with HCV1 (a and b) infection. Patients with cirrhosis may have a better response with longer treatments (86 and 82% vs 100%)	Moderate (Gilead)
ION-3 **NCT 01851330** **Kowdley** **NEJM 2014**	HCV 1 Treatment naïve Without cirrhosis.	RCT Phase 3 (N= 647) Multicenter US	LDV/SOF 8 w LDV/SOF + RBV 8 w LDV/SOF 12 w	LDV/SOF with or without RBV yielded high SVRs (>92%) in patients with HCV1 (a and b) infection without cirrhosis. The addition of RBV increases the risk and severity of AEs	Moderate (Gilead)
ION-4 **NCT02073656** **Naggie** **NEJM 2015**	HCV 1-4 HIV co-infected Treatment naïve and experienced With and without cirrhosis	Open label single arm (N= 335) Multicenter	LDV/SOF 12 w	LDV/SOF yielded high SVR rates (96%) in patients with HCV1 (a and b) infection and HIV co-infection. Treatment was in general safe and did not interfere with antiretrovirals	Moderate (Gilead)
SIRIUS **NCT 01965535** **Bourliere** **Lancet 2015**	HCV 1 Treatment experienced With cirrhosis	RCT Phase 2 (N= 155) Multicenter France	LDV/SOF 24 w LDV/SOF + RBV 12 w	LDV/SOF for 24 weeks yielded high SVR rates (97%). LDV/SOF + RBV for 12 weeks yielded similar SVR rates (96%) among treatment experienced patients with HCV genotype1 infection with cirrhosis. The incidence of AEs was comparable.	Low (Gilead)
Gane **NCT 01826981.** **Gastroenterology 2015**	HCV 3 and 6 Treatment naïve and experienced With and without cirrhosis	RCT Phase 3 Open label (N= 126) Multicenter NZ	HCV3 TN: LDV/SOF 12 w TN: LDV/SOF + RBV 12 w TE: LDVSOF + RBV 12 w HCV 6 TN/TE: LDV/SOF 12 w	Patients with HCV genotype 3 infection benefited from the addition of RBV to LDV/SOF (SVR from 64% to 100% in treatment naïve population, 82% in treatment experienced) Patients with HCV6 infection had high response without RBV (96%) SVR not reported by cirrhosis status	Low (Gilead)
Kohli **NCT 01805882** **Lancet 2014**	HCV 4 Treatment naïve and experienced, With and without cirrhosis	Open label Single arm (N= 24) Single center US	LDV/SOF 12 w	LDV/SOF is overall effective (SVRs >95%) among both treatment naïve and experienced patients with HCV genotype 4 infection. Treatment is well tolerated. SVR not reported by cirrhosis status	Moderate (NIH + Cooperative Research Development Agreement with Gilead)
Abergel **NCT 02081079** **Hepatology 2016**	HCV 4 Treatment naïve and experienced With and without cirrhosis	Open label Single arm (N=44) Multicenter France	LDV/SOF 12 w	LDV/SOF is overall effective (SVRs 93%) among both treatment naïve and experienced patients with HCV genotype 4 infection. Treatment is well tolerated.	Moderate (Gilead Sciences)
Lancet 2016	HCV 5 Treatment naïve and experienced With and without cirrhosis	Open label Single arm (N= 41) Multicenter France	LDV/SOF 12 w	LDV/SOF is overall effective in patients with HCV genotype 5 infection among both treatment naïve and experienced patients (SVR 95%), but less so in patients with cirrhosis (89% vs 97%) Treatment is well tolerated.	Moderate (Gilead)
Charlton **SOLAR-1** **NCT 01938430** **Gastroenterology 2015**	HCV 1 and 4 Advanced liver disease Pre and post liver transplant	RCT Phase 2 Open label (N= 337) Multicenter US	LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w 10 arms CTP classes A,B,C Pre and Post-transplant-	LDV/SOF + RBV for 12 or 24 weeks achieved high SVR rates in patients with advanced liver disease and decompensated cirrhosis before liver transplantation (SVR >87%). SVR remained high after liver transplantation in patients without decompensated cirrhosis, but was much lower among post-liver transplant patients with decompensated liver disease. Treatment did not interfere with immunosuppressive management	Low (Gilead)
SOLAR-2 **NCT 02010255** **Manns** **Lancet 2016**	HCV 1 and 4 Advanced liver disease Pre and post liver transplantation	RCT Phase 2 Open label (N= 333) Multicenter	LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w 10 arms CTP classes A,B,C Pre vs Post-transplant-	LDV/SOF+ RBV for 12 or 24 weeks achieved high SVR rates in patients with advanced liver disease and decompensated cirrhosis before liver transplantation(SVR >85%). SVR remained high after liver transplantation in patients without decompensated cirrhosis, but was much lower among post-liver transplant patients with	Low (Gilead)

				decompensated liver disease. Treatment did not interfere with immunosuppressive management	
ASTRAL 1 **NCT 02201940** **Feld** **NEJM 2015**	HCV 1, 2,4 and 6 Treatment naïve and experienced With and without cirrhosis	RCT Phase 3 (N= 706) Multicenter	VEL/SOF 12w Placebo + Deferred treatment	VEL/SOF for 12 weeks achieved high SVR rates across multiple HCV genotypes among treatment naïve and experienced patients, with and without cirrhosis. Treatment was well tolerated.	Low (Gilead)
ASTRAL 2 **NCT 02220998** **Foster** **NEJM 2015**	HCV 2 Treatment naïve and experienced With and without cirrhosis	RCT Phase 3 (N= 266) Multi Center US	VEL/SOF 12w SOF + RBV 12w	VEL/SOF achieved higher SVR rates than SOF + RBV (99 vs 94%) in treatment naïve and experienced patients with HCV2 infection, with and without cirrhosis	Low (Gilead)
ASTRAL 3 **NCT 02201953** **Foster** **NEJM 2015**	HCV 3 Treatment naïve and experienced With and without cirrhosis	RCT Phase 3 (N= 552) Multicenter	VEL/SOF 12w SOF + RBV 24w	VEL/SOF for 12 weeks achieved higher SVR rates than SOF + RBV for 24 weeks (95 vs 80%) in treatment naïve and experienced patients with HCV3 infection with and without cirrhosis and was associated with fewer AEs.	Low (Gilead)
ASTRAL 4 **NCT 02201901** **Curry** **NEJM 2015**	HCV 1-6 decompensated cirrhosis (Child Pugh class B)	RCT Phase 3 N= 267) Multi Center US	VEL/SOF 12w VEL/SOF + RBV 12w VEL/SOF 24w	VEL/SOF + RBV for 12 weeks achieved high SVR rates across multiple HCV genotypes within patients with decompensated cirrhosis. Lower SVRs were seen for patients with HCV 3 infection. Treatment was well tolerated.	Moderate (Gilead)

HCV = Hepatitis C Virus; RCT = Randomized Control Trial; TN = Treatment Naïve; TE = Treatment experienced; CTP = Child Turcotte Pugh; GZP = Grazoprevir; EBV = Elbasvir; RBV = Ribavirin; PTV/r = Paritaprevir/Ritonavir; OBV = Ombitasvir; DAV = Dasabuvir; SOF = Sofosbuvir; SIM = Simeprevir; DCV = Daclatasvir; LDV = Ledipasvir; VEL = Velpatasvir; AEs = Adverse events

Table 2. Follow up and adverse event summary table by clinical trial and oral DAA regimen

Study, Author, Year, Country	Target population	DAA Regimen	Patients enrolled/lost to follow up	Serious AEs	Fatigue	Headache	Anemia	Nausea	Rash
C-WORTHY	HCV 1	Treatment Naive With cirrhosis					Hb >8.5 <10 g/dl	NR	NR
NCT 01717326	Treatment naïve or	GZP/EBV12w	29/ 0	2 (7)	5 (17)	5 (17)	0		
	experienced	GZP/EBV + RBV 12w	31/ 0	0	9 (29)	2 (6)	5 (16)		
Lawitz	With and without	GZP/EBV 18w	31/ 0	0	5 (16)	10 (32)	0		
Lancet 2015	cirrhosis	GZP/EBV + RBV 18w	32/ 1	1 (3)	9 (29)	11 (34)	2 (6)		
		Treatment Experienced With/Without					0		
		cirrhosis	33/ 0	1(3)	9 (27)	6 (18)	1 (3)		
		GZP/EBV 12w	32/ 2	2 (6)	6 (19)	9 (28)	0		
		GZP/EBV + RBV 12w	32/ 0	1 (3)	8 (25)	10 (31)	3 (9)		
		GZP/EBV 18w	33/ 0	0	15 (45)	6 (18)			
		GZP/EBV + RBV 18w							
Sulkowski	HCV 1 Treatment	Monoinfected					Hb >8.5 <10 g/dl		NR
Lancet 2015	naive	GZP/EBV +RBV 8w	30/1	0	14 (47)	7 (23)	1 (3)	8 (27)	
	Without cirrhosis.	GZP/ EBV +RBV 12w	85/3	1 (1)	23 (27)	17 (20)	8 (10)	16 (19)	
	With and without HIV coinfection	GZP/EBV 12w	44/0	0	10 (23)	15 (35)	0	7 (16)	
		Coinfected		1 (3)	2 (7)	4 (14)	1 (3)	0	
		GZP/EBV +RBV 12w	29/0	1 (3)	2 (7)	1 (3)	0	1 (3)	
		GZP/EBV 12w	30/2						
C-EDGE	HCV 1, 4, & 6						Anemia (total)		
	Treatment naïve	GZP/EBV 12w	316/4	9(3)	49(16)	52(17)	9 (1.1%)	NR	NR
Zeuzem	With and without	Placebo + Deferred treatment	105/0	3(3)	18(17)	19(18)	4 (4%)		
Annals 2015	cirrhosis								
Rockstroh	HCV 1-4-6*	GZP/EBV 12w	218/1	2 (1)	29 (13)	27 (12)	0	20 (9)	NR
Lancet 2015	Treatment naïve								
	With and without cirrhosis.								
	With HIV coinfection								
C-EDGE TE	HCV 1, 4, & 6	GZP/EBV 12w	105/2	4 (4)	20 (19)	22 (21)	0 (0)	9 (9)	NR
NCT 02105701	Treatment experienced	GZP/EBV +RBV 12w	104/0	3 (3)	28 (27)	21 (20)	12 (12)	15 (14)	
Kwo	With and without	GZP/ EBV 16w	105/1	3 (3)	17 (16)	20 (19)	0 (0)	4 (4)	
Gastroenterology	cirrhosis	GZP/EBV +RBV 16w	106/2	4 (4)	32 (30)	20 (19)	17 (16)	18 (17)	
2016	With and without HIV infection								
C-SURFER	HCV 1						Hb < 8.5 g/dl		
NCT 02092350	Treatment naïve	GZP/EBV 12w	111/4	16 (15)	11 (10)	19 (17)	5 (4.5)	17 (15)	NR
Roth	CKD stage 4-5	Placebo + Deferred treatment	113/1	19 (17)	17 (15)	19 (17)	5 (4.4)	18 (16)	
Lancet 2015									
Pearl 1	HCV 1b	Without cirrhosis					Hb <8 g/dl		
NCT 01685203	Treatment naïve or	TN: PTV/r/OBV + RBV 12w	42/2	1 (2.4)	6 (14)	14 (33)	0	8 (19)	7 (16.7)
	experienced	TE: PTV/r-OB + RBV 12w	40/0	1 (2.5)	0	10 (25)	0	0	0
Lawitz	With and without	With cirrhosis							
Gastroenterology	cirrhosis	TN: PTV/r/OBV+ RBV 24w	47/1	3 (6.4)	4 (8)	9 (19)	1 (1)	5 (11)	1 (1)
2015		TE: PTV/r-OBV + RBV 24w	52/0	0	6 (11)	9 (17	1 (2)	5 (10)	1 (2.1)

Hezode Lancet 2015	HCV 4 Treatment naïve or experienced Without cirrhosis	UT: PTV/r/OBV 12 w UT : PTV/r/OBV+ RBV 12 w T: PTV/r/OBV+ RBV 12 w	44 /1 42/ 0 49/ 0	1 (2) 0 0	3(7) 5(12) 9(18)	13(30) 14 (33) 14 (29)	Hb <10 g/dl 1 (2) 2 (4) 1 (2)	4 (9) 7 (17) 6 (12)	NR
Pearl II **NCT 01674725** **Andreone Gastroenterology 2014**	HCV 1b Treatment naive Without cirrhosis	PTV/r/OBV + DAV+ RBV 12 w PTV/r/OBV + DAV + Plac 12 w	91/0 95/0	2 (2) 2 (2)	29 (32) 15 (16) P = 0.02	22 (24) 22 (23)	Hb <ULN 37 (42) 5 (5) P<0.001	19 (21) 6 (6)	8 (9) 1 (1)
Pearl III **NCT 01767116** **Ferenci NEJM 2014**	HCV 1b Treatment naïve Without cirrhosis	PTV/r/OBV + DAV + RBV 12 w PTV/r/OBV + DAV + Plac 12 w	210/1 209/1	2 (1) 1 (0.5)	45 (21) 48 (23)	51 (24) 49 (23)	Hb <ULN 106/207 (51) 7/205 (3.4) P<0.001 Hb <10 g/dl 19 (9) 0 (-) P<0.001	23 (11) 9 (4)	NR
Pearl IV **NCT 01833533** **Ferenci 2014**	HCV 1a Treatment naïve Without cirrhosis	PTV/r-OBV + DAV + RBV 12 w PTV/r-OBV + DAV + Plac 12 w	100/0 205/5	2 (2) 4 (2)	46 (46) 72 (35)	25 (25) 58 (23)	Hb <ULN 42/100 (42) 8/203 (4) P<0.001 Hb <10 g/dl 4 (4) 0 (-) P= 0.01	21 (21) 28 (14)	NR
Sapphire I **NCT 01716585** **Feld NEJM 2014**	HCV 1 Treatment naïve Without cirrhosis	PTV/r/OBV + DAV + RBV 12 w Placebo + Deferred treatment	473/5 158/0	10 (2.1) 0	164 (35) 45 (28)	156 (33) 42 (27)	Grade 3-4 0 0	112 (24) 21 (13)	51 (11) 9 (6)
Sapphire II **NCT 01715415** **Zeuzem NEJM 2014**	HCV 1 Treatment experienced Without cirrhosis	PTV/r/OBV + DAV + RBV 12 w Placebo + Deferred treatment	297/2 97/1	6 (2) 1 (1)	99 (33) 22 (23)	108 (36) 34 (35)	Grade 3-4 1/296 (0.3) 0	60 (20) 17 (17)	NR
TURQUOISE I **NCT 01717326** **Sulkowski JAMA 2015**	HCV 1 and HCV/HIV coinfection	PTV/r/OBV+ DAV+ RBV 12 w PTV/r/OBV+ DAV + RBV 24w	31/1 32/0	0 0	18 (58) 12 (38)	6 (19) 4 (13)	Hb 10 g/dl 4 (13) 3 (9)	5 (16) 6 (19)	NR
TURQUOISE II **NCT 01704755** **Poordad NEJM 2014**	HCV 1 Treatment naïve and experienced With cirrhosis	PTV/r/OBV +DAV + RBV 12w PTV/r /OBV + DAV + RBV 24w	208/0 172/3	13 (6) – 1 death 8 (5) - 0 death	68 (33) 80 (46)	58 (28) 53 (31)	Grade 3-4 abnormality 3 (1.5) 1 (0.6)	37 (18) 35 (20)	23 (11) 25 (14)
CORAL-1 **NCT 01782495** **Kwo NEJM 2014**	HCV Post liver transplant 12 months prior	PTV/r/OBV+ DAV+ RBV 24 w	34/0	2 (6)	17 (50)	15 (40)	Grade 3 Hb 1 (3)	8 (24)	7 (21)

RUBY-1 **NCT 02207088** **Pockros** **Gastroenterology 2016**	HCV 1 Treatment naïve CKD stage 4-5 Without cirrhosis	HCV 1a PTV/r/OBV+ DAV+ RBV 12 w HCV 1b PTV/r/OBV+ DAV 12 w	13/0 7/0	3 (23) 1 (14)	5 (38) 2 (29)	3 (23) 0 (-)	Hb Grade 2 7 (54) 2 (29) Hb Grade 3 1 (8) 0 (0)	5 (38) 0 (-)	NR
OPTIMIST 1 **NCT 02114177** **Kwo** **Hepatology 2016**	HCV 1 Treatment naïve and experienced Without cirrhosis	SIM +SOF 8 w SIM + SOF 12 w	155/2 155/2	3 (2) 1 (1)	23 (15) 19 (12)	26 (17) 22 (14)	NR	14 (9) 23 (15)	12 (8) 10 (6)
OPTIMIST 2 **NCT 02114151** **Lawitz** **Hepatology 2016**	HCV 1 Treatment naïve and experienced With cirrhosis	SIM + SOF 12 w	103/3	5 (5) 1 death	21 (20)	21 (20)	NR	11 (11)	16 (16)
Cosmos **NCT 01466790** **Lawitz** **Lancet 2014**	HCV 1 Treatment naïve and experienced	SIM + SOF 12 w SIM + SOF + RBV 12 w SIM + SOF 24 w SIM + SOF+ RBV 24 w	28/1 54/1 31/1 54/4	0 0 1 (3) 3(6)	NR	NR	0 7(13) 1 (3) 16 (30)	NR	3(11) 11(20) 5(16) 10(19)
OSIRIS **Raziky** **J Viral Hep 2016**	HCV 4 Treatment Naïve and Experienced	Non cirrhotic SIM + SOF 8 weeks SIM + SOF 12 weeks Cirrhotic SIM + SOF 12 weeks	20/0 20/0 23/0	0 0 1 (4)	1 (5) 3 (15) 1 (4)	2 (10) 1 (5) 5(22)	NR	NR	NR
AI444040 **NCT 01359644** **Sulkowski** **NEJM 2015**	HCV 1, 2 and 3 Treatment naïve and experienced Without cirrhosis	<u>TN x 24 weeks</u> Grp A GT 1 SOF 7d+DCV+ SOF 23w And Grp B GT2/3 SOF 7d then DCV +SOF 23w Grp C GT 1 DCV + SOF 24w and Grp D GT 2/3DCV + SOF 24w Grp E GT 1 DCV + SOF + RBV 24w and Grp F GT 2/3 DCV + SOF + RBV 24w <u>HCV 1 TN x 12 weeks</u> Grp G GT 1 DCV + SOF 12w' Grp H DCV + SOF+RBV 12w Treatment experienced <u>HCV1 –TE</u> Grp I DCV + SOF 24w Grp J DAC + SOF + RBV 24w	31/0 28/0 29/1 41/0 41/0 21/0 20/0	2(6) 4(14) 2(7) 1(2) 0 0 1(5)	9(29) 14(50) 9(31) 16(39) 15(37) 6(29) 9(45)	5(16) 8(29) 11(38) 14(34) 9(22) 7(33) 7(35)	0 0 3 (10) 0 7(17) 0 3(15)	5(16) 9(32) 9(31) 8(20) 8(20) 0 2(10)	3(10) 4(14) 1(3) 0 6(15) 0 2(10)
ALLY-1 **NCT02032875** **Poordad** **Hepatology**	HCV 1-4 and 6 Pre and Post liver transplant	Advanced cirrhosis DCV +SOF+ RBV 12 w Post-Transplant DCV +SOF + RBV 12 w	60/0 53/0	10 (17) 5 (9) No deaths	11 (18) 15 (28)	9 (15) 19 (36)	Hgb < 9 5 (8) 2 (4)	10 (17) 3 (6)	NR
ALLY-2 **NCT 02032888** **Wyles** **NEJM**	HCV 1-4 Treatment naïve and experienced WITH HIV co-infection	TN: DCV + SOF 8w TN: DCV+ SOF 12w TE: DCV + SOF 12w	50/1 101/1 52/0	0 1 (1) 3 (6)	5 (10) 19 (19) 10 (19)	3 (6) 12 (12) 8 (15)	NR	4(8) 14(14) 8(15)	0 6 (6) 3 (6)

ALLY-3	HCV 3						Hgb < 9		
NCT 02032901	Treatment naïve and	TN: DCV + SOF 12 w	101/0	1 (1)	29 (19)	30 (20)	0	18 (12)	NR
Nelson	experienced	TE: DCV + SOF 12 w	51/0						
Hepatology 2015	With or without cirrhosis								
ALLY 3 Plus	HCV 3			2 (8)			Grade 3-4		
NCT02319031	Treatment naïve and	DCV + SOF+ RBV 12 w	24/1	1 death	6 (25)	7 (29)	0 (-)	NR	NR
Leroy	experienced	DCV + SOF+ RBV 16 w	26/0	3 (11)	7 (27)	5 (19)	1 (4)		
Hepatology 2016	With advanced fibrosis including cirrhosis			0 deaths					
LONESTAR	HCV 1	TN: LDV/SOF 8 w	20/0	0	NR	2 (10)	NR		2 (10)
NCT 01726517	Treatment naïve and	TN: LDV/SOF + RBV 8 w	21/0	1 (5)		3 (14)			3 (14)
Lawitz	experienced	TN: LDV/SOF 12 w	19/1	1 (5)		0			0
Lancet 2014	With and without	TE : LDV-SOF 12 w	19/0	1 (5)		1 (5)			1 (5)
	cirrhosis	TE: LDV-SOF + RBV 12 w	21/0	1 (5)		1 (5)			1 (5)
ION-1	HCV1						Hb (<10 g/dl)		
NCT 01701401	Treatment naïve	LDV/SOF 12 w	214/ 2	1 (<1)	44 (21)	53 (25)	0 (-)	24 (11)	16 (7)
Afdhal,	With and without	LDV/SOF + RBV 12 w	217/ 4	7 (3)	79 (36)	49 (23)	20 (9)	37 (17)	21 (10)
NEJM 2014	cirrhosis	LDV/SOF 24 w	217/ 2	18 (8)	53 (24)	54 (25)	0 (-)	29 (13)	16 (7)
		LDV/SOF + RBV 24 w	217 /2	7 (3)	82 (38)	65 (30)	16 (7)	32 (15)	27 (12)
ION-2	HCV 1						Hb (<10 g/dl)		
NCT 01768286	Treatment experienced	LDV/SOF 12 w	109/0	0	23 (21)	28 (26)	0 (-)	13 (12)	2 (2)
Afdhal,	With and without	LDV/SOF + RBV 12 w	111/0	0	45 (41)	26 (23)	2 (2)	20 (18)	11 (10)
NEJM 2014	cirrhosis	LDV/SOF 24 w	109/2	6 (6)	26 (24)	25 (23)	0 (-)	7 (6)	6 (6)
		LDV/SOF + RBV 24 w	111/1	3 (3)	50 (45)	35 (32)	9 (8)	25 (23)	16 (14)
ION-3	HCV 1						Hb (<10 g/dl)		
NCT 01851330	Treatment naïve	LDV/SOF 8 w	215/ 1	4 (2)	45 (21)	30 (14)	0 (-)	15 (7)	3 (1)
Kowdley	Without cirrhosis	LDV/SOF + RBV 8 w	216/ 5	1 (<1)	75 (35)	54 (25)	11 (5)	38 (18)	19 (9)
NEJM 2014		LDV/SOF 12 w	216/ 7	5 (2)	49 (23)	33 (15)	1 (<1)	24 (11)	5 (2)
ION-4	HCV 1-4	LDV/SOF 12 w	335/1	8 (2)	71 (21)	83 (25)	NR	33 (10)	NR
NCT02073656	Treatment naïve and experienced								
Naggie	With and without cirrhosis								
NEJM 2015	With HIV co-infection								
SIRIUS	HCV 1						Hb (<10 g/dl)		
NCT 01965535	Treatment naive	LDV/SOF 24 w	78/0	8 (10)	15 (19)	31 (40	1 (1)	8 (10)	4 (5)
Bourliere	With cirrhosis	LDV/SOF + RBV 12 w	77/0	4 (5)	7 (9)	21 (27)	2 (3)	14 (18)	12 (16)
Lancet 2015									
Gane	HCV 3 and 6	HCV3					Hgb < 9		
NCT 01826981.	Treatment naïve and	TN- LDV/SOF 12 w	25/0	4 (16)	5 (20	10 (40)	0	9 (36)	1 (4)
Gastroenterology	experienced	TN – LDV/SOF + RBV 12 w	26/0	0 (-)	2 (8)	8 (31)	5 (19)	4 (15)	1 (4)
2015	With and without	TE – LDV/SOF + RBV 12 w	50/0	1 (2)	13 (26)	13 (26)	3 (6)	5 (10)	7 (14)
	cirrhosis	HCV 6	25/0						
		TN/TE – LDV/SOF 12 w		1 (4)	6 (24)	2 (8)	0	0	2 (8)
				No deaths					

Kohli **NCT 01805882** **Lancet 2014**	HCV 4 Treatment naïve and experienced With and without cirrhosis	LDV/ SOF 12 w	21/1	0	3 (14)	NR	NR	2 (10)	NR
Abergel **NCT 02081079** **Hepatology 2016**	HCV 4 Treatment naïve and experienced With and without cirrhosis	LDV/ SOF 12 w	44/0	0	9 (20)	11 (25)	1 (2)	4 (9)	NR
Abergel **NCT 02081079** **Lancet 2016**	HCV 5 Treatment naïve and experienced With and without cirrhosis	LDV/SOF 12 w	41/0	1 (2)	4 (10)	11 (27)	1 (2)	NR	NR
Charlton **SOLAR-1** **NCT 01938430** **Gastroenterology 2015**	HCV 1-4 Advanced liver disease Pre and post liver transplant	Pre transplant- CTP B LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Pre transplant- CTP C LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- No Cirrhosis LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPA LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPB LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPC LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- FCH LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w	 30/0 29/2 23/1 26/3 55/0 56/2 26/1 25/1 26/1 26/2 5/0 4/0 4/0 2/0	 3(10) 10(34) 6(26) 11(42) 6 (11) 12(21) 3 (12) 4 (16) 5 (19) 11(42) 1(20) 3(75) 1 (25) 1(50)	NR	NR	NR	NR	NR
Manns **SOLAR-2** **NCT 02010255** **Lancet 2016**	HCV 1 and 4 Advanced liver disease Pre and Post liver transplant	Pre transplant- CTP B LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Pre transplant- CTP C LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- No Cirrhosis LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPA LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPB LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPC LDV/SOF + RBV 12 w	 28/1 28/3 25/5 26/3 52/0 49/0 34/0 33/0 22/1 23/0 3/0	 3 (11) 6(21) 13(52) 9(35) 9(17) 5(10) 3(9) 7(21) 5(23) 6(26) 1(33)	Death 0 0 1 (4) 3 (12) 1(2) 0 1(3) 0 1(5) 0 1(33)	NR	0 1(4) 3(12) 3(12) 2(4) 1(2) 0 3(9) 2(9) 4(17) 1(33)	NR	0 0 0 0 0 0 0 0 1(5) 0 0

		LDV/SOF + RBV 24 w	5/0	2 (40)	1(20)		0		0
		Post-transplant- FCH							
		LDV/SOF + RBV 12 w	3/0	2(67)	0		0		0
		LDV/SOF + RBV 24 w	3/1	1(50)	0		0		0
ASTRAL 1	HCV 1, 2,4 and 6						Hb <10 g/dl		NR
NCT 02201940	Treatment naïve and	VEL/SOF 12w	624/2	15 (2)	126 (20)	182 (29)	2 (<1)	75 (12)	
Feld	experienced	Placebo + Deferred treatment	116/0	0	23 (20)	33 (28)	0 (-)	13 (11)	
NEJM 2015	With and without cirrhosis								
ASTRAL 2	HCV 2						Hb <10 g/dl		
NCT 02220998	Treatment naïve and	VEL/SOF 12w	134/0	2 (1)	20 (15)	24 (18)	0 (-)	14 (10)	NR
Foster	experienced	SOF - RBV 12w	132/2	2 (2)	47 (36)	29 (22)	6 (5)	19 (14)	
NEJM 2015	With and without cirrhosis								
ASTRAL 3	HCV 3						Hb <10 g/dl		
NCT 02201953	Treatment naïve and	VEL/SOF 12w	277/2	6 (2)	71 (26)	90 (32)	0 (-)	46 (17)	NR
Foster	experienced	SOF - RBV 24w	275/6	15 (2)	105 (38)	89 (32)	10 (4)	58 (21)	
NEJM 2015	With and without cirrhosis								
ASTRAL 4	HCV 1-6						Hb <10 g/dl		
NCT 02201901	Decompensated	VEL/SOF 12w	90/1	17 (19)	23 (26)	23 (26)	7 (8)	22 (24)	NR
Curry	cirrhosis (CTP class	VEL/SOF- RBV 12w	87/0	14 (16)	34 (39)	18 (21)	20 (23)	22 (25)	
NEJM 2015	B)	VEL/SOF 24w	90/3	16 (18)	21 (23)	17 (19)	8 (9)	18 (20)	

HCV = Hepatitis C Virus; TN = Treatment Naïve; TE = Treatment experienced; CTP = Child-Turcotte-Pugh; GZP = Grazoprevir; EBV = Elbasvir; RBV = Ribavirin; PTV/r = Paritaprevir/Ritonavir; OBV = Ombitasvir; DAV = Dasabuvir; SOF = Sofosbuvir; SIM = Simeprevir; DCV = Daclatasvir; LDV = Ledipasvir; VEL = Velpatasvir

Table 3: Study characteristics and outcomes for HCV genotype 1 infection by clinical trial

Study	Population included	DAA Regimen	SVR12 All HCV1	SVR12 HCV1a	SVR12 HCV1b	Serious adverse events n (%)	Discontinuation (n)
C-EDGE Zeuzem Annals 2015	HCV 1, 4, & 6 Treatment naïve With and without cirrhosis	GZP/EBV 12w Placebo 12 w + Deferred treatment	NR	92% (95%CI 86-96) SVR by presence of baseline NS5A RASs Without NS5A RASs 99%(133/135) With NS5A RASs 58% (11/19)	99% (95%CI 95-100)	9(3) 3(3)	NR
C-EDGE TE Kwo Gastroenterology 2016	HCV 1, 4, & 6 Treatment experienced With and without cirrhosis With and without HIV infection	GZP/EBV 12w GZP/EBV +RBV 12w GZP/ EBV 16w GZP/EBV +RBV 16w		All Patients 92% (55/60) 93% (56/60) 94% (45/48) 100% (55/55) SVR by presence of baseline NS5A RAVs Without With 98% (49/50) 60% (6/10) 98% (50/51) 67% (6/9) 100% (42/42) 50% (3/6) 100% (49/49) 100% (6/6)	All Patients 100% (34/34) 97% (28/29) 98% (46/47) 100% (37/37) SVR by presence of baseline NS5A RAVs Without With 100%(30/30) 100% (4/4) 100% (24/24) 80% (4/5) 100% (35/35) 92% (11/12) 100% (28/28) 100% (9/9)	4 (4) 3 (3) 3 (3) 4 (4)	1 (1) 1 (1) 0 5 (5)
C-WORTHY Lawitz Lancet 2015	HCV 1 Treatment naive or experienced With and without cirrhosis	Treatment naive with cirrhosis GZP/EBV12w GZP/EBV + RBV 12w GZP/EBV 18w GZP/EBV + RBV 18w Treatment experienced W/Without cirrhosis GZP/EBV 12w GZP/EBV + RBV 12w GZP/EBV 18w GZP/EBV + RBV 18w	<u>All patients</u> 95% (95%CI 91 - 97) <u>With cirrhosis</u> 97% (95%CI 82- 100) 90% (95%CI 74-98) 94% (95%CI 79-99) 97% (95%CI 84-100) <u>Without cirrhosis</u> 91% (95%CI 76-98) 94% (95%CI 79-99) 100% (95%CI 89-100) 97% (95%CI 84-100)	Data not given for HCV1a and HCV 1b separately	Data not given for HCV1a and HCV 1b separately	2 (7) 0 0 1 (3) 1(3) 2 (6) 1 (3) 0	<u>Treatment naïve</u> 0 <u>Previously treated</u> 1
PEARL I Lawitz Gastroenterology 2015	HCV 1b Treatment naïve or experienced With and without cirrhosis	Without cirrhosis TN: PTV/r/OBV + RBV 12w TE: PTV/r/OBV + RBV 12w With cirrhosis TN: PTV/r/OBV + RBV 24w TE: PTV/r/OBV + RBV 24w	NA	NA	With cirrhosis 98% (95%CI 89-100) 96% (95%CI 87-99) Without cirrhosis 95% (95%CI 84-99) 90% (36/40; CI, 76-97)	1 1 3 2	0 0 3 0

PEARL II **Andreone** **Gastroenterology** **2014**	HCV 1b Treatment experienced Without cirrhosis	PTV/r/OBV + DAV + RBV 12w PTV/r/OBV + DAV+ Plac 12w	NA	NA	97% (95%CI 93-100) 100% (95%CI 96-100) (All without cirrhosis)	2 (2) 2 (2)	2 0
PEARL III **Ferenci** **NEJM 2014**	HCV 1b Treatment naïve Without cirrhosis	PTV/r/OBV + DAV + RBV 12w PTV/r/OBV + DAV + Plac 12w	NA	NA	99% (95%CI 99-100) 99% (95%CI 98-100) (All without cirrhosis)	2 (1) 1 (0.5)	0 0
PEARL IV **Ferenci** **NEJM 2014**	HCV 1a Treatment experienced Without cirrhosis	PTV/r/OBV + DAV + RBV 12w PTV/r/OBV + DAV + Plac 12w	NA	97% (95%CI 94-100) 90% (95%CI 87-94)	NA	2 (2) 4 (2)	0 3
SAPPHIRE I **Feld** **NEJM 2014**	HCV 1 Treatment naïve Without cirrhosis	PTV/r/OBV + DAV + RBV 12w Placebo + Deferred treatment	96% (95%CI 94-98) (All without cirrhosis)	95% (95%CI 93-99) (All without cirrhosis)	98% (95%CI 96 -100) (All without cirrhosis)	10 (2) 0	3 1
SAPPHIRE II **Zeuzem** **NEJM 2014**	HCV 1 Treatment experienced Without cirrhosis	PTV/r/OBV + DAV + RBV 12w Placebo + 12 w open label active regimen	97% (95%CI 94-98) (All without cirrhosis)	96% (95%CI 93-99) (All without cirrhosis)	97% (95%CI 94-100) (All without cirrhosis)	6 (2) 1 (1)	5 1
TURQUOISE II **Poordad** **NEJM 2014**	HCV 1 Treatment naïve and experienced With cirrhosis	PTV/r/OBV + DAV + RBV 12w PTV/r/OBV + DAV + RBV 24w	92%(95% CI 88-96) 96% (95% CI 92-99) P=0.09	88.6% 94.2%	98.5% 100%	13 (6) – 1 death 8 (5) - 0 death	NR
COSMOS Lawitz **Lancet 2014**	HCV 1 Treatment naïve and experienced	Previous non-responders METAVIR F0-F1 SIM + SOF + RBV 12 w SIM + SOF 12 w SIM + SOF + RBV 24 w SIM + SOF 24 w Non responders + TN with METAVIR score F3-F4 SIM + SOF + RBV 12 w SIM + SOF 12 w SIM + SOF + RBV 24 w SIM + SOF 24 w		Cohort 1 HCV 1a 95% (20/21) 90% (9/10) 75% (15/20) 100% (11/11) Cohort 2 HCV 1a 91% (20/22) 91% (10/11) 96% (20/23) 100% (12/12)	Cohort 1 HCV 1b 100% (6/6) 100% (4/4) 100% (4/4) 75% (3/4) Cohort 2 HCV 1b 100% (5/5) 100% (3/3) 86% (6/7) 100% (4/4)	0 0 1 (3) 3 (6)	0 0 2 (7) 2 (4)
OPTIMIST 1 **Kwo** **Hepatology 2016**	HCV 1 Treatment naïve and experienced Without cirrhosis	SIM + SOF 8 w SIM + SOF 12 w	83% (95%CI 76-89) 97% (95%CI 94-100)	79% (95%CI 72-87) 97% (95%CI 93-100)	92% (95%CI 79-98) 97% (95%CI 87-100)	1 3	0 0

OPTIMIST 2 **Lawitz** **Hepatology 2016**	HCV 1 Treatment naïve and experienced With cirrhosis	SIM + SOF 12 w	83% (95%CI 76-91) TN 88% (95% CI 78-98) TE 79% (95% CI 67-91)	83% (95% CI 74-93) Q80K present 74% (95% CI 57-90) Q80K absent 92% (95% CI 82-100)	84% (95% CI 69-98%)	5(5)	3
AI444040 **Sulkowski** **NEJM 2014**	HCV 1, 2 and 3 Treatment naïve and experienced Without cirrhosis	HCV1 - TN Grp ASOD 7d then DCV+ SOF 23w Grp C DCV + SOF 24w Grp E DCV + SOF + RBV 24w Grp G DCV + SOF 12w Grp H DCV + SOF+RBV 12w	HCV 1 TN 100% (15/15) 100% (14/14) 100% (15/15) 100% (41/41) 95% (39/41)	98% (129/132)	100% (35/35)	Unclear Unclear Unclear 1 (2) 0 0	 0 1 0 0 0
		HCV1 –TE Grp I DCV + SOF 24w Grp J DCV+ SOF + RBV 24w	HCV 1 TE 100% (21/21) 95% (19/20)			0 1(5)	0 0
LONESTAR **Lawitz** **Lancet 2014**	HCV 1 Treatment naïve and experienced With and without cirrhosis	TN LDV/SOF 8 w TN LDV/SOF + RBV 8 w TN LDV/SOF 12 w TE LDV/SOF 12 w TE LDV/SOF + RBV 12 w	95% (95%CI 75-100) 100% (95%CI 84-100) 95% (95%CI 74-100) 95% (95%CI 74-100) 95% (95%CI 84-100)	SVR not reported by subtype or cirrhosis status	SVR not reported by subtype or cirrhosis status	0 1 (5) 1 (5) 1 (5) 1 (5)	NR
ION-1 **Afdhal,** **NEJM 2014**	HCV 1 Treatment naïve With and without cirrhosis	LDV/SOF 12 w LDV/SOF + RBV 12 w LDV/SOF 24 w LDV/SOF + RBV 24 w	99% (95%CI 96-100) 97%; (95%CI 94-99) 98%; (95%CI 95-99) 99%; (95%CI 97-100) <u>With cirrhosis</u> 97% (95%CI 84- 100) 100% (95%CI 89-100) 97% (95%CI 84-100) 100% (95%CI 90-100) <u>Without cirrhosis</u> 100% (95%CI 98-100) 100% (95%CI 98-100) 99% (95%CI 97-100) 100% (95%CI 98-100)	99 % (95%CI 96-100) 100% (95%CI 97-100) 100% (95%CI 97-100) 100% (95%CI 97-100) SVR not reported by cirrhosis status on subtype	100% (95%CI 94-100) 100% (95%CI 94-100) 97% (95%CI 90-97) 100% (95%CI 95-100) SVR not reported by cirrhosis status on subtype	1 (<1) 7 (3) 18 (8) 7 (3)	0 0 4 6

ION-2 **Afdhal,** **NEJM 2014**	HCV 1 Treatment experienced With and without cirrhosis	LDV/SOF 12 w LDV/SOF + RBV 12 w LDV/SOF F 24 w LDV/SOF + RBV 24 w	94% (95%CI 87-97) 96% (95%CI 91-99) 99% (95%CI 95-99) 99% (95%CI 95-99) <u>With cirrhosis</u> 86% (95%CI 65-97) 82% (95%CI 60-95) 100% (95%CI 85-100) 100% (95%CI 85-100) <u>Without cirrhosis</u> 95% (95%CI 89- 99) 100% (95%CI 96- 100) 99% (95%CI 94- 99) 99% (95%CI 94- 99)	95% (95%CI 88- 99) 95% (95%CI 89- 99) 99% (95%CI 94- 100) 99% (95%CI 94- 100) SVR not reported by cirrhosis status on subtype	87% (95%CI 66 -97) 100% (95%CI 85-100) 100% (95%CI 86-100) 100% (95%CI 85-100) SVR not reported by cirrhosis status on subtype	0 0 6 (6) 3 (3)	0
ION-3 **Kowdley,** **NEJM 2014**	HCV 1 Treatment naïve Without cirrhosis.	LDV/SOF 8 w LDV/SOF + RBV 8 w LDV/SOF 12 w	94% (95%CI 90-97) 93% (95%CI 89-96) 95% (95%CI 92-98)	93% (95%CI 88-97) 92% (95%CI 87-96) 95% (95%CI 90 -98)	98% (95%CI 88-100) 95% (95%CI 84-99) 98% (95%CI 88-100)	4 (2) 1 (<1) 5 (2)	0 1 2
SIRIUS **Bourliere,** **Lancet 2015**	HCV 1 Treatment experienced With cirrhosis	LDV/SOF 24 w LDV/SOF + RBV 12 w	97% (95%CI 91-99) 96% (95%CI 89-99) (All without cirrhosis)	Data not given for HCV1a and HCV 1b separately	Data not given for HCV1a and HCV 1b separately	8 (10) 4 (5)	NR
ASTRAL 1 **Feld** **NEJM 2015**	HCV 1, 2,4 and 6 Treatment naïve and experienced, with and without cirrhosis	VEL/SOF 12w Placebo +Deferred treatment VEL/SOF	<u>All HCV 1</u> 98.5% (95%CI 96-99) <u>With cirrhosis</u> 99% (95%CI 95-100) <u>Without cirrhosis</u> 99% (95%CI 97-98) <u>Treatment naïve</u> 99% (95%CI 97-100) <u>Treatment Experienced</u> 99.5% (95%CI 97-100)	<u>All HCV 1a</u> 98% (95%CI 95- 99) <u>With cirrhosis</u> 100% (95%CI 93-100) <u>Without cirrhosis</u> 98% (95%CI 94-99) <u>Treatment naïve</u> 97% (95%CI 92-99) <u>Treatment Experienced</u> 100% (95%CI 95-100)	<u>All HCV 1b</u> 99% (95%CI 95- 100) <u>With cirrhosis</u> 96% (95%CI 79-100) <u>without cirrhosis</u> 100% (95%CI 96-100) <u>Treatment naïve</u> 100% (95%CI 95-100) <u>Treatment experienced</u> 97% (95%CI 84-100)	15 (2) 0	1

Table 4: Study characteristics and outcomes for HCV genotypes 2-4 infection by clinical trial

Study	Population included	DAA Regimen	SVR12 HCV2	SVR12 HCV3	SVR12 HCV4	Serious adverse events n (%)	Discontinuation (n)
OSIRIS	HCV 4	Non cirrhotic	NA	NA			0
Raziky	Treatment	SIM + SOF 8w			75% (95% CI 51-91)	0	
J. Viral hepatitis	naïve and	SIM + SOF 12w			(15/20)	0	
2016	experienced				100% (95% CI 83-100)		
	with and	Cirrhotic			(20/20)	1 (2)	
	without	SIM + SOF 12w					
	cirrhosis				100% (95% CI 85-100)		
					(23/23)		
ALLY-2	HCV 1-4 and	TN DCV + SOF 8w	83% (5/6 CI, 36-99)	67% (2/3 CI, 9-99)	NA	NR	NR
Wyles	Treatment	TN DCV + SOF 12w	100% (11/11 CI, 71-100)	100% (6/6 CI, 54-100)	100% (2/2 CI, 16-100)		
NEJM 2015	naïve and	TE DCV + SOF 12w	100% (2/2 CI, 16-100)	100% (4/4 CI, 40-100)	100% (1/1 CI, 2.5-100)		
	experienced						
	With HIV co-infection						
ALLY-3	HCV 3		NA	90% (95%CI 83-95)	NA		0
Nelson	Treatment	TN DCV + SOF 12w		86% (95%CI 74-94)			0
Hepatology 2015	naïve and	TE DCV + SOF 12w					
	experienced						
	With and without cirrhosis						
ALLY-3 +	HCV 3		NA	Advanced fibrosis/cirrhosis			
Leroy	Treatment	DCV + SOF + RBV 12w		88% (95%CI 68-97)	NA	2 (8)	0
Hepatology 2016	naïve and	DCV + SOF + RBV 16w					
	experienced			92% (95%CI 75-99)		3 11)	0
	With advanced fibrosis						
				100% (14/14) with advanced fibrosis achieved SVR			
				Among patients with cirrhosis Overall 86% (31/36) 12 weeks 83% (15/18) 16 weeks 89% (16/18)			
AI444040	HCV 1, 2 and 3	HCV2/3 TN	92% with or without RBV	89% with or without RBV	NA	Unclear	0
Sulkowski	Treatment naïve	DCV + SOF 23w	(24/26)				1
NEJM 2014	and experienced	DCV + SOF 24w					0
	without cirrhosis	DCV + SOF + RBV 24w					
ASTRAL 1	HCV 1, 2,4 and	VEL/SOF 12w	<u>All HCV 2</u>	NR	<u>All HCV 4</u>	15 (2)	1
Feld	6	Placebo +Deferred	100% (95%CI 96- 100)		100 % (95%CI 97-100)	0	
NEJM 2015	Treatment	treatment SOF+VEL					
	naïve and		<u>With cirrhosis</u>		<u>With cirrhosis</u>		
	experienced		100% (95%CI 69 -100)		100% (95%CI 87 -100)		
	With and		<u>without cirrhosis</u>		<u>Without cirrhosis</u>		
	without		100% (95%CI 96 – 100)		100% (95%CI 96-100)		

	cirrhosis		Treatment naïve 100% (95%CI 95-100) Treatment Experienced 100% (95%CI 86-100)		Treatment naïve 100%(95%CI 94-100) Treatment Experienced 100% (95%CI 93-100)		
ASTRAL 2 **Foster** **NEJM 2015**	HCV 2 Treatment naïve and experienced With and without cirrhosis	VEL/SOF 12w SOF + RBV 12w	99% (95%CI 96-100) 94% (95%CI 88-97) SVR not reported by cirrhosis status	NA	NA	2 (1) 2 (2)	1 2
ASTRAL 3 **Foster** **NEJM 2015**	HCV 3 Treatment naïve and experienced With and without cirrhosis	VEL/SOF 12w SOF + RBV 24w	NA	95% (95%CI 92-98) 80% (95%CI 75-85) With cirrhosis 91% (95%CI 83-96) 66% (95%CI 55-76) without cirrhosis 97% (95%CI 93-99) 87% (95%CI 81-92)	NA	6 (2) 15 (2)	2 9
Gane **Gastroenterology** **2015**	HCV 3 and 6 Treatment naïve and experienced With and without cirrhosis	TN LDV/SOF 12w TN LDV/SOF + RBV 12w TE LDV/SOF + RBV 12w (1 other arm for HCV6 without RBV)	NA	64% (95%CI 43-82) 100% (95%CI 87-100) 82% (95%CI 69-91) SVR not reported by cirrhosis status	NA	4 0 1	1 0 1
C-EDGE Zeuzem **Annals 2015**	HCV 1, 4, & 6 Treatment naïve With and without cirrhosis	GZP/ELB 12w Placebo 12 w + Deferred treatment	NA	NA	100% (18/18 95%CI 82 - 100)	9(3) 3(3)	NR
C-EDGE TE **Kwo** **Gastroenterology** **2016**	HCV 1, 4, & 6 Treatment experienced With and without cirrhosis With and without HIV infection	GZP/EBV 12w GZP/EBV +RBV 12w GZP/ EBV 16w GZP/EBV +RBV 16w	NA	NA	All Patients 88% (7/8) 93% (14/15) 60% (3/5) 100% (8/8) SVR by presence of baseline NS5A RAVs Without With 86%(6/7) 100% (1/1) 92% (11/12) 100% (3/3) 100% (3/3) 0% (0/2) 100% (7/7) 100% (1/1)	4 (4) 3 (3) 3 (3) 4 (4)	1 (1) 1 (1) 0 5 (5)
PEARL I **Hezode** **Lancet 2015**	HCV 4 Treatment naïve and experienced Without cirrhosis	TN PTV/r/OBV 12w TN PTV/r/OBV+ RBV 12w TE PTV/r/OBV+ RBV 12w	NA	NA	91% (95%CI 78-97) 100% (95%CI 92-100) 100% (95%CI 93-100)	2 0 0	0 0 1

Kohli Lancet 2014	HCV 4 Treatment naïve and experienced With and without cirrhosis	LDV/SOF	12w	NA	NA	95% (95%CI 76-100) SVRs not given for sub-populations separately	10 (48)	1
Abergel Hepatology 2016	HCV 4 Treatment naïve and experienced With and without cirrhosis	LDV/SOF	12w	NA	NA	93% (95% CI 81-99)	0	0

Table 5: Study characteristics and outcomes for HCV genotypes 5 and 6 infection by clinical trial

Study	Population included	DAA Regimen	SVR12 HCV5	SVR12 HCV6	Serious adverse events n (%)	Discontinuation (n)
C-EDGE Zeuzem Annals 2015	HCV 1,4,& 6 Treatment naïve With and without cirrhosis	GZP/ELB 12w Placebo 12 w to GZP + ELB 12w	NA	(8/10) 80% (95%CI 44-98)(8/10)	9(3) 3(3)	NR
C-EDGE TE Kwo Gastroenterology 2016	HCV 1, 4, & 6 Treatment experienced With and without cirrhosis With and without HIV infection	GZP/EBV 12w GZP/EBV +RBV 12w GZP/ EBV 16w GZP/EBV +RBV 16w		None none 100% (2/2) 100% (2/2)	4 (4) 3 (3) 3 (3) 4 (4)	1 (1) 1 (1) 0 5 (5)
ASTRAL 1 Feld NEJM 2015	HCV 1, 2,4 and 6 Treatment naïve and experienced, with and without cirrhosis	VEL/SOF 12w Placebo (+Deferred treatment SOF+VEL)	<u>All HCV 5</u> 97% (95%CI 85- 100) <u>With cirrhosis</u> 100% (95%CI 48 -100) <u>without cirrhosis</u> 97% (95%CI 82 – 100) <u>Treatment naïve</u> 100% (95%CI 95-100) <u>Treatment Experienced</u> 100% (95%CI 86-100)	<u>All HCV 6</u> 100% (95%CI 91 – 100) <u>HCV 6 With cirrhosis</u> 100% (95%CI 54 -100) <u>HCV 6 without cirrhosis</u> 100% (95%CI 90 – 100) <u>Treatment naïve</u> 100% (95%CI 91-100) <u>Treatment Experienced</u> 100% (95%CI 29-100)	15 (2) 0	1
Gane Gastroenterology 2015	HCV 3 and 6 Treatment naïve and experienced With and without cirrhosis	LDV /SOF 12 w (3 other arms for HCV3 with and without RBV)	NA	96% (95%CI 80-100) SVR not reported by cirrhosis status	1	0
Abergel Lancet 2016	HCV 5 Treatment naïve and experienced With and without cirrhosis	LDV /SOF 12w	95% (95%CI 83-99) <u>With cirrhosis</u> 89% (8/9) <u>without cirrhosis</u> 97% (31/32) <u>Treatment naïve</u> 95% (95%CI 76-100) <u>Treatment experienced</u> 95% (95%CI 75-100)	NA	1	0

Table 6: Study characteristics and outcomes for subpopulations by clinical trial

Study	Population included	DAA Regimen	SVR all study	SVR other		Serious adverse events n (%)	Discontinuation (n)
C-WORTHY **Sulkowski** **Lancet 2015**	HCV 1 Treatment naïve With and without cirrhosis With and without HIV coinfection	Monoinfected GZP/EBV +RBV 8w GZP/EBV +RBV 12w GZP/EBV 12w Coinfected GZP/EBV +RBV 12w GZP/EBV 12w	80% (95%CI 61-92) 93% (95%CI 85 -97) 98% (95%CI 88- 100) 97% (95%CI 82- 100) 87% (95%CI 69- 96)	NA	NA	0 1 (1) 0 1 (3) 1 (3)	0
C-EDGE **Rockstroh** **Lancet 2015**	HCV 1-4-6* Treatment naïve With and without cirrhosis With HIV coinfection	GZP/EBV 12w	96% (95%CI 93-98)	NA	NA	2 (1)	0
TURQUOISE I **Sulkowski** **JAMA 2015**	HCV 1 With HIV coinfection	PTV/r/OBV + DAV + RBV 12 w PTV/r/OBV + DAV + RBV 24 w	94% (95%CI 79-98) 91% (95%CI 76-97)	NA	NA	0 0	NR
ALLY-2 **Wyles** **NEJM**	HCV 1-4 Treatment naïve and experienced With HIV co-infection	DCV + SOF 8w (TN) DCV + SOF 12w (TN) DCV + SOF 12w (TE)	76% (95%CI 62 – 87) 97% (95%CI 92- 99) 98% (95%CI 90-100)	NA	NA	0 1 (1) 3 (6)	0 0 0
ION-4 **Naggie** **NEJM 2015**	HCV 1-4 Treatment naïve and experienced With and without cirrhosis With HIV co-infection	LDV/SOF 12 weeks	96% (95%CI 93-98)	<u>With cirrhosis</u> 66% (10/10; CI, 69 -100) <u>without cirrhosis</u> 100% (95%CI 96- 100)	NA	8 (2)	0
ASTRAL 4 **Curry** **NEJM 2015**	HCV 1-6 Decompensated cirrhosis (Child Pugh class B)	VEL/SOF 12w VEL/SOF + RBV 12w VEL/SOF 24w	<u>HCV 1a</u> 88% (95%CI 76-96) 94% (95%CI 85- 99) 93% (95%CI 82-98) <u>HCV 1b</u> 89% (95%CI 65-99) 100% (95%CI 77-100) 88% (95%CI 62-98)	<u>HCV 2</u> 100% (95%CI 40-100) 100% (95%CI 40-100) 75% (95%CI 19-99) <u>HCV 3</u> 50% (95%CI 23-77) 85% (95%CI 55-98) 50% (95%CI 21-79)	<u>HCV 4</u> 100% (95%CI 40-100) 100% (95%CI 16-100) 100% (95%CI 16-100) <u>HCV 6</u> 0 0 100% (95%CI 3-100)	17 (19) 14 (16) 16 (18)	1 4 4

SOLAR-1 Gastroenterology 2015	HCV 1/4 Advanced liver disease Pre and post liver transplant	Pre transplant- CTP B LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Pre transplant- CTP C LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- No Cirrhosis LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPA LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPB LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPC LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- FCH LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w	87% (95%CI 72-95) 89% (95%CI 74-97) 86% (95%CI 68-96) 87% (95%CI 70-96) 96% (95%CI 89-99) 98% (95%CI 92-100) 96% (95%CI 83-100) 96% (95%CI 82-100) 85% (95%CI 68-95) 88% (95%CI 73-97) 60% (95%CI 19-92) 75% (95%CI 25-99) 100% (95%CI 47-100) 100% (95%CI 22-100)	Only 5 (1%) had HCV GT 4. Data not provided separately for HCV subtypes	3 (10) 10 (34) 6 (26) 11(42) 6 (11) 12(21) 3(12) 4(16) 5(19) 11(42) 1(20) 3(75) 1(25) 1(25)	0 2 1 2 0 2 1 0 2 3 0 0 0 0
SOLAR-2 Lancet 2015	HCV 1/4 advanced liver disease Pre and post liver transplantation	Pre transplant- CTP B LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Pre transplant- CTP C LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- No Cirrhosis LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPA LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPB LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- CTPC LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w Post-transplant- FCH LDV/SOF + RBV 12 w LDV/SOF + RBV 24 w	<u>HCV 1</u> 87% (95%CI 70-96) 96% (95%CI 81-100) 85% (95%CI 66-96) 78% (95%CI 60-91) 93% (95%CI 84-98) 100% (95%CI 93-100) 100% (95%CI 91-100) 96% (95%CI 84-100) 95% (95%CI 78-100) 100% (95%CI 86-100) 50% (95%CI 3-98) 80% (95%CI 34-99) 100% (95%CI 37-100) 100% (95%CI 22-100)	<u>HCV 4</u> 67% (95%CI 14-98) 100% (95%CI 22-100) 0% (95%CI 0-95) 50% (95%CI 3-98) 100% (95%CI 65-100) 100% (95%CI 55-100) 75% (95%CI 25-99) 100% (95%CI 55-100) 100% (95%CI 22-100) 100% (95%CI 37-100) 0% (95%CI 0-95) - - -	3 (11) 6 (21) 13 (52) 9 (35) 9 (17) 5 (10 3 (9) 7 (21) 5 (23) 6 (26) 1 (33) 2 (40) 2 (67) 1 (50)	1 2 2 5 2 0 0 2 1 0 1 1 0 0
CORAL-1 Kwo NEJM 2014	HCV 1 Post liver transplant 12 months prior	PTV/r/OBV + DAV + RBV	97% (95%CI 85-100)		2 (6)	1

ALLY-1 **Poordad** **Hepatology**	HCV 1-4 and 6 Pre and Post Liver transplant	Pre Transplant DCV +SOF+ RBV 12w Post-Transplant DCV +SOF + RBV 12w	<u>All patients</u> 83% (95%CI 71-92) 94% (95%CI 84-99) <u>HCV1</u> 82% (95%CI 68-92) 95% (95%CI 84-99)	<u>HCV 1a</u> 76% (26/34) 97% (30/31) <u>HCV 1b</u> 100 (11/11) 90% (9/10) <u>HCV 2</u> 80% (4/5) 0	<u>HCV 3</u> 83% (5/6) 91% (10/11) <u>HCV 4</u> 100% (4/4) 0 <u>HCV 6</u> 0 100% (1/1)	10(17) 5(9)	1 1
C-SURFER **Roth** **Lancet 2015**	HCV 1 Treatment naïve With and without cirrhosis CKD stage 4-5	GZP/EBV 12w Placebo 12 w to GZP + ELB 12w	NR	<u>HCV1a</u> 100% (95%CI 94-100 <u>HCV1b</u> 98% (95%CI 90-100)	<u>In cirrhotic patients</u> 100% (95%CI 54-100) <u>In non-cirrhotic patients</u> 99% (95%CI 95-100)	16 (15) 19 (17)	0 5
RUBY-1 **Pockros** **Gastroenterology 2016**	HCV 1 Treatment naive Without cirrhosis CKD stage 4-5	HCV 1a PTV/r/OBV/ DAV + RBV 12w HCV 1b PTV/r/ OBV + DAV 12w	NR	<u>HCV1a</u> 85% (11/13) (+ RBV) <u>HCV1b</u> 100% (7/7) (- RBV)	NA	3 (23) 1 (14)	0 0

Table 7: Ongoing and Future Hepatitis C Oral DAA Clinical Trials

Study	Planned Study Population	Size	Start date	Estimated Primary Completion date	Main outcome
HCV Genotype3					
Efficacy and Safety of Sofosbuvir/ Velpatasvir Fixed Dose Combination (FDC) and Sofosbuvir/ Velpatasvir FDC and Ribavirin in Participants With Chronic Genotype 3 HCV Infection and Cirrhosis **NCT02781558**	HCV genotype 3 and compensated cirrhosis	200	July 2016	March 2017	SVR 12 Proportion who permanently discontinue study drug due to an adverse event
Safety and Efficacy of SOF/VEL/VOX FDC for 8 Weeks and SOF/VEL for 12 Weeks in Adults Chronic Genotype 3 HCV Infection and Cirrhosis **NCT02639338**	HCV genotype 3 Treatment naive or experienced With Cirrhosis	220	December 2015	October 2016	SVR 12 Proportion who permanently discontinue study drug due to an adverse event
HCV Genotype 2					
Efficacy and Safety of ABT-493/ABT-530 in Adults With Chronic Hepatitis C Virus (HCV) Genotype 2 Infection (ENDURANCE-2) **NCT02640482**	Treatment naive or experienced HCV genotype 2 Non-cirrhotic	321	November 2015	September 2016	SVR 12
HCV Genotype 4, 5 and 6					
A Study of Glecaprevir/Pibrentasvir in Adults With Chronic Hepatitis C Virus (HCV) Genotype 5 or 6 Infection **Non-cirrhotic x 8 weeks** **Cirrhotic x 12 weeks** **NCT02966795**	Treatment naive or experienced With or without cirrhosis	80	December 2016	January 2018	SVR 12
Efficacy and Safety of ABT-493/ABT-530 in Adults With Chronic Hepatitis C Virus Genotype 4, 5, or 6 Infection (ENDURANCE-4) **NCT02636595**	Treatment naïve or experienced Genotype 4, 5 or 6 Non-cirrhotic	130	November 2015	October 2016	SVR 12
HCV Genotypes 1-6					
Efficacy and Safety of ABT-493/ABT-530 in Adults With Chronic Hepatitis C Virus Genotype 1, 2, 4, 5 or 6 Infection and Compensated Cirrhosis (EXPEDITION-1) **NCT02642432**	HCV genotype 1,2, 4, 5 and 6 Treatment naïve or experienced Compensated Cirrhosis	175	December 2015	October 2016	SVR 12
Safety and Efficacy of Sofosbuvir/Velpatasvir/ Voxilaprevir and Sofosbuvir/Velpatasvir in Adults With Chronic HCV Infection Who Have Not Previously Received Treatment With Direct-Acting Antiviral Therapy	HCV infection Treatment naive or experienced with an interferon (IFN)-based regimen	943	November 2015	October 2016	SVR 12 Proportion who permanently discontinue study drug

(POLARIS-2) **NCT02607800**					due to an adverse event
Efficacy and Safety of Experimental Drugs ABT-493/ABT-530 in Adults With Chronic Hepatitis C Virus Genotype 1-6 Infection and Human Immunodeficiency Virus -1 Coinfection (EXPEDITION-2) **NCT02738138**	HCV GT 1-6 Treatment naïve or experienced HIV infected ART naïve CD4 >500 On stable ART CD4 >200	160	May 2016	January 2017	SVR 12
Efficacy and Safety of MK-3682 + Ruzasvir (MK-8408) x 12 weeks **NCT02956629**	HCV Genotypes 1-6 Treatment naïve and experienced With and without cirrhosis With and without HIV infection	250	November 2016	August 2017	SVR 12
Efficacy and Safety of Combinations of AL-335, Odalasvir (ODV) and Simeprevir (SMV) in the Treatment of Chronic Hepatitis C Infection **NCT02765490**	HCV genotype 1, 2, 4, 5 or 6 infected subjects without cirrhosis	300	November 2015	August 2016	SVR 12
Chronic Kidney Disease					
Efficacy and Safety of ABT-493/ABT-530 in Renally Impaired Adults With Chronic Hepatitis C Virus Genotype 1 - 6 Infection (EXPEDITION-4) **NCT02651194**	HCV genotypes 1-6 Treatment naïve or experienced With underlying chronic renal impairment	100	December 2015	October 2016	SVR 12
Decompensated Cirrhosis					
Efficacy and Safety of Sofosbuvir/ Velpatasvir ± Ribavirin for 12 Weeks in Adults With Chronic HCV Infection and Decompensated Cirrhosis **NCT02996682**	HCV infection CTP Class C	100	December 2016	March 2018	SVR 12 Proportion who permanently discontinue study drug due to an adverse event
Post liver transplant					
Pilot Study to Evaluate Efficacy of Grazoprevir + Elbasvir for 12 or 16 Weeks in Liver Transplant Recipients. (EGRADICATE) **NCT02890719**	Genotype 1 and 4 Treatment naïve or experienced Post liver transplant	30	September 2016	May 2018	SVR 12
Sofosbuvir/Velpatasvir Fixed Dose Combination in Participants With Chronic Hepatitis C Virus Infection Who Have Received a Liver Transplant **NCT02781571**	HCV genotype 1, 2, 3, 4, 5, 6, or indeterminate ≥ 3 months post-liver transplant with chronic HCV reoccurrence	80	July 2016	March 2017	SVR 12 Proportion who permanently discontinue study drug due to an adverse event
Safety and Efficacy of ABT-493/ABT-530 in Adult Post-Liver or Post-Renal Transplant Recipients With Chronic Hepatitis C Virus (MAGELLAN-2)	Post liver/renal transplant HCV Genotypes 1-6	90	April 2016	March 2017	SVR 12

NCT02692703 **HIV Co-infection** **Efficacy and Safety of Experimental Drugs ABT-493/ABT-530 in Adults With Chronic Hepatitis C Virus Genotype 1-6 Infection and Human Immunodeficiency Virus -1 Coinfection (EXPEDITION-2)** **NCT02738138**	HCV GT 1-6 Treatment naïve or experienced HIV infected ART naïve CD4 >500 On stable ART CD4 >200	160	May 2016	January 2017	SVR 12
Oral Direct Acting Agent Failures **Safety and Efficacy of Sofosbuvir/Velpatasvir/ Voxilaprevir Fixed-Dose Combination With or Without Ribavirin in Participants With Chronic Genotype 1 HCV Infection Previously Treated With a Direct Acting Antiviral Regimen** **NCT02536313**	HCV genotype 1 Treatment experienced with oral direct acting agent	49	July 2015	March 2016	SVR 12 Proportion who permanently discontinue study drug due to an adverse event
Safety and Efficacy of Sofosbuvir/Velpatasvir/ Voxilaprevir in Adults With Chronic HCV Infection Who Have Previously Received Treatment With Direct-Acting Antiviral Therapy (POLARIS-1) **NCT02607735**	HCV infection Treatment experienced with oral direct acting agent	416	November 2015	October 2016	SVR 12 Proportion who permanently discontinue study drug due to an adverse event
Safety, Tolerability and Efficacy of Sofosbuvir, Velpatasvir, and GS-9857 for 12 weeks in Subjects With Previous DAA Experience **NCT02745535**	GT 1a and b With and without Previously failed Viekira Pak or Harvoni	120	March 2016	December 2016	SVR 12 Grade 3 and 4 adverse events
Efficacy and Safety of MK-3682B (MK-5172 + MK-3682 + MK-8408) Fixed Dose Combination in Chronic HCV Participants Failing Prior Antiviral Treatment (MK-3682-021) **NCT02613403**	HCV GT1 or GT3 Who Have Failed a Direct Acting Antiviral Regimen	200	December 2015	June 2018	SVR 12
Safety and Efficacy of SOF/VEL/VOX FDC for 12 Weeks and SOF/VEL for 12 Weeks in DAA-Experienced Adults With Chronic HCV Infection Who Have Not Received an NS5A Inhibitor **NCT02639247**	Chronic HCV infection (≥ 6 months) Treatment experienced with a direct acting antiviral medication not including a NS5A Inhibitor for HCV	333	December 2015	October 2016	SVR 12 Proportion who permanently discontinue study drug due to an adverse event

Table 8: Risk of bias assessment based on the Cochrane Risk of Bias tool for Randomized Controlled Trials

Study	Sequence generation	Allocation scheme concealed	Blinding	Incomplete outcome data	Selective reporting	Other biases	Overall Risk of Bias
LONE STAR	Low	Low	Low	Low	Low	Low	Low
ION-1	Unclear	Unclear	High	Low	Low	Low	Moderate
ION-2	Unclear	Unclear	High	Low	Low	Low	Moderate
ION-3	Low	Unclear	Unclear	Low	Low	Low	Moderate
SIRIUS	Low	Low	Low	Low	Low	Low	Low
Pearl II	Low	Low	Low	Low	Low	Low	Low
Pearl III	Low	Low	Low	Low	Low	Low	Low
Pearl IV	Low	Low	Low	Low	Low	Low	Low
Sapphire I	Low	Low	Low	Low	Low	Low	Low
Sapphire II	Low	Low	Low	Low	Low	Low	Low
Turquoise II	Unclear	Unclear	Unclear	Low	Low	Low	Moderate
Pearl I Hezode	Low	Low	High	Low	Low	Low	Low
Pearl I Lawitz	High	High	High	Low	Low	Low	Moderate
Cosmos	Low	Low	High	Low	High	Low	Moderate
ASTRAL-1	Low	Low	Low	Low	Low	Low	Low
ASTRAL 2	Low	Low	High	Low	Low	Low	Low
ASTRAL 3	Low	Low	High	Low	Low	Low	Low
ASTRAL 4	Unclear	Unclear	High	Low	High	Low	Moderate
C-EDGE Zeuzem	Low	Low	Low	Low	High	Low	Moderate
C-WORTHY Lawitz	Low	Low	High	Low	High	Low	Moderate
C-WORTHY Sulkowski	Low	Low	Low	Low	Low	Low	Low
TURQUOISEI Sulkowski	Low	Low	High	Low	Low	Low	Low
C-SURFER Roth	Low	Low	Low	Low	Low	Low	Low
OPTIMIST-1	Low	High	High	Low	Low	Low	Low
Gane	Low	Low	High	Low	Low	Low	Low

AI444040	Low	Unclear	High	Low	High	Low	Moderate
SOLAR 1	Low	Low	Low	Low	Low	Low	Low
SOLAR 2	Low	Low	Low	Low	Low	Low	Low
ALLY 2	Unclear	Unclear	High	Low	Low	Low	Moderate
ALLY3plus	Unclear	Unclear	High	Low	Low	Low	Moderate
C-EDGE-TE	Low	Low	High	Low	low	Low	Low
OSIRIS	Unclear	Unclear	High	Low	Low	Low	Moderate

Table 9: Risk of bias assessment based on Cochrane tool for assessment of the risk of bias in nonrandomized trials and observational studies

Study	Bias due to confounding	Bias in selection of participants into the study	Bias in measurement of interventions	Bias due to departures from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall Risk of Bias
C-EDGE Rockstrohm	N/A	N/A	Low	Low	Low	Low	low	Moderate
OPTIMIST 2	N/A	N/A	Low	Low	Low	Low	low	Moderate
ALLY-1	N/A	N/A	Low	Low	Low	Low	low	Moderate
ALLY-3	N/A	N/A	Low	Low	Low	Low	low	Moderate
ION-4	N/A	N/A	Low	Low	Low	Low	low	Moderate
Kohli	N/A	N/A	Low	Low	Low	Low	low	Moderate
Abergel GT 5	N/A	N/A	Low	Low	Low	Low	low	Moderate
Ruby 1	N/A	N/A	Low	Low	Low	Low	low	Moderate
Coral 1	N/A	N/A	Low	Low	Low	Low	low	Moderate
Abergel GT 4	N/A	N/A	Low	Low	Low	Low	Low	Moderate