Review: In chronic hepatitis C virus infection, oral direct-acting antivirals have high sustained virologic response

Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, et al. ***Oral direct-acting agent therapy for hepatitis C virus infection: a systematic review.*** *Ann Intern Med. 2017;166:637-48.*

Clinical impact ratings: HO ★★★★★☆☆ ID ★★★★★☆☆

Question

In patients with chronic hepatitis C virus (HCV) infection, what are the efficacy and safety of oral direct-acting antiviral (DAA) regimens?

Review scope

Included English-language studies assessed interferon-free treatment regimens of ≥ 2 DAAs that were approved by the US Food and Drug Administration and lasted ≥ 8 weeks in adults with chronic HCV infection, regardless of cirrhosis, HIV, or liver transplantation status. DAA combinations included inhibitors of HCV NS3 protease (grazoprevir, paritaprevir, and simeprevir), NS5A (daclatasvir, elbasvir, ledipasvir, ombitasvir, and velpatasvir), and NS5B polymerase (sofosbuvir and dasabuvir), with or without oral antiviral ribavirin. Outcomes were sustained virologic response (SVR) and adverse events.

Review methods

MEDLINE and EMBASE/Excerpta Medica (both to Nov 2016), ClinicalTrials.gov, and reference lists were searched for randomized controlled trials (RCTs) and cohort studies. 42 studies met selection criteria: 32 RCTs and 10 cohort studies. 19 RCTs had low risk for bias, and 13 had moderate risk. Comparison groups were deferred treatment (5 RCTs); varying duration of DAAs with or without ribavirin (11 RCTs); DAAs with or without ribavirin for the same duration (5 RCTs); varying duration of DAAs with ribavirin (6 RCTs) and without ribavirin (3 RCTs); or another active HCV treatment regimen (2 RCTs). Results from RCTs are presented in this abstract.

Main results

The main results for HCV genotype 1 and 3 are in the Table; SVR varied according to treatment experience, cirrhosis status, and addition of ribavirin. SVR rates for genotypes 2, 4, 5, and 6 were > 90%. Rates of serious adverse events were < 10%.

Conclusion

In patients with chronic hepatitis C virus infection, oral direct-acting antiviral regimens have high sustained virologic response rates.

Source of funding: Patient-Centered Outcomes Research Institute.

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Commentary

Of the estimated 3.5 million people in the USA infected with chronic HCV, roughly half have been diagnosed and < 10% have been successfully treated (1). The review by Falade-Nwulia and colleagues shows that we now have oral treatments of shorter duration that are simple, effective, and well-tolerated, including the combination of velpatasvir plus sofosbuvir ± ribavirin, which is effective for all 6 genotypes. There will likely be even better drugs in the near future, and vaccines are being developed, but it is now easier for primary care providers to play a major role in diagnosis and treatment of HCV. Barriers to care include access to treatment, cost, and practitioner expertise. Guidance on HCV from the American Association for the Study of Liver Diseases/Infectious Diseases Society of America is frequently updated and addresses testing and linkage to care (crucial first steps in improving health outcomes) and optimal treatment regimens in various situations (2).

Because concurrent hepatitis B infection is possible and may reactivate during HCV therapy, it is important for patients to be screened with HBsAg, HBsAb, and core Ab (3).

Even at today's outrageous prices, screening and treating *all* patients with chronic HCV would be cost-effective—and likely cost-saving—because cirrhosis, hepatocellular carcinoma, and mortality in infected persons, as well as transmission to others, can be reduced (4). However, some payers remain resistant and providers will need to be strong and vocal advocates for their patients.

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Effect of oral direct-acting antiviral (DAA) treatments on sustained virologic response (SVR) in patients with chronic hepatitis C virus (HCV) infection*

HCV genotype	DAA regimen	Number of trials (n)	SVR at 12 wk (patient group)
HCV-1	GZP-EBV	4 (1644)	≥ 92%†
	PTV-r-OBV-DAV ± RBV	10 (2702)	97% to 100% (genotype 1b); 97% (genotype 1a +RBV); 90% (genotype 1a −RBV); 87% (cirrhosis)
	SIM + SOF ± RBV	2 (478)	97% (TN); 91% (TN, cirrhosis); 79% (TE, cirrhosis)
	DCV + SOF	2 (238)	95% to 100% (TN/TE)
	LDV-SOF ± RBV	7 (2718)	≥ 95% (TN); 86% (TE, cirrhosis); 97% (TE, cirrhosis, +RBV); 85% to 87% (decompensated cirrhosis, +RBV)
	VEL-SOF ± RBV	2 (600)	> 95%†; 94% (decompensated cirrhosis, +RBV)
HCV-3	DCV + SOF ± RBV	3 (107)	94% to 95% (TN/TE); 58% to 69% (TN/TE, cirrhosis); 83% to 89% (cirrhosis, +RBV)
	LDV-SOF ± RBV	1 (26)	100% (+RBV); 64% (−RBV)
	VEL-SOF ± RBV	2 (591)	95%†; 85% (decompensated cirrhosis, +RBV); 50% (decompensated cirrhosis, −RBV)

**DAV = dasabuvir; DCV = daclatasvir; EBV = elbasvir; GZP = grazoprevir; LDV = ledipasvir; OBV = ombitasvir; PTV-r = paritaprevir-ritonavir; RBV = ribavirin; SIM = simeprevir; SOF = sofosbuvir; TE = treatment-experienced; TN = treatment-naive; VEL = velpatasvir.*

†TN/TE, with or without cirrhosis.

References

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doi:10.7326/ACPJC-2017-167-2-003

