

LONG-TERM EFFICACY OF SECOND-GENERATION DIRECT-ACTING ANTIVIRAL AGENTS (DAAs-2) FOR HCV TREATMENT:

A META-ANALYSIS



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Background

Efficacy of second generation direct-acting antiviral agents (DAAs-2) in terms of sustained viral response (SVR) 12 weeks after the end of treatment (EOT) has widely been proven¹⁻⁵; however, long-term efficacy is still controversial due to the low number of available studies with a small number of patients.



Purpose

The objective of the study is to conduct a systematic review and, if possible, a meta-analysis of existing clinical evidence in terms of long-term efficacy (SVR longer than 12 weeks after EOT) of DAAs-2 for HCV treatment.

Material and methods

A systematic review was performed with the use of CENTRAL, MEDLINE, Embase, Pubmed and SBBL-CILEA/METACRAWLER databases. Trials were initially screened by the title; secondly, full papers and abstracts were analysed. The meta-analysis included randomised controlled trials (RCTs) with adult patients affected by HCV, treated with DAAs-2 and assessed for longer than 12 weeks after EOT. Study quality assessment was undertaken using the Jadad scale. Heterogeneity analysis of the studies was conducted with chi-square and I²; the statistical analysis of the efficacy rate was performed using the meta package with the R software⁶. The effect estimate was expressed in risk ratio (RR) with 95% confidence interval (CI 95%) and pooled using a random effects model

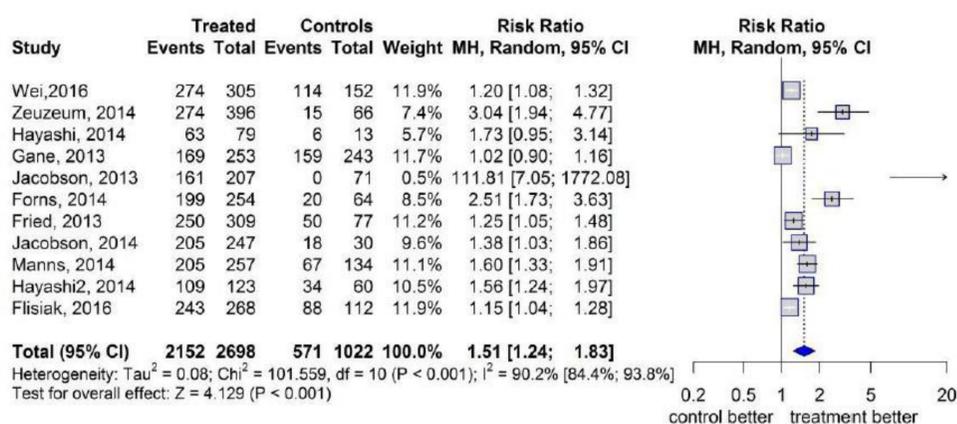


Figure 1. Meta-analysis results

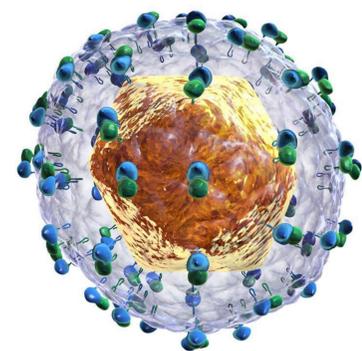


Figure 2. Hepatitis Virus C

Results

Of the 106 identified studies, 11 high quality RCTs were included for meta-analysis (25 were duplicate publications, 70 did not meet the inclusion criteria). Considered genotypes were 1 (9), 2 (1), 3 (1). Meta-analysis included 3720 patients (2698 treated with DAAs-2; 1022 treated with placebo or a first generation DAA ± Ribavirin ± PEG-interferon). Heterogeneity between studies was high (p<0.001; I²=90.2%), however it was absorbed by the model (τ²=0,08). Long-term efficacy was expressed as SVR 24 weeks after EOT, since longer timescales were not available. According to the pooled RR, the incidence of efficacy was 1.5 (CI 95%: 1.24-1.83, p<0.001).

Conclusion

The meta-analysis demonstrated that DAAs-2 for HCV treatment have long-term efficacy at SVR 24 weeks after the EOT; however, the number of studies is mostly based on genotype 1. More RCTs are required to confirm long-term efficacy at more than 6 months after EOT for all treated genotypes.

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References 1. EpaC portal 2. Statistical software R V. 3.3.3



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