Bayesian network meta-analysis to evaluate interferon-free treatments in naive patients with genotype 1 hepatitis C virus infection

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Interferon-free antiviral treatments represent the newest therapeutic option for previously untreated patients with genotype 1 hepatitis C [1,2]. In Europe, six antiviral combinations have received regulatory approval,
namely, sofosbuvir + simeprevir for 12 weeks (SOF/SIM-12 weeks), sofosbuvir + ledipasvir for 12 weeks (SOF/LED-12 weeks), sofosbuvir + daclatasvir for 12 weeks (SOF/DAC-12 weeks), ABT-450/ritonavir/ombitasvir/dasabuvir for 12 weeks (ARIOD-12 weeks) and ABT-450/ritonavir/ombitasvir/dasabuvir/ribavirin for 12 weeks (ARIODR-12 weeks).

Bayesian meta-analysis [3] is a new statistical technique for synthesis of outcome data from different sources. The typical application of this analysis is when the treatments studied in the randomized trials are inter-connected through one common comparator. However, when common comparators are not available, a modified Bayesian model [4] has been developed that retains the ability to make indirect comparisons and rank the treatments according to their effectiveness.

We carried out a Bayesian network meta-analysis of interferon-free treatments for hepatitis C virus. The trials evaluated in our analysis fulfilled the following criteria: (a) enrolment of previously untreated patients with genotype 1 infection; (b) administration of one of the combination treatments indicated above; and (c) end-point represented by sustained virologic response at week 12 after completion of treatment (SVR12). Further details of this selection process have been reported elsewhere [5].

Figure 1 shows the estimates of SVR12 achievement calculated by the modified Bayesian model (a) and the ranking histograms (b); SOF/SIM-12 weeks was not evaluated because there were seven patients in the COSMOS trial.

The median rankings estimated by our probabilistic analysis were as follows (rank 1: most effective; rank 5: least effective): SOF/LED-12 weeks, 2 [95% credible intervals (CrIs): 1–5]; SOF/LED-8 weeks, 4 (95% CrI: 2–5); SOF/DAC-12 weeks, 1 (95% CrI: 1 to 5); AROID-12 weeks, 4 (95% CrI: 2–5); and AROIDR-12 weeks, 3 (95% CrI: 1–4).

The CrIs indicate that the effectiveness data for SOF/DAC-12 weeks, SOF/LED-12 weeks and AROIDR-12 weeks are quite robust from a statistical point of view, whereas the remaining two treatments have a less predictable effectiveness (or anyhow their lower extreme of 95% CrIs is around 75–80%). Interestingly enough, the rates of SVR12 were close to 100% for three treatments (ARID-12 weeks, SOF/LED-12 weeks, SOF/DAC-12 weeks). The rates for AROID-12 weeks and SOF/LED-8 weeks were somewhat lower, and so their rankings were the worst among the five treatments.

The advantages of the Bayesian approach include the ‘all-in-one’ modelling approach, the standardization of the statistical procedures and the robustness of the results. Our study, however, had some limitations. For example, genotype 1a and genotype 1b were pooled into a single category; furthermore, our inclusion criteria did not stratify the patients according to the presence of cirrhosis.

In conclusion, despite the lack of common comparators, our analysis was successful in synthesizing the effectiveness of these five treatments according to Bayesian modelling.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

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