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Title **Direct-Acting Antiviral Agents for Chronic Hepatitis C Genotype 1**

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Reference Canadian Agency for Drugs and Technologies in Health. CADTH therapeutic review. Direct-acting antiviral agents for chronic hepatitis C genotype 1 [Internet]. Ottawa: The Agency; 2014 Oct. (CADTH Therapeutic Review vol.2, no.2b). Available from: http://www.cadth.ca/en/products/therapeutic-reviews/chronic-hep-c/reports
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Aim

To evaluate the comparable benefits, harms, and cost-effectiveness of boceprevir, telaprevir, sofosbuvir and simeprevir, combined with pegylated interferon and ribavirin (PR), for patients with genotype 1 chronic hepatitis C.

Conclusions and results

Results from the systematic review and indirect treatment comparison suggest that direct-acting antiviral agents (DAAs) in combination with PR are more effective in achieving a sustained virologic response (SVR) than 48 weeks of PR in adults with genotype 1 chronic hepatitis C infection. No DAA was found to be more effective than another in achieving SVR among treatment-naive or the overall treatment-experienced population, based on indirect comparisons.

In terms of safety, boceprevir, and telaprevir showed an increased risk of anemia relative to PR alone in treatment-naive and treatment-experienced patients, and an increased risk of rash versus PR alone in treatment-experienced patients. The indirect comparisons between DAA regimens did not consistently show an increased risk of anemia for boceprevir or telaprevir versus simeprevir. Similarly, in treatment-experienced patients, no consistent increased risk of rash was found between boceprevir or telaprevir and simeprevir. Comparative safety data for sofosbuvir were limited.

The pharmacoeconomic analysis suggests that, for all populations assessed (treatment-naive and those with prior relapse or prior partial response to PR therapy), at least one of the new DAA-based therapies appears to be economically attractive compared with PR alone. The drug that is the most cost-effective varies by population, but was generally consistent across fibrosis stages. For treatment-naive patients, simeprevir is likely to be the most cost-effective option at $32,230 per quality-adjusted life-year (QALY) gained, and for patients with genotype 1 and prior relapse, telaprevir is likely to be the most cost-effective option at $19,808 per QALY gained compared with PR therapy alone. For patients with prior partial response, treatment with boceprevir is likely to be the most cost-effective option; however, due to large degree of uncertainty around the efficacy data, there is significant uncertainty in the cost-effectiveness estimate for this population.

Recommendations

Available in a separate report from: http://www.cadth.ca/media/pdf/TR0007_HepC_RecsReport_e.pdf

Methods

Peer reviewed literature searches and consultations with experts and stakeholders were used to identify potential prospective studies evaluating DAA plus PR regimens in patients with genotype 1 hepatitis C. Two reviewers independently screened citations, selected studies according to predefined criteria, and assessed study quality of eligible studies. Direct pairwise meta-analyses and Bayesian network meta-analyses were conducted for efficacy and safety outcomes. An economic model was developed in the form of a cost-utility analysis. The primary outcome was the number of QALYs, with treatments compared in terms of the incremental cost per QALY (incremental cost-utility ratio [ICUR]).

Further research/reviews required

Considering the rapid pace of development of treatments for hepatitis C, updated and expanded therapeutic reviews will be necessary to incorporate the all-oral, interferon-free regimens that may be approved by regulatory agencies in the near future.

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