



ORIGINAL ARTICLE

Predictive variables of sustained virological response after early discontinuation of triple therapy with telaprevir for genotype-1 HCV infection



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KEYWORDS

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Early discontinuation

Abstract

Background: Pivotal phase studies of telaprevir (TLV) and boceprevir (BOV) showed 10–56% rates of early treatment interruption. However, there have been no reports on the sustained virological response (SVR) rates of these patients.

Aim: To assess the SVR rate in a large cohort of patients who discontinued triple therapy with TLV or BOV for reasons other than stopping rules and to identify variables predicting SVR.

Abbreviations: BOV, boceprevir; TLV, telaprevir; PI, protease inhibitor; RVR, rapid virological response; eRVR, extended virological response; P, pegylated-interferon; R, ribavirin; PR, pegylated-interferon plus ribavirin; SAE, severe adverse effect; ROC, receiver operating characteristics.

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Material and method: A survey was sent to 15 hospitals in Catalonia asking them to report all TLV/BOV treatments finished by 31 May 2014. Demographic, clinical, laboratory, liver fibrosis and therapeutic data were recorded for treatments with early discontinuation. Logistic regression analysis, ROC curves and prognostic assessment of the variables identified were calculated.

Results: Twelve hospitals responded to the survey, representing 467 treatments and 121 (21.2%) early discontinuations, 76 (62.8%) due to stopping rules and 45 (37.2%) for other reasons. Early discontinuation was more frequent with BOV [38.2% (50/131) versus 21.1% (71/336) $p < 0.005$], mainly due to stopping rules [78% (39/50) versus 52.1% (37/71); $p = 0.004$]. SVR was achieved in 21/121 patients (17.4%), 19/71 (26.8%) treated with TLV and 2/50 (4.0%) treated with BOV. In patients discontinuing treatment for reasons other than stopping rules, SVR was achieved in 19/37 (55.9%) treated with TLV and in 2/11 (18.2%) treated with BOV. The SVR rate in patients treated with TLV who discontinued due to a severe adverse event was 61.5% (16/26). A logistic regression analysis was performed only with triple therapy with TLV and early discontinuation. The predictive variables of SVR were undetectable HCV-RNA at treatment week 4 and treatment length longer than 11 weeks. Treatment duration longer than 11 weeks showed the best accuracy (0.794), with a positive predictive value of 0.928.

Conclusions: Early discontinuation of TLV-based triple therapy due to reasons other than stopping rules still have a significant SVR rate (55.9%). Undetectable HVC-RNA at week 4 of treatment and treatment duration longer than 11 weeks are predictive of SVR in this subset of patients.

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PALABRAS CLAVE

Telaprevir;
Boceprevir;
Respuesta virológica sostenida;
Hepatitis crónica C;
Interrupción precoz

Variables pronósticas de respuesta virológica sostenida tras la interrupción precoz del tratamiento triple con telaprevir de la infección por genotipo 1 del virus de la hepatitis C

Resumen

Antecedentes: Los estudios de registro de telaprevir (TLV) y boceprevir (BOV) han mostrado tasas de interrupción precoz del tratamiento del 10-56%, pero no se ha comunicado la respuesta virológica sostenida (RVS) de estos pacientes.

Objetivos: Analizar la RVS, y los factores predictivos de esta, en una cohorte extensa de pacientes que pararon precozmente el tratamiento triple con TLV/BOV por causas diferentes a reglas de parada.

Material y método: Se envió a 15 de hospitales de Cataluña un cuestionario relativo a los tratamientos con TLV/BOV finalizados antes del 31 de mayo de 2014, incluyendo información clínica, analítica, elastométrica y terapéutica de aquellos interrumpidos precozmente. Se realizaron análisis de regresión logística, curvas ROC y estimaciones pronósticas de las variables identificadas.

Resultados: Contestaron la encuesta 12 hospitales, sumando un total de 467 tratamientos con 121 (21,2%) interrupciones precoces del mismo, 76 (62,8%) por reglas de parada y 45 (37,2%) por otras causas. Hubo más paradas precoces en los tratamientos con BOV (38,2% [50/131] versus 21,1% [71/336]; $p < 0,005$), principalmente debidas a reglas de parada (78% [39/50] versus 52,1% [37/71]; $p = 0,004$). Alcanzaron RVS 21/121 pacientes (17,4%), 19/71 (26,8%) tratados con TLV y 2/50 (4,0%) tratados con BOV. En los pacientes que pararon el tratamiento por causas distintas a reglas de parada se alcanzó la RVS en 19/37 (55,9%) tratados con TLV y en 2/11 (18,2%) tratados con BOV. Los pacientes tratados con TLV que pararon el tratamiento por efecto adverso grave tuvieron una tasa de RVS del 61,5% (16/26). El análisis de regresión logística se hizo solo con los tratamientos triples con TLV parados precozmente. Las variables predictivas de RVS fueron el ARN-VHC indetectable en semana 4 y la duración del tratamiento mayor de 11 semanas. El mejor valor pronóstico (0,794) lo tuvo la duración total del tratamiento mayor de 11 semanas, con un VPP de 0,928.

Conclusiones: Los pacientes que paran precozmente el tratamiento triple con TLV por causas diferentes a reglas de parada conservan una tasa de RVS relevante (55,9%) en esta cohorte. El ARN-VHC indetectable en semana 4 y la duración del tratamiento mayor de 11 semanas son predictivas de RVS de este subgrupo de pacientes.

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