Poster #253

Opioid Maintenance Therapy Is Not Associated With Treatment Failure to Hepatitis C Therapy in a Large German Multicenter Cohort

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Abstract

Objective: The largest group of newly infected individuals with chronic hepatitis C in the Western World are intravenous drug users. Emerging data support treating individuals with peginterferon and ribavirin for chronic hepatitis C after stabilisation on opioid maintenance therapy (methadone or buprenorphine). However these data are based on small cohorts or substrata from trials with small patient numbers. Here we report data from a cohort of 2422 patients including 333 patients on opioid maintenance therapy.

Methods: A total of 3547 patients treated with at least one dose of peginterferon alfa-2b and weight based ribavirin are currently included in a German multicentre cohort. Only patients included in this cohort beyond 72 weeks of baseline were included in this analysis (n = 2422). Patients with missing data at week 72 were counted as treatment failures. Univariate analysis was performed for comparison of demographics in patients on opioid maintenance vs. remaining patients (age, sex, ALT, BMI, HCV-RNA, genotype, ribavirin dose, peginterferon dose). For logistic regression analysis sex, age, baseline HCV-RNA, HCV-genotype, BMI and opioid maintenance were used as independent variables. The dependent variable being HCV-RNA negative (<400 IU/mL) or positive at week 72 (SVR).

Results: Patients on opioid maintenance were younger (35.0 ± 9 vs. 42.2 ± 12 years, $P < 0.001$), and more had genotype 3 (46.0% vs. 31.4%, $P < 0.001$). HCV-RNA levels were lower (45.8% vs. 61.2% <400,000 IU/mL, $P < 0.001$). SVR in all patients on opioid maintenance (n = 333) was 64.1% vs. 56.0% in the remaining patients (n = 2089) ($P < 0.05$, univariate). In logistic regression analysis, variables positively associated with SVR were younger age, HCV-genotype 2/3 and baseline HCV-RNA <400,000 IU/mL (all $P < 0.001$). Female sex showed a trend for SVR ($P = 0.055$). Opioid maintenance therapy was not associated with treatment outcomes in the logistic regression analysis.

Conclusion: Efficacy of peginterferon and ribavirin was not different for patients on opioid maintenance therapy. Due to favourable factors for SVR such as HCV-genotype 3, younger age, and lower HCV-RNA, patients on opioid maintenance therapy showed a better unadjusted SVR compared to patients not on this therapy. Treatment of patients on opioid maintenance therapy in daily practice is feasible and success rates are not inferior to results from prospective, controlled studies.

Background

- Intravenous (IV) drug users are the largest group of individuals newly infected with the hepatitis C virus (HCV) in the Western World. Emerging data support treating these individuals with peginterferon (PEG-IFN) plus ribavirin (RBV) for chronic hepatitis C after stabilization using opioid maintenance therapy (methadone or buprenorphine). However, these data are based on small cohorts or substrata from clinical trials with small patient numbers.

Aim

- To determine sustained virologic response (SVR) rates after treatment with PEG-IFN alfa-2b (PegIntron®) and weight-based RBV among a large German multicenter cohort of HCV-infected IV drug users (N = 4130), which included 391 patients undergoing opioid maintenance therapy

Methods

Patients

- 4130 patients treated with at least 1 dose of weight-based PEG-IFN alfa-2b (1.5 µg/kg body weight) and weight-based RBV (according to the prescription label) were included in this analysis
  - — Only patients who started treatment at least 48 weeks (genotype [G] 2 or G3) or 72 weeks (G1, G4, G5, G6) before the time of this analysis were included (n = 2016)
  - — Patients with missing data at follow-up were classified as "treatment failures"

Analyses

- Univariate analysis using age, sex, alanine aminotransferase (ALT) levels, body mass index (BMI), baseline HCV RNA levels, genotype, RBV dose, and PEG-IFN dose as variables was performed for comparison of demographics in patients undergoing opioid maintenance against those not undergoing maintenance therapy
- For logistic regression analysis, independent variables were sex, age, baseline HCV RNA, genotype, BMI, and opioid maintenance; the dependent variable was SVR (HCV RNA undetectable, <400 IU/mL) or no SVR (HCV RNA detectable) at week 48 (G2/3) or 72 (G1, G4, G5, G6)

Results

Baseline Patient Characteristics

- Baseline characteristics are shown in **Table 1**
- Patients undergoing opioid maintenance therapy
  - — Were significantly younger (36.0 ± 8 years) than those not receiving maintenance therapy (42 ± 12 years; $P < .0001$)
  - — Had significantly more HCV G3 infection (51%) than those not receiving maintenance therapy (35%, $P < .0001$)
  - — Had significantly lower baseline HCV RNA levels (<600,000 IU/mL; 66%) than those not undergoing maintenance therapy (50%; $P < .0001$)

Table 1. Baseline Patient Demographics

	Patients Not Receiving Opioid Maintenance Therapy	Patients Receiving Opioid Maintenance Therapy	*P*
n	1761	255	
Female, n (%) Male, n (%)	721 (41) 1011 (57)	69 (27) 182 (72)	<.0001
Median age (range), y	42 (18-78)	36 (18-63)	<.0001
Median BMI (range), kg/m²	24.5 (11.5-49.3)	23.8 (11.5-57.4)	.002
G1, n (%)	924 (53)	91 (36)	<.0001
G2, n (%)	162 (9)	25 (10)	.73
G3, n (%)	608 (35)	130 (51)	<.0001
G4, G5, G6, n (%)	52 (3)	6 (2)	.84
Median HCV RNA (range), IU/mL	540,000 (20×10^3-860×10^6)	439,000 (48×10^3-17×10^6)	.02
HCV RNA <600,000 IU/mL, n (%)	882 (50)	167 (66)	<.0001
Normal ALT level, n (%)	203 (12)	49 (19)	.001

Sex data were missing for 33 patients.
ALT = alanine aminotransferase; BMI = body mass index; G = genotype; HCV = hepatitis C virus.

Sustained Virologic Response Rates

- SVR rate was 64% in patients undergoing opioid maintenance therapy (n = 255) and 59% in patients not receiving opioid maintenance therapy (n = 1761; $P = .133$, univariate) (**Figure 1**)
- SVR occurred more frequently in G2 or G3 patients than in G1 patients (**Figure 2**)

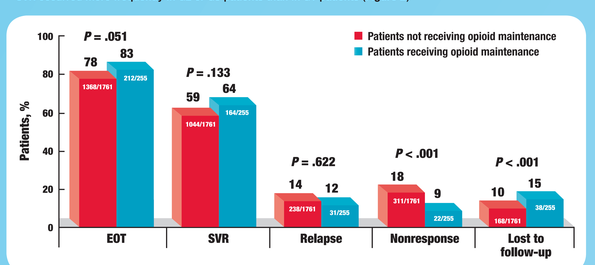

Figure 1. Efficacy of treatment with PEG-IFN alfa-2b plus RBV. EOT = end of treatment response; PEG-IFN = pegylated interferon; RBV = ribavirin; SVR = sustained virologic response.

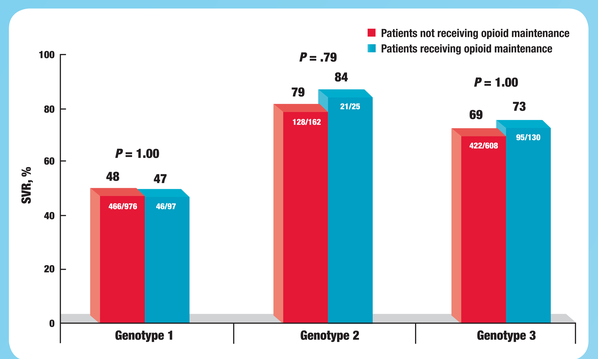

Figure 2. Efficacy of PEG-IFN alfa-2b plus RBV according to genotype. PEG-IFN = pegylated interferon; RBV = ribavirin; SVR = sustained virologic response.

Logisitic Regression Analyses

- HCV G2/3 and baseline HCV RNA <600,000 IU/mL were positively associated with SVR and older age was negatively associated with SVR (**Figure 3**)
- Female sex was not significantly associated with SVR ($P = .1$; data not shown)
- Opioid maintenance therapy was not associated with treatment outcome
- After adjusting for the effects of age, genotype, and baseline HCV RNA, the predicted probability of SVR was 71% ± 4% in patients receiving opioid maintenance and 72% ± 2% in patients not receiving opioid maintenance (**Figure 4**)

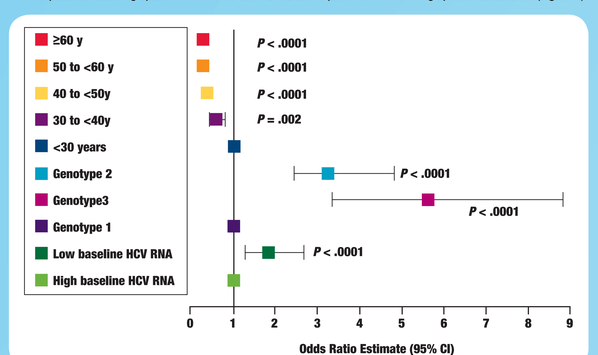

Figure 3. Logistic regression analyses: variables associated with SVR. References were age <30 years, HCV G1, and high baseline HCV RNA >600,000 IU/mL. CI = confidence interval; HCV = hepatitis C virus; SVR = sustained virologic response.

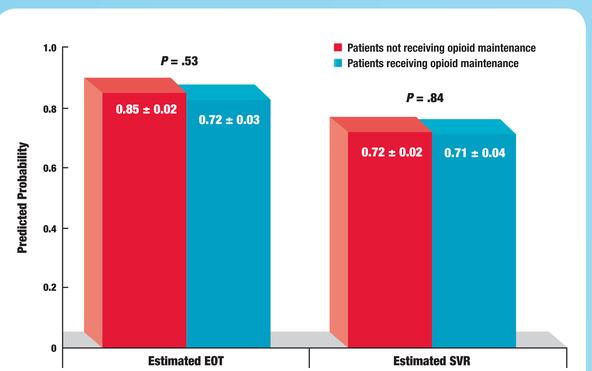

Figure 4. Predicted probability for EOT response and SVR after adjustment for age, HCV genotype, and baseline HCV RNA. EOT = end of treatment; HCV = hepatitis C virus; SVR = sustained virologic response.

Conclusions

- The efficacy of PEG-IFN alfa-2b plus RBV was not different between chronic hepatitis C patients receiving opioid maintenance therapy and patients not receiving opioid maintenance therapy.
- Because of favorable factors for SVR such as HCV G3 infection, young age, and low baseline HCV RNA, patients undergoing opioid maintenance therapy showed a trend for better unadjusted SVR rates.
- However, after adjusting for variables associated with treatment outcome (age, genotype, baseline HCV RNA), treatment outcome did not differ between patients receiving and not receiving opioid maintenance therapy.
- In conclusion, treatment of chronic hepatitis C patients undergoing opioid maintenance therapy in daily clinical practice is feasible, and success rates are not inferior to results from prospective, controlled studies.

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