Poster #816

Impaired Fasting Glucose Is Associated With Lower Rates of Sustained Virologic Response (SVR) in Patients With Genotype 1 Chronic Hepatitis C (CHC): Retrospective Analysis of the IDEAL Study

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Abstract

Background/Aims: Impaired fasting glucose is independently associated with reduced likelihood of SVR with current therapy (*NEJM*, 2009;361:580). However, the relationship between SVR, fasting blood glucose (FBG) and HBA1c has not been defined.

Methods: 3070 treatment-naive, CHC genotype 1 patients (pts) received peginterferon (PegIFN) alfa-2b or alfa-2a plus ribavirin (RBV). All pts underwent pretreatment FBG determination and were categorized by their medical history of diabetes. Based on American Diabetes Association definition, pts with FBG ≥100mg/dL were defined as having impaired fasting glucose (IFG). Per protocol, pts with known diabetes and/or FBG ≥116mg/dL underwent HBA1c testing; those with HBA1c >8.5% were excluded. Pts with FBG between 100 and 115mg/dL did not have HBA1c testing. Virologic response rates were analyzed.

Results: 3068 pts were included in the analysis. The frequency of IFG of ≥100mg/dL was 28.7% (880/3068) and of a medical history of diabetes was 6.7% (206/3068). Among those who underwent testing (n=324), median HBA1c was 6.1% (interquartile range 5.6% - 6.6%). SVR according to baseline FBG for all pts and according to HBA1c for the subset with testing are shown (Table). SVR rate was significantly lower among pts with IFG compared to those with FBG <100mg/dL (*P*<0.001); relapse rate was also higher in those with IFG. Pts with a history of diabetes had lower SVR rates than those without (21.4% [44/206] vs 41.0% [1161/2833]). However, among those tested, the SVR rate was not associated with HBA1c level (<6% vs ≥6%; *P*=0.88).

Conclusions: Impaired fasting glucose and the clinical diagnosis of diabetes were each strongly associated with lower SVR and higher relapse rates in CHC genotype 1 pts treated with PegIFN/RBV. Among those who underwent testing, no association between HBA1c level and SVR was apparent; however, pts with HBA1c >8.5% were excluded from treatment. These data suggest that FBG should be routinely assessed prior to therapy; randomized trials are needed to determine if improvement in glucose control prior to treatment will lead to improved viral response.

	SVR (%)	EOT Response (%)	Relapse (%)
Fasting Blood Glucose (pretreatment)			
All Pts (n=3068)	40	56	26
<100 mg/dL (n=2188)	43	58	22
100 – 125 mg/dL (n=747)	31	50	34
>125 mg/dL (n=133)	25	44	40
HBA1c (pretreatment)			
Pts with protocol-defined criteria of diabetes and/or FBG ≥116mg/dL (n=324)	26	45	40
<6% (n=139)	25	45	44
6 – <7% (n=133)	23	46	46
7 – 8.5% (n=52)	33	40	15

Background

- A number of previous studies have reported that insulin resistance is negatively associated with sustained virologic response (SVR) in patients receiving peginterferon alfa plus ribavirin for chronic hepatitis C (as reviewed by Harrison et al[1])
- In the IDEAL study, stepwise multivariable logistic regression analysis identified normal baseline fasting glucose as an independent predictor of SVR[2]
  - SVR rates were 42% to 44% in patients with baseline fasting glucose <5.6 mmol/L (<100 mg/dL) and 28% to 33% in those with baseline fasting glucose ≥5.6 mmol/L (≥100 mg/dL)

Aim

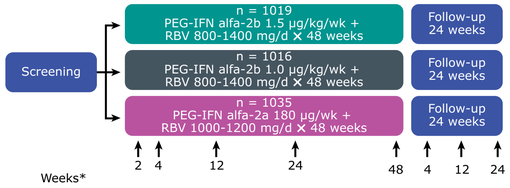
- To define the relationship between SVR, fasting blood glucose, and HbA_{1c} in patients receiving peginterferon (PEG-IFN) plus ribavirin in the IDEAL trial

Patients and Methods

Study Design

- IDEAL was a phase 3b, randomized, parallel-arm trial conducted at 118 academic and community centers in the United States (**Figure 1**)
  - PEG-IFN alfa-2b dose was double-blinded, and PEG-IFN alfa-2a and RBV were administered as open-label treatments
  - Patients with a detectable, <2-$\log_{10}$ decline in HCV-RNA at week 12, or with detectable HCV-RNA at week 24 were discontinued from treatment

Figure 1. IDEAL study design.



*HCV-RNA assessments
PEG-IFN = peginterferon; RBV = ribavirin.

Patients

- 3070 treatment-naive patients with chronic hepatitis C, genotype 1 infection, aged 18 to 70 years and weighing 40 to 125 kg

Assessments

- All patients underwent pretreatment fasting blood glucose (FBG) determination and were categorized by their medical history of diabetes
  - Based on the American Diabetes Association definition, patients with baseline FBG ≥100 mg/dL were defined as having impaired fasting glucose (IFG)
- Per protocol, patients with a medical history of diabetes and/or FBG ≥116 mg/dL underwent HbA_{1c} testing
  - Those with pretreatment baseline HbA_{1c} >8.5% were excluded from participation in the study
  - Patients with a baseline FBG <116 mg/dL did not require HbA_{1c} testing
- FBG (in all patients) and HbA_{1c} (in diabetics or those with FBG ≥116 mg/dL) levels were assessed at pretreatment baseline visit, treatment weeks 12, 24, 36, and 48, and follow-up week 24. In addition, patients with diabetes had an additional HbA_{1c} assessment at treatment week 4
- SVR was defined as undetectable HCV-RNA (lower limit of quantitation of 27 IU/mL by Roche COBAS TaqMan HCV-RNA assay) at the end of the 24-week follow-up period

Results

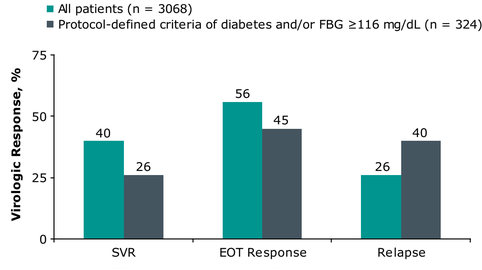
Patients

- 3068 patients were included in the analysis
  - 28.7% (880/3068) of patients had baseline FBG ≥100 mg/dL and were considered to have IFG
  - 6.7% (206/3068) of patients had a medical history of diabetes
  - Among those who underwent testing (n = 324), median HbA_{1c} was 6.1% (interquartile range, 5.6%–6.6%)

Virologic Response

- Virologic response rates were lower in patients with a medical history of diabetes and/or baseline FBG ≥116 mg/dL compared with the study population (**Figure 2**)

Figure 2. Virologic response rates in all patients and those with a medical history of diabetes and/or baseline fasting blood glucose ≥116 mg/dL.

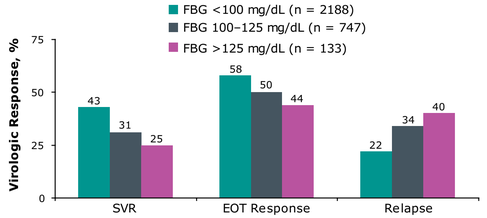


EOT = end-of-treatment; FBG = fasting blood glucose; SVR = sustained virologic response.

Virologic Response in Patients With Impaired Fasting Glucose

- SVR rate was significantly lower among patients with IFG (FBG ≥100 mg/dL) compared with those with baseline FBG <100 mg/dL (30.3% [267/880] vs 43.3% [947/2188]; *P* < .001) (**Figure 3**)
  - Relapse rate was also higher in those with IFG (34.7% [141/406] vs 22.4% [270/1203])

Figure 3. Virologic response rates according to baseline fasting blood glucose.



EOT = end-of-treatment; FBG = fasting blood glucose; SVR = sustained virologic response.

Virologic Response in Patients With Diabetes or Elevated Fasting Blood Glucose

- SVR rate for patients with diabetes and/or FBG ≥116 mg/dL was 26% (83/324)
  - End-of-treatment (EOT) response rate was 45% (145/324), with a relapse rate of 40% (56/139)
- Among this subgroup of patients, there was a trend for lower SVR rates in patients with lower baseline HbA_{1c} levels (**Table 1**)
  - However, the SVR rate was not associated with HbA_{1c} level (<6% vs ≥6%; *P* = .88)

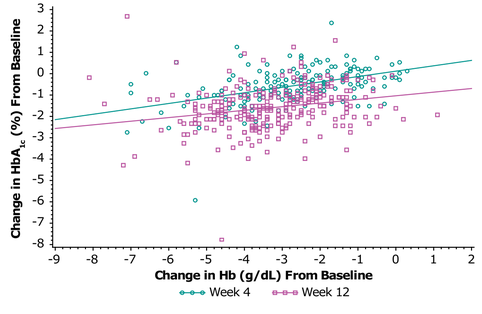
Table 1. Virologic Response Rates According to Baseline HbA_{1c} Level

	SVR, % (n/N)	EOT Response, % (n/N)	Relapse, % (n/N)
Pretreatment baseline HbA_{1c}			
<6%	25 (35/139)	45 (63/139)	44 (27/62)
6% – <7%	23 (31/133)	46 (61/133)	46 (26/57)
7% – 8.5%	33 (17/52)	40 (21/52)	15 (3/20)

EOT = end-of-treatment; SVR = sustained virologic response.

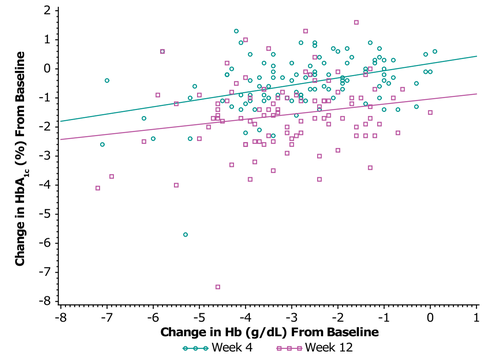
- Changes in hemoglobin (Hb) concentrations correlated with changes in HbA_{1c} levels at treatment weeks 4 (n = 170) and 12 (n = 271) (**Figure 4**)
  - Pearson correlation coefficient was estimated as 0.44 at treatment week 4
  - Pearson correlation coefficient was estimated as 0.24 at treatment week 12
  - Given a decrease in Hb of 1 g/dL, the predicted decrease of HbA_{1c} would be 0.24% at treatment week 4 and 0.16% at treatment week 12

Figure 4. Relationship between hemoglobin concentration and HbA1c at treatment weeks 4 (n = 170) and 12 (n = 271).



- Patients with a history of diabetes had a lower SVR rate than those with no history of diabetes (21.4% [44/206] vs 41.0% [1161/2833])
- For patients with both treatment-week-4 and week-12 values, changes in Hb concentrations correlated with changes in HbA_{1c} levels at treatment weeks 4 and 12 (n = 103) (**Figure 5**)
  - Pearson correlation coefficient was estimated as 0.39 at treatment week 4
  - Pearson correlation coefficient was estimated as 0.20 at treatment week 12
  - Given a decrease in Hb of 1 g/dL, the predicted decrease of HbA_{1c} would be 0.25% at treatment week 4 and 0.17% at treatment week 12

Figure 5. Relationship between hemoglobin concentration and HbA_{1c} at treatment weeks 4 and 12 for patients with values at both time points (n = 103).



Summary

- IFG and the clinical diagnosis of diabetes were each strongly associated with lower SVR and higher relapse rates
- There was no apparent association between HbA_{1c} level and SVR; however, patients with HbA_{1c} >8.5% were excluded from treatment

Conclusions

- These data suggest that FBG should be routinely assessed prior to treatment of chronic hepatitis C
  - Randomized trials are needed to determine if improvement in glucose control prior to treatment would lead to improved viral response
- Anemia may be associated with a decrease in HbA_{1c}
  - Clinicians should be aware of this relationship, and perhaps use alternative measures of glucose control (eg, fingerstick glucose monitoring and/or fructosamine)

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1. Harrison SA. *Clin Gastroenterol Hepatol*. 2008;6(8):864-76.
2. McHutchison JG, et al. *N Engl J Med*. 2009;361(6):580-93.

Disclosures

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Impaired Fasting Glu Patients With Geno

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Abstract

Background/Aims: Impaired fasting glucose is independently associated with reduced likelihood of SVR with current therapy (*NEJM*, 2009;361:580). However, the relationship between SVR, fasting blood glucose (FBG) and HBA1c has not been defined.

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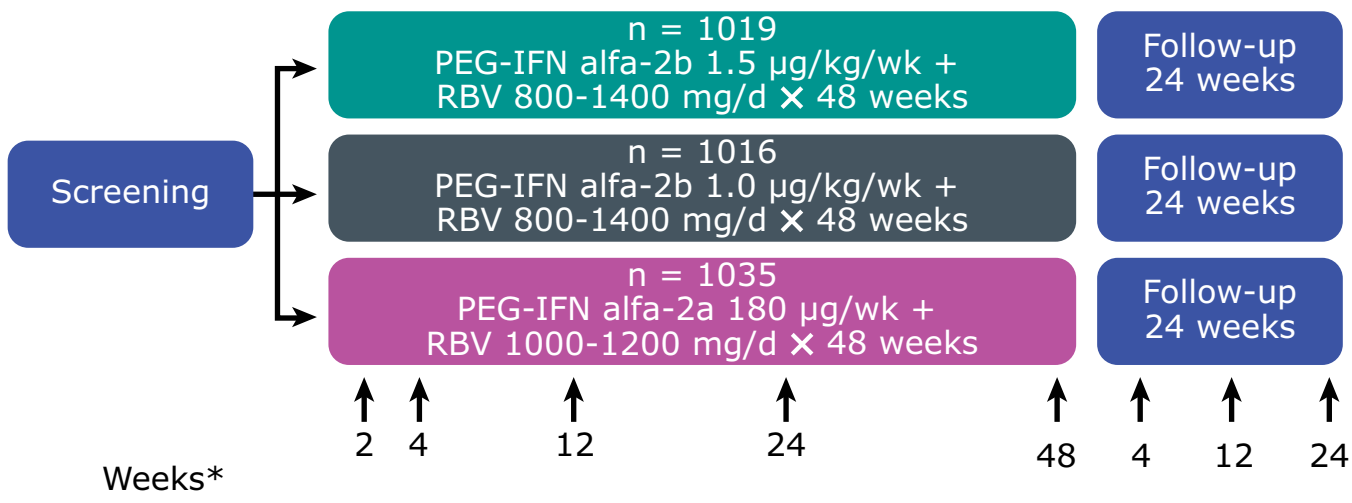

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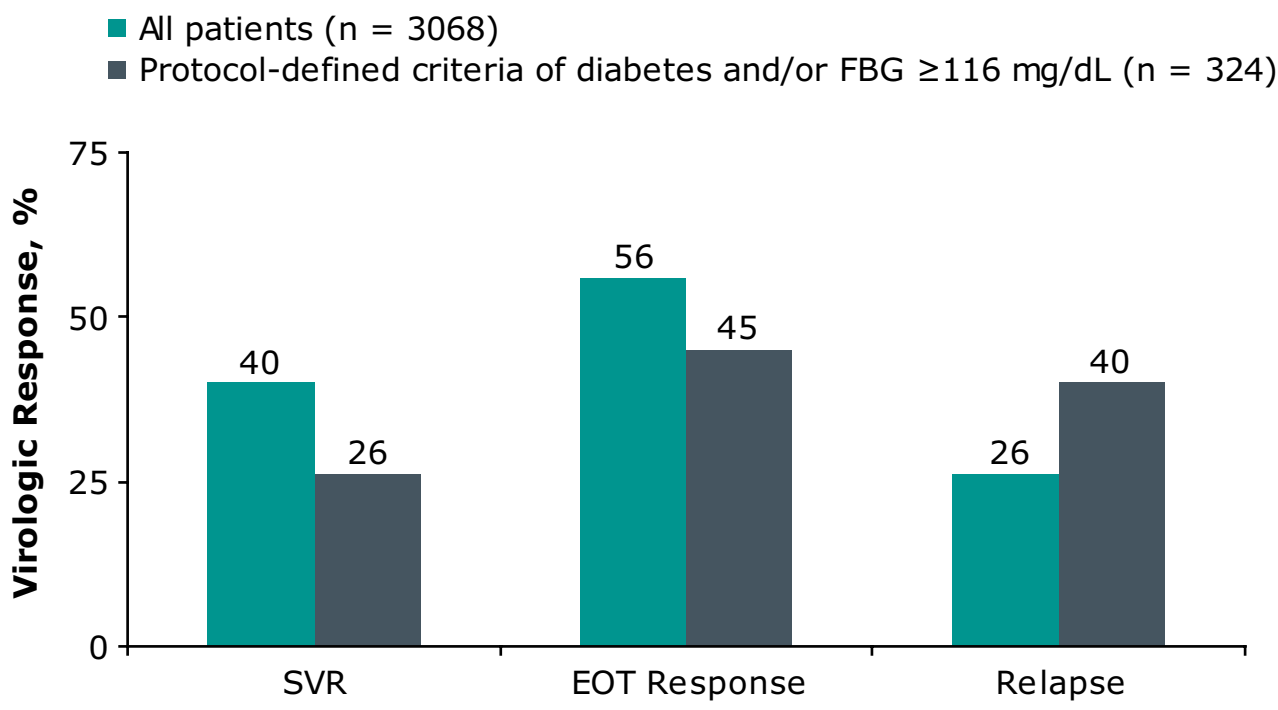

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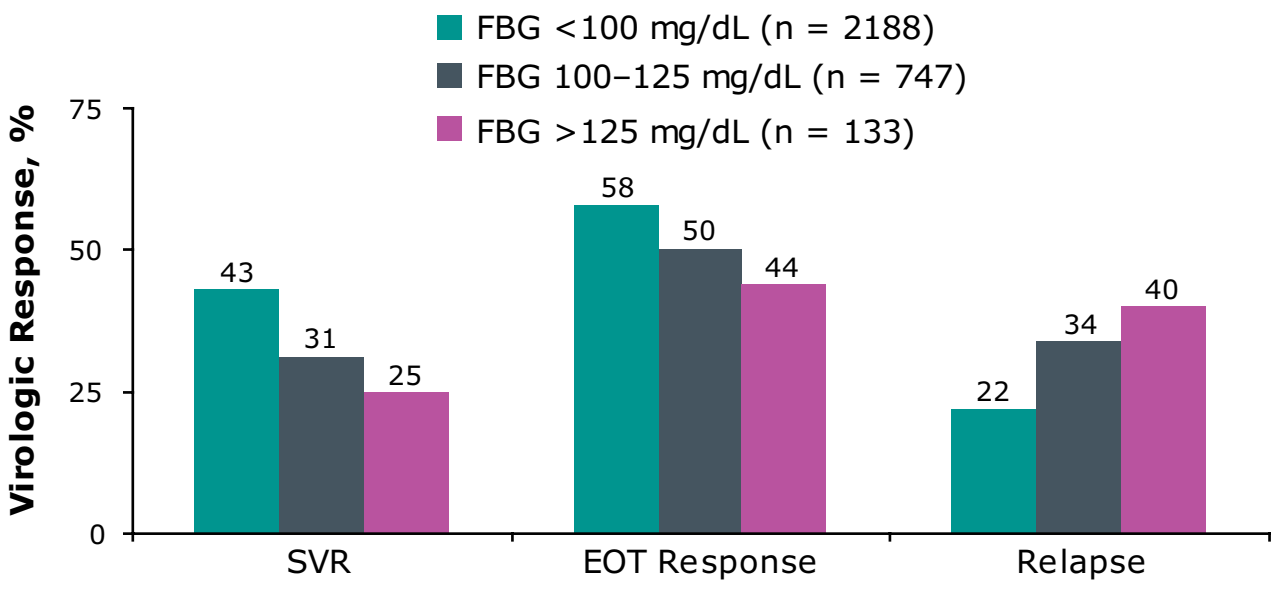

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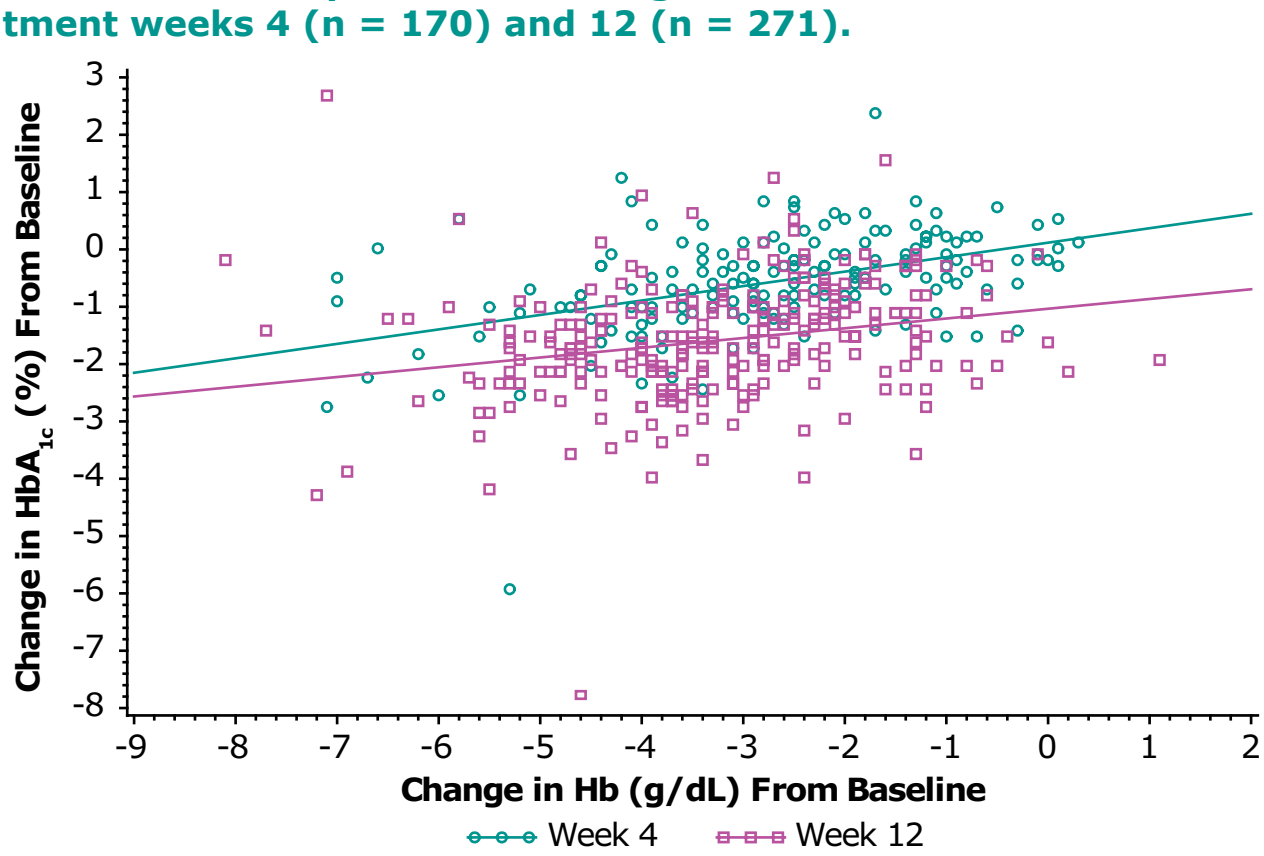
	SVR, % (n/N)	EOT Response, % (n/N)	Relapse, % (n/N)
Pretreatment baseline HbA_{1c}			
<6%	25 (35/139)	45 (63/139)	44 (27/62)
6% – <7%	23 (31/133)	46 (61/133)	46 (26/57)
7% – 8.5%	33 (17/52)	40 (21/52)	15 (3/20)

EOT = end-of-treatment; SVR = sustained virologic response.

- Changes in hemoglobin (Hb) concentrations correlated with changes in HbA_{1c} levels at treatment weeks 4 (n = 170) and 12 (n = 271) (**Figure 4**)
  - — Pearson correlation coefficient was estimated as 0.44 at treatment week 4
  - — Pearson correlation coefficient was estimated as 0.24 at treatment week 12
  - — Given a decrease in Hb of 1 g/dL, the predicted decrease of HbA_{1c} would be 0.24% at treatment week 4 and 0.16% at treatment week 12

Figure 4. Relationship between hemoglobin concentration and HbA1c at treatment weeks 4 (n = 170) and 12 (n = 271).



- Patients with a history of diabetes had a lower SVR rate than those with no history of diabetes (21.4% [44/206] vs 41.0% [1161/2833])
- For patients with both treatment-week-4 and week-12 values, changes in Hb concentrations correlated with changes in HbA_{1c} levels at treatment weeks 4 and 12 (n = 103) (**Figure 5**)
  - — Pearson correlation coefficient was estimated as 0.39 at treatment week 4
  - — Pearson correlation coefficient was estimated as 0.20 at treatment week 12
  - — Given a decrease in Hb of 1 g/dL, the predicted decrease of HbA_{1c} would be 0.25% at treatment week 4 and 0.17% at treatment week 12

gic Response (SVR) in of the IDEAL Study

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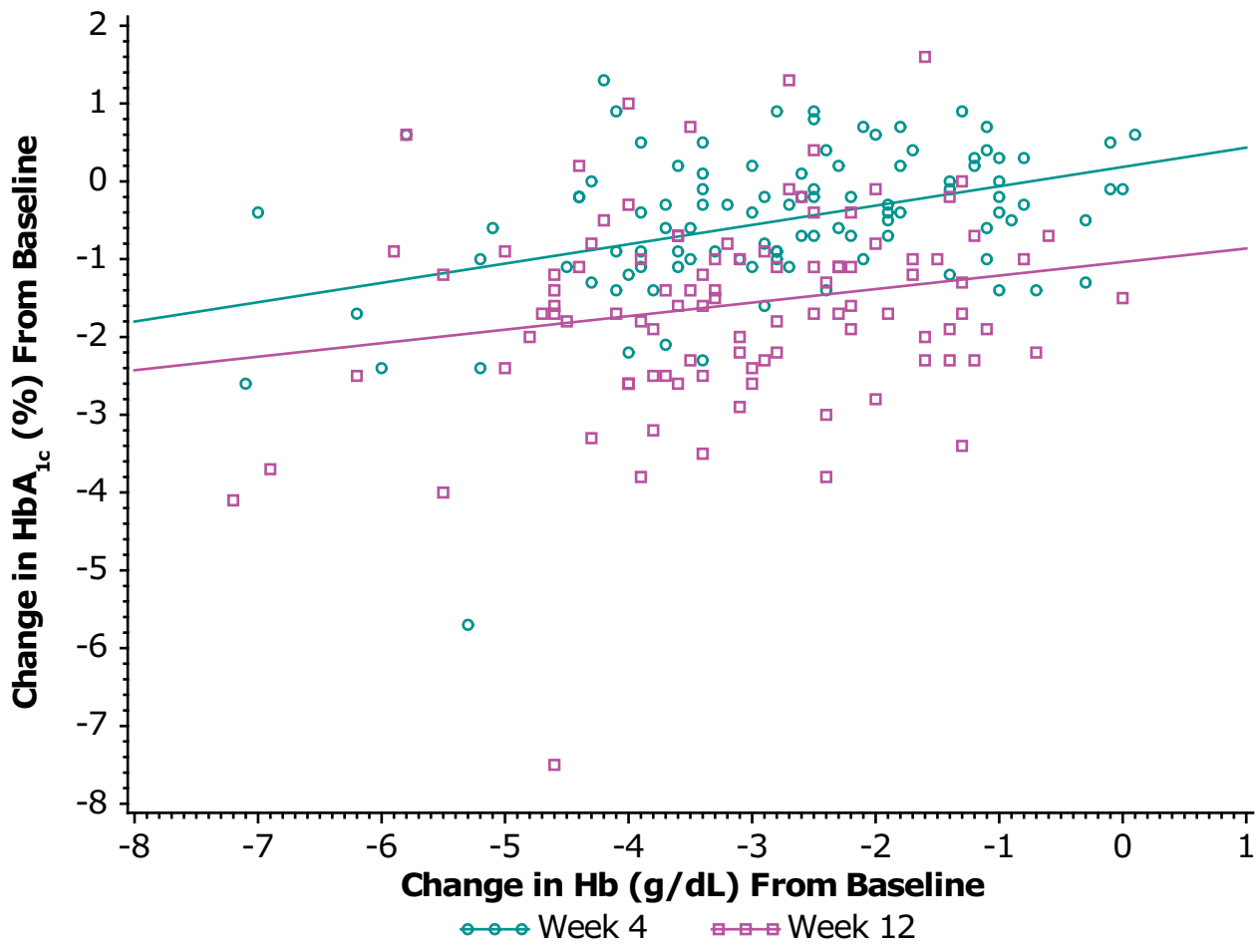
Figure 5. Relationship between hemoglobin concentration and HbA_{1c} at treatment weeks 4 and 12 for patients with values at both time points (n = 103).



Summary

- IFG and the clinical diagnosis of diabetes were each strongly associated with lower SVR and higher relapse rates
- There was no apparent association between HbA_{1c} level and SVR; however, patients with HbA_{1c} >8.5% were excluded from treatment

Conclusions

- These data suggest that FBG should be routinely assessed prior to treatment of chronic hepatitis C
  - — Randomized trials are needed to determine if improvement in glucose control prior to treatment would lead to improved viral response
- Anemia may be associated with a decrease in HbA_{1c}
  - — Clinicians should be aware of this relationship, and perhaps use alternative measures of glucose control (eg, fingerstick glucose monitoring and/or fructosamine)

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