Published in final edited form as:
Pharmacogenet Genomics. 2013 November ; 23(11): 619–623. doi:10.1097/FPC.0000000000000002.

Predictors of consent to pharmacogenomics testing in the IDEAL study

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Abstract

Pharmacogenomic (PG) testing is important in developing individualized therapeutic approaches. In the phase 3 IDEAL clinical trial, a subset of patients receiving peginterferon and ribavirin for treatment of chronic hepatitis C agreed to provide blood samples for genetic testing. Genome-wide association studies subsequently identified associations between *IL28B* polymorphism and sustained virologic response, and *ITPA* polymorphism and ribavirin-associated anemia.

Objective—To characterize the groups of patients who accepted or declined PG testing in the IDEAL study.

Methods—Clinical and demographic factors and treatment outcomes were compared at all sites that had approved PG testing. Differences between patients who consented to and declined PG testing were analyzed using Student *t* and chi-square tests.

Results—In total, 109 of 118 sites participated in the PG sub-study, and 1674 of 2949 (57%) patients enrolled at these sites consented to PG testing. More patients treated in academic medical centers than in community centers (60% vs. 52%, $P < 0.001$) provided consent. More males than females (58% vs. 54%, $P = 0.04$) consented to PG testing. There was no significant difference in PG participation between patients from different racial groups, including whites and African Americans (58% vs. 54%, $P = 0.07$). Treatment outcomes were also similar according to PG participation.

Conclusions—In the IDEAL study, patient consent to PG testing did not introduce selection bias. Treatment at an academic center and male gender were associated with higher rates of PG

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Statement of Conflict of Interest: PJC and ABJ have nothing to disclose.

testing consent. Efficacy and safety outcomes were similar in patients who accepted and declined PG testing.

Keywords

pharmacogenomics; hepatitis C; peginterferon; ribavirin

Introduction

Response to therapeutics is governed by a complex interaction of genetic and environmental factors, disease determinants, and drug pharmacodynamics and pharmacokinetics. The field of pharmacogenomics has provided valuable insight into individual variability in response to therapeutic agents; however, large cohorts of patients who are representative of the target population are required to validate associations between genomics and therapeutic response. Historically, patient consent rates for genetic studies are lower than for non–genetic-based studies, and consent rates to genetics research are also known to vary according to race, age, and socioeconomic and education status. [1] Theoretically, these imbalances could lead to selection bias and therefore affect the interpretation of data from pharmacogenomic (PG) studies.

The IDEAL (Individualized Dosing to Assess Optimal Pegylated Interferon Therapy) study was a phase 3, large clinical trial that compared treatment with peginterferon alfa-2a or -2b in combination with ribavirin in 3070 patients with chronic hepatitis C infection. [2] This study also included a pharmacogenomic sub-study to identify genetic predictors of response to treatment and treatment-limiting side effects. This sub-study required a separate consent process, enabling patients to participate in the clinical trial without requiring participation in the pharmacogenomic sub-study. As a result of this sub-study, a polymorphism near the *IL28B* gene was discovered and subsequently found to be the strongest baseline predictor of response to peginterferon plus ribavirin in patients with chronic hepatitis C. [3] Additionally, polymorphisms in the *ITPA* gene were associated with the development of anemia in patients receiving peginterferon and ribavirin. [4] These findings have had a profound impact on the treatment of patients with hepatitis C and in the design and interpretation of clinical trials.

The aim of this post hoc analysis was to assess differences in patient characteristics and treatment outcomes between individuals who agreed and did not agree to participate in the IDEAL pharmacogenomic sub-study.

Methods

IDEAL study

The IDEAL study design has been described in detail previously. In brief, this was a phase 3b, randomized, parallel-group study conducted at 118 centers (76 academic and 42 community) in the United States (www.ClinicalTrials.gov number, NCT00081770). [2] Treatment-naive patients with chronic hepatitis C genotype 1 infection aged 18 to 70 years and weighing 40 to 125 kg, with compensated liver disease were enrolled. Patients received peginterferon alfa-2a (180 μg/week) plus ribavirin (1000–1200 mg/day) or peginterferon alfa-2b (1.0 μg/kg/week or 1.5 μg/kg/week) plus ribavirin (800–1400 mg/day). The primary outcome of the study was to compare safety and efficacy (achievement of sustained virological response [SVR], defined as undetectable HCV RNA at week 24 after treatment completion) between the different treatment regimens.

Pharmacogenomic testing

Consent for pharmacogenomic testing at study centers was obtained separately from study consent and prior to the initiation of treatment. A blood sample was obtained and stored for later use from patients who provided consent for pharmacogenomic testing.

Statistical analysis

Individuals were classified into 2 groups according to their decision to accept or decline participation in the pharmacogenomic sub-study. Descriptive statistics were generated using means with standard deviation and frequency. Differences between the 2 groups were tested using Student *t* test for continuous variables and chi-square for categorical variables. An alpha level of 0.05 was defined to be statistically significant.

Results

Overall, 3070 patients were enrolled in the IDEAL study across 118 study sites, of which 109 sites participated in the pharmacogenomics sub-study. A total of 1674 of 2949 patients (57%) from the 109 sites agreed to participate in the pharmacogenomics sub-study. Participation rates in the pharmacogenomic sub-study were higher at academic medical centers than at community centers (60% vs. 52%, $P < 0.001$).

Demographic features

Males were more likely than females to consent to pharmacogenomic testing (58% vs. 54%, $P = 0.04$) (Table 1). Consent rates did not differ according to ethnicity with similar rates found in whites (58%), African Americans (54%), and Hispanics (57%). Consent rates among Asian patients were lower than seen in other ethnic groups (41%); however, the total number of Asian patients was limited (n = 51) and this difference was not statistically significant. Rates of participation in the pharmacogenomic sub-study did not differ according to patient age, baseline HCV viral load, baseline fibrosis score, smoking, history of heavy alcohol use, or medical co-morbidities, including depression (Table 1).

Treatment outcomes

SVR rates were similar between patients who consented to pharmacogenomic testing and those who did not (41% vs. 38%, Table 2). Rates of complete early virological response, end of treatment response, and relapse were also similar between the consent groups (Table 2). There was no difference between the groups with respect to discontinuation of therapy secondary to side effects, serious adverse events, or treatment adherence.

Discussion

The discovery of the association between *IL28B* genotype and treatment outcome in patients with chronic hepatitis C is an example of the power of pharmacogenomic studies in clinical research. Subsequent trials of hepatitis C therapies have utilized this important information to either focus on the favorable or less favorable *IL28B* genotypes or to stratify randomization according to *IL28B* genotype. Additionally, *IL28B* genotyping has been incorporated into patient care algorithms and is used to counsel patients on their likelihood of responding to hepatitis C therapy. This discovery was made possible through the participation of patients enrolled in the large IDEAL study.

In our post-hoc analysis of the IDEAL study, we show that the patients who agreed to participate in the pharmacogenomics sub-study had similar demographic factors, medical co-morbidities, and treatment outcomes when compared with those patients who did not provide consent. This lack of selection bias indicates that the results can be generalized to

the population of patients who participated in the IDEAL study. These results are significant, since for many years, a concern within the field of clinical pharmacogenomics was whether those patients who consented to PG testing represented a pharmacodynamically different cohort than those who did not.

In our analysis, pharmacogenomic testing consent rates were higher at academic centers than community centers. In a similar study involving patients with acute myocardial infarction, the strongest factor associated with consent to participate in the genetic sub-study was study site. [5] We did not have individual site data to determine whether there was significant variability between the sites. Additionally, we did not have data related to the consent process, but believe that one factor contributing to differences in consent rate could be site differences in the motivation of study coordinators and the level of information provided to patients. Notably, the pharmacogenomics participation rate of 57% in this study is lower than pharmacogenomics participation rates of approximately 70% in recent clinical trials [6–8]. However, the IDEAL study was conducted before the importance of DNA collection and pharmacogenomics studies were widely recognized in clinical research.

Many studies have described gender and ethnicity differences in consent to genomics research. In our study, male sex was the only significant demographic factor associated with participation in the pharmacogenomics sub-study. The difference in participation rates between sexes was small and hence the clinical significance of this finding is unclear. However, several other studies have also reported that women are less likely than men to participate in both genetic and non–genetic-based research and more frequently have negative perceptions of genetic-based research. [9–12] Despite this reported finding, we were unable to identify any study that evaluated social, political or ethical mechanisms of gender difference to consent for genetics research.

Additionally, though not seen in our study, African American race and age >65 years are commonly cited demographic factors associated with lower rates of participation in clinical studies with both a genetic and non-genetic focus. [9–22] The majority of these earlier studies evaluated participation in cancer registries or clinical trials; however, within the general population, the National Health and Nutrition Examination Survey (NHANES) found that women and non-Hispanic black patients were less likely than men and non-black patients to contribute material for future genetic analysis. [9,10] In 1999, pharmacogenomic study participation rates were lower in women compared with men (82% vs. 86%, $P < 0.05$) and in non-Hispanic black compared with white patients (73% vs. 86%, $P < 0.05$). [9] Similarly in 2000, participation rates were again lower in women compared with men (84% vs. 87%, $P < 0.05$) and in non-Hispanic black compared with white patients (81% vs. 88%, $P < 0.05$). [10] Interestingly, these differences disappeared when the pharmacogenomics portion of the consent form was removed. While these analyses were performed some time ago, they are contemporary with enrollment in the IDEAL study. Re-assessment of gender and ethnic differences in consent may be warranted with more recent data.

In the IDEAL study, we did not assess factors that might influence consent but other studies exploring perceptions of genetic research have identified concerns about discrimination and misuse of information. [1,23] As recently as 2011, a study evaluating perceptions of genetics research reported that 63% of black respondents and 57% of white respondents indicated that they were “very” or “moderately concerned” about genetic research data being used to discriminate against people. In that study, 64% of black and 34% of white respondents reported that their willingness to donate a blood sample would be substantially reduced because of their concerns about potential discrimination. [23] There added layers of complexity when considering issues surrounding the consent process in countries such as Africa, where the population has lower income and literacy levels. [24–26] This was nicely

illustrated in a description of the consent process for the MalariaGEN project conducted in Africa and Oceania. [27]

As discussed above, there are several limitations to this study. First, we did not have access to site-specific data to determine whether the difference in consent rates between academic and community sites was reflective of differences in site environment, principal investigator/study coordinator motivation, or patient-related factors. We were unable to analyze factors related to the consent process, such as time spent discussing the study and reasons that patients agreed or disagreed to participate in the genetics sub-study. Finally, our analysis is restricted to the IDEAL study, and similar comparisons should be conducted in independent cohorts. However, despite these limitations, we report the first systematic evaluation of demographic factors associated with consent to genetic testing in patients with chronic hepatitis C. Additionally, we provide evidence that the IDEAL genetic sub-study leading to the discovery of the *IL28B* and *ITPA* polymorphisms included individuals who were representative of the wider IDEAL population in terms of demographic factors and treatment outcomes, such that no selection bias was identified that might have affected the interpretation of the results.

Future research to understand patient factors that are associated with consent to genetics research should examine reasons that patients agree or refuse to participate. A particular focus on ethnic and gender differences would be of interest. Additionally, study of how consent/nonconsent impacts the broader field of –omics sciences is needed. One of the newest OMICs technologies to emerge is metabolomics, a field in which sex differences are particularly important. In a recent study of body fat distribution and cardiovascular risk, the metabolite profiles and phenotypic parameters were significantly different between men and women, necessitating separate analyses to increase power. [28] This further illustrates our major point, which is that in -omics research in general, ensuring that the study group is a pharmacodynamically similar group to the population in which the results will be applied is crucial. This will require continued vigilance that those patients being used to generate pharmacogenomics data are representative of the larger population in whom the results will be applied.

Acknowledgments

LDP, JKA, and CAB are former employees and shareholders of Merck & Co., Inc. AJT has received research/grant support from Merck, Roche, Gilead Sciences; has served in a consulting or advisory capacity for Merck, Roche, Janssen, Bristol-Myers Squibb, GlaxoSmithKline; and has received Speaker's fees from Merck, Roche, Gilead Sciences, Bristol-Myers Squibb and Bayer; AJT is also co-inventor of a patent related to the IL28B-HCV discovery. SCG has received grant or research support from Merck, Abbott, Bristol-Myers Squibb, Vertex, Gilead; has served on Data Monitoring Boards for Janssen; and has served as a consultant or on advisory boards for Merck, Abbott, Bristol-Myers Squibb, Vertex, Gilead, Novartis, and CVS-Caremark. AJM has served as a consultant for Achillion, Bristol-Myers Squibb, Gilead, GlaxoSmithKline, Merck, Profectus, and Vertex; and has received grants from Abbott, Achillion, Bristol-Myers Squibb, Gilead, Merck, Pfizer, Profectus, Salix, and Vertex. SN is a current employee of Bristol-Myers Squibb, a former employee of Schering-Plough Research Institute, now Merck Research Laboratories, and a stockholder of Merck & Co., Inc. MSS serves as advisor for Roche, Schering-Plough, Merck, Human Genome Sciences, BIPI, Gilead, Vertex, Tibotec, Bristol-Myers Squibb, and Pfizer and receives grant/research support from Mederax, Peregrine, Debiopharm, and Abbott. EJL has received grants and consulting fees from Merck and Co., Inc. and has served as a consultant and received grants from Abbott, Achillion, Anadys, Biolex Therapeutiocs, GlobeImmune, Inhibitex, Pharmasset, Santaris, Tibotec, and Theravance. EJL has also received grants from Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline, Idenix Pharmaceuticals, Idera Pharmaceuticals, Intercept Pharmaceuticals, Janssen, Medarex, Medtronic, Novartis, Roche, Schering-Plough, Scynexis Pharmaceuticals, Vertex Pharmaceuticals, ViroChem Pharma, ZymoGenetics.

The IDEAL study was sponsored by Schering-Plough (now Merck & Co., Inc.)

Editorial assistance was provided by Tim Ibbotson, PhD, and Bianca Ruzicka, PhD, of ApotheCom (Yardley, PA). This assistance was funded by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ.

Source of funding, ABJ:

Grant #	NIH 5T32DK007568-20
Title	Duke Training Grant in Digestive Diseases and Nutrition
Period	7/1/2010 – 6/30/2011

References

1. Sterling R, Henderson GE, Corbie-Smith G. Public willingness to participate in and public opinions about genetic variation research: a review of the literature. American journal of public health. 2006; 96(11):1971–1978. doi: 10.2105/AJPH.2005.069286. PubMed PMID: 17018829; PubMed Central PMCID: PMC1751820. [PubMed: 17018829]
2. McHutchison JG, Lawitz EJ, Shiffman ML, Muir AJ, Galler GW, McCone J, et al. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. The New England journal of medicine. 2009; 361(6):580–593. Epub 2009/07/25. doi: 10.1056/NEJMoa0808010. PubMed PMID: 19625712. [PubMed: 19625712]
3. Ge D, Fellay J, Thompson AJ, Simon JS, Shianna KV, Urban TJ, et al. Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance. Nature. 2009; 461(7262):399–401. Epub 2009/08/18. doi: 10.1038/nature08309. PubMed PMID: 19684573. [PubMed: 19684573]
4. Fellay J, Thompson AJ, Ge D, Gumbs CE, Urban TJ, Shianna KV, et al. ITPA gene variants protect against anaemia in patients treated for chronic hepatitis C. Nature. 2010; 464(7287):405–408. Epub 2010/02/23. doi: 10.1038/nature08825. PubMed PMID: 20173735. [PubMed: 20173735]
5. Lanfear DE, Jones PG, Cresci S, Tang F, Rathore SS, Spertus JA. Factors influencing patient willingness to participate in genetic research after a myocardial infarction. Genome medicine. 2011; 3(6):39. Epub 2011/06/17. doi: 10.1186/gm255. PubMed PMID: 21676259; PubMed Central PMCID: PMC3218813. [PubMed: 21676259]
6. Franc MA, Warner AW, Cohen N, Shaw PM, Groenen P, Snapir A. Current practices for DNA sample collection and storage in the pharmaceutical industry, and potential areas for harmonization: perspective of the I-PWG. Clinical pharmacology and therapeutics. 2011; 89(4):546–553. Epub 2011/03/04. doi: 10.1038/clpt.2010.338. PubMed PMID: 21368755. [PubMed: 21368755]
7. Warner AW, Bhathena A, Gilardi S, Mohr D, Leong D, Bienfait KL, et al. Challenges in obtaining adequate genetic sample sets in clinical trials: the perspective of the industry pharmacogenomics working group. Clinical pharmacology and therapeutics. 2011; 89(4):529–536. Epub 2011/02/25. doi: 10.1038/clpt.2010.305. PubMed PMID: 21346757. [PubMed: 21346757]
8. Ricci DS, Broderick ED, Tchelet A, Hong F, Mayevsky S, Mohr DM, et al. Global requirements for DNA sample collections: results of a survey of 204 ethics committees in 40 countries. Clinical pharmacology and therapeutics. 2011; 89(4):554–561. Epub 2011/02/25. doi: 10.1038/clpt.2010.319. PubMed PMID: 21346753. [PubMed: 21346753]
9. McQuillan GM, Porter KS, Agelli M, Kington R. Consent for genetic research in a general population: the NHANES experience. Genetics in medicine : official journal of the American College of Medical Genetics. 2003; 5(1):35–42. Epub 2003/01/25. doi: 10.1097/01.GIM.0000048372.64172.15. PubMed PMID: 12544474. [PubMed: 12544474]
10. McQuillan GM, Pan Q, Porter KS. Consent for genetic research in a general population: an update on the National Health and Nutrition Examination Survey experience. Genetics in medicine : official journal of the American College of Medical Genetics. 2006; 8(6):354–360. Epub 2006/06/17. doi: 10.1097/01.gim.0000223552.70393.08. PubMed PMID: 16778597. [PubMed: 16778597]
11. Ford BM, Evans JS, Stoffel EM, Balmana J, Regan MM, Syngal S. Factors associated with enrollment in cancer genetics research. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. 2006; 15(7):1355–1359. Epub 2006/07/13. doi: 10.1158/1055-9965.EPI-05-0816. PubMed PMID: 16835336.

12. Murthy VH, Krumholz HM, Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. JAMA : the journal of the American Medical Association. 2004; 291(22):2720–2726. Epub 2004/06/10. doi: 10.1001/jama.291.22.2720. PubMed PMID: 15187053. [PubMed: 15187053]

13. Corbie-Smith G, Thomas SB, Williams MV, Moody-Ayers S. Attitudes and beliefs of African Americans toward participation in medical research. Journal of general internal medicine. 1999; 14(9):537–546. Epub 1999/09/22. PubMed PMID: 10491242; PubMed Central PMCID: PMC1496744. [PubMed: 10491242]

14. Sateren WB, Trimble EL, Abrams J, Brawley O, Breen N, Ford L, et al. How sociodemographics, presence of oncology specialists, and hospital cancer programs affect accrual to cancer treatment trials. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2002; 20(8):2109–2117. Epub 2002/04/17. PubMed PMID: 11956272. [PubMed: 11956272]

15. Hutchins LF, Unger JM, Crowley JJ, Coltman CA Jr, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. The New England journal of medicine. 1999; 341(27):2061–2067. Epub 1999/12/30. doi: 10.1056/NEJM199912303412706. PubMed PMID: 10615079. [PubMed: 10615079]

16. Lewis JH, Kilgore ML, Goldman DP, Trimble EL, Kaplan R, Montello MJ, et al. Participation of patients 65 years of age or older in cancer clinical trials. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2003; 21(7):1383–1389. Epub 2003/03/29. PubMed PMID: 12663731. [PubMed: 12663731]

17. Bogner HR, Wittink MN, Merz JF, Straton JB, Cronholm PF, Rabins PV, et al. Personal characteristics of older primary care patients who provide a buccal swab for apolipoprotein E testing and banking of genetic material: the spectrum study. Community genetics. 2004; 7(4):202–210. Epub 2005/02/05. doi: 10.1159/000082263. PubMed PMID: 15692195; PubMed Central PMCID: PMC2804857. [PubMed: 15692195]

18. Wang SS, Fridinger F, Sheedy KM, Khoury MJ. Public attitudes regarding the donation and storage of blood specimens for genetic research. Community genetics. 2001; 4(1):18–26. Epub 2001/08/09. doi: 10.1159/000051152. PubMed PMID: 11493749. [PubMed: 11493749]

19. Shavers VL, Lynch CF, Burmeister LF. Racial differences in factors that influence the willingness to participate in medical research studies. Annals of epidemiology. 2002; 12(4):248–256. Epub 2002/05/04. PubMed PMID: 11988413. [PubMed: 11988413] Unson CG, Dunbar N, Curry L, Kenyon L, Prestwood K. The effects of knowledge, attitudes, and significant others on decisions to enroll in a clinical trial on osteoporosis: implications for recruitment of older African-American women. Journal of the National Medical Association. 2001; 93(10):392–401. discussion 2–4. PubMed PMID: 11688920; PubMed Central PMCID: PMC2594076. [PubMed: 11688920]

20. Robinson SB, Ashley M, Haynes MA. Attitude of African-Americans regarding prostate cancer clinical trials. Journal of community health. 1996; 21(2):77–87. PubMed PMID: 8728357. [PubMed: 8728357]

21. Harris Y, Gorelick PB, Samuels P, Bempong I. Why African Americans may not be participating in clinical trials. Journal of the National Medical Association. 1996; 88(10):630–644. PubMed PMID: 8918067; PubMed Central PMCID: PMC2608128. [PubMed: 8918067]

22. Mouton CP, Harris S, Rovi S, Solorzano P, Johnson MS. Barriers to black women's participation in cancer clinical trials. Journal of the National Medical Association. 1997; 89(11):721–727. PubMed PMID: 9375475; PubMed Central PMCID: PMC2608280. [PubMed: 9375475]

23. Goldenberg AJ, Hull SC, Wilfond BS, Sharp RR. Patient perspectives on group benefits and harms in genetic research. Public health genomics. 2011; 14(3):135–142. Epub 2010/10/13. doi: 10.1159/000317497. PubMed PMID: 20938159; PubMed Central PMCID: PMC3104869. [PubMed: 20938159]

24. Tindana PO, Singh JA, Tracy CS, Upshur RE, Daar AS, Singer PA, et al. Grand challenges in global health: community engagement in research in developing countries. PLoS medicine. 2007; 4(9):e273. doi: 10.1371/journal.pmed.0040273. PubMed PMID: 17850178; PubMed Central PMCID: PMC1989740. [PubMed: 17850178]

25. Molyneux CS, Wassenaar DR, Peshu N, Marsh K. 'Even if they ask you to stand by a tree all day, you will have to do it (laughter)…!': community voices on the notion and practice of informed

consent for biomedical research in developing countries. Social science & medicine. 2005; 61(2): 443–454. doi: 10.1016/j.socscimed.2004.12.003. PubMed PMID: 15893058. [PubMed: 15893058]

26. Molyneux CS, Peshu N, Marsh K. Understanding of informed consent in a low-income setting: three case studies from the Kenyan Coast. Social science & medicine. 2004; 59(12):2547–2559. doi: 10.1016/j.socscimed.2004.03.037. PubMed PMID: 15474208. [PubMed: 15474208]
27. Tindana P, Bull S, Amenga-Etego L, de Vries J, Aborigo R, Koram K, et al. Seeking consent to genetic and genomic research in a rural Ghanaian setting: a qualitative study of the MalariaGEN experience. BMC medical ethics. 2012; 13:15. doi: 10.1186/1472-6939-13-15. PubMed PMID: 22747883; PubMed Central PMCID: PMC3441464. [PubMed: 22747883]
28. Szymanska E, Bouwman J, Strassburg K, Vervoort J, Kangas AJ, Soininen P, et al. Gender-dependent associations of metabolite profiles and body fat distribution in a healthy population with central obesity: towards metabolomics diagnostics. Omics : a journal of integrative biology. 2012; 16(12):652–667. doi: 10.1089/omi.2012.0062. PubMed PMID: 23215804. [PubMed: 23215804]

Table 1

Consent for Pharmacogenomic Testing Across Various Patient Subgroups

	Consented to PG sampling (n = 1674)	Did not consent to PG sampling (n = 1275)	*P*
Gender, n (%)			0.04
Male	1021 (58)	729 (42)	
Female	653 (54)	546 (46)	
Race, n (%)			0.07
White	1214 (58)	882 (42)	
African American	293 (54)	254 (46)	
Hispanic	121 (57)	90 (43)	
Asian	21 (41)	30 (59)	
Other	25 (57)	19 (43)	
Age, y, mean (SD)	47.4 (7.9)	47.6 (8.3)	0.71
Baseline HCV RNA, n (%)			0.17
>600,000 IU/mL	1388 (57)	1032 (43)	
≤600,000 IU/mL	286 (54)	243 (46)	
METAVIR fibrosis score, n (%)*			0.7
F0	25 (54)	21 (46)	
F1	1160 (58)	857 (42)	
F2	235 (55)	192 (45)	
F3	66 (55)	54 (45)	
F4	112 (58)	80 (42)	
Baseline smoking history, n (%)†			0.39
Current smoker	620 (57)	470 (43)	
Ex-smoker	626 (58)	455 (42)	
Non-smoker	390 (54)	327 (46)	
History of alcohol abuse, n (%)	153 (58)	109 (42)	0.58
History of depression, n (%)	391 (57)	299 (43)	0.95
History of diabetes, n (%)	112 (57)	85 (43)	0.98
History of hypertension, n (%)	454 (57)	342 (43)	0.86
History of coronary artery disease, n (%)	25 (57)	19 (43)	0.99

*Missing 76 of those who participated in pharmacogenomic testing and 71 of those who did not.

†Missing 38 of those who participated in pharmacogenomic testing and 23 of those who did not.

Abbreviations: PG, pharmacogenomics testing.

Table 2

Treatment Outcomes

	PG subjects (n = 1674)	Non-PG subjects (n = 1275)	*P*
cEVR, n (%)	696 (42)	493 (39)	0.11
SVR, n (%)	683 (41)	485 (38)	0.13
EOT, n (%)	938 (56)	705 (55)	0.69
Relapse, n (%)	215/886 (24)	180/661 (27)	*
Discontinuation for AE, n (%)	196 (12)	151 (12)	0.91
SAE, n (%)	164 (10)	128 (10)	0.83
12-week PEG adherence> 80%, n (%)	1527 (91)	1141 (89)	0.11
12-week RBV adherence> 80%, n (%)	1485 (89)	1144 (90)	0.38

* Not tested since denominator for comparison groups (EOT responder) is not based on factor determined at randomization.

Abbreviations: cEVR, complete early virological response; PG, pharmacogenomics; SVR, sustained virological response; EOT, end of treatment response; AE, adverse event; SAE, serious adverse event; PEG, pegylated interferon-alfa; RBV, ribavirin.