Insights on GRACE (Gender, Race, And Clinical Experience) from the Patient's Perspective: GRACE Participant Survey

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Abstract

The Gender, Race And Clinical Experience (GRACE) study was conducted between October 2006 and December 2008 to evaluate sex- and race-based differences in outcomes after treatment with a darunavir/ritonavir-based antiretroviral regimen. Between June 2010 and June 2011, former participants of the GRACE trial at participating sites were asked to complete a 40-item questionnaire as part of the GRACE Participant Survey study, with a primary objective of assessing patients' characteristics, experiences, and opinions about participation in GRACE. Of 243 potential survey respondents, 151 (62%) completed the survey. Respondents were representative of the overall GRACE population and were predominantly female (64%); fewer were black, and more reported recreational drug use compared with nonrespondents (55% vs. 62% and 17% vs. 10%, respectively). Access to treatment (41%) and too many blood draws (26%) were reported as the best and worst part of GRACE, respectively. Support from study site staff was reported as the most important factor in completing the study (47%). Factors associated with nonadherence, study discontinuation, and poor virologic response in univariate analyses were being the primary caregiver for children, unemployment, and transportation difficulties, respectively. Patients with these characteristics may be at risk of poor study outcomes and may benefit from additional adherence and retention strategies in future studies and routine clinical care.

Introduction

ALTHOUGH GLOBALLY APPROXIMATELY HALF of all HIV-infected individuals are women,¹ they have historically been under-represented in clinical trials examining the effect of antiretroviral drugs in treatment-experienced patients.^{2,3} Between 2000 and 2008, only 15% of treatment-experienced patients enrolled in the 18 randomized controlled trials of HIV drugs submitted for approval to the Food and Drug Administration (FDA) were women.³ Women of color have been particularly under-represented, despite the fact that they comprise a large portion of new infections.^{4,5} In addition to HIV-related stigma, women of color may face both sex-based and race-based discrimination, culminating in increased rates

of mental health issues.⁴ Challenges to recruitment and retention have been observed and exist for studies in other therapeutic areas as well.^{6,7} Sex-based statistical analyses and conclusions are limited when female enrollment is low; therefore, female enrollment in HIV clinical trials should be representative of the infected population.⁸

The Gender, Race, And Clinical Experience (GRACE) trial was designed to evaluate sex- and race-based differences in the outcomes associated with darunavir/ritonavir-based therapy in treatment-experienced HIV-infected adults.⁹ This was a phase 3b, open-label, multicenter trial that enrolled 429 patients. The trial successfully enrolled a high percentage of women (67%) across North America, including women of color, through specific recruitment and retention strategies.¹⁰

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TABLE 1. CHARACTERISTICS AT BASELINE AND KEY OUTCOMES OF THE GRACE PARTICIPANT SURVEY RESPONDENTS VERSUS THOSE FROM THE SAME SITES WHO DID NOT PARTICIPATE IN THE SURVEY

	GRACE sites that participated in survey			GRACE sites that did not participate in survey (n = 186)	Total GRACE population (N = 429)
	Respondent (n = 151)	Nonrespondent (n = 92)	Total (n = 243)		
<i>Characteristics at baseline</i>					
Sex, n (%)					
Female	97 (64.2)	60 (65.2)	157 (64.6)	130 (69.9)	287 (66.9)
Male	54 (35.8)	32 (34.8)	86 (35.4)	56 (30.1)	142 (33.1)
Age, years					
Median (range)	44 (19–74)	43 (20–78)	44 (19–78)	42 (19–78)	43 (19–78)
Race, n (%)					
Black	83 (55.0)	57 (62.0)	140 (57.6)	124 (66.7)	264 (61.5)
Caucasian	24 (15.9)	13 (14.1)	37 (15.2)	28 (15.1)	65 (15.2)
Hispanic	43 (28.5)	21 (22.8)	64 (26.3)	32 (17.2)	96 (22.4)
Other	1 (0.7)	1 (1.1)	2 (0.8)	2 (1.1)	4 (0.9)
Tobacco use, n (%)	58 (38.4)	31 (33.7)	89 (36.6)	68 (36.6)	157 (36.6)
Alcohol use, n (%)	57 (37.7)	30 (32.6)	87 (35.8)	64 (34.4)	151 (35.3)
Recreational drug use, n (%)	26 (17.2)	9 (9.8)	35 (14.4)	26 (14.0)	61 (14.2)
HIV stage C disease, n (%)	52 (34.4)	37 (40.2)	89 (36.6)	80 (43.0)	169 (39.4)
Baseline viral load, log ₁₀ copies/mL					
Median (range)	4.75 (1.9–6.1)	4.76 (1.7–6.8)	4.76 (1.7–6.8)	4.63 (2.4–6.5)	4.71 (1.7–6.8)
Baseline CD4 cell count, cells/mm ³					
Median (range)	221 (1–1125)	186.5 (1–868)	211 (1–1125)	180 (3–826)	200 (1–1125)
<i>Key outcomes</i>					
Adherence ≥95%, n (%)	99 (65.6)	54 (58.7)	153 (63.0)	129 (69.4)	282 (65.8)
Discontinued GRACE, n (%)	40 (26.5)	37 (40.2)	77 (31.7)	50 (26.9)	127 (29.6)
Virologic response rates					
Week 48 ITT-TLOVR (<50 HIV-1 RNA copies/mL)	92 (60.9)	42 (45.7)	134 (55.1)	95 (51.1)	229 (53.4)
Week 48 TLOVR non-VF censored (<50 HIV-1 RNA copies/mL)	92 (76.7) ^a	42 (70.0) ^b	134 (74.4) ^c	95 (71.4) ^d	229 (73.2) ^e

^an, 120; ^bn, 60; ^cn, 180; ^dn, 133; ^en, 313.

ITT-TLOVR, intent-to-treat time-to-loss of virologic response; VF, virologic failure.

Patients received darunavir/ritonavir plus an optimized background regimen for 48 weeks. Sex-based safety and efficacy results have been previously reported.⁹

We present here the findings from an exploratory patient survey conducted after the GRACE trial was completed, with the purpose of collecting additional data regarding issues inherent to clinical trials (such as retention). The impact of patients' characteristics, experiences, and opinions on treatment outcomes was assessed.

Methods

Study design of GRACE trial

Detailed study design and results of GRACE have been reported.^{9–15} Briefly, GRACE was a phase 3b, multicenter, open-label, 48-week study conducted in treatment-experienced HIV-infected adults at 65 sites throughout the United States, Puerto Rico, and Canada between October 2006 and December 2008. Patients enrolled in GRACE were treated with darunavir/ritonavir 600/100 mg twice daily in addition to an investigator-selected optimized background regimen.

GRACE participant survey design and objectives

The present study was a noninterventive, multicenter, cross-sectional survey completed by former participants of the GRACE trial. Of the 57 GRACE sites located in the United States and Puerto Rico that enrolled patients, 22 chose to participate in the survey study, which was conducted between June 2010 and June 2011. The primary objective of the survey was to examine GRACE participants' characteristics (beyond data obtained during the study), experiences, and opinions about study participation. The secondary objective was to explore statistically the associations between survey responses and adherence to study medications, study discontinuation, and virologic response. Patients completed a 40-question multiple-choice and open-ended survey in a single visit.

Statistical analyses

Descriptive statistics of survey responses were compiled. Univariate logistic regression was performed to determine the importance of individual survey responses on each of the following GRACE study outcomes: study discontinuation,

TABLE 2. SURVEY RESPONSES RELATED TO RESPONDENTS' CHARACTERISTICS, SUCH AS MEDICAL COVERAGE, EMPLOYMENT/EDUCATION, LIVING SITUATION, HEALTH BEHAVIOR PRIOR TO GRACE, AND SOCIAL SUPPORT

	n (total 151 ^a)	%
<i>Medical coverage</i>		
During your participation in the GRACE study, did you have health insurance? (one that is the main source)		
No health insurance	27	18
Medicaid	41	27
Medicare	30	20
Private health insurance	36	24
Other	16	11
When you are not in a study, how do you pay for your HIV medications? (the one that is used the most)		
ADAP	37	25
Medicaid	31	21
Medicare	24	16
Private insurance	27	18
Other (PAPs, self-pay)	32	21
If you have drug coverage, how much do you pay in co-pays?		
Nothing	73	51
Less than \$10 per prescription	36	25
\$10–\$25 per prescription	13	9
More than \$25 per prescription	22	15
<i>Employment/education</i>		
At the time you started GRACE, were you working?		
Yes	64	42
No	87	58
At the time you started GRACE, were you in school?		
Yes	10	7
No	140	93
Did you find a new job or start school while you were in GRACE?		
Yes	15	10
No	135	90
Have you graduated from high school?		
Yes	110	73
Highest educational degree = high-school diploma	67	62
Highest educational degree = associate degree or higher	41	38
No	40	27
<i>Living situation</i>		
How would you describe your living situation while participating in GRACE?		
Moved at least once during the study	23	15
Lived in one place the whole time	125	83
Homeless	4	3
Lived in a shelter	4	3
Did you spend any nights in jail while you were in GRACE?		
Yes	3	2
No	147	98
Do you have children?		
Yes	107	71
No	44	29
Are you the primary caregiver for any children or grandchildren?		
Yes	58	38
No	93	62
<i>Health behaviors prior to GRACE</i>		
Before GRACE, did you have trouble taking your HIV medications as you were supposed to?		
Yes	58	39
Didn't like how they made me feel	18	31
Forgot to take my medicine regularly	13	22
Too many pills	10	17
Other	17	29
No	92	61

(continued)

TABLE 2. (CONTINUED)

	n (total 151 ^a)	%
When you were in care before GRACE, did you have trouble keeping your medical appointments?		
Yes	23	15
Too busy to keep appointments/couldn't get off work	11	48
Lack of transportation/couldn't get there	7	30
Other	5	22
No	127	85
Where do you obtain most of your information about HIV?		
From my health care provider (doctor, nurse practitioner, physician assistant)	117	78
From the research coordinator	10	7
From reading HIV magazines or brochures	7	5
Other	16	11
<i>Social support</i>		
Which best describes you (as it relates to your HIV-infection)?		
I feel like I am in this alone	31	21
I get some help from my friends/partner/or family	35	23
I get lots of support from my friends/partner/or family	84	56
Have you disclosed your HIV status to others?		
No	41	27
Yes, but only to a few very close people	54	36
Yes, to several friends/family	39	26
Yes, I am completely open about my status	16	11

^aNot all survey respondents answered every question, resulting in an *n* that does not always add up to 151. Percentages were calculated based on actual number of responses. ADAP, AIDS Drug Assistance Program; PAPs, Prescription Assistance Programs.

adherence, and virologic response. Although the current study was not powered for statistical analyses, a *p* value < 0.10 was used as a broad selection criteria for association of survey responses with respective end points.

Results

Patient population and baseline characteristics of survey respondents versus nonrespondents

In the total GRACE population (*N* = 429), 67% were female, with a median age of 43 years (range 19–78; Table 1). Sixty-two percent were black, 22% Hispanic, and 15% Caucasian. Tobacco, alcohol, and recreational drug use were reported by 37%, 35%, and 14% of patients, respectively, and 39% had HIV stage C disease. Median baseline CD4 cell count was 200 cells/mm³ (range 1–1125). Median baseline viral load was 4.71 log₁₀ copies/mL (range 1.7–6.8).

In all, 243 patients who took part in the GRACE trial (57% of the total GRACE population), across 22 participating sites (39% of total GRACE sites), were asked to complete the survey. Of these 243 potential survey participants, 151 (62%) completed the survey; this represents 35% of the overall GRACE population. Survey respondents were predominantly female (64%), with a median age of 44 years (range 19–74), which was similar to nonrespondents (Table 1). However, fewer respondents were black (55% vs. 62% for nonrespondents) and more respondents were Hispanic (29% vs. 23% for nonrespondents). More survey respondents reported tobacco, alcohol, and recreational drug use during their participation in GRACE, compared with nonrespondents (38%, 38%, and 17% vs. 34%, 33%, and 10%, respectively). Fewer respondents had HIV stage C disease (34% vs. 40% for nonrespondents) and more had a higher median baseline CD4 cell count (221 vs. 187 cells/mm³ for nonrespondents). There was no differ-

ence in median baseline viral load (4.75 log₁₀ copies/mL for respondents vs. 4.76 log₁₀ copies/mL for nonrespondents). No significant differences in baseline characteristics were observed between sites that participated in the survey versus those that did not participate, ruling out potential bias in participating site selection (Table 1).

Adherence, discontinuation, and virologic response rates of survey respondents versus nonrespondents during participation in GRACE

Adherence rates of ≥ 95% were reported in 65.6% of survey respondents compared with 58.7% of nonrespondents. Similar rates were observed between survey respondents and participants of the GRACE trial as a whole (65.8% reported ≥ 95% adherence).⁹ Fewer survey respondents had discontinued participation in the GRACE trial compared with nonrespondents (27% vs. 40%), and similar rates of discontinuation were observed between survey respondents and participants in the GRACE trial as a whole (27% vs. 30%, respectively).⁹ Survey respondents achieved higher rates of HIV-1 RNA suppression below 50 copies/mL, with week 48 intent-to-treat time-to-loss of virologic response (ITT-TLOVR) values of 61%, compared with 46% for nonrespondents, and TLOVR nonvirologic failure (VF) censored values of 77%, compared with 70% for nonrespondents. However, among the overall GRACE population, 53.4% and 73.2% achieved HIV-1 RNA below 50 copies/mL in the ITT-TLOVR and TLOVR non-VF censored populations.⁹

Characteristics of survey participants

While participating in the GRACE trial, 18% of survey respondents did not have health insurance and 27% were on Medicaid (Table 2). When not in the study, 25% of

TABLE 3. SURVEY RESPONSES RELATED TO RESPONDENTS' EXPERIENCES DURING THE GRACE TRIAL, SUCH AS MOTIVATION FOR PARTICIPATION, TRANSPORTATION TO STUDY SITE, COMMUNICATION/COMFORT WITH STUDY SITE, AND KEY STUDY CONTACT

	n (total 151 ^a)	%
<i>Motivation for participation in GRACE trial</i>		
What is your experience with HIV studies?		
GRACE was my first study	107	71
I had participated in studies before GRACE	44	29
How did you learn about GRACE?		
Someone at my clinic	124	82
Other (family, ASO, media)	27	18
What was the main reason you wanted to participate in GRACE?		
Needed the medications	56	37
Thought a study about women and people of color was important	32	21
Wanted to help others/contribute to something bigger	55	36
Other	8	5
How important was it to your participation in GRACE that medications other than the main study drug, Prezista, were also provided by the study as part of your combination therapy?		
Not important	12	8
Somewhat important	20	13
Very important	118	79
<i>Transportation to study site</i>		
Did you participate in GRACE at your primary care site (place where you usually receive your HIV care) or did you have to go to a different location?		
Primary care site	115	76
Different location	36	24
Different location, but site where received services before	20	56
How did you usually get to your study visits?		
Drove my own car	80	53
Public transportation (bus, train)	37	25
Got a ride from a friend/family member	12	8
Transportation provided by a community organization	11	7
Took a taxi	11	7
How difficult was it to arrange or get transportation to your study visits?		
Not at all difficult	116	77
Somewhat difficult	28	19
Very difficult	6	4
How long did it usually take for you to get to the GRACE site?		
Less than 30 min	66	44
30–60 min	66	44
1–2 h	16	11
More than 2 h	3	2
<i>Communication/comfort with study site</i>		
What is your primary language?		
English	108	72
Spanish	38	25
Creole	5	3
Did any of the staff at your study clinic speak your primary language?		
Yes	146	99
No	2	1
How would you rate your comfort level with your study site and staff?		
Not comfortable	1	1
Comfortable	26	17
Very comfortable	123	82
How well did the study site work around your schedule/availability for visits?		
The site was not flexible at all	1	1
The site was somewhat flexible	10	7
The site was very flexible	139	93

(continued)

TABLE 3. (CONTINUED)

	n (total 151 ^a)	%
<i>Key study contact</i>		
Did you have a key contact person at the study site?		
No key contact	5	3
The study nurse	105	70
The study physician	24	16
Social worker	2	1
Other	14	9
Was this person the same race or ethnic background as you?		
Yes	68	46
No	79	54
How important was it that this person was the same race or ethnic background as you?		
Not important	107	73
Somewhat important	20	14
Very important	20	14
Was this person the same sex as you?		
Yes	92	61
No	58	39
How important was it that this person was the same sex as you?		
Not important	112	76
Somewhat important	16	11
Very important	20	14

^aNot all survey respondents answered every question, resulting in an n that does not always add up to 151. Percentages were calculated based on actual number of responses. ASO, AIDS Service Organization.

respondents relied on the AIDS Drug Assistance Program, other prescription assistance programs, or paid on their own for their HIV medications. In all, 73% of respondents were high-school graduates. At the time of entry into GRACE, 58% were not working and only 7% were in school. Less than 5% of the survey respondents were homeless or lived in a shelter, and only 2% spent a night in jail while participating in the GRACE trial. The majority (71%) of respondents had children, but only 38% reported that they were the primary caregiver for children/grandchildren. Before enrolling in GRACE, 39% of respondents reported having difficulty taking HIV medications as directed, mainly because they did not like how the drugs made them feel; 15% had trouble keeping medical appointments, which was primarily due to a busy lifestyle. Most respondents (73%) had disclosed their HIV status to others and over half (56%) reported receiving strong support from friends/family.

Survey participants' experiences during the GRACE trial

The majority (71%) reported that GRACE was their first HIV study and that they learned about the study from the staff at their clinic (82%; Table 3). The most common reasons to participate in GRACE were the need to access medications (37%) and the desire to contribute to something bigger/help others (36%). Most (79%) felt that receiving other medications in addition to the main study drug, darunavir, was very important in their decision to participate in the GRACE study. The majority (76%) participated in GRACE at their primary HIV care location, and 77% did not have any difficulty arranging transportation to the study site. Nearly all (99%) participants reported being comfortable or very comfortable with the study site, indicating that the site was very flexible with scheduling visits (93%). In most cases, the key contact

person at the study site was the study nurse (70%) and most respondents reported that it was not important to them that the key contact person was of the same race/ethnicity (73%) or sex (76%) as themselves.

Survey respondents' opinions about the GRACE trial

Respondents reported that the best part of the GRACE experience was access to treatment (41%), being part of something bigger (18%), and feeling better (17%) (Table 4). Seventy-six percent felt that the GRACE trial made them feel differently about their health/HIV care, and most (82%) became more focused on their health, with 87% of respondents continuing treatment after GRACE. In all, 68% would be interested in sharing their GRACE experience, and 96% would recommend participation in a clinical trial to others. Some of the worst parts of the GRACE experience as reported by respondents were too many blood draws (26%), travel to the study site (13%), and the opinion that medicines were hard to take (12%). Although 88% reported having completed the GRACE trial, only 74% actually did so. Support from site study staff (47%) was noted as the most important factor in completing the study. Other common success factors were feeling better or healthier (16%), receiving support from family/friends (15%), and having access to medications (13%). Of the 12% who reported not completing the study, the most cited reason for discontinuation was intolerable side effects/not liking how they felt (50%).

Themes from the open-ended question

The survey respondents were asked to share additional opinions about their experience during GRACE through the open-ended question: "Is there anything else you would like to share about your experience in participating in

TABLE 4. SURVEY RESPONSES RELATED TO RESPONDENTS' OPINIONS ASSOCIATED WITH PARTICIPATION, SATISFACTION, AND COMPLETION OF THE GRACE TRIAL

	n (total 151 ^a)	%
<i>Best and worst parts of participating in the GRACE trial</i>		
What was the best part of your experience?		
Access to treatment	61	41
Being part of something bigger	27	18
Feeling better	26	17
Interaction with study staff	18	12
Pride in helping others	15	10
Interaction with other participants	1	1
Other	2	1
What was the worst part of your experience?		
Too many blood draws	38	26
Getting to the study site	19	13
Medicines were hard to take	18	12
Made my life too complicated/too much	5	3
Other	69	46
<i>Satisfaction/benefits of participating in the GRACE trial</i>		
Have you stayed on treatment since GRACE?		
Yes	130	87
No	20	13
Did participating in GRACE make you feel differently about your own health or HIV care in general?		
No	36	24
Yes	115	76
More focused on my health ^b	94	82
More active in my own care ^b	44	38
Would you be interested in sharing your experience in the GRACE study with others?		
Yes	103	68
No	48	32
Would you recommend participating in a study to someone else?		
Yes	144	96
No	6	4
<i>Completing the GRACE trial</i>		
Did you complete the study (finish 48 weeks of treatment)?		
Yes	133	88
What things/people were most important in helping you complete the study? ^c		
Support from study/site staff	61	47
Felt better or healthier	21	16
Family/friend support	19	15
Access to the treatments	17	13
Wanting to contribute to something bigger	11	8
Other	1	1
No	18	12
Why? ^d		
I had side effects that I could not tolerate/I didn't like how I felt	9	50
Other	9	50
Too busy	2	22
Jail	2	22
Moved	1	11
Did not work	1	11
Others thought I should stop	1	11
Allergic reaction to medication	1	11
I did not do everything I was supposed to do	1	11

^aNot all survey respondents answered every question, resulting in an n that does not add up to 151. Percentages were calculated based on actual number of responses. ^bMultiple answers were permitted. ^cFour of the 133 survey respondents who answered yes did not clarify what was most important in helping them complete the study. ^dFour of the 18 survey respondents who answered no did not give a reason.

FIG. 1. Associations with adherence. Univariate analysis was used to examine associations ($p < 0.1$) between survey responses and adherence to study medication. The p value for univariate selection is based on all levels (survey answers) of the variable (survey question); only one level is shown here. Adherence was defined as compliance with study medications $\geq 95\%$ over the course of the trial.

the GRACE study?" The following themes emerged: (1) Improved adherence: respondents reported an increased awareness of the importance of continuing to take their medications. "I became more aware of the importance of the meds and I take my care more serious now." (2) Increased self-confidence: respondents reported feeling more confident about themselves and their future. "More self-confident being with the staff that help me a lot." (3) Better health: respondents felt healthier since participating in GRACE, with

improved energy and quality of life. "Thank God for the GRACE study! I loved it. My health was a mess. After I took the medicine, my health was back on track. I am still taking the same medications." (4) Access to effective HIV medications: respondents reported that the study provided them with medications that they would not otherwise have been able to afford. "I am very blessed to be in this study, because I can't afford the meds for a whole year." (5) Race: respondents felt that the fear among people of color regarding

FIG. 2. Associations with study discontinuation. Univariate analysis was used to examine associations ($p < 0.1$) between survey responses and discontinuation from study for reasons other than virologic failure or adverse events. The p value for univariate selection is based on all levels (survey answers) of the variable (survey question); only one level is shown here.

FIG. 3. Associations with virologic response. Univariate analysis was used to examine associations ($p < 0.1$) between survey responses and virologic response. Responders were defined as patients achieving intent-to-treat time-to-loss of virologic response < 50 HIV-1 RNA copies/mL at week 48. The p value for univariate selection is based on all levels (survey answers) of the variable (survey question); only one level is shown here.

participation in clinical trials needed to be dispelled and that people of color are now able to access effective treatment. "As a black woman the fear from clinical trials had to be dispelled." (6) Positive relationship with study staff: respondents felt that the staff was professional, supportive, comforting, nonjudgmental, confidential, caring, and spent extra time to help the study participants. "The most important was the staff because I just felt like I was normal and however I could deal with the medicine and they were there. I appreciated the medicine because I didn't have any. When doing a survey or hiring staff the most important thing is that the staff doesn't judge the people. That's what I like, they were very confidential. They saved my life as well as the medicine. Thanks!"

Associations of responses with clinical outcomes

Univariate analyses were performed to assess any associations between survey responses and clinical outcomes, including adherence to treatment, study discontinuation, and virologic response to study medications.

Adherence was defined as $\geq 95\%$ compliance with study medications over the course of the study. The following associations were found to be significant at a level of $p < 0.1$ (Fig. 1): increased adherence was associated with not feeling differently about one's own health or HIV care since participating in GRACE, not having children and working. Less adherence was associated with having some difficulties with transportation to study site, not being very comfortable with study site and staff, having trouble taking HIV medications prior to the GRACE trial, or being a primary caregiver for children.

Study discontinuation was defined as discontinuing the study for reasons other than VF or adverse events. The following factors associated with study discontinuation

were significant at a level of $p < 0.1$ (Fig. 2): having spent at least one night in jail during the trial; not staying on treatment after GRACE; having Medicaid; having difficulty with transportation to study site; choosing not to disclose their HIV status to others; not having a high-school diploma; not feeling it was important that medications other than darunavir were provided during the study; or feeling that it was important that the study nurse was the same sex. Factors associated with study completion (significant at a level of $p < 0.1$) were having private insurance, working, or not having children.

Virologic response to study medications was defined as ITT-TLOVR < 50 HIV-1 RNA copies/mL at week 48, and the following factors were significant at a level of $p < 0.1$ (Fig. 3): paying for HIV medications with private insurance, being educated about HIV by research coordinator/HIV magazines/brochures/other, working, having private insurance and having the need to access medications as a main reason for participation in GRACE. Factors associated with not achieving a virologic response were difficulty keeping appointments prior to the GRACE trial, not feeling it was important that medications other than darunavir were provided during the study, having Medicaid, problems with transportation to study site, paying for HIV medications with Medicaid or Medicare, feeling it was important that the study nurse was the same sex, having trouble taking HIV medications prior to the GRACE trial, traveling to study site via transportation other than personal car, or being a primary caregiver.

Discussion

GRACE was reported as a very positive experience for most survey participants. Although other reports have

assessed patient experiences as they relate to HIV care in general,¹⁶ to our knowledge, this is the first report of a post-trial exploratory survey to assess patient experiences as they relate to clinical outcomes following a large trial. Most respondents were recruited to participate in GRACE via their clinic, suggesting that media outreach programs may have less impact than originally thought or hoped. GRACE's enrollment success may be attributed to the access to treatment it provided for participants, as this was often cited as an important reason for participation. In addition, people who felt that availability of medications other than darunavir during GRACE was important were more likely to complete the study and had better virologic responses. The main factors linked to completion of the GRACE study were access to treatment and family and study site support. Although most survey respondents reported having no difficulty with arranging transportation to the GRACE site, those that did have difficulty and/or used a mode of transportation other than their own vehicle were more likely not to achieve a virologic response. Past experiences as they relate to difficulties adhering to HIV medications and keeping medical appointments were associated with lower adherence, study discontinuation, and lower virologic response rates while participating in GRACE. Similar respondent characteristics/responses were observed to be associated with adherence, study discontinuation, and virologic outcomes; this was not surprising given the fact that a lack of adherence to study medication, as well as study discontinuation are likely to affect virologic response. A prospective survey of antiretroviral-naïve and -experienced HIV-infected patients treated once daily with single-pill, fixed formulations of nucleoside/nucleotide reverse transcriptase inhibitors found that the reported adherence rate was more than 90%. Adjusting treatment regimens to more convenient formulations upon identification of patients with or likely to have poor adherence may ultimately improve patient outcomes.¹⁷

There were some limitations of the survey. This was a post-hoc analysis, not prespecified in the protocol, and only 35% of the overall GRACE population (151 of 429) completed the survey. The survey was conducted 1.5 years after completion of the GRACE trial. This limitation may actually be beneficial because better insight may have been obtained after the excitement and emotion of the trial were over. A potential confounding factor may be HIV care providers' negative perceptions of female versus male patients, resulting in gender disparities in HIV care.¹⁸ This may potentially lead to lower adherence rates in women compared with men. Although the survey respondents overall represented the participants in the GRACE trial, there were some small differences. Fewer respondents were black, more used recreational drugs, responders had less HIV stage C disease (which is indicative of progression to AIDS), and they had a higher median baseline CD4 cell count. Fewer respondents had discontinued GRACE and more had achieved higher response rates. As survey completion was not mandated for GRACE trial participants, those who had a lower discontinuation rate, higher response rate, and greater adherence were more likely to (and did) complete the survey.

Patients with certain characteristics or lifestyles may be at greater risk for experiencing poor study outcomes. Study respondents with or who are the primary caregiver of children and/or grandchildren, those who were not working, and those

who experienced difficulties arranging transportation experienced less adherence, study completion, and virologic response.

Conclusions

Overall, baseline characteristics of survey respondents were representative of participants in the GRACE trial. Respondents cited access to treatment as the main reason for participation in the study, and completion of the study was attributable to support from the study site staff. Patients with certain characteristics may be at risk for poor study outcomes and may benefit from additional efforts with the aim of improving drug adherence, study retention, and, ultimately, clinical outcomes. Acknowledging these characteristics may be useful when designing future clinical trials for patients with HIV, especially women.

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