

The GRACE Study: A Unique Clinical Trial in Treatment-Experienced Women With HIV

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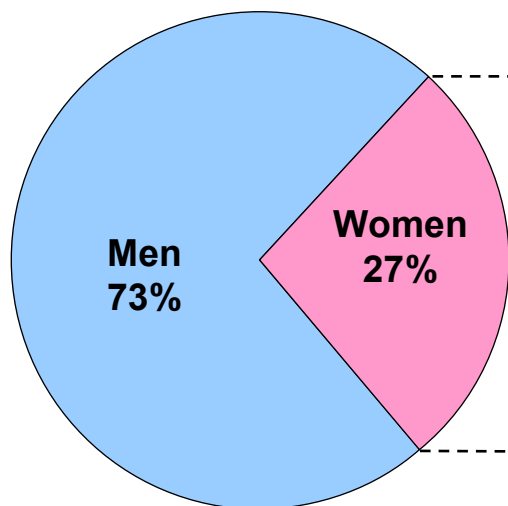
Introduction

- Despite research suggesting sex-based differences in drug efficacy, toxicity, and tolerability profiles, women have been underrepresented in HIV clinical trials¹
- Recent data suggest that sex has a small but significant influence on the clinical and laboratory outcomes of HIV infection²
- Late initiation and premature discontinuation of antiretroviral therapy has been shown to reduce life-expectancy
 - These losses have been reported with higher frequency in racial and ethnic minorities, especially black and Hispanic women³

Adults and Adolescents Living with HIV/AIDS in the US

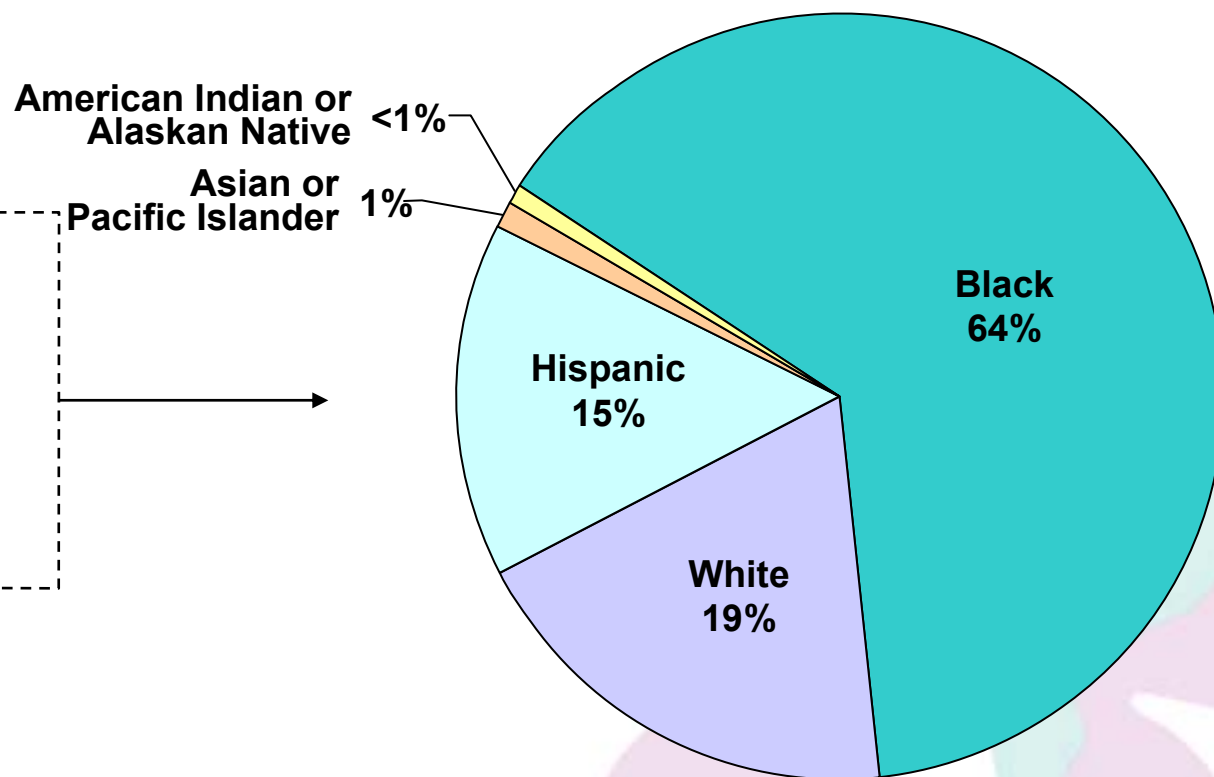
Total adults, by sex

N = 468,488



Women, by race/ethnicity

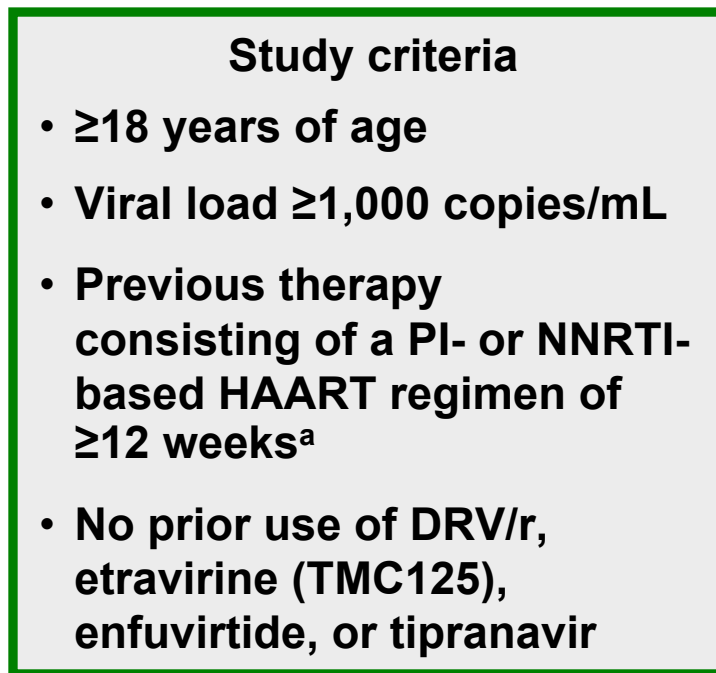
n = 126,964



- Women account for over one-quarter of all adults and adolescents in the US living with HIV/AIDS; infection rates are particularly high among women of color

GRACE

- GRACE is the largest treatment trial to focus on women with HIV in North America, and the first to focus on antiretroviral treatment-experienced women in North America
- GRACE is a multicenter, open-label phase IIIb trial designed to assess sex and race differences in efficacy, safety, and tolerability of darunavir/ritonavir (DRV/r) over 48 weeks in treatment-experienced patients



Target Enrollment^c
N = 420

**DRV/r 600/100mg bid
+ investigator-selected OBR^b**

48 Weeks

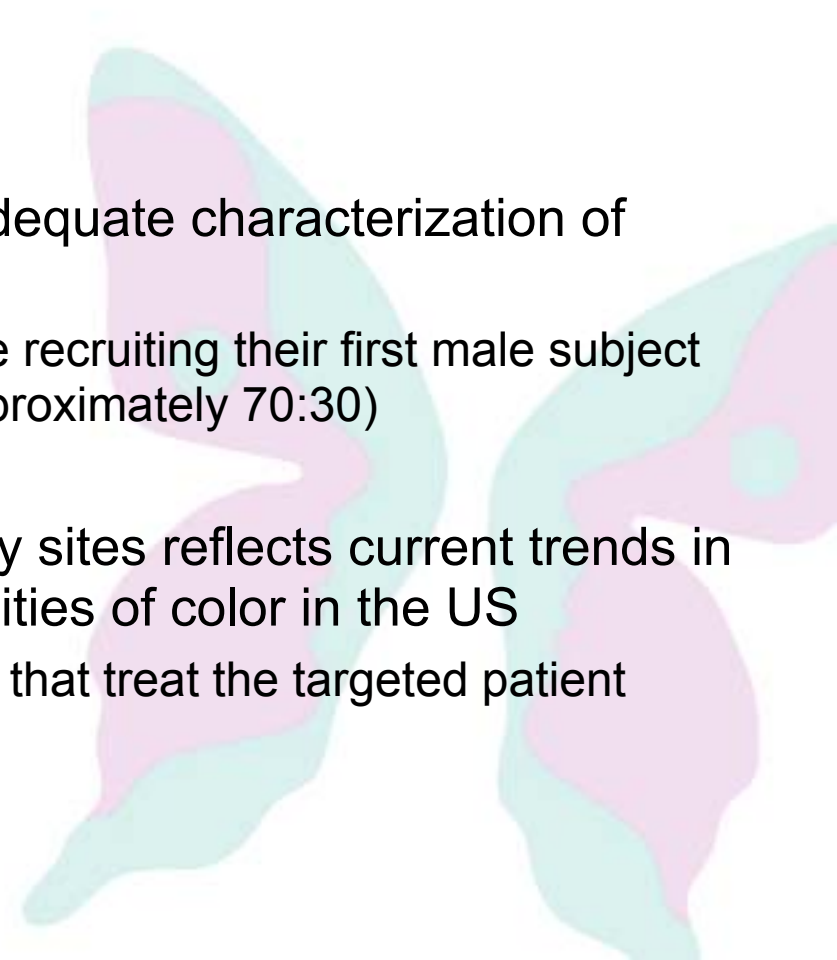
4-Week follow-up

^cTarget enrollment ratio was approximately 70:30 (women-to-men)

^aPatients were allowed to enter the study on treatment interruption of ≥4 weeks;
^bNNRTIs and NNRTIs included; ENF, TPV, or agents from novel classes were not allowed; OBR = optimized background regimen; DRV/r = darunavir/ritonavir

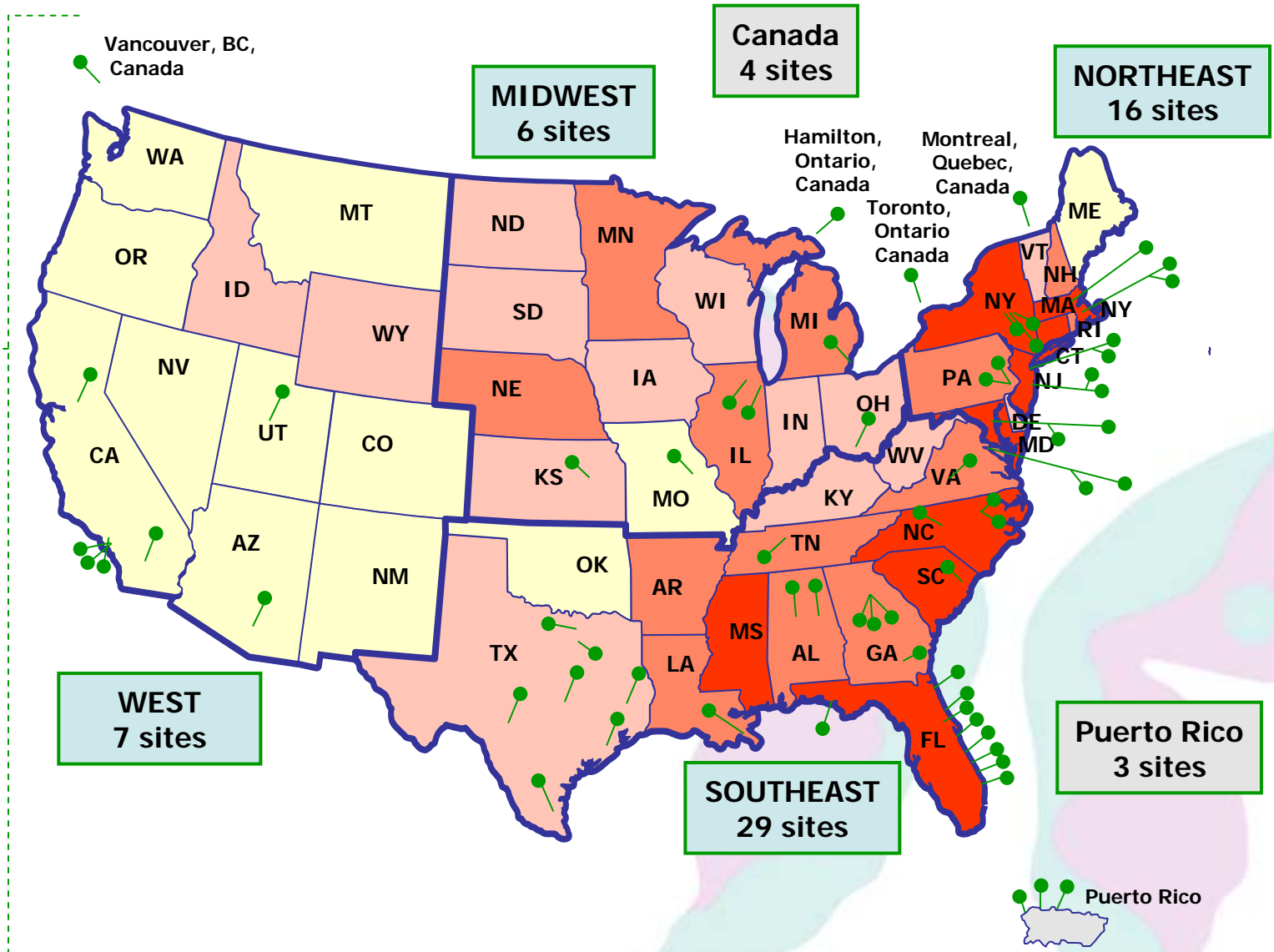
GRACE Enrollment

- Target enrollment of 420 patients was achieved (November 2006 - November 2007)
- 429 patients have enrolled in the GRACE study
 - 67% (n=287) women, 33% (n=142) men
 - 62% (n=266) black, 22% (n=94) Hispanic
- Women were over-represented to allow for adequate characterization of safety and tolerability in this population
 - Sites were required to recruit 3 women before recruiting their first male subject in order to meet the pre-determined ratio (approximately 70:30)
- The geographical distribution of GRACE study sites reflects current trends in HIV/AIDS cases among women and communities of color in the US
 - The study team solicited novel research sites that treat the targeted patient populations



Number of Active GRACE Study Sites in North America

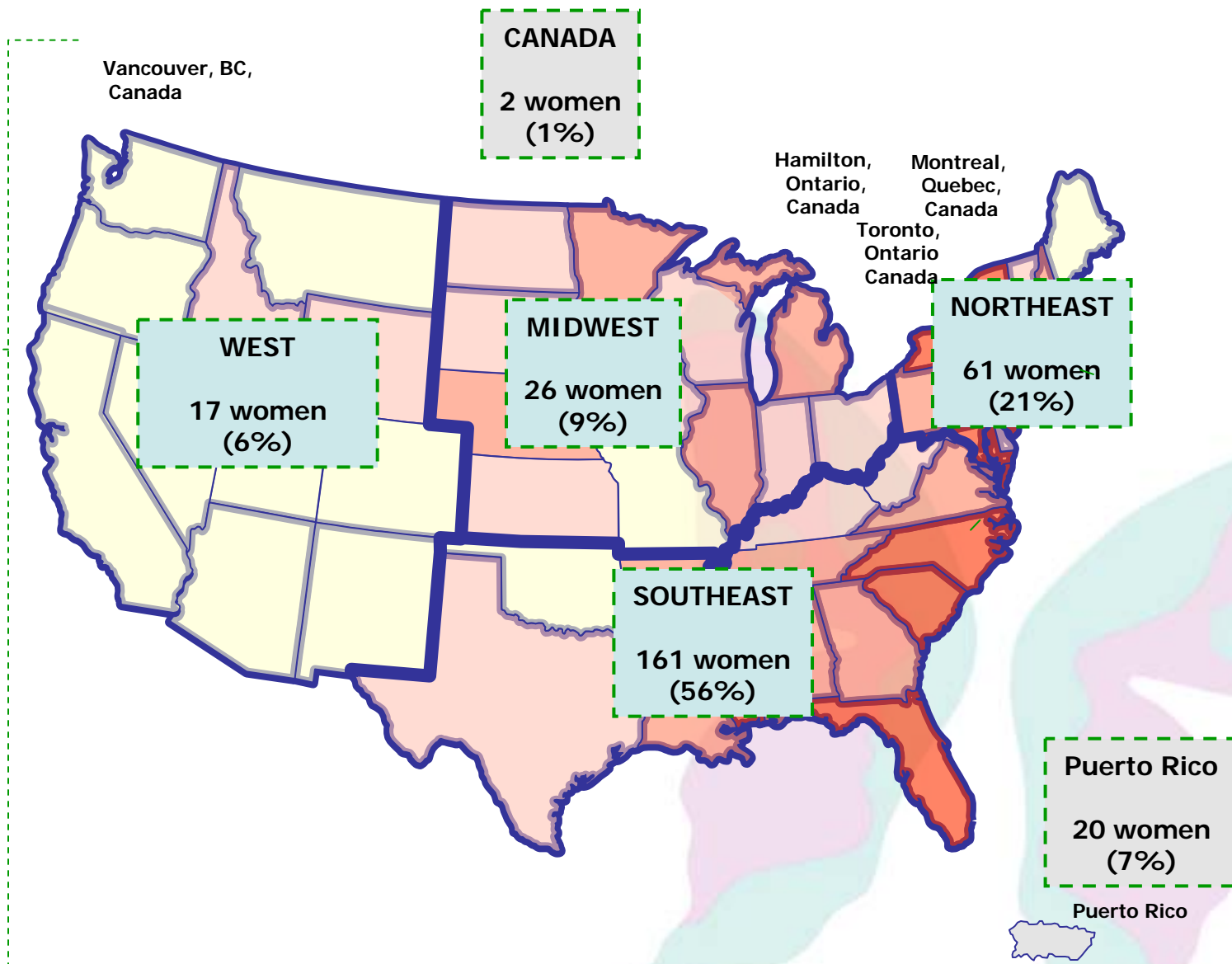
Region	n
USA	58
Canada	4
Puerto Rico	3



¹CDC. *HIV/AIDS Surveillance Report*. 2005;17:9. Revised June 2007.

Geographical Distribution of 287 Women Enrolled in GRACE

Region	Study sites (n)
USA	
Southeast	29
Northeast	16
West	7
Midwest	6
Canada	4
Puerto Rico	3



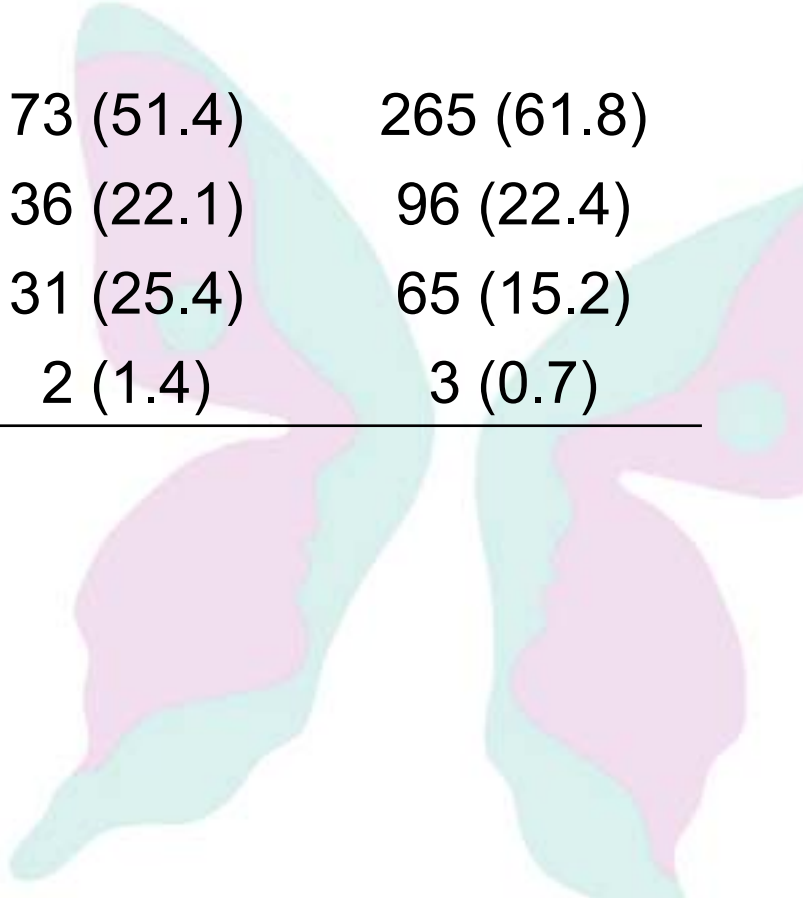
Proportion of HIV/AIDS cases that are female, by state¹

- 10.4% – 16.0%
- 16.4% – 19.6%
- 20.1% – 26.2%
- 26.4% – 33.2%

¹CDC. *HIV/AIDS Surveillance Report*. 2005;17:9. Revised June 2007.

GRACE Demographics

	Women (n = 287)	Men (n = 142)	All patients (N = 429)
Age, mean (range), years	42.5 (19–79)	45.8 (22–78)	43.6 (19–79)
Race/ethnicity, n (%)			
Black	192 (66.9)	73 (51.4)	265 (61.8)
Hispanic	60 (20.9)	36 (22.1)	96 (22.4)
White	34 (11.8)	31 (25.4)	65 (15.2)
Other	1 (0.3)	2 (1.4)	3 (0.7)



Strategies for Site Outreach and Patient Support for the GRACE Study

- Reducing barriers to care
 - Provision of some commonly used NRTIs for use in OBR
 - Provision of an experimental antiretroviral (etravirine)
 - Per diem for child care and travel
- Awareness and outreach
 - Unique study branding, including logo and colors
 - Targeted awareness campaigns in minority media
- Recruitment
 - Inclusion of sites with a focus on the care of women
 - Regular site visits, site support meetings, and site-specific enrollment plans
- Study retention
 - Supplemental site grants for patient support activities
 - Site and patient toolkits
 - Increased flexibility and availability of healthcare practitioners at study sites
- Continuous involvement with patient advocates, study sites and investigators throughout all phases of the study



GRACE Toolkit Contents

Site Outreach

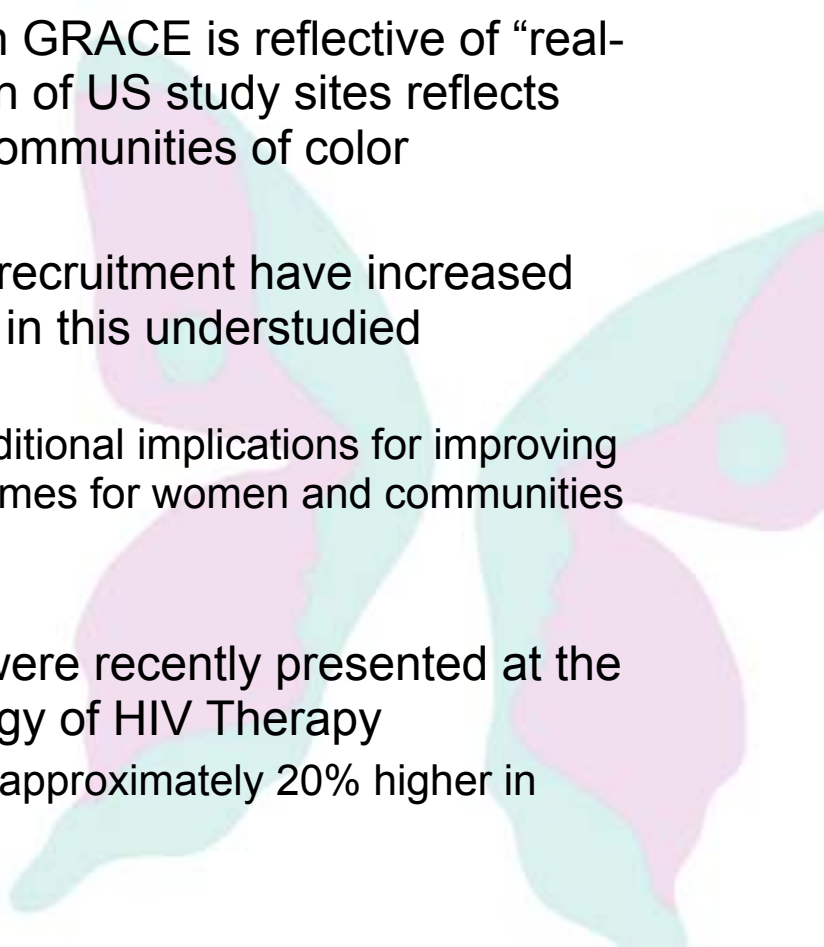
- CD
 - Templates for public service announcements
 - “Dear Colleague” letter
 - Templates for flyers and ads
 - Grant applications
- Balloons and buttons
- Inclusion/exclusion cards
- Novel activity reporting form
- GRACE pens
- Site pamphlet on women in research

Patient Support

- Black tote bag with GRACE embroidery
- Day planner with calendar
- GRACE pen
- Water bottle
- Single-dose pill box
- Site contact card
- Insulated cooler bag



GRACE Summary

- GRACE is the largest treatment trial to date in North America to focus on women with HIV
 - GRACE target enrollment figures were met according to schedule, including sex-specific targets
 - The racial/ethnic composition of women enrolled in GRACE is reflective of “real-world” HIV demographics in the US and distribution of US study sites reflects current epidemiologic trends among women and communities of color
 - Novel approaches to site selection, outreach, and recruitment have increased awareness and overcome hurdles for participation in this understudied population
 - The effectiveness of these strategies may have additional implications for improving access to HIV care and enhancing treatment outcomes for women and communities of color outside of a clinical trial setting
 - Preliminary PK data from a sub-study of GRACE were recently presented at the 9th International Workshop on Clinical Pharmacology of HIV Therapy
 - Median exposure to DRV (AUC_{12h}) at Week 4 was approximately 20% higher in women compared with men
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Acknowledgments

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