Prevention of Events with Angiotensin Converting Enzyme Inhibition (PEACE) Trial

CRP Ancillary Data
(High sensitivity C-reactive protein)
Limited Access Data Set Documentation

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1 Overview of the CRP Ancillary Limited Access Data Set

This CD contains documentation and data comprising the CRP Ancillary Limited Access Data Set for the Prevention of Events with Angiotensin Converting Enzyme Inhibition (PEACE) trial. This data release includes data collected as ancillary data to the main PEACE trial. These data include the biomarker, high sensitivity C-reactive protein. The commercial purpose data set is the same as the non-commercial data set, so only one data set is provided.

2 Overview of the Main Study Limited Access Data Set

The Limited Access Data Set for the Prevention of Events with Angiotensin Converting Enzyme Inhibition (PEACE) trial is available as a separate data set. Data from the main study includes baseline and follow-up data collected from initiation of the trial (November 1996) through the conclusion of the trial (December 2003).

3 PEACE Publications and Ancillary Studies Committee

The PEACE Publications and Ancillary Studies Committee plans to remain active and requests that investigators share their proposals/analysis plans with the Committee so that the Committee can encourage collaborations and avoid redundancies. Please send an e-mail to Drs. Eugene Braunwald, Marc Pfeffer and Bernard Gersh, expressing your interest in and your proposed use of the PEACE limited access data set. Their e-mail addresses are: EBraunwald@partners.org, MPfeffer@rics.bwh.harvard.edu, Gersh.Bernard@mayo.edu

4 Description of the Trial

4.1 Purpose

The goal of the PEACE trial was to test whether ACE-inhibitor therapy, when added to modern conventional therapy, would reduce the rate of nonfatal myocardial infarction, death from cardiovascular causes, or coronary revascularization in low-risk patients with stable coronary artery disease and normal or slightly reduced left ventricular function.

4.2 Overall Study Design

The trial was a double-blind, placebo-controlled study in which 8290 patients were randomly assigned to receive either trandolapril at a target dose of 4 mg per day (4158 patients) or matching placebo (4132 patients). Patients underwent randomization from November 1996 to June 2000 and were followed at six-month intervals for up to 7 years (median, 4.8 years) through December 2003.

4.3 Inclusion Criteria

- Age 50 years or older
- Coronary artery disease documented by at least one of the following:
  - Myocardial infarction at least 3 months before enrollment

- Coronary-artery bypass grafting or percutaneous transluminal coronary angioplasty at least 3 months before enrollment
- Obstruction of ≥50% of the luminal diameter of at least one native vessel on coronary angiography

- Left ventricular ejection fraction >40% on contrast or radionuclide ventriculography or echocardiography, a qualitatively normal left ventriculogram, or the absence of left ventricular wall-motion abnormalities on echocardiography (a subgroup of echocardiograms was reviewed by a core laboratory to confirm eligibility)
- Toleration of the medication and successful completion of the run-in phase, with ≥80% compliance with the medication

4.4 Exclusion Criteria

- Current use of or a current condition requiring use of an ACE inhibitor or a contraindication to ACE inhibitors
- Current use of an angiotensin II–receptor antagonist
- Hospitalization for unstable angina within the preceding 2 months
- Valvular heart disease deemed to require surgical intervention
- Coronary-artery bypass grafting or percutaneous transluminal angioplasty within the preceding 3 months
- Planned elective coronary revascularization
- Serum creatinine >2.0 mg/dl (177 μmol/liter)
- Serum potassium >5.5 mmol/liter
- Limited chance of 5-yr survival
- Psychosocial condition precluding long-term adherence
- Unable or unwilling to give consent
- Female sex and of childbearing potential and not using contraception
- Current use in a research trial of medication not approved by the U.S. Food and Drug Administration or the Health Protection Branch of the Canadian Department of National Health and Welfare

4.5 Study Organization

The PEACE trial was sponsored by the National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI). An independent data and safety monitoring board reviewed patient safety data and interim results. An executive committee and a steering committee provided scientific leadership and a clinical and statistical coordinating center coordinated all elements of the trial. An Italian coordinating center oversaw the data collection process in Italy. Patients were enrolled from 187 clinics in the United States (including Puerto Rico), Canada, and Italy. Study medication was distributed by a central pharmacy. All specimens went to a central laboratory and a morbidity and mortality review committee adjudicated outcomes. A publications and ancillary studies committee reviewed and approved proposals, manuscripts and presentations.

4.6 Outcomes Documentation and Adjudication

The following outcomes were classified by centrally-trained, local staff and confirmed by outcomes staff at the coordinating center through review of medical records:

- Coronary-artery bypass grafting

- Percutaneous coronary intervention
- Hospitalization for unstable angina
- Peripheral vascular disease requiring angioplasty, bypass grafting, or aneurysm repair
- Hospitalization for congestive heart failure
- Hospitalization for cardiac arrhythmia

A morbidity and mortality review committee conducted a further review of medical records, and classified and adjudicated the following outcomes:

- Cardiovascular death
- Non-cardiovascular death
- Death from unknown causes
- Myocardial infarction

Further review of medical records by one of the morbidity and mortality review committee members was conducted for the following outcome:

- Stroke

All reviews were blinded to the study intervention.

The following outcome was ascertained by patient self-report:

- New-onset diabetes

5 Description of the CRP Ancillary Data

5.1 Purpose

To examine whether concentrations of high sensitivity C-reactive protein (hs-CRP) is associated with outcomes in PEACE patients who provided EDTA plasma specimens.

5.2 Overall Biospecimen Collection in PEACE

Blood and urine samples (serum, EDTA plasma, citrate plasma and urine) were obtained at the clinical centers. Blood samples were centrifuged at room temperature, processed per standard laboratory methods, then frozen within 90 minutes of collection at -20°C at the individual centers. Within 2 weeks (clinics with a -20°C freezer) or 2 months (clinics with a -70°C freezer) of collection, samples were shipped on dry ice via over-night delivery to the PEACE central laboratory for storage at -70°C. A baseline blood sample was obtained in approximately 3786 participants. A follow-up blood sample was obtained in approximately 2081 participants whom also had a baseline blood sample and in 696 participants whom did not have a baseline blood sample. A baseline urine sample was obtained in approximately 3414 participants. A follow-up urine sample was obtained in approximately 1891 participants whom also had a baseline urine sample and in 606 participants whom did not have a baseline urine sample. The follow-up sample was not standardized with regards to time since randomization and was obtained in a time period from just after randomization to 6 years, 3 months from randomization; for a median

of 3 years. Sample collection was not standardized with regards to time of day or time since last meal. All participants from the US and Canada were eligible for biospecimen collection.

5.3 Biomarker Information

Biomarker measurements were performed by personnel blinded to clinical outcomes and treatment allocation.

EDTA plasma was thawed and aliquots shipped frozen from the PEACE central laboratory on dry ice to the Thrombolysis in Myocardial Infarction (TIMI) Biomarker Laboratory (Boston, MA) for hs-CRP testing using the CRP-Latex (II) immunoturbidimetric assay (Denka Seiken, Tokyo, Japan) on a Hitachi 911 immunoanalyzer (Roche Diagnostics, Indianapolis, IN, USA). This assay has a minimal detectable concentration of 0.03 mg/L and a total imprecision of 5.1% and 2.5% at concentrations of 0.2 and 1.9 mg/L, respectively.*

Baseline hs-CRP was measured in 3771 participants and follow-up hs-CRP was measured in 1961 participants.

* Roberts WL, Moulton L, Law TC, Farrow G, Cooper-Anderson M, Savory J, Rifai N. Evaluation of nine automated high-sensitivity C-reactive protein methods: implications for clinical and epidemiological applications, part 2. Clin Chem. 2001;47:418–425.

5.4 Study Design

The study design is a cohort study design, conducted among patients providing EDTA plasma samples. The follow-up measurements were in participants whom also had a baseline sample.

6 Files and Documents on the CD

6.1 Limited Access Data Set as a SAS CPORT Transport Library

- *CRP.LADS* (SAS CPORT transport library)
    - This transport library can be imported into any system (PC, Unix, Mainframe OS, etc.). For instructions on importing the file, please see Section 8 "***Installing the SAS Files.***" Conversion of the files using CIMPORT is required.

6.2 Limited Access Data Set as a PC SAS Data Set

- *CRP.sas7bdat*
    - For investigators that use PC SAS, this file can be read in directly by PC SAS versions 7, 8 and 9. No import program is necessary.

6.3 Import Program

- *PEACE_Import.sas* (SAS program that can be used to import the file)

6.4 Readme Document (this document)

- *PEACE readme CRP.pdf* (pdf document)

6.5 List of Publications Associated with these Ancillary Data

- *List of Publications PEACE CRP.pdf* (pdf document)

7 Description of System Requirements

- CD-ROM drive
- A working installation of the SAS system version 8 or later

8 Installing the SAS Files

8.1 PC SAS Users:

- Copy the PC SAS data set from the CD to a directory on the system running the SAS software. The PC SAS format file can be read in directly by PC SAS versions 7, 8 and 9. No import program is necessary.

8.2 All Other Users (Unix, Mainframe OS, etc.):

- Transfer the SAS CPORT transport library from the CD to a directory on the system running the SAS software. The transfer must be made using binary format.

- Execute a program such as the one below to read the transport library and convert it to a native SAS library format suitable for your operating system. Remember to change the directory and file names appropriately. This program is included on the CD, called "*PEACE_Import.sas*"

```
filename xin 'C:\Peace\SAS Data\CRP.lads';
LIBNAME CRP 'C:\Peace\SAS Data';
PROC CIMPORT LIBRARY=CRP INFILE=XIN MEMTYPE=ALL;
run;
```

- The imported data set is:
  - *CRP.sas7bdat* (SAS data file)

9 Contents of the CRP Ancillary Limited Access Data Set

The table below lists all variables in the CRP ancillary limited access data set. The data set file includes a participant ID (NEW_ID) that links all data set files. Merge data files by this variable.

Variable	Comments
NEW_ID	**Merge data files by this variable**
B_CRP	Baseline hs-CRP Units = mg/L Recoded baseline hs-CRP < 0.15 = 0.09 Recoded baseline hs-CRP > 40.00 = 58.41
F_CRP	Follow-up hs-CRP Units = mg/L Recoded follow-up hs-CRP < 0.20 = 0.15 Recoded follow-up hs-CRP > 25.00 = 32.90
DAYSBLOOD	Days since randomization for blood draw for follow-up hs-CRP (F_CRP) Units = days