SC WEBINAR

ISCHEMIA Case Studies
Finding the Right Patients

ISCHEMIA

Moderator

Mary Anne Cox
Program Deputy Director
Ischemia Clinical Coordinating Center
NYU Cardiovascular Clinical Research Center

Housekeeping

- All phone lines will remain unmuted to allow for questions during presentations. Please mute your own phone if there is noise in the background.
- You may also type any questions you have into the chat box located on the side of your screen.
- During Case Presentation we will ask you to answer questions in the chat box also.

AGENDA

- Study Update
- Inclusion / Exclusion Review
- Case Studies
- Q&A

General Study Update

David Maron, MD
ISCHEMIA Trial Co-Chair/PI
Clinical Professor of Medicine (Cardiovascular)
Director, Preventive Cardiology
Stanford University School of Medicine

1924 Enrolled

- Insufficient ischemia = 285/1924 (14.8%)
- No obstructive disease = 158/1228[1] (12.9%)
- Left Main disease = 113/1228[1] (9.2%)
- Incidental Findings = 5/1228[1] (0.4%)
- Other = 127/1924 (6.6%)
- 122 Pending Confirmation of Eligibility

1114 Randomized

As of 10/20/14

[1] Denominator = CCTA screened

Enrolled Pt Demographics (n=1924)

Mean age = 64
Female = 489 (25.4%)
eGFR 30-59 = 199(10.3%; no CCTA)

Excluded Pt Demographics (n=688)

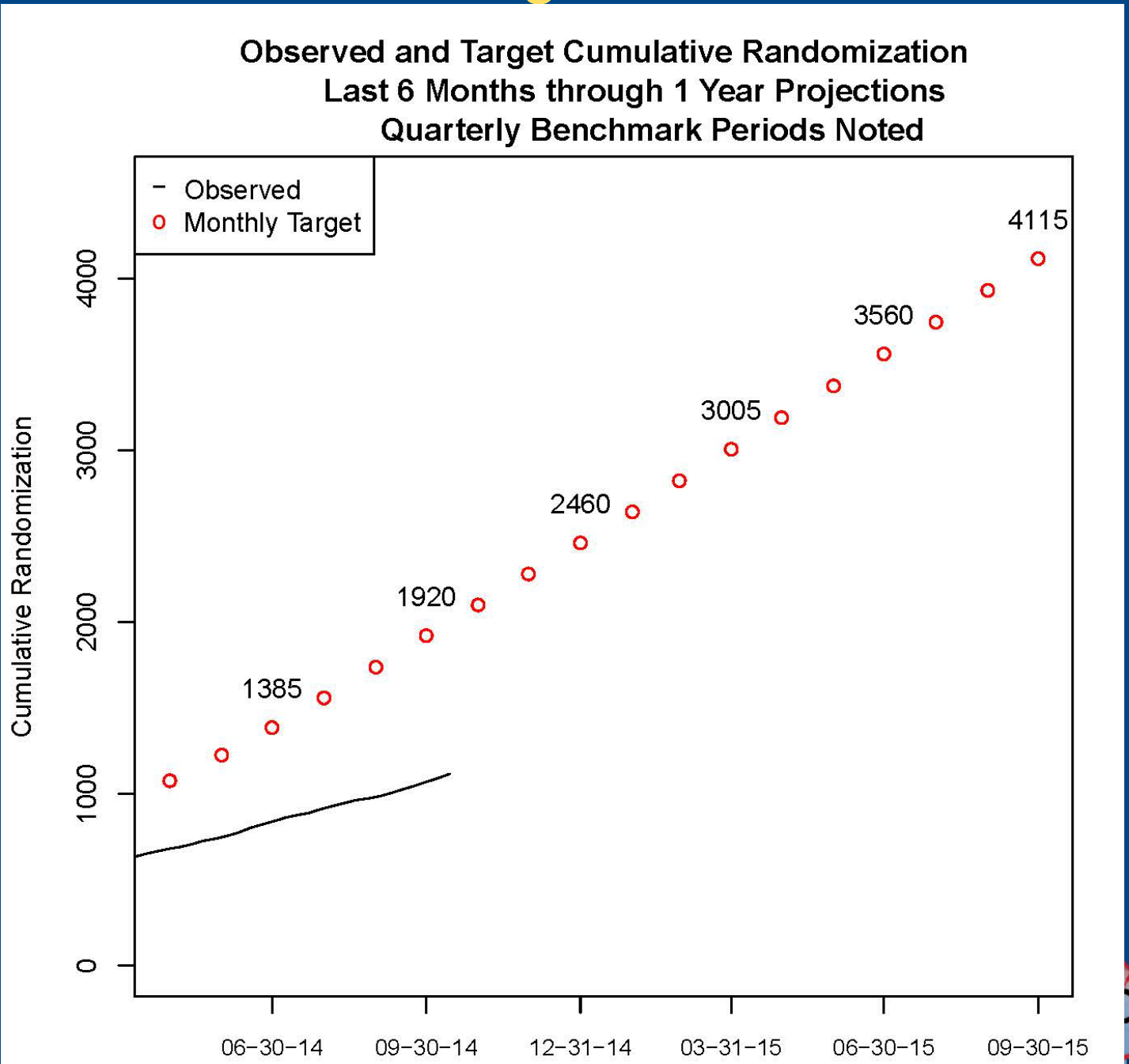
Mean age = 63
Female = 221 (32.1%)

Rand. Pt Demographics (n=1114)

Mean age = 64
Female = 243 (21.8%)
eGFR 30-59 = 141 (12.7%)

Countries	
Argentina: 14	Lithuania: 17
Australia: 7	Mexico: 12
Austria: 19	New Zealand: 11
Belgium: 2	Poland: 112
Brazil: 25	Russia: 29
Canada: 163	Saudi Arabia: 3
China: 20	Serbia: 8
France: 9	Singapore: 5
Germany: 2	Spain: 37
Hungary: 17	Sweden: 4
India: 85	Switzerland: 4
Israel: 9	Macedonia: 11
Italy: 67	United Kingdom: 133
Japan: 3	United States: 286

Observed vs. Target Randomizations



As of
10/15/14

Top Randomizers

Country	Site Name	Investigator	Study Coordinator	Enrolled	Randomized	Pending
United Kingdom	Northwick Park Hospital-Royal Brompton Hospital, London	Roxy Senior	Jo Evans, Sothinathan Gurunathan, Linda Haimbodi, Raisa Kavalakkat, Christopher Kinsey	102	**62**	3
Poland	Coronary and Structural Heart Diseases Department, Institute of Cardiology, Warsaw	Marcin Demkow	Radek Pracon, Olga Chojnacka	46	**41**	2
Canada	Montreal Heart Institute, QC	Gilbert Gosselin	Rima Amche, Magalie Corfias	64	**37**	2
India	Medical College Calicut	Mangalath Krishnan	Sajeesh Pontrasseri	45	**33**	5
Spain	Hospital Universitario La Paz	Jose Lopez-Sendon	Almudena Castro, Silvia Valbuena	45	**28**	3

As of 10/20/14

Inclusion/Exclusion Criteria

Inclusion Criteria: Stress Imaging Criteria

Nuclear Perfusion via SPECT or PET	**Echo**	**CMR**	**ETT** *(for Protocol v2.0)*
≥10% myocardium ischemic	≥3/16 segments with stress-induced severe hypokinesis or akinesis	perfusion: ≥12% myocardium ischemic and/or wall motion: ≥3/16 segments with stress-induced severe hypokinesis or akinesis	See criteria on next slide

Inclusion Criteria: ETT

Exercise Testing ***without*** Imaging (all 4 criteria must be met)

1. Clinical history of typical angina or typical angina during the exercise test
2. Absence of resting ST segment depression ≥1.0 mm or confounders that render exercise ECG non-interpretable (LBBB, LVH with repolarization, pacemaker, etc.)
3. As compared to the baseline tracing, additional exercise-induced horizontal or downsloping ST segment depression ≥1.5 mm in 2 leads *or ≥2.0 mm in any lead*
4. Either of the following:
   a. Workload at which ST segment criteria are met is not to exceed completion of stage 2 of a standard Bruce protocol or 7 METS if a non-Bruce protocol is used *or*
   b. ST segment criteria are met at <75% of the maximum predicted HR

Major Exclusion Criteria

- LVEF < 35%
- History of unprotected left main stenosis ≥50% on prior coronary computed tomography angiography (CCTA) or prior cardiac catheterization (if available)
- Finding of “no obstructive CAD” (<50% stenosis in all major epicardial vessels) on prior CCTA or prior catheterization, performed within 12 months
- Coronary anatomy unsuitable for either PCI or CABG
- Unacceptable level of angina despite maximal medical therapy
- Very dissatisfied with medical management of angina
- Canadian Cardiovascular Society Class III angina of recent onset, or angina of **any class** with a rapidly progressive or accelerating pattern
- Canadian Cardiovascular Society Class IV angina, including unprovoked rest angina
- History of noncompliance with medical therapy

Exclusion:
Participant-reported unacceptable level of angina despite maximal medical therapy

- Ask the question "Over the past 4 weeks, on average, how many times have you had chest pain, chest tightness, or angina?"
  - Potential responses:
    - 4 or more times per day
    - 1-3 times per day
    - 3 or more times per week but not every day
    - 1-2 times per week
    - Less than once a week
    - None over the past 4 weeks

At least daily angina without ability to further titrate medical or anti-anginal therapy excludes the participant.

Exclusion:
Very dissatisfied with medical management of angina

- Ask the question "How bothersome is it for you to take your pills for chest pain, chest tightness, or angina as prescribed?"
  - Potential responses:
    - Extremely bothersome
    - Quite a bit bothersome
    - Moderately bothersome
    - Slightly bothersome
    - Not bothersome at all
    - My doctor has not prescribed pills

"Extremely bothersome" excludes the participant

Major Exclusion Criteria

- LVEF < 35%
- History of unprotected left main stenosis ≥50% on prior coronary computed tomography angiography (CCTA) or prior cardiac catheterization (if available)
- Finding of “no obstructive CAD” (<50% stenosis in all major epicardial vessels) on prior CCTA or prior catheterization, performed within 12 months
- Coronary anatomy unsuitable for either PCI or CABG
- Unacceptable level of angina despite maximal medical therapy
- Very dissatisfied with medical management of angina
- Canadian Cardiovascular Society Class III angina of recent onset, OR angina of **any class** with a rapidly progressive or accelerating pattern
- Canadian Cardiovascular Society Class IV angina, including unprovoked rest angina
- History of noncompliance with medical therapy

Canadian Cardiovascular Society (CCS) Angina Classification

Class I

- **Ordinary physical activity does not cause angina**, such as walking, climbing stairs. Angina occurs with strenuous, rapid or prolonged exertion at work or recreation.

Class II

- **Slight limitation of ordinary activity**. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, or in wind, or under emotional stress, or only during the few hours after awakening. Angina occurs on walking more than 2 blocks on the level and climbing more than one flight of ordinary stairs at a normal pace and in normal conditions.

Class III OF RECENT ONSET

- **Marked limitation of ordinary physical activity**. Angina occurs on walking one to two blocks on the level and climbing one flight of stairs in normal conditions and at a normal pace.

Class IV

- **Inability to carry on any physical activity without discomfort**—anginal symptoms may be present at rest.

Angina and Noncompliance Exclusion Criteria

- The reason for these criteria is to exclude participants who, if randomized to CON, will need cardiac catheterization because their angina symptoms cannot be controlled with medical therapy because they are refractory to medications, dissatisfied with taking medications, or won't take them.

Exclusion: ACS syndrome within the previous 2 months

- Patients with acute coronary syndrome within the previous 2 months, defined as STEMI, non-STEMI, or rest angina subset of unstable angina, is excluded.
- Low risk unstable angina such as new onset angina that does not include rest angina or a rapid, high risk crescendo pattern on minimal exertion does NOT exclude patient.

Exclusion: Prior CABG

- Prior CABG, unless CABG was performed more than 12 months ago, and coronary anatomy has been demonstrated to be suitable for PCI or repeat CABG to accomplish complete revascularization of ischemic areas (CCC approval required)
- Rationale: patients with prior CABG initially permitted for enrollment, high rate of inability to revascularize in INV group

Case Studies