A Registry-Based Randomized Trial Comparing Radial and Femoral Approaches In Women Undergoing Percutaneous Coronary Intervention: The Study of Access Enhancement of PCI for Women (SAFE-PCI for Women) Trial

Sunil V. Rao MD, Connie N. Hess MD, Britt Barham, Laura H. Aberle, Kevin Anstrom PhD, Tejan B. Patel MD, Jesse P. Jorgensen MD, Ernest L. Mazzaferri MD, Sanjit S. Jolly MD, Alice Jacobs MD, L. Kristin Newby MD, C. Michael Gibson MD, David F. Kong MD, Roxana Mehran MD, Ron Waksman MD, Ian C. Gilchrist MD, Brian J. McCourt, Eric D. Peterson MD MPH, Robert A. Harrington MD, Mitchell W. Krucoff MD *on behalf of the SAFE-PCI for Women Investigators*

DCRI

Disclosures

- **Sunil V. Rao**
  - Consultant: The Medicines Company, Astra Zeneca
- **The SAFE-PCI for Women Trial was conducted in collaboration with the American College of Cardiology and funded by a consortium of academic, industry, and government entities**
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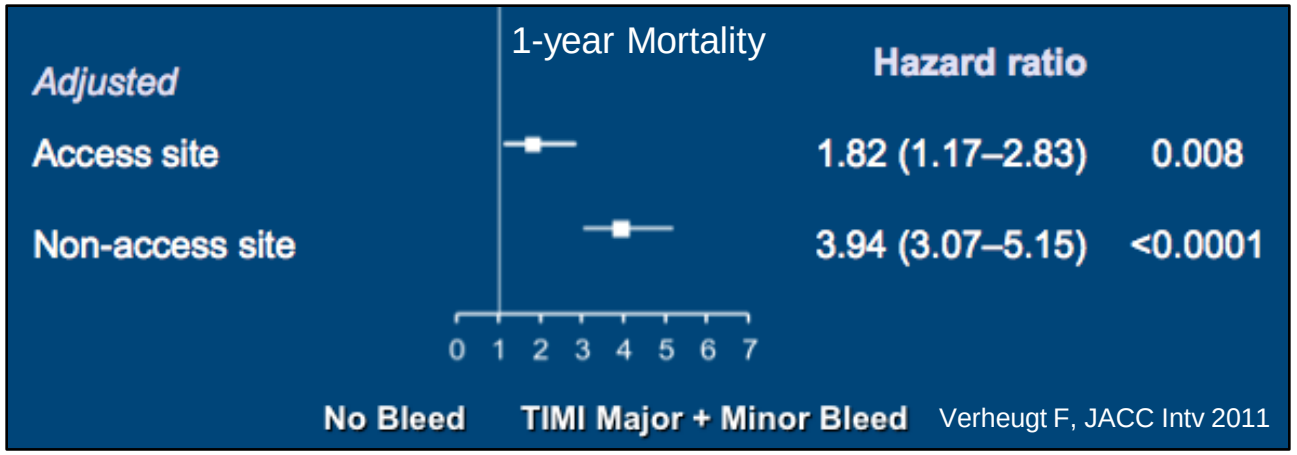
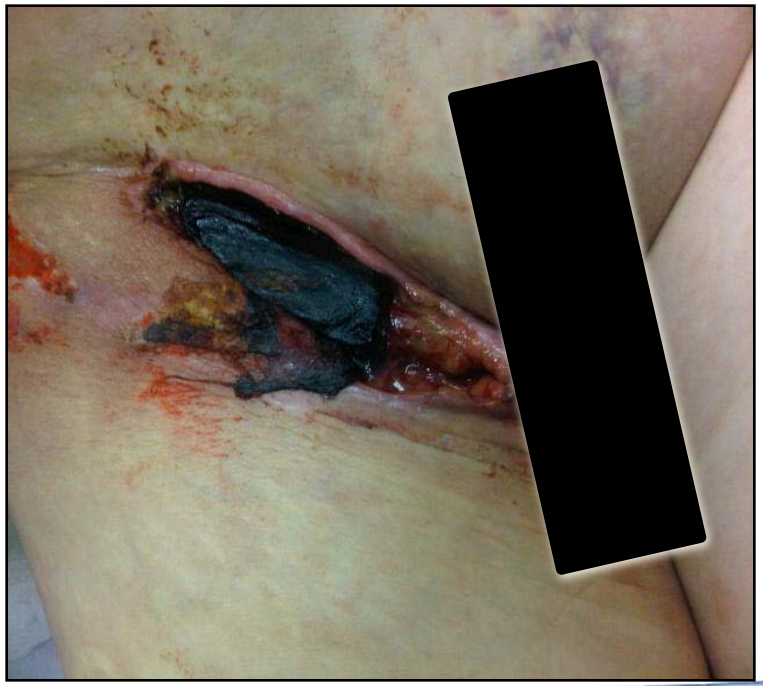
Post-PCI Bleeding and Outcomes



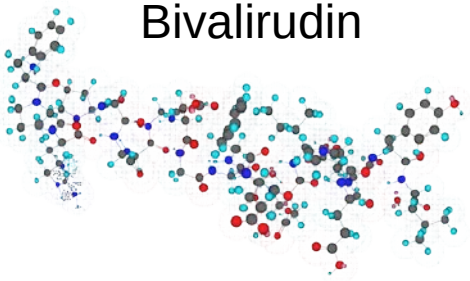
Verheugt F, JACC Intv 2011

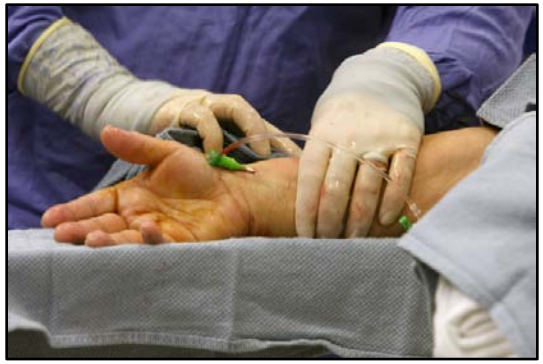
Kugelmass A, AJC 2006

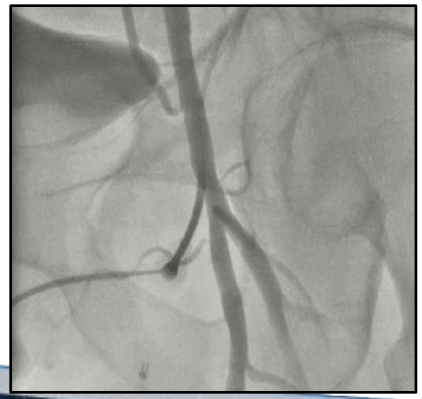


Bleeding avoidance strategies

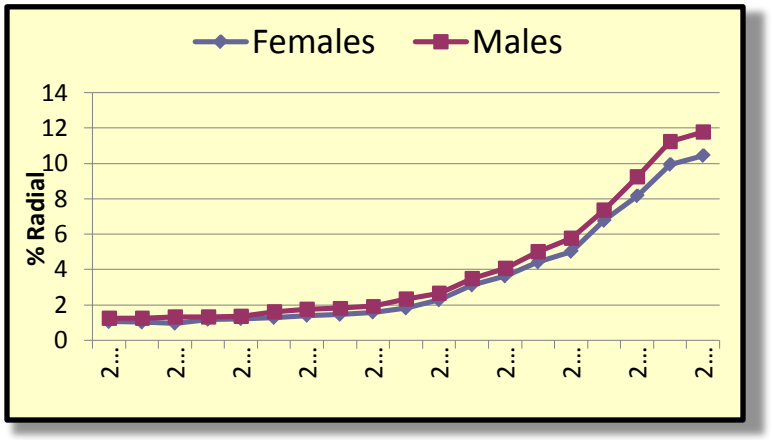
Bivalirudin

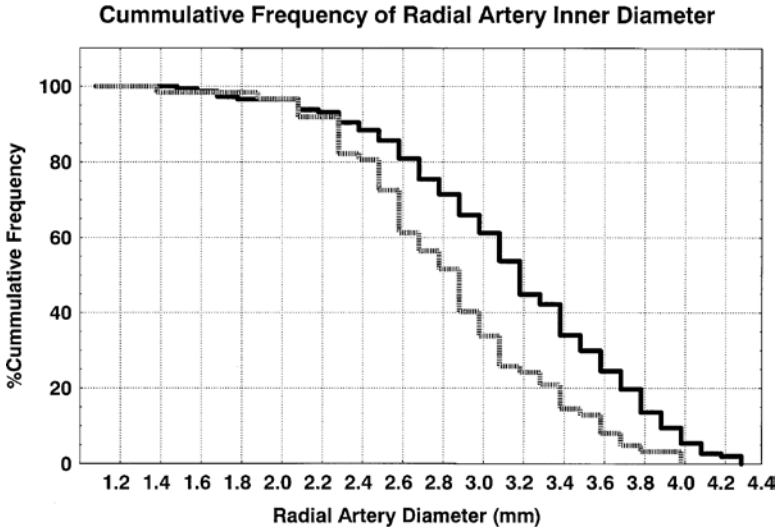






Radial approach in men vs. women
From the NCDR CathPCI Registry®





Dauerman HL, et. al. *JACC* 2011
Feldman DN, et. al. *Circ* 2013
Saito S, *CCI* 1999

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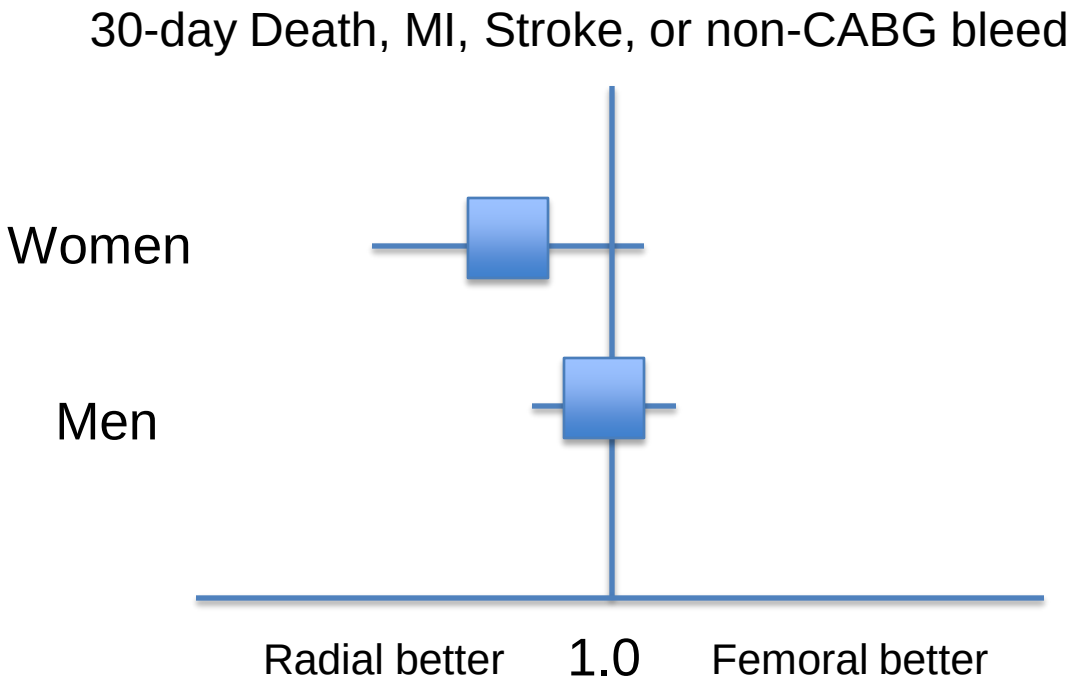
RIVAL Trial – Men vs. Women



- **Although PCI success was high, 7.6% crossover rate from radial to femoral**
- **Rate of primary outcome not different among women, crossover rates not examined**

The role of radial access in women is unclear

Jolly SS, et. al. *Lancet* 2011

SAFE-PCI for Women Objective

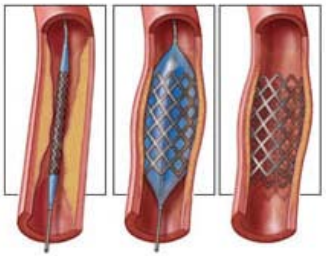
To determine the efficacy and feasibility of transradial PCI in women

National Cardiovascular Research Infrastructure

- **Embeds randomization into the NCDR CathPCI Registry**
- **Mechanism for identifying appropriate trial sites**
- **Estimation of endpoint event rates for sample size estimation**
- **Leverages the workflow of registry participants by electronically exporting trial-relevant data into an electronic case report form**
  - Reduction of redundant data entry (~60% data needed for study patients from CathPCI registry)
  - Reduced trial costs due to reduced site-level workload
- **Data output using CDISC SDTM standards**
- **21 CFR 11 compliant – IND and IDE applications**

SAFE-PCI for Women workflow

Randomization



Demographics
Medical Hx
Procedural data

NCDR® National Cardiovascular Data Registry
CathPCI Registry®

Autopopulate

ORACLE

Unique pages for trial

Analytic Database

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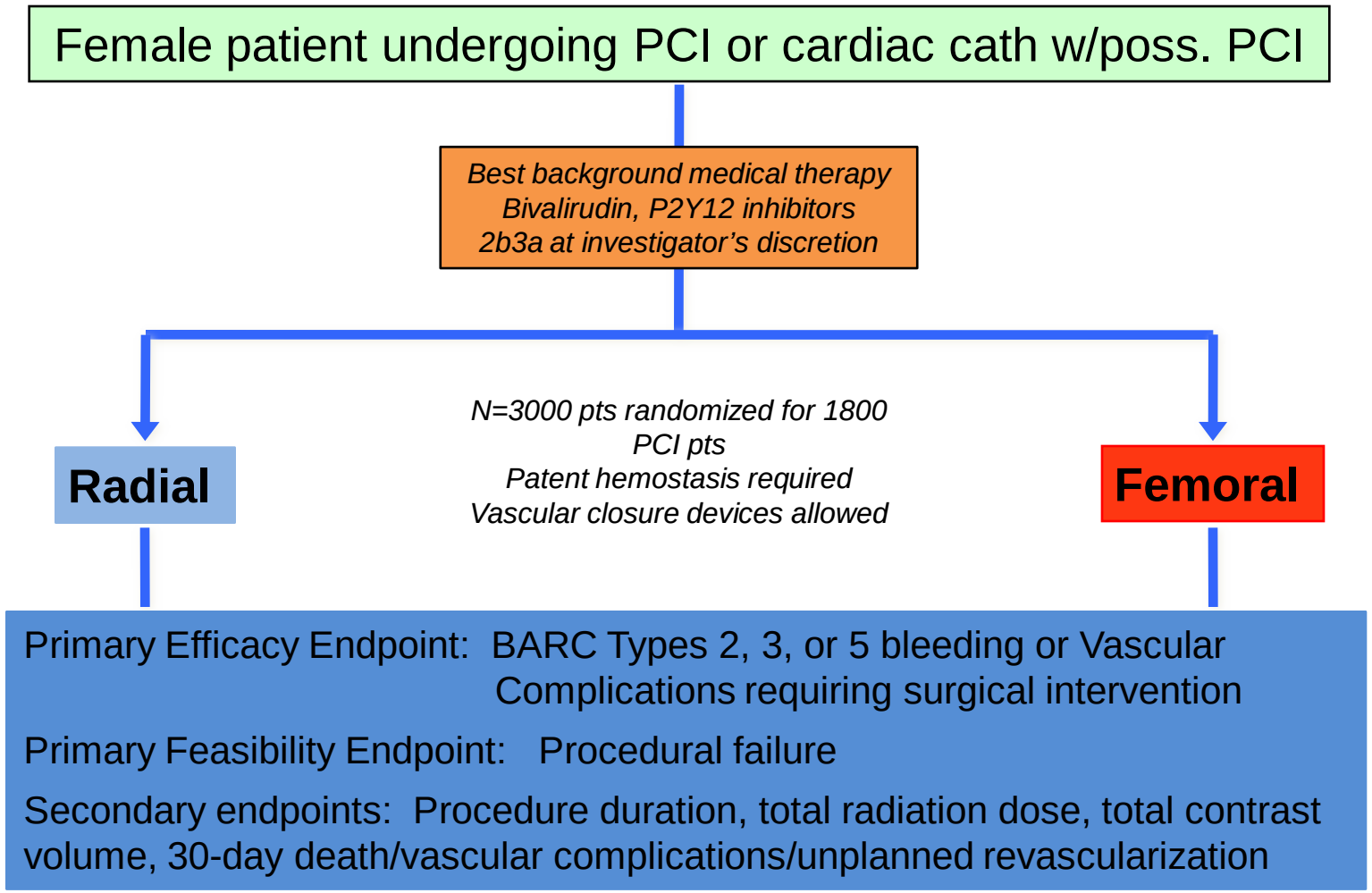
Study of Access site For Enhancing PCI for Women (SAFE-PCI for Women)



Methods – Patient population

Inclusion

- **Age > 18 years**
- **Female patient undergoing elective or urgent PCI or**
- **Undergoing diagnostic angiography to evaluate ischemic symptoms with the possibility of PCI**
- **Have capacity to sign informed consent**

Exclusion

- **Conditions precluding safe arterial access**
  - Non-palpable radial or femoral pulses
  - Bilateral abnormal Barbeau tests
  - Hemodialysis AV fistula or graft in arm to be used for arterial access
  - INR ≥ 1.5 if on warfarin
- **Bilateral IMA grafts**
- **Planned staged PCI within 30d of index PCI**
- **Valvular heart disease requiring surgery**
- **Planned RHC**
- **Primary PCI for STEMI**

Two cohorts specified:

- **Total randomized – all patients who are randomized regardless of whether they undergo PCI**
- **PCI cohort – defined as a guidewire exiting the guide catheter for diagnosis or treatment and therapeutic anticoagulation given; Primary analysis cohort**

Endpoint definitions

Primary efficacy endpoint

- **BARC Bleeding**
  - Type 2: Overt, actionable bleeding not meeting criteria for type 3, 4, or 5 bleeding
  - Type 3:
    - Overt bleeding with hgb drop ≥ 3 g/dL (corrected for transfusion)
    - Transfusion with overt bleeding
    - cardiac tamponade
    - bleeding requiring surgical intervention or intravenous vasoactive drugs
    - intraocular bleeding or ICH
  - Type 5: Fatal bleeding
- **Vascular complications requiring intervention**
  - AV fistula
  - Pseudoaneurysm
  - Arterial occlusion

Primary Feasibility Endpoint

- **Procedural failure**
  - Inability to complete the procedure from the assigned access site (access site crossover)

CEC Adjudication of all suspected bleeding or vascular complication events

Secondary endpoints – assessed only in PCI patients

- Procedure duration
- Total radiation dose (Air Kerma, mGy)
- Total contrast volume (mL)
- 30-day death, vascular complications, or unplanned revascularization
- Access site preference for next procedure

Methods

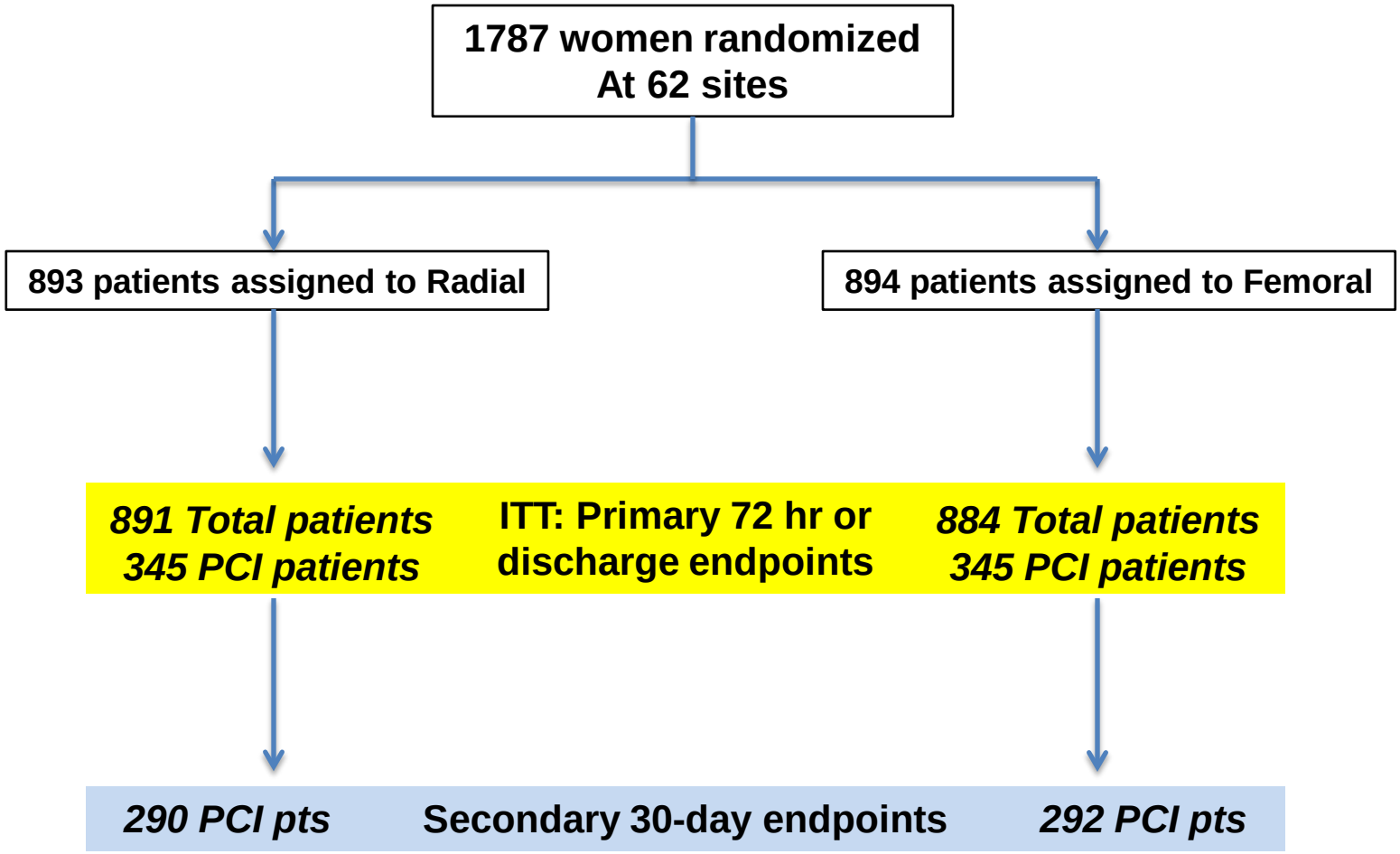
- **Sample size calculation**
  - Rate of BARC-type bleeding in NCDR CathPCI Registry among women without STEMI ~ 8.7%[1]
  - Assumptions
    - Femoral access bleeding or vascular complication rate – 8%
    - 50% reduction with radial access
    - 1576 patients provides 90% power at alpha 0.05
    - Sample size increased to 1800 due to uncertainty around event rates
    - 3000 total randomized patients to obtain 1800 PCI patients
- **All primary analyses performed according to the intention-to-treat principle; P-value ≤ 0.05 for statistical significance**
- **Three prespecified subgroups**
  - Planned use of Glycoprotein IIb/IIIa inihibitors during PCI, ACS vs. non-ACS, Site radial volume

[1]Rao SV, et. al. *JACC Intv* 2013

Results

- **After 1120 patients had been randomized, 446 of whom had undergone PCI, an unplanned meeting of the DSMB was convened**
  - Primary efficacy event rate markedly lower than expected
  - Trial unlikely to show a difference at the planned sample size
  - No harm noted in either arm
  - Recommended termination of the trial
- **Steering committee voted to continue study until enrollment in a quality-of-life substudy was complete (N=300)**

Final Recruitment



96.7% of sites enrolled ≥ 1 patient
70.9% of sites enrolled ≥ 10 patients

Results – Baseline characteristics

Total randomized cohort

	Radial (N=893)	Femoral (N=894)
Median age, yrs	63.4 (55.1, 72.2)	63.9 (55.7, 72.0)
Median BMI, kg/m2	30.5 (26.1, 35.1)	30.8 (26.5, 35.8)
Current or Recent smoker	27.2%	24.2%
HTN	79.5%	79.9
Prior MI	17.9%	19.6%
Prior CABG	4.5%	6.4%
Dialysis	0.3%	0.3%
PAD	5.7%	6.0%
Diabetes	35.2%	35.0%
CAD presentation		
Non-ACS	46.8%	43.5%
NSTEACS	52.7%	56.3%
STEMI	0.4%	0.2%

Results – Baseline characteristics

PCI cohort

	Radial (N=345)	Femoral (N=346)
Median age, yrs	65.1 (56.5, 73.7)	63.9 (56.5, 72.9)
Median BMI, kg/m2	30.1 (25.9, 34.5)	30.5 (26.9, 35.4)
Current or Recent smoker	30.7%	29.5%
HTN	85.8%	85.0%
Prior MI	23.8%	27.7%
Prior CABG	7.2%	9.9%
Dialysis	0.6%	0.6%
PAD	6.7%	8.4%
Diabetes	41.7%	44.5%

Results – Procedure characteristics

PCI cohort

	Radial (N=345)	Femoral (N=346)
PCI status		
Elective	46.5%	43.6%
Urgent	52.1%	55.7%
Emergent	1.4%	0.7%
Bivalirudin used	59.1%	65.8%
Glycoprotein IIb/IIIa	11.4%	11.6%
Vascular closure device	5.1%*	65.5%

Table excludes patients who underwent FFR, IVUS, or OCT

*Patients who had any femoral access

Results – Primary efficacy and feasibility endpoints

Total randomized cohort

	Radial (N=893)	Femoral (N=894)	OR (95% CI)	P
BARC 2, 3, 5 bleeding or Vasc Complications	0.6%	1.7%	0.3 (0.1-0.9)	0.03
Procedural failure	6.7%	1.9%	3.7 (2.1-6.4)	<0.001

- Most common reason for needing to convert from radial to femoral access to complete the procedure was radial artery spasm (43.6%)

Results – Primary efficacy and feasibility endpoints

PCI cohort

	Radial (N=345)	Femoral (N=346)	OR (95% CI)	P
BARC 2, 3, 5 bleeding or Vasc Complications	1.2%	2.9%	0.4 (0.1-1.3)	0.12
Procedural failure	6.1%	1.7%	3.6 (1.5-9.2)	0.006

- Most common reason for needing to convert from radial to femoral access to complete the procedure was radial artery spasm (42.9%)
- Interactions not significant for ACS vs. Non-ACS, Use of 2b3a vs. not, site radial volume

Results – Secondary endpoints

PCI cohort

	Radial (N=290)	Femoral (N=291)	P
Procedure duration (min)	51.6 ± 32.3	49.9 ± 30.5	0.46
Total radiation dose (mGy)	1604 ± 1394	1472 ± 1274	0.26
Total contrast volume (mL)	152.7 ±76.9	165.6 ± 82.7	0.03
30-day death, vascular complications, or unplanned revasc	5.2%	3.4%	0.26
Patient prefers assigned access site for next procedure	71.9%	23.5%	

Conclusions – Implications for clinical practice

- **Despite using the CathPCI Registry to determine bleeding or vascular complication rates, the actual rates were lower than expected, leading to early termination of the trial**
- **The treatment benefit of radial access over femoral access was larger than expected (~60%) in both the PCI and Total randomized cohorts**
- **The need for conversion to femoral access was significantly higher and was primarily due to spasm, representing an area needing improvement in technology to offer wider application of transradial PCI to women**
- **The SAFE-PCI for Women trial suggests an initial strategy of radial access is reasonable and may be preferred in women, with the recognition that a proportion of patients will require conversion to femoral access.**
  - Proportional bleeding reduction similar to that seen in prior studies[1]
  - Conversion to femoral rate similar to that seen in RIVAL (7.6%)[2]

[1]Bertrand OF, et. al. *AHJ* 2012
[2]Jolly SS, et. al. *Lancet* 2011

Conclusions – Implications for clinical research

- **As the first registry-based randomized trial in the US, the SAFE-PCI for Women trial demonstrates a new paradigm for conducting efficient practical clinical trials using The National Cardiovascular Research Infrastructure**
  - High quality data
  - Adjudication possible
  - CFR Part 11 compliant – IND and IDE applications
  - Faster enrollment, Reduced site workload
  - Reduced costs (total budget for SAFE-PCI for Women ~ $5 million)
- **This trial construct is a promising approach for future clinical investigations**

Acknowledgements

Clinical and Data Coordinating Center	DCRI
Steering Committee	Mitchell W. Krucoff MD (Chair) Sunil V. Rao MD (PI) Connie N. Hess MD Kevin Anstrom MD Sanjit S. Jolly MD Alice Jacobs MD L. Kristin Newby MD C. Michael Gibson MD David F. Kong MD Roxana Mehran MD Ron Waksman MD Ian C. Gilchrist MD
Project Team	Britt Barham (Project lead) Laura Aberle (Stats) Richard Brown, Cherie Barnes (data) Tracy Robinson, Ryan Stults, Wendy Lavender Schuyler Jones MD (CEC PI)
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NCRI	Robert A. Harrington MD, Eric D. Peterson MD MPH, Brian J. McCourt

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