



# MICHELANGELO: OASIS 5 Women's Substudy



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Disclosure

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Dr. Swahn has no conflicts of interest



## Background

- **Women with NSTEMI ACS have less severe CAD and better prognosis than men.**
- **Some treatments (eg LMWH or CABG surgery) are associated with a higher risk in women. Others (GPIIIB/ IIIa inhib) appear ineffective.**
- **Randomized trials of routine invasive strategy in NSTEMI ACS show benefits in men but the results in women are contradictory.**



## Death/MI

	Routine invasive	Selective invasive
FRISCII (2001) (12 m f-u)	43 (12.4%)	34 (8.5%)
RITA3 (2002) (12 m f-u)	30 (8.6%)	17 (5.1%)
TACTICS (2002) (6 m f-u)	26 (6.6%)	35 (9.7%)



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Female Patients Randomized to OASIS 5

(NSTE ACS)

Fondaparinux vs Enoxaparin

Randomized to WSS

Routine Invasive

Selective Invasive

Cath followed by  
PCI/CABG within 7  
days

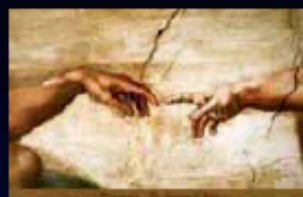
Primary Outcomes

over duration of 2 yr follow-up

1. Death/MI/Stroke/Refractory ischemia
2. Death/MI/Stroke

Only in presence  
of symptoms or  
severe ischemia

184 patients randomized



## Study Design

**A randomized, international, multi-center open trial  
Sub-study of MICHELANGELO: OASIS-5 trial.**

**Eligible female patients in participating OASIS 5 centers  
were randomized to receive either:**

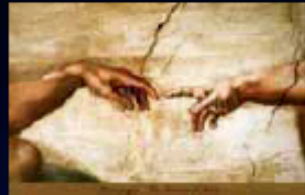
- **routine early coronary angiography and, if appropriate, intervention within 7 days of randomization**
- or**
- **selective invasive strategy  
(coronary angiography only in case of symptoms  
i.e. severe ischemia during index hospital admission  
or on a stress test).**



## **Study Objectives**

**To evaluate whether, among women with NSTACS,  
an early invasive strategy,  
is superior  
to a selective invasive strategy  
in terms of Death/MI/Stroke  
over a duration of 2 year follow-up**

**All patients were concurrently managed with intense  
anti-ischemic and antithrombotic medication during  
index hospitalization.**



## **Indications for revascularization in the selective invasive group**

- **Refractory ischemia.**
- **New ST elevation.**
- **Development of hemodynamic instability or CHF.**
- **Intractable life-threatening arrhythmia.**
- **Incapacitating angina or severe ischemia at a stress test .**
- **Incapacitating angina despite optimal medical therapy during follow-up.**
- **Reinfarction during follow-up.**



## Follow-up Schedule

- As per the main study at 30, 90 and 180 days
- Out-patient visit or telephone contact with survivors at 1 and 2 years.
- Appropriate CRF and event forms filled in according to the protocol.



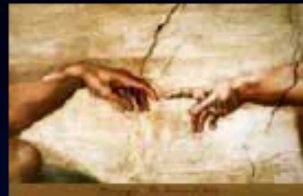
## Statistical Considerations

- Based on the overall results of the FRISC II trial we assumed a reduction in the rate of death, MI from 17.5% to 12.5% at 3 years with a routine invasive strategy. To detect a relative risk reduction of 28.5 %, with 80% power, a sample size of 1,600 was planned.
- The curtailment in the sample size as well as follow-up time reduced the effective power to about 12% to detect the hypothesized reduction in outcome(2 sided  $\alpha=0.05$ ). The effect of Invasive strategy on outcomes was assessed using Cox's Proportional Hazard Model.



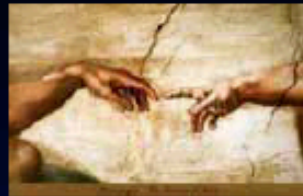
## Baseline Characteristics

	Selective Invasive (n = 92)		Routine Invasive (n = 92)	
Age (SD)	67.8 (8.8)		68.2 (9.2)	
	n	%	n	%
Previous MI	18	19.6	22	23.9
Previous PCI	11	12.0	7	7.6
CABG Surgery	3	3.3	5	5.4
Stroke	4	4.3	4	4.3
PAD	2	2.2	4	4.3
Hypertension	62	67.4	57	62.0
Diabetes	27	29.3	19	20.7
Current Smoker	24	26.1	9	9.8
Onset to Rand (hrs)	92	13.3 +/- 6.3	92	12.5 +/- 6.6



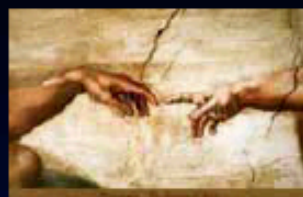
# Ischemic Symptoms/ECG/ Enzymes, Biomarkers

	Selective Invasive (n = 92)		Routine Invasive (n = 92)	
	n	%	n	%
<b>Troponin or CK-MB &gt; ULN</b>	<b>72</b>	<b>78.3</b>	<b>73</b>	<b>79.3</b>
<b>ECG compatible with ischemia</b>	<b>65</b>	<b>70.7</b>	<b>70</b>	<b>76.1</b>
<b>ST depression <math>\geq</math> 0.5 mm</b>	<b>45</b>	<b>49.0</b>	<b>47</b>	<b>51.8</b>
<b>Any ECG abnormality</b>	<b>79</b>	<b>86.0</b>	<b>79</b>	<b>86.0</b>



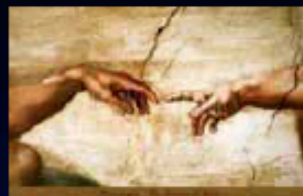
# Concomitant Medications during Initial Hospitalization

	Selective Invasive (n = 92)		Routine Invasive (n = 92)	
	n	%	n	%
<b>ASA</b>	<b>91</b>	<b>98.9</b>	<b>92</b>	<b>100</b>
<b>Clopidogrel/Ticlopidine</b>	<b>70</b>	<b>76.1</b>	<b>79</b>	<b>85.9</b>
<b>Dual Anti-platelet Rx</b>	<b>69</b>	<b>75.0</b>	<b>79</b>	<b>85.9</b>
<b>GP IIb/IIIa</b>	<b>7</b>	<b>7.6</b>	<b>11</b>	<b>12.0</b>
<b>IV UFH</b>	<b>6</b>	<b>6.5</b>	<b>11</b>	<b>12.0</b>
<b>LMWH</b>	<b>20</b>	<b>21.7</b>	<b>22</b>	<b>23.9</b>
<b>Only LMWH</b>	<b>14</b>	<b>15.2</b>	<b>19</b>	<b>20.7</b>
<b>Beta Blocker</b>	<b>86</b>	<b>93.5</b>	<b>87</b>	<b>94.6</b>
<b>ACE/ARB</b>	<b>74</b>	<b>80.4</b>	<b>65</b>	<b>70.7</b>
<b>Statins</b>	<b>77</b>	<b>83.7</b>	<b>81</b>	<b>88.0</b>



# Interventions during Initial Hospitalization

	Selective Invasive (n = 92)		Routine Invasive (n = 92)	
	n	%	n	%
<b>Coronary Angiography</b>	<b>37</b>	<b>40.2</b>	<b>88</b>	<b>95.7</b>
<b>PCI</b>	<b>22</b>	<b>23.9</b>	<b>42</b>	<b>45.7</b>
<b>CABG Surgery</b>	<b>6</b>	<b>6.5</b>	<b>11</b>	<b>12.0</b>



# Interventions during Long term Follow-up

	Selective Invasive (n = 92)		Routine Invasive (n = 92)	
	n	%	n	%
<b>Coronary Angiography</b>	<b>60</b>	<b>65.2</b>	<b>89</b>	<b>96.7</b>
<b>PCI</b>	<b>36</b>	<b>39.0</b>	<b>44</b>	<b>48.0</b>
<b>CABG Surgery</b>	<b>11</b>	<b>12.0</b>	<b>15</b>	<b>16.0</b>

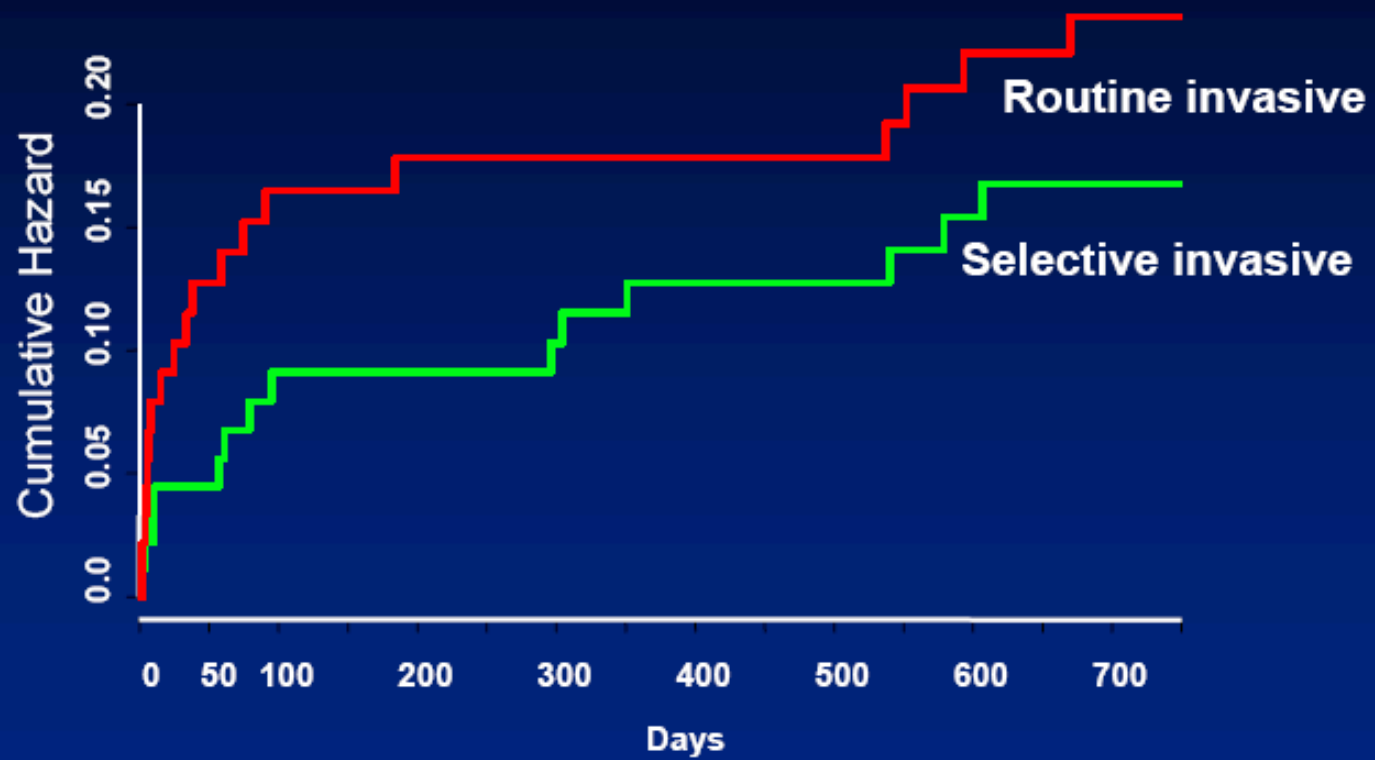


## Cox PH Ratios: 2 yr outcome

	Selective Invasive (n = 92)		Routine Invasive (n = 92)		Hazard Ratio (95% CI)
	n	%	n	%	
Death/MI/Stroke	16	15.4	19	21.0	1.46 (0.73 – 2.94)
Death/MI/RI	19	20.8	19	21.0	0.99 (0.52 – 1.90)
Death/MI	13	14.3	17	18.8	1.39 (0.67 – 2.88)
Death	2	2.2	8	8.8	4.65 (0.97 – 22.2)
MI	12	13.3	11	12.9	0.95 (0.42 – 2.19)
Stroke	4	4.4	2	2.3	0.67 (0.12 – 3.70)
Major Bleeding	2	2.2	9	10.0	6.90 (1.48 – 32.1)
Death/MI/Stroke/ Major Bldg	14	15.4	25	27.4	2.16 (1.11 – 4.20)



# Death/MI/Stroke





# Death





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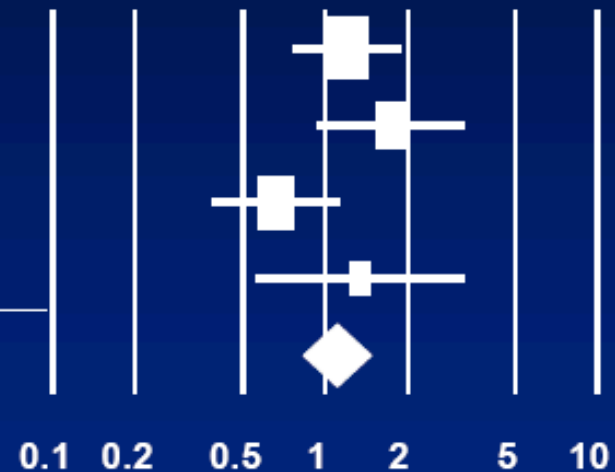


# Meta analysis - Death/MI

Study name   Death or MI / Total   Statistics for each study   Odds ratio and 95% CI

Routine Invasive   Selective Invasive   Odds ratio   Lower limit   Upper limit   p-Value

<b>FRISC II</b>	43 / 348	42 / 401	1.21	0.77	1.89	0.42
<b>RITA 3</b>	30 / 350	17 / 332	1.74	0.94	3.21	0.08
<b>TACTICS</b>	26 / 395	35 / 362	0.66	0.39	1.12	0.12
<b>OASIS 5</b>	13 / 92	10 / 92	1.35	0.56	3.25	0.50
	112 / 1185	104 / 1187	1.11	0.83	1.47	0.48



Favours Early Invasive   Favours Selective Invasive



# Meta analysis - Death

Study name Dead / Total      Statistics for each study      Odds ratio and 95% CI

	Routine Invasive	Selective Invasive	Odds ratio	Lower limit	Upper limit	p-Value
<b>FRISC II</b>	14 / 348	13 / 401	1.25	0.58	2.70	0.57
<b>RITA 3</b>	18 / 350	8 / 332	2.20	0.94	5.12	0.07
<b>TACTICS</b>	15 / 395	13 / 362	1.06	0.50	2.26	0.88
<b>OASIS 5</b>	8 / 92	1 / 92	8.67	1.06	70.77	0.04
	55 / 1185	35 / 1187	1.50	0.96	2.35	0.07

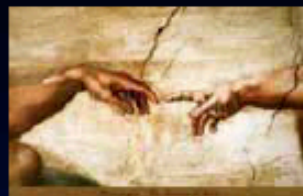


**Favours Early Invasive**      **Favours Selective Invasive**



## FINAL Enrollment by Country

Country	No. of Sites	No. of Patients
Argentina	2	2
Sweden	14	108
Poland	6	73
South Africa	1	1
<b>TOTAL</b>	<b>23</b>	<b>184</b>



## Conclusions

In this study, women with NSTEMI ACS did not benefit from a routine invasive strategy.

On the contrary, patients randomised to a routine invasive strategy had a higher mortality rate.

The results taken together with the results of previous larger trials suggest that the results from men do not necessarily apply to women and that large scale randomised trials in women are needed to determine the optimal strategy in NSTEMI ACS.