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Cost-Effectiveness of Prasugrel vs. Clopidogrel for PCI Patients with Acute Coronary Syndromes:

Results from the TRITON-TIMI 38 Trial

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Disclosures

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Background

- Recently, the TRITON-TIMI 38 study has demonstrated that for pts with ACS undergoing PCI, treatment with prasugrel as compared with clopidogrel over ~14 months of f/u led to a 19% reduction in CV death, MI, or stroke at the expense of an increased risk of major bleeding
- On the basis of these results, prasugrel has recently been approved for use in the United States and in many other countries
- Given the higher acquisition cost of prasugrel and the substantial population who may be candidates for treatment, economic factors may be an important consideration in identifying the optimal patient population and treatment duration

TRITON-TIMI 38 Economic Study: Objectives

1. To compare total medical care costs for ACS patients undergoing PCI and treated with prasugrel vs. clopidogrel over the duration of the TRITON trial

2. If prasugrel is found to be both more costly and more effective than clopidogrel, to assess its cost-effectiveness measured in terms of:
   - *Cost per year of life gained (primary analysis)*
   - *Cost per quality-adjusted year of life gained*

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Economic Study Design

Study population: All patients from 8 countries

- United States
- Canada
- Australia
- Germany
- Italy
- Spain
- UK
- France

n = 6705

Selected for similar resource patterns to US practice and feasibility of collecting detailed resource utilization

Analytic Perspective: U.S. healthcare system

Time Horizon: Lifetime

Economic Study Methods

- Medical resource utilization tracked for all patients from randomization through last f/u visit
- Costs for hospitalizations and physician services calculated by multiplying resource counts by U.S.-specific unit costs (in 2005 dollars) derived from Medicare data
- Study drug costs based on net wholesale price as of August 2009
  - *Clopidogrel = $4.62/day ($141/month)*
  - *Prasugrel = $5.45/day ($166/month)*

Incremental Cost of In-Hospital Complications

In-hospital bleeding

- *Based on published regression analyses of PCI patients from the REPLACE-2 trial (for PCI patients) and MEDPAR data (for CABG patients)*
- *PCI-related major bleeding (TIMI major+minor) = $7176/event*
- *PCI-related minor bleeding (TIMI minimal) = $451*
- *CABG-related major bleeding = $9,366*

Periprocedural MI

- *Based on REPLACE-2 trial*
- *Incremental cost = $2,543/event*

Cohen DJ, et al. J Am Coll Cardiol 2004;44:1792-800

Brown PP, et al. Ann Thorac Surg 2008;85:1980-6

Life Expectancy Analysis

- Saskatchewan Health data used to develop survival estimates for an ACS population similar to TRITON, conditional on occurrence of primary endpoint events over median follow-up duration in trial
  - *Because of observed excess of major bleeds in the prasugrel arm, fatal bleeding was also included in the life expectancy calculations*
- Lost life expectancy associated with non-fatal events (MI, stroke) calculated as difference between LE with and without the event of interest
- Lost life expectancy calculated for each trial patient based his/her specific characteristics (e.g., age, gender, diabetes, ACS type, etc.) + event status at completion of trial

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Saskatchewan Data: Lost Life Expectancy

Projected Survival

	No Event	MI x 1	Severe Stroke
Male			
Age 55	19.48	11.54	12.50
Age 75	6.48	5.12	3.03
Female			
Age 55	21.71	13.73	12.94
Age 75	7.98	5.95	3.55

Lost Life Expectancy (yrs)

	Death	MI x 1	Severe Stroke
Male			
Age 55	19.48	7.95	6.98
Age 75	6.48	1.36	3.46
Female			
Age 55	21.71	7.98	8.77
Age 75	7.98	2.03	4.43

* Population adjusted to TRITON covariates (undiscounted life expectancy)

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Baseline Characteristics:

Economic Substudy vs. Overall Trial

	Economic Study (n=6705)	Overall Trial (n=13,608)
Age	60.8 ± 11.1	60.9 ± 11.3
Female	25.4%	25.9%
ACS Type: STEMI	21.4%	26.0%
Cardiac Marker > ULN	84.5%	79.2%
Diabetes	24.3%	23.1%
Hypertension	67.0%	64.2%
Current Smoker	55.8%	58.0%
Prior MI	18.5%	17.9%
Prior PCI	15.5%	13.4%
Prior CABG	9.7%	7.6%

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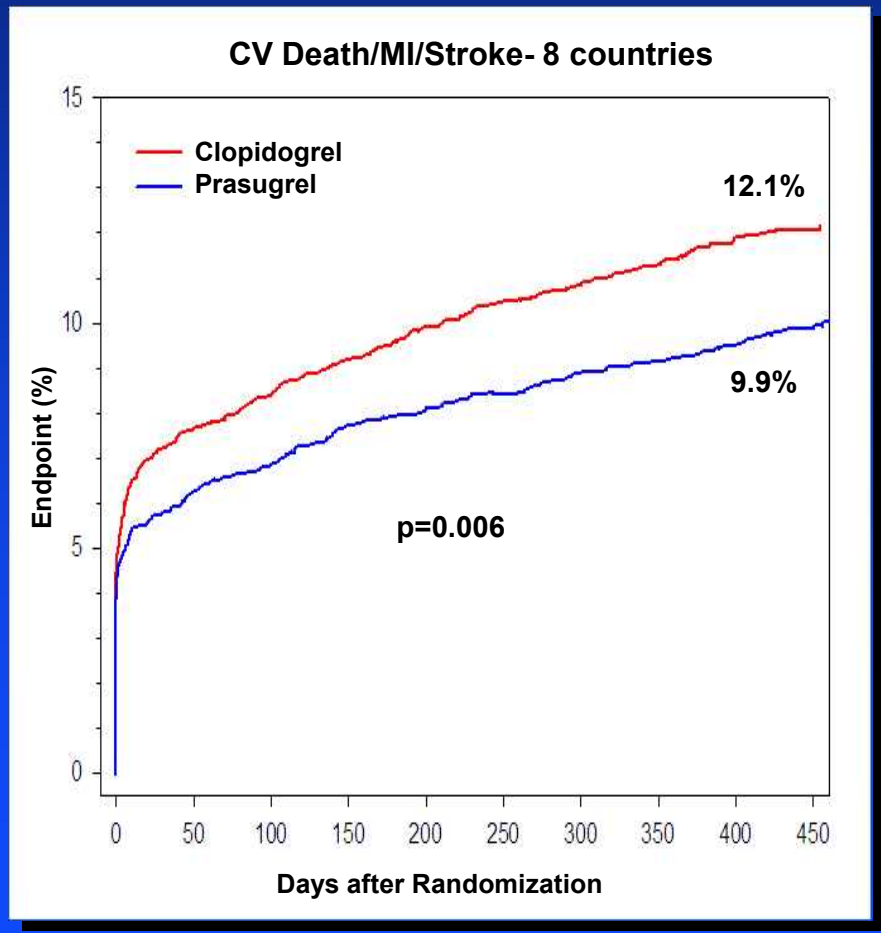
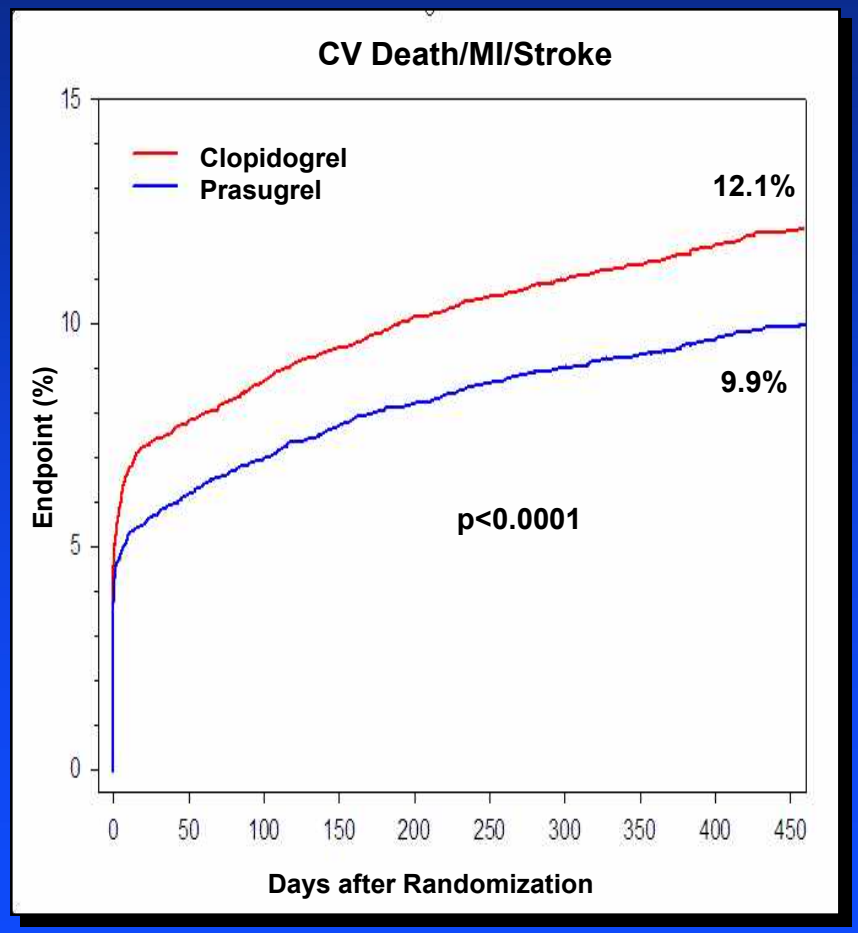
Primary Endpoint:

Economic Subset vs. Overall Trial

Economic Study Subset (n=6705)



Overall Study Population (n=13,608)



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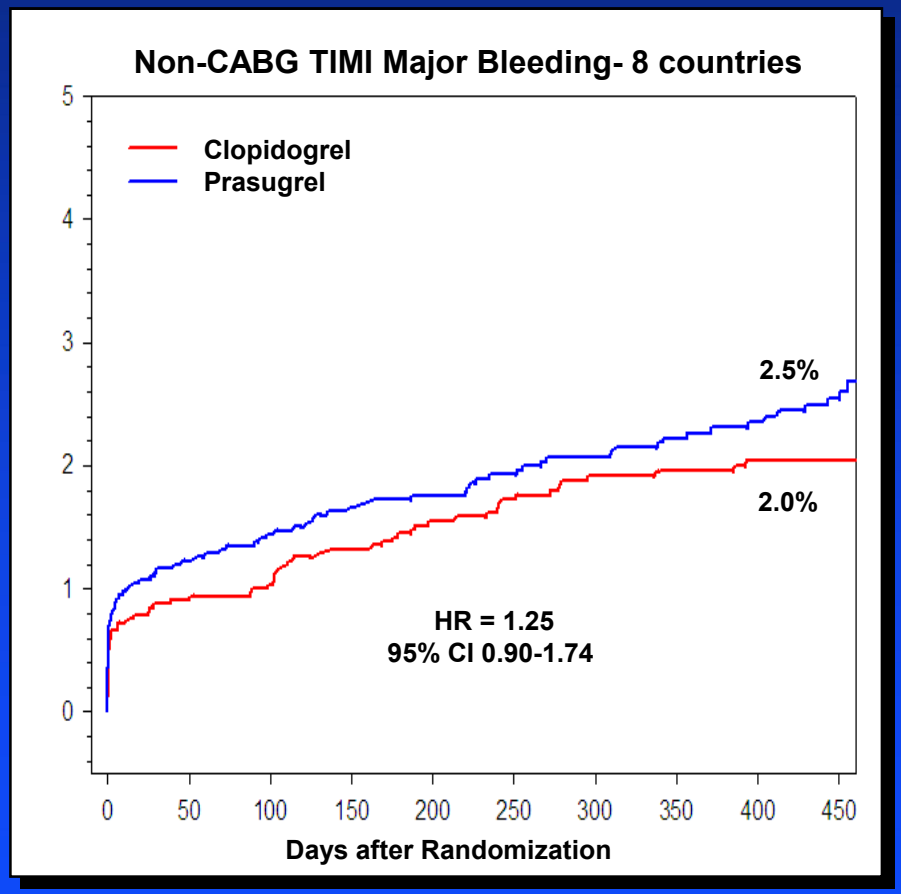
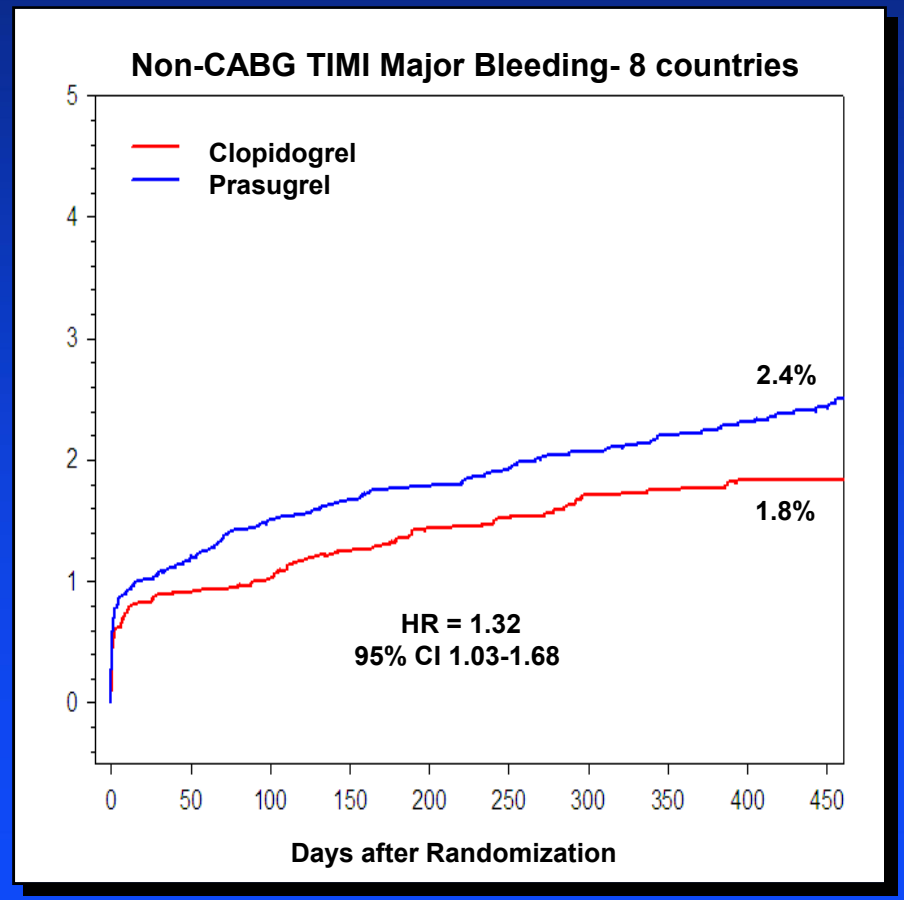
Non-CABG TIMI Major Bleeding:
Economic Subset vs. Overall Trial

Economic Study Subset (n=6705)



Overall Study Population (n=13,608)



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Peri-procedural bleeding and MI events* during index hospitalization

	Prasugrel	Clopidogrel	Δ_{P-C}
Peri-procedural MI	154 (4.6%)	175 (5.3%)	-21
Any bleed	180 (5.3%)	151 (4.5%)	+29
major TIMI bleed	32 (1%)	27 (0.8%)	+5
minor TIMI bleed	57 (1.7%)	47 (1.4%)	+10
minimal TIMI bleed	91 (2.7%)	77 (2.3%)	+14

•All periprocedural events were related to PCI procedures, except 1 MI (prasugrel) and 2 bleeds (both clopidogrel; 1 minor, 1 minimal)

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Index Hospitalization Costs*

	Prasugrel	Clopidogrel	Δ_{P-C}
DRG-related	$19,422	$19,453	-$31
Complication-related			
Periprocedural MI	$115	$134	-$18
Major bleeding	$203	$165	+$38
TOTAL Cost	**$19,740**	**$19,752**	**-$12**

* Costs exclude study medications

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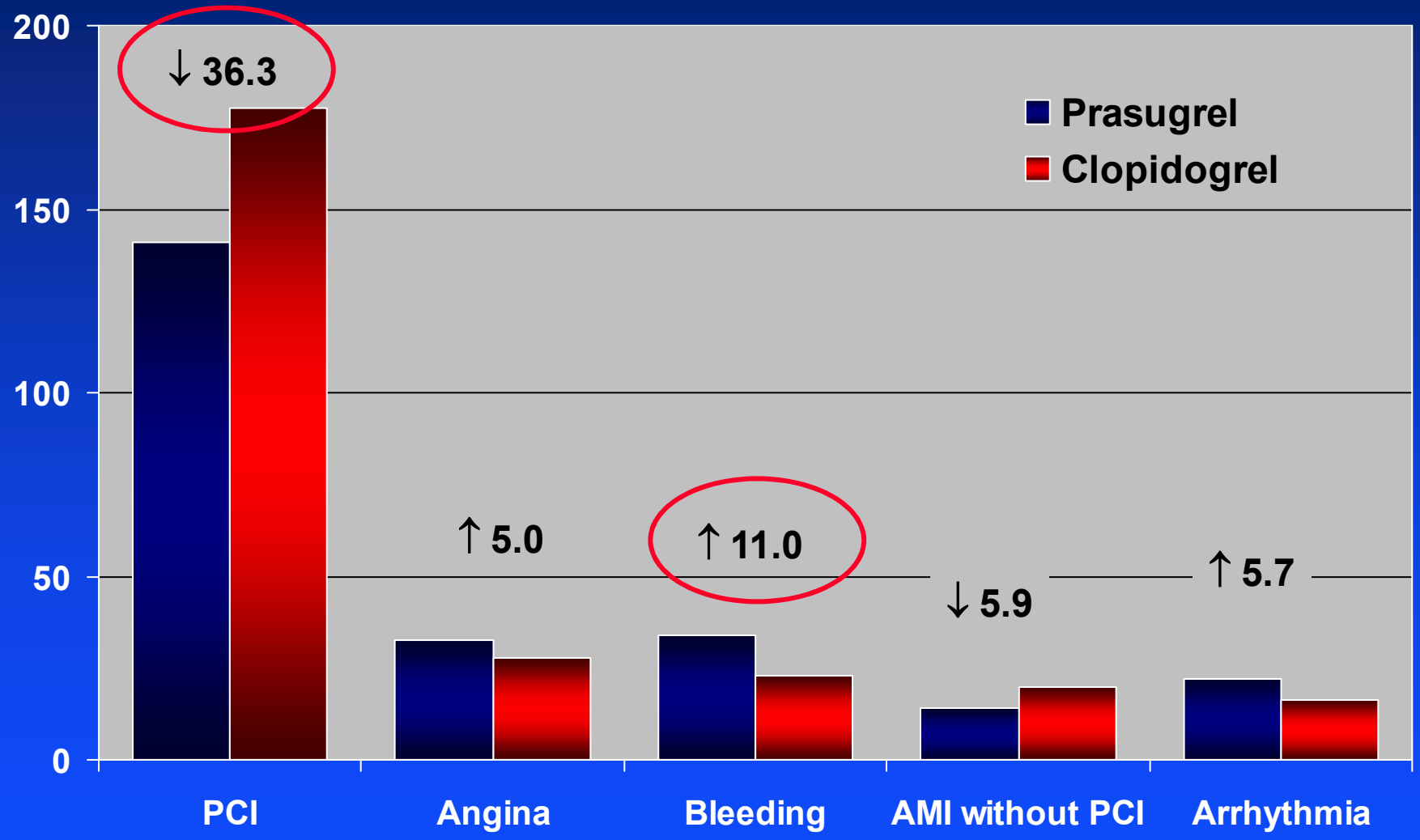
Number of Rehospitalizations (per 1000 pts)



* Conditions with fewer than 2% of events or differences < 2 per 1000 pts not shown

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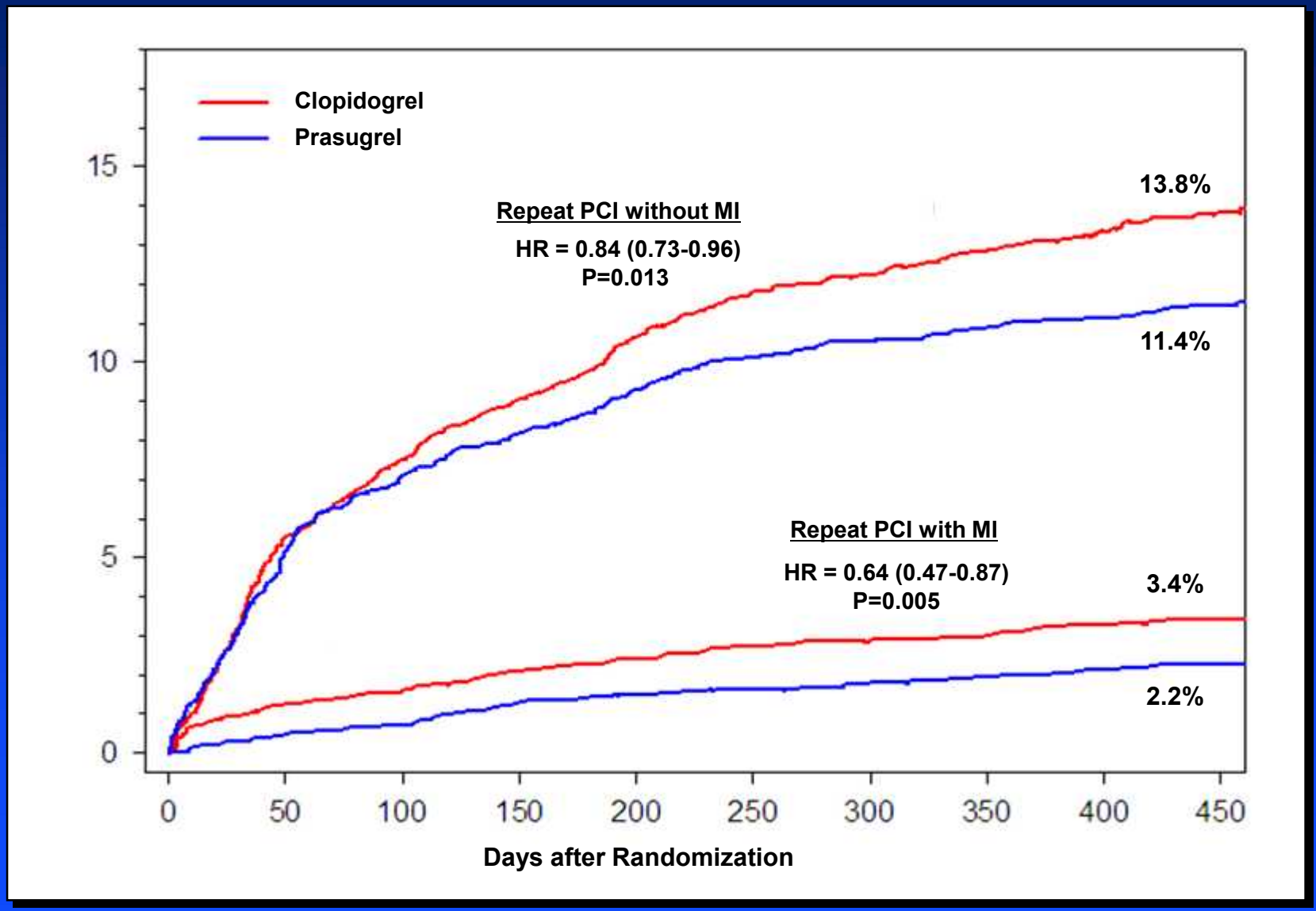
Repeat PCI with or without MI



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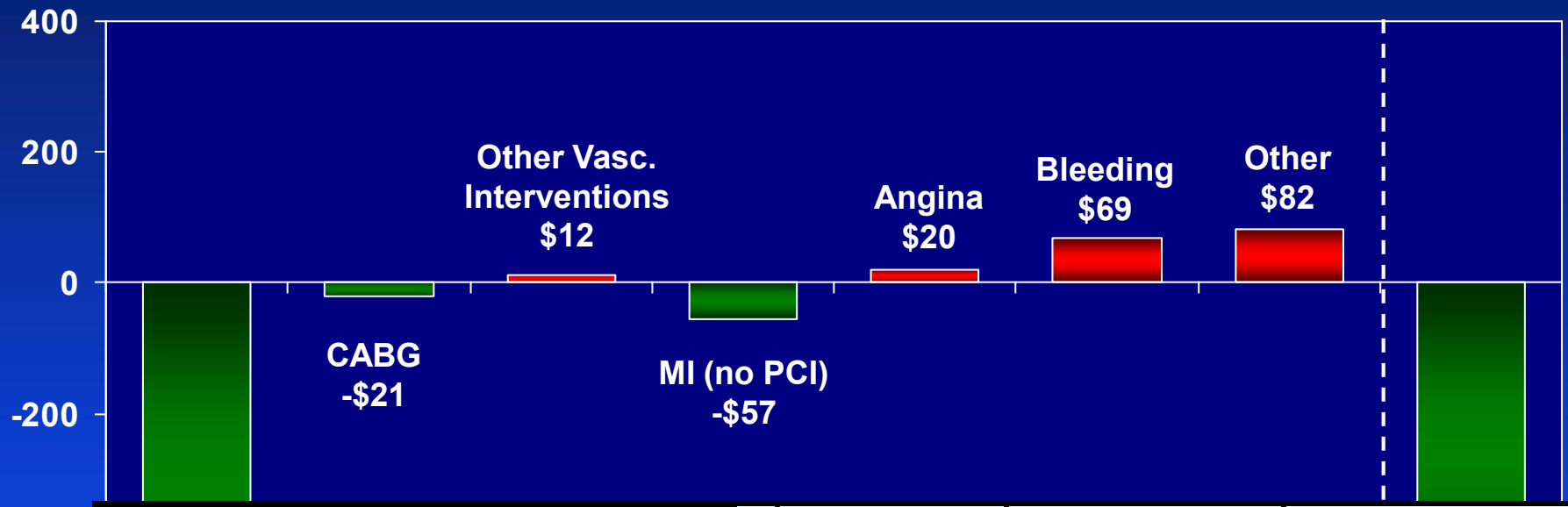
Incremental Costs/Cost Offsets with Prasugrel*



	Prasugrel	Clopidogrel	Difference (P-C)
Index Hospitalization Costs	$19,740	$19,752	-$12
Rehospitalization Costs	$4,465	$4,982	-$517
Study Drug Costs	$1,862	$1,554	$308
TOTAL COSTS	**$26,067**	**$26,288**	**-$221**

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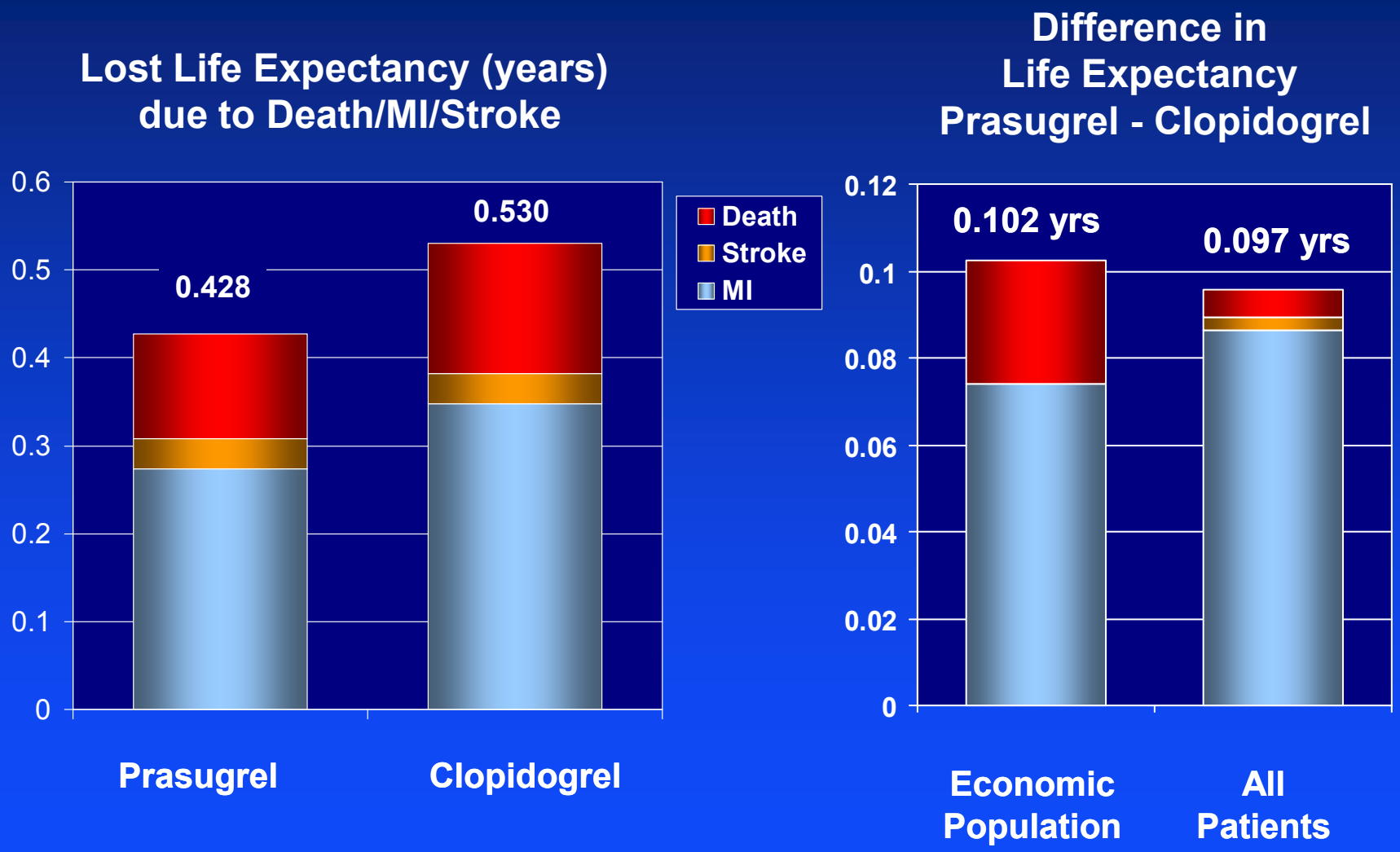
Life Expectancy Results



* Projections based on TRITON-eligible pts from Saskatchewan Health database

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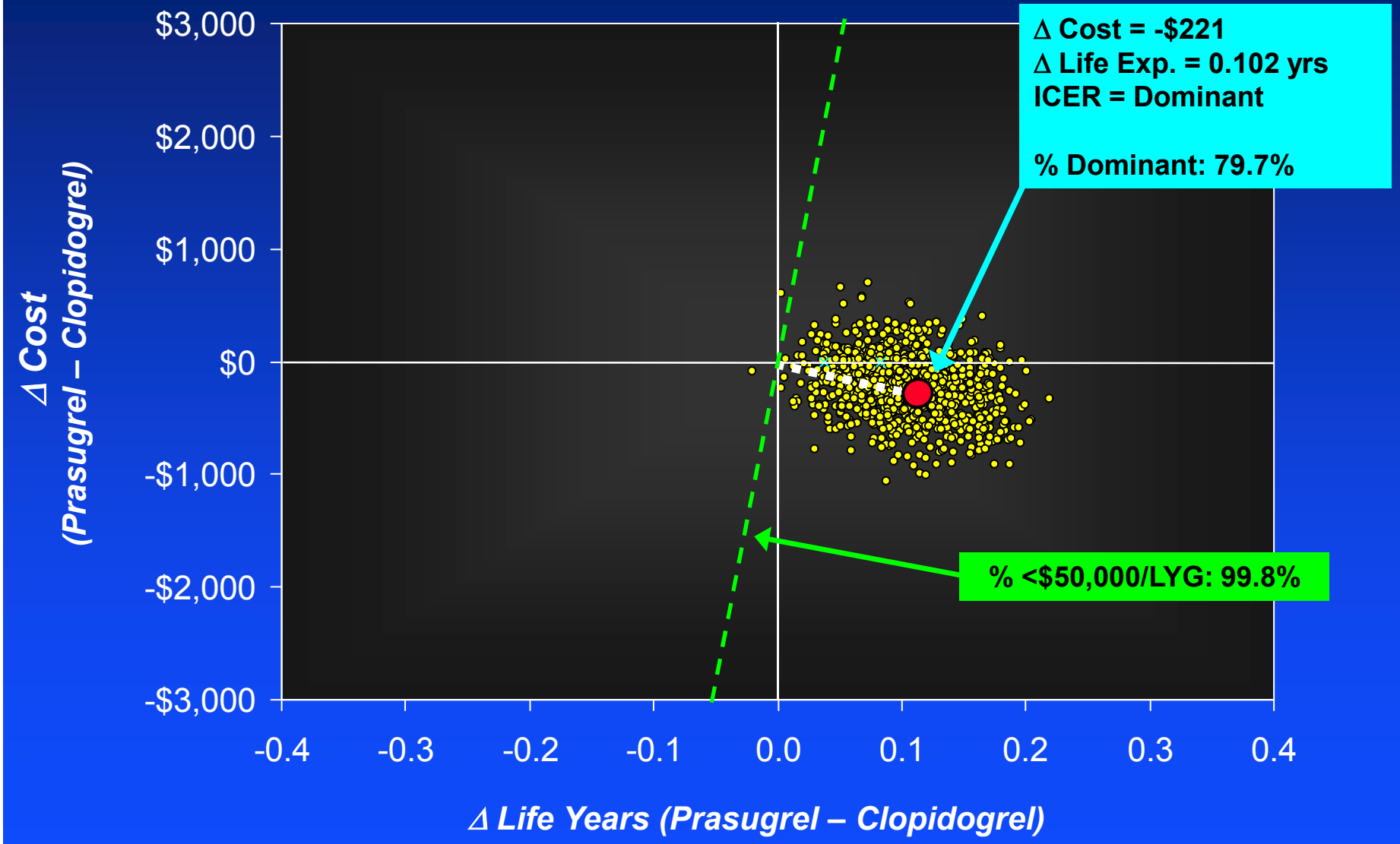
Cost-Effectiveness: *Base Case*



Subgroup Analyses

	Δ Cost	Δ Life Expect.	ICER	% Dom-inant	% Dom-inated	% < $50K/LYG
Diabetes	-$695	0.183	**Dominant**	86.5%	0.6%	**97.9%**

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Subgroup Analyses

	Δ Cost	Δ Life Expect.	ICER	% Dom-inant	% Dom-inated	% < $50K/LYG
Diabetes	-$695	0.183	Dominant	86.5%	0.6%	97.9%
No Diabetes	-$94	0.078	**Dominant**	63.2%	2.9%	**95.0%**

Subgroup Analyses

	Δ Cost	Δ Life Expect.	ICER	% Dominant	% Dominated	% < $50K/LYG
Diabetes	-$695	0.183	Dominant	86.5%	0.6%	97.9%
No Diabetes	-$94	0.078	Dominant	63.2%	2.9%	95.0%
STEMI	-$547	0.145	**Dominant**	78.5%	1.6%	**95.5%**

Subgroup Analyses

	Δ Cost	Δ Life Expect.	ICER	% Dominant	% Dominated	% < $50K/LYG
Diabetes	-$695	0.183	Dominant	86.5%	0.6%	97.9%
No Diabetes	-$94	0.078	Dominant	63.2%	2.9%	95.0%
STEMI	-$547	0.145	Dominant	78.5%	1.6%	95.5%
NSTEMI/UA	-$139	0.091	**Dominant**	70.3%	0.9%	**98.3%**

Subgroup Analyses

	Δ Cost	Δ Life Expect.	ICER	% Dom-inant	% Dom-inated	% < $50K/LYG
Diabetes	-$695	0.183	Dominant	86.5%	0.6%	97.9%
No Diabetes	-$94	0.078	Dominant	63.2%	2.9%	95.0%
STEMI	-$547	0.145	Dominant	78.5%	1.6%	95.5%
NSTEMI/UA	-$139	0.091	Dominant	70.3%	0.9%	98.3%
DES	$26	0.080	**$326/LYG**	44.0%	3.0%	**95.1%**

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Subgroup Analyses

	Δ Cost	Δ Life Expect.	ICER	% Dom-inant	% Dom-inated	% < $50K/LYG
Diabetes	-$695	0.183	Dominant	86.5%	0.6%	97.9%
No Diabetes	-$94	0.078	Dominant	63.2%	2.9%	95.0%
STEMI	-$547	0.145	Dominant	78.5%	1.6%	95.5%
NSTEMI/UA	-$139	0.091	Dominant	70.3%	0.9%	98.3%
DES	$26	0.080	$326/LYG	44.0%	3.0%	95.1%
No DES	-$875	0.180	**Dominant**	92.3%	0.2%	**99.2%**

Subgroup Analyses

	Δ Cost	Δ Life Expect.	ICER	% Dom-inant	% Dom-inated	% < $50K/LYG
Diabetes	-$695	0.183	Dominant	86.5%	0.6%	97.9%
No Diabetes	-$94	0.078	Dominant	63.2%	2.9%	95.0%
STEMI	-$547	0.145	Dominant	78.5%	1.6%	95.5%
NSTEMI/UA	-$139	0.091	Dominant	70.3%	0.9%	98.3%
DES	$26	0.080	$326/LYG	44.0%	3.0%	95.1%
No DES	-$875	0.180	Dominant	92.3%	0.2%	99.2%
“On-Label” *	-$234	0.128	**Dominant**	78.4%	0.1%	**99.9%**

* Age <75, weight >=60kg, no h/o stroke or TIA (post-hoc)

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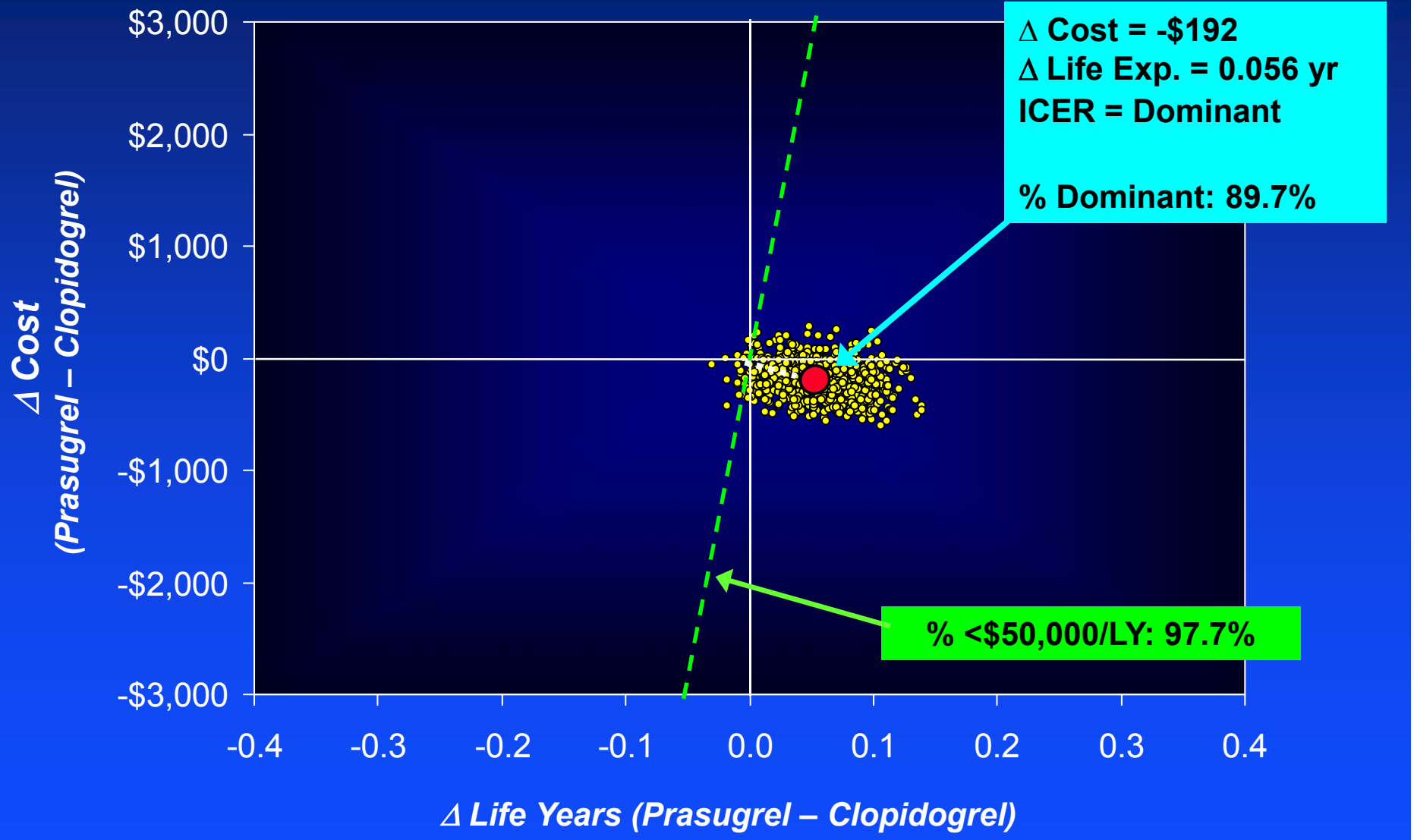
Cost-Effectiveness: *Days 1-30*



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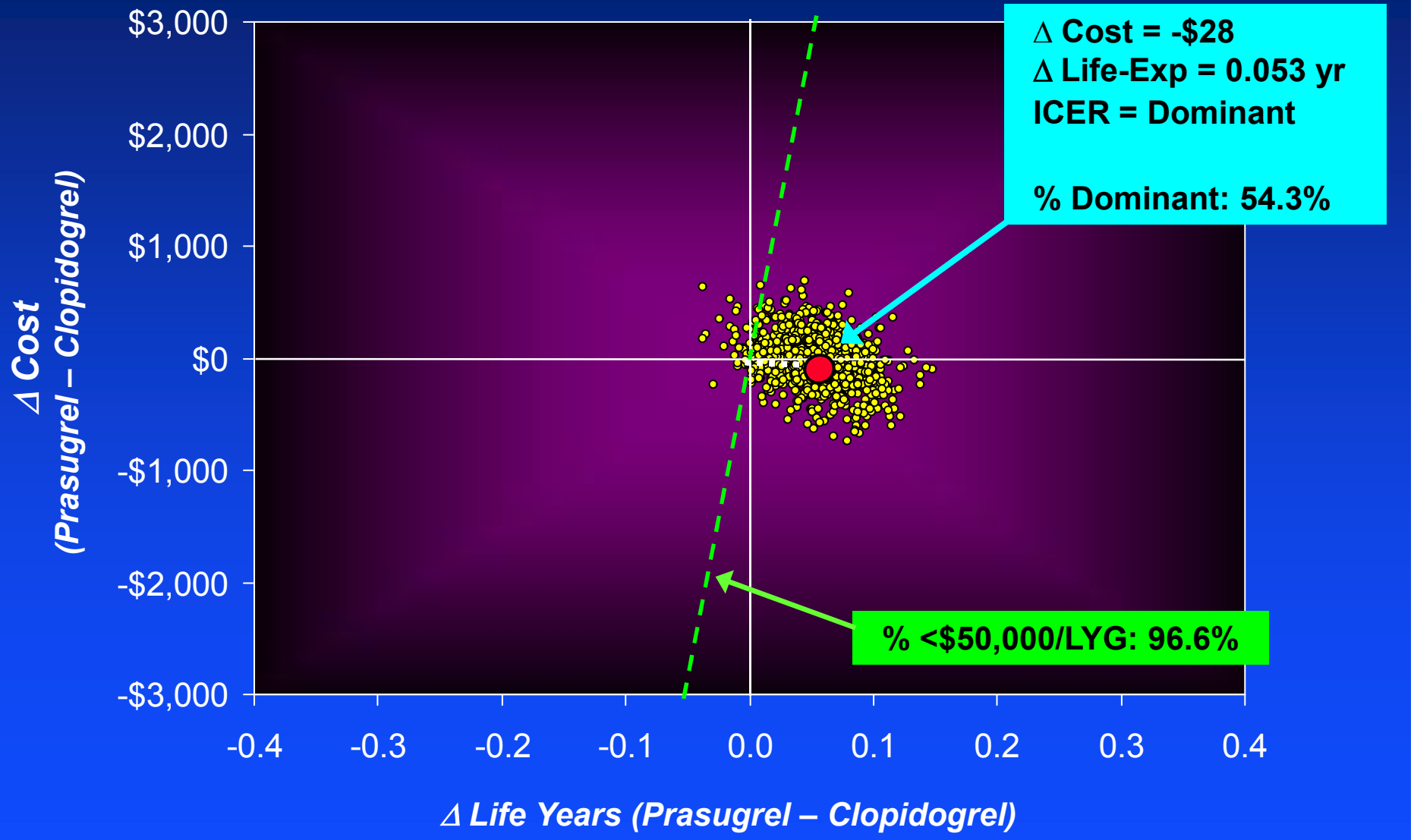
Cost-Effectiveness: *Days 31-EOS*



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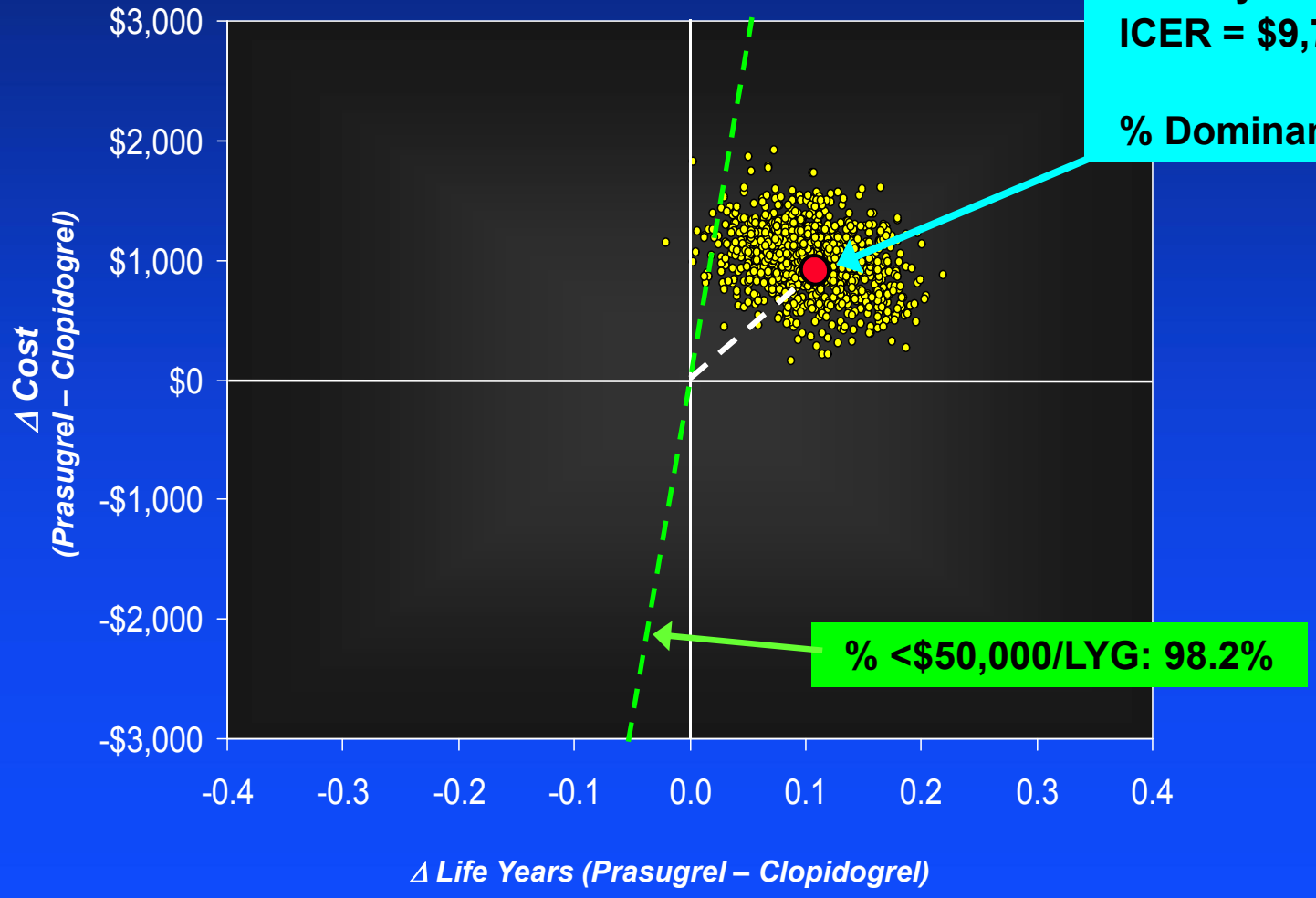
Impact of Generic Clopidogrel

Treatment Over Full Trial Duration
Cost of Generic Clopidogrel = $1/day



Δ Cost = +$996
Δ Life-years= 0.102
ICER = $9,727/LYG

% Dominant: 0%

% <$50,000/LYG: 98.2%

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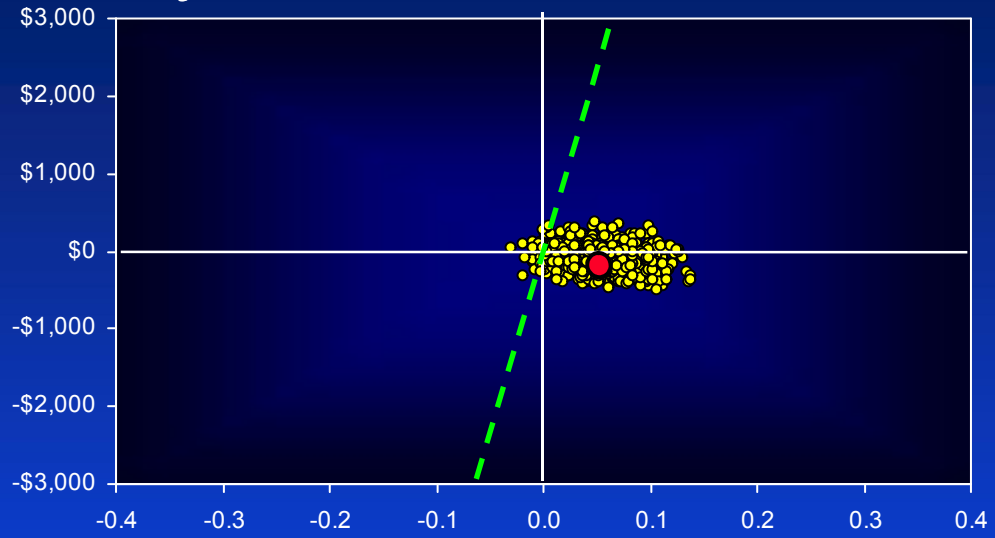
Impact of Generic Clopidogrel by Time Period

Treat Days 1-30

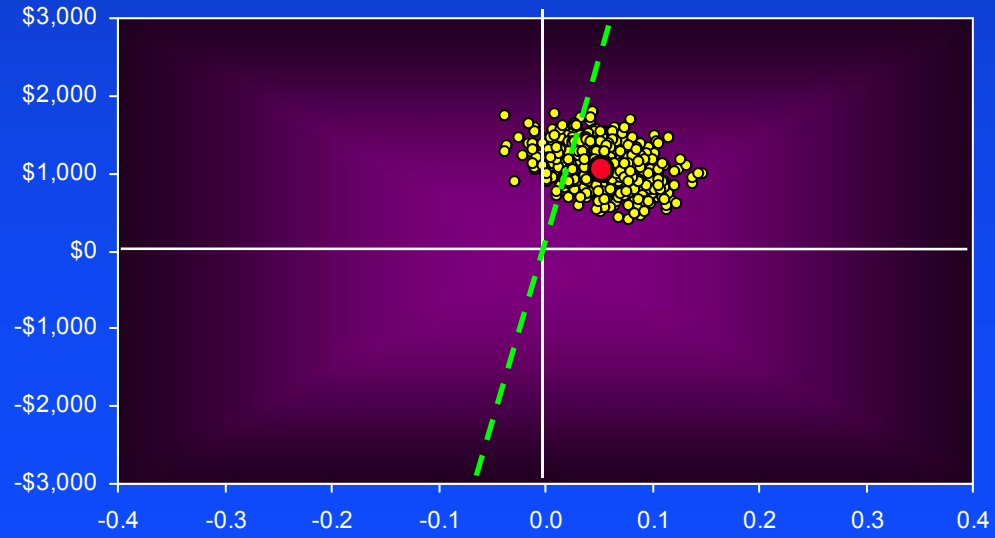


Summary Statistics

Δ Cost = -$92
Δ Revasc = 0.056
ICER = Dominant

% Dominant: 70.1%
% <$50K/LYG: 96.9%

Extend treatment from Day 31 to End of Trial



Summary Statistics

Δ Cost = +$1088
Δ Revasc = 0.053
ICER = $20,714/LYG

% Dominant: 0.0%
% <$50K/LYG: 84.5%

Subgroup Analyses (vs. Generic Clopidogrel)

	Δ Cost	Δ Life Expect.	ICER	% Dom-inant	% Dom-inated	% < $50K/LYG
Diabetes	$470	0.18	**$2565**	23%	1%	**97%**
No Diabetes	$1140	0.08	**$15,582**	0%	4%	**88%**
STEMI	$760	0.14	**$5254**	10%	5%	**92%**
NSTEMI/UA	$1054	0.09	**$11,571**	0%	2.2%	**93%**
DES	$1284	0.08	**$16,065**	0%	5%	**87%**
No DES	$292	0.18	**$1626**	31%	1%	**99%**
"On-Label" *	$1020	0.13	**$7926**	0%	1%	**98%**

* Age <75, weight >=60kg, no h/o stroke or TIA (post-hoc)

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Summary

- For patients with ACS undergoing PCI, treatment with prasugrel as compared with clopidogrel was associated with *significant cost offsets* in both the first 30 days as well as longer term treatment (median 14.7 months)
- These cost offsets were derived predominantly from *reductions in repeat PCI*– both with and without subsequent MI– and occurred despite a modest increase in costs related to bleeding events
- Although the acquisition cost of prasugrel was ~$300 greater than clopidogrel, total medical care costs remained lower for prasugrel both during the first 30 days as well as the subsequent ~13 months

Summary

- Compared with generic clopidogrel (expected cost $1/day), prasugrel was cost saving during the first 30 days but resulted in higher costs beyond this time period
- Nonetheless, the *cost-effectiveness* of prasugrel vs. generic clopidogrel was favorable (<$20,000/LYG) for both the subacute and longer term phases of treatment
- These results were consistent across most subgroups with the exception of pts with previous stroke/TIA and patients at high risk of bleeding (age >75, wt < 60 kg)

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Conclusions

- For patients undergoing PCI in the ACS setting, treatment with prasugrel compared with clopidogrel is highly cost-effective– and in many cases cost-saving– over both the subacute and longer term phases of treatment
- Further studies will be necessary to understand the optimal duration of treatment and the cost-effectiveness of prasugrel in other, non-ACS settings