PREVENTion of Non-Surgical Bleeding by Management of HeartMate II Patients without Antiplatelet Therapy (PREVENT II) Trial

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Relevant Financial Relationship Disclosure Statement

PREVENT II Study Results

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I will not discuss off label use and/or investigational use of the HeartMate II left ventricular assist device.

The following relevant financial relationships exist related to this presentation:

Dr. Jorde: Consultant (no Honoraria) for Abbott

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Dr. Adamson: personal fees from Abbott

Drs. Crandall and Franke: employees of Abbott

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PREVENT II Study Design

PREVENT II was a prospective, multicenter, randomized, double-blind, placebo-controlled trial of aspirin 81 mg versus placebo once-daily in subjects ≥ 50 years of age receiving warfarin, after initial implantation of a HeartMate II left ventricular assist system.

- Investigators implanted and managed subjects in accordance with the original PREVENT recommended practices to reduce pump thrombosis.
- PREVENT II aimed to enroll up to 350 subjects to demonstrate, with 80% power, the non-inferiority of the primary safety and superiority of the primary efficacy endpoint
  - Enrollment was stopped early due to the start of MOMENTUM3
- 65/72 (31 placebo, 34 ASA) enrolled subjects met criteria for initiation of the study drug.

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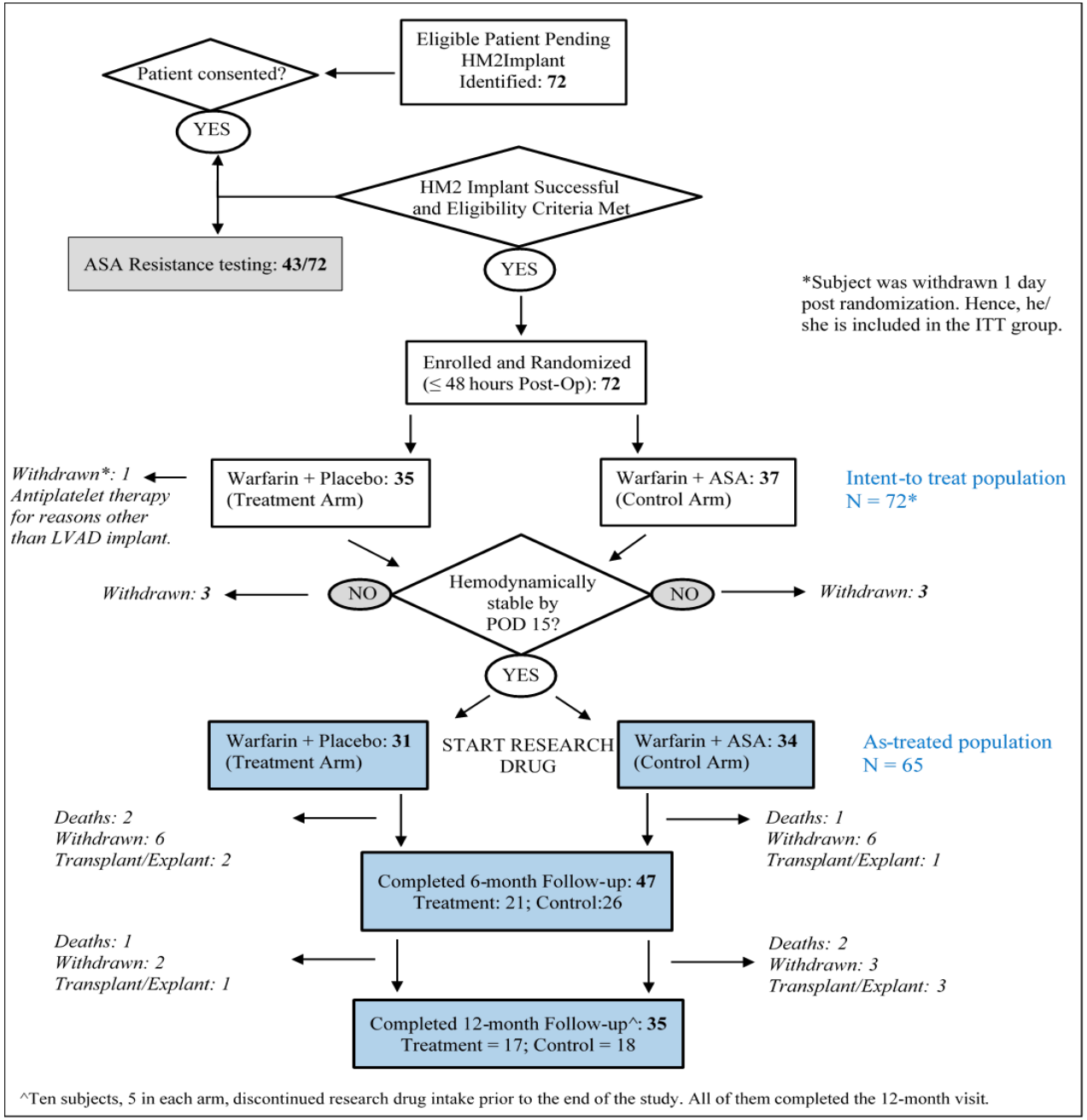
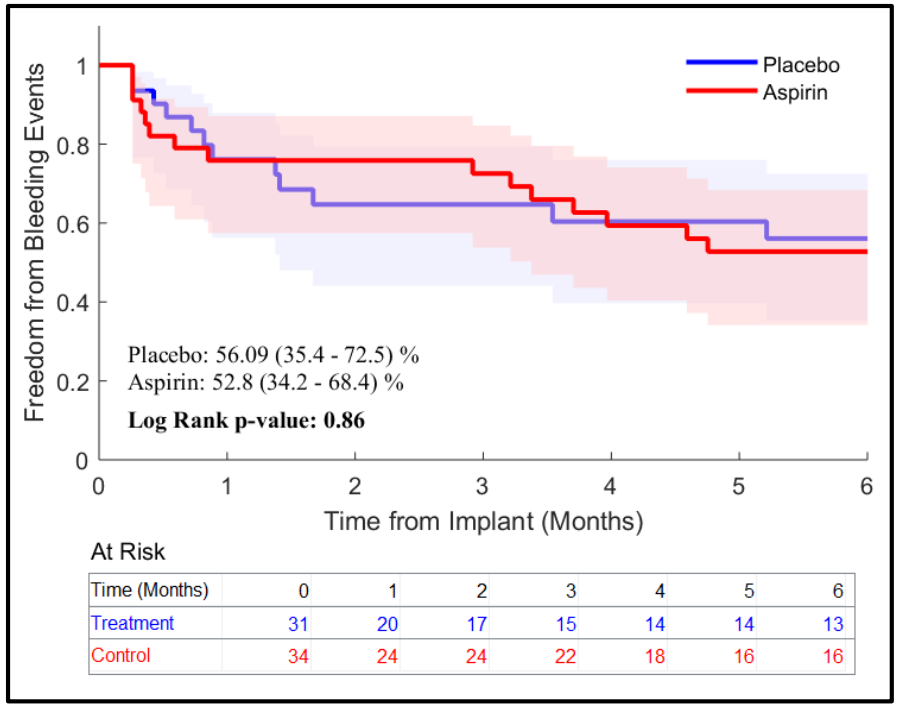
Disposition of Subjects

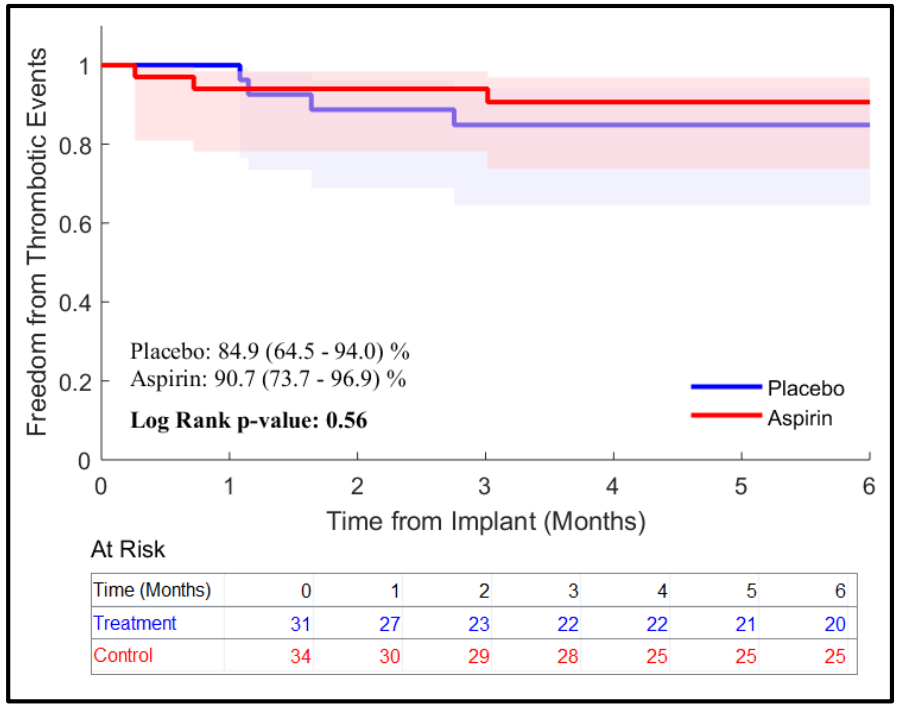


Baseline Characteristics	Placebo (N=31)	Aspirin (N=34)
Mean Age ± SD - years	68 ± 6	66 ± 7
Females – % (n)	19% (7)	9% (3)
BMI - Kg/m^2	28 ± 6	28 ± 5
Race White – % (n)	74% (23)	71%(24)
Ischemic Heart Failure – % (n)	48% (15)	71% (24)
History of Atrial Fibrillation – % (n)	42% (13)	41% (14)
History of Stroke – % (n)	19% (6)	6% (2)
History of Bleed – % (n)	3.2% (1)	15% (5)
GI Bleed / Ulcer – % (n)	0% (0)	6% (2)
History of MI – % (n)	39% (12)	63% (21)
History of Diabetes – % (n)	58% (18)	53% (18)
History of Aortic Stenosis – % (n)	0% (0)	3% (1)
History of Carotid Artery Disease – % (n)	10% (3)	12% (4)
LVEF (%) – mean ± SD (n)	18 ± 6	17 ± 5
Right Atrial Pressure – mmHg	11 ± 7	10 ± 6
Mean Blood Pressure – mmHg	84 ± 10	86 ± 14
Cardiac Index – L/min/m^2	2.0 ± 0.6	2.0 ± 0.8
NYHA Class IIIB or IV – % (n)	97% (30)	97% (33)
Intent for Therapy – % (n)		
BTT	10% (3)	15% (5)
DT	90% (28)	85% (29)
INTERMACS Profile – % (n)		
1	3% (1)	9% (3)
2	32% (10)	21% (7)
3	55% (17)	47% (16)
4 - 7	10% (3)	21% (7)

Primary Endpoints in the As-Treated Population at 6 months Post-Randomization

	Events included in Composite Endpoint	Placebo % [95% CI]	Aspirin % [95% CI]
Safety	Non-surgical bleeding and primary hemorrhagic stroke	38 [21.6 – 55.9] %	44 [27.4 – 60.8] %
Efficacy	Pump thrombosis and thromboembolic stroke	12.9 [1.1 – 24.7] %	8.8 [0.0 – 18.4] %





Descriptive Endpoints in the As-Treated Population at 12 months Post-Randomization

	Placebo (N=31)		Aspirin (N=34)	
	Events (EPPY)	% [95% CI]	Events (EPPY)	% [95% CI]
Major Bleeding	20 (0.92)	38.7 [21.9 – 57.8]	35 (1.36)	64.7 [46.5 – 80.3]
GI Bleeding	13 (0.6)	25.8 [11.9 – 44.6]	16 (0.62)	29.4 [15.1 – 47.5]
Non-Surgical Bleeding^	18 (0.83)	38.7 [21.9 – 57.8]	29 (1.13)	52.9 [35.1 – 70.2]
Major Bleeding in patients with no history of Bleeding	20 (0.92)	38.7 [21.9 – 57.8]	29 (1.13)	50.0 [32.4 – 67.6]
Neurological Dysfunction	12 (0.55)	32.3 [16.7 – 51.4]	9 (0.35)	23.5 [10.8 – 41.2]
TIA	3 (0.14)	9.7 [2.0 – 25.8]	0	0 [0.0 – 10.3]
Hemorrhagic Stroke	2 (0.09)	6.5 [0.79 – 21.4]	2 (0.08)	5.9 [0.72 – 19.7]
Ischemic Stroke	4 (0.18)	12.9 [3.6 – 29.8]	5 (0.19)	14.7 [5.0 – 31.0]
Other	3 (0.14)	6.5 [0.79 – 21.4]	2 (0.08)	5.9 [0.72 – 19.7]
Suspected Pump Thrombosis	4 (0.23)	9.7 [2.0 – 25.8]	3 (0.12)	8.8 [1.9 – 23.7]
Subsequently Confirmed	2 (0.09)	6.5 [0.79 – 21.4]	2 (0.08)	5.9 [0.72 – 19.7]

^Bleeding occurring post-op day 8 or later.

Conclusions

- First attempt of a double-blinded RCT in the history of MCS, occurring nearly two decades after the seminal REMATCH trial
- Low dose aspirin therapy was not found to significantly alter the risk of thrombosis in HMII recipients
- Bleeding risk was higher with Aspirin at 12 months, but not at 6 months
- Overall results are also comparable to those observed in PREVENT study (GI Bleeding 21%, ischemic stroke 4%, hemorrhagic stroke 2.7%, pump thrombosis 4.8%)
- Results should be considered an incremental contribution to the hypothesis that ASA therapy may not be needed for the HMII device
  - originally suggested by the TRACE study findings

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THANK YOU !!

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