MDP477. The Effects Of Anacetrapib Therapy On Occlusive Vascular Events During Post-Trial Follow-Up of the REVEAL Randomized Trial

Presented on behalf of the REVEAL Collaborative Group

Financial Disclosures

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- Designed, conducted and analyzed independently of the funders

- University of Oxford is the trial sponsor

Background

- In statin trials there is a lag to onset of benefit and a persistence of effect for several years beyond the end of treatment
- Anacetrapib is a potent inhibitor of Cholesteryl Ester Transfer Protein (CETP) which doubles HDL-cholesterol and lowers LDL-cholesterol
- Anacetrapib accumulates in adipose tissue during prolonged dosing
- Therefore additional follow-up of REVEAL trial participants was planned

REVEAL Trial Design

Eligibility: 30,449 patients aged over 50 years with occlusive vascular disease

Background statin: Atorvastatin 20 or 80 mg daily (China: 10 or 20 mg)

Randomized: Anacetrapib 100 mg daily vs. matching placebo

In-Trial Follow-Up: median 4.1 years

Post-Trial Follow-Up: median 2.3 years off study treatment, biannual telephone interview/medical record review

Primary outcome: Major Coronary Event

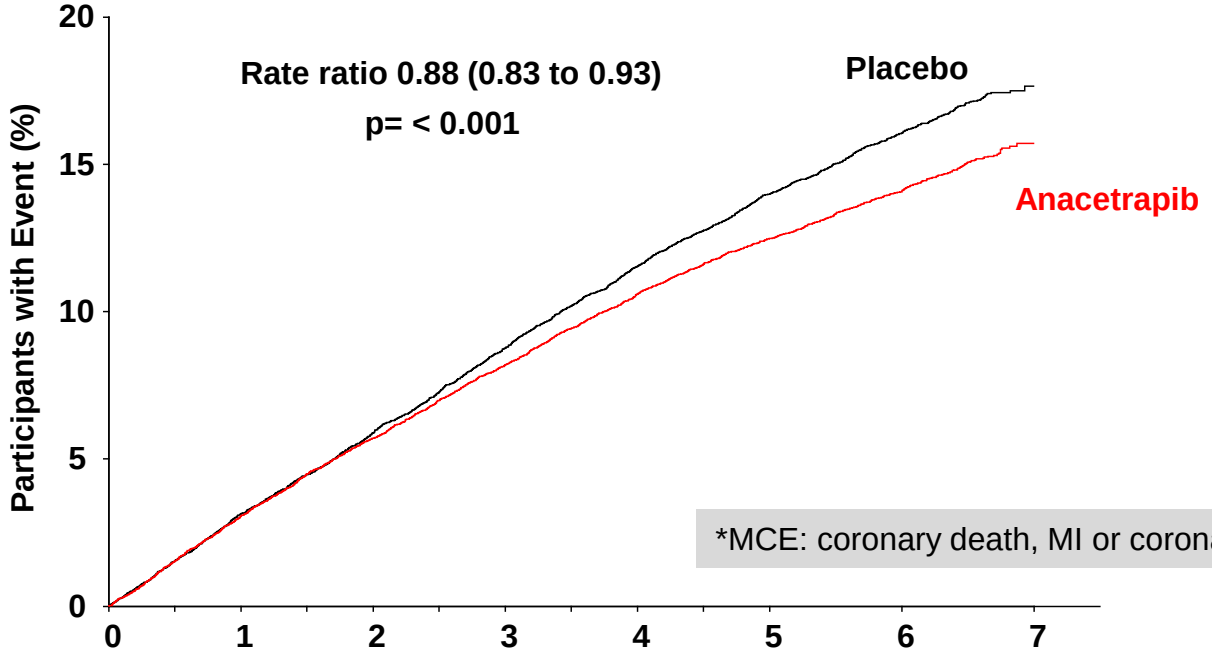
(i.e. Coronary death, myocardial infarction, or coronary revascularization)

HPS 3/TIMI 55-REVEAL Collaborative Group. Am Heart J 2017;187:182-90
The HPS3/TIMI55–REVEAL Collaborative Group. N Engl J Med 2017; 377:1217-1227

Baseline Characteristics

Characteristic		Total (N = 30,449)
Age (years)	Mean	67
Gender	Male	25,534 (84%)
Region	Europe	15,738 (52%)
	North America	6082 (20%)
	China	8629 (28%)
Prior Disease	Coronary heart disease	26,679 (88%)
	Cerebrovascular disease	6781 (22%)
	Peripheral arterial disease	2435 (8%)
	Diabetes mellitus	11,320 (37%)

Primary Endpoint: Major Coronary Event*



*MCE: coronary death, MI or coronary revascularization

No. at Risk								
Placebo	15,224	14,649	14,088	13,451	12,616	11,173	9124	276
Anacetrapib	15,225	14,656	14,104	13,531	12,708	11,389	9389	289
Benefit		1±2	2±3	6±3	9±4	15±4	20±4	19±5

Per 1000 participants in anacetrapib group

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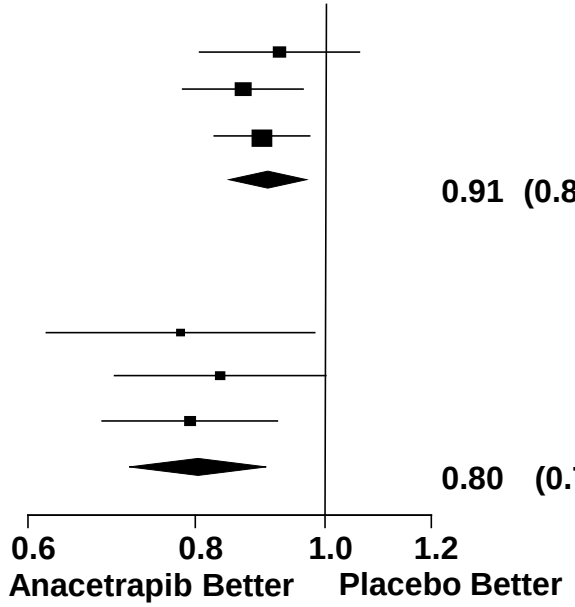
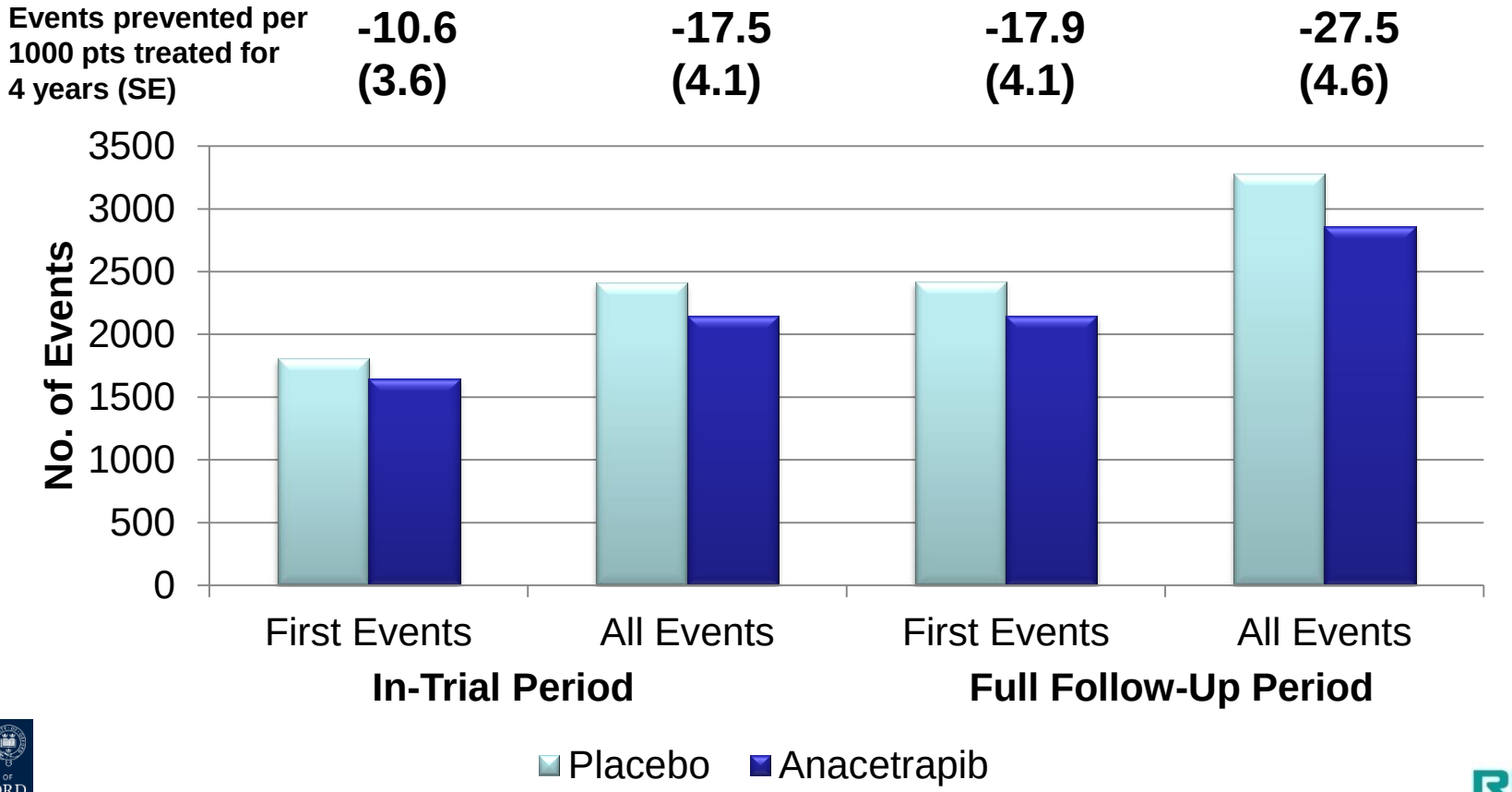
Components of Primary Endpoint by Trial Period

Type of Event	Anacetrapib (N=15,225) No. of participants with events	(%)	Placebo (N=15,224) No. of participants with events	(%)	Rate Ratio (95% CI)	P Value
In-trial						
Coronary death	389	(2.6)	420	(2.8)		
Myocardial infarction	670	(4.4)	769	(5.1)		
Coronary revascularization	1083	(7.1)	1203	(7.9)		
Major coronary event	**1643**	**(10.8)**	**1805**	**(11.9)**	**0.91 (0.85–0.97)**	**0.004**
Post-trial						
Coronary death	127	(1.0)	162	(1.3)		
Myocardial infarction	215	(1.7)	254	(2.1)		
Coronary revascularization	300	(2.5)	372	(3.2)		
Major coronary event	**503**	**(4.3)**	**614**	**(5.3)**	**0.80 (0.71–0.90)**	**<0.001**



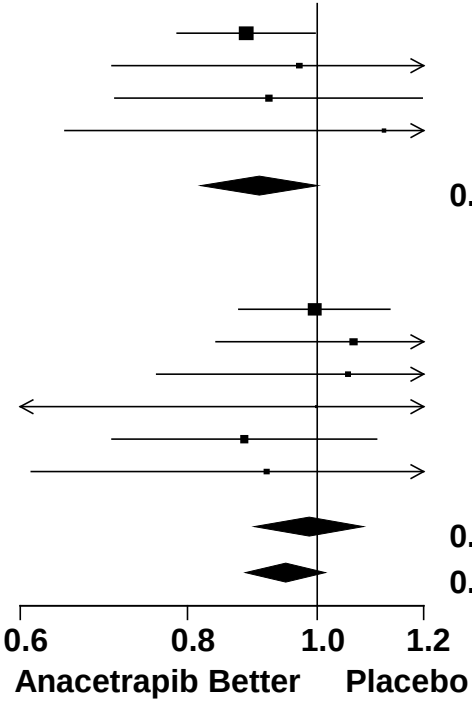
Effect on Recurrent Major Coronary Events



Effect on Mortality

(Overall and by Cause: Full Follow-Up Period)

Cause of Death	Anacetrapib (N=15,225) No. of participants with events (%)		Placebo (N=15,224) No. of participants with events (%)		Rate Ratio (95% CI)	P Value
Cardiovascular causes						
Coronary death	516	(3.4)	582	(3.8)		
Other cardiac	73	(0.5)	75	(0.5)		
Stroke	106	(0.7)	115	(0.8)		
Other vascular	27	(0.2)	24	(0.2)		
Subtotal: Any cardiovascular	**722**	**(4.7)**	**796**	**(5.2)**	**0.90 (0.82–1.00)**	**0.05**
Non-cardiovascular causes						
Cancer	455	(3.0)	456	(3.0)		
Infection	142	(0.9)	133	(0.9)		
Respiratory	73	(0.5)	69	(0.5)		
Hepatic	6	(0.0)	6	(0.0)		
Other medical	139	(0.9)	157	(1.0)		
Non-medical	45	(0.3)	49	(0.3)		
Subtotal: Any non-cardiovascular	**860**	**(5.6)**	**870**	**(5.7)**	**0.99 (0.90–1.08)**	**0.76**
All causes	**1582**	**(10.4)**	**1666**	**(10.9)**	**0.95 (0.88–1.01)**	**0.12**



Conclusion

- Between-group differences in the risk of coronary death emerged in later years of follow-up that were not seen in-trial
- Absolute reduction in MCE at 6 years was nearly double that seen at the end of the 4 year treatment period.
- No safety concerns emerged for non-vascular mortality or morbidity
- Results reinforce importance of post-trial follow-up in lipid-modifying trials to evaluate the efficacy and safety