RESVERLOGIX

TSX: RVX

Detailed Preliminary Results of BETonMACE

Strengthening Opportunities Through Positive Findings & Synergy

November 18th, 2019

Forward Looking Statement

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Executive Summary (1)

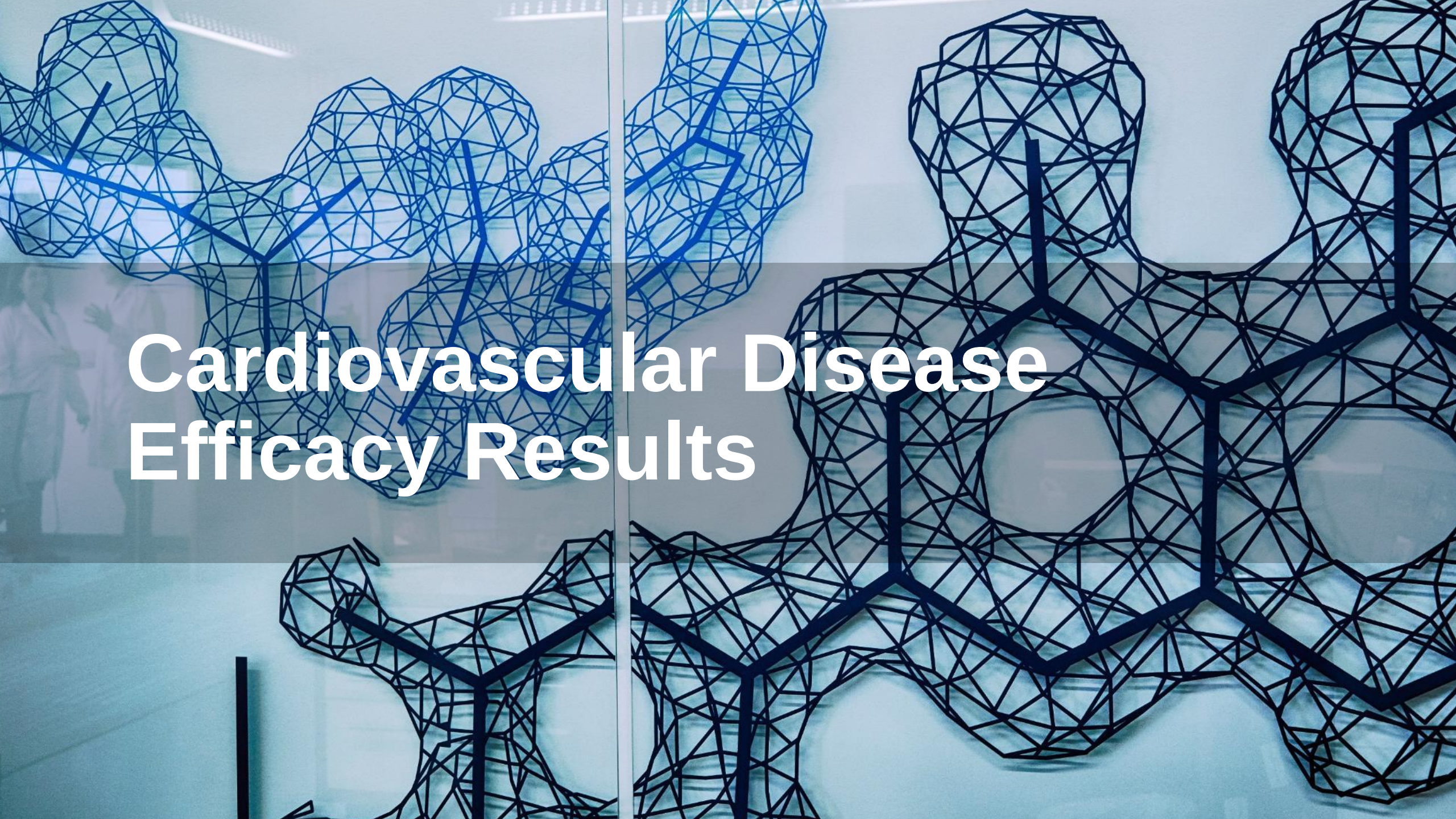
- **Very Encouraging Cardiovascular Disease Efficacy Results**
  - Narrow Miss on Primary: 18% Hazard Reduction (95% CI; 0.65-1.04) p=0.11
    - 21% Hazard Reduction (95% CI; 0.62-1.01) p=0.06, excluding undetermined cause of death
  - Trending MACE Improvements on Multiple Endpoints (see Forest plots) with Survival Curves Consistently Separating Early
  - Hit on Hospitalization for Congestive Heart Failure: 41% Hazard Reduction (95% CI; 0.38-0.94) p=0.03

- **Most Pronounced Primary Endpoint Hits in Prespecified Subgroups vs Top Standard of Care**
  - Impaired Renal Function: 50% Hazard Reduction (95% CI; 0.26-0.96) p=0.03
  - Baseline LDL Below Median: 40% Hazard Reduction (95% CI; 0.42-0.86) p=0.02

- **Critically Important Finding, Patents Filed – Potential Synergy with New Generation of Diabetes Drugs**
  - Primary Endpoint in Patients Receiving SGLT2i
    - All SGLT2i's: 60% Hazard Reduction (95% CI; 0.16-1.00) p=0.05 (non-QC'd)
    - Empagliflozin: 66% Hazard Reduction (95% CI; 0.12-1.01) p=0.05 (non-QC'd)

Executive Summary (2)

- **Early December Release of Cognitive Impairment Data**
  - Embargoed until Clinical Trials on Alzheimer's Disease conference (CTAD: Dec. 4 – 7, 2019)
  - Additional BETonMACE results to be presented; details to come
- **Significantly Enhanced Intellectual Property Position from Additional and Future Patent Filings**
  - Composition, use, and manufacturing, with long patent life for Apabetalone
  - Additional, important patent filings to come
- **Further Development of Apabetalone Well Underway Based on Key BETonMACE Findings**
  - Consider multiple paths forward (breakthrough status filings with FDA and EMA, partnering for multiple indications and synergistic combination trials)
- **Appendix**
  - BETonMACE Review, Study Design and Baseline Characteristics
  - Safety Evaluation
  - Apabetalone MoA details



Cardiovascular Disease Efficacy Results

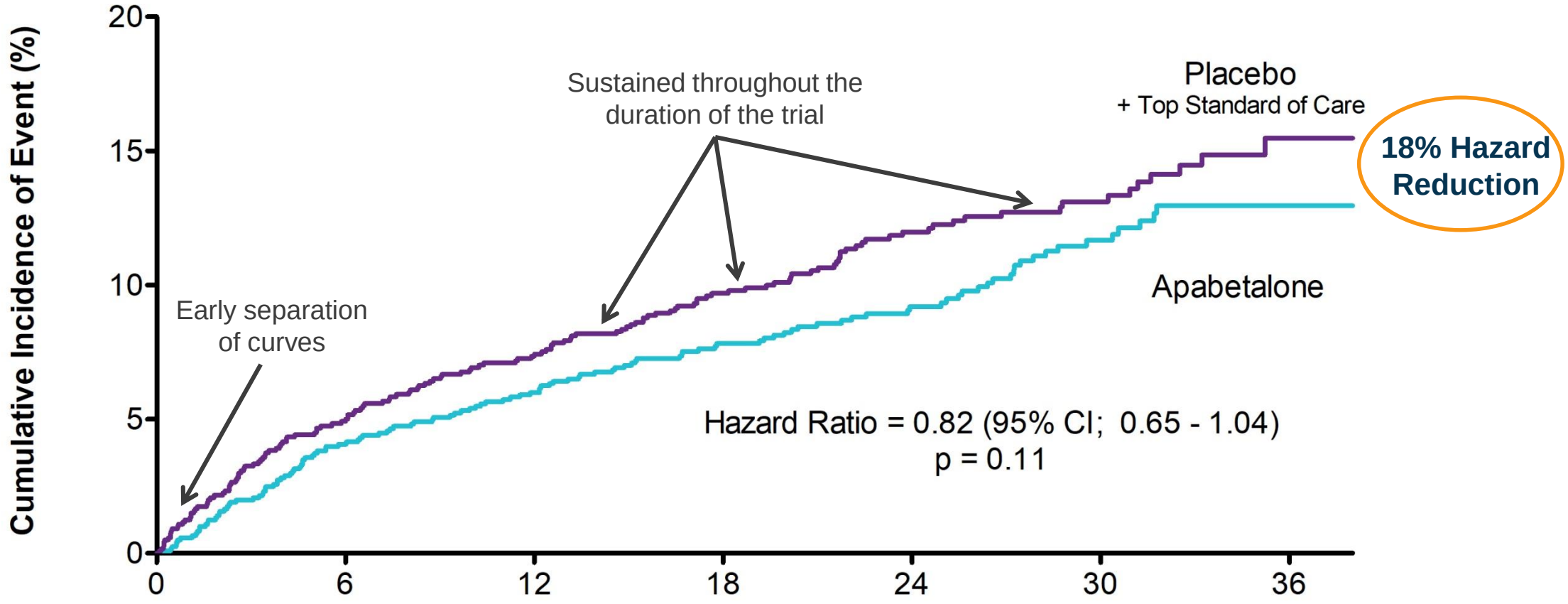
Primary Endpoint

Primary Outcome Measure and Components

Endpoint, n(%)	Apabetalone (N=1212)	Placebo (N=1206)	HR (95% CI)	Log-rank p-value
MACE	**125**	**149**	**0.82 (0.65-1.04)**	**0.11**
Non-fatal MI	77	94	0.80 (0.59,1.08)	0.15*
Stroke	17	17	1.01 (0.52, 1.98)	0.99*
CV Death	45	55	0.81 (0.54, 1.19)	0.29*

***Nominal p value**

Primary Endpoint: Narrowly Defined MACE

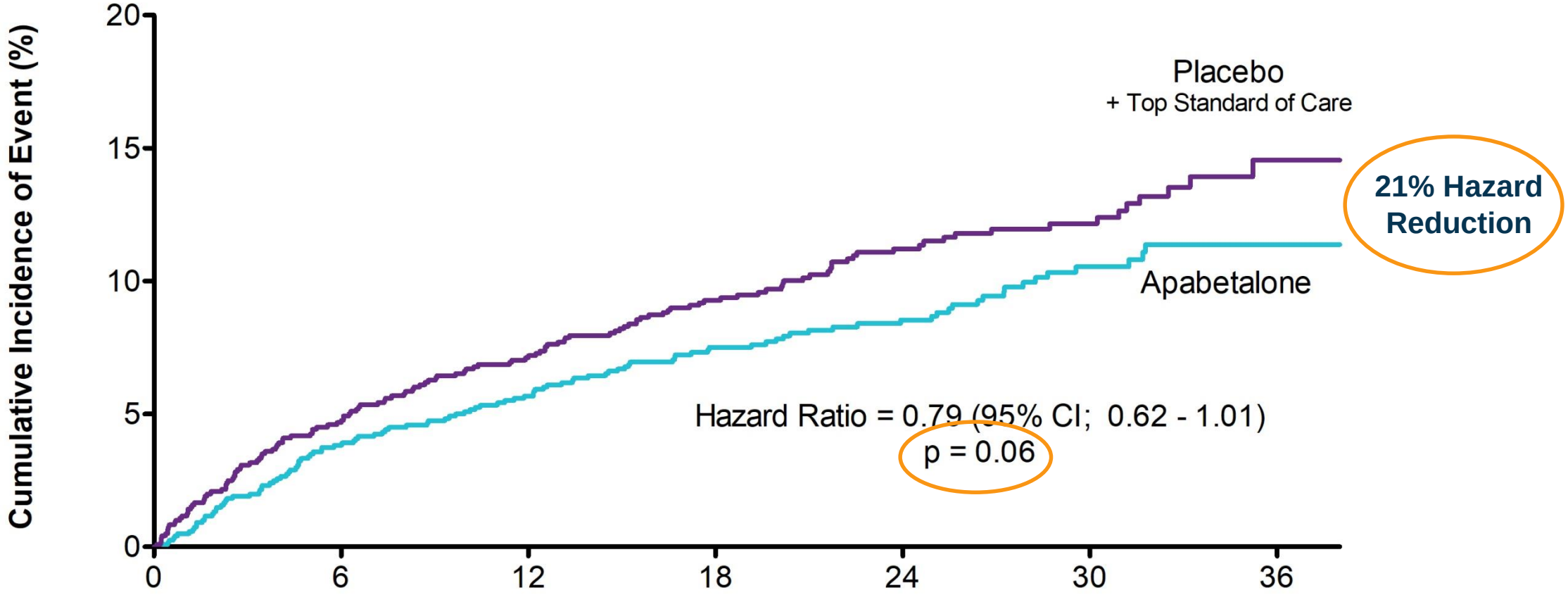


No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

Primary Endpoint Excluding Undetermined Deaths

Sensitivity Analysis

MACE defined as CV Death, non-fatal MI, stroke (excluding undetermined cause of death patients)

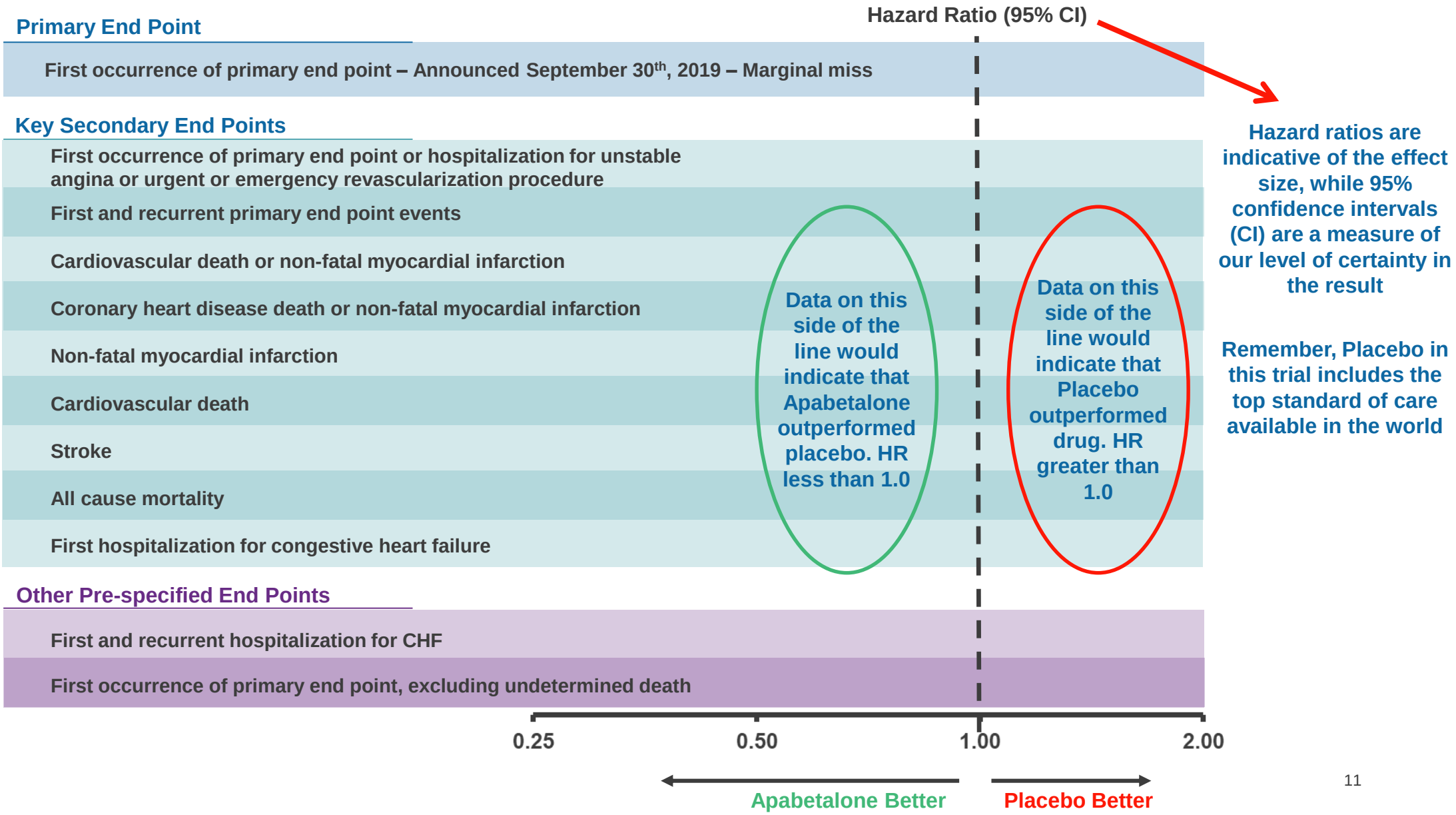


No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

*excludes undetermined cause of death patients

Secondary and Other Prespecified Endpoints

Forest Plot Primer – Presented at AGM

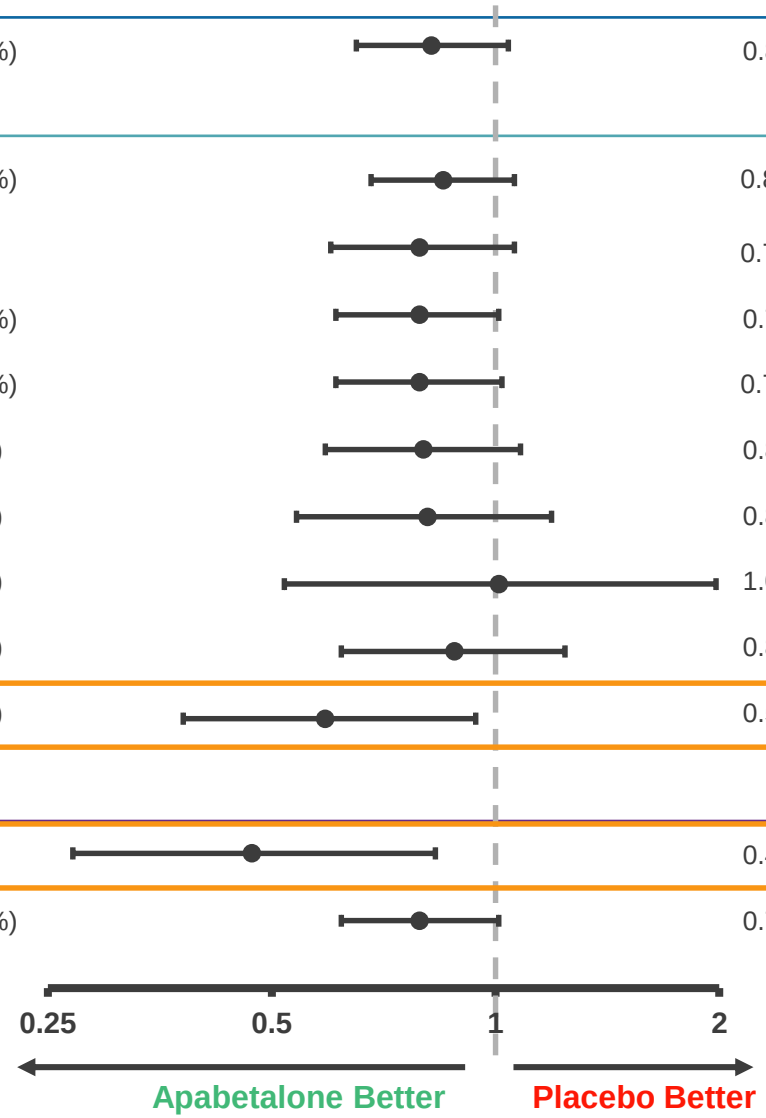


Hazard ratios are indicative of the effect size, while 95% confidence intervals (CI) are a measure of our level of certainty in the result

Remember, Placebo in this trial includes the top standard of care available in the world

Cardiovascular Endpoints

Primary End Point	Apabetalone (no. of events (%))	Placebo (no. of events (%))	Hazard Ratio (95% CI)	P Value
First occurrence of primary end point	125 (10.3%)	149 (12.4%)	0.82 [0.65, 1.04]	0.11
Key Secondary End Points				
First occurrence of primary end point or hospitalization for unstable angina or urgent or emergency revascularization procedure	144 (11.9%)	166 (13.8%)	0.85 [0.68, 1.06]	
First and recurrent primary end point events	171	203	0.79 [0.60, 1.06]	
Cardiovascular death or non-fatal myocardial infarction	112 (9.2%)	139 (11.5%)	0.79 [0.61, 1.01]	
Coronary heart disease death or non-fatal myocardial infarction	110 (9.1%)	136 (11.3%)	0.79 [0.61, 1.02]	
Non-fatal myocardial infarction	77 (6.4%)	94 (7.8%)	0.80 [0.59, 1.08]	
Cardiovascular death	45 (3.7%)	55 (4.6%)	0.81 [0.54, 1.19]	
Stroke	17 (1.4%)	17 (1.4%)	1.01 [0.52, 1.98]	
All cause mortality	61 (5.0%)	69 (5.7%)	0.88 [0.62, 1.24]	
First hospitalization for congestive heart failure	29 (2.4%)	48 (4.0%)	0.59 [0.38, 0.94]	
Other Pre-specified End Points				
First and recurrent hospitalization for congestive heart failure	35	70	0.47 [0.27, 0.83]	
First occurrence of primary end point, excluding undetermined death	113 (9.3%)	140 (11.6%)	0.79 [0.62, 1.01]	



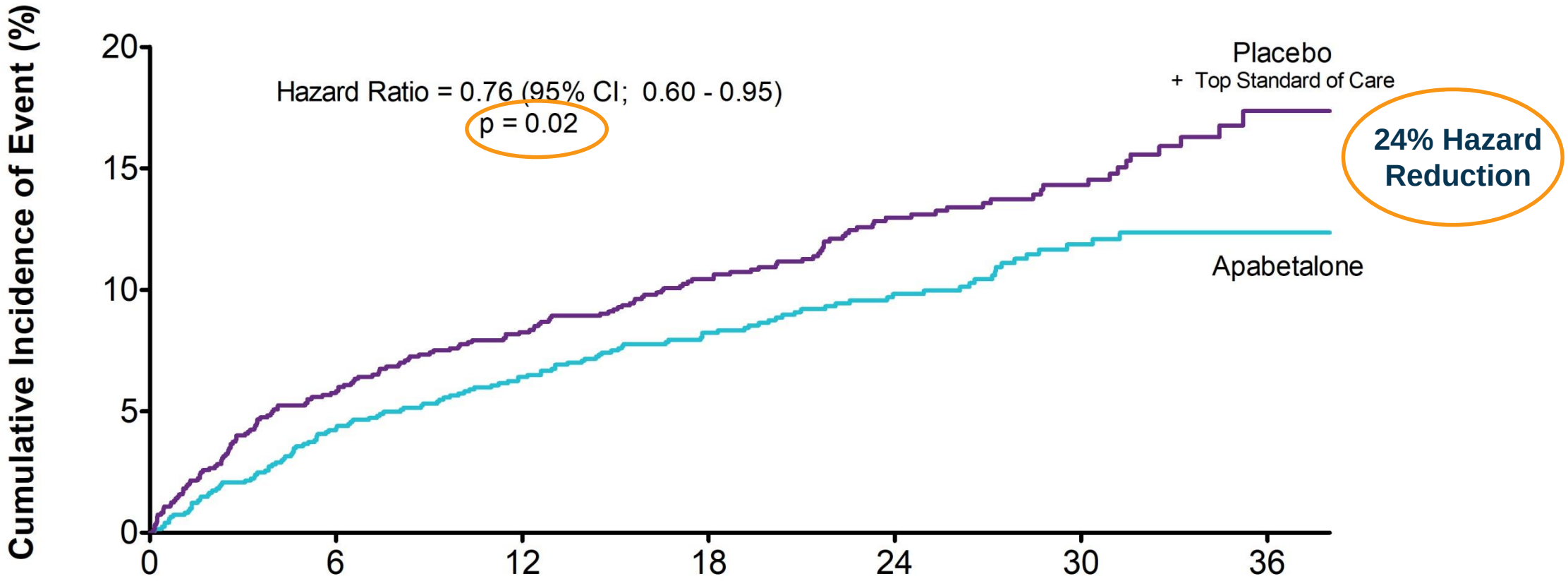
Alternative Primary Outcome Measure and Components

Endpoint, n(%)	Apabetalone (N=1212)	Placebo (N=1206)	HR (95% CI)	Log-rank p-value
MACE	**126**	**163**	**0.76 (0.60, 0.95)**	**0.02***
Non-fatal MI	77	94	0.80 (0.59,1.08)	0.15*
CV Death	45	55	0.81 (0.54, 1.19)	0.29*
Hosp. for CHF	29	48	0.59 (0.38, 0.94)	0.03*

Non-QC'd

***Nominal p value**

Alternative Primary Outcome Measure – Survival Curve



No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

Source: RVX Internal Analysis – Non-QC'd

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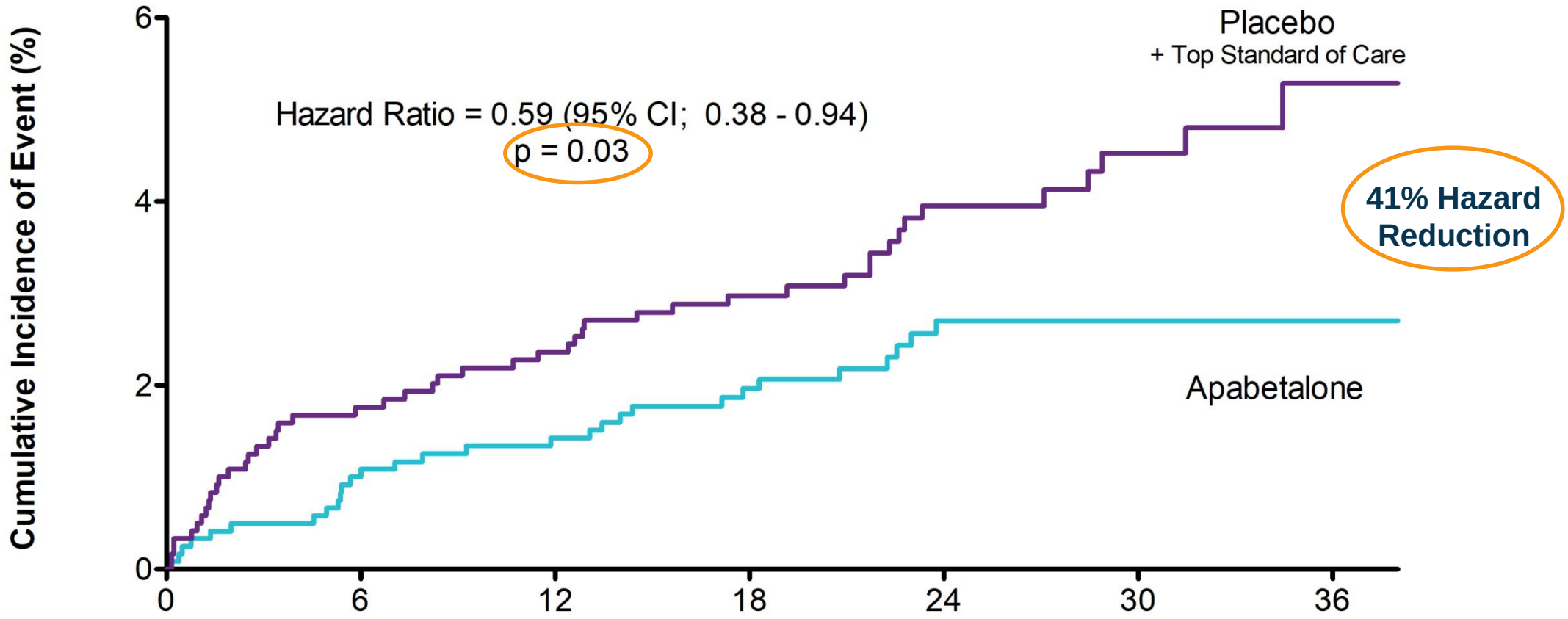
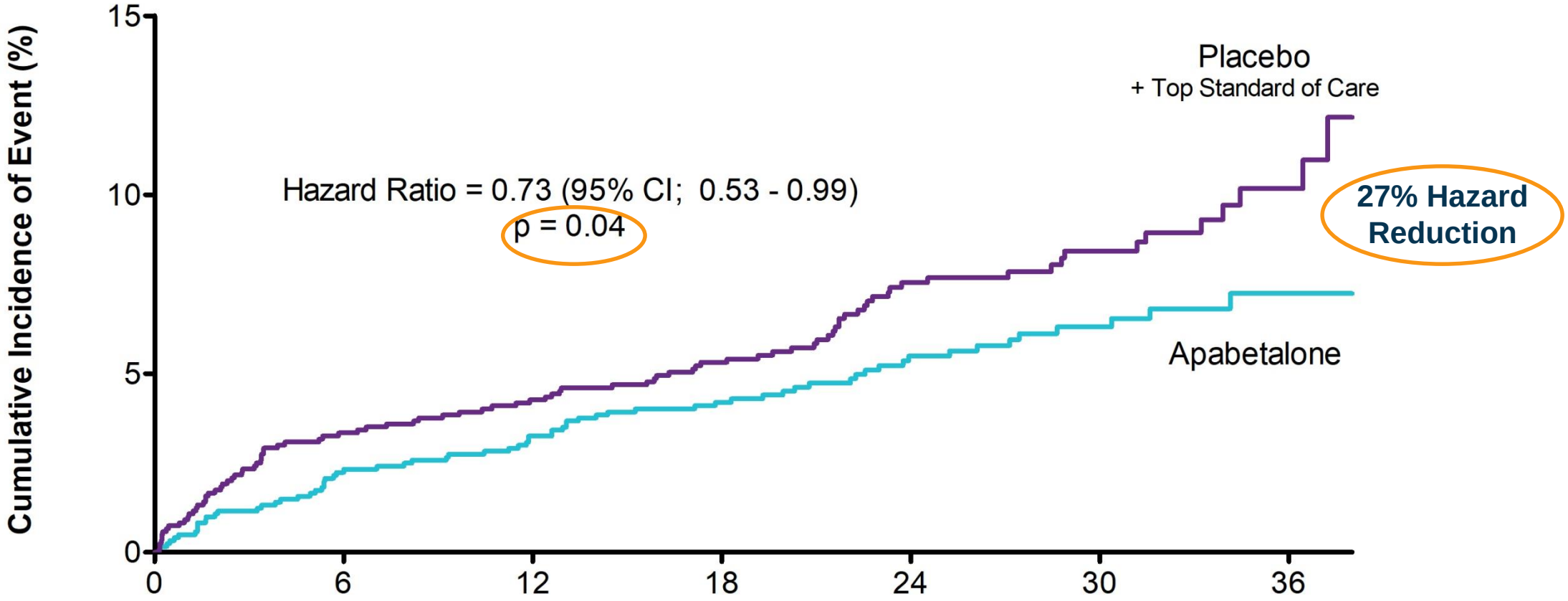
Hospitalization for Congestive Heart Failure (CHF)

Key Secondary Endpoint – First Hospitalizations for CHF



No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

Exploratory Endpoint – First Hospitalizations for CHF or CV Death

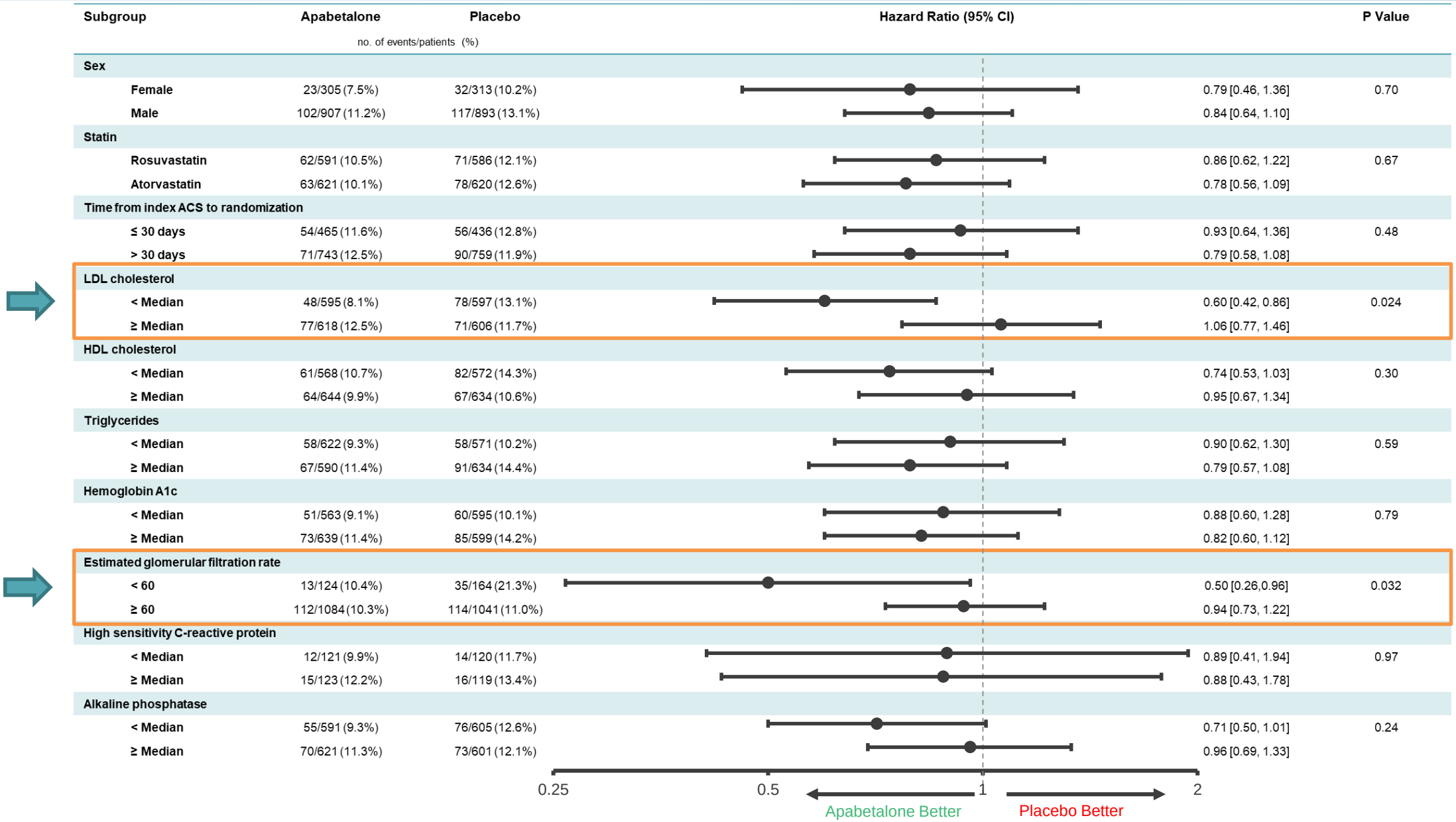


No. at Risk							
Placebo	1206	1135	1102	937	641	383	108
Apabetalone	1212	1151	1114	950	672	397	107

Source: RVX Internal Analysis – Non-QC'd

Prespecified Subgroups

Endpoint Significance Reached in Prespecified Subgroups



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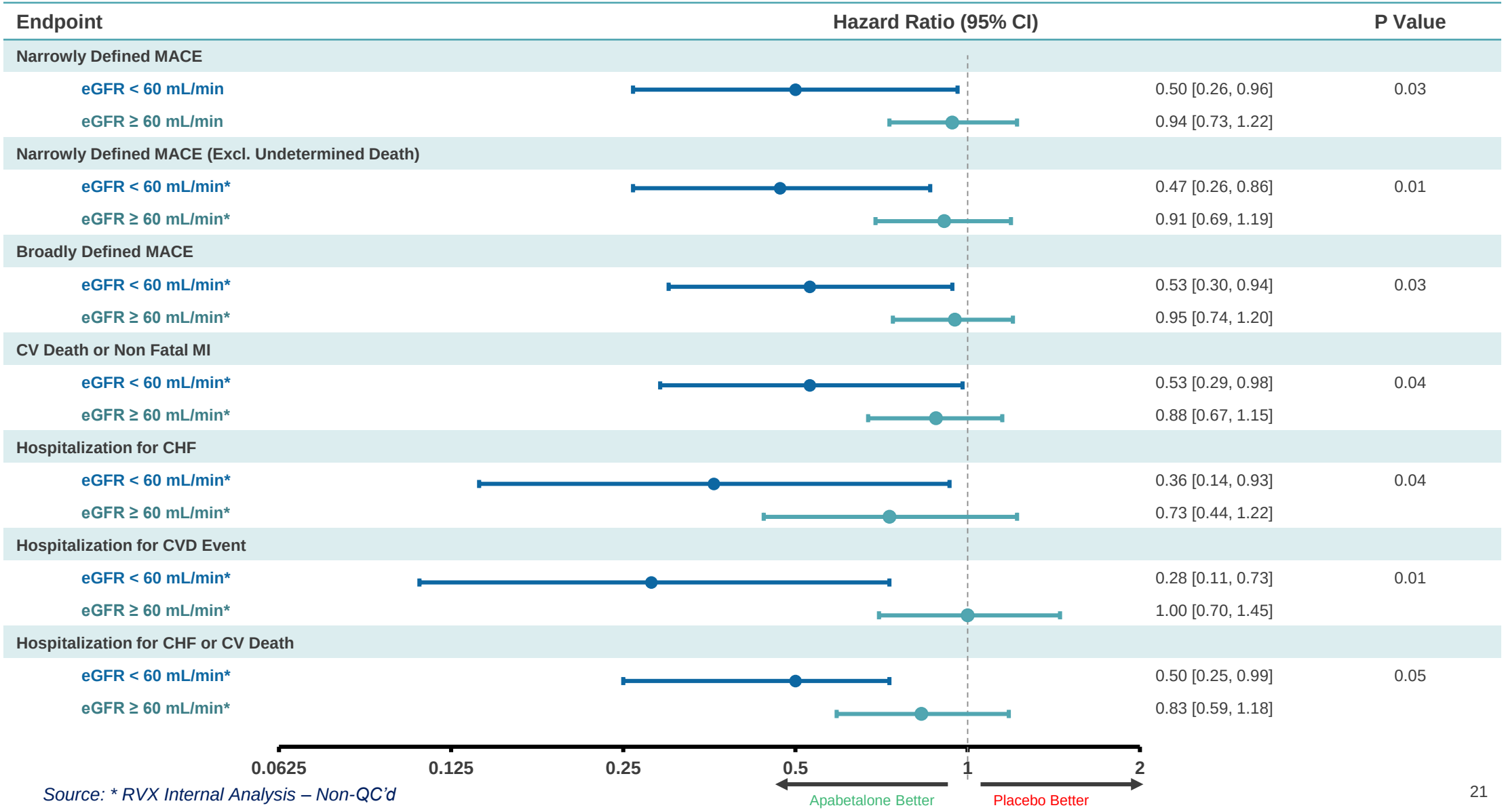
Apabetalone Overperforms in Patients with Renal Impairment

(Baseline eGFR Below 60 mL/min)

Apabetalone Improved CVD Outcomes in Impaired Renal Subgroup

Baseline eGFR Below 60 mL/min



*Source: * RVX Internal Analysis – Non-QC'd*

Apabetalone Improved CVD Outcomes in Impaired Renal Subgroup

Baseline eGFR Below 60 mL/min

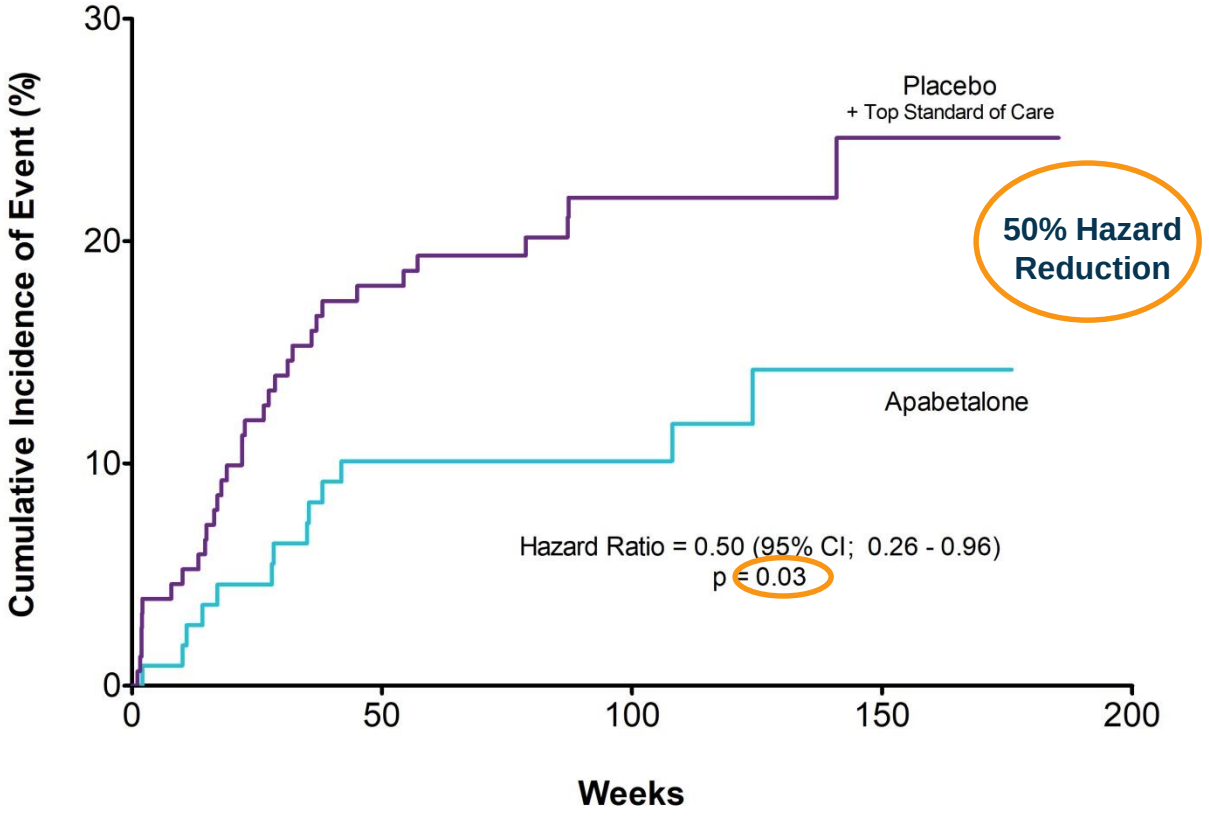
		Apabetalone		Placebo			
Endpoint	**Subgroup**	**No. of Patients**	**No. of Events**	**No. of Patients**	**No. of Events**	**Hazard Ratio**	**p-value**
Narrowly Defined MACE	eGFR <60 mL/min as calculated at baseline	110	13	153	33	0.50	0.03
Narrowly Defined MACE (excluding undetermined cause of death)			11		33	0.47	0.01
Broadly Defined MACE			13		34	0.53	0.03
CV Death or Non-Fatal MI			12		31	0.53	0.04
CHD Death or Non-Fatal MI			12		29	0.57	0.07
Non-Fatal MI			9		19	0.63	0.23
CV Death			6		16	0.53	0.14
Stroke			2		6	0.47	0.29
All Cause Mortality			10		23	0.62	0.17
Hospitalization for CHF			3		14	0.36	0.04
Hospitalization for CVD Events			2		15	0.28	0.01
Hospitalization for CHF or CV Death			9		25	0.50	0.05
Narrowly Defined MACE	eGFR ≥60 mL/min as calculated at baseline	1100	112	1051	116	0.94	0.51
Narrowly Defined MACE (excluding undetermined cause of death)			102		107	0.91	0.48
Broadly Defined MACE			131		132	0.95	0.65
CV Death or Non-Fatal MI			100		108	0.88	0.35
CHD Death or Non-Fatal MI			98		107	0.87	0.31
Non-Fatal MI			68		75	0.86	0.37
CV Death			39		39	0.96	0.84
Stroke			15		11	1.31	0.49
All Cause Mortality			51		46	1.05	0.82
Hospitalization for CHF			26		34	0.73	0.23
Hospitalization for CVD Events			61		58	1.00	0.96
Hospitalization for CHF or CV Death			60		69	0.83	0.30

Source: RVX Internal Analysis – Non-QC'd

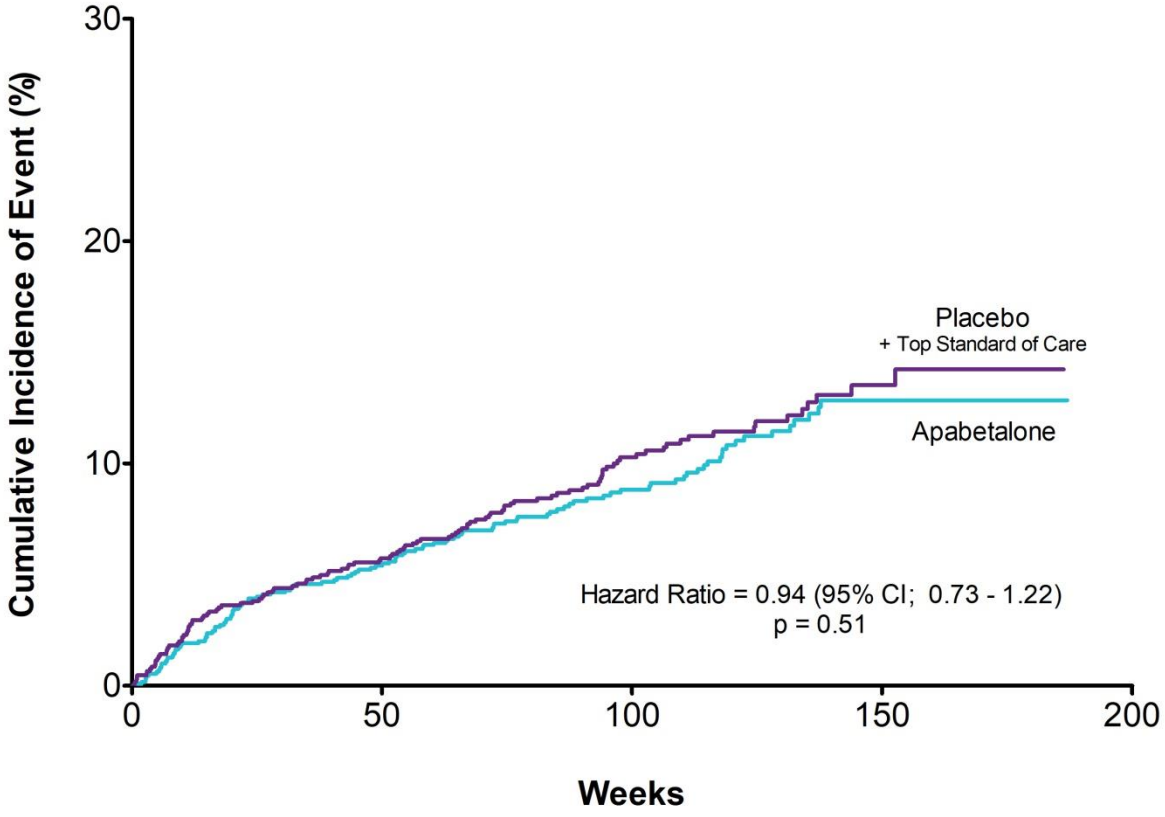
Renal Subgroup – Narrowly Defined MACE

MACE defined as CV death, non-fatal MI, and stroke

Patients with eGFR < 60 at Baseline



Patients with eGFR ≥ 60 at Baseline

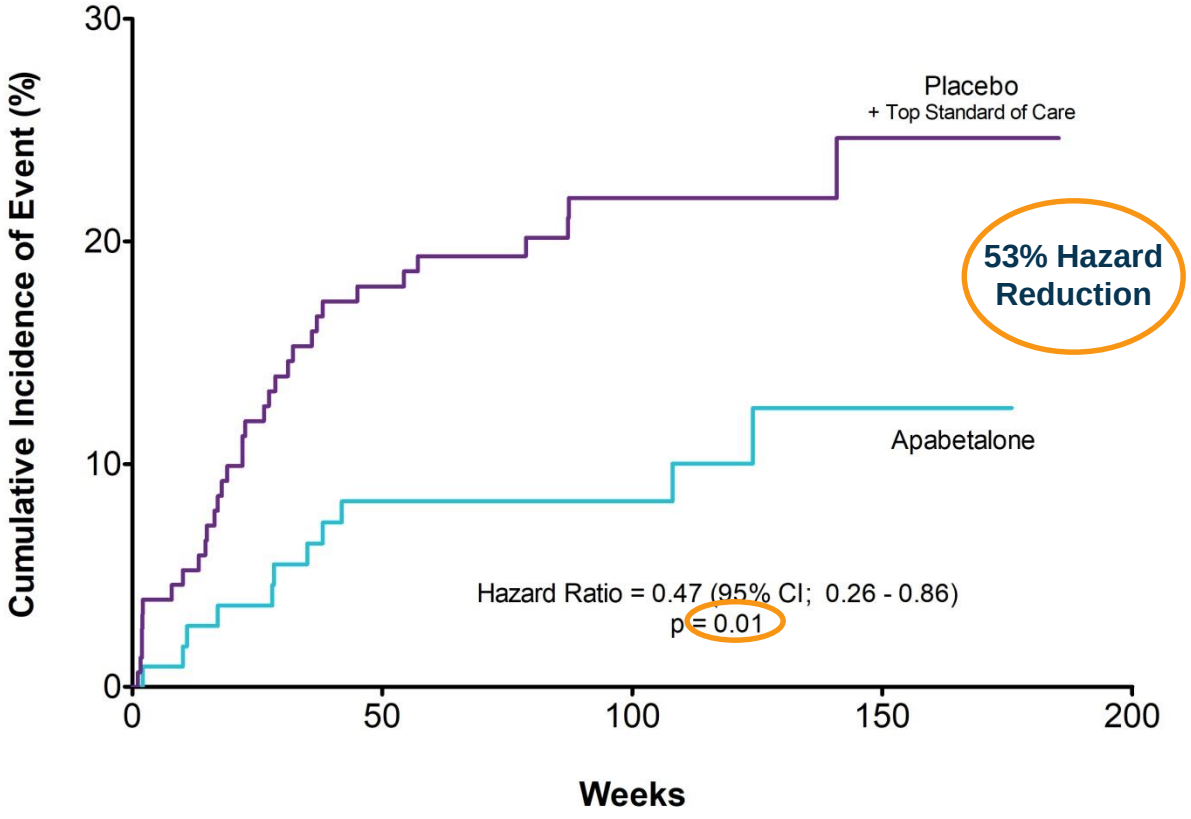


Source: RVX Internal Analysis – Non-QC'd

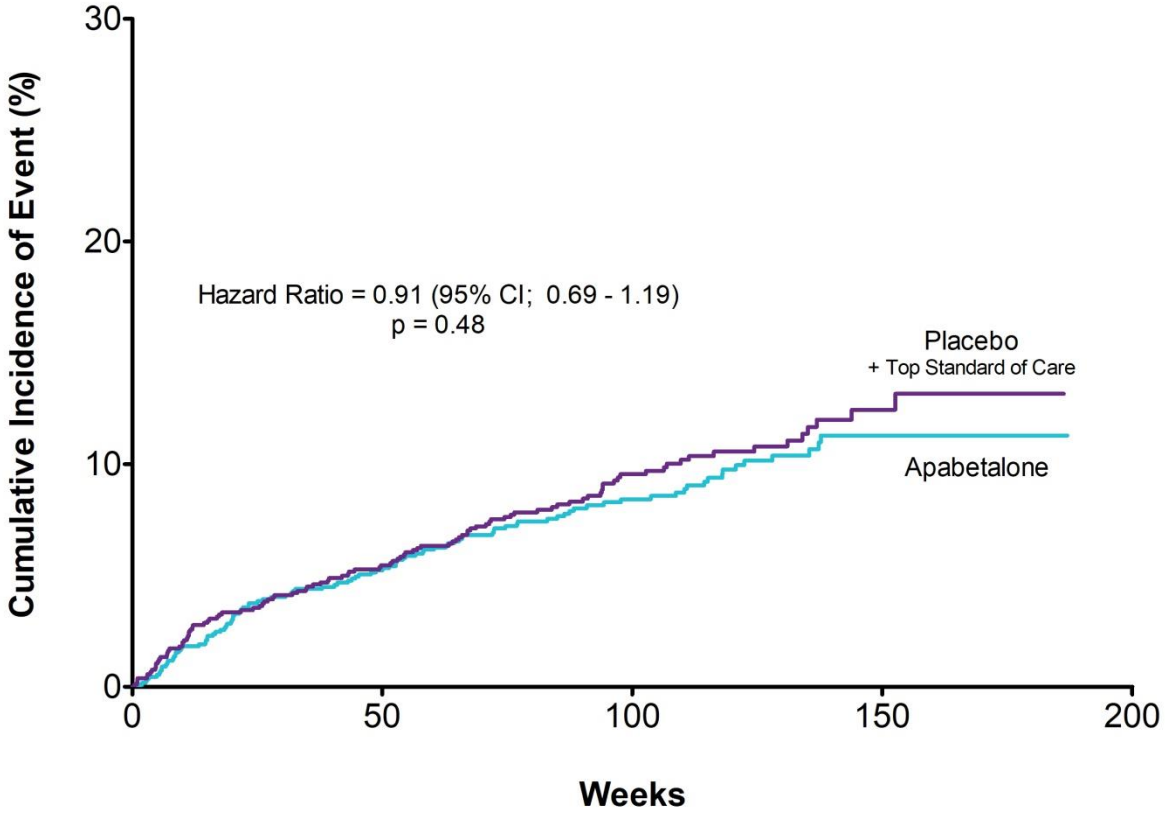
Renal Subgroup – Narrowly Defined MACE

MACE defined as CV death, non-fatal MI, and stroke excluding undetermined cause of death

Patients with eGFR < 60 at Baseline



Patients with eGFR ≥ 60 at Baseline

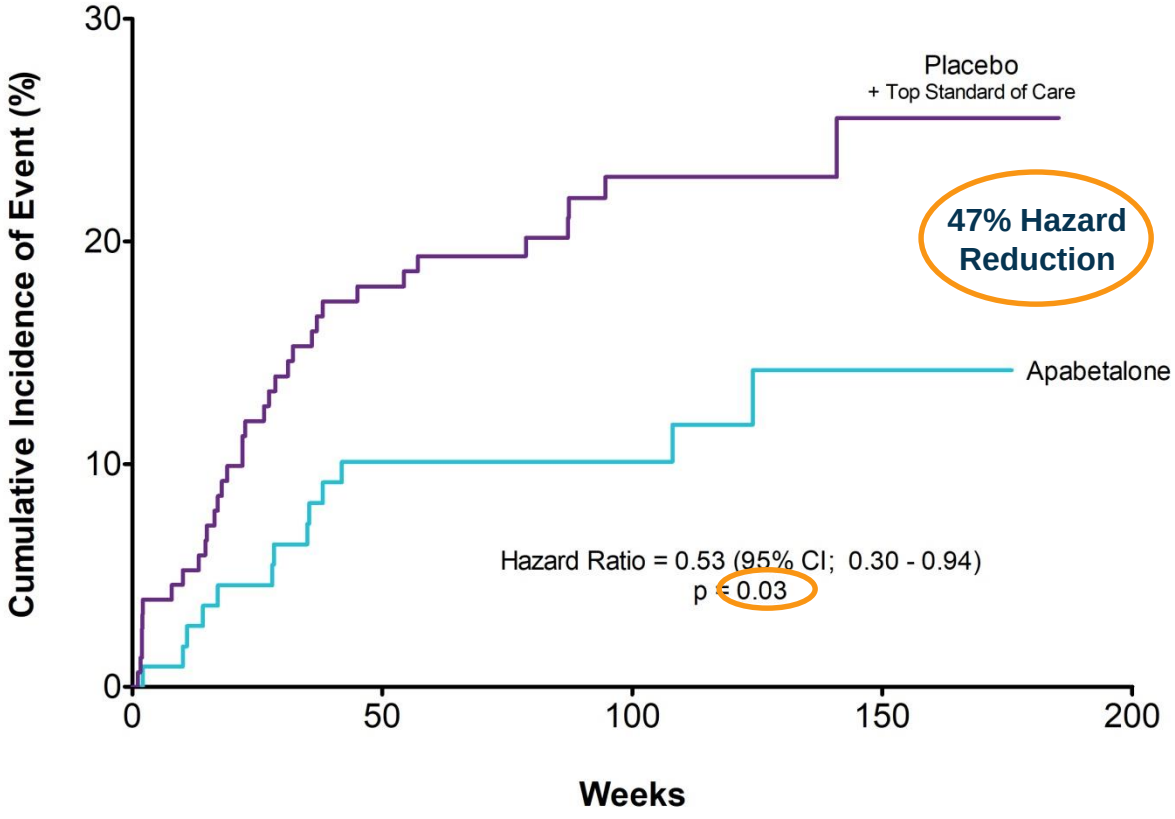


Source: RVX Internal Analysis – Non-QC'd

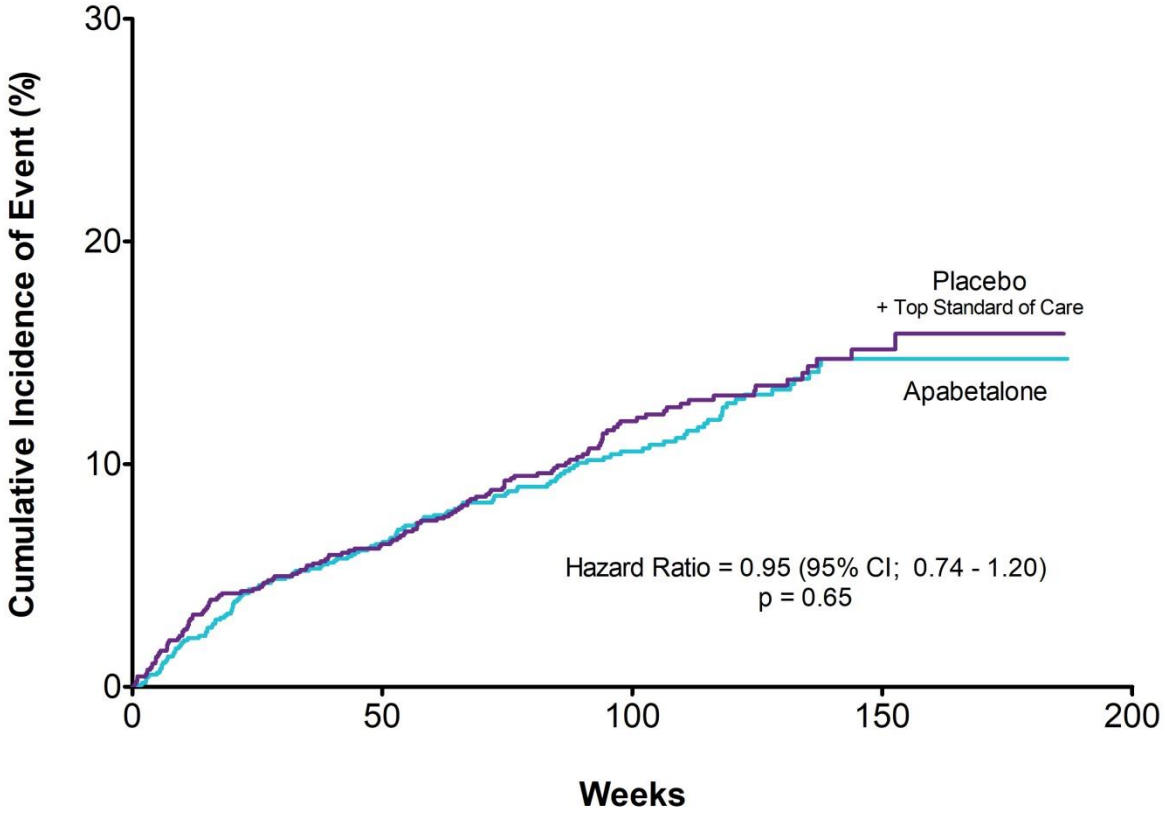
Renal Subgroup – Broadly Defined MACE

Broad MACE defined as CV death, non-fatal MI, stroke, and hospitalizations for CVD events

Patients with eGFR < 60 at Baseline



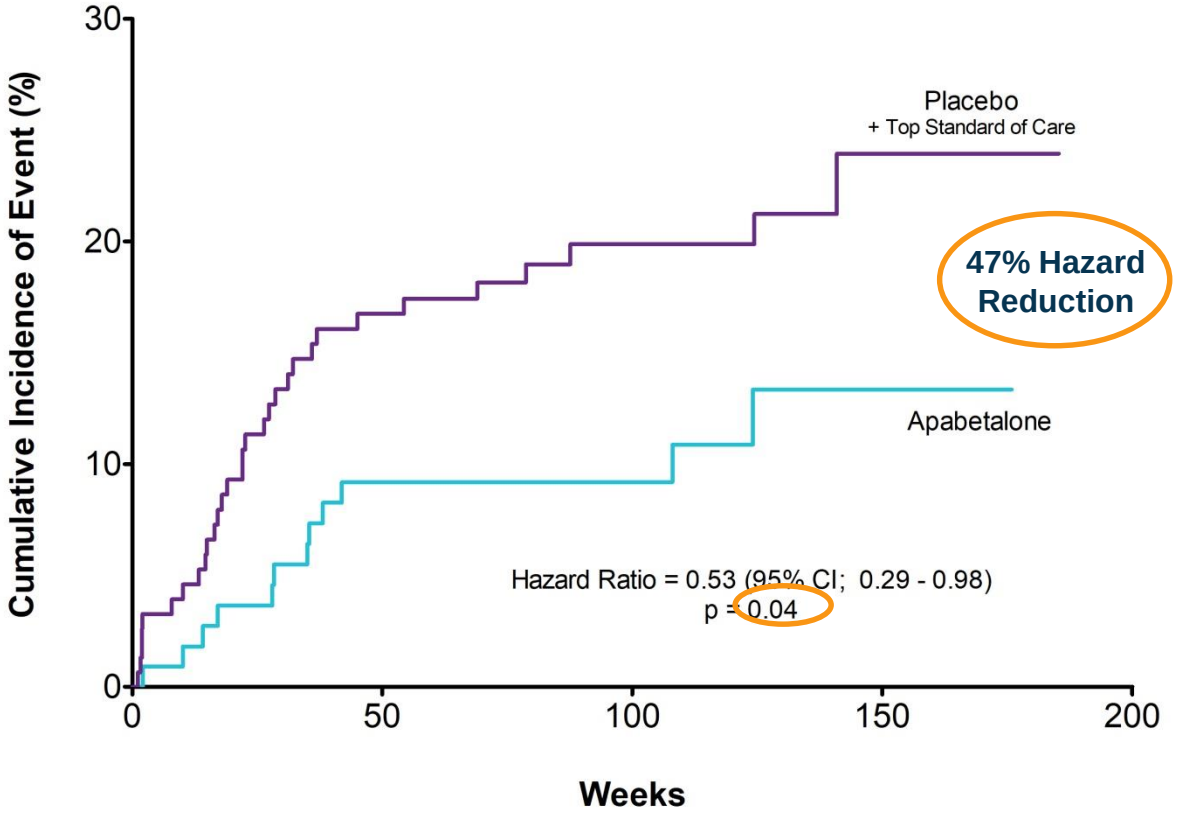
Patients with eGFR ≥ 60 at Baseline



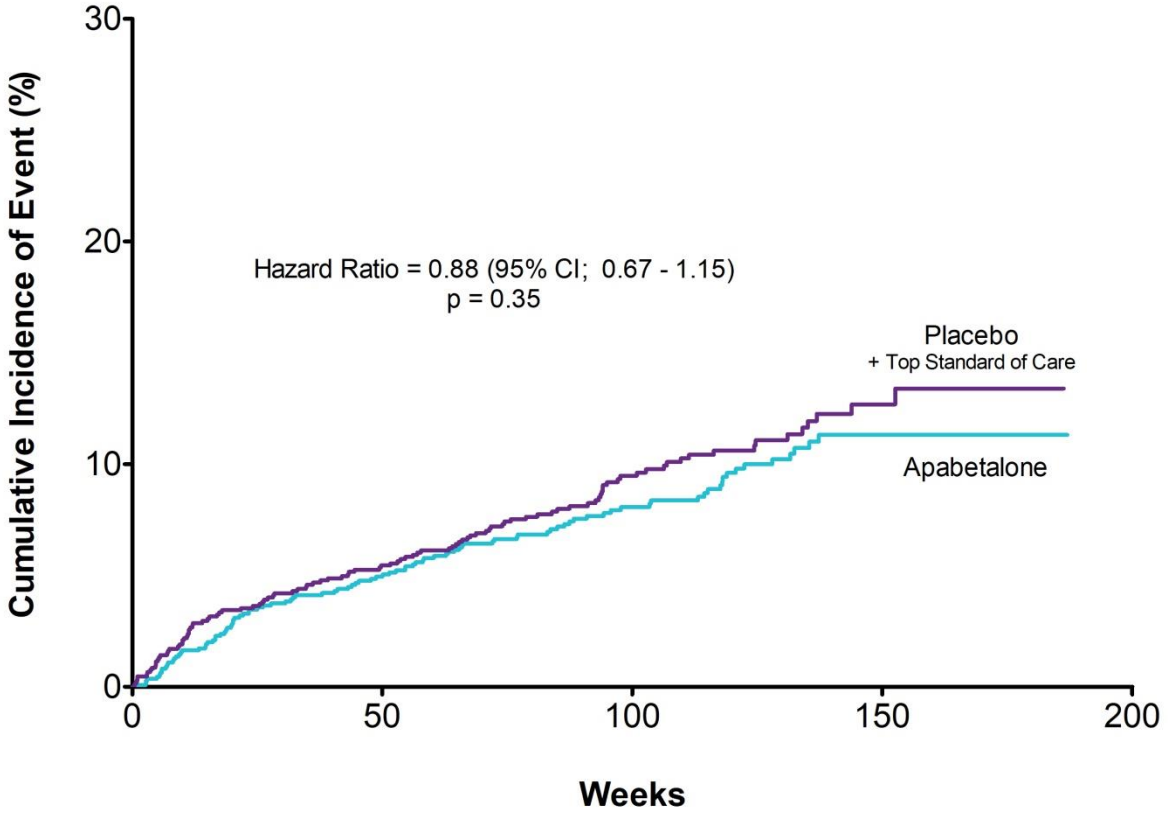
Source: RVX Internal Analysis – Non-QC'd

Renal Subgroup – CV Death or Non Fatal MI

Patients with eGFR < 60 at Baseline



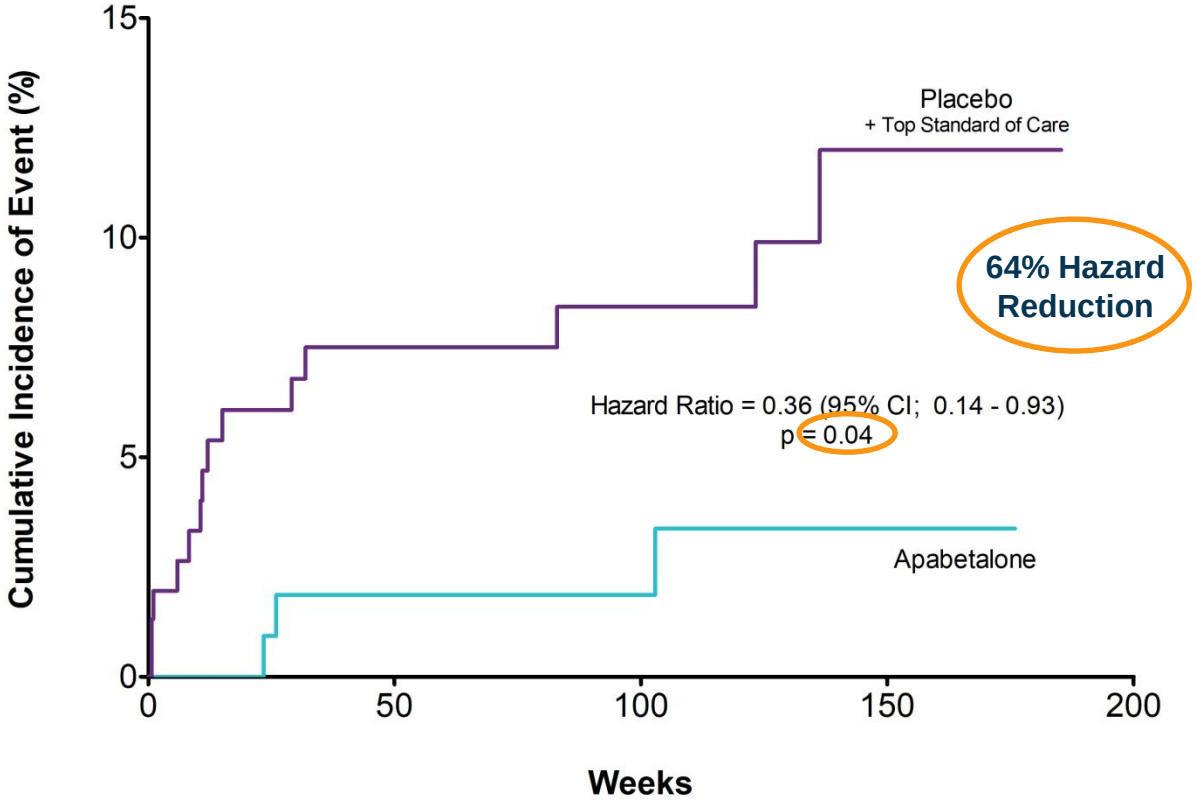
Patients with eGFR ≥ 60 at Baseline



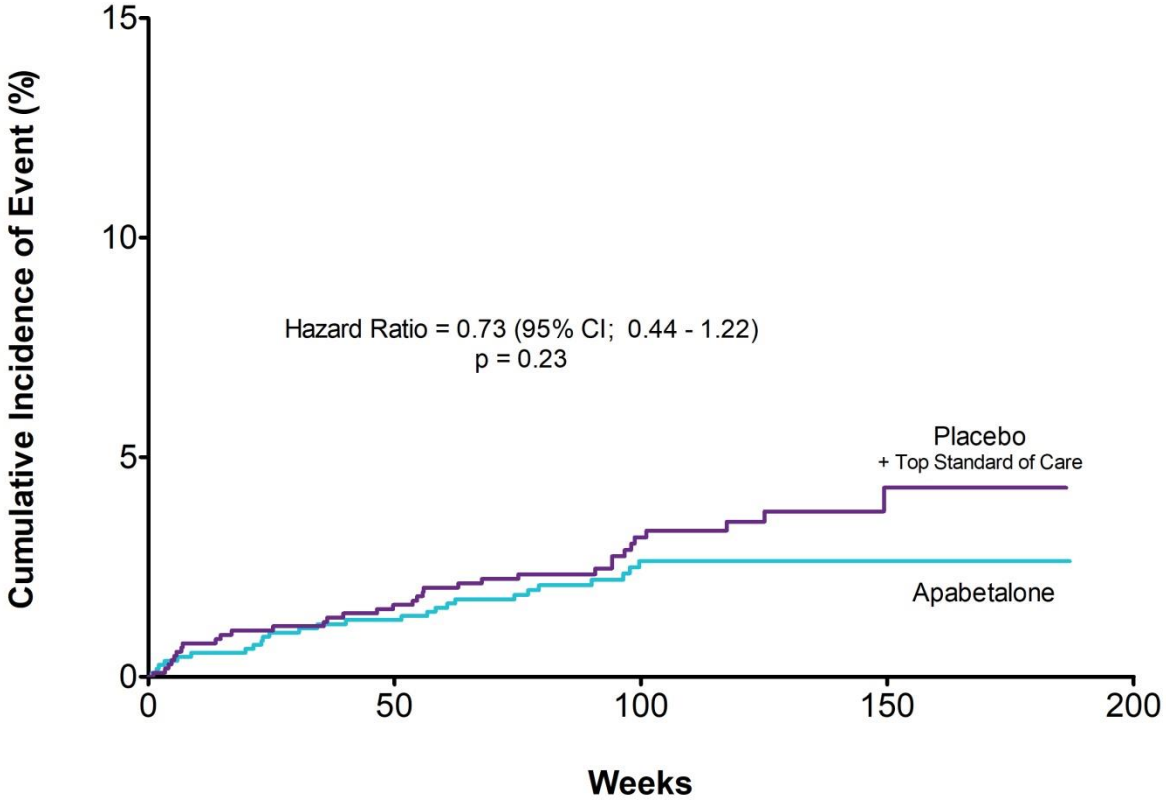
Source: RVX Internal Analysis – Non-QC'd

Renal Subgroup – Hospitalization for CHF

Patients with eGFR < 60 at Baseline



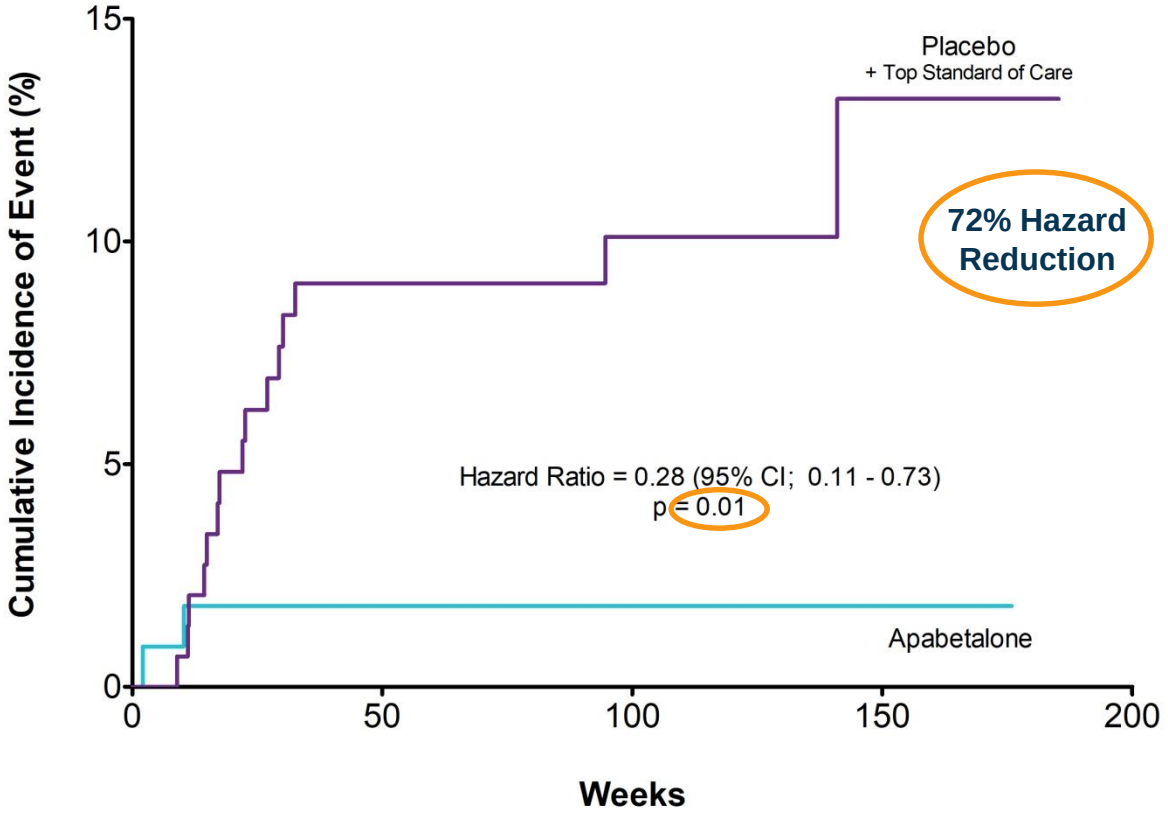
Patients with eGFR ≥ 60 at Baseline



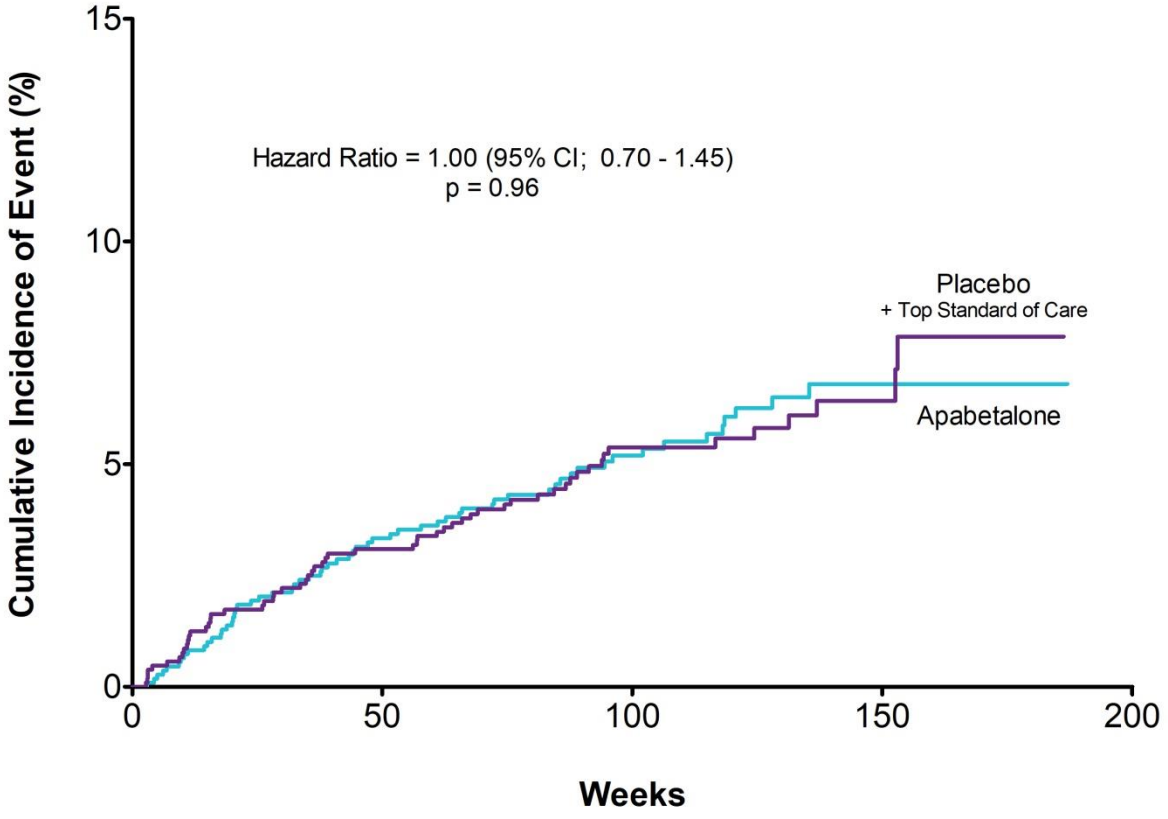
Source: RVX Internal Analysis – Non-QC'd

Renal Subgroup – Hospitalization for CVD Events

Patients with eGFR < 60 at Baseline



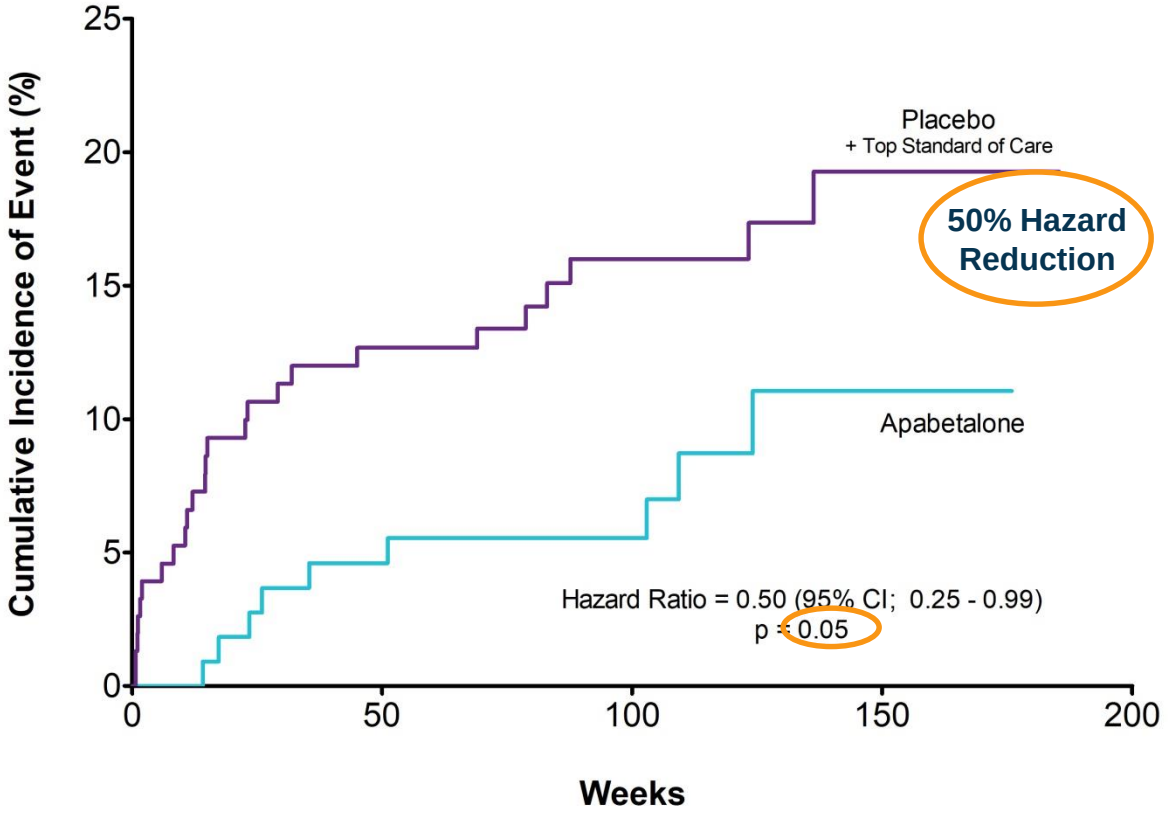
Patients with eGFR ≥ 60 at Baseline



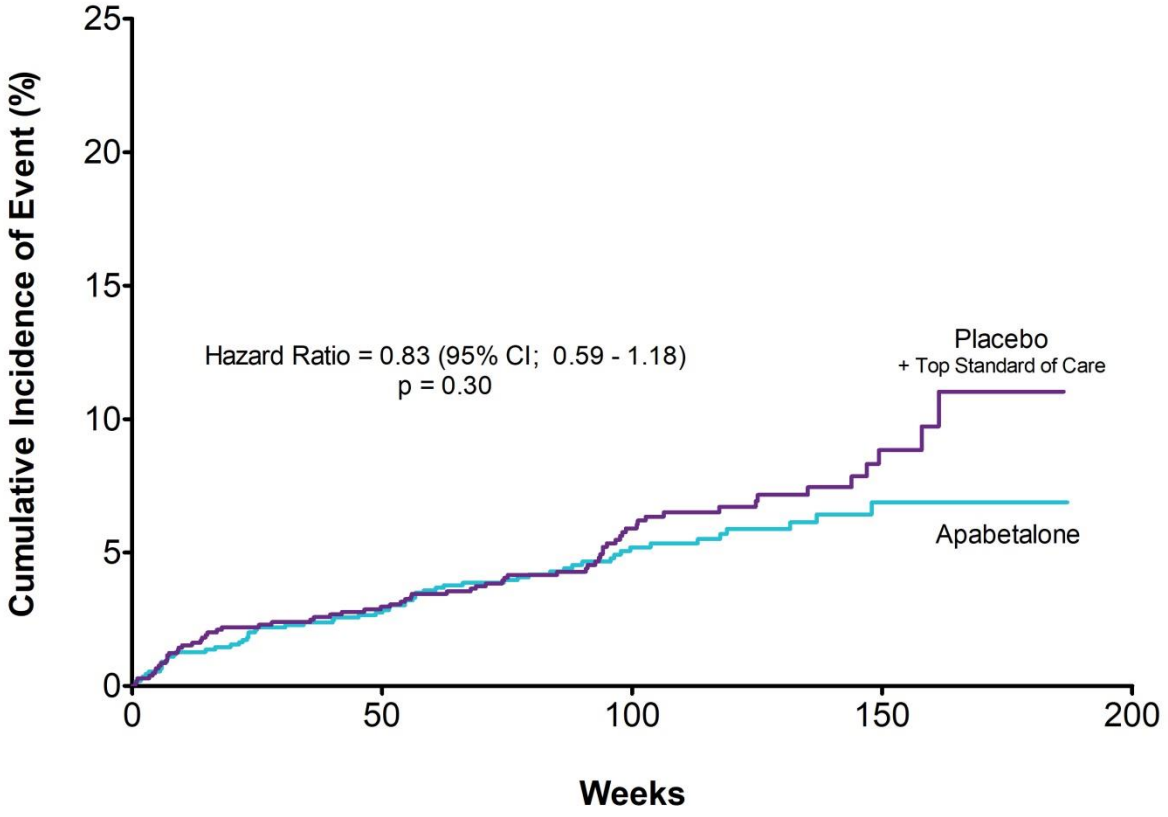
Source: RVX Internal Analysis – Non-QC'd

Renal Subgroup – Hospitalization for CHF or CV Death

Patients with eGFR < 60 at Baseline



Patients with eGFR ≥ 60 at Baseline



Source: RVX Internal Analysis – Non-QC'd

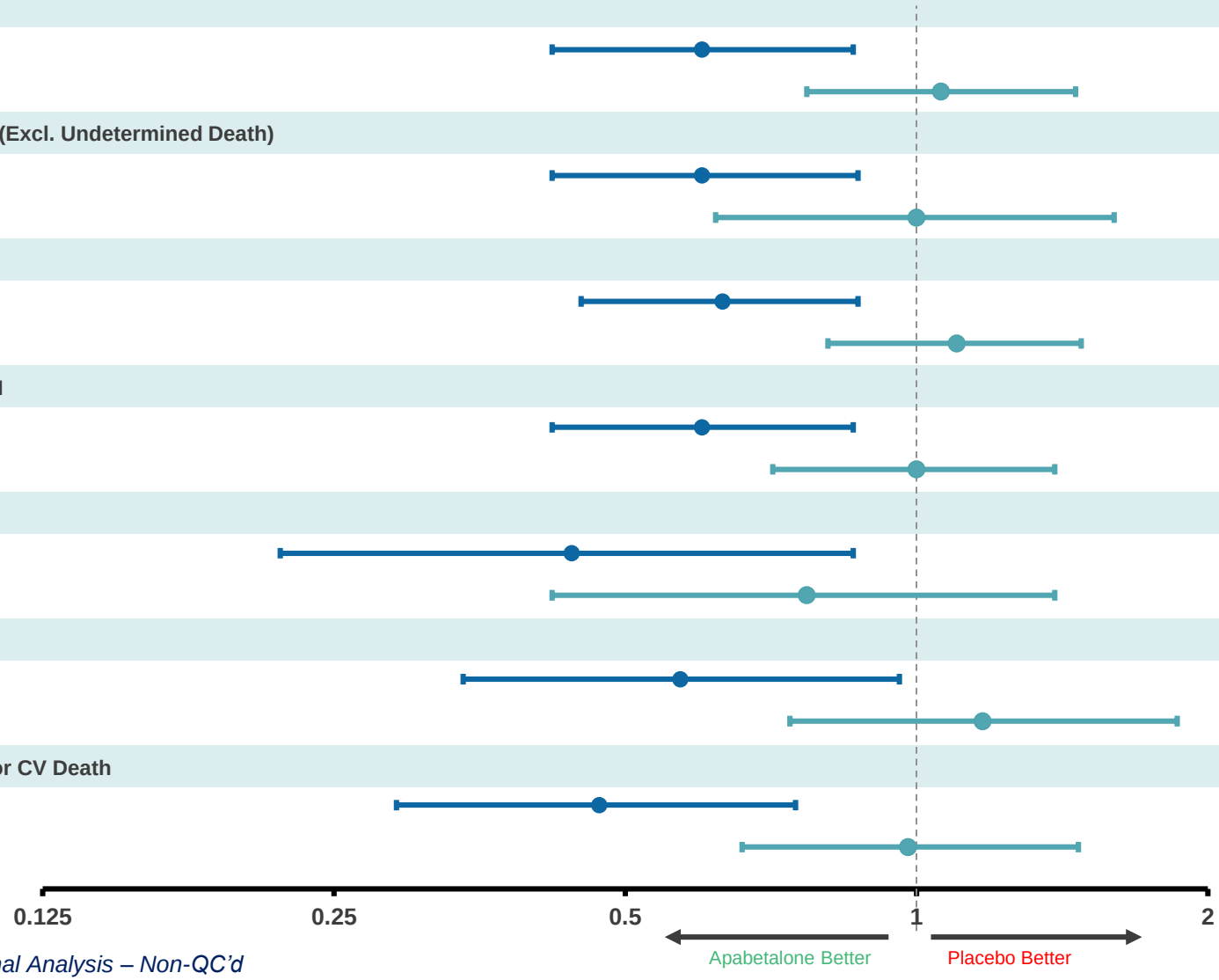
Apabetalone Significantly Reduced MACE Risk in Low LDL Subgroup

(Baseline LDL Below Median)

Apabetalone Reduced MACE Risk in Low LDL Subgroup

Baseline LDL Below Median

Endpoint	Hazard Ratio (95% CI)	P Value
Narrowly Defined MACE		
LDL < Median	0.60 [0.42, 0.86]	0.02
LDL ≥ Median	1.06 [0.77, 1.46]	
Narrowly Defined MACE (Excl. Undetermined Death)		
LDL < Median*	0.60 [0.42, 0.87]	0.01
LDL ≥ Median*	1.00 [0.62, 1.60]	
Broadly Defined MACE		
LDL < Median*	0.63 [0.45, 0.87]	0.01
LDL ≥ Median*	1.10 [0.81, 1.48]	
CV Death or Non Fatal MI		
LDL < Median*	0.60 [0.42, 0.86]	0.01
LDL ≥ Median*	1.00 [0.71, 1.39]	
Hospitalization for CHF		
LDL < Median*	0.44 [0.22, 0.86]	0.02
LDL ≥ Median*	0.77 [0.42, 1.39]	
All-cause Mortality		
LDL < Median*	0.57 [0.34, 0.96]	0.04
LDL ≥ Median*	1.17 [0.74, 1.86]	
Hospitalization for CHF or CV Death		
LDL < Median*	0.47 [0.29, 0.75]	0.002
LDL ≥ Median*	0.98 [0.66, 1.47]	



*Source: * RVX Internal Analysis – Non-QC'd*

Apabetalone Reduced MACE Risk in Low LDL Subgroup

Baseline LDL Below Median

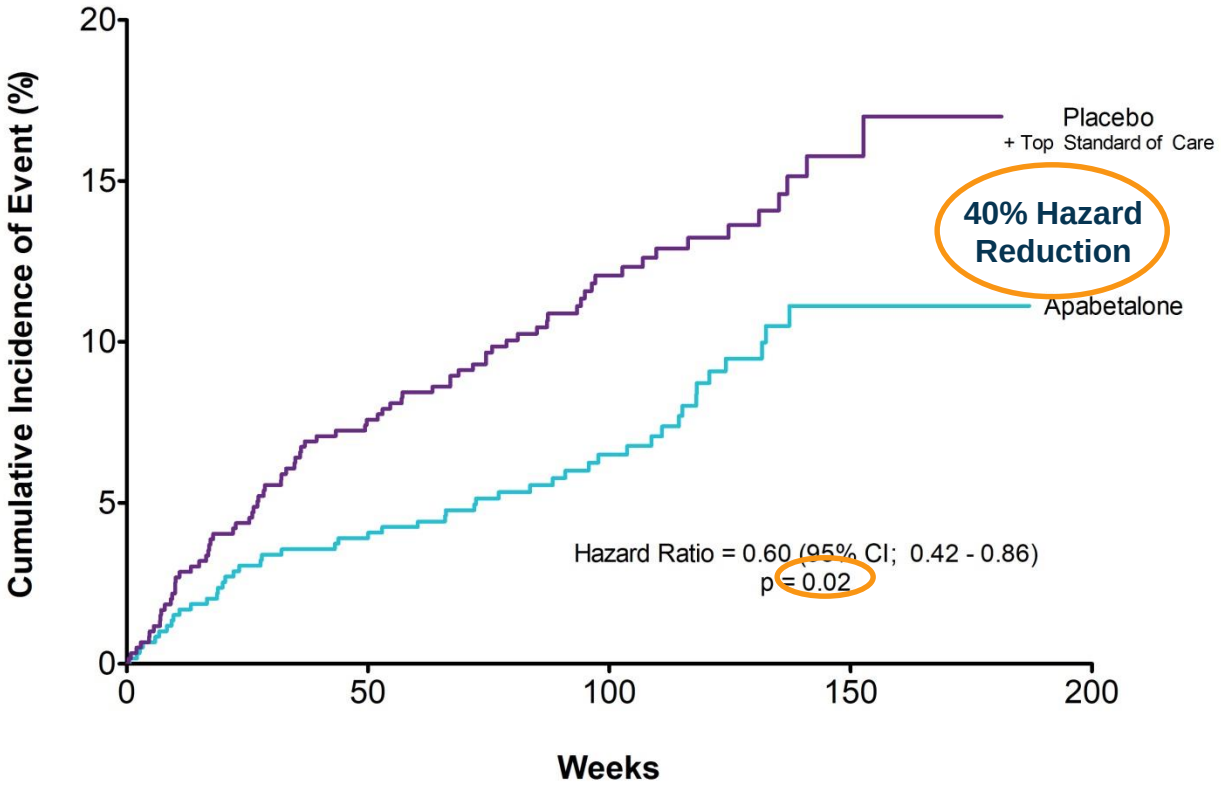
		Apabetalone		Placebo			
Endpoint	**Subgroup**	**No. of Patients**	**No. of Events**	**No. of Patients**	**No. of Events**	**Hazard Ratio**	**p-value**
Narrowly Defined MACE	LDL below median value for the study sample	594	48	597	78	0.60	0.02
Narrowly Defined MACE (excluding undertermined cause of death)			44		73	0.60	0.01
Broadly Defined MACE			54		86	0.63	0.01
CV Death or Non-Fatal MI			43		72	0.60	0.01
CHD Death or Non-Fatal MI			43		71	0.61	0.01
Non-Fatal MI			31		47	0.66	0.07
CV Death			12		31	0.42	0.004
Stroke			5		9	0.56	0.29
All Cause Mortality			21		36	0.57	0.04
Hospitalization for CHF			10		24	0.44	0.02
Hospitalization for CVD Events			28		39	0.72	0.19
Hospitalization for CHF or CV Death			21		47	0.47	0.002
Narrowly Defined MACE	LDL above median value for the study sample	618	77	606	71	1.06	0.76
Narrowly Defined MACE (excluding undertermined cause of death)			69		67	1.00	1.00
Broadly Defined MACE			90		80	1.10	0.55
CV Death or Non-Fatal MI			69		67	1.00	0.98
CHD Death or Non-Fatal MI			67		65	1.00	0.98
Non-Fatal MI			46		47	0.95	0.79
CV Death			33		24	1.32	0.29
Stroke			12		8	1.46	0.39
All Cause Mortality			40		33	1.17	0.49
Hospitalization for CHF			19		24	0.77	0.38
Hospitalization for CVD Events			35		34	1.00	1.00
Hospitalization for CHF or CV Death			48		47	0.98	0.93

Source: RVX Internal Analysis – Non-QC'd

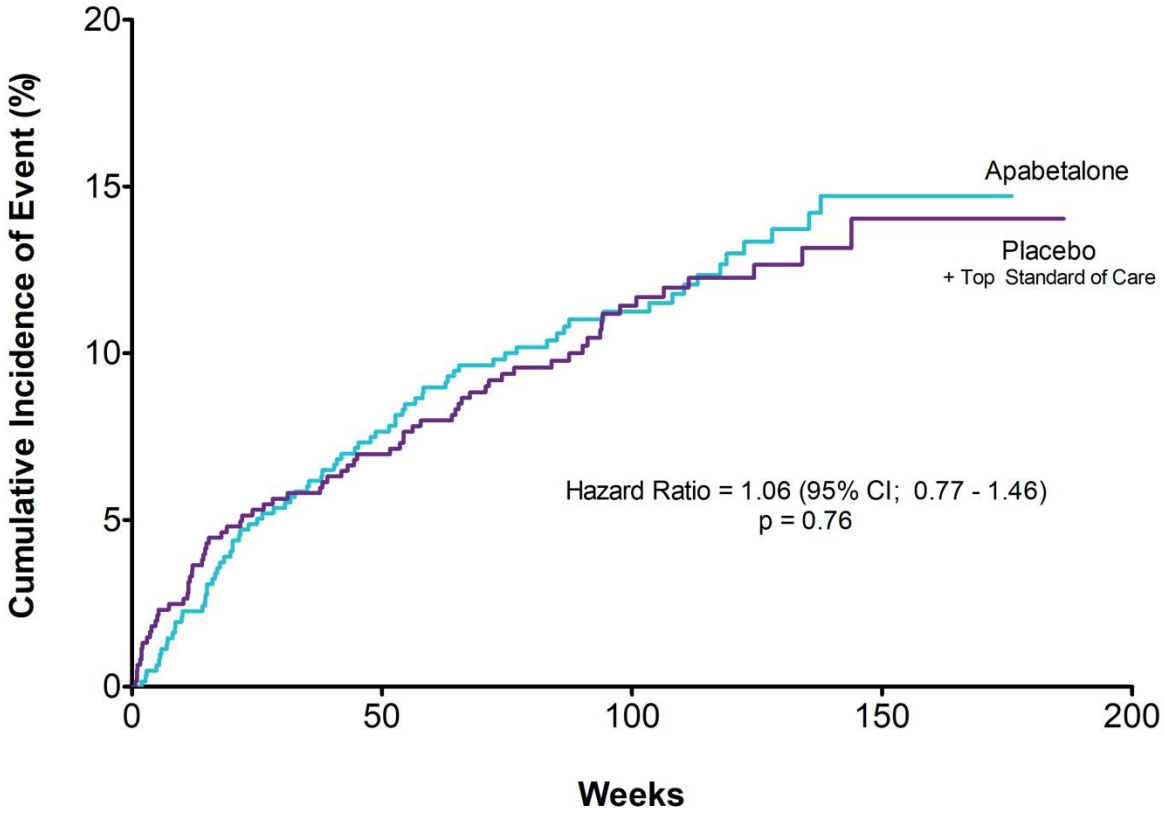
LDL Subgroup – Narrowly Defined MACE

MACE defined as CV death, non-fatal MI, and stroke

Patients with LDL < Median



Patients with LDL ≥ Median



Source: RVX Internal Analysis – Non-QC'd


Surprise Finding!
Potential Synergy with New Generation of Diabetes Drugs

Baseline Characteristics: Cardiovascular and Diabetes Medications

Cardiovascular and Diabetes Medications	Apabetalone (N=1212)	Placebo (N=1206)
Atorvastatin	621 (51.2)	620 (51.4)
Rosuvastatin	591 (48.8)	586 (48.6)
High intensity statin	1089 (89.9)	1092 (90.5)
ACE inhibitors/ angiotensin II blockers	1119 (92.3)	1110 (92.0)
Beta blockers	1103 (91.0)	1088 (90.2)
Antiplatelet agents	1196 (98.7)	1195 (99.1)
Dual antiplatelet agents	1057 (87.2)	1065 (88.3)
Metformin	1009 (83.3)	989 (82.0)
Insulin	445 (36.7)	464 (38.5)
Sulfonylureas	363 (30.0)	344 (28.5)
DPP4 inhibitors	181 (14.9)	178 (14.8)
SGLT2 inhibitors	150 (12.4)	148 (12.3)
GLP1 receptor agonists	41 (3.4)	45 (3.7)

Comparison to Other Major Therapeutic Classes

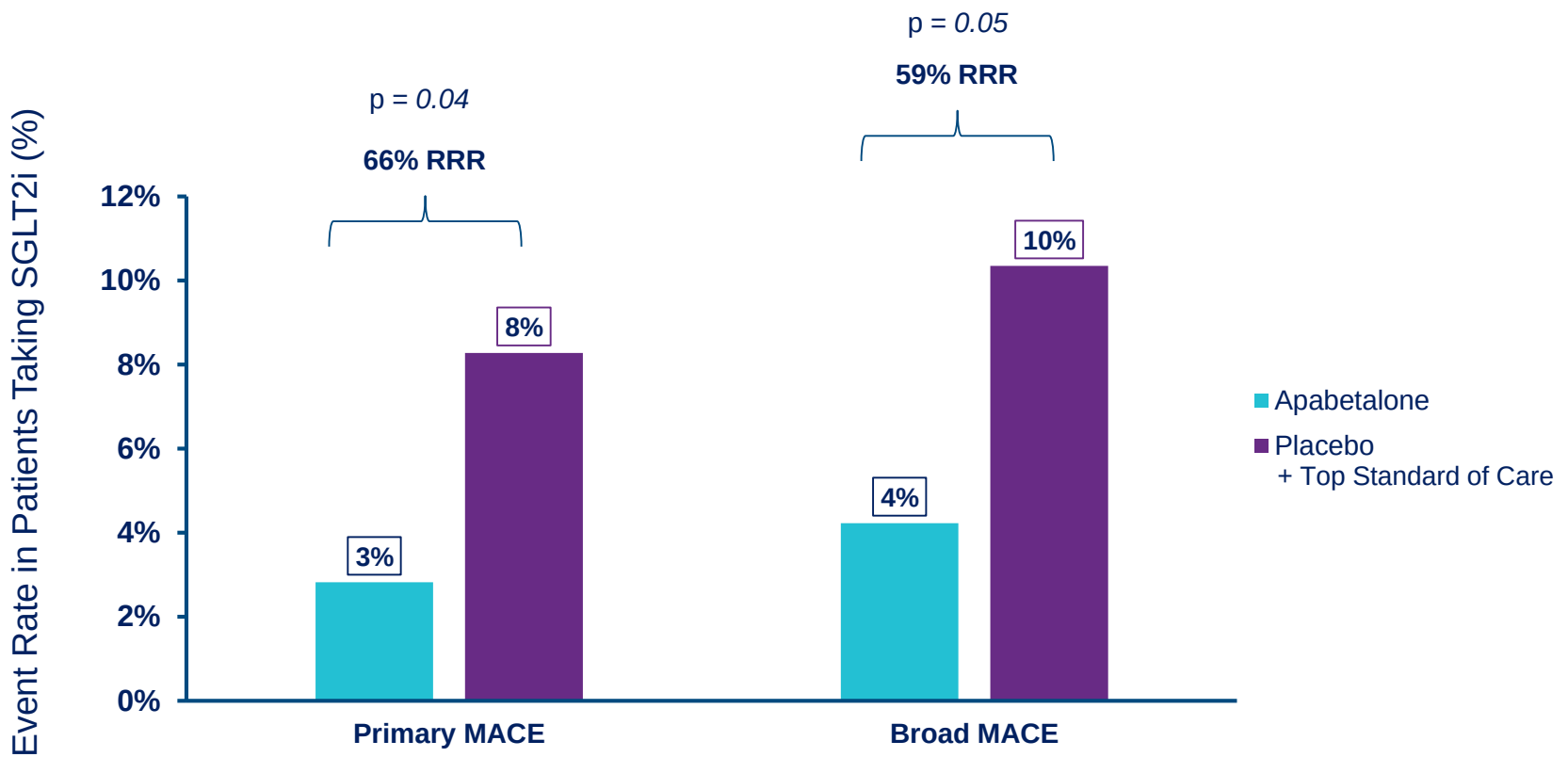
Impact on MACE in Patients with Type 2 Diabetes

Therapeutic	Trial Name	# Patients	Effect on MACE
Apabetalone	**BETonMACE**	**2,425**	**-18%***
Apabetalone + SGLT2i	**BETonMACE**	**298**	**-60%****
DDP-4 inhibitors[1,2]	CAROLINA	6,042	no effect
Insulin[3]	ORIGIN	12,537	no effect
SGLT2i[4]	CANVAS	10,142	-14%
PCSK9i[5]	ODYSSEY OUTCOMES	18,924	-15%
GLP-1 Receptor Agonists[6]	REWIND	9,091	-12% to -26%

*p-value = 0.11
**p-value = 0.05; patients receiving any SGLT2i during the study

1. Rosenstock, J et al. JAMA. (2019) Sep 19. doi: 10.1001/jama.2019.13772
2. Green, JB et al. N Engl J Med. (2015) 373:232–42. doi: 10.1056/NEJMoa1501352
3. ORIGIN trial Investigators, N. Engl. J. Med. (2012) 367, 319–328
4. Zelniker, TA et al. Lancet (2019) Jan 5;393(10166):31-39. doi: 10.1016/S0140-6736(18)32590-X.
5. Schwartz, GG et al. N Engl J Med (2018); 379:2097-2107 doi: 10.1056/NEJMoa1801174
6. Zelniker, TA et al. Circulation. (2019);139(17):2022-2031. doi: 10.1161/CIRCULATIONAHA.118.038868.

Apabetalone Reduces MACE Beyond Benefit of New Diabetes Drugs



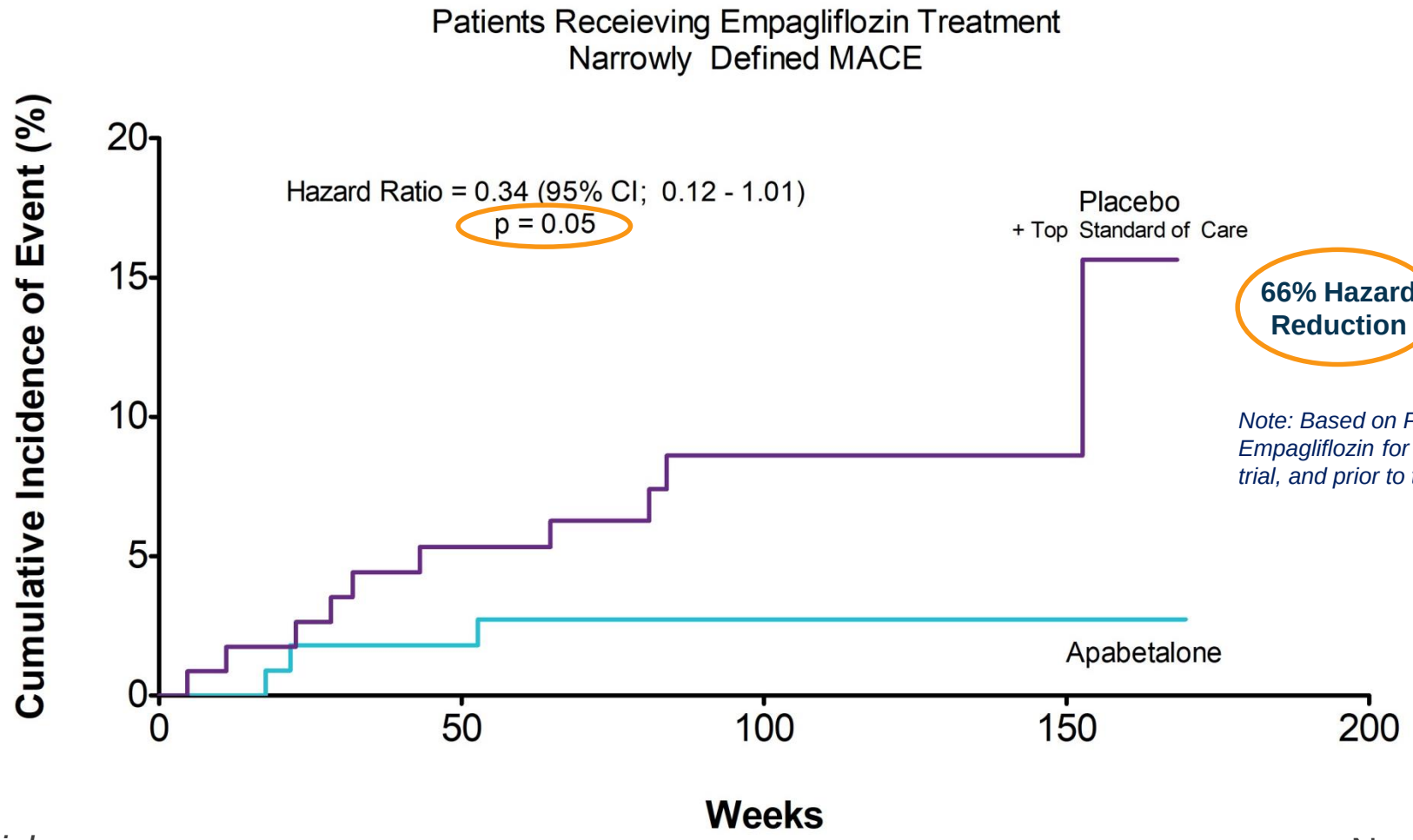
No. of Events	4	12	6	15
Patients Taking SGLT2i	142	145	142	145

Patent Filed,
Additional Patents
in Progress

Note: Based on Patients who were taking SGLT2 inhibitors for at least 30 days during the trial, and prior to their MACE

Source: RVX Internal Analysis – Non-QC'd

Apabetalone and Empagliflozin (Jardiance)



Note: Based on Patients who were taking Empagliflozin for at least 30 days during the trial, and prior to their MACE

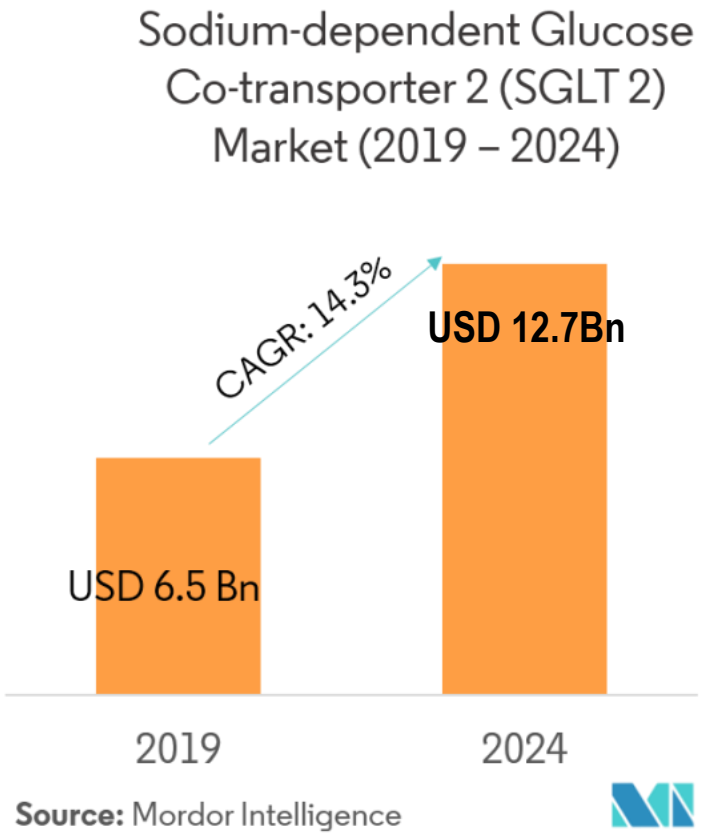
No. at Risk				
Apabetalone	113	108	67	13
Placebo	115	104	59	18

Narrowly Defined MACE:
- CV Death
- Non Fatal MI
- Stroke

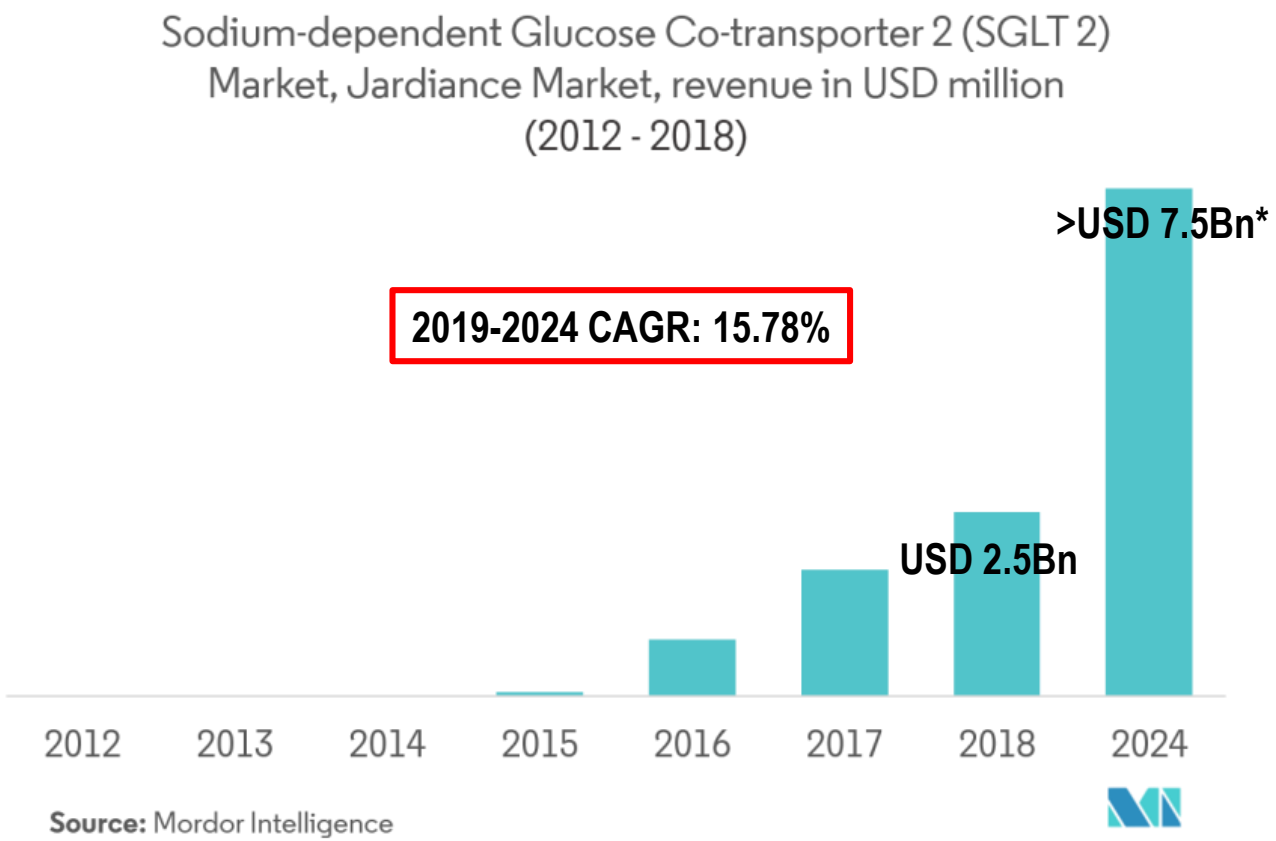
Source: RVX Internal Analysis – Non-QC'd

Market Growth of SGLT2 Inhibitors

Global Market Growth



Jardiance Market Growth



*Source: *RVX Internal Estimate*

New Findings Presented at CtAD Symposium – December 5th, 2019

Epigenetics and the BET-system in vascular dementia, Alzheimer's disease and mixed dementia – the problem and potential remedies

Chairman: Bengt Winblad, *Karolinska Institutet, Sweden*

- Dementias, who and how to treat and by what specialty. Addressing problem and current and potential future therapeutic practices
  - Charles DeCarli*, UC Davis, USA*
- Fluid biomarkers that predict and project brain health
  - Henrik Zetterberg*, University of Gothenburg, Sweden*
- The epigenetic inhibitor Apabetalone corrects pathophysiological brain endothelial and microglial cell activation that contributes to neurodegenerative disease
  - Ewelina Kulikowski*,, Resverlogix Corporation, Canada*
- Epigenetics, the BET-system, Alzheimer's Disease and Vascular Cognitive Impairment; The BETonMACE study and effects of apabetalone 100 mg b.i.d. two years treatment on cognition in diabetes patients with established cardiovascular disease
  - Jeffrey Cummings, *Cleveland Clinic Lou Ruvo Center for Brain Health, USA*

Summary

- The first approach at confirming a Primary endpoint was narrowly missed **with consistent positive trend in key secondary endpoints**
  - Clinically relevant MACE reductions
  - Lower than anticipated placebo event rate (5.8/100 pt yrs) due to new drugs entering today's market
  - Apabetalone further decreases MACE risk on top of best available standard of care

Strengthening Opportunities Through Positive Findings & Synergy

Narrow MACE (with CHF)
24% Hazard Reduction
(95% CI; 0.60-0.95)
p=0.02

Renal Subgroup
eGFR < 60 at Baseline
50% Hazard Reduction
(95% CI; 0.26-0.96)
p=0.03

Apabetalone & SGLT2i (Empagliflozin)
66% Hazard Reduction
(95% CI; 0.12-1.01)
p=0.05

Source: RVX Internal Analysis – Non-QC'd

Near Term Commercialization Steps

In the near term we will continue our five point approach to progressing our corporate commercial value. This approach involves aggressive exploratory development of the following:

- Breakthrough Therapy status filings, both FDA and EMA, over the next 90-120 days
- SGLT2i partnering discussions, one has already been initiated, key patent already filed
- Renal partnering discussions ASAP
- Congestive Heart Failure partnering discussions ASAP, already initiated
- Orphan partnering discussions initially focused on PAH and HIV only at this time. PAH enrollment has already commenced. HIV funding being derived from a yet to be named US based organization

RESVERLOGIX

TSX: RVX

Detailed Preliminary Results of BETonMACE

Strengthening Opportunities Through Positive Findings & Synergy

November 18th, 2019


Appendix

Study Design

BETonMACE Study Parameters

Primary Objective

- To evaluate if treatment with apabetalone as compared to placebo increases time to the first occurrence of triple MACE. Triple MACE is defined as a single composite endpoint of CV death or non fatal MI or stroke.

Key Inclusion Criteria

- Type 2 Diabetes Mellitus
  - HbA1c >6.5% or history of diabetes medications
- Acute coronary syndrome 7-90 days prior to the screening visit
  - Unstable angina (Limited to 25% of total participants) or acute myocardial infarction
- Low HDL cholesterol
  - <40 mg/dL (1.04 mmol/L) for males; <45 mg/dL (1.17 mmol/L) for females at the screening visit

Primary Endpoint

- Time to first occurrence of adjudication-confirmed triple MACE

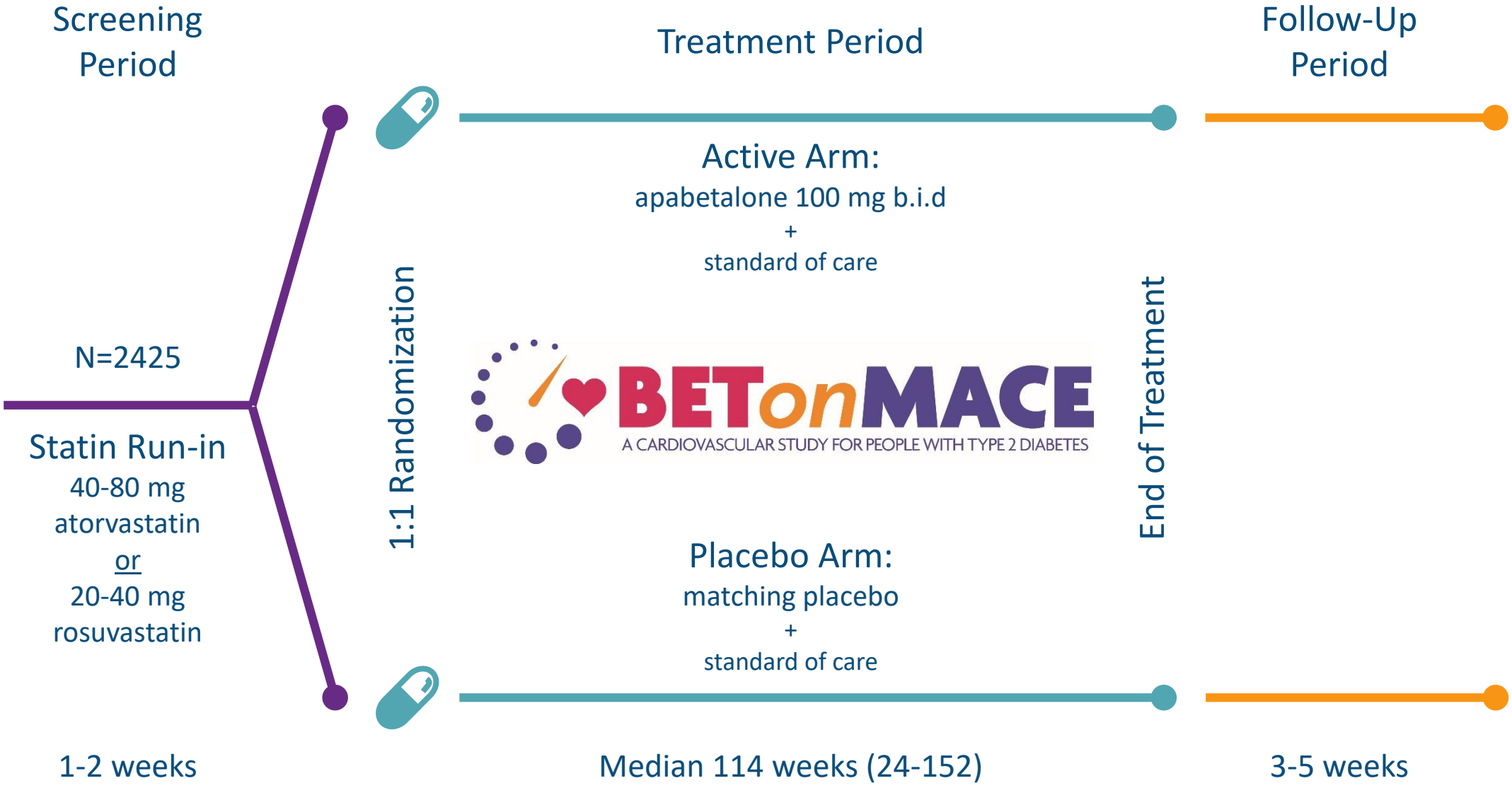
Key Secondary and Exploratory Endpoints

- Change in kidney function in chronic kidney disease sub-population
  - Baseline estimated glomerular filtration rate (eGFR) <60 mL/min/1.7m^2
- Change in Montreal Cognitive Assessment (MoCA)
  - Evaluated in at-risk sub-population (>70 years old at randomization)

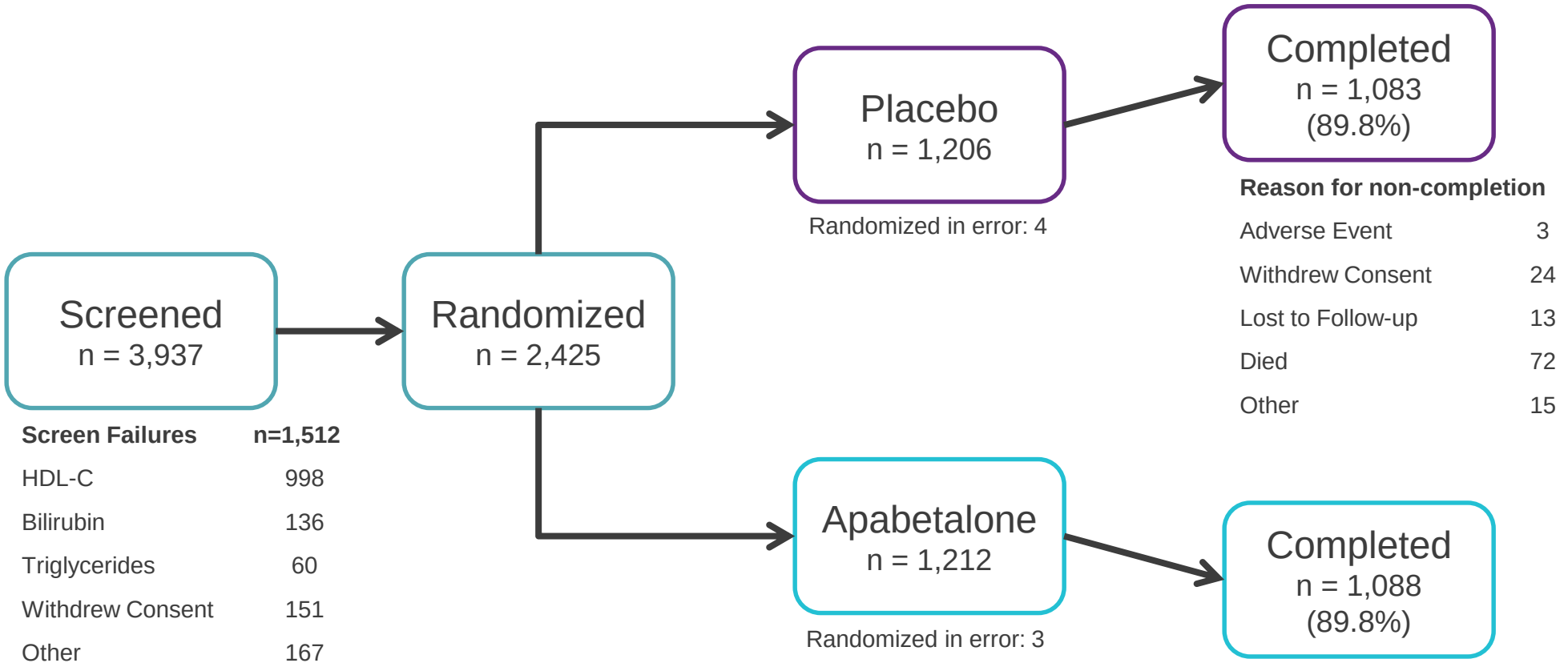
BETonMACE a Global, Multi-centered Clinical Trial

With 14 approved countries around the world,
BETonMACE included patients randomized at 220 different sites

BETonMACE Study Design



BETonMACE: Patient Disposition



Screen Failures	n=1,512
HDL-C	998
Bilirubin	136
Triglycerides	60
Withdrew Consent	151
Other	167

Reason for non-completion	
Adverse Event	3
Withdrew Consent	24
Lost to Follow-up	13
Died	72
Other	15

Reason for non-completion	
Adverse Event	2
Withdrew Consent	31
Lost to Follow-up	7
Died	61
Other	26

Baseline Characteristics

Baseline Characteristics, Prior Medical and Index ACS History

	Apabetalone (n=1212)	Placebo (n=1206)
Median age, yrs	62.0	62.0
Male sex- %	74.8	74.0
Body mass index, kg/m^2	30.2	30.3
Hypertension - %	89.4	87.8
eGFR Mean ± SD, mL/min/1.73m^2	104.9	101.7
Duration of diabetes – yrs	8.4	8.7
Index acute coronary syndrome – %		
Myocardial infarction	73.0	74.0
STEMI	38.4	38.6
NSTEMI	34.1	35.1
Unstable angina	26.7	25.0
PCI for index acute coronary syndrome	79.8	79.2
Time from index ACS to randomization – days	38	38

Baseline Characteristics: Cardiovascular and Diabetes Medications

Cardiovascular and Diabetes Medications (%)	Apabetalone (N=1212)	Placebo (N=1206)
Atorvastatin	51.2	51.4
Rosuvastatin	48.8	48.6
High intensity statin	89.9	90.5
ACE inhibitors/ angiotensin II blockers	92.3	92.0
Beta blockers	91.0	90.2
Antiplatelet agents	98.7	99.1
Dual antiplatelet agents	87.2	88.3
Metformin	83.3	82.0
Insulin	36.7	38.5
Sulfonylureas	30.0	28.5
DPP4 inhibitors	14.9	14.8
SGLT2 inhibitors	12.4	12.3
GLP1 receptor agonists	3.4	3.7

BETonMACE: Baseline Laboratory Parameters

Baseline Laboratory Parameters	Apabetalone (n=1212)	Placebo (n=1206)
Serum glucose, mg/dL	152.2 ± 60.7	150.7 ± 62.5
eGFR, ml/min/1.73m^2 †	104.9 ± 39.3	101.7 ± 38.6
Total cholesterol, mg/dL	134.8 ± 35.3	136.8 ± 38.2
LDL cholesterol, mg/dL	69.7 ± 29.8	70.9 ± 32.4
HDL cholesterol, mg/dL	33.3 ± 5.1	33.3 ± 5.1
Triglycerides, mg/dl	144.4 (110.7-194.9)	149.7 (116.0-201.9)
Alkaline phosphatase, U/L	83.3 ± 38.2	81.9 ± 34.8
Alanine aminotransferase, units/L	25.3 ± 14.3	25.4 ± 14.7
Total bilirubin, µmol/L	9.8 ± 4.2	9.9 ± 4.2
High sensitivity C-reactive protein §	2.9 (1.3-5.9)	2.7 (1.1-6.1)

† Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft Gault method, based on age and weight at baseline.
§ High-sensitivity C-Reactive Protein was assessed in only a subset of patients. Triglycerides expressed as median and IQR

Biochemical Parameters at 100 weeks and changes from baseline

Biochemical parameters	Apabetalone (N=1212)	Placebo (N=1206)	P value
HDL cholesterol, mg/dL	38.1 (+16.4%)	36.4 (+10.4%)	0.001
LDL cholesterol, mg/dL	69.6 (+11.5%)	72 (+14.9%)	0.35
eGFR, ml/min/1.73m^2	104.3 (-0.4)	105.2 (+2.1)	0.03
Alkaline phosphatase, U/L	77.6 (-4.8)	84.2 (+2.2)	0.003
Hemoglobin A1c, %	7.76 (+0.12)	7.76 (+0.04)	0.39
Serum glucose, mg/dL	161.1 (+9.2)	160.5 (+10.5)	0.74
hCRP §	2.2 (-17.1%)	2.3 (-16.2%)	0.74

§-only at centers in Hungary and Argentina

RESVERLOGIX

Safety Results

Top Line Data: Safety

Variable	Apabetalone (N=1212)	Placebo (N= 1207)
Adverse events - n (%)		
Patients with at least one adverse event	830 (68.5)	820 (67.9)
Adverse event leading to discontinuation	114 (9.4)	69 (5.7)
Serious adverse events – n (%)		
Patients with at least one SAE	354 (29.2)	339 (28.1)
Death	61 (5.0)	72 (6.0)
Cardiovascular deaths	34 (2.8)	42 (3.5)
Laboratory results – n (%)		
Liver Function ALT >3x ULN	78 (6.4)	18 (1.5)
ALT >5x ULN	40 (3.3)	9 (0.7)
Bilirubin >2x ULN	7 (0.6)	9 (0.7)
Hy's law	0	0
Discontinuation due to LFT elevation – n (%)	35 (2.9)	11 (0.9)

- **Well tolerated with similar AE's and SAE's to placebo**
- **Rate raised LFT's >5xULN low and only 2.6 % greater than placebo**
- **No Hy's law cases reported by DSMB**

Top Line Data: Safety

Adverse Events, System Organ Classes with at least one AE > 2% incidence either group*

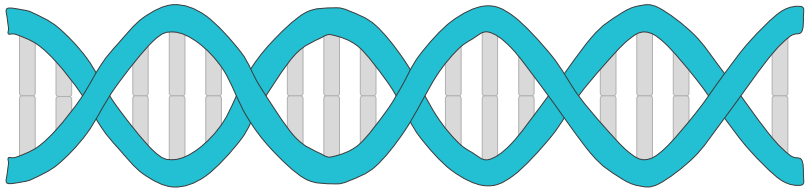
System Organ Class, Adverse Event	Apabetalone (N=1212)	Placebo (N= 1207)
Infections and Infestations	291 (20.6)	296 (19.3)
Nasopharyngitis	46 (3.8)	56 (4.6)
Urinary tract infection	58 (4.8)	40 (3.3)
Influenza	43 (3.5)	47 (3.9)
Bronchitis	25 (2.1)	32 (2.7)
Pneumonia	27 (2.2)	26 (2.2)
URTI	29 (2.4)	24 (2.0)
Cardiac Disorders	260 (19.1)	278 (21.2)
Angina	74 (6.1)	76 (6.3)
Angina unstable	58 (4.8)	41 (3.4)
Acute myocardial infarction	42 (3.5)	50 (4.1)
Cardiac failure	22 (1.8)	38 (3.1)
Gastrointestinal Disorders	186 (15.3)	170 (14.1)
Diarrhea	43 (3.5)	44 (3.6)
Abdominal pain	12 (1.0)	24 (2.0)
Nausea	26 (2.1)	7 (0.6)
Musculoskeletal	143 (11.8)	183 (15.2)
Myalgia	37 (3.1)	33 (3.7)
Back pain	17 (1.4)	28 (2.3)
Pain in extremity	15 (1.2)	26 (2.2)
Arthralgia	11 (0.9)	24 (2.0)
Metabolism and nutrition disorders	148 (12.2)	170 (14.1)
Diabetes mellitus	93 (7.7)	93 (7.7)
Vascular Disorders	135 (11.1)	142 (11.8)
Hypertension	72 (5.9)	72 (6.0)
Investigations	160 (13.2)	86 (7.1)
ALT increase	64 (5.3)	18 (1.5)
General Disorders	111 (9.2)	109 (9.0)
Non-cardiac chest pain	33 (2.7)	39 (3.2)
Blood and Lymphatic System Disorders	52 (4.3)	52 (4.3)
Anemia	36 (3.0)	40 (3.3)

Background Slides

BETonMACE: Background & Rationale

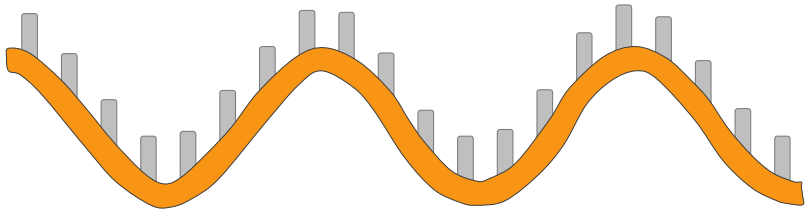
Apabetalone Mechanism of Action

DNA



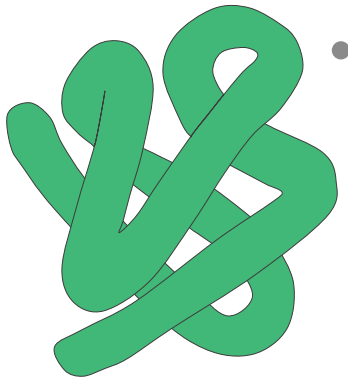
Transcription

RNA



Translation

Protein



Genome Editing

Altering the sequence of DNA itself and then reintroducing **modified genes** into the body

*There are currently **no FDA-approved** therapies based on gene editing*

Transcriptional Regulation

Adjusting the levels of **multiple** disease proteins by modulating their expression at the gene level

***Apabetalone**, acting upstream of traditional pharmaceuticals, represents a **paradigm shift** in the treatment of chronic disease*

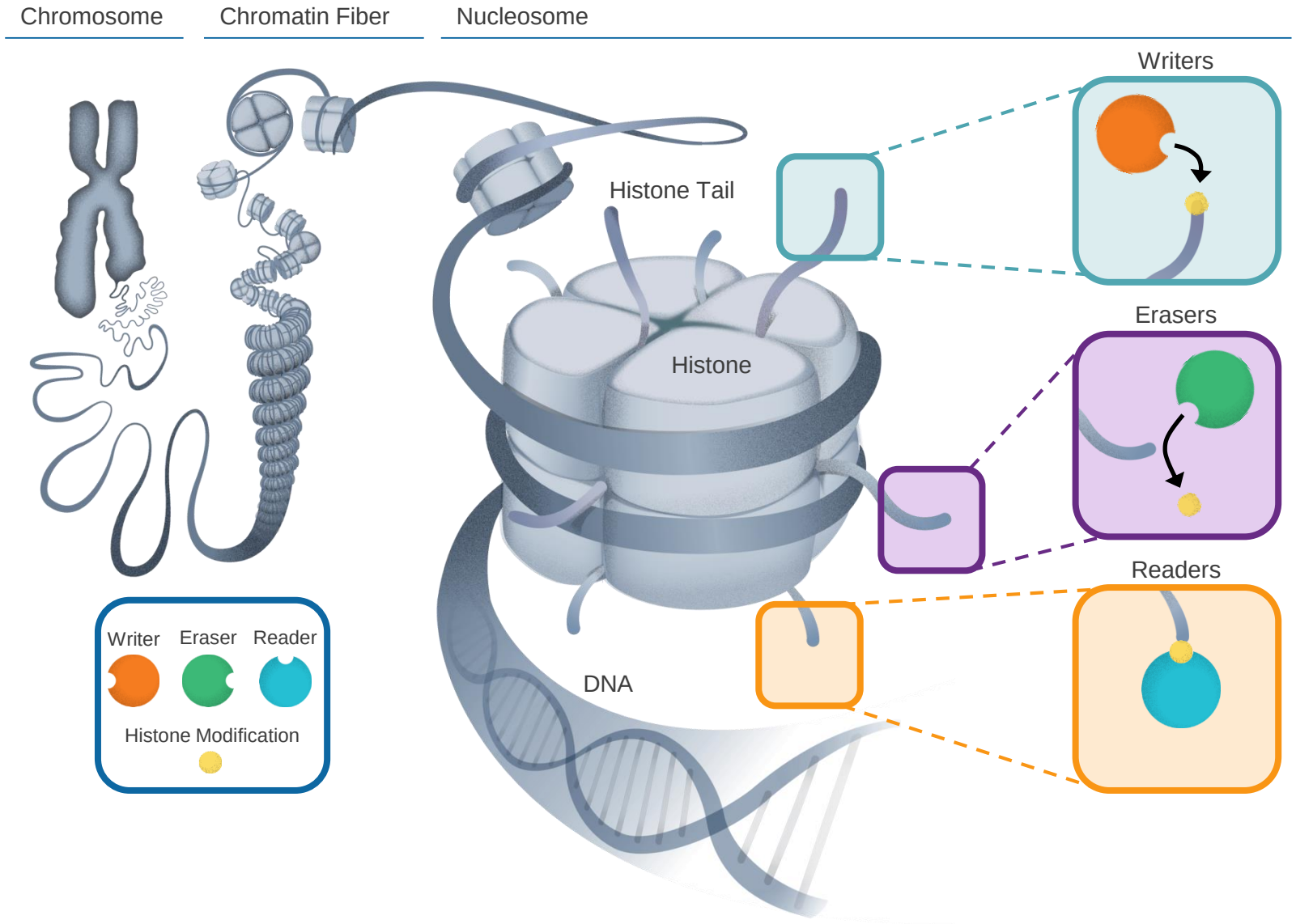
Protein Inhibition

Reducing or blocking the activity of **one** disease protein by using an inhibitor or antibody

Almost all **current therapeutics** function via protein inhibition

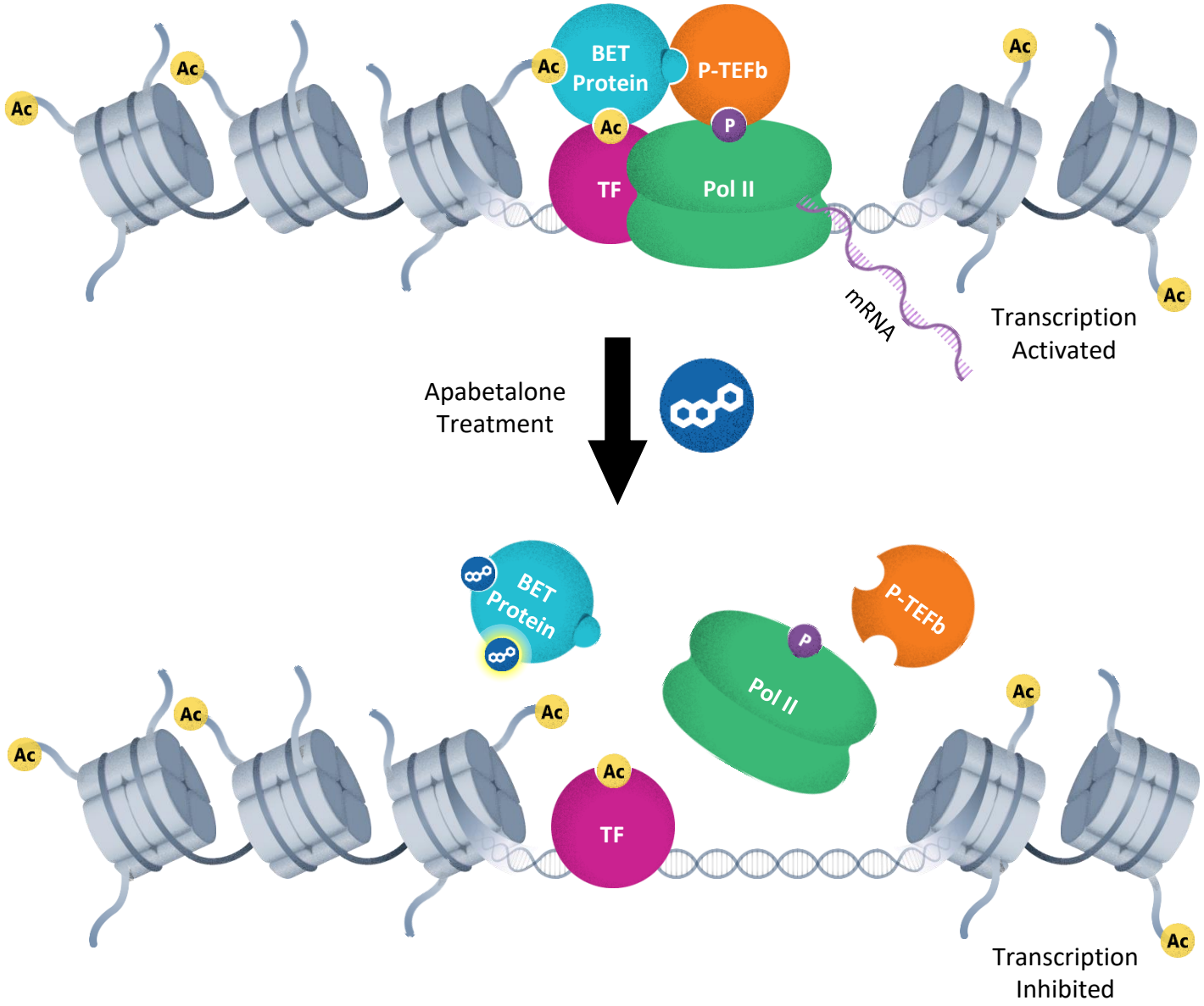
BETonMACE: Background & Rationale

Epigenetics Regulate Gene Activity



- Epigenetics refers to **modifications** to chromatin that regulate it's activity
- Transcription is regulated by **addition, removal, or recognition** of these modification
- **Acetylation** is associated with **active transcription** regions of chromatin
- **Bromodomain and Extraterminal Domain (BET)** proteins bind to acetylated histones and recruit additional transcription factors to drive gene expression

Apabetalone Mechanism of Action



BETi Impacts the Pathways that Drive CV and Kidney Disease

Apabetalone reduces the expression of multiple components of the complement cascade

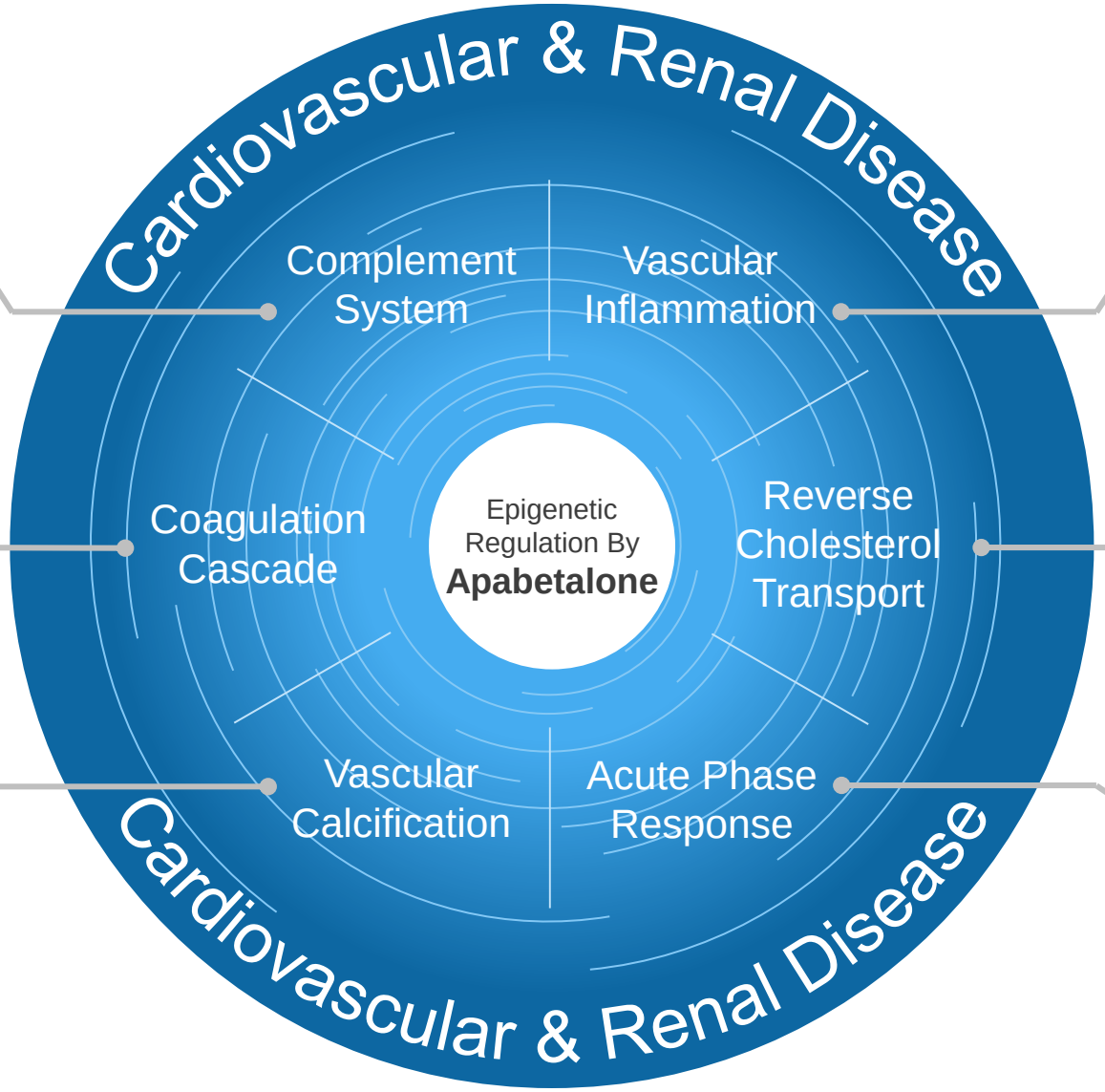
Wasiak et al. 2017

Apabetalone reduces the expression of several factors within the coagulation system

Wasiak et al. 2017

Levels of alkaline phosphatase and other drivers of vascular calcification are lowered by apabetalone

Gilham et al. 2019



Treatment with apabetalone reduces mediators that drive endothelial activation, monocyte recruitment and plaque destabilization

Tsujikawa et al. 2019

Apabetalone contributes to remodeling of the HDL proteome and lipidome, including increased ApoA-1 and HDL particle size

Jahagirdar et al. 2014

Apabetalone reduces markers of systemic inflammation including acute phase reactants

Wasiak et al. 2019 (Under Review)

Addressing Critical Unmet Needs

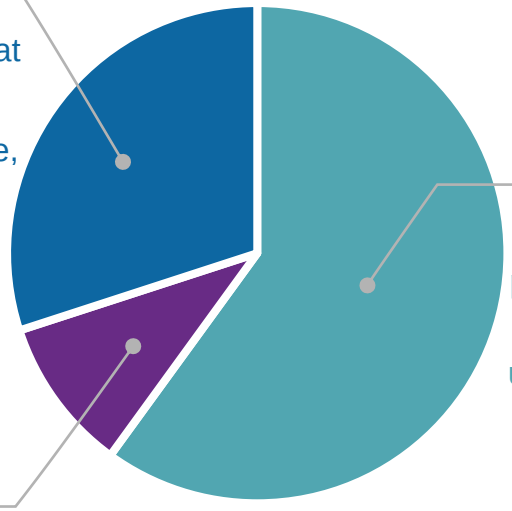
Cardiovascular Disease

Still the number one killer of both males and females and costs the US healthcare system over $500B per year

Current CVD Therapies - 30%

Statins are the top medication used to treat CVD

Despite maximized use, current therapies only manage about 30% of CVD events



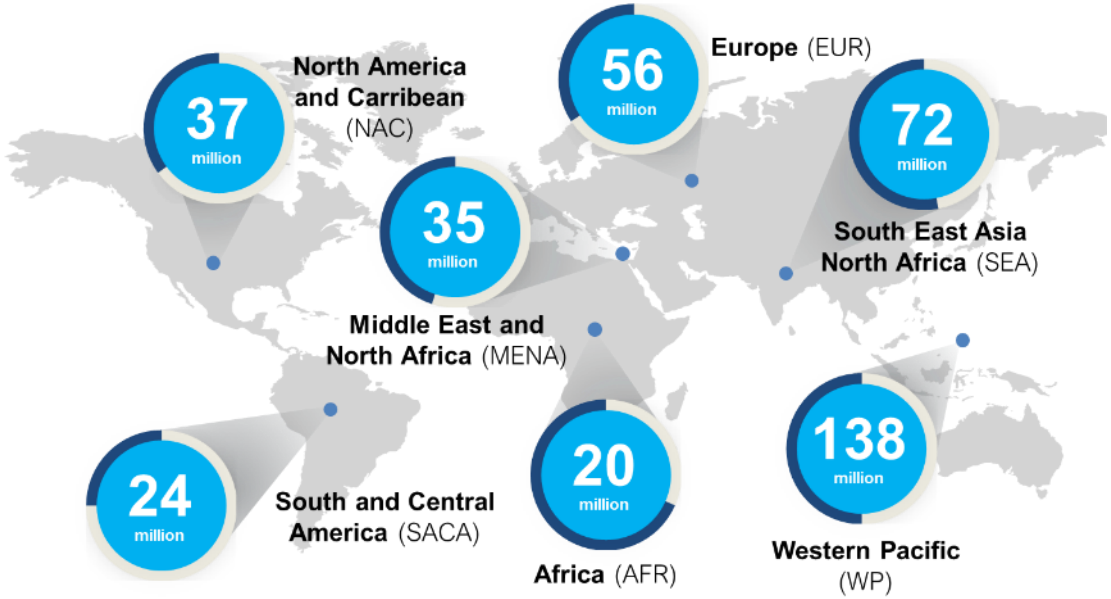
60% Opportunity

Huge market potential resides in the remaining 60% unmet need in CVD management

New LDL Modulators - 10%

Several new types of LDL modulators are in clinic. Leading are the very expensive PCSK9's

Diabetes Epidemic



Globally **382 Million** People living with diabetes

46% Undiagnosed

Diabetes prevalence; will increase by 55% in the next 30 years, with the Middle east region showing an increase of 96%.

IDF Diabetes Atlas | 6th edition