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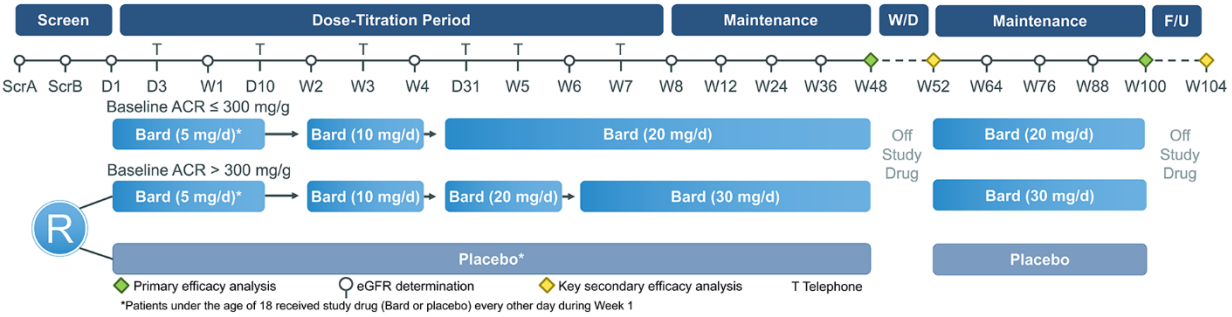
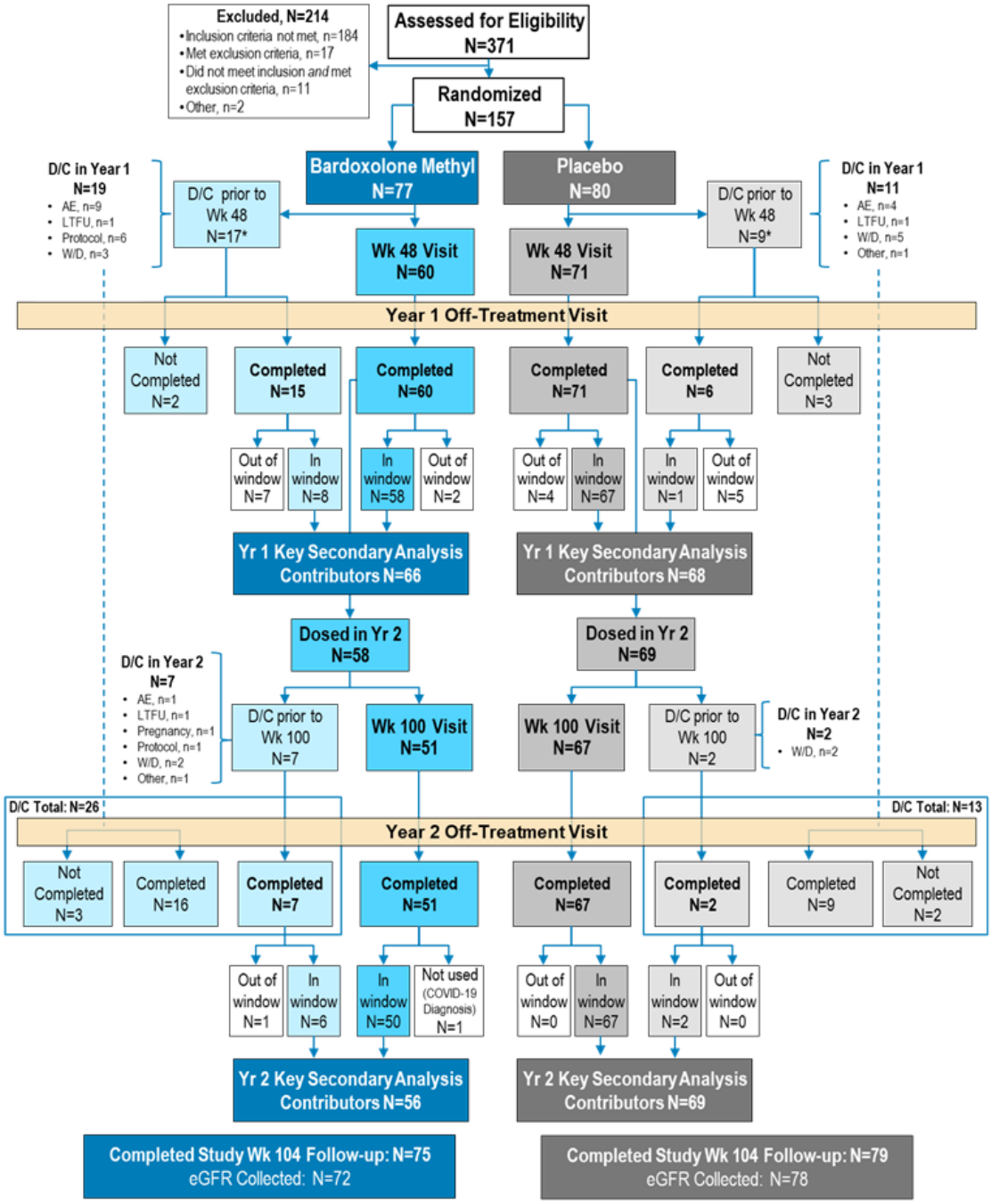
Supplemental Figure 1: Study Design and Schema

Adult patients started once-daily dosing by receiving 5 mg and increased the dose every two weeks to their target dose of 20 mg or 30 mg (the latter for patients with baseline UACR >300 mg/g only). Patients <18 years of age started dosing by receiving 5 mg every other day during the first week, 5 mg daily during the second week, and then increased the dose every two weeks following the dose-titration scheme noted above for adults. Patients did not receive study drug during a 4-week withdrawal period between 48 and 52 weeks, after which treatment was re-started at the same dose received at Week 48 and continued through 100 weeks; patients were reassessed after a second 4-week withdrawal period at 104 weeks.



Abbreviations: Bard=bardoxolone methyl; eGFR=estimated glomerular filtration rate; F/U=follow-up; R=randomization; W/D=withdrawal

Supplemental Figure 2: CONSORT Diagram



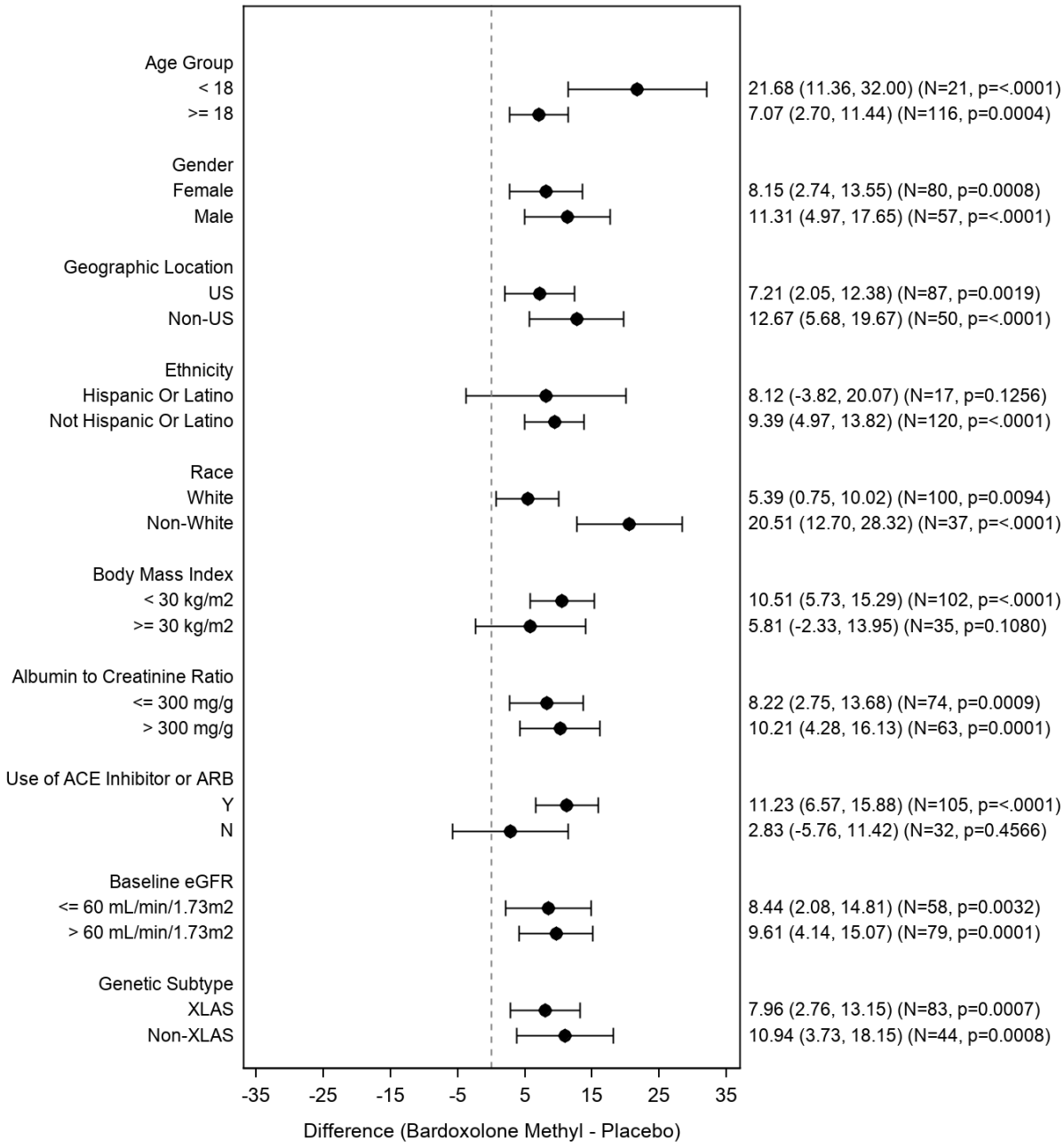
Abbreviations: AE=adverse event; D/C=discontinued treatment; LTFU=Lost to Follow-up; Protocol=protocol specified criterion met; W/D=withdrew consent; Wk=week.

Week 52 analysis window was 14 to 35 days after last dose and Week 104 analysis window was ≥ 14 days after last dose.

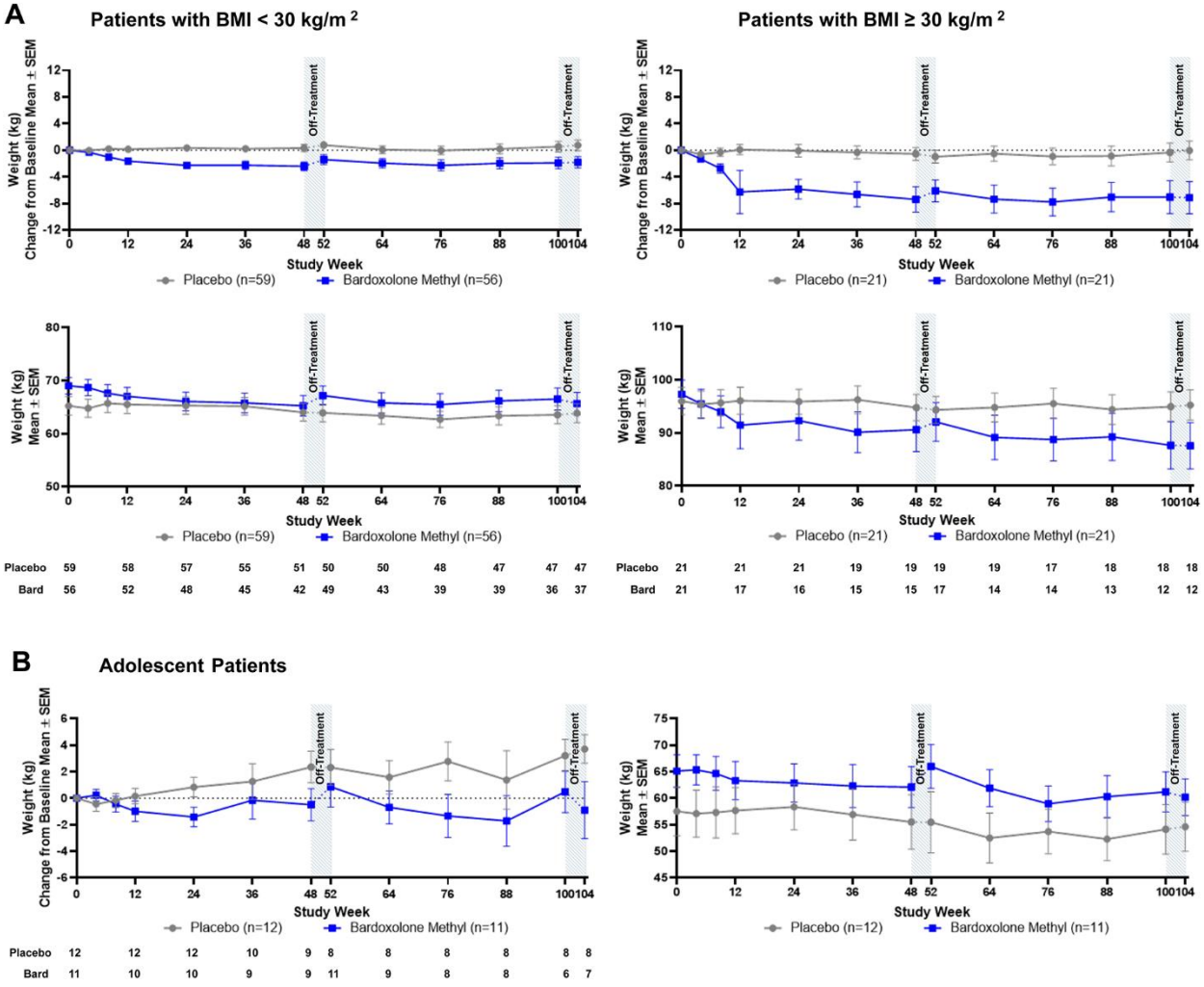
*Two additional bardoxolone methyl patients and 2 additional placebo patients discontinued at Week 48: 1 additional bardoxolone methyl patient discontinued due to an AE; 1 additional bardoxolone methyl patient and 2 additional placebo patients withdrew consent.

Note: Two patients in the placebo group did not have Year 2 follow-up visits, but one completed phone follow-up. Three patients in the bardoxolone methyl group did not have Year 2 off-treatment lab values, but 2 of those patients did have follow-up visits.

Supplemental Figure 3: Forest Plot of eGFR Change from Baseline to Week 48 by Subgroups
Forest plot summarizing LS mean ± 97.5% CI difference between bardoxolone methyl and placebo groups in the change from baseline in eGFR at 48 weeks for subgroups based on baseline characteristics at randomization. Mean difference between treatment groups at 48 weeks were analyzed for each subgroup by MMRM and included all available eGFR values collected through Week 48 for the intention-to-treat (ITT) population, with the number of patients with Week 48 data for each subgroup noted in the figure.



Supplemental Figure 4: Mean Changes from Baseline in Body Weight by Baseline BMI and Age Subgroups
Mean (± SEM) and mean (± SEM) change from baseline in body weight for BMI <30 and BMI ≥ 30 kg/m^2 subgroups of patients (A) and adolescent patients (B) randomized to bardoxolone methyl (n=77) or placebo (n=80) through the 104 weeks of the study. On-treatment is represented by the solid line, and off-treatment is represented by the dashed line. Mean values at 52 and 104 weeks include data collected 28 days after last dose for patients that discontinued early in the first or second year of treatment, respectively.



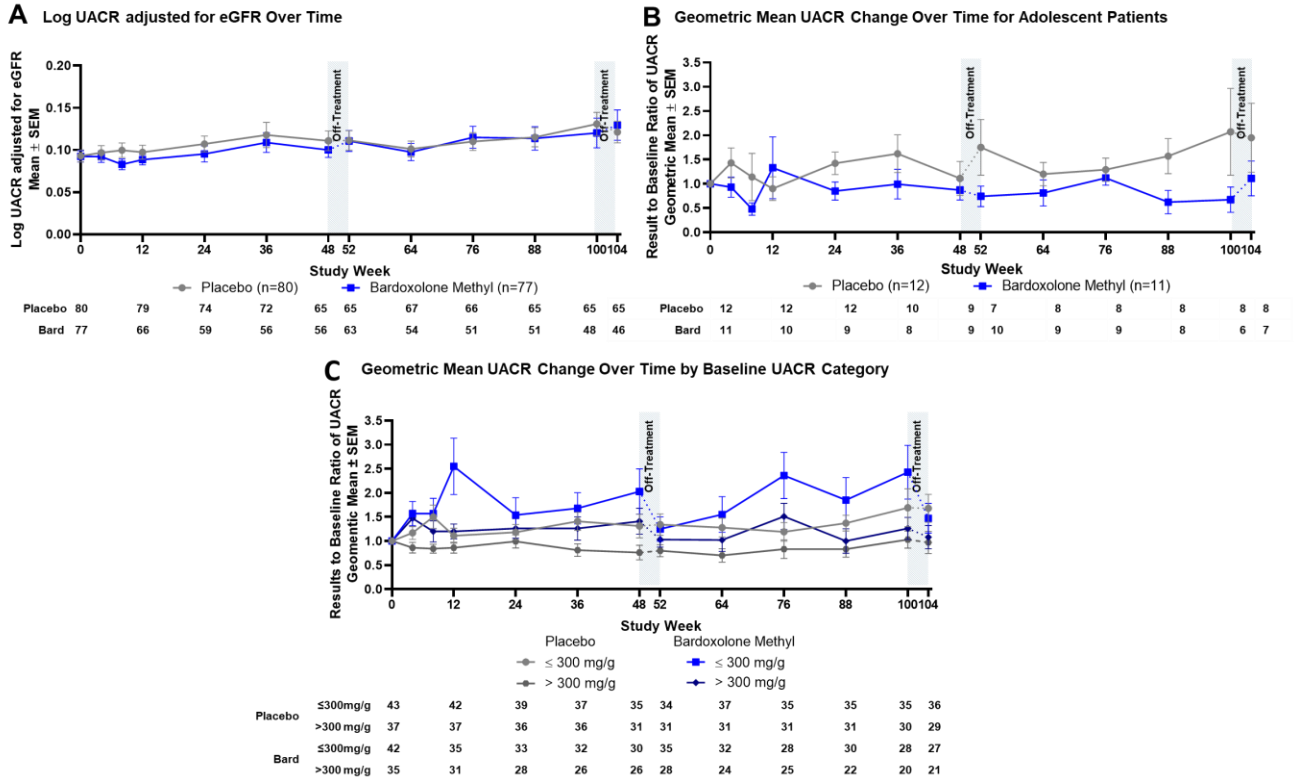
Supplemental Figure 5: Log UACR Adjusted for eGFR Over Time for ITT Population and Geometric Mean UACR Change Over Time for Adolescent Patients and ITT Patients by Baseline UACR Category

A. Mean (± SEM) for the ratio of log UACR/eGFR values for the patients randomized to bardoxolone methyl (n=77) or placebo (n=80) through the 104 weeks of the study. On-treatment data are represented by the solid line, and off-treatment data are represented by the dashed line.

B. Geometric mean (± SEM) to baseline ratio in UACR for adolescent patients randomized to bardoxolone methyl (n=11) or placebo (n=12) through the 104 weeks of the study. On-treatment is represented by the solid line, and off-treatment is represented by the dashed line. Mean values at 52 and 104 weeks include data collected 28 days after last dose for patients that discontinued early in the first or second year of treatment, respectively.

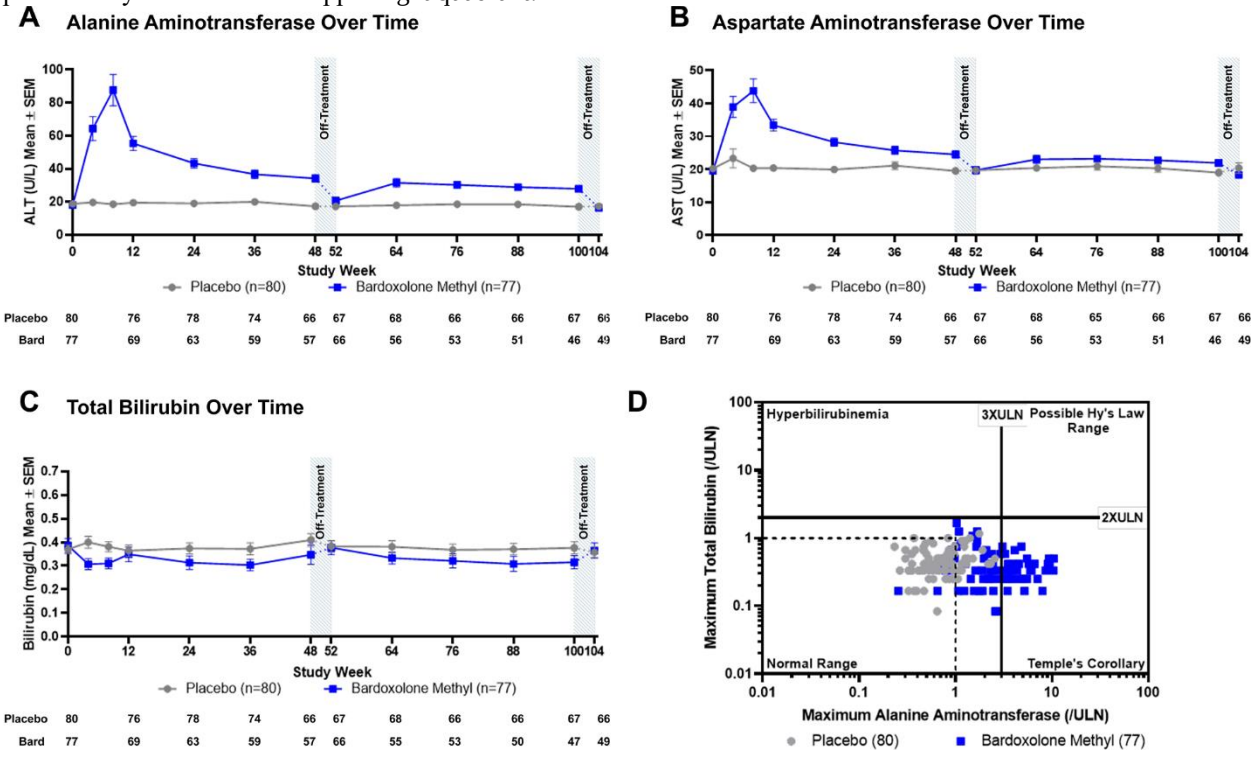
Mean values at 52 and 104 weeks include data collected 28 days after last dose for patients that discontinued early in the first or second year of treatment, respectively.

C. Geometric mean (± SEM) to baseline ratio in UACR for patients randomized to bardoxolone methyl or placebo by baseline UACR category through the 104 weeks of the study. On-treatment is represented by the solid line, and off-treatment is represented by the dashed line. Mean values at 52 and 104 weeks include data collected 28 days after last dose for patients that discontinued early in the first or second year of treatment, respectively.



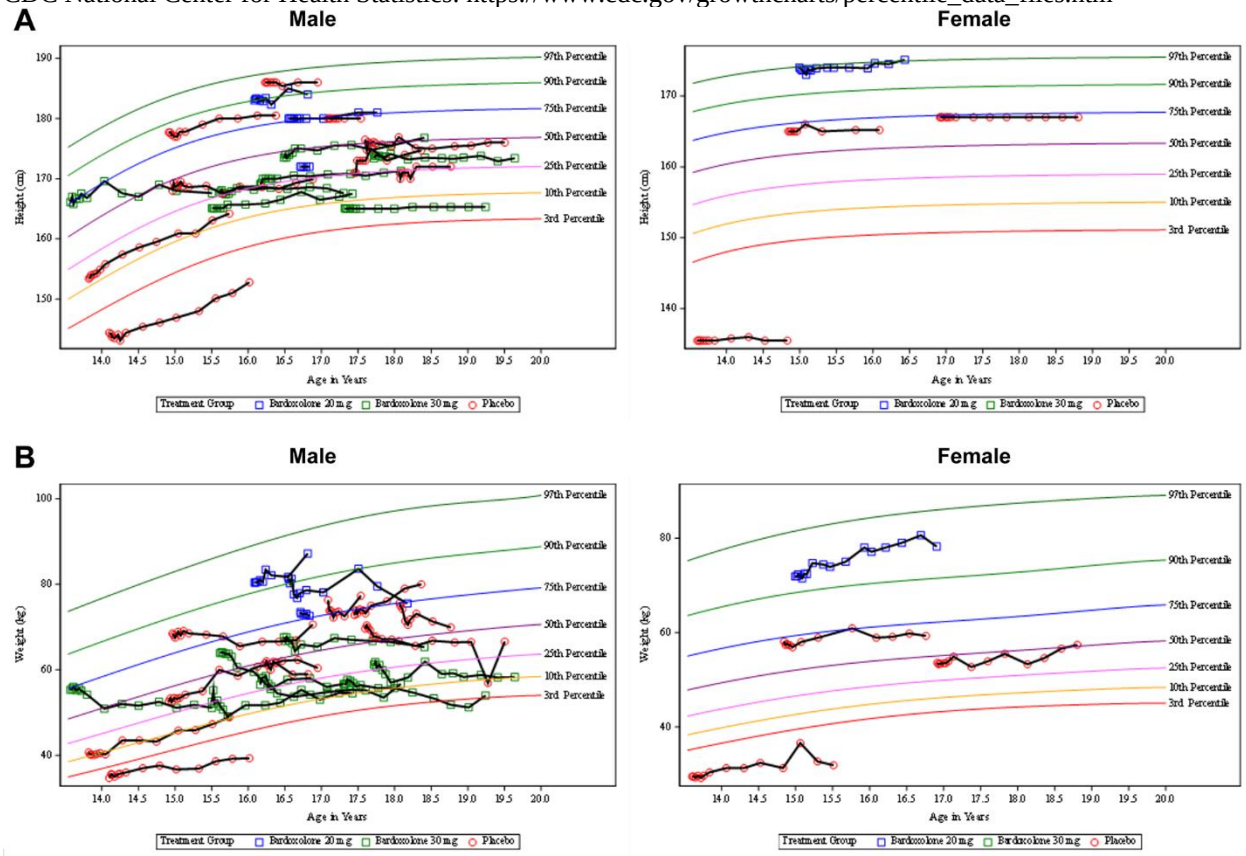
Supplemental Figure 6: Laboratory Evaluations Related to Hepatic Function

Mean (± SEM) (A) alanine aminotransferase (ALT); (B) aspartate aminotransferase (AST); and (C) total bilirubin values for patients randomized to bardoxolone methyl (n=77) or placebo (n=80) through 104 weeks of trial. On-treatment is represented by the solid line, and off-treatment is represented by the dashed line. Mean values at 52 and 104 weeks include data collected 28 days after last dose for patients that discontinued early in the first or second year of treatment, respectively. (D) An evaluation of drug-induced hepatotoxicity (eDISH) plot. Vertical lines correspond to 3 x ULN for ALT. Horizontal lines correspond to 2 x ULN for total bilirubin. No patients met potential Hy's criteria in the upper-right quadrant.

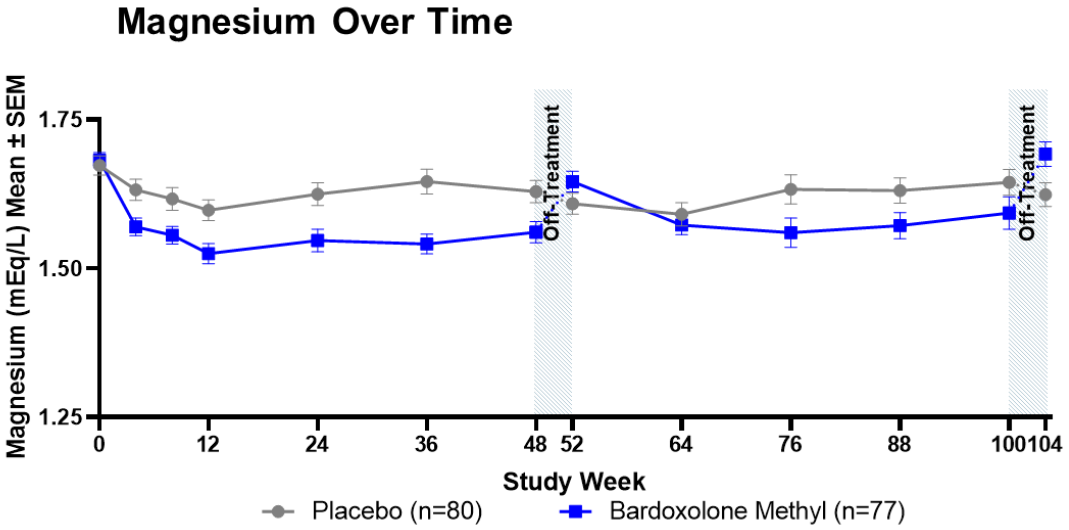


Supplemental Figure 7: Growth Chart for Adolescent Patients

Scatter plots for height (A) and weight (B) of adolescent patients. Reference lines for percentiles are taken from CDC National Center for Health Statistics: https://www.cdc.gov/growthcharts/percentile_data_files.htm



Supplemental Figure 8: Serum Magnesium Over Time for ITT Population
Mean (± SEM) serum magnesium levels for patients randomized to bardoxolone methyl (n=77) or placebo (n=80) through 104 weeks of trial. On-treatment is represented by the solid line, and off-treatment is represented by the dashed line. Mean values at 52 and 104 weeks include data collected 28 days after last dose for patients that discontinued early in the first or second year of treatment, respectively.



Placebo	80	79	78	74	67	68	68	66	66	67	67
Bard	77	69	63	59	57	66	57	53	51	48	49

Supplemental Table 1: Eligibility and Exclusion Criteria

Inclusion criteria

1. Male or female patients between 12 and 70 years old, inclusive, upon study consent;
2. Were diagnosed with Alport syndrome by genetic testing (documented mutation in a gene associated with Alport syndrome, including *COL4A3*, *COL4A4*, or *COL4A5*) or histologic assessment using electron microscopy;
3. Had a screening eGFR (average of Screen A and Screen B eGFR values) ≥ 30 and ≤ 90 mL/min/1·73 m^2. The two eGFR values collected at Screen A and Screen B visits used to determine eligibility must have a percent difference ≤25%;
4. Had UACR ≤3500 mg/g at Screen B visit. Up to 50% of patients in the Phase 2 cohort and approximately 40% of patients enrolled in the Phase 3 cohort could have had UACR of 301 to 3500 mg/g. Once enrolment of these patients was complete, the UACR inclusion criterion was ≤300 mg/g;
5. Patients receiving an ACE inhibitor and/or an ARB should be receiving the maximally tolerated labelled daily dose, for at least 6 weeks prior to the Screen A visit. The dosage of ACE inhibitor and/or ARB should have remained the same throughout the remainder of the study, and any potential changes were to be discussed with the medical monitor. Patients not currently taking an ACE inhibitor and/or ARB because they were not indicated or because of a medical contraindication may have been eligible provided the patient has not taken an ACE inhibitor and/or ARB at least 8 weeks prior to the Screen A visit (these patients were to be discussed with the medical monitor prior to enrolment);
6. Had adequate bone marrow reserve and organ function at the Screen A visit as follows:
    a. Hematologic: Absolute neutrophil count >1.5 × 10^9/L, platelets >100 × 10^9/L, hemoglobin ≥9 g/dL;
    b. Hepatic: Total bilirubin ≤1.5 × ULN, ALT and AST ≤1.5 × ULN;
7. Were able to swallow capsules;
8. Were willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures;
9. Had a signed and dated informed consent document (assent form if necessary) indicating that the patient (or a legally acceptable representative) was informed of all pertinent aspects of the study prior to initiation of any patient-mandated procedures.

Exclusion criteria

1. Had prior exposure to bardoxolone methyl;
2. Had ongoing chronic hemodialysis or peritoneal dialysis therapy;
3. Were a renal transplant recipient;
4. Had BNP >200 pg/mL at Screen A visit;
5. Had uncontrolled diabetes (HbA1c >11.0%) at Screen A visit;
6. Had acute dialysis or acute kidney injury within 12 weeks prior to Screen A visit or during Screening;
7. Had serum albumin < 3 g/dL at Screen A visit;
8. Had a history of clinically significant left-sided heart disease and/or clinically significant cardiac disease, including but not limited to any of the following:
    a. Clinically significant congenital or acquired valvular disease;
    b. Left ventricular ejection fraction < 40% (based on echocardiogram performed at Screen A visit or within 6 months prior to Day 1);
    c. Pericardial constriction (based on echocardiogram performed at Screen A visit or within 6 months prior to Day 1);
    d. Restrictive or congestive cardiomyopathy (based on echocardiogram performed at Screen A visit or within 6 months prior to Day 1);
    e. Symptomatic coronary disease (prior myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft surgery, or angina);
    f. History of hospitalization for heart failure;
    g. Cardiac insufficiency, defined as New York Heart Association Class > 2;
    h. History of atrial fibrillation;
    i. History of unstable arrhythmias;
9. Had uncontrolled systemic hypertension (sitting systolic blood pressure >160 mmHg or sitting diastolic blood pressure >100 mmHg at Screen A visit after a period of rest;
10. Had systolic blood pressure <90 mmHg at Screen A visit after a period of rest;
11. Had a history of malignancy within 5 years prior to Screen A visit, with the exception of localized skin or cervical carcinomas;
12. Had systemic immunosuppression for more than 2 weeks, cumulatively, within the 12 weeks prior to randomization or anticipated need for immunosuppression during the study;
13. Had untreated or uncontrolled active bacterial, fungal, or viral infection;
14. Had participated in other investigational clinical studies within 30 days prior to Day 1;
15. Were unwilling to practice acceptable methods of birth control (both males who have partners of childbearing potential and females of childbearing potential) during Screening, while taking study drug, and for at least 30 days after the last dose of study drug was ingested;
16. Women who were pregnant or breastfeeding;
17. Had a known hypersensitivity to any component of the study drug;
18. Had any abnormal laboratory level that, in the opinion of the investigator, would put the patient at risk by trial enrolment;
19. Patient was, in the opinion of the investigator, unable to comply with the requirements of the study protocol or was unsuitable for the study for any reason.

Abbreviations: ACE=angiotensin converting enzyme; ALT=alanine aminotransferase; ARB=angiotensin II receptor blocker; AST= aspartate aminotransferase; BNP=B-type natriuretic peptide; eGFR=estimated glomerular filtration rate; HbA1c= hemoglobin A1C; UACR=urinary albumin-to-creatinine ratio; ULN=the upper limit of normal

Supplemental Table 2: Full List of Efficacy Endpoints in CARDINAL

Primary efficacy endpoints
• Change from baseline in eGFR at Weeks 48 and 100
Key secondary endpoints
• Change from baseline in eGFR, following a 4-week drug treatment withdrawal period, at Weeks 52 and 104
Exploratory endpoints
• Time to first kidney failure composite event, defined as the composite endpoint consisting of: - 30% decline from baseline in eGFR; - eGFR <15 mL/min/1.73 m^2; - ESKD (initiation of maintenance dialysis or kidney transplant). • Percentage of patients with a kidney failure event by Weeks 48 and 100, defined as the composite endpoint consisting of: - 30% decline from baseline in eGFR; - eGFR <15 mL/min/1.73 m^2; - ESKD (initiation of maintenance dialysis or kidney transplant). • Percentage of patients with an increase from baseline in eGFR of 30% or more by Weeks 48 and 100 • Percentage of patients with a decrease from baseline in eGFR of 30% or more by Weeks 48 and 100 • Distribution of changes from baseline in eGFR at Weeks 48 and 100 • Distribution of the PGIC scores at Weeks 48 and 100 • Distribution of the CGI-I scores at Weeks 48 and 100

Abbreviations: CGI-I=Clinical Global Impression-Improvement; eGFR=estimated glomerular filtration rate; ESKD=end-stage kidney disease; PGIC=Patient Global Impression of Change

Supplemental Table 3: Detailed Description of CARDINAL Analysis Methodologies

Longitudinal Model for Primary Efficacy Analyses	Baseline eGFR was defined as the average of screening and Day 1 eGFR measurements, where screening eGFR was the average of the last two eGFR measurements collected prior to the Day 1 eGFR collection and Day 1 eGFR is the measurement on the date of first study drug administration prior to the first study drug administration. The change from baseline eGFR for patients treated with bardoxolone methyl was compared with placebo at Week 48 or Week 100 using a mixed model repeated measures (MMRM) analysis, with baseline eGFR, baseline UACR strata and geographical region (Week 100 only) as covariates and the following fixed factors as covariates: treatment group, time (i.e., analysis visit number), the interaction between treatment and time, and the interaction between baseline eGFR and time. The covariate for geographical region (US versus non-US) was included in the model used to analyze the primary endpoint for the second year of the trial to account for regional differences in the impact of the novel coronavirus SARS-CoV2 (COVID-19).
ANCOVA Model for Key Secondary Analyses	The change from baseline eGFR at Week 52 and Week 104 (or 4 weeks after last dose for patients who discontinued early) for patients treated with bardoxolone methyl was compared with placebo using an analysis of covariance (ANCOVA) model, with baseline eGFR and geographical region (Week 104 only) as covariates and treatment group and randomized UACR strata as a fixed effect. If off-treatment eGFR was measured more than once, the value collected closest to 28 days after last dose was used for analysis. Treatment-based multiple imputation was used to impute missing off-treatment values. The point estimate for each treatment group at Week 104 was based on a model that used two UACR categories (≤300; >300) to account for the small sample size in the two higher categories.
Prespecified Modified ITT (mITT) Sensitivity Analysis for Primary Endpoint	A modified intention-to-treat (mITT) analysis was performed to evaluate the treatment effect in the ITT population while receiving study drug. The same mixed model repeated measures approach used for the primary efficacy analysis, including covariates and fixed factors, was also used for the mITT analysis, but excluded any eGFR values collected after final dose.
Prespecified Analysis using Control-based Multiple Imputation	All missing eGFR values are imputed with multiple imputation using the Week 100 or the Week 104 data from the placebo group.
Prespecified Tipping Point Analyses for Primary and Key Secondary Endpoints	Tipping point sensitivity analyses were performed to assess how severe departures from the missing at random (MAR) assumption must be in order to overturn conclusions from the methods employed in the primary and key secondary efficacy analyses. Patients in the bardoxolone methyl group with a missing eGFR value were multiply imputed separately from the placebo arm and were assigned a shift parameter in the imputation procedure for progressively worse (lower) scores to find the point at which statistical significance was lost. Data for the placebo arm remained unchanged.
Post-hoc Sensitivity Analysis for Key Secondary Endpoint	All available eGFR values collected approximately 104 weeks after randomization, irrespective of time off study drug. This included data from 96% (150/157) of all randomized patients, including 78 patients randomized to placebo and 72 patients randomized to bardoxolone methyl. Missing data were not imputed.
Post-hoc Sensitivity Analysis for Imputation of ESKD in Key Secondary Endpoint	An alternate imputation method was used for patients (3 bardoxolone methyl and 3 placebo patients) who progressed to kidney failure, whereby Week 104 eGFR values were assumed to be 0 mL/min/1.73 m^2 or 5 mL/min/1.73 m^2.

Abbreviations: ANCOVA=analysis of covariance; eGFR=estimated glomerular filtration rate; ESKD=end-stage kidney disease; ITT=intention-to-treat; mITT=modified intention-to-treat; MMRM=mixed model repeated measures; SARS-CoV2= severe acute respiratory syndrome coronavirus 2; UACR=urinary albumin-to-creatinine ratio; US=United States

Supplemental Table 4: Detailed Disposition and Reasons for Discontinuation in CARDINAL

	Placebo (n=80)	**Bardoxolone methyl (n=77)**
ITT Population	80 (100%)	77 (100%)
Completed Study Follow-up through Week 104	79 (99%)	75 (97%)
eGFR Values Collected at Follow-up[a]	78 (98%)	72 (94%)
Year 1		
On Treatment at Week 48	71 (89%)	60 (78%)
Week 48 eGFR data	71 (89%)	66 (86%)
Week 52 eGFR data	68 (85%)	66 (86%)
Discontinued study treatment prior to Week 48	9 (11%)	17 (22%)
Reason for discontinuing treatment prior to Week 48		
Adverse Event	4 (5%)	8 (10%)
Lost to Follow-Up	1 (1%)	1 (1%)
Protocol-Specified Withdrawal Criterion Met	0	6 (8%)
Withdrawal by Subject	3 (4%)	2 (3%)
Other	1 (1%)	0
Discontinued treatment at Week 48	2 (3%)	2 (3%)
Adverse Event	0	1 (1%)
Withdrawal by Subject	2 (3%)	1 (1%)
Year 2		
On treatment at Week 100	67 (84%)	51 (66%)
Week 100 eGFR data	73 (91%)	65 (84%)
Week 104 eGFR data	69 (86%)	56 (73%)
Discontinued study treatment prior to Week 100	2 (3%)	7 (9%)
Reason for discontinuing treatment prior to Week 100		
Adverse Event	0	1 (1%)
Lost to Follow-Up	0	1 (1%)
Other	0	1 (1%)
Pregnancy	0	1 (1%)
Protocol-Specified Withdrawal Criterion Met	0	1 (1%)
Withdrawal by Subject	2 (3%)	2 (3%)

[a]Patients with eGFR values collected approximately 104 weeks after randomization
Abbreviations: eGFR=estimated glomerular filtration rate; ITT=intention-to-treat.

Supplemental Table 5: Summary of Protocol-Specified Criteria Leading to Study Drug Discontinuation

Event	Placebo (n=80)	Bardoxolone methyl (n=77)
Number (%) of patients	**0**	**7 (9%)**
Alanine aminotransferase increased	0	5 (7%)
End stage kidney disease[a]	0	2 (3%)

[a] An additional 3 patients randomized to placebo and 1 patient randomized to bardoxolone methyl experienced end stage kidney disease during the trial but the discontinuations were not categorized as a 'protocol-specified criteria' as the primary reason for study drug discontinuation.

Supplemental Table 6: Summary of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation

Event	Placebo (n=80)	Bardoxolone methyl (n=77)
Number (%) of patients reporting TEAEs resulting in study drug discontinuation	**4 (5%)**	**10 (13%)**
Investigations	**0**	**3 (4%)**
B-type natriuretic peptide increased	0	2 (3%)
Alanine aminotransferase increased	0	1 (1%)
Glomerular filtration rate decreased	0	1 (1%)
N-terminal prohormone brain natriuretic peptide increased	0	1 (1%)
Renal and urinary disorders	**2 (3%)**	**2 (3%)**
End stage kidney disease	1 (1%)	1 (1%)
Acute kidney injury	0	1 (1%)
Proteinuria	1 (1%)	0
Gastrointestinal disorders	**0**	**2 (3%)**
Gastroesophageal reflux disease	0	2 (3%)
Musculoskeletal and connective tissue disorders	**0**	**2 (3%)**
Muscle spasms	0	2 (3%)
General disorders and administration site conditions	**1 (1%)**	**1 (1%)**
Peripheral edema	1 (1%)	1 (1%)
Metabolism and nutrition disorders	**0**	**1 (1%)**
Dehydration	0	1 (1%)
Skin and subcutaneous tissue disorders	**0**	**1 (1%)**
Alopecia	0	1 (1%)
Ear and labyrinth disorders	**1 (1%)**	**0**
Deafness	1 (1%)	0

Abbreviation: TEAE=treatment-emergent adverse event

Supplemental Table 7: Treatment-Emergent Serious Adverse Events

Patients with Adverse Event System Organ Class/Preferred Term	**Placebo (n=80)**	**Bardoxolone methyl (n=77)**
General disorders and administration site conditions	**2 (3%)**	**0**
Non-cardiac chest pain	1 (1%)	0
Edema peripheral	1 (1%)	0
Immune system disorders	**1 (1%)**	**0**
Anaphylactic reaction	1 (1%)	0
Infections and infestations	**2 (3%)**	**0**
Pneumonia	2 (3%)	0
Empyema	1 (1%)	0
Injury, poisoning and procedural complications	**2 (3%)**	**1 (1%)**
Clavicle fracture	0	1 (1%)
Rib fracture	0	1 (1%)
Scapula fracture	0	1 (1%)
Animal bite	1 (1%)	0
Laceration	1 (1%)	0
Metabolism and nutrition disorders	**0**	**1 (1%)**
Dehydration	0	1 (1%)
Musculoskeletal and connective tissue disorders	**1 (1%)**	**0**
Osteoarthritis	1 (1%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2 (3%)**	**1 (1%)**
Colon adenoma	0	1 (1%)
Carcinoid tumor	1 (1%)	0
Prostate cancer	1 (1%)	0
Nervous system disorders	**2 (3%)**	**0**
Ischemic stroke	1 (1%)	0
Status migrainosus	1 (1%)	0
Renal and urinary disorders	**3 (4%)**	**4 (5%)**
End stage renal disease	2 (3%)	2 (3%)
Proteinuria	1 (1%)	1 (1%)
Acute kidney injury	0 (0)	1 (1%)
Reproductive system and breast disorders	**1 (1%)**	**0**
Ovarian mass	1 (1%)	0
Respiratory, thoracic and mediastinal disorders	**1 (1%)**	**2 (3%)**
Pneumomediastinum	0	1 (1%)
Pneumothorax	0	1 (1%)
Asthma	1 (1%)	0
Vascular disorders	**0**	**1 (1%)**
Hypertensive crisis	0	1 (1%)

Supplemental Table 8: Treatment-Emergent Adverse Events by System Organ Class

Patients with Adverse Event System Organ Class	Placebo (N = 80)	Bardoxolone Methyl (N = 77)
Blood and lymphatic system disorders	3 (4%)	5 (7%)
Cardiac disorders	7 (9%)	4 (5%)
Congenital, familial and genetic disorders	0	1 (1%)
Ear and labyrinth disorders	7 (9%)	4 (5%)
Endocrine disorders	1 (1%)	3 (4%)
Eye disorders	9 (11%)	5 (7%)
Gastrointestinal disorders	29 (36%)	41 (53%)
General disorders and administration site conditions	30 (38%)	32 (42%)
Hepatobiliary disorders	0	4 (5%)
Immune system disorders	3 (4%)	3 (4%)
Infections and infestations	45 (56%)	46 (60%)
Injury, poisoning and procedural complications	11 (14%)	11 (14%)
Investigations	32 (40%)	59 (77%)
Metabolism and nutrition disorders	25 (31%)	25 (33%)
Musculoskeletal and connective tissue disorders	44 (55%)	48 (62%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3 (4%)	3 (4%)
Nervous system disorders	33 (41%)	24 (31%)
Psychiatric disorders	14 (18%)	5 (7%)
Renal and urinary disorders	18 (23%)	19 (25%)
Reproductive system and breast disorders	5 (6%)	6 (8%)
Respiratory, thoracic and mediastinal disorders	17 (21%)	25 (33%)
Skin and subcutaneous tissue disorders	13 (16%)	11 (14%)
Vascular disorders	13 (16%)	10 (13%)

Supplemental Table 9: Change from Baseline in Laboratory Results at Week 100

Laboratory parameter	Placebo (n=80)	Bardoxolone methyl (n=77)	Difference between treatment groups
ALT (U/L)			
Least Square Means (SE)	-1.37 (1.295)	9.44 (1.487)	10.81 (1.975)
p-value	-	-	<0.0001
95% Confidence Interval	-3.93, 1.20	6.50, 12.39	6.90, 14.72
AST (U/L)			
Least Square Means (SE)	-1.12 (0.644)	2.06 (0.755)	3.18 (0.994)
p-value	-	-	0.0017
95% Confidence Interval	-2.39, 0.16	0.57, 3.56	1.21, 5.15
Bilirubin (mg/dL)			
Least Square Means (SE)	0.00 (0.018)	-0.07 (0.021)	-0.07 (0.028)
p-value	-	-	0.009
95% Confidence Interval	-0.04, 0.04	-0.11, -0.03	-0.13, -0.02
B-type Natriuretic Peptide (ng/L)			
Least Square Means (SE)	5.37 (8.308)	30.47 (9.452)	25.10 (12.578)
p-value	-	-	0.0576
95% Confidence Interval	-11.86, 22.60	11.02, 49.92	-0.87, 51.08
Creatine Kinase (U/L)			
Least Square Means (SE)	-16.27 (8.171)	-48.27 (9.383)	-32.01 (12.458)
p-value	-	-	0.011
95% Confidence Interval	-32.44, -0.10	-66.83, -29.72	-56.65, -7.37
Serum Creatinine (mg/dL)			
Least Square Means (SE)	0.45 (0.103)	0.27 (0.115)	-0.18 (0.154)
p-value	-	-	0.26
95% Confidence Interval	0.24, 0.67	0.03, 0.51	-0.50, 0.14
Magnesium (mEq/L)			
Least Square Means (SE)	-0.02 (0.017)	-0.09 (0.020)	-0.07 (0.027)
p-value	-	-	0.011
95% Confidence Interval	-0.06, 0.01	-0.13, -0.05	-0.12, -0.02
Potassium (mEq/L)			
Least Square Means (SE)	0.03 (0.055)	0.23 (0.063)	0.20 (0.084)
p-value	-	-	0.02
95% Confidence Interval	-0.08, 0.14	0.10, 0.35	0.03, 0.36
Urate (mg/dL)			
Least Square Means (SE)	-0.15 (0.143)	-0.43 (0.162)	-0.28 (0.217)
p-value	-	-	0.19
95% Confidence Interval	-0.43, 0.13	-0.75, -0.11	-0.71, 0.15
Urea Nitrogen (mg/dL)			
Least Square Means (SE)	3.74 (0.934)	5.03 (1.060)	1.29 (1.415)
p-value	-	-	0.36
95% Confidence Interval	1.88, 5.60	2.92, 7.14	-1.52, 4.11
UACR (mg/g)			
Least Square Means (SE)	0.33 (0.133)	0.56 (0.150)	0.23 (0.201)
p-value	-	-	0.25
95% Confidence Interval	0.07, 0.59	0.27, 0.86	-0.16, 0.63
Systolic blood pressure (mm Hg)			
Least Square Means (SE)	0.83 (1.625)	-0.50 (1.880)	-1.33 (2.486)
p-value	-	-	0.59
95% Confidence Interval	-2.39, 4.05	-4.23, 3.22	-6.25, 3.59
Diastolic blood pressure (mm Hg)			
Least Square Means (SE)	1.93 (1.182)	1.70 (1.368)	-0.23 (1.810)
p-value	-	-	0.90
95% Confidence Interval	-0.41, 4.27	-1.01, 4.41	-3.82, 3.35
Weight (kg)			
Least Square Means (SE)	0.41 (0.680)	-3.47 (0.749)	-3.88 (1.013)
p-value	-	-	0.0002
95% Confidence Interval	-0.93, 1.76	-4.95, -1.98	-5.89, -1.87

Abbreviations: ALT=alanine aminotransferase; AST= aspartate aminotransferase; SE=standard error; UACR=urinary albumin-to-creatinine ratio

The change from baseline for each parameter, except for UACR, was estimated for patients randomized to bardoxolone methyl or placebo using all available data collected through Week 100 for the randomized population (n=77 for bardoxolone methyl and n=80 for placebo). Changes from baseline and differences between treatment groups were estimated using mixed models repeated measures analysis, with baseline value, randomized UACR strata, and geographical location as covariate and the following fixed factors: treatment group, , the interaction between treatment and time, and the interaction between baseline value and time. Within-patient errors are modelled

using an unstructured covariance matrix. Changes in UACR were calculated as the logarithm of UACR ratio relative to baseline. Statistical significance for the between group changes determined from a test comparing the difference in mean changes between placebo and bardoxolone methyl groups.