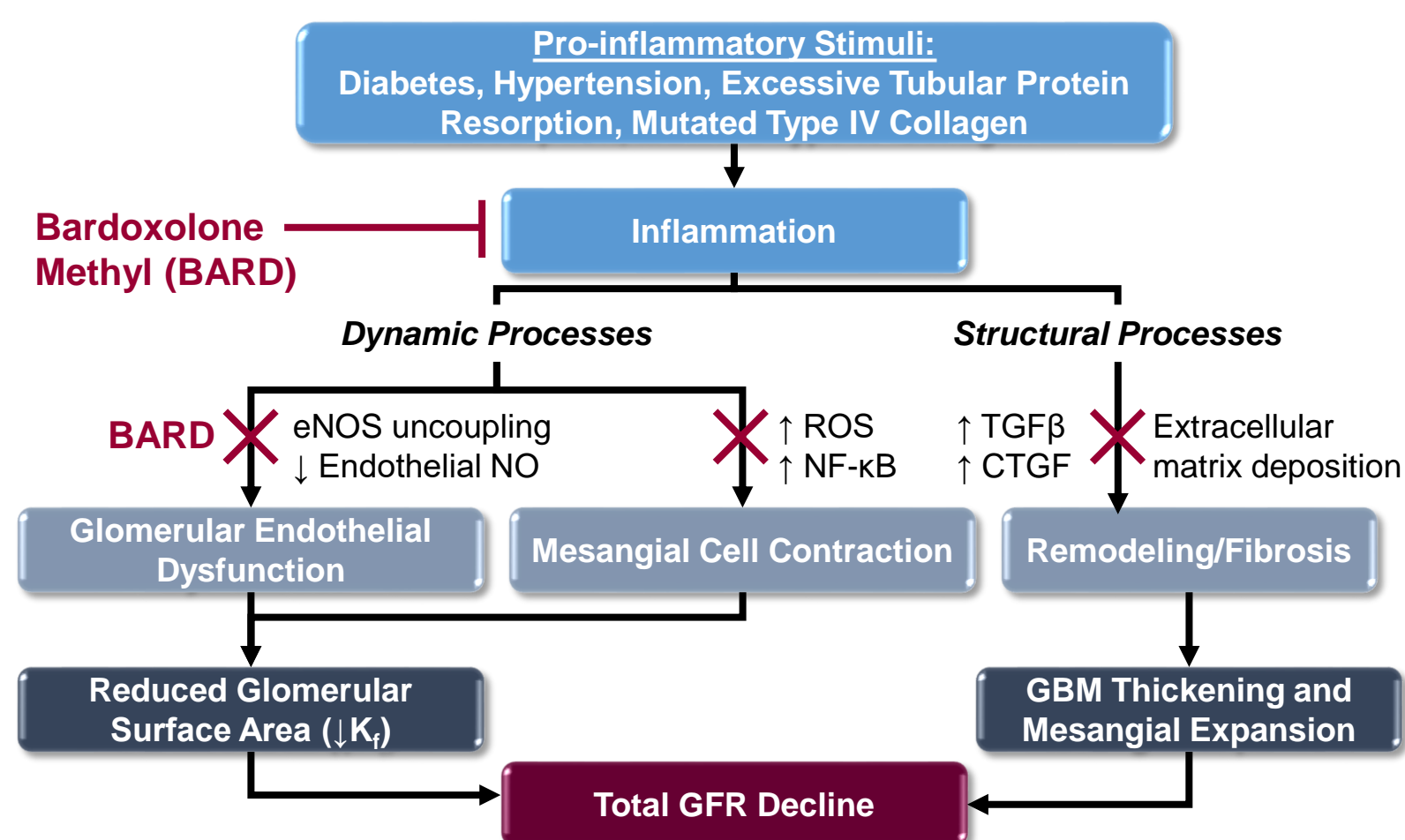


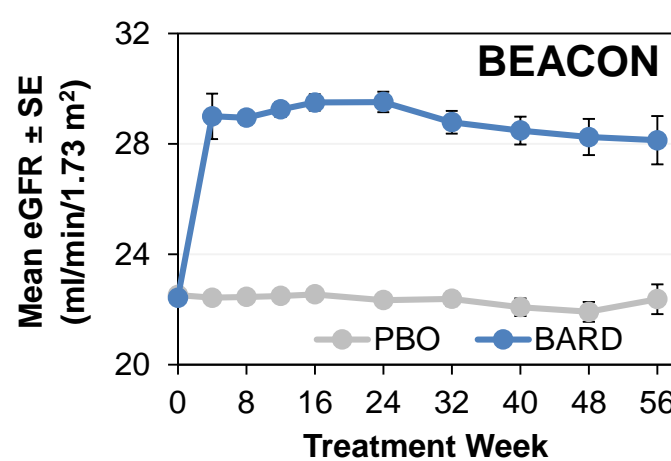
Colin Meyer, David G. Warnock, Melanie Chin, Angie Goldsberry, Peter A. McCullough, Megan O'Grady, Robert Toto, Keith Ward, Geoffrey Block, Pablo E. Pergola

BARDOXOLONE METHYL

- Bardoxolone methyl (BARD) activates Nrf2 and suppresses NF-κB
 - Nrf2 activation is reno-protective in kidney disease models^{1,2}
 - BARD increases expression of antioxidant genes to reduce inflammation and pro-proliferative drive^{3,4}
- BARD targets inflammatory pathways that contribute to GFR loss in chronic kidney diseases⁵⁻⁷



- BARD significantly increases eGFR, inulin clearance, creatinine clearance, and other markers of kidney function across 7 clinical trials in patient with CKD that enrolled over 2,600 patients with CKD⁸⁻¹¹
- In Phase 2 BEAM and Phase 3 BEACON studies^{10,11}
 - BARD increased eGFR ($p < 0.0001$)
 - Durable eGFR change through 1 year and retained benefit four weeks after drug cessation, suggesting disease-modifying activity
 - Fewer renal SAEs and ESRD events in BARD vs placebo patients



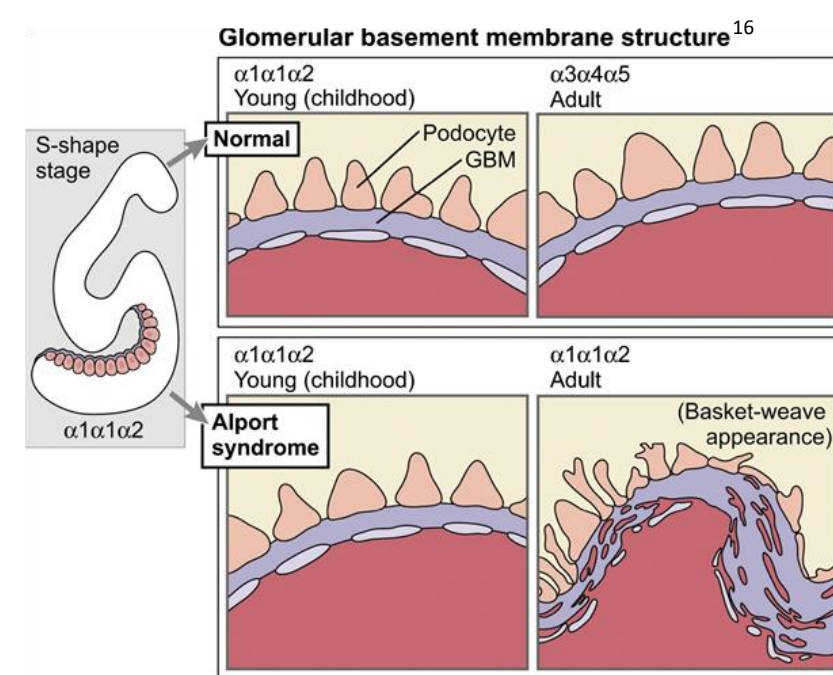
	Baseline eGFR ml/min/1.73m ²	PBO-Corrected Post-TX ΔeGFR ml/min/1.73m ²	P-value
BEAM (n=172)			
Low Dose	33	0.6	p>0.05
Mid Dose	32	4.7	p<0.05
High Dose	32	5.0	p<0.05
BEACON (n=498)			
20 mg	23	1.8	p<0.001

- BEACON study was terminated early due to increased risk for fluid overload hospitalizations within first four weeks. The average age of patients in the study was 68.5±9.6
- Post-hoc analyses identified baseline BNP > 200 pg/ml and prior history of heart failure were risk factors for fluid overload in BEACON¹² and these were used to exclude at-risk patients in subsequent studies
- BARD has potential to prevent kidney function decline and delay or prevent ESRD in patients with Alport syndrome
- Reata has initiated a pivotal Phase 2/3 study (CARDINAL) in patients with Alport syndrome

ALPORT SYNDROME

- Alport syndrome is a hereditary disease caused by mutations in genes that code for type IV collagen
 - Affects approximately 1 in 50,000 in the US¹³
 - Defective glomerular basement membrane leads to:
 - Leakage of proteins
 - Inflammation, glomerular sclerosis, tubular atrophy and interstitial fibrosis
- Like other chronic kidney diseases, progressive eGFR loss (~4 ml/min/1.73 m² per year¹⁴) leads to ESRD
- Median age at onset of ESRD for male hereditary Alport (XLAS) patients is 25¹⁵
- Standard of care involves off-label ACEi/ARBs, with no approved therapies

Inflammation, fibrosis and mitochondrial dysfunction contribute to GFR loss and decreased kidney function in patients with Alport Syndrome¹⁷⁻¹⁹



CARDINAL STUDY DESIGN

CARDINAL STUDY (NCT03019185)

- Multicenter, multinational phase 2/3 study
- Patients 12 to 60 years of age with genetic or histologic confirmation of Alport syndrome
- Broad range of kidney function (eGFR between 30-90 mL/min/1.73 m²) and urine ACR ≤ 3500 mg/g
- Patients with history of cardiovascular disease or baseline risk for increased fluid retention (BNP > 200 pg/ml) will be excluded
- Dose-titration to goal BARD dose of 20 or 30 mg given orally, once daily

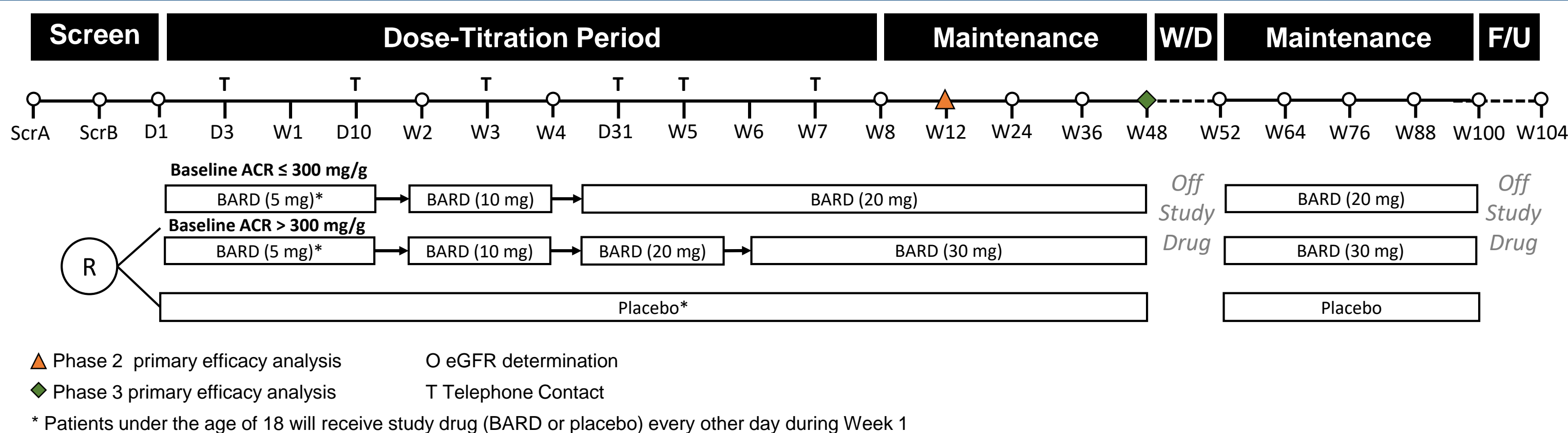
Phase 2 Cohort

- Open-label cohort enrolling a total of 30 patients: 15 with normo- or micro-albuminuria; 15 with macroalbuminuria
- Primary endpoint: change from baseline in eGFR at Week 12
- Following analysis at 12 weeks, patients will remain on treatment for 2 years

Phase 3 Cohort

- Enroll up to 180 patients for 2 years of treatment
- Placebo-controlled, double-blind, 1:1 randomization
- Primary endpoint - change in eGFR at Week 48
- Key secondary endpoint - change from baseline in eGFR at Week 52 following a 4-week drug withdrawal period

CARDINAL STUDY - SCHEMA AND DOSING SCHEDULE



CONCLUSION

CARDINAL is the first trial to test the hypothesis that BARD will improve kidney function in patients with Alport syndrome

DISCLOSURES

CM, MC, AG, MO and KW are employees of Reata Pharmaceuticals.
 DW is an investor in Reata Pharmaceuticals
 PAM, RT, GB and PP are consultants to Reata Pharmaceuticals

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