Topline Results of ACCOLADE Trial of Avacopan for C3 Glomerulopathy (C3G)

December 21, 2020

Forward-Looking Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "contemplate," "believe," "estimate," "predict," "project," "seek," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties and other factors are described more fully in our periodic reports filed with the Securities and Exchange Commission (SEC), including our Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on March 10, 2020 and our Form 10-Q filed on November 9, 2020, particularly in the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations". In light of the significant uncertainties in our forward-looking statements, you should not place undue reliance on these statements or regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all. The forward-looking statements contained in this presentation represent our estimates and assumptions only as of the date of this presentation and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this presentation.

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ACCOLADE Trial Topline Results Summary

- Modeled C3G Histologic Index of Disease Activity of >35% mean difference between avacopan and placebo was achieved in ACCOLADE
  - High variability patient-to-patient prevented achievement of statistical significance against primary endpoint
- Importantly, avacopan was observed to significantly improve kidney function vs. placebo, as measured by improvement in estimated glomerular filtration rate (eGFR)
  - Unprecedented in C3G patients; consistent with data from ADVOCATE trial in ANCA vasculitis
- Avacopan therapy also demonstrated reduction in proteinuria, reduction in urinary MCP1, significant improvement in C3G Histologic Index of Disease Chronicity
- Avacopan safety profile in C3G unremarkable; observed to be well tolerated
- Company plans to explore with regulators the use of avacopan in C3G

Avacopan: Clinical Development in C3G

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Overview

- Uncontrolled activation of complement system leading to complement protein deposition in the kidney (glomeruli), disrupting kidney function
- Can be life-threatening; half of all with C3G ultimately have kidney failure
- Kidney transplant does not cure disease; relapse is common
- Primarily affects the young; huge economic burden on HC systems
- US prevalence between ~1000 – 3800
- Incidence ~300 -700 new cases / yr

Rationale

- Characterized by C3 but also C5 / C5a deposition in glomeruli
- C5a contributes to inflammatory hypercellularity in the glomeruli, leading to kidney damage
- Avacopan targets C5aR, which blocks the effects of C5a

Current Treatments

No Approved Therapies

- Non-specific treatment approaches include blood pressure control and broad immunosuppression

FDA and EMA Orphan Drug Designations

See J.J.E. Koopman et al, Netherlands Journal of Medicine 2019;
https://www.kidney.org/sites/default/files/C3G_EL-PFDD_VoP-Report_3-29-18.pdf
https://rarediseases.org/rare-diseases/c3-glomerulopathy-dense-deposit-disease-and-c3-glomerulonephritis/

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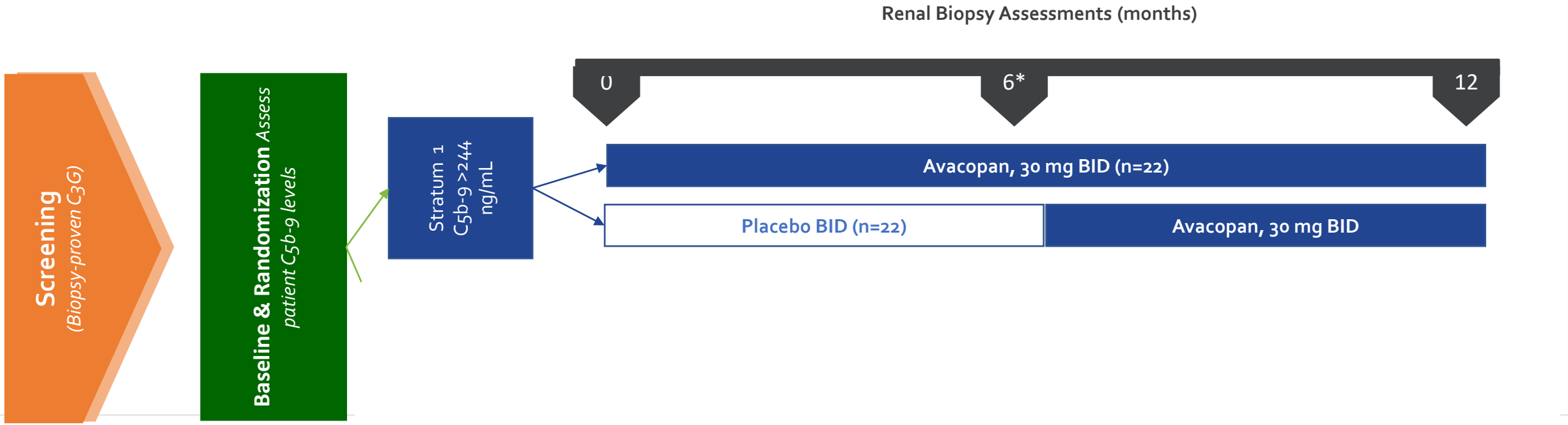
C3 Glomerulopathy: ACCOLADE Trial Design

ACCOLADE

Original Design and Primary Patient Population



Study Design

- Randomized (1:1), double-blind, placebo controlled clinical trial in patients with a biopsy confirmed diagnosis of C3G
- Originally only C5b-9 level >244 ng/mL (primary patient population); later added second stratum C5b-9 level ≤244 ng/mL

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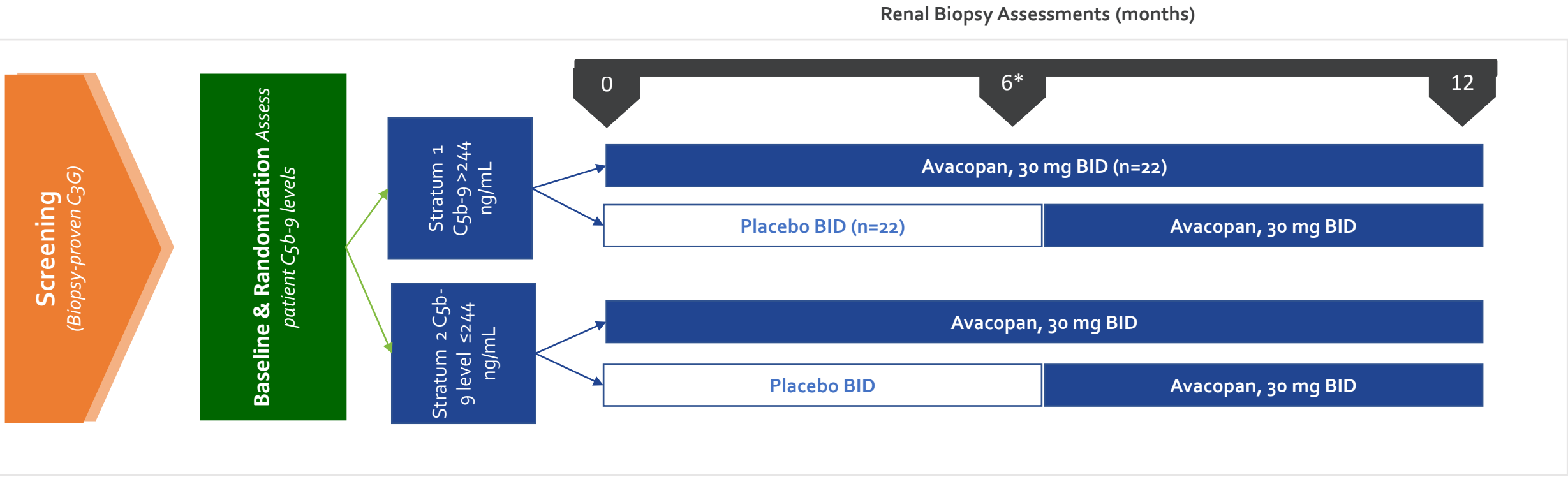
C3 Glomerulopathy: ACCOLADE Trial Design



New Observations Resulting from ACCOLADE Trial Design:

- Higher C5b-9 stratum correlated with increased rate of biopsy-proven C3G
- By Contrast lower (normal) C5b-9 only verified by biopsy ~1/5 of subjects
- But no obvious difference in treatment effect by stratum

Primary Patient Population Disposition and Baseline Characteristics (Elevated C5b-9)

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Characteristic	Placebo N = 21 subjects	Avacopan N = 19 subjects	Total N = 40
C3G	19 (90.5%)	18 (94.7%)	37 (92.5%)
DDD	2 (9.5%)	1 (5.3%)	3 (7.5%)
History of Kidney Transplant	1 (4.8%)	1 (5.3%)	2 (5.0%)
Mean duration of C3G (months), calculated from the time of first diagnosis based on renal biopsy	52.1 months	48.7 months	50.5 months
Mean eGFR ml/min/1.73 m^2	82.19	73.58	78.10
Mean UPCR (g/g)	3.29	4.43	3.83
UPCR g/g > 1 g/g	15 (71.4%)	16 (84.2%)	31 (77.5%)
UPCR g/g < = 1 g/g	6 (28.6%)	3 (15.8%)	9 (22.5%)
Mean Urinary MCP-1: creatinine ratio pg/mg creatinine	768.28	1472.14	1101.69
Mean BMI	24.15	24.89	24.50

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Combined Patient Population Disposition and Baseline Characteristics (Elevated and Normal C5b-9)

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Characteristic	Placebo N = 26 subjects	Avacopan N = 26 subjects	Total N = 52
C3G	22 (84.6%)	22 (84.6%)	44 (84.6%)
DDD	4 (15.4%)	3 (11.5%)	7 (13.5%)
History of kidney transplant	1 (3.8%)	1 (3.8%)	2 (3.8%)
C5b-9 > 244 ng/ml	21 (80.8%)	19 (73.1%)	40 (76.9%)
C5b-9 < 244 ng/ml	5 (19.2%)	7 (26.9%)	12 (24.0%)
Mean duration of C3G (months), calculated from the time of first diagnosis based on renal biopsy	46.5 months	49.3 months	47.9 months
Mean eGFR ml/min/1.73 m2	73.42	76.27	74.85
Mean UPCR (g/g)	2.92	3.84	3.38
Mean UPCR g/g > 1 g/g	18 (69.2%)	20 (76.9%)	38 (73.1)
Mean UPCR g/g < = 1 g/g	8 (30.8%)	6 (23.1%)	14 (26.9%)
Mean Urinary MCP-1: creatinine ratio pg/mg creatinine	756.14	1263.62	1014.38
Mean BMI	24.39	26.20	24.57

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ACCOLADE Trial Endpoints

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ACCOLADE believed to be the largest randomized blinded controlled trial in C3G

- Primary endpoint data based on renal biopsy compared between baseline and 26 weeks of blinded treatment
  - Difference in the biopsy-based C3G Histologic Index of Disease Activity between avacopan group and placebo group
- Secondary endpoints:
  - Renal function as assessed by change from baseline in estimated Glomerular Filtration Rate (eGFR)
  - Change from baseline in Urinary Protein to Creatinine ratio (proteinuria)
  - Change from baseline in Urinary MCP1 to creatinine ratio (MCP-1 is a marker of kidney inflammation)
  - Change from baseline in biopsy-based C3G Histologic Index of Disease Chronicity
    - Chronicity score mainly measures rate of progression of fibrosis in the kidney

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Primary Endpoint: C3G Histologic Score for Disease Activity Percent Change from Baseline to Week 26 (mean ± SEM)

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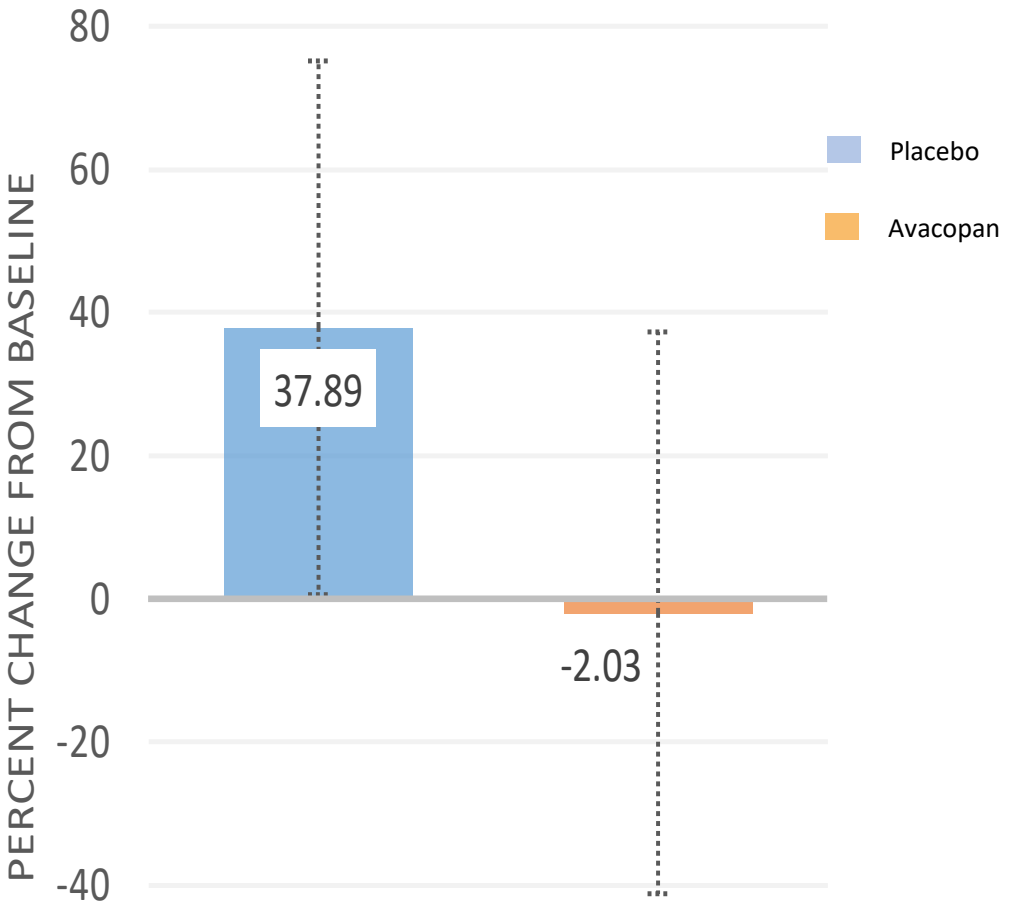
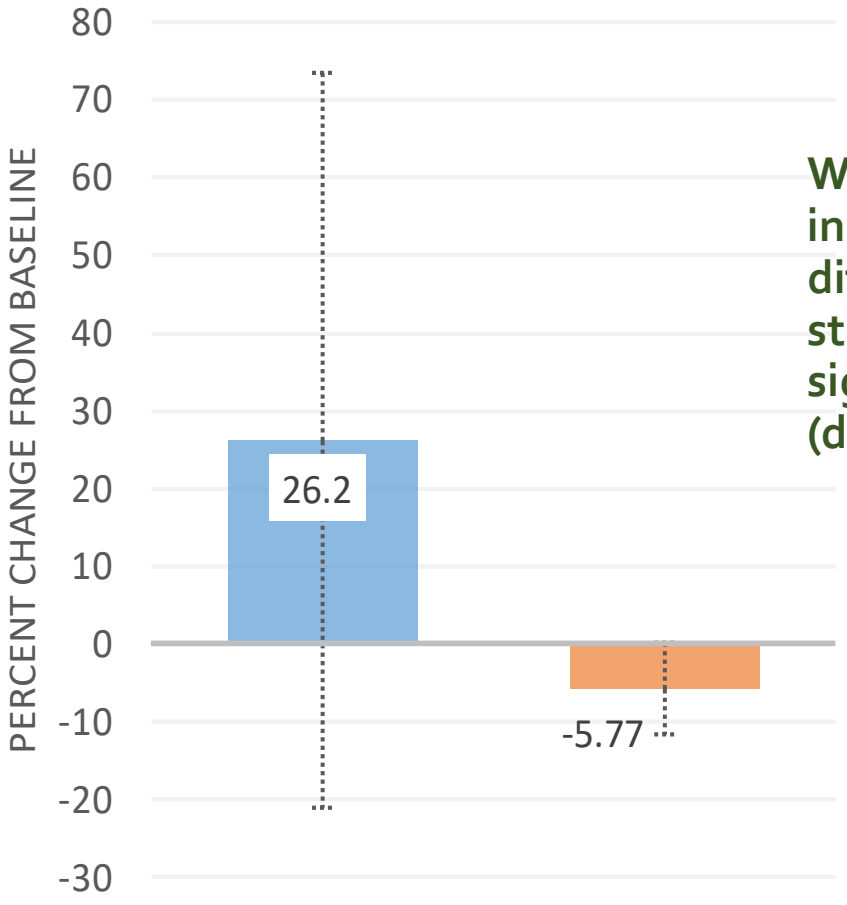
Elevated C5b-9 Stratum



Both C5b-9 Stratum Combined



While mean change indicates beneficial difference, no statistically significant separation (due to variability)

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Considering Endpoints in C3G

- Ultra-rare disorder. No Approved therapy with no standard regulatory path
- Biopsy-based C3G Histologic Index: *Activity* Score or *Chronicity* Score*
  - Biopsy has the advantage of 'a direct look' at the kidney but disadvantage of sampling only ~ 10-20 glomeruli out of the total ~1,000,000 glomeruli in the kidney
  - For C3G Histology Index -- each 1-unit increase in total chronicity score at baseline increased the risk for doubling of creatinine, progression to CKD stage 5, ESRD, transplantation, or death by 59% ($P < 0.001$).
  - In fact, a 1-unit increase in baseline chronicity score had 3 times greater effect on long term outcome than 1-unit increase in the activity score at baseline. *[Note: this is using the baseline chronicity score to predict the long outcome, not a direct measure response to drug treatment.]*
    - Chronicity Score thought to be the best prognosticator of delaying ESRD by many.
- Estimated glomerular filtration rate (eGFR)
  - Advantage – a functional readout *of all the glomeruli* in the kidney
  - Pre-specified secondary endpoint, though advice suggested seeing an effect minimal due to small N, short duration
  - Pre-ADVOCATE trial results, eGFR generally measured in terms of smaller rate of decline, not improvement
  - Not aware of precedent for significant eGFR improvement from a blinded study in C3G

* *Bomback AS, et al. C3 glomerulonephritis and dense deposit disease share a similar disease course in a large United States cohort of patients with C3 glomerulopathy. Kidney Int. 2018*

C3G Histologic Score for Chronicity

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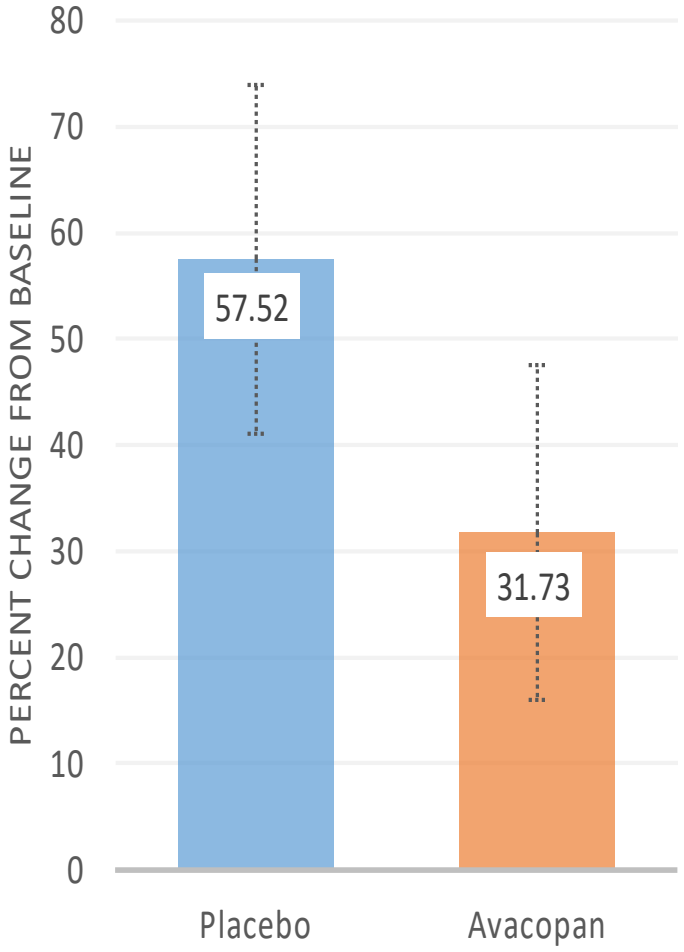
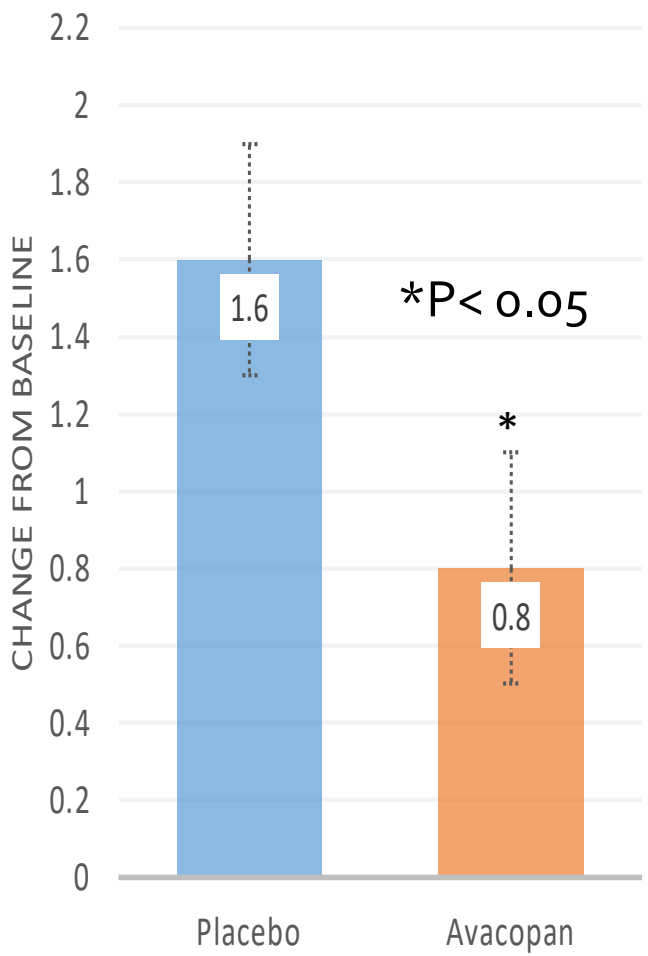
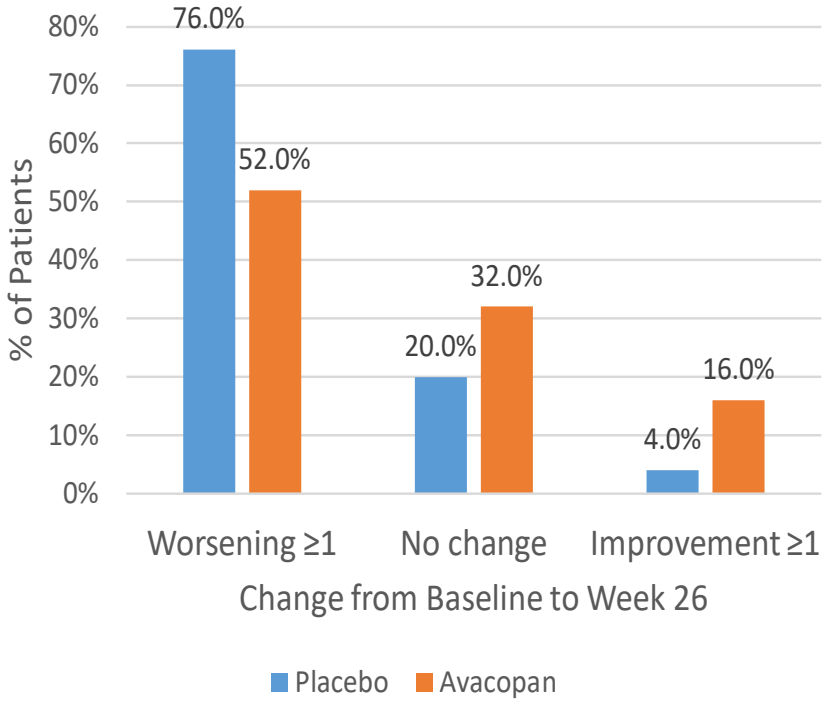
Evidence for Slowing of Progression







C3G Histologic Score for Chronicity; Percentage Change and Unit from Baseline to Week 26, mean ± SEM; Both C5b-9 Strata

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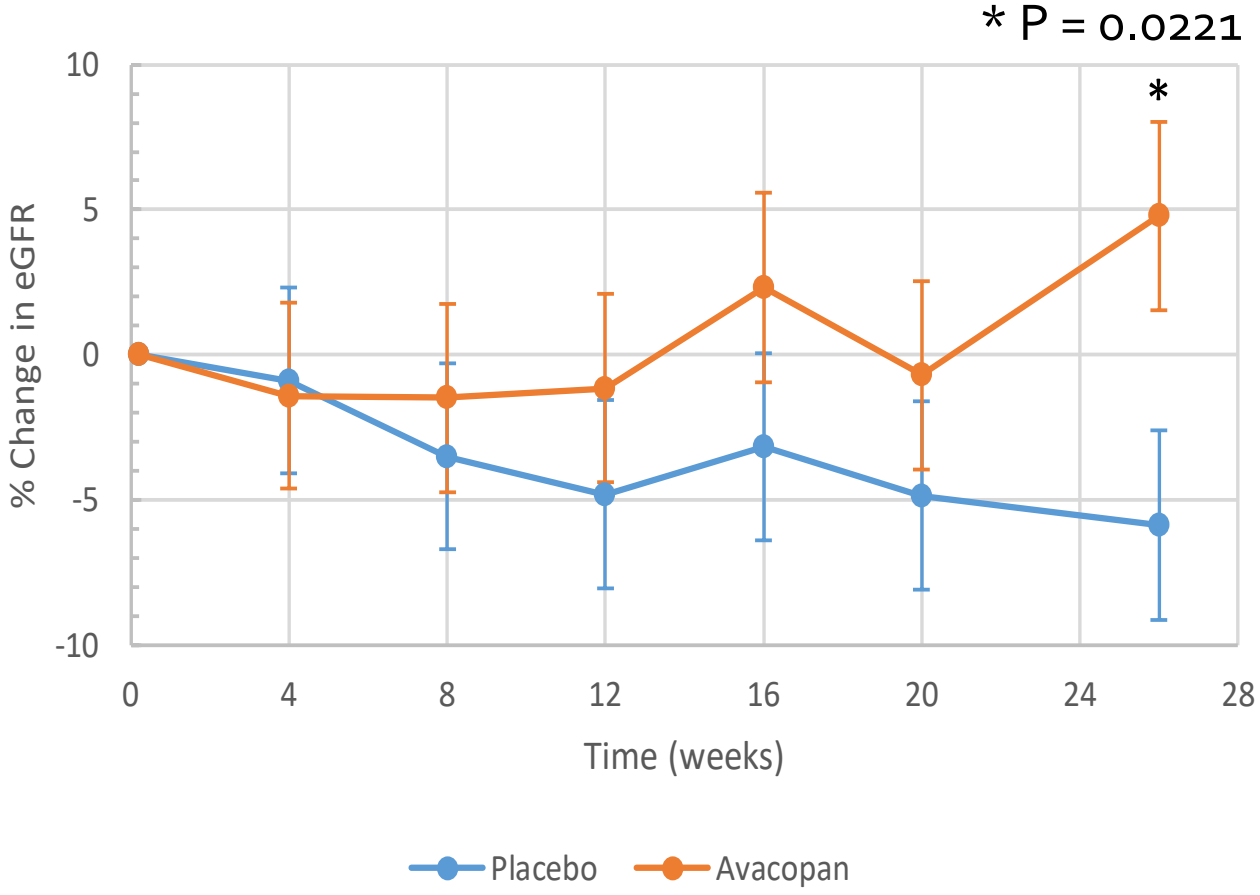
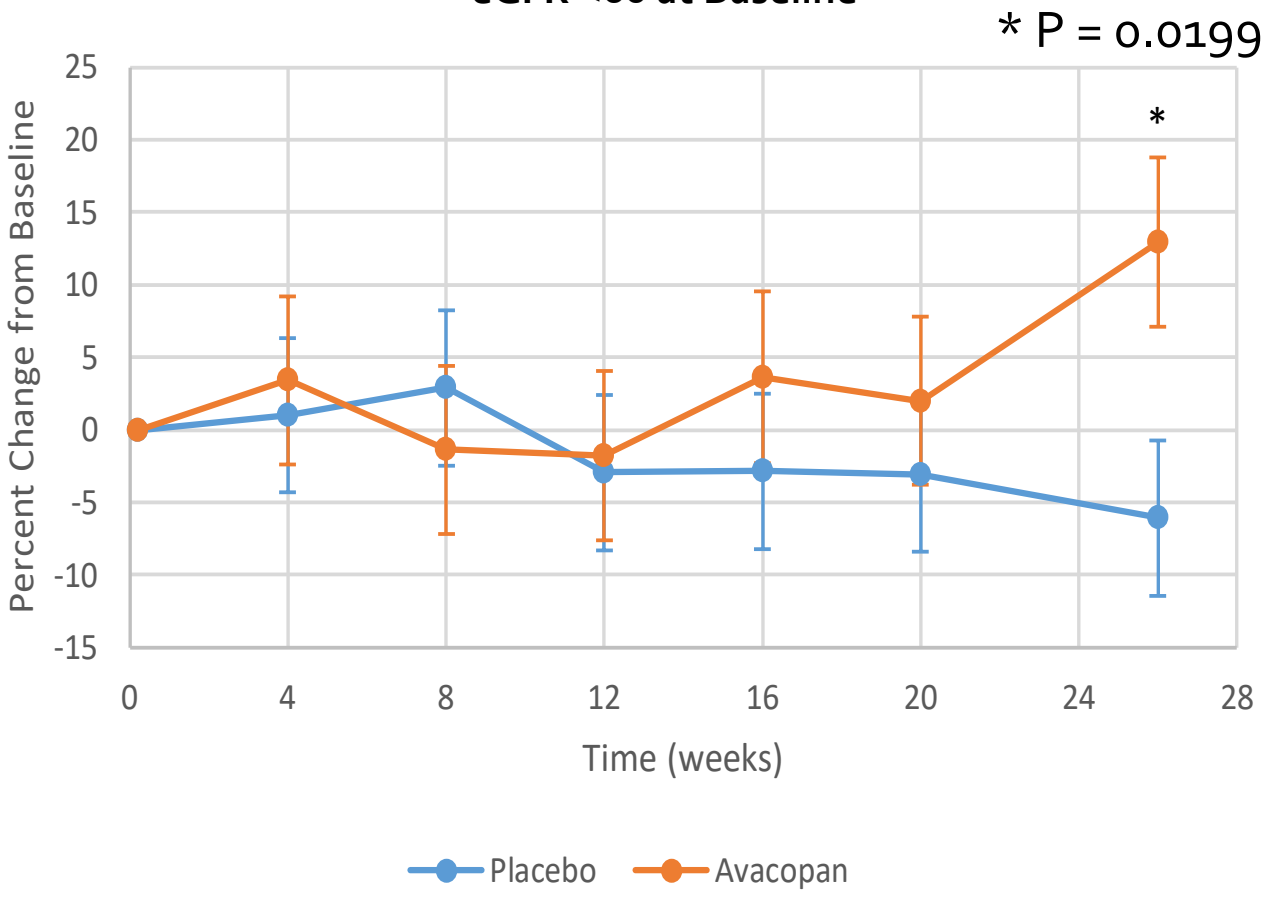
Avacopan Demonstrates Significant Improvement in Renal Function

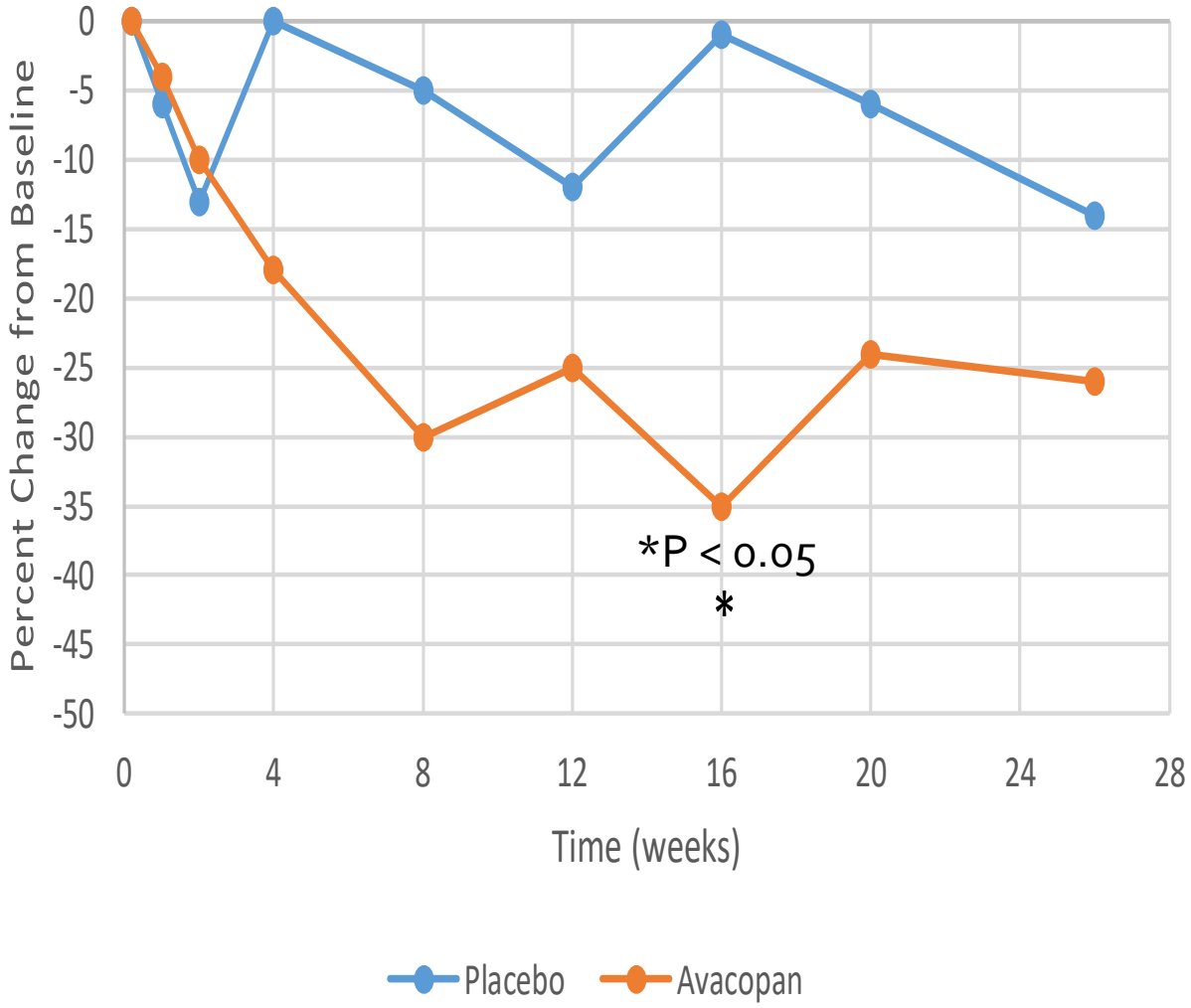
Improvement from Baseline in eGFR in all Patients

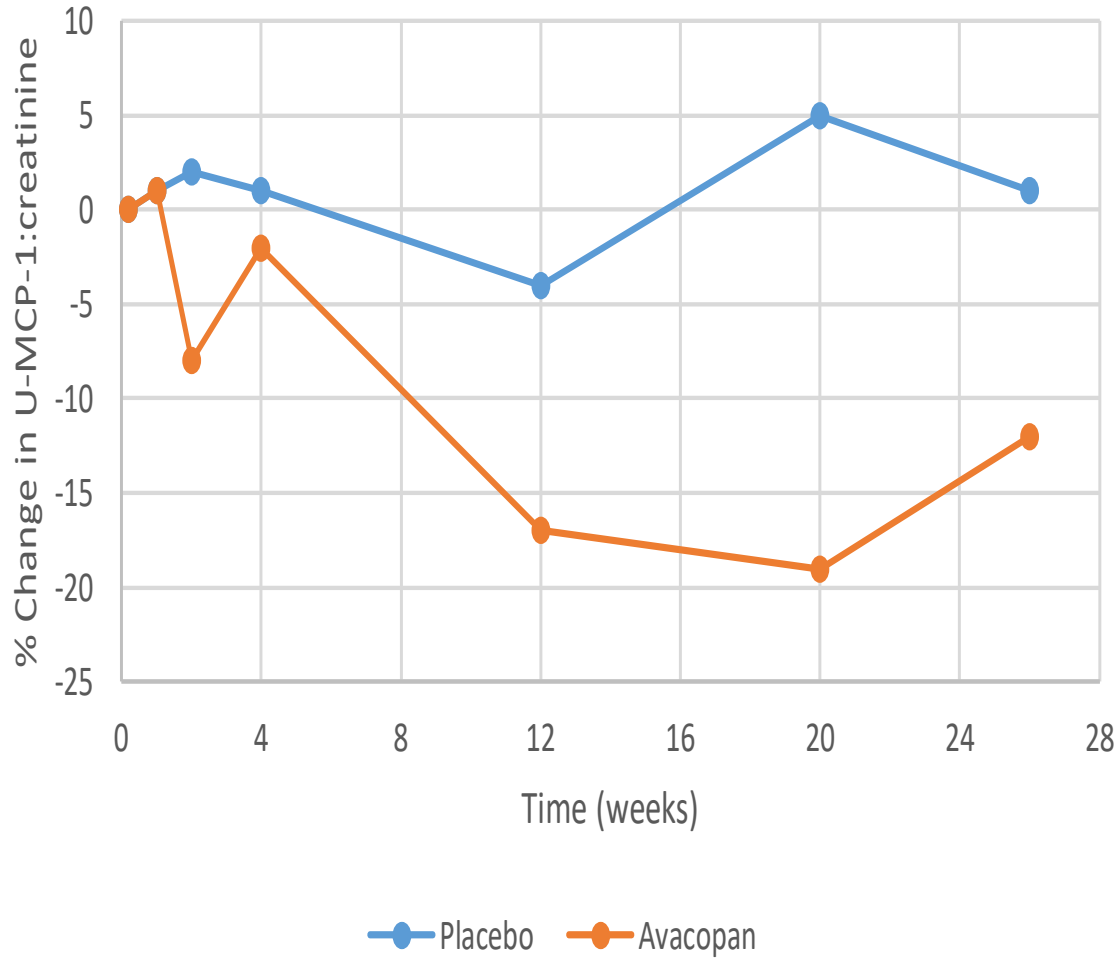


Improvement from Baseline in eGFR in Patients with eGFR <60 at Baseline



Urinary Protein:Creatinine Ratio and Urinary MCP-1 :Creatinine Ratio Percent Change from Baseline





ACCOLADE and Avacopan

Safety profile of avacopan in C3G unremarkable -

- Adverse events incidence similar between the 2 groups
- AE's associated generally to underlying C3G condition or background medications
- 1 subject in each group discontinued for AE
- Serious Adverse events incidence (SAE's) – 3 each group (~10%) ; no obvious pattern
- No deaths in study

Next Steps in U.S.: Avacopan in C3G

- This is an ultra rare condition with no approved therapy
- Declining kidney function is the central issue in C3G
- Evidence that avacopan enhances kidney function in C3G
- Precedent for approvals in chronic kidney diseases based on eGFR
- We will present ACCOLADE data to FDA
- Explore utility of avacopan in this indication based on the data
- No additional clinical development contemplated at present

Thank You

December 21, 2020

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