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ASSIST Study Design:
A Randomized, Double-blind, Placebo-controlled, Crossover Study of Atrasentan* in Patients with IgA Nephropathy on SGLT2i

Jonathan Barratt, MD
University of Leicester, Leicester, UK

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***Atrasentan is an investigational drug that has not been approved by regulatory authorities.**

The 17th International Symposium on IgA Nephropathy

COI disclosure

presenter: Dana V. Rizk, University of Alabama at Birmingham

I have the following relationships to disclose any COI for this research presentation within the period of 36 months:

Employment/Leadership position/Advisory role:	**Chinook Therapeutics; Novartis**
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Stock ownership or options, Patent royalties/licensing fees, Honoraria (e.g. lecture fees), Manuscript fees, Subsidies or Donations, Endowed departments by commercial entities, Travel fees, gifts, and others: **None**

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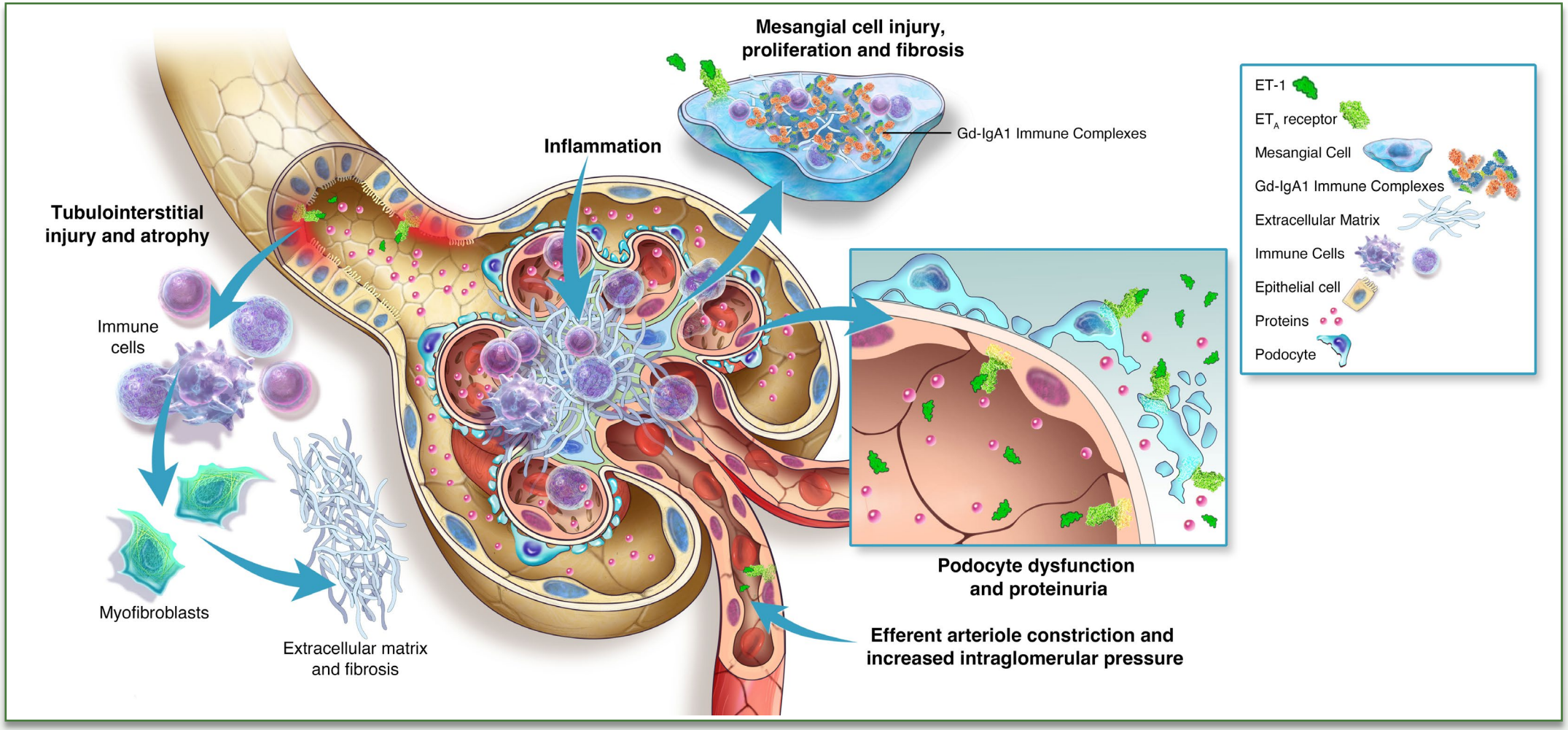
Endothelin-A Receptor Activation Drives the Hallmarks of IgA Nephropathy Progression through Multiple Mechanisms[1,2]



1. Lai KN, et al. *Nat Rev Dis Primers*. 2016;2(1):16001. 2. Kohan DE, et al. *Kidney Int*. 2014;86(5):896-904; Kohan et al, Kidney Int Rep, 2023.
ET-1, endothelin-1; ET$_A$, endothelin-A; Gd-IgA1, galactose deficient IgA1; IgA, immunoglobulin A

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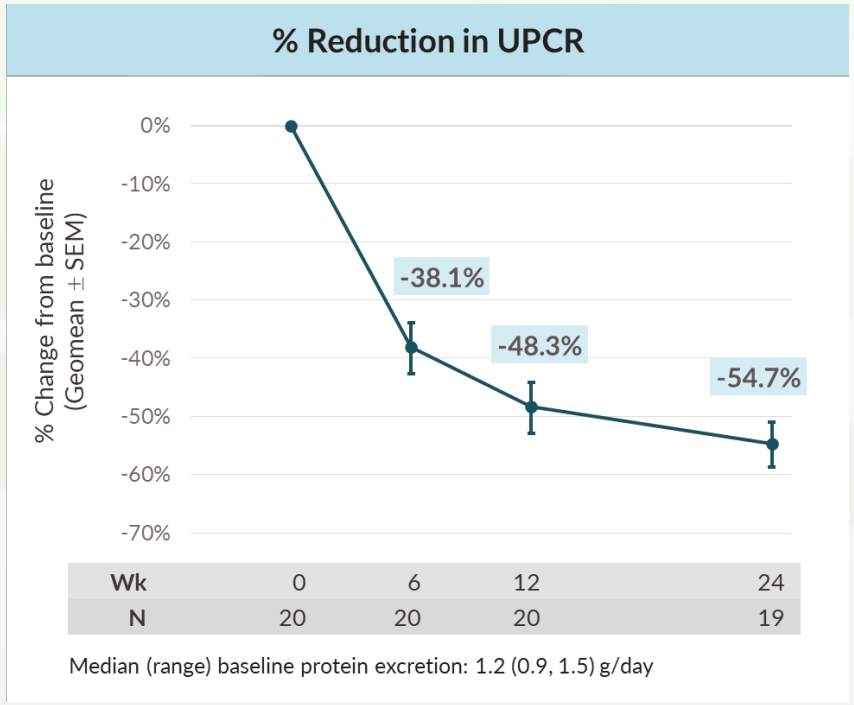
Atrasenan*

Atrasentan is a potent and selective ET_A antagonist that has potential to reduce proteinuria and preserve kidney function in IgAN

- Interim results of a phase 2, open-label study in patients with IgAN (AFFINITY, NCT04573920) demonstrated that atrasentan was generally well tolerated and resulted in clinically meaningful and sustained proteinuria reductions in patients receiving a maximally tolerated and optimized dose of a RAS inhibitor (Rastogi et al, 2022, ASN Kidney Week).



* Atrasentan is an investigational drug that has not been approved by regulatory authorities. Efficacy and safety have not been established. There is no guarantee that it will become commercially available for the use(s) under investigation.

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Sodium glucose cotransporter-2 inhibitors (SGLT2is)

SGLT2is are approved in the U.S. for use in adults with CKD at risk of kidney disease progression, including IgAN.[1,2]

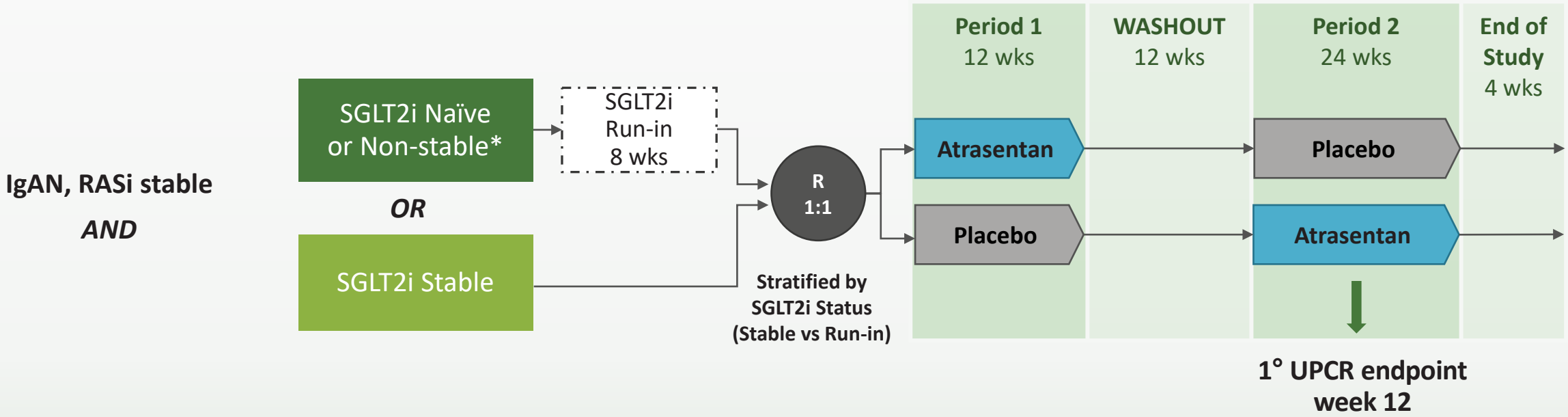
- In a post-hoc analysis of the global phase 3 SONAR study in patients with type 2 diabetes and CKD, 6-week treatment with atrasentan and SGLT2i in a small number of patients (n=14) further decreased albuminuria and decreased body weight, a surrogate for fluid retention, vs. atrasentan alone.[3]

1. Jafar et al, 2021 Lancet; 2. Wheeler et al, 2021, Kidney Int;11. Heerspink et al, 2021, Kidney Intl.

ASSIST Study Design

Study Objective

ASSIST™ (NCT05834738) is a randomized, double-blind, placebo-controlled, crossover study to evaluate the safety and efficacy of atrasentan vs. placebo in adults with IgAN on stable SGLT2i and RASi with persistent proteinuria.



** Subjects who have not been on a stable dose of SGLT2i prior to study entry are required to complete the 8-week run-in period.*

ASSIST Key Inclusion Criteria

All patients	• Adults with biopsy-proven IgAN, not due to secondary causes • Receiving max tolerated and stable RASi ≥ 12 weeks prior to screening • eGFR ≥ 30 mL/min/1.73 m^2 (CKD-EPI) at screening
SGLT2i stable	• Receiving SGLT2i at stable dose ≥ 8 weeks prior to screening • 24-hour total urine protein > 0.5 g/d at screening
SGLT2i naïve or non-stable	• 24-hour total urine protein > 0.85 g/d at screening • Complete 8-week run-in period on a stable and well tolerated dose of an SGLT2i • After run-in: ➢ 24-hour total urine protein > 0.5 g/d confirmed at end of run-in ➢ eGFR of ≥ 30 mL/min/1.73 m^2 (CKD-EPI) at end of run-in

ASSIST Study Endpoints

ASSIST™

Primary	Change in proteinuria (UPCR from a 24-hour urine collection) from baseline to week 12
Key secondary	In Treatment Period 2, the change in proteinuria (UPCR from a 24 hr urine collection) from baseline to week 24
Safety	Type, incidence, severity and relatedness of adverse events (AEs) and serious AEs
Exploratory	In Treatment Period 2, change in eGFR from baseline to week 24

Summary

Atrasentan, a potent and selective ET_A antagonist, has potential to reduce proteinuria and preserve kidney function in IgAN

The ASSIST crossover study will evaluate the safety and efficacy of atrasentan in combination with SGLT2i in patients with IgAN with persistent proteinuria despite maximized RASi

The ASSIST study is currently enrolling

For more information, scan QR or visit
https://clinicaltrials.gov/ct2/show/NCT05834738