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Sparsentan (SPAR) Added to Stable Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2is) in Adults With IgA Nephropathy (IgAN) in the Phase 2 SPARTACUS Trial

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INTRODUCTION

- SPAR, a non-immunosuppressive, dual endothelin and angiotensin receptor antagonist (DEARA),[1,2] showed sustained albuminuria reduction and kidney function preservation in patients with IgAN in PROTECT[2]
- A subgroup analysis from DAPA-CKD and EMPA-KIDNEY independently showed that SGLT2is also reduced albuminuria and kidney disease progression in patients with IgAN[3,4]

AIM

- To report the final analysis of the phase 2 SPARTACUS trial (NCT05856760), which evaluated the efficacy and safety of replacing RASi with SPAR in adults with IgAN receiving stable SGLT2i therapy

METHOD

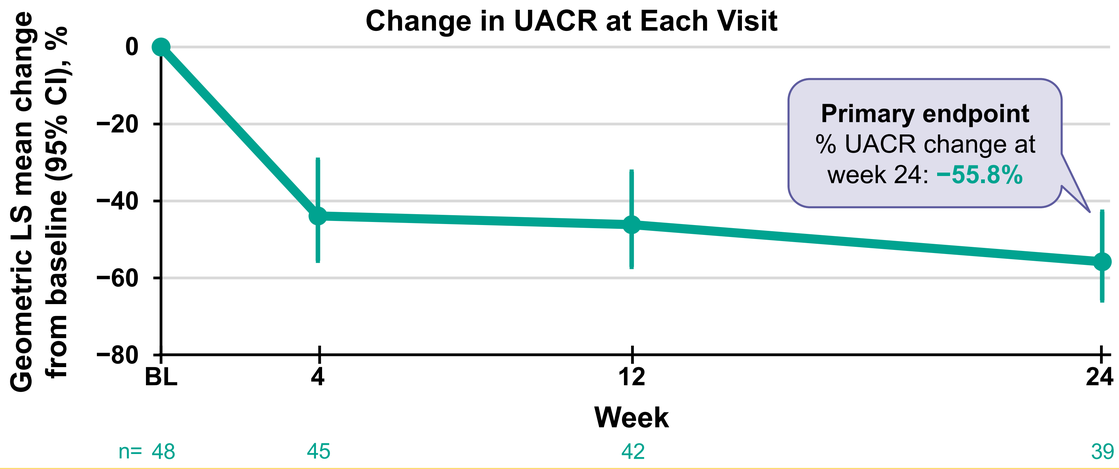
Eligibility criteria:
Biopsy-proven IgAN; UACR ≥0.3 g/g
eGFR ≥25 mL/min/1.73 m^2
Stable SGLT2i ≥12 weeks
Max tolerated dose RASi ≥12 weeks

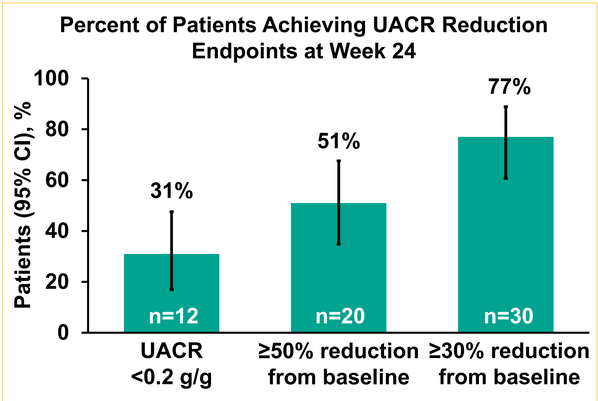
N=48 adults with IgAN

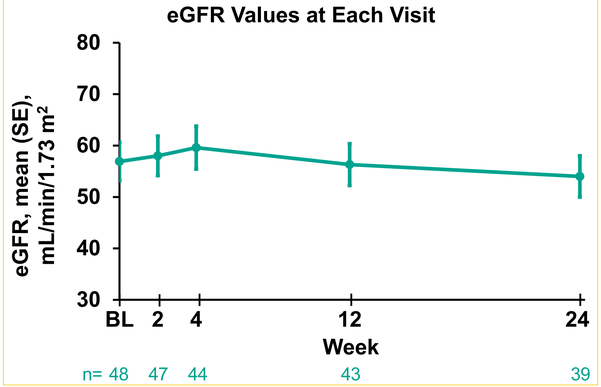
SGLT2i/SPAR treatment:
Continue stable SGLT2i; discontinue RASi
SPAR: 200 mg/d (first 2 weeks); 400 mg/d up to 24 weeks

Endpoints:
Change from baseline in UACR at week 24
UACR reduction thresholds
Change in UACR, UPCR, eGFR, and BP
Adverse events

RESULTS







- Thirty (63%) patients experienced a TEAE; the most common was hypotension (15%)
- One patient each discontinued SPAR treatment due to a TEAE of vertigo, hypotension, peripheral edema, and Henoch-Schönlein purpura
- No patients experienced abnormal liver function test results >3 × the upper limit of normal

CONCLUSIONS

- In patients with IgAN receiving SGLT2i therapy, replacing maximally tolerated RASi with SPAR resulted in rapid and sustained albuminuria reduction, suggesting a potential to further decrease the risk of kidney disease progression
- Nearly one-third of patients achieved UACR <0.2 g/g
- SPAR combined with an SGLT2i is generally well tolerated, with no unexpected safety signals

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ABBREVIATIONS

BL, baseline; BP, blood pressure; DEARA, dual endothelin and angiotensin receptor antagonist; eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; LS, least squares; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose cotransporter-2 inhibitor; SPAR, sparsentan; TEAE, treatment-emergent adverse event; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

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