INTRODUCTION

• People of East Asian ancestry have the highest likelihood of all race categories to progress to kidney failure as a result of IgAN.1

• Nefecon is a novel, oral, targeted-release bissudoformide formulation specifically designed to treat IgAN by acting locally in the distal ileum2

• Nefecon has received full FDA approval to reduce the loss of kidney function in adults with primary IgAN who are at risk for disease progression, irrespective of proteinuria levels, whereas the EMA indication requires patients to have UPCR ≥1.5 g/g.

• In the interim analysis of the Phase 3 NefIgArd trial, treatment with Nefecon 16 mg/day for 9 months resulted in a significant reduction in UPCR and significant eGFR benefit compared with placebo at 3 months post treatment3

– The observed benefits were maintained over a further 12-month off-treatment period. 4

– Here, we present the full 2-year NefIgArd trial data to assess responses to Nefecon treatment in patients identifying as Asian or White.

METHODS

• The Phase 3 NefIgArd trial was designed to assess whether 9 months of treatment with Nefecon 16 mg/day leads to a significant reduction in kidney function decline compared with placebo over 2 years; the trial comprised 9 months of treatment and 15 months of observational follow-up.

• Inclusion criteria included patients aged ≥18 years with biopsy-proven primary IgAN; UPCR ≥0.8 g/g or proteinuria ≥21 μg/min/1.73 m²; estimated glomerular filtration rate (eGFR) 50 to 90 mL/min/1.73 m².

• Exclusion criteria were poorly controlled diabetes or blood pressure (≥140/90 mmHg); any secondary form of IgAN or non-IgAN glomerulonephritis; systemic diseases that may cause mesangial IgA deposition; and having undergone a kidney transplant.

• The analysis set included 64 White and 60 Asian patients, although race categories were defined based on those specified by the FDA.

• Outcomes of the subgroup race analysis included time-weighted eGFR average over 2 years, UPCR in 30% reduction in eGFR or kidney failure, microhematuria, and safety outcomes.

RESULTS

• Nefecon significantly diminished from placebo in the time-weighted average change in eGFR over 2 years for Asian (p=0.0028*) and White (p=0.0001*) patients, with a favorable estimated average mean change in eGFR over 2 years of 5.5 mL/min/1.73 m² in Asian patients and 4.8 mL/min/1.73 m² in White patients (Figure 1).

• Nefecon showed a significant reduction in UPCR versus placebo at 9 months in both race groups (Asian patients: 23.4%, p=0.0472*; White patients: 32.0%, p=0.0001*), and at 24 months in White patients (Asian patients: 26.7%, p=0.0104*; White patients: 32.1%, p=0.0003*) (Figure 2).

• The time to a confirmed 10% reduction in eGFR or kidney failure event was significantly delayed with Nefecon versus placebo, irrespective of race (Asian patients: HR 0.32, 95% CI 1.12, 0.77; p=0.0035); and White patients (HR 0.48, 95% CI 0.28, 0.83; p=0.0046*) (Figure 3).

• Nefecon significantly reduced the likelihood of microhematuria in both Asian (OR 3.5, 95% CI 1.2, 11.7; p=0.003) and White patients (OR 2.3, 95% CI 1.3, 3.9; p=0.003) (Figure 4).

• Rates of TEAEs were broadly similar across groups, although with a slightly higher overall rate of TEAEs in Asian patients (Table 1).

CONCLUSIONS

• The 2-year full NefIgArd trial demonstrated that treatment with Nefecon 16 mg/day for 9 months provided a statistically significant and clinically relevant preservation of eGFR compared with placebo5.

– Nefecon achieved a durable reduction in proteinuria when evaluated 15 months after end of treatment6

– Nefecon was well tolerated, with a safety profile as expected for a locally acting oral bissudoformide product.

– The results from this subgroup race analysis indicate that, although the number of patients identifying as Asian was considerably lower than the number identifying as White, Nefecon was equally effective and well tolerated, irrespective of race.

REFERENCES


ABBREVIATIONS

AE, adverse event; CI, confidence interval; eGFR, estimated glomerular filtration rate; DAK, European Medicine Agency; FDA, US Food and Drug Administration; HR, hazard ratio; IgA, immunoglobulin A; IgG, immunoglobulin G; IgAN nephropathy; OR, odds ratio; RAS, renin-angiotensin system; SmPC, summary of product characteristics; UPCR, urine protein/creatinine ratio.

DISCLOSURES

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One-sided p-values. Data analyzed using ratios of geometric mean square means; *patient was defined as having hematuria if the urine dipstick returned a result of negative or trace. Patients without at least two valid results from 12 months onwards were excluded from the analysis. There was no overlap reported during treatment with Nefecon for any infection that was considered unrelated to study treatment.

Figure 1: eGFR stratified by race and treatment

Figure 2: UPCR stratified by race and treatment

Table 1: TEAEs and AEs during the 9-month treatment period, stratified by race and treatment