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New Novartis Fabhalta® (iptacopan) data show clinically meaningful and statistically significant proteinuria reduction of 38.3% versus placebo for patients with IgA nephropathy (IgAN)

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- APPLAUSE-IgAN is first and only Phase III study to demonstrate significant proteinuria reduction by targeting the complement system in patients with IgAN[1]
- IgAN is a heterogeneous, progressive, rare kidney disease and is a major cause of chronic kidney disease worldwide[2]; complement activation is a key driver of glomerular inflammation in IgAN[3,4]
- There is a need for effective, targeted therapies for IgAN[2,5]; up to 30% of patients with persistent proteinuria (≥1 g/day) may progress to kidney failure within 10 years, requiring maintenance dialysis and/or kidney transplantation[6]
- Novartis continues to advance broad renal portfolio in late-stage development, exploring the potential to slow disease progression and extend dialysis-free life

EAST HANOVER, N.J., April 15, 2024 -- Novartis today presented results from a pre-specified interim analysis of the Phase III APPLAUSE-IgAN study of Fabhalta® (iptacopan), an investigational Factor B inhibitor of the alternative complement pathway, in patients with IgA nephropathy (IgAN)[1]. In the analysis, patients treated with Fabhalta achieved a 38.3% (p<0.0001) proteinuria reduction (as measured by 24-hour urine protein to creatinine ratio [UPCR]) at 9 months when compared to placebo on top of supportive care[1].

Proteinuria reduction is an increasingly recognized surrogate marker correlating with progression to kidney failure and has been used as an endpoint in IgAN clinical trials to support accelerated approvals[7]. The study also showed that Fabhalta was well tolerated with a favorable safety profile consistent with previously reported data[1,8]. Results were presented today during a late-breaking clinical trials session at the World Congress of Nephrology (WCN) in Buenos Aires, Argentina[1].

"In IgAN, part of the immune system called the alternative complement pathway can become overly activated in the kidneys, which causes an inflammatory response, leading to progressive kidney damage and gradual loss of kidney function. The loss of kidney function, together with potential side effects of IgAN treatments available until recently, significantly impact patients' lives," said Professor Dana Rizk, Investigator and APPLAUSE-IgAN Steering Committee Member and professor in the UAB Division of Nephrology. "Fabhalta is the first potential treatment for IgAN that specifically targets the alternative complement pathway."

This pre-specified interim analysis included 250 patients for the efficacy analysis and 443 for the safety analysis[1]. The APPLAUSE-IgAN study continues in a double-blind fashion, and therefore only limited interim analysis results can be presented[9,10]. Submission for possible accelerated approval to the FDA was accepted and has received priority review. The primary endpoint evaluating Fabhalta's ability to slow IgAN progression by measuring the annualized total estimated glomerular filtration rate (eGFR) slope over 24 months is expected at study completion in 2025[9,10].

"IgAN progresses over many years, and patients' needs may evolve such that different therapies may be best used at different times," said David Soergel, M.D., Global Head, Cardiovascular, Renal and Metabolism Development Unit, Novartis. "Our renal pipeline includes medicines with a variety of mechanisms which may allow them to be targeted to patients based on their clinical characteristics."

Other data presented at WCN include IgAN and C3 glomerulopathy (C3G) real-world studies. Novartis will be presenting further data from the renal portfolio at future medical meetings.

About APPLAUSE-IgAN

APPLAUSE-IgAN (NCT04578834) is a Phase III multicenter, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of twice-daily oral Fabhalta (200 mg) in 518 adult primary IgAN patients[9,10].

The two primary endpoints of the study for the interim and final analysis, respectively, are proteinuria reduction at 9 months as measured by UPCR, and the annualized total eGFR slope over 24 months[9,10]. At the time of final analysis, the following secondary endpoints will also be assessed: proportion of participants reaching UPCR <1 g/g without receiving corticosteroids/immunosuppressants or other newly approved drugs or initiating new background therapy for treatment of IgAN or initiating kidney replacement therapy (KRT), time from randomization to first occurrence of composite kidney failure endpoint event (reaching either sustained ≥30% decline in eGFR relative to baseline or sustained eGFR <15 mL/min/1.73 m^2 or maintenance dialysis or receipt of kidney transplant or death from kidney failure), change from baseline to 9 months in the fatigue scale measured by the Functional Assessment Of Chronic Illness Therapy-Fatigue questionnaire[9,10].

The main study population enrolled patients with an eGFR ≥30 mL/min/1.73 m^2 and UPCR ≥1 g/g at baseline[9,10]. In addition, a smaller cohort of patients with severe renal impairment (eGFR 20–30 mL/min/1.73 m^2 at baseline) was also enrolled to provide additional information but will not contribute to the main efficacy analyses[9,10].

About Fabhalta® (iptacopan)

Fabhalta (iptacopan) is an oral, Factor B inhibitor of the alternative complement pathway[1].

Discovered at Novartis, Fabhalta is currently in development for a range of rare diseases including IgAN, C3G, atypical hemolytic uremic syndrome (aHUS), immune complex membranoproliferative glomerulonephritis (IC-MPGN) and lupus nephritis (LN).

Fabhalta was approved by the FDA in December 2023 for the treatment of adults with the rare blood disorder paroxysmal nocturnal hemoglobinuria (PNH) and received a positive opinion from the CHMP of the EMA in March 2024[11,12].

About IgA nephropathy (IgAN)

IgAN is a heterogeneous, progressive, rare kidney disease[2]. Each year, approximately 25 people per million worldwide are newly diagnosed with IgAN[13].

Up to 30% of people who have IgAN with persistent higher levels of proteinuria (≥1 g/day) may progress to kidney failure within 10 years[6]. There is a need for effective, targeted therapies for IgAN that can help slow or prevent progression to kidney failure[2,5,14].

Novartis commitment in renal

At Novartis, our journey in nephrology began more than 40 years ago when the development and introduction of cyclosporine helped reimagine the field of transplantation and immunosuppression. We continue today with the same bold ambition to transform the lives of people living with kidney diseases.

Through our renal portfolio, we are exploring potential therapeutic options to address the current unmet needs of people living with rare kidney diseases, including IgAN, C3G, aHUS, IC-MPGN and LN. New and innovative treatment options that target the underlying causes of rare kidney diseases may slow disease progression and help people live longer without the need for infusions, dialysis or transplantation.

IgAN is a heterogeneous disease presenting with a variety of clinical manifestations, phenotypes, and variable speeds of progression[2]. In addition to Fabhalta, Novartis is advancing the development of two other therapies in IgAN with highly differentiated mechanisms of action: atrasentan, an investigational oral endothelin A (ETA) receptor antagonist, and zigakibart, an investigational subcutaneously administered anti-APRIL monoclonal antibody, which are both in Phase III development[15,16]. Through our IgAN pipeline, we are committed to creating a portfolio of innovative medicines that improve and extend the lives of people living with kidney disease.

Disclaimer

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About Novartis

Novartis is an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people's lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 250 million people worldwide.

Reimagine medicine with us: Visit us at https://www.novartis.com and https://www.novartis.us and connect with us on LinkedIn, LinkedIn US, Facebook, X/Twitter, X/Twitter US, and Instagram.

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