Rethinking Fabry disease

Facing challenges in diagnosis and renal disease control

Fabry is a rare, chronic, progressive disease with multisystemic involvement[1-4] that can lead to significant renal decline and terminal renal failure.[3] Patients can receive clinical benefit from current therapies, but **disease progression commonly continues to impact the day-to-day quality of life of Fabry patients**—even with standard-of-care management.[5]

It's critical to take a holistic view of the impact of Fabry disease—considering not only the nephrological implications, but also the daily issues and long-term challenges that individual patients may face.

Revealing unmet needs in Fabry disease

The standard of care in Fabry disease hasn't changed for nearly 20 years.[6-10] Current therapies can provide clinical benefit, but significant diagnostic and management challenges remain.[5,6,8-13]

Because of the spectrum of potential manifestations of Fabry disease, patients and physicians continue to encounter unmet needs:

- Time to diagnosis: may be 30 years or more[6]
- Limited treatment options[5,8,10]
- Administration challenges[13]
- Delayed treatment initiation[6,12]
- Continuing daily symptoms despite treatment[5]

Regardless of current management, Fabry disease may eventually progress to severe clinical manifestations—including terminal renal failure.[1,9]

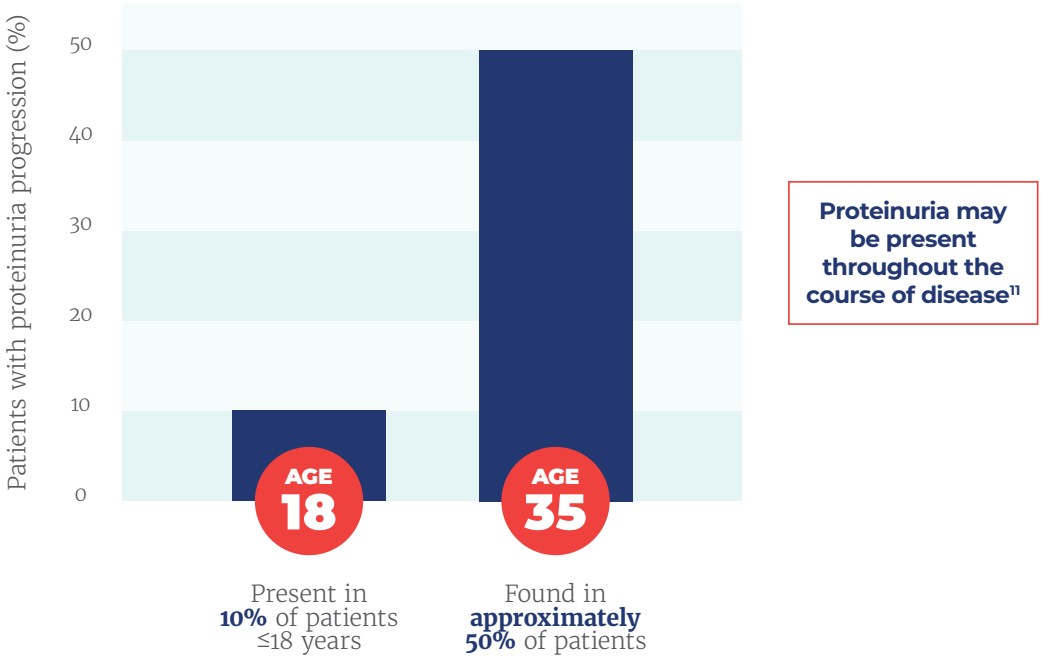
The progressive dangers of renal involvement in Fabry

Patients with Fabry disease may exhibit diverse forms of renal histopathology. Fabry affects all cell types within the kidney, even if patients have minimal proteinuria and a normal estimated glomerular filtration rate (eGFR).[14] Nephrologists will often be able to recognize early and relevant signs of renal disease, thereby helping to ensure early diagnosis and appropriate management, with an optimal clinical outcome for the patient.[3,11,15]

Proteinuria—a telltale sign of renal decline in Fabry

Proteinuria is typically the earliest sign of renal involvement in Fabry disease, found in 10% of pediatric patients—and occurring as young as 2 years of age. By age 35, proteinuria is present in approximately 50% of patients, reinforcing that early intervention is critical in slowing the progression of disease in Fabry.[11]

Proteinuria progression in Fabry disease[11]



eGFR decline and progression to renal failure

Another clinical manifestation of Fabry is decreasing eGFR, progressing to kidney failure over time. This often necessitates clinical intervention by the third or fourth decade of a patient's life. In one trial that assessed the decrease in eGFR, patients who were treated with ERT and whose severity of disease required clinical intervention initiated renal replacement therapy between 33 and 47 years of age.[3]

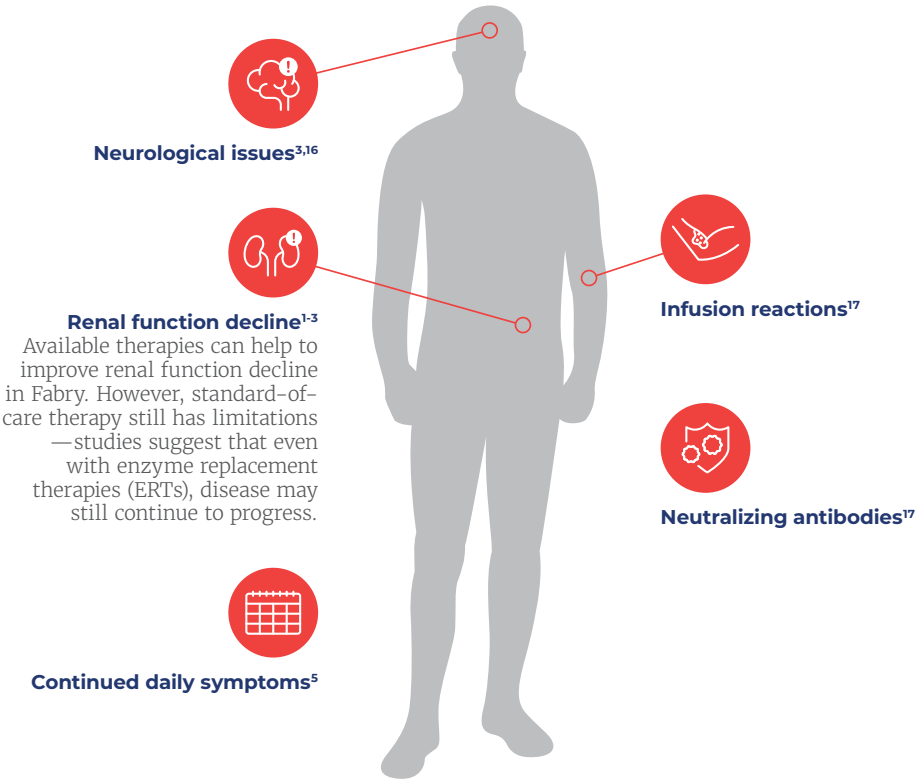
Symptomatic renal complications typically emerge early, in young adulthood. These include chronic kidney disease progression to kidney failure. In fact, according to a review article, **in patients who were not treated with ERT, the mean age at which patients generally reach kidney failure from Fabry disease is 40 years.**[15]

AGE 40 **Mean age of kidney failure[15]**

The hidden impact of Fabry disease—renal involvement and beyond

Even with current, standard-of-care management, patients may still experience a variety of day-to-day symptoms of their disease, particularly pain of differing forms and severity. Patients may even adjust their lives around such symptoms as their disease, including its renal complications, continues to progress.[5]

People being treated for Fabry disease may experience a range of issues, including:



Neurological issues[3,16]

Renal function decline[1-3]
Available therapies can help to improve renal function decline in Fabry. However, standard-of-care therapy still has limitations—studies suggest that even with enzyme replacement therapies (ERTs), disease may still continue to progress.

Continued daily symptoms[5]

Infusion reactions[17]

Neutralizing antibodies[17]

An expert look at existing needs in Fabry disease

Hear from leading nephrologist Dr. Eric Wallace and a panel of healthcare experts as they discuss how far we've come in treating Fabry disease—and what's left to be done

Staying vigilant about the renal warning signs of Fabry disease

Early diagnosis is key

Patients with Fabry often have long delays in their diagnosis and consequent initiation of treatment—sometimes 30 years or more. By the third or fourth decade of life, many patients may already exhibit proteinuria or even reach terminal renal failure.[3,11,15]

Early intervention to maximize clinical benefit[15]

Even with standard-of-care management, Fabry disease may eventually progress to severe clinical manifestations.[1,9] The best way to prevent or slow this progression is by initiating treatment as early as possible.[15]

Awareness and action can create better possibilities for people with Fabry disease.

Keeping these strategies top-of-mind in your practice will optimize care for your patients.

Ongoing and proactive disease management, including elevating the importance of patient-reported outcomes and exploring additional data

Recognition of limitations of current therapies, from quality of life to disease progression

Shortening the time to diagnosis

An eye on the horizon for other strategies

By rethinking our plan today, we may be able to change outcomes tomorrow.

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References: 1. Rombach SM, Smid BE, Bouwman MG, Linthorst GE, Dijkgraaf MGW, Hollak CEM. Long term enzyme replacement therapy for Fabry disease: effectiveness on kidney, heart and brain. *Orphanet J Rare Dis.* 2013;8:47. doi:10.1186/1750-1172-8-47. **2.** Rombach SM, Smid BE, Linthorst GE, Dijkgraaf MGW, Hollak CEM. Natural course of Fabry disease and the effectiveness of enzyme replacement therapy: a systematic review and meta-analysis: effectiveness of ERT in different disease stages. *J Inherit Metab Dis.* 2014;37(3):341-352. doi:10.1007/s10545-014-9677-8. **3.** Weidemann F, Niemann M, Störk S, et al. Long-term outcome of enzyme-replacement therapy in advanced Fabry disease: evidence for disease progression towards serious complications. *J Intern Med.* 2013;274(4):331-341. doi:10.1111/joim.12077. **4.** Desnick RJ, Brady R, Barranger J, et al. Fabry disease, an under-recognized multisystemic disorder: expert recommendations for diagnosis, management, and enzyme replacement therapy. *Ann Intern Med.* 2003;138(4):338-346. doi:10.7326/0003-4819-138-4-200302180-00014. **5.** Morand O, Johnson J, Walter J, et al. Symptoms and quality of life in patients with Fabry disease: results from an international patient survey. *Adv Ther.* 2019;36(10):2866-2880. doi:10.1007/s12325-019-01061-x. **6.** Reisin R, Perrin A, García-Pavía P. Time delays in the diagnosis and treatment of Fabry disease. *Int J Clin Pract.* 2017;71(1). doi: 10.1111/ijcp.12914. **7.** Brady M, Montgomery E, Brennan P, Mohindra R, Sayer JA. Diagnosing Fabry disease—delays and difficulties within discordant siblings. *QJM.* 2015;108(7):585-590. doi:10.1093/qjmed/hct024. **8.** El Dib R, Gomaa H, Carvalho RP, et al. Enzyme replacement therapy for Anderson-Fabry disease. *Cochrane Database Syst Rev.* 2016;7(7):CD006663. doi:10.1002/14651858.CD006663.pub4. **9.** Mehta A, Hughes DA. Fabry Disease. 2002 Aug 5 [Updated 2017 Jan 5]. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews®*. University of Washington, Seattle; 1993-2020. Accessed August 12, 2020. https://www.ncbi.nlm.nih.gov/books/NBK1292/. **10.** Hughes DA, Nicholls K, Shankar SP, et al. Oral pharmacological chaperone migalastat compared with enzyme replacement therapy in Fabry disease: 18-month results from the randomised phase III ATTRACT study. *J Med Genet.* 2017;54(4):288-296. doi:10.1136/jmedgenet-2016-104178. **11.** Hoffmann B, Mayatepek E. Fabry disease—often seen, rarely diagnosed. *Dtsch Arztebl Int.* 2009;106(26):440-447. doi:10.3238/arztebl.2009.0440. **12.** Ramaswami U, Stull ED, Parini R, et al. Measuring patient experiences in Fabry disease: validation of the Fabry-specific Pediatric Health and Pain Questionnaire (FPHPQ). *Health Qual Life Outcomes.* 2012;10:116. doi:10.1186/1477-7525-10-116. **13.** National Fabry Disease Foundation. Fabry disease treatment. Accessed June 30, 2020. https://www.fabrydisease.org/index.php/about-fabry-disease/fabry-disease-treatment. **14.** Waldek S, Feriozzi S. Fabry nephropathy: a review—how can we optimize the management of Fabry nephropathy? *BMC Nephrol.* 2014;15:72. doi:10.1186/1471-2369-15-72. **15.** Ortiz A, Germain DP, Desnick RJ, et al. Fabry disease revisited: management and treatment recommendations for adult patients. *Mol Genet Metab.* 2018;123(4):416-427. doi:10.1016/j.ymgme.2018.02.014. **16.** Schiffmann R, Moore DF. Neurological effects of enzyme replacement therapy in Fabry disease. In: Mehta A, Beck M, Sunder-Plassmann G, eds. *Fabry Disease: Perspectives from 5 Years of FOS.* Oxford PharmaGenesis; 2006. Accessed June 29, 2020. https://www.ncbi.nlm.nih.gov/books/NBK11595/. **17.** Lenders M, Bran E. Effects of enzyme replacement therapy and antidrug antibodies in patients with Fabry disease. *J Am Soc Nephrol.* 2018;29(9):2265-2278. doi:10.1681/ASN.2018030329.

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