

Diane, 31, living with IgAN

# DIANE'S LIFE OUTSIDE YOUR OFFICE CAN BE MORE CHALLENGING THAN IMAGINED

Patient portrayal.

“

I am always worried about how my disease might get worse. The possibility of my kidneys failing is a constant dark cloud over me. I just wish I knew what the future holds.”<sup>1</sup>

Not an actual patient quote. Based on patient insights.

## COULD IT BE IgAN?

**6-month follow-up with nephrologist:**  
worsening back pain and persistent hematuria  
and proteinuria prompt a biopsy<sup>1,2</sup>

### Vital signs<sup>2</sup>

✓ BP (mm Hg): 135/76

### Lab results<sup>2,3</sup>

✓ sCr (mg/dL): 1.1

✓ eGFR (mL/min/1.73 m<sup>2</sup>): 72 (G2)

✓ Proteinuria (g/24 h): 1.7 (A3)

✓ Hematuria: microscopic

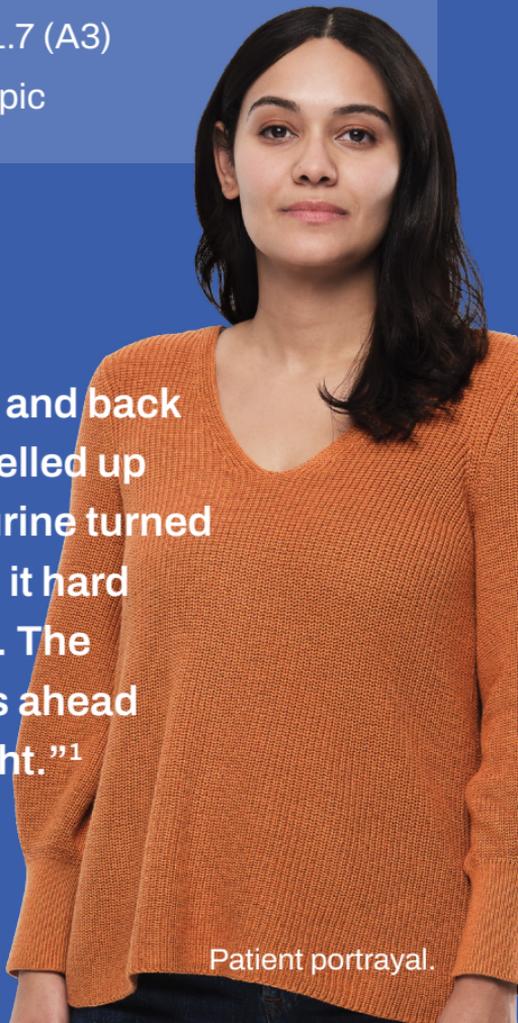


First, it was the fatigue and back pain. Then, my feet swelled up like balloons, and my urine turned dark. Everything made it hard to do as well as I could. The uncertainty of what lies ahead keeps me awake at night.”<sup>1</sup>

Not an actual patient quote.  
Based on patient insights.

BP, blood pressure; eGFR, estimated glomerular filtration rate; sCr, serum creatinine.

Patient portrayal.



## WAVE 1

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### IgAN INSTIGATES: SYMPTOMS APPEAR AND HEALTH WORSENS<sup>4</sup>

Diane wonders why she isn't feeling well

Her first symptoms included<sup>1</sup>:

- ✓ Fatigue
- ✓ Mild back pain
- ✓ Blood in urine

Vital signs<sup>5,6</sup>

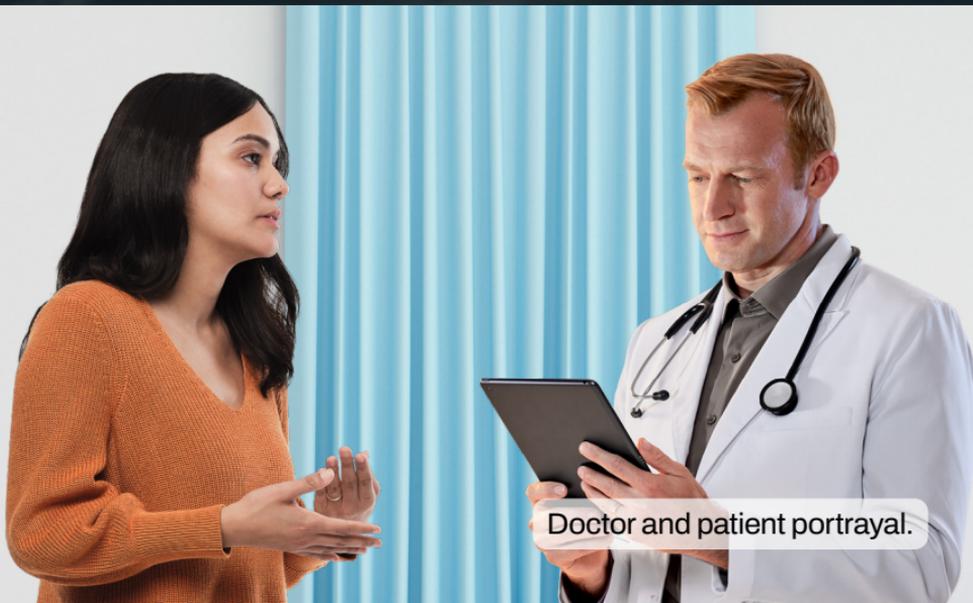
- ✓ BP (mm Hg): 143/90 (hypertension)

Lab results<sup>2</sup>

- ✓ eGFR (mL/min/1.73 m<sup>2</sup>): 75
- ✓ UACR (mg/g): >300

Her PCP prescribes an ACEi and suggests lifestyle changes, including adjustments to her diet and more exercise.<sup>2,7</sup>

ACEi, angiotensin-converting enzyme inhibitor; PCP, primary care provider; UACR, urine albumin-creatinine ratio.



Doctor and patient portrayal.

## WAVE 2 6 MONTHS LATER

### **IgAN INTERRUPTS: PERSISTENT SYMPTOMS PROMPT BIOPSY<sup>2</sup>**

#### **Diane's biopsy results are cause for concern**

- ✓ IgA and C3 deposits are seen in the glomeruli with immunofluorescence<sup>8</sup>
- ✓ MEST-C score: M1, E1, S1, T1, and C0 suggest that complement pathway activity might be contributing to disease<sup>2,9</sup>

#### **COMPLEMENT OVERACTIVITY MAY THREATEN THE FUTURE<sup>10</sup>**



In IgAN, overactivation of the alternative complement pathway can lead to kidney damage<sup>4,10-12</sup>



Overactivation of the alternative pathway, or less often, the lectin pathway, contributes to inflammation and host cell injury. Some studies have found that intensity of C3 staining on kidney biopsy is associated with increased progression to kidney failure.<sup>11,13,14</sup>

MEST-C, mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental glomerulosclerosis (S), tubular atrophy/interstitial fibrosis (T), crescents (C).

## WAVE 3 9 MONTHS LATER

# IgAN INTERFERES: DIANE DEALS WITH DIAGNOSIS AND RISK OF PROGRESSION<sup>13</sup>

Diane's nephrologist identifies clinical and histological risk factors for progression

- ✓ Hypertension<sup>2</sup>
- ✓ Proteinuria continues to fluctuate between 0.8 g/day and 1.4 g/day despite supportive care<sup>2</sup>
- ✓ Signs of kidney damage in biopsy<sup>14</sup>

**30%** of patients

experience kidney failure within 10 years when their time-averaged proteinuria ranges from 0.5 g/day to <1 g/day<sup>15,\*†</sup>

\*0.88 g/g is approximately equivalent to 1 g/day.

†Data from retrospective cohort of 2299 adults and 140 children with IgAN of the UK National Registry of Rare Kidney Diseases (RaDaR). Patients enrolled had a biopsy-proven diagnosis of IgA nephropathy plus proteinuria >0.5 g/day or eGFR <60 mL/min per 1.73 m<sup>2</sup> at any time in their history of their disease. Analyses of kidney survival were conducted using Kaplan–Meier and Cox regression. Recruitment into RaDaR was initiated in 2013. Availability of patient medication and blood pressure data was a limiting factor in this study.



I try my best to live a kidney-friendly life while balancing the side effects of medications like ACEis and steroids. I'm doing everything I can, but my numbers aren't improving."<sup>1</sup>

Not an actual patient quote.  
Based on patient insights.

Patient portrayal.



## WHAT'S NEXT FOR DIANE?

After a course of steroids, Diane's lab results haven't improved and her proteinuria has increased, prompting further concerns over progression.<sup>2,15</sup>

### Vital signs<sup>2,6</sup>

✓ BP (mm Hg): 130/75

### Lab results<sup>2,3</sup>

✓ sCr (mg/dL): 1.6

✓ eGFR (mL/min/1.73 m<sup>2</sup>): 61 (G3a)

✓ Proteinuria (g/24 h): 1.8 (A3)

✓ Hematuria: microscopic



### LEARN MORE

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**References:** 1. Feldman DL, White EM, Julian B, et al. The Voice of the Patient: Externally Led Patient-Focused Drug Development Meeting on IgA Nephropathy. National Kidney Foundation; 2020 2. Rovin BH, Adler SG, Barratt J, et al; Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. *Kidney Int.* 2021;100(suppl 4): S1-S276. doi:10.1016/j.kint.2021.05.021 3. Rajasekaran A, Julian BA, Rizk DV. IgA nephropathy: An interesting autoimmune kidney disease. *Am J Med Sci.* 2021;361(2):176-194. doi:10.1016/j.amjms.2020.10.003 4. Lafayette RA, Kelepouris E. Immunoglobulin A nephropathy: advances in understanding of pathogenesis and treatment. *Am J Nephrol.* 2018;47(suppl 1):43-52. doi:10.1159/000481636 5. National Institute of Diabetes and Digestive and Kidney Diseases. IgA nephropathy. National Institutes of Health; 2015. Accessed April 11, 2023. <https://www.niddk.nih.gov/health-information/kidney-disease/iga-nephropathy> 6. Facts about hypertension. Centers for Disease Control and Prevention. Updated July 6, 2023. Accessed September 21, 2023. <https://www.cdc.gov/bloodpressure/facts.htm> 7. Rovin BH, Adler SG, Barratt J, et al. Executive summary of the KDIGO 2021 guideline for the management of glomerular diseases. *Kidney Int.* 2021; 100:753-779. doi:10.1016/j.kint.2021.05.015 8. Cheung CK, Barratt J. IgA nephropathy: clinical features and diagnosis. Updated Nov 29, 2022. Accessed September 21, 2023. <https://www.uptodate.com/contents/iga-nephropathy-clinical-features-and-diagnosis> 9. Xie J, Kirylyuk K, Wang W, et al. Predicting progression of IgA nephropathy: new clinical progression risk score. *PLoS One.* 2012;7(6):e38904. doi:10.1371/journal.pone.0038904 10. Lai KN, Tang SCW, Schena FP, et al. IgA nephropathy. *Nat Rev Dis Primers.* 2016;2:16001. doi:10.1038/nrdp.2016.1 11. Rizk DV, Maillard N, Julian BA, et al. The emerging role of complement proteins as a target for therapy of IgA nephropathy. *Front Immunol.* 2019;10:504. doi:10.3389/fimmu.2019.00504 12. Barratt J, Feehally J. IgA nephropathy. *J Am Soc Nephrol.* 2005;16(7):2088-2097. doi:10.1681/ASN.2005020134 13. Medjeral-Thomas NR, Cook HT, Pickering MC. Complement activation in IgA nephropathy. *Semin Immunopathol.* 2021;43(5): 679-690. doi:10.1007/s00281-021-00882-9 14. Medjeral-Thomas NR, Trolldborg A, Constantinou N, et al. Progressive IgA nephropathy is associated with low circulating mannan-binding lectin associated serine protease 3 (MASP-3) and increased glomerular factor H-related protein-5 (FHR5) deposition. *Kidney Int Rep.* 2017;3(2):426-438. doi:10.1016/j.ekir.2017.11.015 15. Pitcher D, Braddon F, Hendry B, et al. Long-term outcomes in IgA nephropathy. *Clin J Am Soc Nephrol.* 2023;18:727-738. doi:10.2215/CJN.0000000000000135