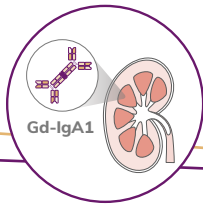


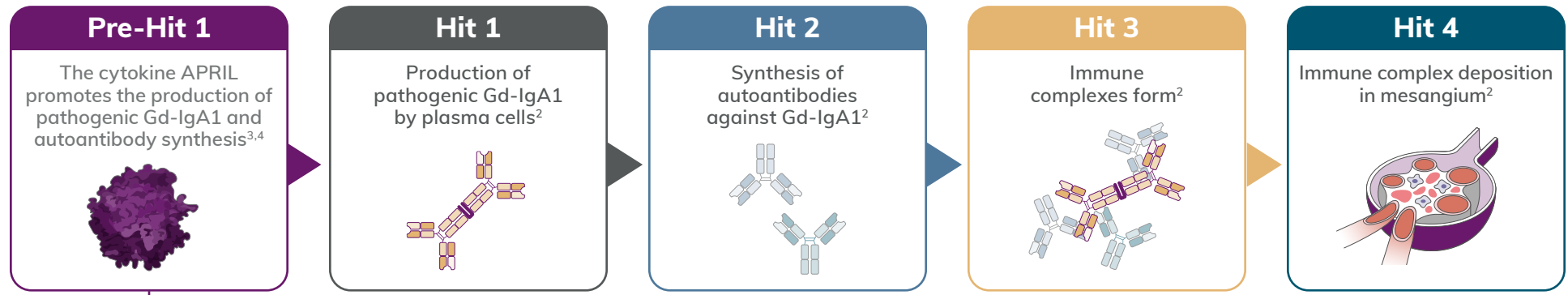
APRIL and the 4-Hit Process of IgA Nephropathy (IgAN)



Pathogenesis of IgAN

- Immunoglobulin A (IgA) is normally produced by cells in the mucosa as part of the innate immune response¹
- Patients with IgAN have elevated levels of pathogenic galactose-deficient IgA1 (Gd-IgA1), which acts as an autoantigen to trigger an immune response²

The pathogenesis of IgAN is explained by the 4-hit process²



Role of APRIL

APRIL acts as a driver of pathogenic Gd-IgA1 production and autoantibody synthesis by mediating antibody class switching in mature B cells and promoting the survival of plasma cells (antibody-producing B cells)^{3,4}

Studies show APRIL acts as an important initiating and sustaining factor in IgAN pathogenesis^{5,6}

The outcome of the 4-hit process is kidney injury, which can progress to kidney failure^{2,7}

- In an observational study, **most patients with IgAN developed kidney failure within 10-15 years** of diagnosis^{7,a}
- In a retrospective study, **36% of patients reached the composite outcome** of $\geq 50\%$ eGFR, kidney failure, or mortality with a median time-to-event of 2.7 years^{8,b,c}

Most current IgAN treatments aim to treat the clinical manifestations of chronic kidney disease, rather than the underlying causes of IgAN^{3,9,10}



Learn More About the Pathogenesis of IgAN

APRIL, a proliferation-inducing ligand; eGFR, estimated glomerular filtration rate.

^aRetrospective cohort study using data from the RaDaR (UK) cohort of 2299 adults and 140 children with biopsy-confirmed IgAN with proteinuria >0.5 g/d or eGFR <60 mL/min/1.73 m² at any point in their clinical history. ^bRetrospective longitudinal cohort study performed using data from US adult patients with biopsy-confirmed IgAN (N=655) within Kaiser Permanente Southern California between January 2000 and November 2022. ^cKidney failure defined as eGFR <15 mL/min/1.73 m², hemodialysis or peritoneal dialysis, or kidney transplant.

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