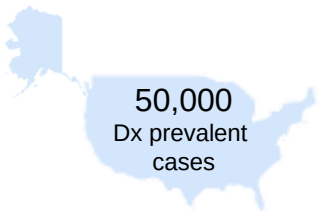
MarketSheet® ANCA-Associated Vasculitis (AAV)

Treatment gaps persist for heterogeneous chronic disorder

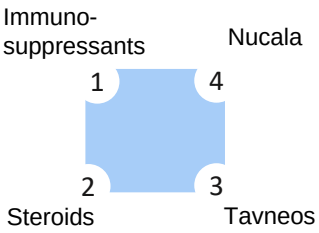
ANCA-associated vasculitis (AAV) is a multisystem autoimmune disorder with heterogeneous presentation occurring between the ages of 50-60 years. Genetic and environmental factors trigger the development of ANCAs that bind healthy neutrophils and induce an attack on small and medium blood vessels leading to increased swelling and inflammation; as a result, patients most commonly experience lung and kidney damage. Patients are segmented into three classifications based on clinical features—MPA, GPA, or EGPA. In recent years, physicians also classify patients based on ANCA type, either PR3 or MPO, to more accurately predict relapse risks and treatment routes.[1]

U.S. PREVALENCE



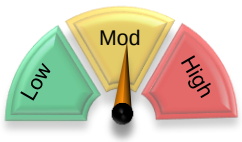
GPA and MPA subtypes comprise around 45,000 of diagnosed AAV cases.[2,3] 80% of patients will receive drug treatment.[4]

CURRENT TREATMENT



AAV is controlled with immunosuppressants and corticosteroids which are used in combination with approved treatments – Tavneos and Nucala.

UNMET NEED



1. Steroid-sparing treatments
2. Longer remission & reduced relapse rates
3. Disease activity reduction

PIPELINE

- **2017-2021:** Approval of Tavneos and Nucala
- **2024:** Additional IL-5 inhibitors for EGPA
- **2026+:** Novel MoA capable of treating all subtypes

Ongoing late-stage trials focus on improving IL-5 mAbs for EGPA and C5a mAbs for MPA/GPA. CAR-T and ERA are novel approaches being investigated for all subtypes.[5]

LACK OF LATE-STAGE PIPELINE DEVELOPMENTS FOR ALL SUBTYPES. Even though the majority of AAV patients are GPA/MPA, late-stage clinical trials by AZ and GSK are centered around the EGPA subtype.

PHYSICIANS SEEK STERIOD-SPARING, SAFE TREATMENTS. Only 25% of patients achieve complete remission off all treatment.[4] Due to complications with long-term steroid and immunosuppressant use, physicians agree there is a gap for maintenance treatments to enable long-term remission off steroids.

TAVNEOS IS WELL-RECEIVED BUT NOT W/OUT DRAWBACKS. Physicians express barriers to access for the new drug, especially since many hospitals don't have it on formulary. The dosing regimen of three pills, twice daily also raises adherence concerns.[4]

ADDITIONAL MARKET FACTS

Treating physicians	EGPA patients are primarily managed by pulmonologists, while MPA and GPA patients are managed by rheumatologists and/or nephrologists. Patients often co-managed due to the multisystem disease.			
Market segments	Patients are segmented by severity and subtype – MPA/GPA (~90%) or EGPA (~10%)			
Standard of care	MPA/GPA – Steroid-sparing immunosuppressant + steroid. Severe MPA/GPA patients can also receive rituximab or Tavneos in addition. Treatment will be tapered as much as possible post-induction. EGPA – Steroid-sparing immunosuppressant + steroid. Severe EGPA may aso receive rituximab or Nucala in addition. Treatment will be tapered as much as possible post-induction.			
Regulatory precedent	Two approved drugs – Amgen's Tavneos (avacopan, approved October 2021) for induction of MPA/GPA and GSK's Nucala (mepolizumab, approved December 2017) for EGPA			
Emerging competitors	5 therapies in development:	Ph III – 2 EGPA	Ph II – 1 all	Ph I – 1 all; 1 MPA/GPA
Clinical considerations	**Pivotal trial**		**Proof-of-concept trial**	
	Primary endpoint: BVAS=0 and steroid ≤ 4 mg/d **Enrollment:** 150 patients (EPGA); 300 (MPA/GPA) **Duration:** 42 weeks (EPGA); 31 weeks (MPA/GPA) to primary completion		**Primary endpoint:** BVAS **Enrollment:** 55 **Duration:** 13 weeks to primary completion	
Druggable targets	EGPA – IL-5, ERA, FcRn, CD20		MPA/GPA – Complement (C5a, C5aR), GM-CSF, ERA, FcRn, CD20	
Pricing potential	Annual U.S. WAC of Tavneos is ~$194,000 and Nucala is ~$125,000			

**MarketSheet trademark pending

MarketSheet® Goodpasture's / Anti-GBM Disease

A rapidly progressing renal and/or lung condition that can be managed if treated early

Goodpasture's syndrome is a rare autoimmune disease that affects the lungs and kidneys. It occurs when the immune system mistakenly produces autoantibodies that attack the basement membrane (called anti-GBM antibodies [ab]) in these organs, leading to bleeding from the lungs, glomerulonephritis, and kidney failure. Symptoms include coughing up blood, difficulty breathing, fatigue, anemia, blood in urine, swelling of the legs, and high blood pressure. Goodpasture's disease mainly affects young adults, particularly males aged 20-30, as well as adults (skewed toward women) aged 60-70 years[1]. The exact cause of GPS is unknown, but it may be related to genetics, exposure to certain chemicals or medications, viral infections, or smoking.

U.S. INCIDENCE

440-500
Incident cases/year

Occurs primarily in whites and some Asians; little presence in African Americans.[2] 30-40% of patients have concomitant ANCA vasculitis[3].

CURRENT TREATMENT

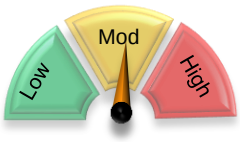
1

There's one treatment regimen for GPS: Plasma exchange + steroid + immunosuppressant; it has been the SOC for 40 years.

Kidney transplant is a limited use option.

The SOC removes circulating anti-GBM abs, dampens inflammation, and suppresses anti-GBM ab production. The goal is to treat quicky after diagnosis to salvage kidney function.

UNMET NEED



1. Avoid dialysis
2. Rapid (i.e., within hours) recovery of independent kidney function

PIPELINE

2023: -

2027: Imlifidase

Hansa's imlifidase, a non-specific IgG degrading enzyme, is the only drug in development. The Ph3 trial concludes in June 2025

Imlifidase is a single dose therapy that is EMA-approved for use for kidney transplants. In GPS, it's a potential replacement for plasma exchange.

TREATMENT IS "ONE-AND-DONE" IN THE 40-50% OF GPS PATIENTS WHO ARE NOT ON DIALYSIS. Non-dialysis patients receive SOC for 3-6 months to eliminate circulating anti-GBM Abs. Of these, only 3% relapse and the majority remain free of anti-GMB Abs.[4] Patients require follow-up at regular intervals (every 3-4 months for CKD management).

"If you start treatment before needing dialysis, you've got a relatively good chance of [kidney function] recovery. *80% to 90% of those patients recover, but the problem is the delayed diagnosis and then being on dialysis before you start treatment."* **– Nephrology KOL, UK**

Patients on dialysis have a 10% chance of recovering independent kidney function.

THE OPPORTUNITY FOR NEW TREATMENTS TARGETING ANTI-GBM ABS IS TWO-FOLD for newly diagnosed patients who present without needing dialysis and for those patients on dialysis who could be made transplantable by eliminating anti-GBM Abs.

ADDITIONAL MARKET FACTS

Treating physicians	Nephrologists for glomerulonephritis; pulmonologists for pulmonary hemorrhage	
Market segments	Dialysis status at presentation: 40-50% not on dialysis, 50-60% on dialysis Organ involvement: 60-80% have renal and lung involvement; 20-40% have renal only[5]	
Standard of care	In non-dialysis patients, 3-6 mos of a combo of plasma exchange for anti-GBM ab removal, corticosteroids to control inflammation, and cyclophosphamide to prevent anti-GBM ab production. Rituximab is sometimes used in place of or in addition to cyclophosphamide.	
Regulatory precedent	There are no FDA or EMA-approved therapies for GPS	
Emerging competitors	• Hansa's imlifidase (Ph 3) • Studies of different types of extracorporeal ab removal have been explored	
Clinical considerations	**Pivotal trial**	**Proof-of-concept trial**
	Primary endpoint: GFR **Enrollment**: 50 patients **Duration**: 2.5 years to primary completion	**Primary endpoint:** % of patients with independent renal function **Enrollment**: 15 patients **Duration**: 3 years to primary completion
Druggable target(s)	Anti-GBM Abs; they are pathogenic and precipitate irreversible, progressive CKD	
Pricing potential	Plasma exchange accounts for the greatest share of costs for SOC at ~$28,000 per cycle (one session of plasma exchange is ~$2,000[6] and patients get an average of 14 sessions).	

**MarketSheet trademark pending