TAVNEOS®: Achieve and sustain remission in severe active ANCA-associated vasculitis (GPA or MPA)

Study overview – The phase 3 ADVOCATE trial compared a TAVNEOS® arm to an Active Control arm in 330 newly diagnosed or relapsing patients with GPA or MPA over 52 weeks in a randomized, double-blind, double-dummy, active-controlled fashion[1,2]

- → **TAVNEOS® arm** = TAVNEOS® + rituximab, or cyclophosphamide (followed by azathioprine or mycophenolate mofetil*)[1]
- → **Active Control arm** = Prednisone taper + rituximab, or cyclophosphamide (followed by azathioprine or mycophenolate mofetil*)[1]

*If azathioprine not tolerated.

The trial sought to evaluate whether patients could achieve remission at Week 26 and sustain remission at Week 52[1]

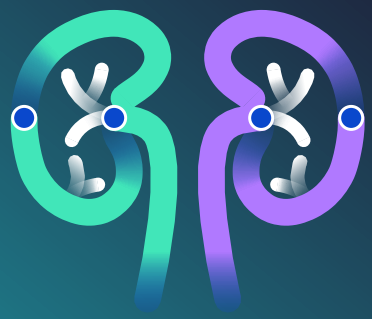
81.2% of patients in the trial had renal involvement based on BVAS prior to treatment[2]

Primary endpoint – The TAVNEOS® arm compared to the Active Control arm was non-inferior in achieving remission† at Week 26 and superior in sustaining remission‡ at Week 52[1,2]

- → Remission at Week 26: 72.3% of patients in the TAVNEOS® arm vs 70.1% of patients in the Active Control arm (non-inferiority, $P < 0.001$)[1,2]
- → Sustained remission at Week 52: 65.7% of patients in the TAVNEOS® arm vs 54.9% of patients in the Active Control arm (superiority, $P = 0.013$)[1,2]

TAVNEOS® Renal Outcomes

The ADVOCATE trial assessed change in eGFR and uACR from baseline in patients in the TAVNEOS® arm and those in the Active Control arm[2,3] **– *see the data inside***



†Remission was defined as achieving a BVAS of 0 and not taking glucocorticoids for treatment of GPA or MPA within 4 weeks prior to Week 26.[2]
‡Sustained remission was defined as remission at Week 26 and at Week 52 and no use of glucocorticoids for the treatment of GPA and MPA for 4 weeks before Week 52, without relapse between Week 26 and Week 52. Relapse was defined as the occurrence of at least 1 major item, at least 3 non-major items, or 1 or 2 non-major items for at least 2 consecutive visits based on BVAS after a BVAS of 0 had been achieved.[1,3]
BVAS = Birmingham Vasculitis Activity Score; eGFR = estimated glomerular filtration rate; GPA = granulomatosis with polyangiitis; MPA = microscopic polyangiitis; uACR = urine albumin-creatinine ratio.

INDICATION

TAVNEOS (avacopan) is indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids. TAVNEOS does not eliminate glucocorticoid use.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

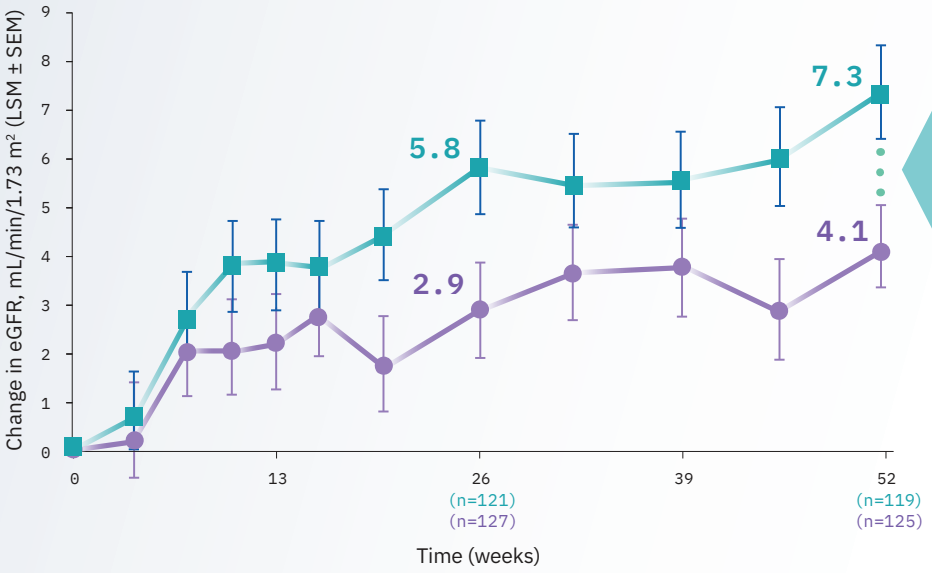
Serious hypersensitivity to avacopan or to any of the excipients.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

In patients with renal impairment at baseline, the TAVNEOS® arm saw an improvement in eGFR over 52 weeks[2]

LSM Change in eGFR from Baseline Over 52 Weeks (ITT Population)[4,*]



3.2 mL/min/1.73 m² LSM difference between the TAVNEOS® and Active Control arms (95% CI, 0.3-6.1)[4]

Baseline Mean eGFR (mL/min/1.73 m²)[2]

TAVNEOS® arm (n = 131) = 44.6

Active Control arm (n = 134) = 45.6

16% improvement from baseline in the TAVNEOS® arm vs 9% in the Active Control arm[2]

Prespecified secondary endpoint not adjusted for multiplicity and should be considered exploratory. Results should be interpreted with caution.[2]

*Least-squares mean (LSM) change in eGFR from baseline to Weeks 26 and 52 in patients with renal involvement at baseline based on the BVAS. BVAS = Birmingham Vasculitis Activity Score; CI = confidence interval; eGFR = estimated glomerular filtration rate; ITT = intent to treat; LSM = least-squares mean; SEM = standard error of the mean.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

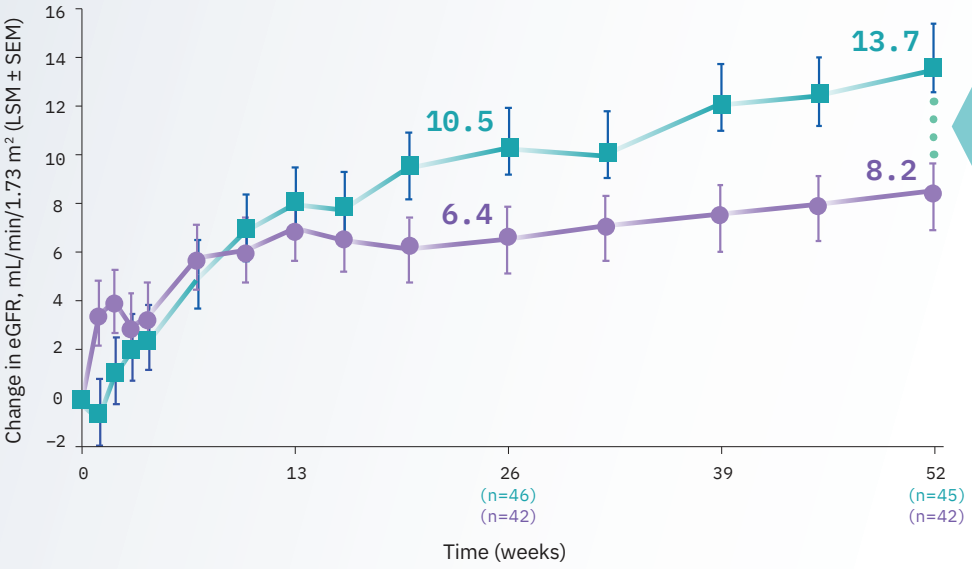
Hepatotoxicity: Serious cases of hepatic injury have been observed in patients taking TAVNEOS, including life-threatening events. Obtain liver test panel before initiating TAVNEOS, every 4 weeks after start of therapy for 6 months and as clinically indicated thereafter. Monitor patients closely for hepatic adverse reactions, and consider pausing or discontinuing treatment as clinically indicated (refer to section 5.1 of the Prescribing Information). TAVNEOS is not recommended for patients with active, untreated, and/or uncontrolled chronic liver disease (e.g., chronic active hepatitis B, untreated hepatitis C, uncontrolled autoimmune hepatitis) and cirrhosis. Consider the risks and benefits before administering this drug to a patient with liver disease.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

Subgroup analysis of patients with a baseline eGFR <30 and ≥15 (mL/min/1.73 m²)[2,5]

LSM Change in eGFR a Prespecified Subgroup Analysis in the 100 Patients with eGFR <30 and ≥15 mL/min/1.73 m² at Baseline[2,5,6]



Baseline mean eGFR (mL/min/1.73 m²)[2,5,6]

TAVNEOS® arm (n = 52) = 21.1

Active Control arm (n = 48) = 21.6

5.5 mL/min/1.73 m² LSM difference between the TAVNEOS® arm and Active Control arm (95% CI, 1.7-9.5)[2,5,6]

65% improvement from baseline in the TAVNEOS® arm vs 38% in the Active Control arm[2,5]

Results from this exploratory subgroup analysis should be interpreted with caution.[2,3]

CI = confidence interval; eGFR = estimated glomerular filtration rate; LSM = least-squares mean; SEM = standard error of the mean.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Serious Hypersensitivity Reactions: Cases of angioedema occurred in a clinical trial, including 1 serious event requiring hospitalization. Discontinue immediately if angioedema occurs and manage accordingly. TAVNEOS must not be readministered unless another cause has been established.

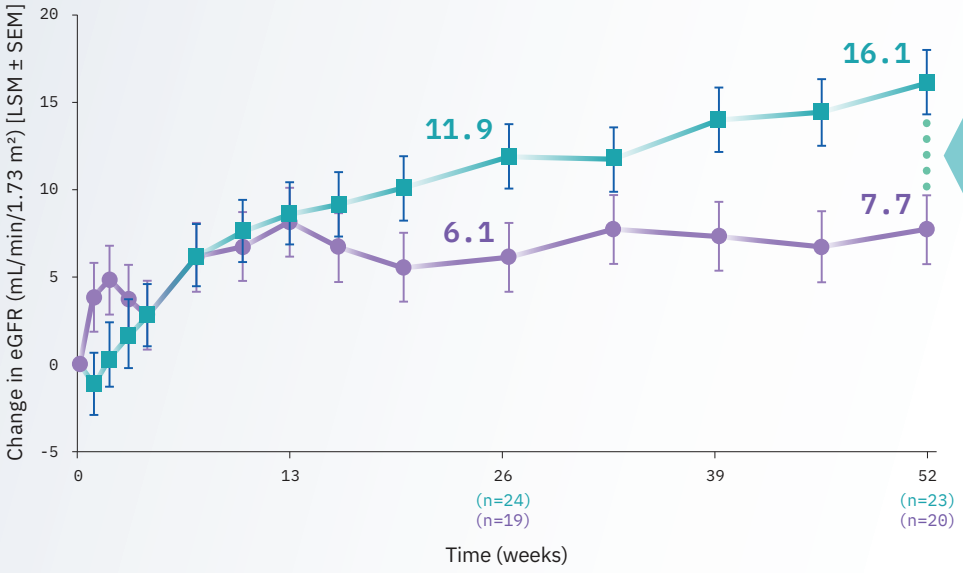
Hepatitis B Virus (HBV) Reactivation: Hepatitis B reactivation, including life-threatening hepatitis B, was observed in the clinical program. Screen patients for HBV. For patients with evidence of prior infection, consult with physicians with expertise in HBV and monitor during TAVNEOS therapy and for 6 months following. If patients develop HBV reactivation, immediately discontinue TAVNEOS and concomitant therapies associated with HBV reactivation, and consult with experts before resuming.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

Post-hoc, exploratory subgroup analysis of patients with a baseline eGFR ≤20 and ≥15 (mL/min/1.73 m²)[7]

LSM Change in eGFR of an Exploratory Subgroup Analysis in the 50 Patients with eGFR ≤20 and ≥15 mL/min/1.73 m² at Baseline[7]



8.4 mL/min/1.73 m² LSM difference between the TAVNEOS® arm and Active Control arm (95% CI, 2.9-13.8)[7]

Baseline mean eGFR (mL/min/1.73 m²)[7]

TAVNEOS® arm (n = 27) = 17.6

Active Control arm (n = 23) = 17.5

improvement from baseline in the TAVNEOS® arm vs 44% in the Active Control arm[7]

Post-hoc analysis is exploratory. No conclusions of statistical or clinical significance can be drawn.[7]

CI = confidence interval; eGFR = estimated glomerular filtration rate; LSM = least-squares mean; SEM = standard error of the mean.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

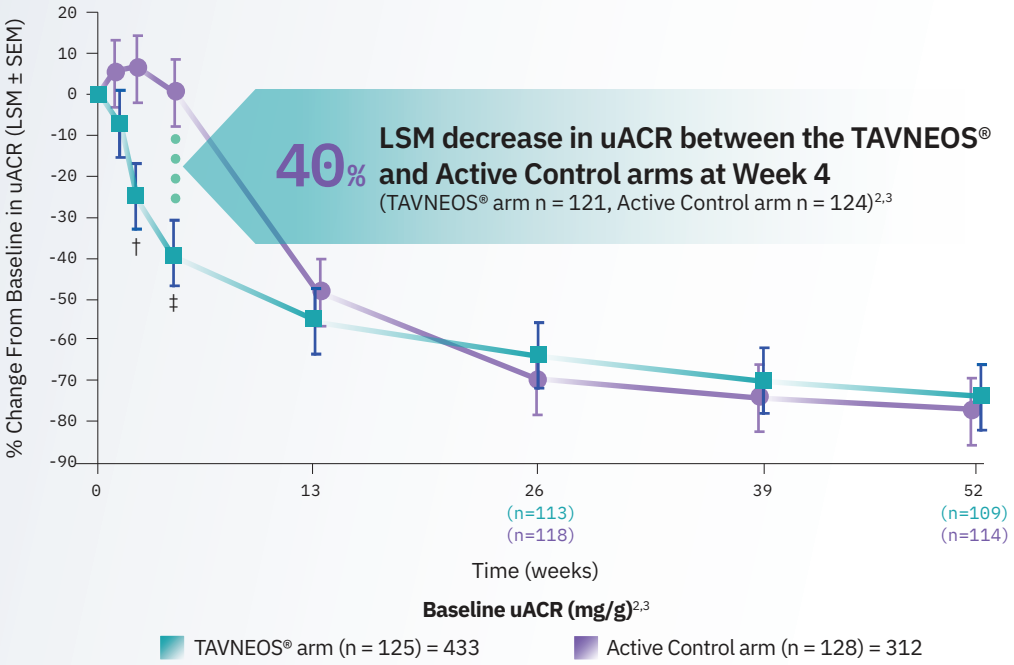
Serious Infections: Serious infections, including fatal infections, have been reported in patients receiving TAVNEOS. The most common serious infections reported in the TAVNEOS group were pneumonia and urinary tract infections. Avoid use of TAVNEOS in patients with active, serious infection, including localized infections. Consider the risks and benefits before initiating TAVNEOS in patients with chronic infection, at increased risk of infection, or who have been to places where certain infections are common.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

Patients in the TAVNEOS® arm saw a decrease in albuminuria by Week 4[2,3,*]

Change in Urinary Albumin-Creatinine Ratio (uACR) Over 52 Weeks (ITT Population)[2,3]



The overall change in uACR was similar between the treatment groups at Week 52[2,3]

Prespecified secondary endpoint of patients with renal involvement and albuminuria at baseline; analysis not adjusted for multiplicity and should be considered exploratory. Results should be interpreted with caution.[2]

- → Elevated albuminuria may reflect underlying impairment of kidney function[8,9]
- → Percent changes from baseline are based on ratios of geometric means of visit over baseline[2]
- → The uACR analysis was only performed in patients who met BVAS criteria for renal involvement at baseline and who also had a uACR ≥10 mg albumin/g creatinine[2]

*Based on percent change from baseline in uACR in patients with baseline renal involvement and baseline uACR ≥10 mg/g (52-week study period).[2,3]
BVAS = Birmingham Vasculitis Activity Score; GM = geometric mean; ITT = intent to treat; LSM = least-squares mean; SEM = standard error of the mean.

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

The most common adverse reactions (≥5% of patients and higher in the TAVNEOS group vs. prednisone group) were nausea, headache, hypertension, diarrhea, vomiting, rash, fatigue, upper abdominal pain, dizziness, blood creatinine increased, and paresthesia.

DRUG INTERACTIONS

Avoid co-administration of TAVNEOS with strong and moderate CYP3A4 enzyme inducers. Reduce TAVNEOS dose when co-administered with strong CYP3A4 enzyme inhibitors to 30 mg once daily.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

TAVNEOS® (avacopan)

In the ADVOCATE trial, patients achieved and sustained remission[1,2]

Remission and superior sustained remission[1,2]

→ Remission at Week 26: **72.3%** in the TAVNEOS® arm vs **70.1%** in the Active Control arm (non-inferiority, $P < 0.001$)

→ Sustained remission at Week 52: **65.7%** in the TAVNEOS® arm vs **54.9%** in the Active Control arm (Superiority, $P = 0.013$)

Patients in the TAVNEOS® arm experienced greater improvement in eGFR compared to those in the Active Control arm.[2]

Renal improvement as measured by eGFR[2,*]

→ Patients in the TAVNEOS® arm saw an LSM eGFR improvement of **16%** (7.3 mL/min/1.73 m^2) from baseline, vs an improvement of **9%** (4.1 mL min/1.73 m^2) in the Active Control arm at Week 52

eGFR improvement in patients with baseline eGFR of <30 and ≥15 (mL/min/1.73 m^2)[2,5,*]

→ Patients in the TAVNEOS® arm saw an LSM eGFR improvement of **65%** (13.7 mL/min/1.73 m^2) from baseline vs an improvement of **38%** (8.2 mL/min/1.73 m^2) in the Active Control arm at Week 52

Further eGFR improvement in patients with baseline eGFR ≤20 and ≥15 (mL/min/1.73 m^2)[7,†]

→ Patients in the TAVNEOS® arm saw an LSM eGFR improvement of **91%** (16.1 mL/min/1.73 m^2) from baseline vs an improvement of **44%** (7.7 mL/min/1.73 m^2) in the Active Control arm at Week 52

Decrease in albuminuria at Week 4[2,3,*]

→ **40%** LSM decrease in uACR in the TAVNEOS® arm vs no change in the Active Control arm at Week 4

***Prespecified secondary endpoint not adjusted for multiplicity and should be considered exploratory. Results should be interpreted with caution.**[2,3]

†Post-hoc analysis is exploratory. No conclusions of statistical or clinical significance can be drawn.[7]

eGFR = estimated glomerular filtration rate; LSM = least-squares mean; uACR = urine albumin-creatinine ratio.

Scan to download the Patient Enrollment Form that will help your patients get started on TAVNEOS®

IMPORTANT SAFETY INFORMATION (CONT'D)

DRUG INTERACTIONS (Cont'd)

Consider dose reduction of CYP3A4 substrates when co-administering TAVNEOS. Co-administration of avacopan and 40 mg simvastatin increases the systemic exposure of simvastatin. While taking TAVNEOS, limit simvastatin dosage to 10 mg daily (or 20 mg daily for patients who have previously tolerated simvastatin 80 mg daily for at least one year without evidence of muscle toxicity). Consult the concomitant CYP3A4 substrate product information when considering administration of such products together with TAVNEOS.

TAVNEOS is available as a 10 mg capsule.

Please see additional **Important Safety Information** throughout and click here for the **Full Prescribing Information** and **Medication Guide** for TAVNEOS.

To report a suspected adverse event, call 1-833-828-6367. You may report to the FDA directly by visiting www.fda.gov/medwatch or calling 1-800-332-1088.

References: 1. TAVNEOS [package insert]. Cincinnati, OH: Amgen Inc. **2.** Jayne DRW, Merkel PA, Schall TJ, Bekker P; ADVOCATE Study Group. *N Engl J Med*. 2021;384(7):599-609. **3.** Data on file, Amgen. Clinical Study Report [92070]; 2020. **4.** Data on file, Amgen. Table 14.2.7.1.1 [100027]; 2024. **5.** Supplement to: Jayne DRW, Merkel PA, Schall TJ, Bekker P; ADVOCATE Study Group. *N Engl J Med*. 2021;384(7):599-609. **6.** Data on file, Amgen. Table 14.2.7.1.2 [92252]; 2023. **7.** Cortazar FB, Niles JL, Jayne DRW, et al. *Kidney Int Rep*. 2023;8(4):860-870. **8.** Kaplan-Pavlovčič S, Cerk K, Kveder R, et al. *Nephrol Dial Transplant*. 2003;18(suppl 5):v5-v7. **9.** Stangou M, Asimaki A, Bamichas G, et al. *J Nephrol*. 2005;18(1):35-44.

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TAVNEOS® (avacopan)