See inside for results from the clinical study FAME
(FYCOMPA® (perampanel) CIII as first Add-on to Monotherapy in patients with Epilepsy)

CaseBriefs®

Addressing Seizure Control in Patients With Partial-Onset Seizures: *Choosing a First Adjunctive Therapy*

Patient Case

George, a real patient with partial-onset seizures

Overview

- Older adult in robust health
- Occupation: Golf course outside service attendant
- **Lack of seizure control on current treatment**
- Needs to control seizures to return to work

Fycompa™ (perampanel) TABLETS 2 • 4 • 6 • 8 • 10 • 12 mg ORAL SUSPENSION 0.5 mg/mL CIII

A Broad-Spectrum First Adjunctive Treatment Option That Offers Potential Control Across Convulsive Seizures

INDICATION

FYCOMPA® (perampanel) is indicated in patients with epilepsy aged 4 years and older for partial-onset seizures (POS) with or without secondarily generalized seizures and adjunctive therapy for patients aged 12 years and older for primary generalized tonic-clonic (PGTC) seizures.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS PSYCHIATRIC AND BEHAVIORAL REACTIONS

- **Serious or life-threatening psychiatric and behavioral adverse reactions including aggression, hostility, irritability, anger, and homicidal ideation and threats have been reported in patients taking FYCOMPA**
- **These reactions occurred in patients with and without prior psychiatric history, prior aggressive behavior, or concomitant use of medications associated with hostility and aggression**
- **Advise patients and caregivers to contact a healthcare provider immediately if any of these reactions or changes in mood, behavior, or personality that are not typical for the patient are observed while taking FYCOMPA or after discontinuing FYCOMPA**
- **Closely monitor patients particularly during the titration period and at higher doses**
- **FYCOMPA should be reduced if these symptoms occur and should be discontinued immediately if symptoms are severe or are worsening**

Please see Important Safety Information throughout, including a **Boxed WARNING for Serious Psychiatric and Behavioral Reactions**. Please see accompanying Prescribing Information.

GEORGE

67-year-old male

Outside service attendant at a golf course

Patient Profile

- Divorced and lives alone, but his younger brother lives nearby
- His most important sources of social support are his brother and golf course co-workers. **He has worked at the same golf course for the last 16 years and lives and breathes golf**
- George is an **older adult in robust health**. He has mild hypertension, which he has managed with lifestyle changes. He is a non-smoker and drinks 1-2 beers every night with his friends or brother

Seizure History and Initial Diagnosis

- **George's first seizure occurred on the golf course at the age of 65 years**
  - He was talking to his friend, started to repeat his words, and then became quiet. George stared off for few seconds and was unresponsive to his friends. When one of his friends tried to shake him, he stumbled and fell to the ground. At that moment he regained awareness and started to speak, but he appeared confused and could not answer questions appropriately. His friends had him sit on a nearby golf cart and gave him water. By this time, George started to speak normally
  - George was taken to the local emergency department where routine labs and a CT of his head were within normal limits. He was thought to have experienced syncope, given that it was a sunny summer day with temperatures in the mid-80s
  - **A similar episode occurred at home a week later** when George was watching a game with his brother. According to his brother, George was sitting on the couch and stopped speaking mid-sentence. He became unresponsive and made some odd movements with his mouth. Then he slumped to his right side on the couch. By the time his brother came up to him, George was coming to and seemed confused. **George asked his brother not to call 911 and instead saw his primary care physician 2 days later. The physician referred him to a cardiologist**
- George was seen by the cardiologist, who was concerned about possible arrhythmia or a vasovagal syncope. The cardiologist ordered a tilt table test and a loop recorder
  - The tilt table test did not reveal any significantly abnormal change in George's blood pressure, heart rate, or rhythm. A loop recorder was implanted
  - George had 2 more of the abovementioned episodes, each lasting 60-90 seconds and occurring within an hour of each other. The loop recorder did not capture any abnormal heart rhythm
  - At this time, t**he cardiologist referred George to a neurology clinic to rule out the possibility of a transient ischemic attack or seizure.** The neurologist ordered a brain MRI and a routine EEG. The MRI revealed only a few non-specific white matter hyperintensities. However, the EEG captured 2 sharp waves in the left fronto-temporal region, leading to the diagnosis of focal epilepsy
  - George was started on oxcarbazepine by the neurologist, which was up-titrated to 450 mg twice a day

IMPORTANT SAFETY INFORMATION (*cont'd*)

SERIOUS PSYCHIATRIC AND BEHAVIORAL REACTIONS

In the partial-onset seizures clinical trials, hostility- and aggression-related adverse reactions occurred in 12% and 20% of patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 6% of patients in the placebo group. These effects were dose-related and generally appeared within the first 6 weeks of treatment, although new events continued to be observed through more than 37 weeks. These effects in FYCOMPA-treated patients led to dose reduction, interruption, and discontinuation more frequently than placebo-treated patients. Homicidal ideation and/or threat have also been reported postmarketing in patients treated with FYCOMPA. The combination of alcohol and FYCOMPA significantly worsened mood and increased anger.

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Presentation

- **George continued to have seizures despite taking oxcarbazepine 600 mg twice daily and maintaining a serum level in the high reference range. At this time, he was referred to the epilepsy clinic**
- At the time of presentation to the clinic, George came with his brother, who had taken up the responsibility of driving him when needed. His general physical examination and neurological examination were within normal limits
- George confided that in the mornings after his brother stays late overnight, he misses his morning dose of oxcarbazepine in a rush to get to the golf course. In fact, **his last 2 seizures occurred on days that he missed his medication**
- At this time, his oxcarbazepine was switched to an extended-release formulation to be taken as a single 1200-mg dose at bedtime

Seizure Description

- George never gets an aura and is completely amnestic to his seizures. As per witnesses, he either starts to repeat words or just stares off. He has a "strange look," puckers his lips, and seems to make chewing movements. He stays like this for 30-60 seconds and then suddenly the facial expression eases and he starts to look around the room. This marks the end of the seizure, and George starts to speak normally within a minute or so
- George reports that his only sign of a seizure is a sudden sense of tiredness, which he complains about to his friends and brother after the seizure has passed

Seizure Frequency

- At least twice a month. His last seizure was 6 days ago

Treatment Goals

- George's biggest complaints are the loss of independence and feelings of guilt because his younger brother has to take time off work to bring him to appointments
- His employers at the golf course are very supportive. However, after his second seizure at the golf course a year ago, he was restricted from driving the golf cart. **Because his seizures are not controlled, he has been taken off his outside service job** and has instead been working in the pro shop
- With the summer coming, George's immediate goal is to return to his former job profile. Given that he is almost always surrounded by other employees or patrons, his employer has agreed to allow him to return to outdoor duties (without driving) if he remains seizure-free for one month

IMPORTANT SAFETY INFORMATION (*cont'd*)

SERIOUS PSYCHIATRIC AND BEHAVIORAL REACTIONS (*cont'd*)

Patients taking FYCOMPA should avoid the use of alcohol. Patients, their caregivers, and families should be informed that FYCOMPA may increase the risk of psychiatric events. Patients should be monitored during treatment and for at least one month after the last dose of FYCOMPA, and especially when taking higher doses and during the initial few weeks of drug therapy (titration period) or at other times of dose increases. Similar serious psychiatric and behavioral events were observed in the primary generalized tonic-clonic (PGTC) seizure clinical trial.

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Treatment Selection

- **Considering George's prior difficulties with adhering to twice-a-day dosing and his epileptologist's concern that extended-release treatment options do not provide true 24-hour therapeutic coverage, FYCOMPA® (perampanel) was selected**
  - Additionally, despite understanding that his serum level was within reference range, George was significantly concerned that the 600- and 1200-mg doses of oxcarbazepine were "too high" due to their numerical value. Therefore, as expected, he was very enthusiastic to try FYCOMPA when informed that he would only be taking few milligrams
- George was started on 2 mg of FYCOMPA to be taken at bedtime, with a titration plan of increasing by 2 mg every other week with a target dose of 6 mg
- At his 3-month visit, George reported one seizure on Day 8 of the 2-mg dose. He has not had any seizure since then, and has remained seizure-free for almost 2.5 months—the longest span in nearly a year
- **George was reinstated to his outdoor job at the golf course.** However, he reported feeling dizzy and experiencing poor balance for the past 1 to 1.5 months. He was unsure if this was because he was acclimatizing to getting back to the more active outdoor job, or if it was due to his medications
- Suspecting that it could be medication related, George's epileptologist lowered his dose of FYCOMPA to 4 mg at bedtime. When the clinical nurse checked on George a month later, he was no longer experiencing any dizziness or imbalance issues

Current Treatment Outcomes

- **George has currently remained seizure-free for almost 14 months** on dual ASM therapy of oxcarbazepine extended-release 1200 mg at bedtime and FYCOMPA 4 mg at bedtime

Patient case is based on an actual patient treated by Dr Vineet Punia. Patient's name and other details have been changed. Photo is not of actual patient. FYCOMPA is not appropriate for all patients. This information should not substitute for the independent medical judgment of the treating physician.

ASM=anti-seizure medication; CT=computed tomography; EEG=electroencephalogram; MRI=magnetic resonance imaging.

IMPORTANT SAFETY INFORMATION (*cont'd*)

SUICIDAL BEHAVIOR AND IDEATION

Antiepileptic drugs (AEDs), including FYCOMPA, increase the risk of suicidal thoughts or behavior in patients. Anyone considering prescribing FYCOMPA or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Patients, their caregivers, and families should be informed of the risk and advised to monitor and immediately report the emergence or worsening of depression, suicidal thoughts or behavior, thoughts about self-harm and/or any unusual changes in mood or behavior. Should suicidal thoughts and behavior emerge during treatment, consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

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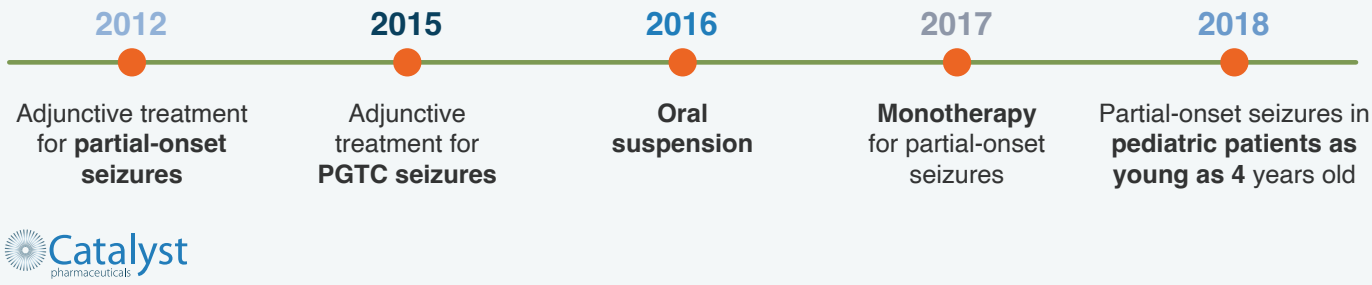
Once-daily FYCOMPA is a broad-spectrum* agent that offers potential seizure control across convulsive seizures

(including **partial-onset** seizures that **secondarily generalize**† and **primary generalized** tonic-clonic seizures‡) and non-convulsive seizures (including **simple** partial seizures† and **complex** partial seizures†).[1-7]

Today, over half a million patients have been prescribed FYCOMPA worldwide.[8§,¶] FYCOMPA has been well-studied, with **80+ global studies** published or ongoing and **10+ years of clinical experience.**[9] FYCOMPA is available in **2 formulations** and approved in **72 countries**.[1,8¶]

FYCOMPA and Catalyst: A Commitment to Treating Epilepsy



Catalyst pharmaceuticals

PGTC=primary generalized tonic-clonic.

*Defined as offering potential seizure control across partial onset, secondarily generalized tonic-clonic, and primary generalized tonic-clonic seizures.
†Adjunctive therapy or monotherapy for patients ≥4 years of age.
‡Adjunctive therapy for patients ≥12 years of age.
§Worldwide figure through December 2021. Over 50,000 patients prescribed FYCOMPA in the United States.
¶Across different indications.

IMPORTANT SAFETY INFORMATION (*cont'd*)

DIZZINESS AND GAIT DISTURBANCE

FYCOMPA caused dose-related increases in events related to dizziness and disturbance in gait or coordination. Dizziness and vertigo were reported in 35% and 47% of patients in the partial-onset seizure trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 10% of placebo-treated patients. Gait disturbance related events were reported in 12% and 16% of patients in the partial-onset seizure clinical trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 2% of placebo-treated patients. These adverse reactions occurred mostly during the titration phase. These adverse reactions were also observed in the PGTC seizure clinical trial.

SOMNOLENCE AND FATIGUE

FYCOMPA caused dose-dependent increases in somnolence and fatigue-related events. Somnolence was reported in 16% and 18% of patients in the partial-onset seizure trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 7% of placebo-treated patients. Fatigue-related events were reported in 12% and 15% of patients in the partial-onset seizure trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 5% of placebo-treated patients. These adverse reactions occurred mostly during the titration phase. These adverse reactions were also observed in the PGTC seizure clinical trial. Patients should be advised against engaging in hazardous activities requiring mental alertness, such as operating motor vehicles or dangerous machinery, until the effect of FYCOMPA is known. Patients should be carefully observed for signs of central nervous system (CNS) depression when FYCOMPA is used with other drugs with sedative properties because of potential additive effects.

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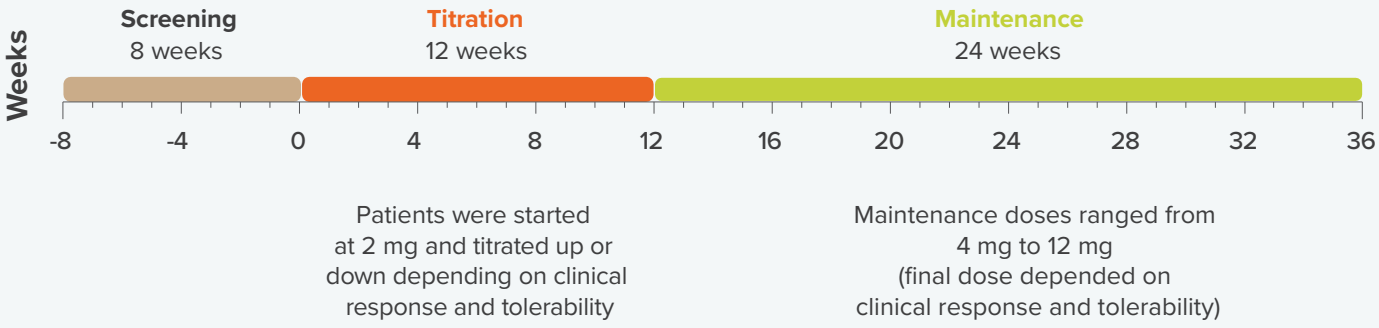
FAME Study Design—FYCOMPA as First Add-on to Monotherapy in Patients With Epilepsy

- The efficacy and safety of FYCOMPA as first adjunctive therapy after ASM monotherapy failure were evaluated in FAME, a 24-week maintenance, multicenter, open-label, prospective trial[10]
  - Included patients aged ≥12 years with partial-onset seizures, with or without secondarily generalized tonic-clonic seizures
- During the titration period of this Phase 4 study, patients received FYCOMPA 2 mg once daily at bedtime[10]
- Daily dose was increased incrementally at ≥2-week intervals, by 2 mg, depending on clinical response and tolerability[10]

FAME Study Design[8,10a]



[a]A South Korean study.

- Patients who were enrolled in this study had ≥2 partial-onset seizures at intervals of ≥24 hours during the 8 weeks prior to Week 0 and had been taking ASM monotherapy administered at a stable dose for 8 weeks prior to Week 0[8]
- TEAEs, withdrawal from treatment, and clinical laboratory evaluations (hematology, clinical chemistry, and urinalysis) were assessed[10]
- The primary endpoint was the percentage of patients with a ≥50% reduction in total seizure frequency during the maintenance period as compared to baseline (50% responder rate)[8,10]
- Secondary endpoints included the percentage of patients with ≥75% reduction in total seizure frequency (75% responder rate); percentage of patients with a 100% reduction in total seizure frequency (100% responder rate); and 50%, 75%, and 100% responder rates for secondarily generalized tonic-clonic seizures[8,10]

TEAEs=treatment-emergent adverse events.

IMPORTANT SAFETY INFORMATION (*cont'd*)

FALLS

Falls were reported in 5% and 10% of patients in the partial-onset seizure clinical trials randomized to receive FYCOMPA at doses of 8 mg and 12 mg per day, respectively, compared to 3% of placebo-treated patients.

DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS)

DRESS, also known as **multiorgan hypersensitivity**, has been reported in patients taking AEDs, including FYCOMPA. DRESS may be fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling, in association with other organ system involvement. If signs or symptoms are present, immediately evaluate the patient and discontinue FYCOMPA if an alternative etiology for signs or symptoms cannot be established.

WITHDRAWAL OF AEDs

A gradual withdrawal is generally recommended with AEDs to minimize the potential of increased seizure frequency, but if withdrawal is a response to adverse events, prompt withdrawal can be considered.

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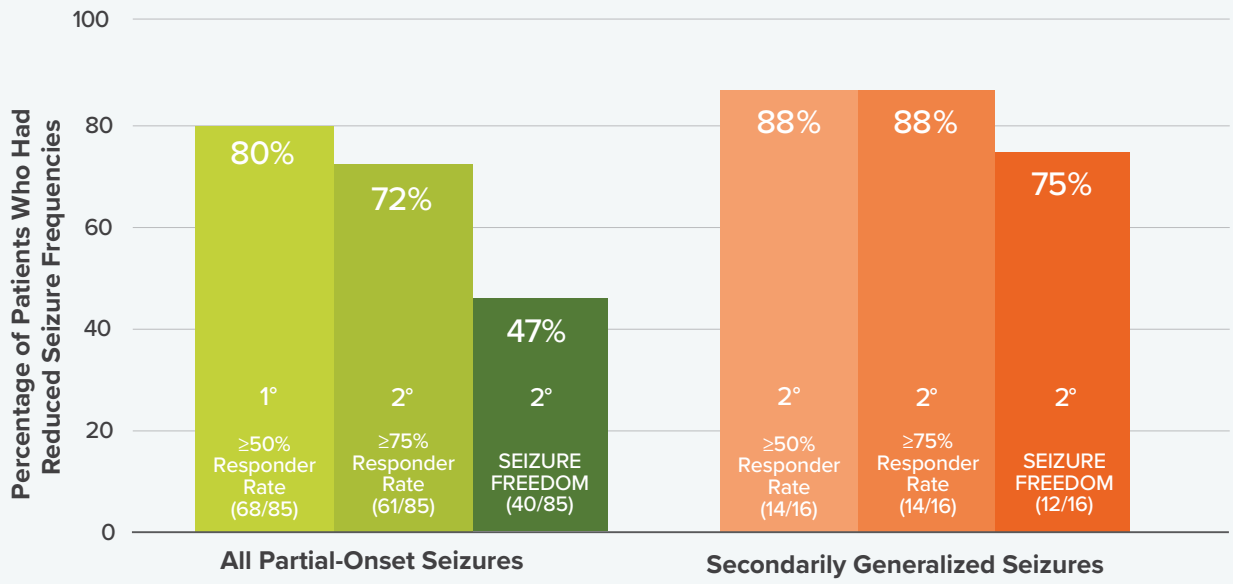
FAME Response Rates and Reduction in Seizure Frequency at Week 24

- The ≥50% responder rate at Week 24 was achieved by 80% (68/85) of patients with partial-onset seizures (primary endpoint) and 88% (14/16) of patients with secondarily generalized seizures (secondary endpoint)[10]
- Convulsive seizure patients experienced seizure freedom at a final dose of 4 mg (n=7/8) or 6 mg (n=5/8)[8]

Overall Response Rates During the 24-Week Maintenance Period in the FAME Study[10]



1°=primary endpoint; 2°=secondary endpoint.

Limitations:

- The study was open-label and did not include a control arm
- Appropriate multiplicity adjustments were not applied
- This information is descriptive
- The study included a relatively small number of patients

Patients With Reductions in Seizure Frequency[10]

	All Partial-Onset Seizures	Secondarily Generalized
≥50% reduction	68/85	14/16
≥75% reduction	61/85	14/16
100% reduction	40/85	12/16

IMPORTANT SAFETY INFORMATION (*cont'd*)

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions in patients aged 12 years and older receiving FYCOMPA (≥5% and ≥1% higher than placebo) include dizziness, somnolence, fatigue, irritability, falls, nausea, weight gain, vertigo, ataxia, headache, vomiting, contusion, abdominal pain, and anxiety. Adverse reactions in patients 4 to <12 years were generally similar to patients aged 12 years and older.

DRUG INTERACTIONS

FYCOMPA may decrease the efficacy of contraceptives containing levonorgestrel. Plasma levels of perampanel were decreased when administered with known moderate and strong CYP3A4 inducers, including, carbamazepine, phenytoin, or oxcarbazepine. Multiple dosing of FYCOMPA 12 mg per day enhanced the effects of alcohol on vigilance and alertness, and increased levels of anger, confusion, and depression. These effects may also be seen when FYCOMPA is used in combination with other CNS depressants.

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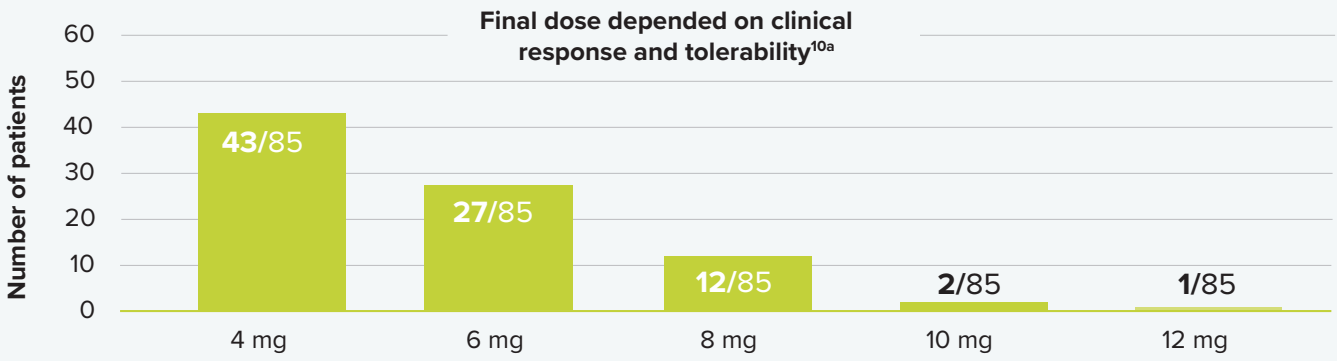
- The majority of patients had a final maintenance dose of FYCOMPA 4 mg or 6 mg[1,8,10*]

Number of Patients With Partial-Onset Seizures at Each Final Maintenance Dose[1,8,10]



[a]According to the investigator's judgment.

Adverse Reactions

- Adverse reactions at 24 weeks from the FAME study are described below
  - Among the 102 patients in the FAME study safety set, 77 (75.5%) reported TEAEs[10]
- Patients included in the analyses[8]:
  - Enrolled subjects: N=106 (3 did not receive drug and 1 was lost to follow-up)
  - Safety set: N=102 (96.23%)
  - Full analysis set: N=85 (80.19%)

Adverse Events at 24 Weeks in the FAME Study[8,10]

Most Common TEAEs	N=102
Dizziness	50.0% (n=51)
Somnolence	9.8% (n=10)
Headache	8.8% (n=9)
Discontinuations During the Study	**24.5% (26/106)**
Adverse event[a]	13.2% (n=14)
Withdrawal of consent	3.8% (n=4)
Major protocol violation	2.8% (n=3)
Lost to follow-up	1.9% (n=2)
Other	2.8% (n=3)

[a]The adverse events most commonly leading to discontinuation (≥1% of patients) were dizziness, headache, and seizure.

*Includes 37 patients taking moderate and strong CYP3A4 inducers, which can cause a reduction in FYCOMPA plasma levels and may require higher doses of FYCOMPA. The study was not designed to evaluate the effect of concomitant inducer/non-inducer ASM.[1,8]

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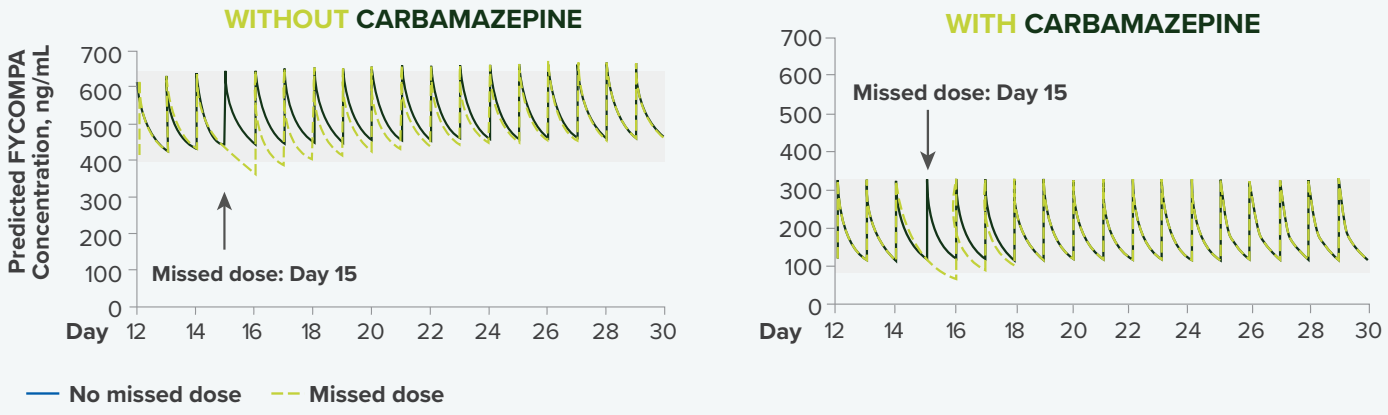
FYCOMPA Has a Long Half-life of Up to 105 Hours[1]*

- FYCOMPA should be administered once daily at bedtime[1]
- In the event of a missed dose, plasma levels of FYCOMPA remain relatively stable[11]
- Patients who miss a dose should resume dosing the following day at their prescribed dose[1]
  - Instruct patients to contact their healthcare provider if more than 1 day of dosing is missed

FYCOMPA Concentration-Time Profiles in Adults (Aged 18+) From Day 12, Following 8 mg/day[11]

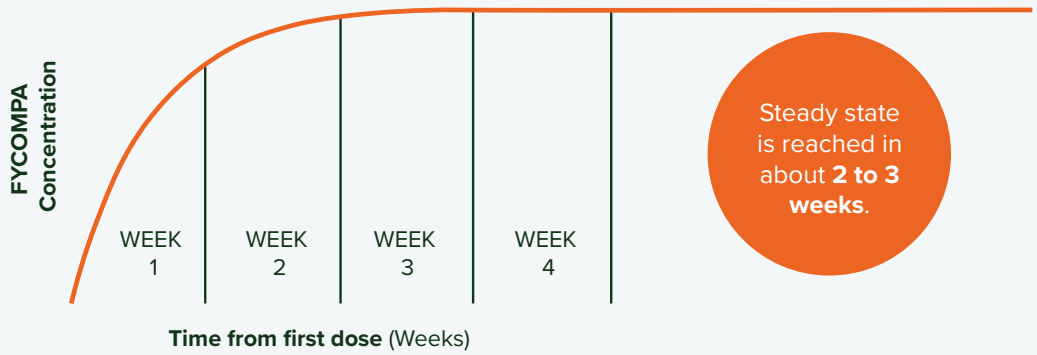


Design: Simulated PK model based on parameters derived from 19 Phase 1 FYCOMPA trials conducted in adults (N=606)[11]
- Nonlinear mixed effects modeling
- Simulations performed for patients receiving FYCOMPA 8 mg/day

Limitations: PK model not prospectively carried out in patients; further studies needed to replicate findings[11]

- Model-predicted concentration following 4 mg/day for 4 weeks is presented here
  - The time to maximum serum concentration of FYCOMPA ranges between 0.5 to 2.5 hours under fasted conditions[1]

Model-Predicted Concentration Following 4 mg/day for 4 Weeks[1]



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FYCOMPA Offers Once-Daily Dosing at Bedtime[1]

- Start patients at 2 mg and increase to 4 mg at 1 to 2 weeks[1]
- Then assess at 4 mg: Some patients with partial-onset seizures may respond to a 4 mg dose, which can be achieved in as little as 2 weeks[1,8]
- Adjust as necessary: Modify dose as needed based on clinical response and tolerability[1]
- May increase dose based on clinical response and tolerability by increments of 2 mg once daily no more frequently than at weekly intervals[1]
- Patients taking moderate or strong CYP3A4 inducers should start at a 4-mg dose. There is no established maintenance dose, and titration should be based on clinical response and tolerability[1]
- **Dosing adjustment and close monitoring** are recommended for patients when starting or withdrawing moderate or strong CYP3A4 inducers (including enzyme-inducing ASMs such as carbamazepine, phenytoin, and oxcarbazepine)[1]

FYCOMPA Dosing Recommendations[1]

In Partial-Onset Seizures
(with or without secondary generalization)

FYCOMPA tablets. Not actual sizes.

The recommended maintenance dose range for partial-onset seizures is 8 mg to 12 mg once daily, although some patients with partial-onset seizures may respond to a dose of 4 mg daily[1]

[a]In partial-onset seizure patients, a dose of 12 mg once daily resulted in somewhat greater reductions in seizure rates than the dose of 8 mg once daily, but with a substantial increase in adverse reactions.[1]

IMPORTANT SAFETY INFORMATION (*cont'd*)

PREGNANCY AND LACTATION

Physicians are advised to recommend that pregnant patients taking FYCOMPA enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry. Caution should be exercised when FYCOMPA is administered to pregnant or nursing women as there are no adequate data on the developmental risk associated with use in pregnant women, and no data on the presence of perampanel in human milk, the effects on the breastfed child, or the effects of the drug on milk production.

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Summary: 3 Pivotal Trials of FYCOMPA in Partial-Onset Seizures With or Without Secondarily Generalized Seizures[1,12-14]

Patients were titrated every week over a 6-week titration period; doses: 2 mg, 4 mg, 6 mg, 8 mg, and 12 mg.[1,12-14]

Primary Endpoint[1,12-14]

Median % reduction in partial-onset seizure frequency per 28 days

- FYCOMPA achieved proven reductions in partial-onset seizure frequency at doses of 4 mg/day, 8 mg/day, and 12 mg/day, with inducer and non-inducer ASMs

Post Hoc Exploratory Endpoint[8]

Seizure freedom in secondarily generalized seizures

- Up to 36% of patients with secondarily generalized seizures were convulsive seizure free during the 13-week maintenance phase

Secondary Endpoint[1]

50% or greater reduction in partial-onset seizure frequency

- Up to 54% of patients experienced a 50% or greater reduction in partial-onset seizure frequency with FYCOMPA

Most Common Adverse Reactions[1]

- Dizziness and disturbance in gait or coordination (including ataxia, gait disturbance, balance disorder, and abnormal coordination)
- Somnolence
- Fatigue-related events (including fatigue, asthenia, lethargy)

Prespecified Exploratory Endpoint[8]

Median % reduction in secondarily generalized seizure frequency per 28 days

- Up to a 75% frequency reduction in secondarily generalized seizures with FYCOMPA

Discontinuations[1]

- Discontinuations due to adverse reactions occurred in participants with placebo (5%), FYCOMPA 4 mg (3%), FYCOMPA 8 mg (8%), and FYCOMPA 12 mg (19%)

*Established in Phase 1 clinical trials with healthy adults. In pediatric patients ages 4 to 11, the half-life of FYCOMPA is long but is reduced by approximately half. In the presence of concomitant moderate or strong CYP3A4 inducers, FYCOMPA continues to have a long half-life, but it is reduced by approximately half in both adults and pediatrics.[8]

PK=pharmacokinetic.

IMPORTANT SAFETY INFORMATION (*cont'd*)

HEPATIC AND RENAL IMPAIRMENT

Use in patients with severe hepatic or severe renal impairment is not recommended. Dosage adjustments are recommended in patients with mild or moderate hepatic impairment. Use with caution in patients with moderate renal impairment.

DRUG ABUSE AND DEPENDENCE

FYCOMPA is a Schedule III controlled substance and has the potential to be abused and lead to drug dependence and withdrawal symptoms including anxiety, nervousness, irritability, fatigue, asthenia, mood swings, and insomnia.

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Vineet Punia, MD, MS
Adult Epileptologist
Epilepsy Center, Cleveland Clinic
Cleveland, Ohio

"Even older adults lead very active routines and would benefit from the once-daily dosing regimen FYCOMPA® (perampanel) offers."

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- **Advise patients and caregivers to contact a healthcare provider immediately if any of these reactions or changes in mood, behavior, or personality that are not typical for the patient are observed while taking FYCOMPA or after discontinuing FYCOMPA**
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Additional Resource: fycompa.com/hcp

References

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