

Izervay versus Syfovre: Two Rivals Recently Approved for Management of Geographic Atrophy

Sir,

Geographic atrophy (GA) is a chronic progressive degeneration of the macula and according to global estimates, GA affects over 5 million individuals globally, accounting for roughly 25% of legal blindness cases in the United Kingdom, and 20% of cases in North America.^[1] GA can lead to irreversible vision loss, one of the most common retinal pathologies that has impacted an estimated 1.5 million people in the United States.^[2] FDA-approved drugs launched this year have had a major impact on GA and now have possibly become rivals as Izervay has overcome the side effects of Syfovre, the monthly intraocular injection that reports to have caused retinal vasculitis.^[3]

Izervay is one of just two GA medications on the market right now, the other being Syfovre, which obtained FDA approval in February. The potential development of retinal vasculitis, a blinding condition, has caused the company to lose over two-thirds of their value and affected the prescription of Syfovre.^[4] Both Izervay and Syfovre have a slight but elevated risk of causing the neovascularization in the eye, which may necessitate further treatment and the risk

could increase with time [Table 1]. According to a research note written by Stifel analyst Annabel Samimy, the labelling for Izervay includes warnings about infections and high ocular pressure, and its safety profile has been noticeably cleaner than Syfovre. However, Iveric's clearance was also based on research findings that were tracked for a year, and the 24-month safety update is yet to come.^[5]

Izervay and Syfovre are the two GA medications on the market currently. When Syfovre was approved in February, a good number of peak sales were expected. However, reports of intraocular inflammation resulting from the drug have weakened its first-to-market advantage. Because both medications function in various ways, patients and health-care professionals can select the course of treatment that could be most effective for them.

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Conflicts of interest

There are no conflicts of interest.

Table 1: Differences between Izervay and Syfovre

Characteristic	Izervay	Syfovre
Mechanism of action	Complement protein-C5 inhibition, preventing the cleavage of C5 to C5a and C5b, that takes part in the formation of MAC	Drug binds to complement C3 and C3b fragments, resulting in inhibition of the complement activation
Pharmacodynamics	Reduction in the growth rate of GA during the baseline year, increased GA area growth is reflective of loss of photoreceptors and AMD disease progression	IVT administration following the subcutaneous administration did not result in QT prolongation
Pharmacokinetics		
Absorption/distribution	C_{max} is estimated to occur approximately 7 days' postdose, the mean plasma C_{max} is estimated to be 68.4 ng/mL. the predicted steady-state avacincaptad pegol C_{max} is 83.9 ng/mL	T_{max} is between 7 and 14 days volume of distribution is approximately 1.85 L following IVT administration
Elimination/metabolism	Systemic half-life of avacincaptad pegol is approximately 12 days, and expected to be excreted renally	The geometric mean half-life of elimination is 4.5 days, and the CL is 0.284 L/day
Dosage forms and strength	It is a clear to slightly opalescent-colorless to slightly yellow solution in a single-dose vial The recommended dose for Izervay is 2 mg (in 0.1 mL of 20 mg/mL solution)	It is a colorless to light yellow aqueous solution in a single-dose vial The recommended dose for Syfovre is 15 mg (0.1 mL of 150 mg/mL solution)
Indications	Geographic atrophy secondary to AMD	Geographic atrophy secondary to AMD
Immunogenicity	Not yet evaluated	There is a low incidence of anti-pegcetacoplan peptide antibodies
Side effects	Ocular and periocular infections, active intraocular inflammation endophthalmitis and retinal detachment, neovascular AMD, increase in intraocular pressure	Ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, conjunctival hemorrhage
Contraindications	Ocular or periocular infection and active intraocular inflammation	Ocular or periocular infection and active intraocular inflammation
Cost	\$2100 for monthly dose	\$2190 for every 25–60 days

MAC=Membrane attack complex, GA=Geographic atrophy, AMD=Age-related macular degeneration, CL=Clearance, IVT=Intravitreal, QT=QT interval in ECG, C_{max} =Maximum plasma concentration / Peak plasma concentration, T_{max} =Time to peak drug concentration

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