Evaluation of Discrimination in Access to Treatments for Geographic Atrophy in Europe: An Analysis of EMA Decision on Pegcetacoplan and the Withdrawal of Avacincaptad Pegol by Astellas

Introduction

Geographic atrophy is an advanced form of age-related macular degeneration (AMD) that affects millions of older individuals, causing irreversible and progressive vision loss. Without approved treatment options in Europe, these patients face a gradual decline in their visual capacity, which affects their autonomy and quality of life. Recently, two drugs, Pegcetacoplan (Apellis) and Avacincaptad Pegol (Astellas), have shown efficacy in slowing down this visual loss and were approved by the FDA in the United States. However, in Europe, these medications have encountered significant regulatory barriers: the European Medicines Agency (EMA) did not approve Pegcetacoplan, and Astellas voluntarily has recently withdrawn the application for Avacincaptad Pegol.

From an equity perspective and the right to health, access to innovative treatments should be considered a fundamental right for all patients, regardless of age or geographical location. The lack of treatment options undermines the right of older individuals to live autonomously and with dignity. This document examines the impact of these decisions on treatment access in Europe, discusses the EMA's assessment, and emphasizes the importance of autonomy for older adults with visual disabilities.

1. Geographic Atrophy, the Importance of Autonomy, and the Problem of Ageism

Studies have shown that autonomy and independence are essential for the well-being and quality of life of older adults with visual impairment. The ability to live independently is linked not only to physical health but also to psychological and social well-being. Older adults with visual impairment often face significant limitations in their daily activities, and maintaining their autonomy requires adaptive strategies and a supportive environment (Rooney et al., 2018).

Ageism, or discrimination based on age, is a bias that often underestimates the needs and the value of treatments for older adults, considering their benefits less of a priority than for younger groups. The lack of therapeutic options for older adults with geographic atrophy, despite their availability in other regions, reflects this bias within the healthcare system. By applying evaluation criteria that do not consider the importance of preserving independence in older individuals, regulatory decisions can perpetuate an ageist outlook that restricts this population's access to therapeutic innovations and also the opportunity to live independently and with dignity.

2. The Role of Complement Therapy in Geographic Atrophy

Complement therapy is an innovative approach that addresses the immune mechanisms involved in the progression of geographic atrophy. Genetic studies have identified variants in complement genes, such as Factor H, associated with an increased risk of AMD. These variants contribute to the inflammation and progressive retinal damage characteristic of this disease (van Lookeren Campagne et al., 2016).

Pegcetacoplan and Avacincaptad Pegol focus on inhibiting specific components of this system: Pegcetacoplan blocks component C3 and Avacincaptad Pegol inhibits C5, thereby reducing inflammation and cellular damage. Although these treatments do not directly improve vision, evidence shows they can slow the expansion of atrophy in the retina, which translates to a positive impact on patient autonomy and well-being. This potential to slow disease progression should be considered sufficient to justify patient access to these treatments.

Studies funded by the National Institutes of Health (NIH) have underscored the importance of C3 and C5 in the context of AMD, supporting the role of these complement inhibitors as promising approaches for treating geographic atrophy:

Yates et al. (2007) explored the association of genetic variants in the C3 gene with AMD risk, finding a strong relationship between certain C3 variants and susceptibility to the disease. These results highlight the essential role of C3 in AMD pathogenesis, supporting the development of therapies targeting this component to control disease progression (Yates et al., 2007).

Gurubaran et al. (2021), using AMD models, discovered that C5a can be activated independently of C3, indicating that both factors may have specific therapeutic effects. This study opens the possibility of using C5 inhibitors as effective strategies to slow the progression of dry AMD (Gurubaran et al., 2021).

Sitnilska et al. (2020) found correlations between imaging biomarkers and C3 and C5 activation in the aqueous humor of patients with early AMD, suggesting that inhibitors of these factors could offer benefits in preventing the progression of geographic atrophy (Sitnilska et al., 2020).

These NIH-funded studies support the use of C3 and C5 inhibitors as effective approaches to control AMD progression, providing a solid basis for considering these therapies in the treatment of geographic atrophy and their positive impact on patient quality of life.

3. EMA and FDA Regulatory Decisions: A Comparison EMA Decision and Voluntary Withdrawal of Avacincaptad Pegol by Astellas

The EMA decided not to approve Pegcetacoplan after re-evaluating the application in September 2024, arguing that the benefits in slowing atrophy did not represent a clinically significant change. On the other hand, Astellas voluntarily withdrew its application for Avacincaptad Pegol approval in October 2024, leaving European patients without access to this treatment, although the EMA did not prohibit it. This withdrawal further restricts access to treatments that could improve patient quality of life and raises questions about regulatory barriers in Europe.

FDA Approval

In the United States, the FDA approved Pegcetacoplan in February 2023 and Avacincaptad Pegol in August 2023, considering that slowing atrophy was a clinically important benefit for patients in terms of preserving their independence and functionality in daily life. This assessment acknowledges the disease's impact on quality of life and the importance of slowing its progression, despite the risks.

Following FDA approval of Pegcetacoplan (Syfovre) and Avacincaptad Pegol (Izervay) for treating geographic atrophy (GA) secondary to age-related macular degeneration (AMD), promising outcomes have been observed in real-world clinical practice in the United States.

Pegcetacoplan (Syfovre): This medication, administered through monthly or bimonthly intravitreal injections, demonstrated in clinical trials a reduction in the progression rate of GA by approximately 14% to 20%. In real-world use, patients have experienced a slowing of atrophic lesion expansion, helping to preserve visual function for a longer period. However, side effects such as ocular inflammation and an increased incidence of wet AMD have been reported, necessitating regular monitoring by specialists (American Academy of Ophthalmology, 2023).

Avacincaptad Pegol (Izervay): Similar to Pegcetacoplan, Avacincaptad Pegol is administered monthly via intravitreal injections and has shown efficacy in slowing GA progression. Treated patients have reported a reduction in the growth rate of atrophic lesions, potentially preserving central vision over an extended period. As with Pegcetacoplan, side effects such us ocular inflammation and an increased risk of developing wet AMD have been observed, highlighting the need for careful monitoring throughout treatment (American Academy of Ophthalmology, 2023).

It is important to note that, while these treatments do not reverse existing vision loss, their ability to slow GA progression offers a valuable option for preserving

vision and quality of life. Clinical experience with these therapies continues to grow, and long-term studies are expected to provide further insights into their effectiveness and safety in real-world settings.

4. Comparison of Risks and Adverse Effects with Other Treatments

Pegcetacoplan and Avacincaptad Pegol present known risks, including an increased likelihood of conversion to wet AMD and potential inflammatory effects. However, halting disease progression is already a significant advancement, and the benefits of preserving current vision and independence should be prioritized. A lack of early intervention can lead to social isolation and dependency, significantly impacting quality of life (Loh & Ogle, 2004; Crews & Campbell, 2001).

Comparison with Brolucizumab for Neovascular AMD

For neovascular AMD, the EMA approved Brolucizumab, an anti-VEGF treatment that also involves risks, including inflammation and retinal vascular occlusion. However, the safety profile of complement inhibitors in treating dry AMD may warrant their consideration, as these treatments target a patient group with no other options and provide a meaningful benefit by preserving central visual function over a longer period (Chuan et al., 2022).

5. Possible Violation of the Right to Health and Equity

The right to health includes access to innovative treatments, and denying it constitutes a form of discrimination against older patients. The lack of access to these treatments in Europe can be perceived as a limitation of this right in several aspects:

Unequal access to innovative treatments: Denying European patients therapeutic advances available in other regions creates an inequality in health access.

Impact on quality of life: Denying access to Pegcetacoplan and Avacincaptad Pegol limits patients' ability to preserve their independence and dignity.

Lack of therapeutic alternatives: Geographic atrophy is a condition with no approved treatment options in Europe, and denying access to these drugs perpetuates a healthcare exclusion based on age, which contradicts principles of equity and justice.

6. The Need to Reconsider EMA's Evaluation Criteria

Since geographic atrophy is a progressive disease with no curative treatment, the EMA must review its risk-benefit evaluation criteria to consider the impact on autonomy, quality of life, and the fight against ageism. These criteria should include the value of functional independence in older patients, which depends on slowing disease progression. Recognizing the impact of ageism in health decisions, the EMA can contribute to a fairer and more inclusive approach to the care of older adults with visual impairment by removing barriers that perpetuate exclusion from innovative treatments.

7. The Impact on Innovation in Europe and the Future of Visual Health

The lack of approval of Pegcetacoplan and the withdrawal of Avacincaptad Pegol raise questions about the future of innovation in treating complex visual diseases in Europe. These decisions not only affect those who suffer from geographic atrophy and lack options, but they also send a worrying message to researchers and companies about the challenges of introducing advanced therapies in the region.

For millions of older Europeans, access to new therapies means the opportunity to maintain their autonomy, enjoy their surroundings, and keep essential social connections. Regulatory barriers that hinder access to these treatments may be seen as a setback in efforts to improve the quality of life of an aging population that demands solutions that fit their real needs.

Limiting access to innovation could lead Europe to lose ground in a rapidly evolving medical field. Precision therapies, such as complement inhibitors, represent the future of personalized medicine and need a regulatory environment that fosters innovation and is open to advances. If Europe does not respond with openness, it risks losing crucial research investments, encouraging innovators to seek more favorable conditions outside the region.

Conclusion

Access to innovative treatments is not merely a matter of medical advancement; it is a matter of justice, the right to health, and equity. Older adults with geographic atrophy face an uncertain future, where each day without treatment brings them closer to losing their autonomy, becoming disconnected from the world, and, in many cases, experiencing profound isolation. Granting them access to therapies that can slow disease progression offers real hope—hope for

maintaining independence, seeing loved ones, moving safely, and living a full dignified life.

Regulatory decisions that limit access to these treatments often reflect an ageist bias, one that underestimates the needs and potential well-being of older adults. Ageism, present in how the benefits of new therapies are assessed, prevents this vulnerable population from fully exercising their right to health and equity. The dignity of older adults demands a more inclusive approach, one that appreciates the impact of these therapies on daily quality of life, looking beyond narrow clinical metrics.

Europe has the opportunity to lead a shift towards an evaluation framework that values not only immediate medical benefits but also considers the impact on its citizens' daily lives and their right to equitable access to innovation. This inclusive fair approach would position Europe as a leader in upholding the right to health for all, regardless of age, and reinforcing its commitment to a society where every medical advancement reaches those in greatest need.

Ultimately, prioritizing equity, rejecting ageism, and guaranteeing the right to health are essential pillars for inbuilding a more just, innovative, and humane Europe.

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