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What does the future hold for Light-chain Amyloidosis?

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Recent advances in the understanding and treatment of Light-chain (AL) Amyloidosis, including the availability of biomarkers and novel therapies, are reforming pharma's approach to the management of this rare disease and giving physicians new options to treat their patients. With a new standard of care rapidly developing, what does the landscape look like?

Amyloidosis is a group of rare, serious conditions caused by the abnormal folding of amyloid proteins that build up in tissue throughout the body. The accumulation of these insoluble deposits causes organs such as the heart, kidneys, stomach, and liver to thicken which then leads to organ toxicity, irreversible damage, and dysfunction that can ultimately be fatal.

With a protracted and often difficult patient journey, little is still known about the burden of AL amyloidosis on health-related quality of life, because it is a complex disease with a variety of clinical manifestations. Physicians we've asked, report the kidneys and heart are the most commonly involved organs and that just over a third of patients also have multiple myeloma. Depending on the tissues and organs that are affected, non-specific symptoms can include loss of appetite, fatigue, shortness of breath and tingling in the wrists, hands and fingers.

As with any disease, the prognosis for patients with AL amyloidosis is improved by early diagnosis and treatment. However, owing to these diverse presentations and a tendency to mimic many other more common medical conditions, it often takes patients an extended period of time to be referred to the right specialist. In our research, we have found the average time between initial presentation to diagnosis is over six months. Consequently, the condition is often diagnosed late and organ dysfunction is advanced by the time treatment is initiated.

A concoction of treatments

Until recently, what had complicated the patient journey further was the lack of treatments officially approved for the management of AL Amyloidosis. This rather predictably led to a medley of inconsistent treatment pathways across the globe. Corticosteroids, alkylating agents, proteasome inhibitors, and immunomodulatory drugs were just some of the off-label treatments that had been used by physicians in various combinations to treat AL Amyloidosis. In the absence of approved therapies, the treatment strategy being adopted was very much aligned with that recommended for Multiple Myeloma, with Velcade (bortezomib), used in combination with cyclophosphamide and dexamethasone (CyBorD) being considered the standard of care in the frontline setting. However, with very few controlled studies investigating the most appropriate approach for different settings, various treatment strategies have evolved over the past decade, primarily based on the opinion of experts in AL Amyloidosis.

Recently, Darzalex (daratumumab), a monoclonal antibody developed by Genmab and Janssen, that has been available for the management of patients with multiple myeloma across Europe for 5 years, was granted accelerated approval in combination with CyBorD for the treatment of newly diagnosed adult patients with AL amyloidosis. This followed the presentation of data from the Phase 3 ANDROMEDA study at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting and at the 26th European Haematology Association (EHA) Congress.

Research to understand the current market landscape

Earlier this year, we conducted research with physicians across Europe to understand the current situation and the impact new entrants may have on the marketplace going forward. Conducting tracking research to get a picture of the market for a rare disease such as AL Amyloidosis can be challenging. Firstly, and perhaps most obviously, the patient populations are small, which of course means that market research sample sizes are limited as a result. Secondly, diagnosis barriers can make it more difficult to accurately size the market. This is a common goal of demand assessment research, but often something we think about in tracking as well. Finally, the marketing process and lifecycle for a rare disease drug are very different to a mass-market product. These treatments are often approved based on single arm clinical trials via an accelerated process. For market researchers, this means we are often working with less complete information, which in turn forces us to make more assumptions when designing research.

At Research Partnership, we understand these challenges and come up with creative solutions to overcome them. Our Quantitative Centre of Excellence and in-house advanced analytics team are equipped with the skills, knowledge and creative flair to design and implement quantitative solutions that make tracking research in rare diseases feasible.

Prior to the approval of a new combination treatment for use across Europe, we conducted the first wave of our research to generate a baseline measure of the market situation. We found spontaneous awareness of new developments and approvals to be very limited in all markets. However, we also found there was some off-label use of regimens under development but not yet approved, with high levels of satisfaction.

The road ahead

Looking ahead, it would seem there is a large appetite for new therapies and the uptake, once they are approved, will be substantial. For example, more than half the physicians in our study who had experience prescribing new non-approved combination therapies said they would be likely or very likely to prescribe them again in the future. Furthermore, amongst the physicians who had not yet prescribed them, almost half said they would be likely to prescribe them in the future. These included not only the recently approved Darzalex regimen, but also regimens in development, e.g. Sanofi's Isatuximab, and a potentially first-in-class fibril-reactive mAb from AstraZeneca's Alexion division. However, while a large appetite for new therapies is promising, in order to secure high uptake pharma will need to ensure they are doing enough to increase awareness of newly approved therapies. Our research found more than two-thirds of physicians strongly agreed that they would be more likely to use a regimen if it was specifically approved for AL Amyloidosis, and more than half strongly agreed that they would be more likely to prescribe a regimen if it were recommended by a local/national AL Amyloidosis expert.

The future looks somewhat brighter, but despite recent advances in treatment strategies, delayed diagnosis of AL Amyloidosis remains a challenge to physicians and the disease continues to disrupt patients' lives. For companies with assets in development, further research to understand the patient journey would provide the insights needed to develop impactful disease awareness campaigns that not only improve the journey but enhance recognition of AL Amyloidosis itself and the therapies that are now available.

As with any rare disease, sensitively conducted market research can help pharma to truly understand the burden of AL amyloidosis, highlight the unmet need for treatment, and help both the industry and physicians identify treatments and patient support programmes aimed at improving patients' functioning, well-being, and overall health-related quality of life.behaviours of European and Japanese patients toward their CD are important to understand so that not only are their needs identified, but these needs are met in an appropriate manner that resonates with patients' respective experiences with CD.