hATTR Patient Screening Questionnaire – Proposal to CNSF

Background

Hereditary transthyretin (hATTR) amyloidosis is a relatively rare multi-system genetic disorder whose major disease manifestations include peripheral neuropathy, autonomic dysfunction and cardiomyopathy. Patients can present with predominantly neurologic or predominantly cardiac involvement, although most have a mixed phenotype. While the overall incidence in Canada is low, it is a common disease in some parts of the world (up to 1:538 in parts of Portgual) and is increasingly found in immigrant populations in Canada.

Historically, this was an invariably fatal disorder with liver transplant serving as the only treatment option associated with improved survival, although some patients would still have a degree of ongoing amyloid disease progression after transplant. The recent advent of two genetic therapies which have been approved for use in Canada (patisiran and inotersen) has completely changed the prognosis of patients with neurologic involvement from hATTR. Both treatments are designed to silence TTR amyloid production and based on two pivotal clinical trials, are shown to result in disease stability in most patients and even improvement in some.

With the development of an effective genetic therapy for a previously incurable disease, new tools are needed to aid in the early diagnosis of patients with hATTR amyloidosis. This form of amyloidosis can be a challenging diagnosis when a typical family history is not present; as a result, the diagnosis is delayed by 3 or more years in up to 30% of patients. Significant disease progression can occur in this short time period as overall survival ranges from 5-10 years from onset of symptoms.

The early symptoms of hATTR polyneuropathy are often difficult to distinguish from other more common causes of polyneuropathy, particularly if autonomic dysfunction is absent or minimally symptomatic. As a result, when suspecting the diagnosis, it is essential to screen for the involvement of other organ systems, especially cardiac symptoms.

With this in mind, we have developed a questionnaire to screen for common cardiac, neurologic and autonomic symptoms.

Purpose

The purpose of this initiative was to develop simple and easy to use patient questionnaire screening tool to assess for important signs, symptoms and historical features that might heighten the index of suspicion that a patient has hATTR. The objective is to provide healthcare providers with a tool that may facilitate easier screening of patients presenting with signs or symptoms suggestive of hATTR, in the hopes of enhancing earlier clinical recognition, diagnosis and treatment before advanced and irreversible organ damage occurs.

The questionnaires are designed to be used in multiple clinical settings to increase their ease of implementation. For example, they could be answered by the patient in an ambulatory clinic waiting room, hospital bed, administered by a healthcare provider during a clinical appointment, or even sent to a patient and completed in their home, either on paper or electronically.

As a multisystem disease, hATTR patients may be assessed by multiple medical specialists prior to the correct diagnosis being made. In light of this, different versions of the questionnaires were designed for

administration in different clinical settings. For example, a focused cardiac questionnaire could be administered by a healthcare provider who may be less familiar with cardiac manifestations of hATTR, such as a neurologist. Similarly, a focused neurologic questionnaire may be more useful to a cardiologist assessing a patient for possible hATTR who is less familiar with neurologic manifestations. A more comprehensive questionnaire was also created to assist any healthcare provider who may be less familiar with hATTR.

These questionnaires were developed by hATTR specialists at the University of Calgary. They were developed independently and without any commercial influence. Alnylam Inc has provided support for graphical design of the questionnaires but provided no input of content.

Roll-out Plan

These questionnaires will be used by the Amyloidosis Program at the University of Calgary where they were developed to help screen patients for possible hATTR.

The developers of these questionnaires hope that other clinical programs and centers across Canada may benefit from their use to aid in the earlier recognition and diagnosis of hATTR patients. The Canadian Neurological Sciences Federation (CNSF) and the Canadian Heart Failure Society (CHFS, affiliate of the Canadian Cardiovascular Society) have both been approached to assess interest in making these questionnaires available free of charge to their respective memberships. If successful, making the questionnaires available to other medical societies in Canada (such as general medicine and family medicine) may be considered.