

171

### Characterizing Familial Chylomicronemia Syndrome: Baseline data of the APPROACH Study



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**Background/Synopsis:** Familial Chylomicronemia Syndrome (FCS) is a rare, recessive genetic disorder caused by mutations in Lipoprotein Lipase (LPL) or genes required for LPL functionality. FCS is characterized by hyperchylomicronemia, recurrent abdominal pain, hepatosplenomegaly and recurrent episodes of acute pancreatitis that may result in pancreatic insufficiency. There are no FDA approved treatments for FCS and patients are managed with a low-fat diet. Due to the rarity of FCS there are few case series describing phenotypic variability in this disorder.

**Objective/Purpose:** To describe demographic and clinical characteristics of adult FCS patients enrolled in a clinical trial.

**Methods:** We analyzed baseline data from 67 patients with FCS, participating in a Phase III study of volanesorsen (apoC-III antisense oligonucleotide).

**Results:** Sixty-seven patients with a mean age of  $46 \pm 13$  years were enrolled. In 54 patients (80%) the diagnosis was confirmed genetically with LPL mutations accounting for 41 (81%) cases. The median age (P25, P75) at diagnosis was 27 (15, 36) years. Fifty four percent were female and 81% were Caucasian with a mean body mass index of  $24.9 \pm 5.7$  kg/m<sup>2</sup>. Median fasting TG (P25, P75) were 2012 (1247, 3117) mg/dL despite 43% of patients receiving fibrates, 27% fish oils and 21% statins. Eruptive xanthomas and lipemia retinalis were identified in 15 (22%) and 14 (21%) of patients, respectively. Forty-nine patients (73%) had a documented history of acute pancreatitis and among those, 27 patients experienced 83 pancreatitis events within the past 5 years. Twenty five percent of patients (17 out of 67) reported abdominal pain events during the 6-8 week screening period. Magnetic resonance imaging demonstrated that liver and splenic volumes were increased and that splenic volume had a mild inverse correlation with platelet counts ( $r = -0.1200$ ,  $p = 0.0052$ ). Postprandial TG clearance was severely impaired (Figure).

**Conclusions:** Our data confirm that TGs remain significantly elevated in most FCS patients despite dietary restrictions and TG-lowering therapies and that FCS is frequently complicated by acute pancreatitis. A relatively late age of diagnosis suggests a likely under diagnosis and appreciation of this rare genetic disorder.

172

### Familial Chylomicronemia Syndrome (FCS): Medical Nutrition Therapy for Patients and Providers



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**Background/Synopsis:** FCS is a rare autosomal recessive disorder due mainly to loss of function mutations of lipoprotein lipase. This results in severe elevation of triglycerides (TG) and massive accumulation of chylomicrons in plasma, often leading to pancreatitis. This underdiagnosed disorder causes decreased quality of life (QoL) and increased ER visits and hospitalizations. Many FCS patients live in isolation, experience employment difficulties and have trouble socializing due to its consequences.

**Objective/Purpose:** An unmet need came out of an FCS expert committee of Registered Dietitians/Nutritionists (RDNs) and patients, sharing challenges and adherence to dietary restrictions, meeting nutrient requirements and improving QoL. The aim was to share best practices, and ultimately provide tools and relevant resources to support patients, caregivers and healthcare professionals, and raise awareness of the dietary impact of managing the disease.

**Methods:** RDNs were interviewed to assess their expertise and interest in joining the expert group. Each RDN was assigned a topic in their area of expertise for the development of the consensus report. A patient with FCS was also included in the group to provide a personal perspective of the challenges of living with FCS. The report included patient-centered nutrition recommendations to optimize nutritional needs to manage and prevent complications of FCS. The report also provided resources for healthcare professionals. Topic-specific presentations were developed for future education.

**Results:** The RDN expert committee incorporated topic-specific presentations into a consensus report on diet and FCS. Topics provided current information on FCS, pancreatitis, implementing current nutrition recommendations,