Examining the high disease burden and impact on quality of life in familial chylomicronemia syndrome

Michael Davidson¹, Andrew Hsieh², Karren R. Williams², Zahid Ahmad³, Jeanine Roeters van Lennep⁴, Michael Stevenson² ¹Department of Medicine, University of Chicago, Chicago, IL, USA; ²Akcea Therapeutics, Cambridge, MA, USA; ³Division of Nutrition and Metabolic Disease, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, USA; ⁴Division of Internal Medicine, Erasmus MC, University Medical Center Rotterdam, The Netherlands

THERAPEUTICS

Introduction

- Familial chylomicronemia syndrome (FCS) is a rare genetic disorder characterized by severe chylomicronemia, leading to high serum triglycerides (TGs) and consequent risk of recurrent and acute, potentially fatal, pancreatitis²
- FCS is caused by a deficiency in the production or functionality of lipoprotein lipase (LPL), the enzyme that breaks down plasma TGs¹
- Patients with FCS typically present with multiple symptoms as a result of severely high TG levels, including intense abdominal pain, nausea and vomiting, and fatigue¹⁻⁴

FCS: Summary of disease manifestation



- The only currently available management option for patients with FCS is to follow an extremely restrictive low-fat diet (≤ 20 g daily), limit simple carbohydrates and abstain from alcohol^{1,2,4,5}
- Compliance with this diet is difficult; even with strict adherence, TGs commonly remain high, resulting in patients remaining at risk of AP⁴
- Although the acute clinical manifestations of FCS have been well documented, cognitive and psychosocial effects have been less well described
- The Investigation of Findings and **Observations Captured in Burden of Illness** Survey in FCS Patients (IN-FOCUS) was a multinational web-based survey conducted to

Methods

• IN-FOCUS was a self-reported, online, anonymous quantitative research survey (approx. 45 mins), conducted with patients diagnosed with FCS (n = 166)

• All research materials were approved by relevant country-level ethics committees



characterize and quantify the burden of illness associated with FCS across all possible dimensions from the patient's perspective⁴

Daily Fat Limit and Difficulty Managing Fat Intake

40%

• 93% of respondents indicate it is challenging to

1=Strongly disagree 7=Strongly agree

Rating 1–3 Rating 4 Rating 5–7

93%

60% 70% 80% 90% 100%

50%

1=Very easy 7=Very challenging

Rating 1–3 Rating 4 Rating 5–7

• IP hospitalization duration Testing volume due to FCS professionals and main FCS-treating physician

- Emotional well-being

- Childbearing (women only)

– Financial



Results

Attitudes Towards Social Relationships and Activities



Current FCS Management Strategies



Diet/lifestyle Medical Social

- FCS patients not only seek to restrict fat from their diets, but also employ other methods to attempt to reduce TGs and potential symptoms, including pancreatitis
- On average, patients reported using six different approaches to reduce plasma TGs

Dietary Modifications by Patient Group

2%-

0%

5%

10%

20%

30%

maintain restricted fat levels

How Difficult is it

to Manage Your

Fat Intake?

I always avoid alcohol in order to avoid developing symptoms of my FCS	8% 8%	84%
I often eat repetitive meals because my dietary restrictions limit variety in the types of foods I can eat	<mark>7%</mark> 13%	80%
I tend to replace the fat in my meals with protein	4 <mark>%</mark> 16%	80%
I find it difficult not having the simple comforts that most people turn to for relieving stress, like eating	11% 14%	75%
I feel guilty if I drink even a small amount of alcohol because I have been told to avoid it	10% 10%	80%
I do not smoke cigarettes specifically because it would make my FCS worse	<mark>9%</mark> 16%	76%
I often find myself craving foods with higher fat content	12% 12%	76%
I sometimes fast (avoid eating for extended periods of time) in order to avoid or manage my FCS symptoms	<mark>11%</mark> 9%	80%
I am afraid to eat anything without first reading the nutritional label	10% 12%	78%
I have trouble focusing because my diet leaves me feeling hungry or unsatisfied with my food	<mark>9%</mark> 15%	76%
I spend a lot of my day thinking about food because of my FCS	12% 11%	77%
The thought of going out for meals or ordering food at a restaurant makes me very anxious	<mark>10%</mark> 16%	74%
I spend hours at the grocery store when I go shopping, looking for foods that will fit in my restricted diet	13% 12%	75%
I feel scared or anxious if I eat more than the very low amount of fat I am allowed in a given day	<mark>8%</mark> 18%	74%
When cooking for family or company, I always need to prepare a separate meal for myself	9% 17%	73%
I tend to replace the fat in my meals with carbohydrates	15% 12%	73%
I sometimes eat higher amounts of fat than I should to avoid drawing attention to my FCS	18% 14%	68%
I have developed strange eating habits due to my FCS, like throwing up after I eat or using laxatives to clear food from my system	25% 9%	66%
	0% 20% 40%	60% 80% 100%



• Respondents felt socially restricted because of their FCS; most reported that FCS affects multiple aspects of their social life and relationships



• FCS significantly interferes with mental and emotional well-being across multiple domains

• A vast majority of respondents reported being concerned about the potential long-term impact of FCS on their health as well as other aspects of their life, including work



• Dietary adherence is not only restrictive, but can also affect patients' mental/emotional health

• The majority of respondents strongly agree that they make extreme dietary restrictions as a means to control their FCS symptoms and strongly agree that they experienced food cravings (76%) and have trouble focusing due to restricted diet (76%)

• The majority of respondents felt scared/anxious if they exceeded the permitted daily level of fat intake (74%), and spend considerable time choosing and preparing meals due to FCS (73%)



• 70%, 81%, and 71% of respondents find managing symptoms extremely energy draining, time consuming, and rigid/prohibitive respectively • Despite adherence to diet, 53% of respondents still experienced symptoms associated with FCS

Conclusions

Largest Burden of Illness study in patients with FCS (N = 166) to date, filling a major gap in the literature

Patients face many comorbidities associated with FCS, the most serious of which is acute pancreatitis

- 40% of patients reported experiencing an event of pancreatitis
- Average of 13 events over their life so far

The burden of FCS goes far beyond physical symptoms & impacts patients' mental & emotional well-being & even professional endeavors

- Only 23% of patients reported full time employment, with 65% of unemployed patients reporting it was largely due to FCS
- FCS negatively effects patients stress/anxiety levels, mental ability, and feeling of self worth

Management strategies are incredibly challenging and time consuming to adhere to

- 53% of patients reported still experiencing symptoms even with rigorous adherence
- Diet is a frequent source of anxiety, worry and fear for patients with FCS and make social activities extremely challenging

References

- 1. Gaudet D et al. *N Engl J Med* 2014;371:2200–2206.
- 2. Brahm AJ and Hegele RA. *Nat Rev Endocrinol* 2015;11: 352–62.
- 3. Symersky T, van Hoorn B, Masclee AAM. *JOP* 2006;7:447–53.
- 4. Davidson M et al. Expert Rev Cardiovasc Ther 2017;15:415–423.
- 5. Valdivielso P, Ramirez-Bueno A, Ewald N. Eur J int Med 2014;25:689–694.

Disclosures

- This study was funded by Akcea Therapeutics, Inc.
- Michael Davidson is a scientific advisory board member of Abbott, Amgen, AstraZeneca, Merck and Sanofi, Regeneron.
- Michael Stevenson, Andrew Hsieh, and Karren R. Williams are employees of Akcea Therapeutics, Inc.
- Zahid Ahmad has received research support from the National Institutes of Health, Regeneron and the FH Foundation, and has received honorarium from Amgen and Sanofi, Regeneron.
- Jeanine Roeters van Lennep has received grants from the Dutch Heart Foundation, serves on the Governance advisory board of Amryt and has received honorarium from Akcea Therapeutics, Inc.

Acknowledgments

make you feel?

- The authors would like to recognize and thank the patients with FCS who completed the survey. Their answers provided insight into the broader ramification of FCS outside of the physical symptoms.
- The authors also like to recognize Alan Gilstrap for his tireless efforts to advocate for patients with FCS and Jill Prawer: Patient, Founder and Chair of LPLD Alliance.
- Trinity Partners (Waltham, MA) provided survey support and analysis.
- ApotheCom and Brant Hubbard provided poster production support.

European Conference on Rare Diseases & Orphan Products • Vienna, Austria • May 10-12, 2018