Severe Hypertriglyceridemia to Familial Chylomicronemia Syndrome: Roadmap to Reduce Pancreatitis

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DISCLOSURES

Dr. Cobble serves on the advisory board of Novo Nordisk and on the speakers bureaus for Johnson & Johnson and Vanda Pharmaceuticals. He is on both the advisory board and speakers bureau for AbbVie and Amgen.

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INTRODUCTION

Severe hypertriglyceridemia (sHTG), defined as fasting triglycerides (TGs) ≥500 mg/dL, increases the risk of acute pancreatitis due to the presence of TG-carrying lipoproteins called chylomicrons in the circulation.[1,2] Often first detected in primary care settings on a routine lipid panel, sHTG commonly reflects interactions between inherited susceptibility, insulin resistance, diet, alcohol use, and the use of TG-raising medications.[2,3] Primary care clinicians (PCCs) are positioned to detect sHTG early in patients with predisposing conditions including diabetes, obesity, hypothyroidism, and chronic kidney disease; timely recognition and intervention can reduce the risk of pancreatitis and cardiovascular (CV) complications.[1]

Hypertriglyceridemia (HTG) occurs in ~28% of the general population (1 in 4).[4,5] In comparison, the estimated prevalence of sHTG globally is 1.14% (1 in 88).[4,5] In a US claims-based analysis of 1.8 million adults with TG values, 12,050 (0.7%) individuals had TGs 500 to 879 mg/dL and 3944 (0.2%) had TGs ≥880 mg/dL, indicating that sHTG may be uncommon enough to be overlooked but common enough to appear routinely in patient panels.[6] The primary immediate risk of sHTG is acute pancreatitis, and the long-term risk is atherosclerotic cardiovascular disease (ASCVD).[7] Acute pancreatitis and CV event rates are higher in patients with higher TG levels. Among adults with TGs <150 mg/dL, acute pancreatitis rates are 0.6 per 1000 person-years and CV events rates are 3.3 per 1000 person-years. Among adults with TGs ≥880 mg/dL, acute pancreatitis rates are 9.9 per 1000 person-years (a nearly 20-fold increase from TGs <150 mg/dL) and CV event rates are 10.3 per 1000 person-years.[1,6]

Key takeaways

- sHTG (fasting TGs ≥500 mg/dL) is associated with an increased risk of acute pancreatitis and CV events.
- Most sHTG in primary care is polygenic and multifactorial, so assessment should consider risk factors such as diabetes, obesity, alcohol use, medications, kidney disease, hypothyroidism, pregnancy, and acute illness.
- Chylomicronemia syndromes may occur with TGs ≥880 mg/dL and include familial chylomicronemia syndrome (FCS), which is characterized by persistent chylomicronemia and responds poorly to standard TG-lowering therapy.
- Treatment of sHTG begins with pancreatitis risk reduction through dietary changes, correction of hyperglycemia if present, and removal of TG-raising drugs, followed by pharmacologic TG lowering and reassessment of CV risk.
- Lifestyle interventions are critical to treating sHTG and include reducing total fat, avoiding alcohol, limiting refined carbohydrates and sugar-sweetened beverages, consuming lean protein and non-starchy vegetables, and pursuing weight reduction when appropriate.
- Apolipoprotein C-III (apoC-III)-targeted treatments, such as olezarsen and plozasiran, are changing the sHTG landscape, showing >80% reductions in the risk of acute pancreatitis.

CASE STUDY

You are seeing a 47-year-old man for a visit regarding type 2 diabetes and hypertension. He reports mild epigastric discomfort after meals, and weekend alcohol use of up to 14 beers. His medications include metformin, valsartan, and hydrochlorothiazide. On a quick dietary review, he reports consumption of high-carbohydrate, high-fat foods (including doughnuts, bagels/cream cheese, pancakes/syrup, fruit juices) on a daily basis. His body mass index (BMI) is 29 kg/m^2, glycated hemoglobin (HbA1c) 7.1%, blood pressure 128/84 mmHg, fasting TGs 930 mg/dL, direct low-density lipoprotein cholesterol (LDL-C) 94 mg/dL, and high-density lipoprotein cholesterol (HDL-C) 27 mg/dL.

THE SPECTRUM OF HTG

Physiology of HTG

TGs are a source of fat derived from food and produced by the liver. TGs are primarily carried in chylomicrons, derived from food, and in very low-density lipoprotein (VLDL), derived from synthesis by the liver.[2] TG-carrying lipoproteins are cleared from the circulation by the enzyme lipoprotein lipase (LPL), which is found in adipose tissue, skeletal muscle, and the heart. LPL hydrolyzes TGs in chylomicrons and VLDL into free fatty acids for storage or energy use; the chylomicron remnants and VLDL remnants thus formed are then cleared by the liver.[2] ApoC-III is carried on TG-rich lipoproteins and inhibits LPL activity, resulting in elevated TG levels.[8]

TG levels reflect the production and clearance of TG-rich lipoproteins from the liver and chylomicrons from the intestine. When production of TGs is increased or clearance is impaired, TG-rich particles accumulate and severely elevated levels of TGs can result, increasing pancreatitis risk.[2,9]

Pathophysiology of sHTG and its complications

sHTG commonly encountered in clinical practice is polygenic rather than caused by a single-gene disorder. When ≥1 secondary factors such as diabetes, obesity/weight gain, excessive alcohol use, suboptimal eating patterns, chronic kidney disease, hypothyroidism, pregnancy, and TG-increasing medications are present, TG levels rise and contribute to the onset and severity of HTG.[2,3]

Pancreatitis is the most urgent and immediate consequence of sHTG, particularly if TGs are ≥880 mg/dL. Acute pancreatitis due to HTG is thought to involve hydrolysis of excess TGs by pancreatic lipase, local free fatty acid toxicity, microvascular injury, inflammatory signaling, and acinar cell damage.[9] Clinically, HTG-induced acute pancreatitis may present with epigastric pain, nausea, vomiting, and systemic illness, and it can progress to pancreatic necrosis, organ failure, prolonged hospitalization, and recurrent episodes if TG levels remain uncontrolled.[9,10] Although mild acute pancreatitis usually resolves with supportive care, severe acute pancreatitis carries substantial morbidity, and mortality can reach approximately 15% to 30% in severe or infected necrotizing disease.[10,11]

CV risk in sHTG is phenotype specific; sHTG often clusters with high-risk cardiometabolic features and elevated non–HDL-C or apolipoprotein B (apoB).[12,13] Elevated non–HDL-C indicates increased cholesterol across atherogenic particles such as VLDL, intermediate-density lipoproteins, LDL-C, and remnants.[1] Elevated apoB indicates an increased number of atherogenic particles and may better capture residual ASCVD risk when TG-rich lipoproteins are abundant.[1,2] To reduce CV risk in patients with sHTG, after urgent TG lowering, PCCs should reassess ASCVD prevention using LDL-C, non–HDL-C, apoB when available, diabetes control, blood pressure, smoking status, and statin eligibility or intensity.[1,7]

SCREENING, IDENTIFICATION, AND DIAGNOSIS

A standard lipid panel will usually identify sHTG, but fasting confirmation is important when TGs are ≥500 mg/dL or when the result will change management. A fasting repeat lab will help classify HTG severity and determine whether pancreatitis risk reduction measures should begin immediately.[1,2] Very high TGs can interfere with obtaining an LDL-C value, since it is calculated, so a direct LDL-C measurement, non–HDL-C, apoB, or repeat testing after TGs improve is often needed to evaluate ASCVD risk accurately.[1] When TGs are markedly elevated (i.e., ≥880 mg/dL), TG lowering is the primary focus prior to addressing LDL-C lowering.

Confirmation of sHTG should be accompanied by assessment of symptoms and potential urgency for intervention. This should include evaluation for secondary causes of sHTG as they are common and often modifiable. Metabolic contributors include new-onset or suboptimally managed diabetes, obesity, and hypothyroidism, while renal, endocrine, and physiologic contributors include chronic kidney disease or nephrotic syndrome, pregnancy, Cushing syndrome, and acute inflammatory illness.[1,2] Exposure to TG-increasing medications should be reviewed; these include alcohol, estrogens, retinoids, glucocorticoids, atypical antipsychotics, human immunodeficiency virus (HIV) protease inhibitors, some beta blockers, thiazides, bile acid sequestrants, and immunosuppressants.[1,2] Clinical evaluation for abdominal pain, nausea, vomiting, history of prior pancreatitis, alcohol intake, diabetes management if present, pregnancy, and recent medication changes should be performed.

Clinical features and differential diagnosis

Chylomicronemia syndrome is an umbrella term for clinically important chylomicron accumulation, generally with fasting TGs ≥880 mg/dL; causes include FCS (rare, 2% of cases) and the more common multifactorial chylomicronemia syndrome

(MCS, 98% of cases seen in clinical practice).[13,14] Thus, if fasting TGs are ≥880 mg/dL, FCS and MCS should be considered as potential diagnoses. FCS is driven by biallelic loss-of-function variants affecting the LPL pathway. MCS is not associated with single gene mutations and is polygenic in etiology.

Differentiating between MCS and FCS

MCS usually presents in adulthood, fluctuates with secondary triggers, and often improves with glycemic control, alcohol cessation, weight loss, medication changes, and standard TG-lowering therapy including fibrates or omega-3 fatty acids.[2,12] Individuals often have high BMI and high apoB and non–HDL-C levels; TG levels may improve when secondary factors are corrected.[12,13] In contrast, FCS is rare, typically begins in childhood or adolescence, and results in persistent extreme TG elevations that do not respond to conventional TG-lowering therapies. Secondary factors such as diabetes or obesity are absent. These individuals have normal or sometimes low BMI. FCS is associated with recurrent pancreatitis risk.[13] Abdominal pain, eruptive xanthomas (yellowish skin papules encircled by an erythematous halo), lipemia retinalis (creamy white discoloration of retinal blood vessels), and pancreatitis can occur in both MCS and FCS.[1,12,13,15-18] The risk of acute pancreatitis in MCS is less than that observed in FCS. Characteristics of the various hypertriglyceridemic diseases across the TG spectrum are summarized in **TABLE 1**.

Although FCS is rare, the diagnosis should be entertained in an individual with normal or low BMI, childhood or adolescent onset of sHTG, persistent extremely elevated TGs despite the absence of secondary drivers, and history of recurrent pancreatitis. A clinical scoring tool (the North American FCS score) can help with diagnosing FCS and is available at https://www.lipid.org/nla/north-american-familial-chylomicronemia-calculator-or-nafcs-scoring-tool.[17] Based on the score obtained, referral to a lipid specialist for evaluation and genetic testing should be pursued as appropriate.

Patients with symptoms concerning for acute pancreatitis should be promptly referred for emergency evaluation rather than managed in the outpatient setting.[1,9] TG levels fall rapidly after fasting, intravenous fluids, or acute illness management, so delayed sampling can underestimate the triggering TG burden in pancreatitis.[9]

TABLE 1. Spectrum of hypertriglyceridemic diseases by phenotype.[1-3,6,13,17]

Feature	Moderate HTG	sHTG	Very severe/ extreme HTG	MCS	FCS
TG levels	150 to 499 mg/dL	≥500 mg/dL	≥880 mg/dL	Usually ≥880 mg/dL, with levels that fluctuate over time	Usually persistently ≥880 mg/dL; often >1500 to 2000 mg/dL
Causes	Insulin resistance, obesity, type 2 diabetes, metabolic syndrome, alcohol use, high refined-carbohydrate intake, and other secondary causes	Polygenic susceptibility plus secondary triggers such as uncontrolled diabetes, obesity, alcohol use, medications, or hypothyroidism	Major secondary triggers superimposed on polygenic risk or on chylomicronemia syndromes	Polygenic or multifactorial disorder with obesity, insulin resistance or diabetes, alcohol use, and medication triggers	Rare monogenic disorder due to biallelic loss-of-function variants in the lipoprotein lipase pathway
Primary disease mechanism	Increased VLDL production with impaired TG-rich lipoprotein clearance	Marked accumulation of VLDL and TG-rich lipoproteins; pancreatitis risk begins to rise	Chylomicron accumulation with severe impairment of TG-rich lipoprotein clearance	Chylomicronemia driven by combined genetic susceptibility and secondary factors	Profound defect in chylomicron clearance
Clinical hallmark	Usually asymptomatic; cardiometabolic risk phenotype	Often asymptomatic, but postprandial abdominal discomfort may occur; pancreatitis prevention becomes a priority	Abdominal pain, nausea, eruptive xanthomas, lipemia retinalis, and high pancreatitis risk	Adult onset, fluctuating TG levels, recurrent abdominal pain or pancreatitis, and metabolic syndrome features are common	Childhood or adolescent onset, recurrent pancreatitis, eruptive xanthomas, lipemia retinalis, low apoB/LDL-C, and minimal metabolic syndrome
Dietary therapeutic response	Responds to weight loss, reduced refined carbohydrates or sugar-sweetened beverages, less alcohol, and improved overall diet quality	Usually improves with lower fat intake, alcohol elimination, reduced simple sugars, and correction of secondary causes	Requires urgent very low-fat nutrition (about 10% to 15% of calories from fat or ≤20 to 30 g/day), no alcohol, and rapid treatment of hyperglycemia	Often shows substantial improvement when secondary causes are corrected and a very low-fat diet is used short term	Requires lifelong strict very low-fat nutrition; response to conventional TG-lowering drugs is often limited

Abbreviations: apoB, apolipoprotein B; FCS, familial chylomicronemia syndrome; HTG, hypertriglyceridemia; LDL-C, low-density lipoprotein cholesterol; MCS, multifactorial chylomicronemia syndrome; sHTG, severe hypertriglyceridemia; TG, triglyceride; VLDL, very low-density lipoprotein.

Besides dietary nonadherence, PCCs should assess for concomitant diseases and factors that increase the risk of HTG.[3,13] **FIGURE 1** summarizes a diagnostic pathway that can be useful for the workup and clinical decision-making in patients with TGs ≥500 mg/dL and ends with treatment, monitoring, and referral triggers.[1,17]

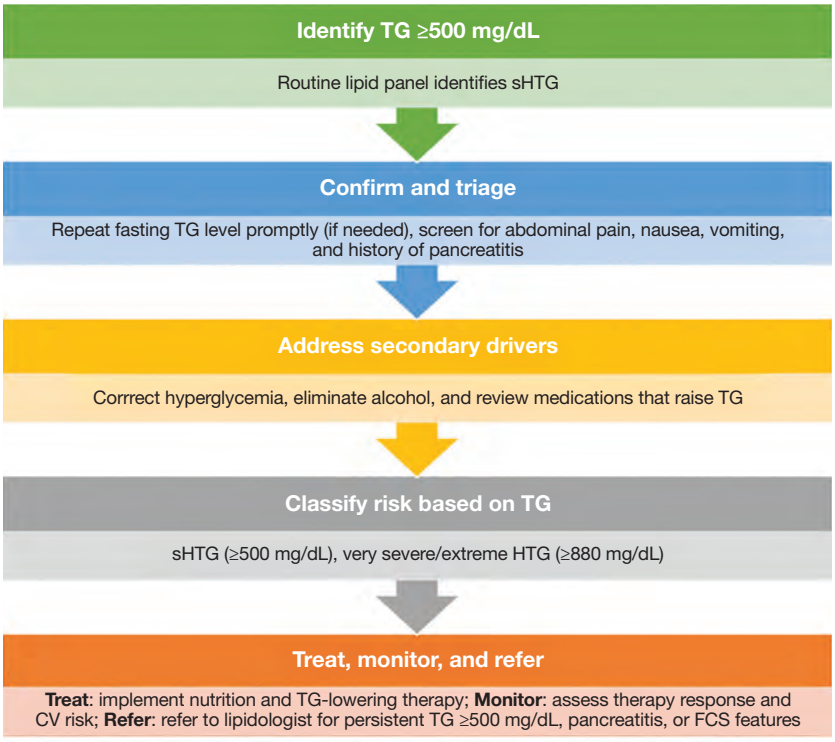
SHTG TREATMENT APPROACHES

The first treatment priority in sHTG is prevention of pancreatitis, especially when TGs are ≥880 mg/dL or symptoms suggest acute pancreatitis.

Immediate approach

For TGs ≥880 mg/dL, clinicians should counsel patients to initiate a chylomicron-clearing very low-fat diet, eliminate alcohol consumption, rapidly correct hyperglycemia if present, and stop or substitute TG-raising medications when clinically feasible.[1,2] Details for rapid TG-lowering nutrition and immediate interventions for reducing pancreatitis risk in patients with TGs ≥880 mg/dL are described in **TABLE 2**.[1,2]

FIGURE 1. Pathway for sHTG in primary care.[1,13]



Abbreviations: CV, cardiovascular; FCS, familial chylomicronemia syndrome; HTG, hypertriglyceridemia; sHTG, severe hypertriglyceridemia; TG, triglyceride.

General principles

Lifestyle measures: Dietary counseling for sHTG should include recommendations to reduce total fat, avoid alcohol, limit refined carbohydrates and sugar-sweetened beverages, use lean protein and non-starchy vegetables, and pursue weight reduction when appropriate.[1,2] When TGs are in the chylomicronemia range (≥880 mg/dL), fat restriction is more stringent than typical cardiometabolic diets and requires referral to a dietitian familiar with counseling for sHTG, particularly when food insecurity, cultural food patterns, or limited access to low-fat options complicate adherence.[1,12] Recommended very low-fat diets typically consist of 10% to 15% of calories from fat or ≤20 to 30 g/day; limiting dietary fat to <5% for a few days until TG falls below 880 mg/dL in severe elevations may be appropriate.[1,2] Of note, low-fat diets can be challenging in patients with concomitant diabetes. Lifestyle interventions are critical for management of

TABLE 2. Rapid TG-lowering interventions for TGs ≥880 mg/dL or impending pancreatitis.[1,2]

Goal for TGs ≥880 mg/dL	Comments/practical actions
Clear chylomicrons quickly	Use a very low-fat diet: 10% to 15% of calories from fat or ≤20 to 30 g/day; consider <5% until TGs fall below 880 mg/dL
Eliminate major triggers	Avoid alcohol completely; avoid sugar-sweetened beverages, added sugars, high-fat foods, and refined carbohydrates
Correct metabolic drivers	Treat hyperglycemia promptly and address insulin deficiency or severe insulin resistance; recommend 150 minutes per week of moderate-intensity aerobic activity or 75 minutes per week of vigorous-intensity aerobic activity; weight loss of 5% to 10%
Review medications	Stop or substitute TG-raising agents when clinically feasible, including thiazides, some beta blockers, estrogens, glucocorticoids, retinoids, and atypical antipsychotics
Support dietary adherence	Use lean protein, non-starchy vegetables, and very low-fat or nonfat foods; involve a dietitian when sHTG is severe, recurrent, or complicated by FCS or access barriers. Dietary plans should account for culture, cost, food access, literacy, and comorbidities
TG-lowering therapies	Initiate TG-lowering therapy based on diagnosis/indication. Conventional TG-lowering therapies are less effective; use apoC-III–targeted therapies for significant reduction in TGs and pancreatitis risk

Abbreviations: apoC-III, apolipoprotein C-III; FCS, familial chylomicronemia syndrome; sHTG, severe hypertriglyceridemia; TG, triglyceride.

sHTG, as significant reductions in TG are associated with certain measures[1]:

- Weight loss (~5% to 10%)—may result in up to a 70% reduction in TGs, although most patients experience about a 10% to 20% reduction
  - o Dietary modification (includes alcohol restriction or abstinence)—70% reduction in TGs or higher depending on baseline TGs and adherence to diet
  - o Physical activity and exercise—up to a 30% reduction in TGs depending on type, duration, and intensity of activity

Conventional TG-lowering therapies: Fibrates and prescription omega-3 fatty acids remain common TG-lowering options for pancreatitis risk reduction in sHTG, while statins are used to reduce ASCVD risk, especially in patients with MCS. Fibrates and prescription omega-3 fatty acids lower TGs by approximately 20% to 50%, and statins lower TGs by about 15% to 30%.[19] Medication selection should account for renal function, drug-drug interactions, tolerability, pregnancy potential, cost, and whether the TG elevation appears driven by a remediable secondary cause.[1,2] If a statin is used, concomitant fenofibrate is generally preferred over gemfibrozil as TG-lowering therapy; gemfibrozil should be avoided in combination with statins because of an elevated risk of muscle-related adverse events.[1,7]

Aspects of management specific to FCS

FCS management centers on lifelong very low-fat nutrition, avoidance of alcohol, prevention of pancreatitis, and care coordination with a lipid specialist and dietitian. Conventional TG-lowering therapies have limited to no effect in FCS because the central defect is in the LPL pathway, causing impaired chylomicron clearance. It is important to note that omega-3 fatty acids may worsen TG levels in FCS as they are an added fat source; therefore, they should be avoided.[2] The new injectable apoC-III–directed therapies olezarsen and plozasiran are now approved as adjuncts to diet to reduce TGs in adults with FCS (see below).[18,20,21]

Monitoring and referral

Monitoring depends on baseline disease severity and the timing of interventions. A fasting TG level should be rechecked 1 to 2 weeks after an immediate intervention, especially when baseline TGs are very high. The monitoring interval should be adjusted according to medication changes, glycemic control, adherence, symptoms, and TG stability. Follow-up should also monitor non–HDL-C, apoB when available, HbA1c/blood glucose, liver enzymes when clinically indicated, renal function for fibrate dosing and/or concomitant kidney disease, and barriers to dietary or medication adherence.[1,2]

Collaboration with a lipidologist is beneficial for patients with sHTG. If specialist involvement is not available, clinicians should be encouraged to use appropriate diagnostic approaches and clinical management strategies to help ensure patients receive optimal care.[2]

CASE STUDY (CONTINUED) – NEXT STEPS

At the visit, due to the identification of sHTG (TGs 930 mg/dL), the patient is first evaluated for pancreatitis symptoms (which only consist of mild abdominal pain after heavy meals). Hydrochlorothiazide is discontinued as it can contribute to raising TGs. He is counseled to avoid alcohol and begin a low-fat diet. He is asked to return in a month to repeat a fasting lipid panel and to discuss dietary changes, alcohol cessation, and weight and glucose management. On his return visit, fasting TGs were 660 mg/dL.

This patient's TGs improved with management of secondary contributors. However, his TGs are still >500 mg/dL, and he can benefit from targeted TG-lowering therapy to further reduce his CV risk and his risk of pancreatitis. ApoC-III–targeted therapies should be considered in addition to ongoing multifactorial management.

NEW TARGETED THERAPIES FOR sHTG

While lifestyle changes and standard therapies remain foundational for sHTG management, many patients with severe, refractory, or genetically driven HTG do not achieve stable TG control and/or remain at risk for pancreatitis. New agents targeting apoC-III are olezarsen for treatment of FCS and sHTG and plozasiran for treatment of FCS.[2,22,23]

Olezarsen is an antisense oligonucleotide targeting apoC-III that was approved in 2024 for treatment of FCS as an 80 mg once-monthly subcutaneous injection.[20] In the Balance trial of 66 adults with genetically identified FCS, olezarsen 80 mg monthly reduced fasting TGs by a placebo-adjusted mean of 43.5% at 6 months.[24] At 53 weeks, the incidence of acute pancreatitis was reduced in the pooled olezarsen groups (80 mg and 50 mg) vs placebo (rate ratio 0.12; 95% confidence interval [CI]: 0.02, 0.66).[24]

In June 2026, olezarsen was approved for sHTG.[20] In the phase 3 CORE-TIMI 72a and CORE2-TIMI 72b trials, which collectively enrolled 1061 patients with sHTG, monthly olezarsen led to placebo-adjusted TG reductions across studied doses and reduced acute pancreatitis incidence compared with placebo.[25] Placebo-adjusted reductions from baseline in TGs were –62.9% (olezarsen 50 mg) and –72.2% (olezarsen 80 mg) in CORE-TIMI 72a, and –49.2% (olezarsen 50 mg) and –54.5% (olezarsen 80 mg) in CORE2-TIMI 72b (P <.001 for all comparisons with placebo).[25] The incidence of acute pancreatitis was 85% lower with olezarsen than placebo (mean rate ratio 0.15; 95% CI: 0.05, 0.40; P <.001).[25] Adverse events were similar across trial groups; injection site reactions and elevations in liver enzymes occurred in ≥2% of patients and more commonly than with placebo. Injection site reactions were seen in 12% of patients receiving ole-

zarsen 50 mg, 18% of those receiving olezarsen 80 mg, and 2% of those receiving placebo; liver enzyme elevations were observed in 3% of the olezarsen 50 mg group, 4% of the olezarsen 80 mg group, and 1% of the placebo group.[20] At baseline, patients in the trials were receiving stable lipid-lowering therapy according to standard of care, which could include statins and other lipid-lowering therapies.[25] Based on results of these phase 3 studies in sHTG, the US Food and Drug Administration (FDA) approved olezarsen for reducing TGs and the risk of acute pancreatitis in adults with sHTG at a dose of 50 mg subcutaneously once monthly, which may be increased to 80 mg once monthly if the 50 mg dose is tolerated and if clinically indicated.[20,23]

Plozasiran is a small interfering RNA (siRNA) therapy targeting apoC-III that was approved in 2025 for FCS and is administered as a 25 mg subcutaneous injection every 3 months.[21] In PALISADE, patients with persistent chylomicronemia (includes FCS) who received plozasiran had significantly lower median placebo-adjusted TG levels at 10 months (–59% in the 25 mg plozasiran group and –53% in the 50 mg plozasiran group; P <.001 for all comparisons with placebo).[26] Additionally, an 83% lower incidence of acute pancreatitis was observed in those receiving plozasiran (pooled 25 mg and 50 mg data) vs placebo (odds ratio 0.17; 95% CI: 0.03, 0.94; P =.03).[26] Plozasiran received an FDA Breakthrough Designation for sHTG, and phase 3 trials are currently ongoing in populations with sHTG.

Additional targets being studied for sHTG treatment include angiopoietin-like protein-3, fibroblast growth factor 21, and gene-editing technologies.[22]

SUMMARY

sHTG carries a significant risk of acute pancreatitis and adverse cardiometabolic outcomes; thus, TGs ≥500 mg/dL are more than a simple laboratory abnormality. Markedly elevated TGs ≥880 mg/dL are more commonly due to polygenic etiology but rarely may indicate the presence of the rare monogenic lipid disorder FCS. PCCs can improve the care of patients with sHTG by identifying severe TG elevations early and initiating appropriate management or referral when necessary. This involves confirming severe TG elevations, screening for pancreatitis symptoms, correcting secondary drivers, initiating low-fat nutrition and standard TG-lowering therapy when indicated, and reassessing ASCVD risk once the immediate TG lowering has been accomplished. Distinguishing multifactorial sHTG from FCS should be a consideration due to the expected lack of response to standard therapy, available treatment options, and the differing needs for referral and treatment. The landscape of sHTG treatment is evolving, with apoC-III–directed therapies demonstrating reductions in TGs and acute pancreatitis risk; as of the time of this writing, olezarsen has been approved to lower TGs and reduce the risk of acute pancreatitis in adults with sHTG, offering a new option for targeted treatment. ●

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