**Supplement**

**Table and Figure Legends**

**Supplement Table 1: Laboratory values and treatment characteristics.**

**w:** weekly; **w2-3**: twice-three times per week; **2w**: biweekly; **ACDA**: anticoagulant citrate dextrose; **UFH**: unfractionated heparin

**Supplement Figure 1a:** **Annual rate of HTG-associated events of acute pancreatitis in patients with severe HTG (n=9).** Decrease from median 2.0 (IQR 0.7–2.8) before to median 0.2 (IQR 0.0–0.4) after commencement of DFPP treatment. (*t* test for paired samples p<0.01). The mean retrospective observation period was 4.2 years (±3.4) before and 4.0 years (±3.1) after commencement of DFPP.

**Supplement Figure 1b: Absolute numbers of AP events before and after commencement of DFPP treatment in patients with severe HTG (n=9).** In total, 452 months were analyzed before commencement and 427 months after commencement of DFPP treatment. AP events were defined as events of acute pancreatitis (AP) or episodes of severe abdominal pain in patients with a history of recurrent AP.

**Supplemental information to the clinical courses of selected patients depicted in Figure 1**

**Patient #3**: Substantial reduction of the AP event rate was achieved with regular DFPP, but AP could not be completely prevented. 13 AP episodes occurred in the two years prior to chronic DFPP treatment. One relapse occurred four months after commencing DFPP treatment, followed by 2.5 years without recurrence. Then three episodes occurred despite chronic DFPP within seven months. Diagnosis of FCS was very likely in this patient according to FCS scoring [14]; a plasma sample gave the typical creamy chylomicron layer, but genetic testing was not available. Comorbid conditions of this patient putatively contributing to this instable course were diabetes mellitus with maximal insulin resistance (HbA1c 12.5%), steroid-dependent minimal change glomerulonephritis, hypothyroidism, steatosis hepatis, adipositas per magna (BMI 42), and limited compliance to diet. Membrane plasma separation was impaired by chylomicrons, resulting in TG reduction rates below average. Centrifugal plasma separation was not available in the patient’s local area. During the last ten months of documentation, no AP was reported.

**Patient #4**: A single episode of AP with regular DFPP must be attributed to temporary non-adherence to apheresis treatment resulting in increase of TG concentration. After continuing chronic DFPP treatment the patient was stable for the last 16 months of the observation period.

**Patient #6**: Available clinical data before commencing DFPP were limited in this case. Three months after pancreatic surgery, the patient experienced a very severe exsudative pancreatitis requiring intensive care. Due to known unsatisfactory control of TG levels with combined lipid lowering medication and dietary restrictions, regular DFPP treatment was commenced to prevent further episodes of AP.

**Severe HTG and pregnancy (#7)**

**Patient #7:** This patient was a 29-year-old woman presenting severe familial HTG with chylomicronemia and initial TG values up to 9000 mg/dl. According to the FCS score, FCS could not be confirmed. Lipoprotein electrophoresis revealed marked elevation in very low density lipoprotein (VLDL) and chylomicron fractions.She had a history of HTG-AP, and most recently, during her first pregnancy at the age of 27, experienced a necrotizing AP. Presumably due to fat embolism, intrauterine fetal death occurred in the 37th gestation week (GW). During further follow-up, including strict diet with one fasting day per week in combination with maximal TG-lowering drug treatment (omega-3 fatty acids, fibrate), TG was reduced to concentrations between 960 mg/dl and a maximum of 2300 mg/dl and the patient remained clinically stable. At the age of 29 years, the patient became pregnant again, requiring the termination of contraindicated lipid-lowering medication. The TG level increased, despite diet, up to >3700 mg/dl. DFPP treatment was commenced to rapidly reduce the TG in plasma and prevent AP. The patient was treated 12 times over a period of 2 months (**Figure 3**). After initiation of DFPP, TG values could be maximally reduced by 2339 mg/dl and 64%. Reduction rates of TG varied—presumably, in some treatments, membrane plasma separation was impaired by chylomicrons. Overall, the treatments were well-tolerated and the pregnancy was without complications. In GW 37 the patient delivered a healthy newborn by cesarean section.

**Severe HTG and FPLD Dunnigan (#8, #9)**

**Patient #8:** HTG was diagnosed at the age of 13 years, and a positive family history for HTG was documented (brother and mother). Comorbidities were diabetes mellitus, which is typically associated with FPLD, and two-vessel coronary artery disease. The first event of AP was reported at the age of 26 years. Until the age of 37 years, the patient had experienced, in total, six AP—three episodes within the last 13 months before commencing regular DFPP treatment with a frequency of twice a week. Initial TG concentration was 14805 mg/dl. At that time the patient showed an FPLD-typical physical appearance with marked loss of subcutaneous fat from the upper and lower extremities and prominent muscles. Gene analysis confirmed the diagnosis of FPLD Dunnigan due to heterozygous mutation in the *LMNA* gene. With regular DFPP treatment the patient had no AP events within the next 3.5 years. After that period, she had a trial with oral metreleptin (5 mg daily) therapy, and frequency of DFPP was reduced to once a week. Subsequently, TG concentrations increased to even above 6000 mg/dl and the patient developed progressive symptoms of TG-associated abdominal pain. Thus, DFPP treatment frequency was increased again to twice per week. A second trial with an increased dose of metreleptin (7.5 mg) and decreased DFPP frequency led to similar symptoms. Consequently, metreleptin therapy was terminated and DFPP treatments continued twice a week. With this regimen the patient was stable within the last three months of the observation period of our study.

**Patient #9:** FPLD Dunniganwas diagnosed, confirmed by gene analysis (*LMNA* gene), at the age of 50 years. She showed an FPLD-typical physical appearance greatly similar to that of her mother, who also suffered from FPLD with associated ASCVD. Comorbidities of the patient were also type 2 diabetes, breast cancer (surgery, chemotherapy, radiotherapy), morbus Crohn, and chronic musculoskeletal pain syndrome. The rationale for commencing regular DFPP treatment in this case was the diagnosis of severe, progressive two-vessel coronary artery disease at the age of 57 years, confirmed by two ASCVD events within one year. Initial TG level was 2587 mg/dl with maximal tolerable lipid-lowering drug treatment; LDL-C was <70 mg/dl. With weekly DFPP treatment the patient had no further progression of ASCVD in 2.5 years. There was no trial with metreleptin due to concerns related to a potential involvement of leptin in the pathogenesis of breast cancer [47].

**Severe HTG with Lp(a)-HLP**

**Patient #10:** Early and severe progressive ASCVD involving coronary and peripheral arteries were underlying a non-fatal myocardial infarction at the age of 38 years. Appropriate diet, antidiabetic drugs (diabetes mellitus diagnosed at the age of 44 years) and maximal lipid-lowering therapy were insufficient to prevent progression of ASCVD and episodes of HTG-AP. Mean concentration of TG during the two years prior to commencing DFPP was 3700 ±1204 mg/dl. Baseline total cholesterol was 373 mg/dl, Lp(a) 89 mg/dl. The patient received DFPP treatment once to twice a week. Extracorporeal elimination of lipoproteins was useful in rapidly lowering elevated serum TG from mean 1686±1492 mg/dl before to 953±847 mg/dl after DFPP. The mean reduction rate for TG was 40%, for LDL-C 67%, and for Lp(a) 68%. DFPP was safe and well-tolerated. The patient was clinically stable without any event 12 months after commencement of regular DFPP.