

Supplementary Materials

S1. Definition of lipid-lowering treatment-naïve status

Patients are considered treatment-naïve to lipid-lowering therapy if they have either never received lipid-lowering therapy or have not received any lipid-lowering therapy for at least 4 weeks before the screening visit (Visit 1). Lipid-lowering therapy for this definition includes statins, ezetimibe, fibrates, bile-acid sequestrants, bempedoic acid, nicotinic acid and derivatives, PCSK9 inhibitors, any other study lipid-lowering drug and/or supplements containing red yeast rice.

S2. Definition of treatment adherence

Treatment adherence is assessed at Visits 3, 4 and 5 on the basis of dispensed study medication, returned unused medication and reported lost tablets. Patients are considered adherent if $\geq 80\%$ of prescribed doses have been administered. In Arm 2, when rosuvastatin/ezetimibe 20/10 mg and rosuvastatin 10 mg are administered concomitantly, adherence is calculated separately for each tablet, and the lower value is used. Patients with adherence $<80\%$ during any treatment period remain in the study but are excluded from the per-protocol analysis; their results are included in the FAS if the FAS criteria are otherwise fulfilled.

S3. Study-treatment discontinuation and withdrawal

Patients may be discontinued from the trial:

- if they request treatment discontinuation and/or withdraw informed consent;
- experience an SAE related to study treatment (serious adverse reaction);
- experience an unrelated SAE for which continued participation is considered by the investigator to pose a significant safety concern;
- develop new or worsening muscle symptoms; protocol-defined muscle symptoms included new-onset or worsening symptoms within 4 weeks of treatment with a typical presentation, defined by at least two features: i) symmetric/bilateral symptoms and ii) proximal muscle ache, weakness, soreness, stiffness, cramping, tenderness, or general fatigue;
- develop new or worsening muscle symptoms accompanied by $CK \geq 4 \times ULN$
- become pregnant;
- develop an acute concomitant disease requiring prohibited medication;
- require major surgery;
- experience clinical deterioration, an intolerable adverse event, or treatment inefficacy warranting discontinuation in the investigator's judgement;

- the clinical trial is prematurely terminated.

Patients withdrawn because of an adverse event or pregnancy discontinue regular trial visits.

Additional follow-up is carried out by the investigator in cases of any serious adverse events, until the condition is resolved or stabilized (in case of a chronic sequel). Pregnancy outcomes are followed according to protocol-specified procedures.

Supplementary Table SI. The list of centers and investigators of the LEASH trial.

CENTER	INVESTIGATOR
Country: Armenia	
N 2 Hospital and Policlinic, 54 Aram street, 0002 Yerevan	Parounak Zelveian
CardioMed Family Medical Centre, Hanrapetutyan ave. 11/5 Building, 2204 Abovyan	Samvel Hayrumyan
Country: Croatia	
KBC Zagreb-klinika za neurologiju; Kišpatićeva 12, 10000 Zagreb	Branko Malojčić
KBC Zagreb - Zavod za bolesti metabolizma; Kišpatićeva 12, 10000 Zagreb	Ivan Pećin
Županijska bolnica Čakovec, Ivana Gorana Kovačića 1e, 40000 Čakovec	Karla Sabolek Lovrec
Dom zdravlja Varaždin, Kolodvorska 20, 42000 Varaždin	Kristina Sambol
Ordinacija opće medicine Balint; Kralja Tomislava 3, 10431 Strmec Samoborski	Ines Balint
Country: Germany	
Cardiologicum Hamburg GbR-Studienzentrum; Schloßstrasse 12, 22041 Hamburg	Martin Bergmann
Country: Hungary	
Békés Vármegyei Központi Kórház Pándy Kálmán Tagkórház 5700 Gyula, Semmelweis u. 1.	László Márk
Dél-budai Centrumkórház Szent Imre Egyetemi Oktatókórház 1115 Budapest, Tétényi út 12-16.	Gábor Simonyi
Balatonfüredi Állami Szívkórház 8230 Balatonfüred, Gyógy tér 2.	József Faluközy
Country: Poland	
Instytut Centrum Zdrowia Matki Polki Ul. Rzgowska 281/289 93-338 Łódź	Maciej Banach
Centrum Medyczne Multimed Sp. z o.o. Os. Wł. Jagiełły 15, 32-800 Brzesko	Karolina Golińska-Grzybała
Pro Life Medica sp. z o.o	Iwona Chmiel -Perzyńska

ETG Poniatowa Ul. Fabryczna 18 24-320 Poniatowa	
Jacek Bil Olga Možeńska Medical Center S.C. Ul. Quo Vadis 1/U6 02-495 Warszawa	Jacek Bil
Country: Serbia	
University Clinical center of Serbia, Pasterova 2, 11000 Beograd	Dragan Simić
Institute for cardiovascular diseases of Vojvodina, Put doktora Goldmana 4, 21204 Sremska Kamenica	Maja Stefanović
University Clinical center Niš, Bulevar dr Zorana Đinđića 48, 18000 Niš	Tomislav Kostić
Clinical - Hospital Center Zvezdara, Dimitrija Tucovića 161, 11120 Beograd	Bojan Jašović