



# Study to Evaluate Efficacy and Safety of Inclisiran in Adolescents With Heterozygous Familial Hypercholesterolemia

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## Main Information

**Primary registry identifying number**

LBCTR2021034776

**Protocol number**

CKJX839C12301

**MOH registration number**

**Study registered at the country of origin**

Yes

**Study registered at the country of origin: Specify**

**Type of registration**

Prospective

**Type of registration: Justify**

N/A

**Date of registration in national regulatory agency**

**Primary sponsor**

Novartis Pharma Services inc.

**Primary sponsor: Country of origin**

Novartis Pharmaceuticals

**Date of registration in primary registry**

11/11/2021

**Date of registration in national regulatory agency**

**Public title**

Study to Evaluate Efficacy and Safety of Inclisiran in Adolescents With Heterozygous Familial Hypercholesterolemia

**Acronym**

**Scientific title**

Two Part (Double-blind Inclisiran Versus Placebo [Year 1] Followed by Open-label Inclisiran [Year 2]) Randomized Multicenter Study to Evaluate Safety, Tolerability, and Efficacy of Inclisiran in Adolescents (12 to Less Than 18 Years) With Heterozygous Familial Hypercholesterolemia and Elevated LDL-cholesterol (ORION-16)

**Acronym**

**Brief summary of the study: English**

This is a pivotal phase III study designed to evaluate safety, tolerability, and efficacy of inclisiran in adolescents with heterozygous familial hypercholesterolemia (HeFH) and elevated low density lipoprotein cholesterol (LDL-C).

This is a two-part (1 year double-blind inclisiran versus placebo / 1 year open-label inclisiran) multicenter study designed to evaluate safety, tolerability, and efficacy of inclisiran in adolescents with heterozygous familial hypercholesterolemia (HeFH) and elevated low density lipoprotein cholesterol (LDL-C) on stable standard of care background lipid-lowering therapy. The primary objective is to demonstrate superiority of inclisiran compared to placebo in reducing LDL-C (percent change) at Day 330.

**Brief summary of the study: Arabic**

[ يتبعه إنكليسيران مفتوح اللصاقَة 1دراسة متعددة المراكز، عشوائية التوزيع من قسمين (إنكليسيران مزدوج التعمية مقابل الدواء الوهمي) السنة [ سنة) المصابين بفرط كوليسترول الدم العائلي18 إلى أقل من 12]] لتقييم سلامة إنكليسيران وقدرة تحملته وفعاليتته لدى المراهقين (من 2السنة [ (ORION-16) متغاير الزيجوت وبارتفاع الكوليسترول الضار (أوريون-

**Health conditions/problem studied: Specify**





Heterozygous Familial Hypercholesterolemia

**Interventions: Specify**

Drug: Inclisiran  
Drug: Placebo

**Key inclusion and exclusion criteria: Inclusion criteria**

Heterozygous Familial Hypercholesterolemia (HeFH) diagnosed either by genetic testing or on phenotypic criteria  
Fasting LDL-C >130 mg/dL (3.4 mmol/L) at screening  
Fasting triglycerides <400 mg/dL (4.5 mmol/L) at screening  
On maximally tolerated dose of statin (investigator's discretion) with or without other lipid-lowering therapy; stable for ≥ 30 days before screening  
Estimated glomerular filtration rate (eGFR) >30 mL/min/1.73 m<sup>2</sup> at screening

**Key inclusion and exclusion criteria: Gender**

Both

**Key inclusion and exclusion criteria: Specify gender**

**Key inclusion and exclusion criteria: Age minimum**

12

**Key inclusion and exclusion criteria: Age maximum**

17

**Key inclusion and exclusion criteria: Exclusion criteria**

Homozygous familial hypercholesterolemia (HoFH)  
Active liver disease  
Secondary hypercholesterolemia, e.g. hypothyroidism or nephrotic syndrome  
Major adverse cardiovascular events within 3 months prior to randomization  
Previous treatment with monoclonal antibodies directed towards PCSK9 (within 90 days of screening)  
Recent and/or planned use of other investigational medicinal products or devices  
Other protocol-defined inclusion/exclusion criteria may apply

**Type of study**

Interventional

**Type of intervention**

Pharmaceutical

**Type of intervention: Specify type**

N/A

**Trial scope**

Therapy

**Trial scope: Specify scope**

N/A

**Study design: Allocation**

Randomized controlled trial

**Study design: Masking**

Blinded (masking used)

**Study design: Control**

Placebo

**Study phase**

3

**Study design: Purpose**

Treatment

**Study design: Specify purpose**

N/A

**Study design: Assignment**

Parallel

**Study design: Specify assignment**

N/A

**IMP has market authorization**

Yes, Worldwide

**IMP has market authorization: Specify**

European Union, United Arab Emirates, Great Britain

**Name of IMP**

inclisiran

**Year of authorization**

**Month of authorization**

**Type of IMP**

Others

**Pharmaceutical class**



cholesterol-lowering small interfering ribonucleic acid (siRNA) that inhibits the production of proprotein convertase subtilisin/kexin type 9

**Therapeutic indication**

heterozygous familial hypercholesterolemia (HeFH) and elevated low density lipoprotein cholesterol (LDL-C)

**Therapeutic benefit**

to demonstrate superiority of inclisiran compared to placebo in reducing LDL-C (percent change) at Day 330 in adolescents (12 to less than 18 years) with heterozygous familial hypercholesterolemia and elevated LDL-cholesterol

**Study model**

N/A

**Study model: Explain model**

N/A

**Study model: Specify model**

N/A

**Time perspective**

N/A

**Time perspective: Explain time perspective**

N/A

**Time perspective: Specify perspective**

N/A

**Target follow-up duration**

**Target follow-up duration: Unit**

**Number of groups/cohorts**

**Biospecimen retention**

Samples with DNA\*\*

**Biospecimen description**

Blood samples collected will be analyzed at Medpace Laboratories, central lab

**Target sample size**

4

**Actual enrollment target size**

**Date of first enrollment: Type**

Anticipated

**Date of first enrollment: Date**

30/04/2021

**Date of study closure: Type**

Anticipated

**Date of study closure: Date**

16/08/2023

**Recruitment status**

Pending

**Recruitment status: Specify**

**Date of completion**

29/07/2021

**IPD sharing statement plan**

Yes

**IPD sharing statement description**



Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data availability is according to the criteria and process described on [www.clinicalstudydatarequest.com](http://www.clinicalstudydatarequest.com).

**Additional data URL**

<https://clinicaltrials.gov/ct2/show/NCT04652726?cond=heterozygous+familial+hypercholesterolemia&draw=2&rank=2>

**Admin comments****Trial status**

Approved

## Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
NCT04652726	Clinical trials.gov

## Sources of Monetary or Material Support

Name
Novartis Pharma Services inc.

## Secondary Sponsors

Name
NA

## Contact for Public/Scientific Queries

Contact type	Contact full name	Address	Country	Telephone	Email	Affiliation
Public	Selim Jambart	Beirut	Lebanon	961 3 406 001	<a href="mailto:sjambart@dm.net.lb">sjambart@dm.net.lb</a>	Hotel Dieu De France
Scientific	Hind Khairallah	Sinelfil	Lebanon	01512002#271	<a href="mailto:Hind.khairallah@fattal.com.lb">Hind.khairallah@fattal.com.lb</a>	Khalil Fattal et Fils s.a.l.
Public	Hala Tfayli	Beirut	Lebanon	71729759	<a href="mailto:HT31@AUB.LB">HT31@AUB.LB</a>	American University of Beirut Medical Center



## Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Hotel Dieu De France	Selim Jambart	Endocrinology	Approved
American University of Beirut Medical Center	Hala Tfayli	Pediatric Endocrinology	Approved

## Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
Hotel Dieu de France	21/12/2020	Sami Richa	cue@usj.edu.lb	961421229
American University of Beirut Medical Center	28/06/2021	Fuad Ziyadeh	irb@aub.edu.lb	00961 -1-350000 or 1 374374, ext: 5445

## Countries of Recruitment

Name
Lebanon
Australia
Germany
Hungary
Norway
Spain
United States of America

## Health Conditions or Problems Studied

Condition	Code	Keyword
heterozygous familial hypercholesterolemia	Hyperlipidaemia, unspecified (E78.5)	heterozygous familial hypercholesterolemia

## Interventions

Intervention	Description	Keyword
Informed Consent/assent form discussion; Inclusion/exclusion assessment; physical examination; neurological examination; blood and urine samples collection; IMP dispensation	Informed Consent/assent form discussion; Inclusion/exclusion assessment; physical examination; neurological examination; blood and urine samples collection; IMP dispensation	ICF, IMP , Lab tests, physical exams



## Primary Outcomes

Name	Time Points	Measure
Percentage (%) change in low-density lipoprotein cholesterol (LDL-C)	baseline to Day 330	baseline to Day 330
Demonstrate superiority of inclisiran compared to placebo in reducing LDL-C [percent change]	Day 330 (Year 1)	Day 330 (Year 1)

## Key Secondary Outcomes

Name	Time Points	Measure
Time-adjusted % change in LDL-C from baseline	Baseline, after Day 90 up to Day 330	Baseline, after Day 90 up to Day 330
Absolute change in LDL-C from baseline to Day 330	Baseline and Day 330	Baseline and Day 330
% change in apolipoprotein B (Apo B), lipoprotein (a) [Lp(a)], non-high density lipoprotein cholesterol (non-HDL-C), and total cholesterol from baseline to Day 330	Baseline and Day 330	Baseline and Day 330
% change and absolute change in LDL-C from baseline up to Day 720	Baseline, up to Day 720	Baseline, up to Day 720
% change and absolute change in other lipoproteins and lipid parameters	Baseline, up to Day 720	Baseline, up to Day 720
% change and absolute change in proprotein convertase subtilisin/kexin type 9 (PCSK9)	Baseline, up to Day 720	Baseline, up to Day 720



## Trial Results

**Summary results**

**Study results globally**

**Date of posting of results summaries**

**Date of first journal publication of results**

**Results URL link**

**Baseline characteristics**

**Participant flow**

**Adverse events**

**Outcome measures**

**URL to protocol files**