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Phase I/II Study of Rapcabtagene Autoleucel in CLL, 3L+ DLBCL, r/r ALL and 1L HR LBCL

Last Update: Apr 10, 2025
Phase I/II, Open Label, Multicenter Study of Rapcabtagene Autoleucel in Adult Patients With CLL/SLL, 3L+ DLBCL, r/r ALL and 1L HR LBCL
ClinicalTrials.gov Identifier:
NCT03960840
Novartis Reference Number:CYTB323A12101
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All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

This is a phase I/II study to evaluate the feasibility, safety and preliminary antitumor efficacy of rapcabtagene autoleucel (also known as YTB323). Rapcabtagene autoleucel will be investigated in combination with ibrutinib in chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and as single agent in diffuse large B-cell lymphoma (3L+ DLBCL), adult acute lymphoblastic leukemia (ALL) and 1st Line High Risk Large B-Cell Lymphoma (1L HR LBCL). This clinical trial is phase I/II open label, multi-center study of rapcabtagene autoleucel.

The Phase I part of the study comprises three independent treatment arms:

* Rapcabtagene autoleucel in combination with ibrutinib in adult CLL/SLL participants with SD or PR after at least 6 months of second or subsequent line ibrutinib therapy. As of 05-May-2021, this arm had completed enrollment.
* Rapcabtagene autoleucel single agent in adult DLBCL participants having failed two or more lines of chemotherapy and either having progressed (or relapsed) after autologous HSCT or being ineligible for or not consenting to the procedure.
* Rapcabtagene autoleucel single agent in adult relapsed/refractory ALL participants

The Phase II part of the study comprises two independent cohorts:

* Rapcabtagene autoleucel single agent in adult 3L + DLBCL participants having failed two or more lines of chemoimmunotherapy and either having progressed (or relapsed) after autologous HSCT or being ineligible for or not consenting to the procedure. This is an extension of the Phase I r/r DLBCL treatment arm to support Phase II objectives
* Rapcabtagene autoleucel single agent in newly diagnosed, adult 1L HR LBCL participants defined as IPI 3-5 and/or DH/TH disease who have completed 2 cycles of CIT and have a response of PR/SD (with a Deauville score of 4-5).

In the Phase I part of the trial, the 3L+ DLBCL and ALL arms consist of two parts: a dose escalation part to evaluate feasibility, characterize safety and identify the recommended dose (RD) of rapcabtagene autoleucel,

and a dose expansion part to further characterize safety, study rapcabtagene autoleucel cellular kinetics and assess preliminary antitumor activity. Once the RD of rapcabtagene autoleucel is determined for each arm, the corresponding expansion part will commence.

In the Phase II part of the trial, approximately 70 additional participants will be enrolled in a 3L+ DLBCL cohort treated at the recommended dose (RD). Including the 3L+ DLBCL participants who were treated at the RD from the Phase I part, it is planned to have in total a cohort of approximately 100 participants included in the primary efficacy analysis based on the efficacy analysis set. In addition, a separate cohort in 1LHR LBCL will be included, with approximately 50-60 participants planned for the primary efficacy analysis based on the efficacy analysis set.

Participants will be followed under the current treatment protocol for safety and efficacy within this trial for a minimum of 2 years before being transferred to the long-term follow-up trial. Once the study is complete, participants will be enrolled in a post-study long term follow-up for lentiviral vector safety for up to 15 years. This post-study long term follow-up for lentiviral vector safety will continue under a separate destination protocol.

Condition
Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma, Diffuse Large B-cell Lymphoma, Acute Lymphoblastic Leukemia, Large B-cell Lymphoma
Phase
Phase1, Phase2
Overall Status
Recruiting
Number of Participants
225
Start Date
Jun 26, 2019
Completion Date
May 31, 2028
Gender
All
Age(s)
18 Years - 100 Years (Adult, Older Adult)

Interventions

Drug

Ibrutinib

Tablets or capsules for oral daily use
Biological

Rapcabtagene autoleucel single agent

Single infusion of rapcabtagene autoleucel

Eligibility Criteria

Inclusion Criteria:

* ECOG performance status 0-1 for ALL and DLBCL
* ECOG performance status 0-2 for 1L HR LBCL at screening
* CLL or SLL diagnosis according to iwCLL criteria
* CLL/SLL in SD or PR after at least 6 months of ibrutinib, either as second or subsequent line of therapy
* DLBCL diagnosis by local histopathology
* DLBCL relapsed or refractory after 2 or more lines of therapy, including autologous hematopoietic stem cell transplantation (HSCT)
* Refractory or relapsed CD19-positive ALL
* ALL with morphologic disease in the bone marrow

1L HR LBCL - Considered to be high-risk based on at least 1 of the following at diagnosis:
* IPI score of 3, 4 or 5
* MYC and BCL2 and/or BCL6 rearrangement (DH/TH lymphoma)
* Participants must have received 2 cycles of frontline therapy for LBCL with R-CHOP or Pola-R-CHP or DA-EPOCH-R. Participants with DH/TH lymphoma must have received at least one cycle (the most recent) DA-EPOCH-R.
* Participants must have a positive PET per Lugano classification (Deauville PET score of 4 or 5 and an overall response of PR/SD) after 2 cycles of frontline CIT. Note: Patient's with Deauville PET score of 5 and overall response of PD, or with Deauville PET score of 1, 2, or 3 and overall response of CR, are not eligible for this trial.

Exclusion Criteria:

* Prior CD19-directed therapy
* Prior administration of a genetically engineered cellular product
* Prior allogeneic HSCT
* Richter's transformation

* For 1L HR LBCL: Richter's transformation, Burkitt lymphoma, primary DLBCL of CNS, DLBCL associated with chronic inflammation, intravascular large B-cell lymphoma, ALK- positive large B-cell lymphoma, HHV8 positive LBCL, DLBCL leg type or EBV positive DLBCL, NOS.
* Active CNS lymphoma

* For 1L HR LBCL: Active or prior history CNS involvement by malignancy
* Targeted small molecule or kinase inhibitor within 2 weeks from leukapheresis

Other protocol-defined inclusion/exclusion may apply.

Australia

Novartis Investigative Site

Recruiting

Melbourne,Victoria,3000,Australia

Novartis Investigative Site

Recruiting

Melbourne,Victoria,3004,Australia

Austria

Novartis Investigative Site

Recruiting

Wien,1090,Austria

France

Novartis Investigative Site

Recruiting

Marseille,13273,France

Novartis Investigative Site

Recruiting

Paris 10,75475,France

Novartis Investigative Site

Recruiting

Pierre Benite,69495,France

Novartis Investigative Site

Recruiting

Rennes,35019,France

Germany

Novartis Investigative Site

Recruiting

Frankfurt am Main,Hessen,60590,Germany

Novartis Investigative Site

Recruiting

Leipzig,Sachsen,04103,Germany

Novartis Investigative Site

Recruiting

Essen,45147,Germany

Italy

Novartis Investigative Site

Recruiting

Bergamo,BG,24127,Italy

Novartis Investigative Site

Recruiting

Milano,MI,20132,Italy

Novartis Investigative Site

Recruiting

Rozzano,MI,20089,Italy

Novartis Investigative Site

Recruiting

Bologna,BO,40138,Italy

Japan

Novartis Investigative Site

Recruiting

Fukuoka city,Fukuoka,812-8582,Japan

Novartis Investigative Site

Recruiting

Sapporo city,Hokkaido,060 8648,Japan

Novartis Investigative Site

Recruiting

Bunkyo ku,Tokyo,113-8677,Japan

Spain

Novartis Investigative Site

Recruiting

Sevilla,Andalucia,41013,Spain

Novartis Investigative Site

Recruiting

Madrid,28009,Spain

Novartis Investigative Site

Recruiting

Salamanca,Castilla Y Leon,37007,Spain

Novartis Investigative Site

Recruiting

Madrid,28041,Spain

Novartis Investigative Site

Recruiting

Badalona,Catalunya,08916,Spain

Novartis Investigative Site

Recruiting

Barcelona,Catalunya,08035,Spain

Novartis Investigative Site

Recruiting

Hospitalet de LLobregat,Catalunya,08907,Spain

Novartis Investigative Site

Recruiting

Valencia,Comunidad Valenciana,46010,Spain

Novartis Investigative Site

Recruiting

Cordoba,Andalucia,14004,Spain

Novartis Investigative Site

Recruiting

Barcelona,08041,Spain

United States

Northside Hospital

Recruiting

Atlanta,Georgia,30342,United States

Adriane Strong

Phone: 404-255-1930
Email: adriane.strong@northside.com

Scott D. Solomon

Northwestern University Northwestern Memorial Hospital Trans

Recruiting

Chicago,Illinois,60611,United States

Shira Dinner

Holly Roberta Krieg

Email: hollyroberta.krieg@northwestern.edu

Sarah Cannon Research Institute

Recruiting

Nashville,Tennessee,37221,United States

Paul Shaughnessy

Kinsey Kozeny

Email: kinsey.kozeny@scri.com

Montefiore Medical Center

Recruiting

Bronx,New York,10461,United States

Vladimir Bonhomme

Phone: 718-920-2680
Email: vbonhomme@montefiore.org

Dennis Cooper

Oregon Health Sciences University

Recruiting

Portland,Oregon,97239,United States

Brandon Hayes-Lattin

Elisa Minerich

Phone: 503-346-7894
Email: minerich@ohsu.edu

Uni of Chi Medi Ctr Hema and Onco

Recruiting

Chicago,Illinois,60637,United States

Bruna Vieira

Phone: 773-834-8980
Email: bruna.vieira@bsd.uchicago.edu

Peter Riedell

Uni Of TX MD Anderson Cancer Cntr

Recruiting

Houston,Texas,77030,United States

Dana Wright

Phone: 713-792-2921
Email: djwright@mdanderson.org

Jason Westin

University of Pennsylvania Clinical

Recruiting

Philadelphia,Pennsylvania,19104,United States

Noelle Frey

Stella Krawiec

Phone: 215-615-6721
Email: stella.krawiec@pennmedicine.upenn.edu

University of Kansas Cancer Center

Recruiting

Westwood,Kansas,66205,United States

Claire McCann

Phone: 913-588-6029
Email: cmccann@kumc.edu

Leyla Shune

University of California LA

Recruiting

Los Angeles,California,90095,United States

Janette Rodriguez

Phone: 310-794-6500
Email: JanetteRodriguez@mednet.ucla.edu

Patricia Young

St Davids South Austin Medical Ctr

Recruiting

Austin,Texas,78704,United States

Amy Hammack

Phone: 512-447-2211
Email: amy.hammack@sarahcannon.com

Aravind Ramakrishnan

Medical College of Wisconsin

Recruiting

Milwaukee,Wisconsin,53226,United States

Jessica Neumann

Phone: 414-805-4600
Email: jneumann@mcw.edu

Nirav Shah

Stanford University Medical Center

Recruiting

Stanford,California,94305-5826,United States

Kendall Levine

Phone: 650-725-0701
Email: klevine@stanford.edu

Saurabh Dahiya

Sarah Cannon Research Institute

Recruiting

Nashville,Tennessee,37203,United States

Ian W Flinn

Savannah Dunston

Phone: 615-329-7274
Email: sdunston@tnonc.com

Mass Gen Hosp Cancer Center

Recruiting

Boston,Massachusetts,02114,United States

Patrick Connor Johnson

Richard Raught Jeffery

Phone: +1 617 726 2000
Email: rjefferyiii@mgh.harvard.edu

H Lee Moffitt Cancer Center and Research Institute

Recruiting

Tampa,Florida,33612,United States

James Rolland

Phone: 888-663-3488
Email: James.Rolland@moffitt.org

Julio Chavez

Worldwide Contacts

If the location of your choosing does not feature any contact detail, please reach out using the information below.

Novartis Pharmaceuticals

Phone: +41613241111
Email:

Novartis Pharmaceuticals

Phone: 1-888-669-6682
Email: novartis.email@novartis.com

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11. tel:773-834-8980
12. mailto:bruna.vieira@bsd.uchicago.edu
13. tel:713-792-2921
14. mailto:djwright@mdanderson.org
15. tel:215-615-6721
16. mailto:stella.krawiec@pennmedicine.upenn.edu
17. tel:913-588-6029
18. mailto:cmccann@kumc.edu
19. tel:310-794-6500
20. mailto:JanetteRodriguez@mednet.ucla.edu
21. tel:512-447-2211
22. mailto:amy.hammack@sarahcannon.com
23. tel:414-805-4600
24. mailto:jneumann@mcw.edu
25. tel:650-725-0701
26. mailto:klevine@stanford.edu
27. tel:615-329-7274
28. mailto:sdunston@tnonc.com
29. tel:+1 617 726 2000
30. mailto:rjefferyiii@mgh.harvard.edu
31. tel:888-663-3488
32. mailto:James.Rolland@moffitt.org
33. tel:+41613241111
34. mailto:
35. tel:1-888-669-6682
36. mailto:novartis.email@novartis.com