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COMPLETED

Study to Evaluate the Safety and Tolerability of Tirabrutinib (ONO/GS-4059) Given as Monotherapy in Participants With Relapsed/Refractory NHL and CLL

ClinicalTrials.gov ID NCT01659255

Sponsor Gilead Sciences

Information provided by Gilead Sciences (Responsible Party)

Last Update Posted 2021-03-16

Study Details Tab

Study Overview

Brief Summary

The primary objective of the study is to evaluate the safety and tolerability of tirabrutinib (formerly ONO/GS-4059) given as monotherapy to participants with relapsed/refractory non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL).

Official Title

An Open-label, Multi-Center, Non-Randomised Phase I Dose-Escalation Study to Investigate the Safety and Tolerability of ONO-4059 (ONO/GS-4059) Given as Monotherapy in Patients With Relapsed/Refractory Non-Hodgkin's Lymphoma (NHL) and Relapsed/Refractory Chronic Lymphocytic Leukaemia (CLL)

Conditions

Feedback

Pharmacyclics LLC
Exhibit 2088
BeiGene v. Pharmacyclics
PGR2024-00009
EX2088.0001

Non Hodgkins Lymphoma | Chronic Lymphocytic Leukaemia

Intervention / Treatment

- Drug: Tirabrutinib

Other Study ID Numbers

- ONO-4059POE001
- 2011-005033-39 (EudraCT Number)

Study Start (Actual)

2012-08-17

Primary Completion (Actual)

2015-02-23

Study Completion (Actual)

2016-01-11

Enrollment (Actual)

90

Study Type

Interventional

Phase

Phase 1

Resource links provided by the National Library of Medicine

MedlinePlus (https://medlineplus.gov/) related topics: Chronic Lymphocytic Leukemia (https://medlineplus.gov/chroniclymphocyticleukemia.html) Leukemia (https://medlineplus.gov/leukemia.html) Lymphoma (https://medlineplus.gov/lymphoma.html)

Genetic and Rare Diseases Information Center (https://rarediseases.info.nih.gov/gard) resources: Lymphosarcoma (https://rarediseases.info.nih.gov/diseases/6946/lymphosarcoma) Chronic Lymphocytic Leukemia (https://rarediseases.info.nih.gov/diseases/6104/chronic-lymphocytic-leukemia) Chronic Graft Versus Host Disease (https://rarediseases.info.nih.gov/diseases/10964/chronic-graft-versus-host-disease)

FDA Drug and Device Resources (https://clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides the contact details for those conducting the study, and information on where this study is being conducted.

France

Lille, France, 59037
CHRU - Hopital Claude HURIEZ

Lyon, France, 69495
Centre hospitalier Lyon Sud

Montpellier, France, 34295
CHU St Eloi

United Kingdom

Cardiff, United Kingdom, CF14 4XW
University Hospital of Wales

Click to view interactive map

Participation Criteria

Researchers look for people who fit a certain description, called eligibility criteria. Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read Learn About Studies (https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Key Inclusion Criteria:

1. Males or females with a confirmed diagnosis of and documented history of relapsed or refractory malignant disease (B-cell lymphoma and/or CLL) for which no therapy of curative or high priority exists and for whom treatment with a Btk inhibitor may be deemed appropriate.
2. Age ≥ 18 years.
3. Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2.

Key Exclusion Criteria:

1. Central nervous system (CNS) lymphoma.
2. Women who are pregnant or lactating.

Note: Other protocol defined Inclusion/Exclusion criteria may apply.

Ages Eligible for Study

18 Years and older (Adult, Older Adult)

Sexes Eligible for Study

All

Accepts Healthy Volunteers

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose : Treatment
Allocation : Non-Randomized
Interventional Model : Parallel Assignment
Masking : None (Open Label)

Arms and Interventions

Participant Group/Arm	Intervention/Treatment
Experimental: Tirabrutinib 20 mg Once Daily (CLL) Participants with relapsed/refractory chronic lymphocytic leukaemia (CLL) received tirabrutinib 20 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 40 mg Once Daily (CLL) Participants with relapsed/refractory CLL received tirabrutinib 40 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 80 mg Once Daily (CLL) Participants with relapsed/refractory CLL received tirabrutinib 80 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 160 mg Once Daily (CLL)	Drug: Tirabrutinib • Capsules administered orally • Other Names:

Participants with relapsed/refractory CLL received tirabrutinib 160 mg once daily.	◦ ONO/GS-4059
Experimental: Tirabrutinib 320 mg Once Daily (CLL) Participants with relapsed/refractory CLL received tirabrutinib 320 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 400 mg Once Daily (CLL) Participants with relapsed/refractory CLL received tirabrutinib 400 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 500 mg Once Daily (CLL) Participants with relapsed/refractory CLL received tirabrutinib 500 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 600 mg Once Daily (CLL) Participants with relapsed/refractory CLL	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059

received tirabrutinib 600 mg once daily.	
Experimental: Tirabrutinib 300 mg Twice Daily (CLL) Participants with relapsed/refractory CLL received tirabrutinib 300 mg twice daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 20 mg Once Daily (NHL) Participants with relapsed/refractory non-Hodgkin's lymphoma (NHL) received tirabrutinib 20 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 40 mg Once Daily (NHL) Participants with relapsed/refractory NHL received tirabrutinib 40 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 80 mg Once Daily (NHL) Participants with relapsed/refractory NHL	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059

received tirabrutinib 80 mg once daily.	
Experimental: Tirabrutinib 160 mg Once Daily (NHL) Participants with relapsed/refractory NHL received tirabrutinib 160 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 320 mg Once Daily (NHL) Participants with relapsed/refractory NHL received tirabrutinib 320 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 480 mg Once Daily (NHL) Participants with relapsed/refractory NHL received tirabrutinib 480 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059
Experimental: Tirabrutinib 600 mg Once Daily (NHL) Participants with relapsed/refractory NHL received tirabrutinib 600 mg once daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059

Experimental: Tirabrutinib 240 mg Twice Daily (NHL) Participants with relapsed/refractory NHL received tirabrutinib 240 mg twice daily.	Drug: Tirabrutinib • Capsules administered orally • Other Names: ◦ ONO/GS-4059

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Percentage of Participants Experiencing Dose-Limiting Toxicities	Dose Limiting Toxicities (DLT) were defined as follows: • All Common Terminology Criteria (CTC) Grade 4 tirabrutinib related adverse events • All CTC Grade 3 tirabrutinib related adverse events, with the exception of the following: ◦ CTC Grade 3 lymphocytosis considered an expected outcome of therapy Any toxicity which in the opinion of the Investigator is attributed to a participant's underlying disease was not considered a DLT.	Day 1 through Day 28

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Overall Response Rate	Overall response rate (ORR) was defined as the percentage of participants who achieve a best overall response of complete remission (CR, unconfirmed complete response (CRu), complete response with incomplete marrow recovery (CRi)) or partial remission (PR, nodal PR) during study as assessed by the investigator. ORR assessment was defined per following standardized criteria: • NHL: Cheson, 1999 • CLL: International Workshop on Chronic Lymphocytic Leukemia (IWCLL) 2008	Up to Cycle 37 (28 days for each cycle) plus 6-month intervals thereafter until disease progression (maximum: up to 39 months)
Pharmacokinetic (PK) Parameter: Cmax of Tirabrutinib	Cmax is defined as the maximum concentration of drug.	Pre-dose, then 30 minutes, 1, 2, 3, 4, 6, 8, 12 hours post-dose at Cycle 1, Day 28
PK Parameter: AUCtau of Tirabrutinib	AUCtau is defined as concentration of drug over dosing interval.	Pre-dose, then 30 minutes, 1, 2, 3, 4, 6, 8, 12 hours post-dose

		at Cycle 1, Day 28

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Gilead Sciences

Collaborators

- Ono Pharmaceutical Co. Ltd

Investigators

- Study Director: Gilead Study Director, Gilead Sciences

Publications

Study Results

These publications are provided voluntarily by the person who enters information about the study and are about the study results.

- Walter HS, Salles GA, Dyer MJ. New Agents to Treat Chronic Lymphocytic Leukemia. N Engl J Med. 2016 Jun 2;374(22):2185-6. doi: 10.1056/NEJMc1602674. No abstract available. (https://pubmed.ncbi.nlm.nih.gov/27248633)
- Walter HS, Rule SA, Dyer MJ, Karlin L, Jones C, Cazin B, Quittet P, Shah N, Hutchinson CV, Honda H, Duffy K, Birkett J, Jamieson V, Courtenay-Luck N, Yoshizawa T, Sharpe J, Ohno T, Abe S, Nishimura A, Cartron G, Morschhauser F, Fegan C, Salles G. A phase 1 clinical trial of the selective BTK inhibitor ONO/GS-4059 in relapsed and refractory mature B-cell malignancies. Blood. 2016 Jan 28;127(4):411-9. doi: 10.1182/blood-2015-08-664086. Epub 2015 Nov 5. (https://pubmed.ncbi.nlm.nih.gov/26542378)
- Fegan, C, Bagshawe J, Salles G, et al. The Bruton's tyrosine kinase (BTK) inhibitor ONO-4059: promising single agent activity and well tolerated in patients with high risk chronic lymphocytic

leukaemia (CLL). Paper presented at: 56th American Society of Hematology Annual Meeting and Exposition; December 6-9, 2014; San Franscisco, CA.

- Morschhauser F, Terriou L, Dyer M, et al. The Bruton's tyrosine kinase (BTK) inhibitor ONO-4059: promising single agent activity in patients with relapsed and refractory NHL. Haematologica. 2014 Jun; 99: 150.

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted
2012-07-06

First Submitted that Met QC Criteria
2012-08-06

First Posted (Estimated)
2012-08-07

Results Reporting Dates

Results First Submitted
2021-01-06

Results First Submitted that Met QC Criteria
2021-01-06

Results First Posted
2021-01-28

Study Record Updates

Last Update Submitted that met QC Criteria
2021-02-22

Last Update Posted
2021-03-16

Last Verified

2021-02

More Information

Terms related to this study

Additional Relevant MeSH Terms

Neoplasms by Histologic Type
Neoplasms
Lymphoproliferative Disorders
Lymphatic Diseases
Immunoproliferative Disorders
Immune System Diseases
Hematologic Diseases
Leukemia, B-Cell
Chronic Disease
Disease Attributes
Pathologic Processes
Lymphoma
Leukemia
Lymphoma, Non-Hodgkin
Leukemia, Lymphoid
Leukemia, Lymphocytic, Chronic, B-Cell

Drug and device information, study documents, and helpful links

Studies a U.S. FDA-Regulated Drug Product

No

Studies a U.S. FDA-Regulated Device Product

No

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National Center for Biotechnology Information

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Study to Evaluate the Safety and Tolerability of Tirabrutinib (ONO/GS-4059) Given as Monotherapy in Participants With Relapsed/Refractory NHL and CLL

ClinicalTrials.gov ID NCT01659255

Sponsor Gilead Sciences

Information provided by Gilead Sciences (Responsible Party)

Last Update Posted 2021-03-16

Researcher View Tab

Trial Contacts

Contacts	ICMJE
Contact information is only displayed when the study is recruiting subjects	

Study Record Dates

First Submitted	ICMJE
2012-07-06	

First Posted	ICMJE

Feedback

2012-08-07

Results First Submitted ICMJE

2021-01-06

Results First Posted ICMJE

2021-01-28

Last Update Posted

2021-03-16

Last Verified *

2021-02

Outcome Measures

Change History

See all versions of this study

Primary (Current) * ICMJE

(Submitted: 2021-01-06)

- Percentage of Participants Experiencing Dose-Limiting Toxicities [Time Frame: Day 1 through Day 28]
  - Dose Limiting Toxicities (DLT) were defined as follows:
    - All Common Terminology Criteria (CTC) Grade 4 tirabrutinib related adverse events
    - All CTC Grade 3 tirabrutinib related adverse events, with the exception of the following:
      - CTC Grade 3 lymphocytosis considered an expected outcome of therapy

  Any toxicity which in the opinion of the Investigator is attributed to a participant's underlying disease was not considered a DLT.

Primary (Original) * ICMJE

(Submitted: 2012-08-06)

- Incidence of dose limiting toxicities (DLTs). DLTs will be assessed within the first 28 days from receiving the first dose of ONO-4059. [Time Frame: up to 12 months]
  - Patients will be monitored frequently during the first 2 days post ONO-4059 dosing as well as throughout the course of the study. Safety measures will include physical examinations (including neurological assessment), vital signs, clinical laboratory tests and twelve-lead electrocardiogram (ECG) along with Computerised Tomography (CT)/ Positron Emission Tomography (PET)-scans to assess efficacy.

Secondary (Current) [*] ICMJE

(Submitted: 2021-02-22)

- Overall Response Rate [Time Frame: Up to Cycle 37 (28 days for each cycle) plus 6-month intervals thereafter until disease progression (maximum: up to 39 months)]
  - Overall response rate (ORR) was defined as the percentage of participants who achieve a best overall response of complete remission (CR, unconfirmed complete response (CRu), complete response with incomplete marrow recovery (CRi)) or partial remission (PR, nodal PR) during study as assessed by the investigator.

    ORR assessment was defined per following standardized criteria:

    - NHL: Cheson, 1999
    - CLL: International Workshop on Chronic Lymphocytic Leukemia (IWCLL) 2008
- Pharmacokinetic (PK) Parameter: Cmax of Tirabrutinib [Time Frame: Pre-dose, then 30 minutes, 1, 2, 3, 4, 6, 8, 12 hours post-dose at Cycle 1, Day 28]
  - Cmax is defined as the maximum concentration of drug.
- PK Parameter: AUCtau of Tirabrutinib [Time Frame: Pre-dose, then 30 minutes, 1, 2, 3, 4, 6, 8, 12 hours post-dose at Cycle 1, Day 28]
  - AUCtau is defined as concentration of drug over dosing interval.

Secondary (Original) [*] ICMJE

(Submitted: 2012-08-06)

- Determine the safety of ONO-4059 in relapsed or refractory NHL [Time Frame: 12 months]
- Pharmacokinetics (PK) assessment [Time Frame: 28 days]
- survival and event free survival [Time Frame: 12 months]

Other Pre-specified (Current)

Not provided

Other Pre-specified (Original)

Not provided

Trial Description

Brief Title * ICMJE

Study to Evaluate the Safety and Tolerability of Tirabrutinib (ONO/GS-4059) Given as Monotherapy in Participants With Relapsed/Refractory NHL and CLL

Official Title *§ ICMJE

An Open-label, Multi-Center, Non-Randomised Phase I Dose-Escalation Study to Investigate the Safety and Tolerability of ONO-4059 (ONO/GS-4059) Given as Monotherapy in Patients With Relapsed/Refractory Non-Hodgkin's Lymphoma (NHL) and Relapsed/Refractory Chronic Lymphocytic Leukaemia (CLL)

Brief Summary *

The primary objective of the study is to evaluate the safety and tolerability of tirabrutinib (formerly ONO/GS-4059) given as monotherapy to participants with relapsed/refractory non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL).

Detailed Description

Not provided

Study Type * ICMJE

Interventional

Study Phase * ICMJE

Phase 1

Study Design *§ ICMJE

Allocation
Non-Randomized

Interventional Model
Parallel Assignment

Masking
None (Open Label)

Primary Purpose
Treatment

Condition * ICMJE

- Non Hodgkins Lymphoma
- Chronic Lymphocytic Leukaemia

Intervention * ICMJE

- Drug: Tirabrutinib
  - Capsules administered orally
  - Other Names:
    - ONO/GS-4059

Study Arms * ICMJE

- Experimental: Tirabrutinib 20 mg Once Daily (CLL)
  - Participants with relapsed/refractory chronic lymphocytic leukaemia (CLL) received tirabrutinib 20 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 40 mg Once Daily (CLL)
  - Participants with relapsed/refractory CLL received tirabrutinib 40 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 80 mg Once Daily (CLL)
  - Participants with relapsed/refractory CLL received tirabrutinib 80 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 160 mg Once Daily (CLL)
  - Participants with relapsed/refractory CLL received tirabrutinib 160 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 320 mg Once Daily (CLL)

- Participants with relapsed/refractory CLL received tirabrutinib 320 mg once daily.
- Interventions:
  - Drug: Tirabrutinib

- Experimental: Tirabrutinib 400 mg Once Daily (CLL)
  - Participants with relapsed/refractory CLL received tirabrutinib 400 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib

- Experimental: Tirabrutinib 500 mg Once Daily (CLL)
  - Participants with relapsed/refractory CLL received tirabrutinib 500 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib

- Experimental: Tirabrutinib 600 mg Once Daily (CLL)
  - Participants with relapsed/refractory CLL received tirabrutinib 600 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib

- Experimental: Tirabrutinib 300 mg Twice Daily (CLL)
  - Participants with relapsed/refractory CLL received tirabrutinib 300 mg twice daily.
  - Interventions:
    - Drug: Tirabrutinib

- Experimental: Tirabrutinib 20 mg Once Daily (NHL)
  - Participants with relapsed/refractory non-Hodgkin's lymphoma (NHL) received tirabrutinib 20 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib

- Experimental: Tirabrutinib 40 mg Once Daily (NHL)
  - Participants with relapsed/refractory NHL received tirabrutinib 40 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib

- Experimental: Tirabrutinib 80 mg Once Daily (NHL)
  - Participants with relapsed/refractory NHL received tirabrutinib 80 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 160 mg Once Daily (NHL)
  - Participants with relapsed/refractory NHL received tirabrutinib 160 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 320 mg Once Daily (NHL)
  - Participants with relapsed/refractory NHL received tirabrutinib 320 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 480 mg Once Daily (NHL)
  - Participants with relapsed/refractory NHL received tirabrutinib 480 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 600 mg Once Daily (NHL)
  - Participants with relapsed/refractory NHL received tirabrutinib 600 mg once daily.
  - Interventions:
    - Drug: Tirabrutinib
- Experimental: Tirabrutinib 240 mg Twice Daily (NHL)
  - Participants with relapsed/refractory NHL received tirabrutinib 240 mg twice daily.
  - Interventions:
    - Drug: Tirabrutinib

Publications

(Includes general and study results' publications, and Pubmed publications referencing this study by ClinicalTrials.gov Identifier (NCT Number))

- Walter HS, Salles GA, Dyer MJ. New Agents to Treat Chronic Lymphocytic Leukemia. N Engl J Med. 2016 Jun 2;374(22):2185-6. (https://pubmed.ncbi.nlm.nih.gov

doi: 10.1056/NEJMc1602674. No abstract available. /27248633)

- Walter HS, Rule SA, Dyer MJ, Karlin L, Jones C, Cazin B, Quittet P, Shah N, Hutchinson CV, Honda H, Duffy K, Birkett J, Jamieson V, Courtenay-Luck N, Yoshizawa T, Sharpe J, Ohno T, Abe S, Nishimura A, Cartron G, Morschhauser F, Fegan C, Salles G. A phase 1 clinical trial of the selective BTK inhibitor ONO/GS-4059 in relapsed and refractory mature B-cell malignancies. Blood. 2016 Jan 28;127(4):411-9. doi: 10.1182/blood-2015-08-664086. Epub 2015 Nov 5. (https://pubmed.ncbi.nlm.nih.gov/26542378)
- Fegan, C, Bagshawe J, Salles G, et al. The Bruton's tyrosine kinase (BTK) inhibitor ONO-4059: promising single agent activity and well tolerated in patients with high risk chronic lymphocytic leukaemia (CLL). Paper presented at: 56th American Society of Hematology Annual Meeting and Exposition; December 6-9, 2014; San Franscisco, CA.
- Morschhauser F, Terriou L, Dyer M, et al. The Bruton's tyrosine kinase (BTK) inhibitor ONO-4059: promising single agent activity in patients with relapsed and refractory NHL. Haematologica. 2014 Jun; 99: 150.

Recruitment Information

Recruitment Status *	ICMJE
Completed	

Enrollment (Actual) *§ **(Submitted: 2016-02-15)**	ICMJE
90	

Original Enrollment (Estimated) *§ **(Submitted: 2012-08-06)**	ICMJE
72	

Study Start Date (Actual) *§	ICMJE
2012-08-17	

Primary Completion Date (Actual) *
2015-02-23 (Final data collection date for primary outcome measure)

Study Completion Date (Actual) *§ ICMJE

2016-01-11

Eligibility Criteria * ICMJE

Key Inclusion Criteria:

1. Males or females with a confirmed diagnosis of and documented history of relapsed or refractory malignant disease (B-cell lymphoma and/or CLL) for which no therapy of curative or high priority exists and for whom treatment with a Btk inhibitor may be deemed appropriate.
2. Age ≥ 18 years.
3. Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2.

Key Exclusion Criteria:

1. Central nervous system (CNS) lymphoma.
2. Women who are pregnant or lactating.

Note: Other protocol defined Inclusion/Exclusion criteria may apply.

Sex/Gender * ICMJE

Sexes Eligible for the Study:
All

Ages * ICMJE

18 Years and older (Adult, Older Adult)

Accepts Healthy Volunteers *§ ICMJE

No

Location Countries ICMJE

France, United Kingdom

Removed Location Countries

Administrative Information

NCT Number ICMJE

NCT01659255

Other Study ID Numbers [*] ICMJE

ONO-4059POE001

2011-005033-39(EudraCT Number)

Has Data Monitoring Committee

No

U.S. FDA-regulated Product *§

Studies a U.S. FDA-regulated Drug Product

No

Studies a U.S. FDA-regulated Device Product

No

IPD Sharing Statement ICMJE

Not provided

Current Responsible Party *

Gilead Sciences

Original Responsible Party *

Ono Pharmaceutical Co. Ltd

Current Study Sponsor * ICMJE

Gilead Sciences

Original Study Sponsor * ICMJE

Ono Pharmaceutical Co. Ltd

Collaborators ICMJE

Ono Pharmaceutical Co. Ltd

Investigators ICMJE

Study Director:

Gilead Study Director

Gilead Sciences

PRS Account

Gilead Sciences

Symbol Legend

*	Required
*§	Required if Study Start Date is on or after January 18, 2017
[*]	Conditionally required
No Symbol	Unmarked fields are optional. If no information is provided, fields will be labeled as "not provided"
ICMJE	Data element required by the International Committee of Medical Journal Editors (https://www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html) and the World Health Organization ICTRP (https://www.who.int/clinical-trials-registry-platform)

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ClinicalTrials.gov ID NCT01659255

Sponsor Gilead Sciences

Information provided by Gilead Sciences (Responsible Party)

Last Update Posted 2021-03-16

Results Posted Tab

Results Overview

Conditions

Non Hodgkins Lymphoma | Chronic Lymphocytic Leukaemia

Intervention/Treatment

- Drug: Tirabrutinib

Other Study ID Numbers

- ONO-4059POE001
- 2011-005033-39 (EudraCT Number)

Study Design

Allocation: Non-Randomized

Feedback

Interventional Model: Parallel Assignment
Masking: None (Open Label)
Primary Purpose: Treatment

Results Point of Contact

Name/Title: Gilead Clinical Study Information Center
Organization: Gilead Sciences
Phone: 1-833-445-3230 (GILEAD-0)
Email: GileadClinicalTrials@gilead.com

Enrollment (Actual)

90

Study Type

Interventional

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates

First Submitted
2012-07-06

First Posted (Estimated)
2012-08-07

Results Reporting Dates

Results First Submitted
2021-01-06

Results First Posted
2021-01-28

Study Record Updates

Last Update Posted
2021-03-16

Last Verified
2021-02

Participant Flow

Recruitment Details

Participants were enrolled at study sites in Europe. The first participant was screened on 17 August 2012. The last study visit occurred on 11 January 2016.

Pre-assignment Details

102 participants were screened.

Arm/Group Title	Tirabrutinib 20 mg Once Daily (CLL)	Tirabrutinib 40 mg Once Daily (CLL)
Arm/Group Description	Participants with relapsed/refractory chronic lymphocytic leukaemia (CLL) received tirabrutinib 20 mg once daily.	Participants with relapsed/refractory CLL receive tirabrutinib 40 mg once daily.

Period Title: **Overall Study**

Started	3	3
Completed	1	2
Not Completed	2	1

Reason Not Completed

Adverse Event	0	0
Death	0	1

Arm/Group Title	Tirabrutinib 20 mg Once Daily (CLL)	Tirabrutinib 40 mg Once Daily (CLL)
Arm/Group Description	Participants with relapsed/refractory chronic lymphocytic leukaemia (CLL) received tirabrutinib 20 mg once daily.	Participants with relapsed/refractory CLL receive tirabrutinib 40 mg once daily.
Progressive Disease	2	0
Withdrew Consent	0	0
Investigator Decision	0	0
Sponsor's Decision	0	0
Completed Treatment Per Protocol at the Time	0	0
Participant Went on to Have an Allograft	0	0

Baseline Characteristics

Arm/Group Title	Tirabrutinib 20 mg Once Daily (CLL)	Tirabrutinib 40 mg Once Daily (CLL)
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib 20 mg once daily.	Participants with relapsed/refractory CLL receive tirabrutinib 40 mg once daily.
Overall Number of Baseline Participants	3	3
Baseline Analysis Population Description	The Full Analysis Set included all the participants who received at least 1 dose of study drug.	

Expand all / Collapse all

Age, Customized

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	3 participants	3 participants
< 65 years	1	0
≥ 65 years	2	3

Sex: Female, Male

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	3 participants	3 participants
Female	0	0
Male	3	3

Race/Ethnicity, Customized

Measure Type: Count of Participants | Unit of measure: Participants

Number Analyzed	3 participants	3 participants
White	2	3
Asian	0	0
Other	1	0

Outcome Measures

Expand all / Collapse all

1. Percentage of Participants Experiencing Dose-Limiting Toxicities

Type: Primary | Time Frame: Day 1 through Day 28

Description	Dose Limiting Toxicities (DLT) were defined as follows: • All Common Terminology Criteria (CTC) Grade 4 tirabrutinib related adverse events • All CTC Grade 3 tirabrutinib related adverse events, with the exception of the following: ◦ CTC Grade 3 lymphocytosis considered an expected outcome of therapy Any toxicity which in the opinion of the Investigator is attributed to a participant's underlying disease was not considered a DLT.
Time Frame	Day 1 through Day 28
Analysis Population Description	The Safety Analysis Set included all the participants who received at least 1 dose of study drug. Per planned analysis, data for DLTs were summarized by dose level received by participants with NHL and CLL.

Arm/Group Title	Tirabrutinib 20 mg Once Daily (CLL)	Tirabrutinib 40 mg Once Daily (CLL)
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib 20 mg once daily.	Participants with relapsed/refractory CLL receive tirabrutinib 40 mg once daily.
Overall Number of Participants Analyzed	3	3
Measure Type: Number | Unit of Measure: percentage of participants	0.0	0.0

2. Overall Response Rate

Type: Secondary | Time Frame: Up to Cycle 37 (28 days for each cycle) plus 6-month intervals thereafter until disease progression (maximum: up to 39 months)

Description	Overall response rate (ORR) was defined as the percentage of participants who achieve a best overall response of complete remission (CR, unconfirmed complete response (CRu), complete response with incomplete marrow recovery (CRi)) or partial remission (PR, nodal PR) during study as assessed by the investigator. ORR assessment was defined per following standardized criteria: • NHL: Cheson, 1999 • CLL: International Workshop on Chronic Lymphocytic Leukemia (IWCLL) 2008
Time Frame	Up to Cycle 37 (28 days for each cycle) plus 6-month intervals thereafter until disease progression (maximum: up to 39 months)
Analysis Population Description	The Full Analysis Set included all the participants who received at least 1 dose of study drug. Per planned analysis, data for overall response rate were summarized by overall CLL group and NHL subgroup.

Arm/Group Title	Chronic Lymphocytic Leukaemia	NHL Subtype FL
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with NHL subtype follicular lymphoma (FL) receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Overall Number of Participants Analyzed	28	5
Measure Type: Number | Unit of Measure: percentage of participants	85.7	0.0

3. Pharmacokinetic (PK) Parameter: Cmax of Tirabrutinib

Type: Secondary | Time Frame: Pre-dose, then 30 minutes, 1, 2, 3, 4, 6, 8, 12 hours post-dose at Cycle 1, Day 28

Description	Cmax is defined as the maximum concentration of drug.
Time Frame	Pre-dose, then 30 minutes, 1, 2, 3, 4, 6, 8, 12 hours post-dose at Cycle 1, Day 28
Analysis Population Description	Participants in the PK Analysis Set (all participants who received at least 1 dose of study drug and had at least 1 nonmissing postdose concentration value for the corresponding analyte in plasma) with available data were analyzed. Per planned analysis, data for PK parameters were summarized by dose cohorts.

Arm/Group Title	Tirabrutinib 20 mg Once Daily (CLL or NHL)	Tirabrutinib 40 mg Once Daily (CLL or NHL)
Arm/Group Description	Participants with relapsed/refractory CLL or NHL received tirabrutinib 20 mg once daily.	Participants with relapsed/refractory CLL or NHL received tirabrutinib 40 mg once daily.
Overall Number of Participants Analyzed	6	6
Mean (Standard Deviation) | Unit of Measure: ng/mL	73.4 (18.26)	164.5 (47.22)

4. PK Parameter: AUCtau of Tirabrutinib

Type: Secondary | Time Frame: Pre-dose, then 30 minutes, 1, 2, 3, 4, 6, 8, 12 hours post-dose at Cycle 1, Day 28

Description	AUCtau is defined as concentration of drug over dosing interval.
Time Frame	Pre-dose, then 30 minutes, 1, 2, 3, 4, 6, 8, 12 hours post-dose at Cycle 1, Day 28
Analysis Population Description	Participants in the PK Analysis Set with available data were analyzed. Per planned analysis, data for PK parameters were summarized by dose cohorts.

Arm/Group Title	Tirabrutinib 20 mg Once Daily (CLL or NHL)	Tirabrutinib 40 mg Once Daily (CLL or NHL)
Arm/Group Description	Participants with relapsed/refractory CLL or NHL received tirabrutinib 20 mg once daily.	Participants with relapsed/refractory CLL or NHL received tirabrutinib 40 mg once daily.
Overall Number of Participants Analyzed	6	6
Mean (Standard Deviation) | Unit of Measure: h*ng/mL	306.4 (74.92)	660.1 (310.95)

Adverse Events

Time Frame
Adverse Events: First dose date up to the last dose date plus 30 days (maximum: 36 months); All-Cause Mortality: First dose date up to 39 months

Adverse Event Reporting Description
The Safety Analysis Set included all the participants who received at least 1 dose of study drug. Per planned analysis, data were summarized by overall groups for NHL and CLL pooling all participants regardless of dose level received.

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
	Affected / at Risk (%)	Affected / at Risk (%)
Total	5/28 (17.86%)	38/62 (61.29%)

Serious Adverse Events

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
	Affected / at Risk (%)	Affected / at Risk (%)
Total	17/28 (60.71%)	23/62 (37.10%)
Blood and lymphatic system disorders		
Anaemia †1	0/28 (0.00%)	1/62 (1.61%)
Febrile neutropenia †1	2/28 (7.14%)	1/62 (1.61%)
Lymphocytic infiltration †1	1/28 (3.57%)	0/62 (0.00%)
Neutropenia †1	1/28 (3.57%)	0/62 (0.00%)
Spontaneous haematoma †1	1/28 (3.57%)	0/62 (0.00%)
Cardiac disorders		

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Cardiac arrest †1	0/28 (0.00%)	1/62 (1.61%)
Cardiac failure †1	0/28 (0.00%)	1/62 (1.61%)
Ear and labyrinth disorders		
Ear haemorrhage †1	0/28 (0.00%)	1/62 (1.61%)
Excessive cerumen production †1	0/28 (0.00%)	1/62 (1.61%)
Gastrointestinal disorders		
Constipation †1	0/28 (0.00%)	1/62 (1.61%)
Inguinal hernia strangulated †1	1/28 (3.57%)	0/62 (0.00%)
Oesophageal haemorrhage †1	0/28 (0.00%)	1/62 (1.61%)
Small intestinal haemorrhage †1	0/28 (0.00%)	1/62 (1.61%)
General disorders		
Adverse drug reaction †1	0/28 (0.00%)	1/62 (1.61%)
General physical health deterioration †1	0/28 (0.00%)	1/62 (1.61%)
Ill-defined disorder †1	0/28 (0.00%)	1/62 (1.61%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Pyrexia †1	3/28 (10.71%)	1/62 (1.61%)
Immune system disorders		
Hypersensitivity †1	0/28 (0.00%)	1/62 (1.61%)
Infections and infestations		
Abdominal abscess †1	1/28 (3.57%)	0/62 (0.00%)
Bacteraemia †1	1/28 (3.57%)	0/62 (0.00%)
Bronchiolitis †1	1/28 (3.57%)	0/62 (0.00%)
Bronchitis †1	1/28 (3.57%)	0/62 (0.00%)
Campylobacter gastroenteritis †1	1/28 (3.57%)	0/62 (0.00%)
Device related infection †1	1/28 (3.57%)	1/62 (1.61%)
Ear infection †1	1/28 (3.57%)	0/62 (0.00%)
Escherichia sepsis †1	1/28 (3.57%)	0/62 (0.00%)
Escherichia urinary tract infection †1	0/28 (0.00%)	1/62 (1.61%)
H1n1 influenza †1	0/28 (0.00%)	1/62 (1.61%)
Hepatitis E †1	1/28 (3.57%)	0/62 (0.00%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Herpes simplex †1	0/28 (0.00%)	1/62 (1.61%)
Herpes zoster oticus †1	0/28 (0.00%)	1/62 (1.61%)
Infection †1	0/28 (0.00%)	1/62 (1.61%)
Influenza †1	0/28 (0.00%)	1/62 (1.61%)
Lower respiratory tract infection †1	4/28 (14.29%)	3/62 (4.84%)
Lower respiratory tract infection bacterial †1	1/28 (3.57%)	0/62 (0.00%)
Lower respiratory tract infection fungal †1	1/28 (3.57%)	0/62 (0.00%)
Lung infection †1	1/28 (3.57%)	0/62 (0.00%)
Neutropenic infection †1	1/28 (3.57%)	0/62 (0.00%)
Neutropenic sepsis †1	2/28 (7.14%)	0/62 (0.00%)
Pneumocystis jirovecii pneumonia †1	0/28 (0.00%)	2/62 (3.23%)
Pneumonia †1	1/28 (3.57%)	2/62 (3.23%)
Pneumonia pneumococcal †1	1/28 (3.57%)	0/62 (0.00%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Respiratory syncytial virus infection †1	1/28 (3.57%)	0/62 (0.00%)
Respiratory tract infection viral †1	1/28 (3.57%)	0/62 (0.00%)
Sepsis †1	1/28 (3.57%)	0/62 (0.00%)
Upper respiratory tract infection †1	0/28 (0.00%)	1/62 (1.61%)
Injury, poisoning and procedural complications		
Cardiac function disturbance postoperative †1	1/28 (3.57%)	0/62 (0.00%)
Investigations		
Activated partial thromboplastin time prolonged †1	0/28 (0.00%)	1/62 (1.61%)
International normalised ratio increased †1	0/28 (0.00%)	1/62 (1.61%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Colorectal cancer †1	1/28 (3.57%)	0/62 (0.00%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Myelodysplastic syndrome †1	0/28 (0.00%)	1/62 (1.61%)
Squamous cell carcinoma of lung †1	1/28 (3.57%)	0/62 (0.00%)
Squamous cell carcinoma of skin †1	1/28 (3.57%)	0/62 (0.00%)
Nervous system disorders		
Dysarthria †1	1/28 (3.57%)	0/62 (0.00%)
Paraesthesia †1	1/28 (3.57%)	0/62 (0.00%)
Seizure †1	1/28 (3.57%)	0/62 (0.00%)
Syncope †1	0/28 (0.00%)	1/62 (1.61%)
Psychiatric disorders		
Anxiety †1	1/28 (3.57%)	0/62 (0.00%)
Disorientation †1	1/28 (3.57%)	0/62 (0.00%)
Renal and urinary disorders		
Calculus ureteric †1	1/28 (3.57%)	0/62 (0.00%)
Myeloma cast nephropathy †1	0/28 (0.00%)	1/62 (1.61%)
Urinary retention †1	0/28 (0.00%)	1/62 (1.61%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc

Pleural effusion †1	0/28 (0.00%)	1/62 (1.61%)

Skin and subcutaneous tissue disorders

Angioedema †1	1/28 (3.57%)	0/62 (0.00%)
Purpura †1	1/28 (3.57%)	0/62 (0.00%)
Rash †1	1/28 (3.57%)	0/62 (0.00%)

† Indicates events were collected by systematic assessment

1 Term from vocabulary, MedDRA 18.1

Other (Not Including Serious) Adverse Events

Frequency Threshold for Reporting Other Adverse Events	5%

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
	Affected / at Risk (%)	Affected / at Risk (%)
Total	28/28 (100.00%)	55/62 (88.71%)

Blood and lymphatic system disorders

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Anaemia †1	9/28 (32.14%)	23/62 (37.10%)
Leukopenia †1	2/28 (7.14%)	2/62 (3.23%)
Lymphopenia †1	2/28 (7.14%)	12/62 (19.35%)
Neutropenia †1	9/28 (32.14%)	9/62 (14.52%)
Thrombocytopenia †1	4/28 (14.29%)	18/62 (29.03%)
Ear and labyrinth disorders		
Ear pain †1	3/28 (10.71%)	0/62 (0.00%)
Eye disorders		
Conjunctival haemorrhage †1	2/28 (7.14%)	1/62 (1.61%)
Eye haemorrhage †1	3/28 (10.71%)	0/62 (0.00%)
Eye pruritus †1	2/28 (7.14%)	2/62 (3.23%)
Glaucoma †1	2/28 (7.14%)	0/62 (0.00%)
Ocular hyperaemia †1	2/28 (7.14%)	2/62 (3.23%)
Gastrointestinal disorders		
Abdominal pain †1	3/28 (10.71%)	8/62 (12.90%)
Abdominal pain upper †1	3/28 (10.71%)	4/62 (6.45%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Constipation †1	6/28 (21.43%)	2/62 (3.23%)
Diarrhoea †1	6/28 (21.43%)	18/62 (29.03%)
Dry mouth †1	2/28 (7.14%)	4/62 (6.45%)
Gastrooesophageal reflux disease †1	3/28 (10.71%)	1/62 (1.61%)
Nausea †1	2/28 (7.14%)	12/62 (19.35%)
Vomiting †1	5/28 (17.86%)	9/62 (14.52%)
General disorders		
Asthenia †1	3/28 (10.71%)	9/62 (14.52%)
Fatigue †1	5/28 (17.86%)	7/62 (11.29%)
Oedema peripheral †1	2/28 (7.14%)	8/62 (12.90%)
Pyrexia †1	7/28 (25.00%)	7/62 (11.29%)
Hepatobiliary disorders		
Cholelithiasis †1	2/28 (7.14%)	1/62 (1.61%)
Immune system disorders		
Hypogammaglobulinaemia †1	2/28 (7.14%)	0/62 (0.00%)
Infections and infestations		

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Bronchitis †1	3/28 (10.71%)	4/62 (6.45%)
Cellulitis †1	3/28 (10.71%)	0/62 (0.00%)
Chronic sinusitis †1	2/28 (7.14%)	0/62 (0.00%)
Ear infection †1	2/28 (7.14%)	1/62 (1.61%)
Eye infection †1	2/28 (7.14%)	0/62 (0.00%)
Herpes zoster †1	4/28 (14.29%)	3/62 (4.84%)
Influenza †1	2/28 (7.14%)	2/62 (3.23%)
Laryngitis †1	2/28 (7.14%)	1/62 (1.61%)
Lower respiratory tract infection †1	5/28 (17.86%)	6/62 (9.68%)
Lung infection †1	2/28 (7.14%)	1/62 (1.61%)
Nasopharyngitis †1	9/28 (32.14%)	11/62 (17.74%)
Oral herpes †1	3/28 (10.71%)	0/62 (0.00%)
Pharyngitis †1	2/28 (7.14%)	0/62 (0.00%)
Rhinitis †1	2/28 (7.14%)	8/62 (12.90%)
Sinobronchitis †1	2/28 (7.14%)	0/62 (0.00%)
Upper respiratory tract	2/28 (7.14%)	5/62 (8.06%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
infection †1		
Urinary tract infection †1	3/28 (10.71%)	3/62 (4.84%)
Injury, poisoning and procedural complications		
Arthropod bite †1	3/28 (10.71%)	1/62 (1.61%)
Contusion †1	10/28 (35.71%)	8/62 (12.90%)
Fall †1	8/28 (28.57%)	5/62 (8.06%)
Laceration †1	4/28 (14.29%)	0/62 (0.00%)
Procedural pain †1	2/28 (7.14%)	0/62 (0.00%)
Tendon rupture †1	2/28 (7.14%)	0/62 (0.00%)
Traumatic haematoma †1	3/28 (10.71%)	1/62 (1.61%)
Investigations		
Blood bilirubin increased †1	1/28 (3.57%)	4/62 (6.45%)
Metabolism and nutrition disorders		
Decreased appetite †1	0/28 (0.00%)	6/62 (9.68%)
Hyperkalaemia †1	4/28 (14.29%)	2/62 (3.23%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Hypoalbuminaemia †1	2/28 (7.14%)	4/62 (6.45%)

Musculoskeletal and connective tissue disorders

Arthralgia †1	8/28 (28.57%)	5/62 (8.06%)
Joint stiffness †1	2/28 (7.14%)	0/62 (0.00%)
Joint swelling †1	2/28 (7.14%)	1/62 (1.61%)
Muscle spasms †1	2/28 (7.14%)	2/62 (3.23%)
Musculoskeletal chest pain †1	2/28 (7.14%)	0/62 (0.00%)
Musculoskeletal pain †1	4/28 (14.29%)	6/62 (9.68%)
Musculoskeletal stiffness †1	2/28 (7.14%)	0/62 (0.00%)
Myalgia †1	2/28 (7.14%)	4/62 (6.45%)
Neck pain †1	0/28 (0.00%)	5/62 (8.06%)
Pain in extremity †1	3/28 (10.71%)	2/62 (3.23%)
Synovial cyst †1	3/28 (10.71%)	0/62 (0.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Basal cell carcinoma †1	6/28 (21.43%)	1/62 (1.61%)
Skin papilloma †1	2/28 (7.14%)	1/62 (1.61%)
Nervous system disorders		
Carpal tunnel syndrome †1	2/28 (7.14%)	0/62 (0.00%)
Dizziness †1	4/28 (14.29%)	1/62 (1.61%)
Dysaesthesia †1	2/28 (7.14%)	1/62 (1.61%)
Headache †1	4/28 (14.29%)	5/62 (8.06%)
Paraesthesia †1	4/28 (14.29%)	0/62 (0.00%)
Psychiatric disorders		
Anxiety †1	2/28 (7.14%)	1/62 (1.61%)
Insomnia †1	2/28 (7.14%)	5/62 (8.06%)
Reproductive system and breast disorders		
Prostatomegaly †1	2/28 (7.14%)	0/62 (0.00%)
Respiratory, thoracic and mediastinal disorders		
Catarrh †1	2/28 (7.14%)	0/62 (0.00%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Cough †1	8/28 (28.57%)	9/62 (14.52%)
Dyspnoea †1	2/28 (7.14%)	6/62 (9.68%)
Epistaxis †1	2/28 (7.14%)	4/62 (6.45%)
Oropharyngeal pain †1	6/28 (21.43%)	4/62 (6.45%)
Productive cough †1	2/28 (7.14%)	5/62 (8.06%)
Rales †1	2/28 (7.14%)	4/62 (6.45%)
Skin and subcutaneous tissue disorders		
Acne †1	3/28 (10.71%)	1/62 (1.61%)
Actinic keratosis †1	3/28 (10.71%)	1/62 (1.61%)
Dry skin †1	6/28 (21.43%)	3/62 (4.84%)
Eczema †1	2/28 (7.14%)	2/62 (3.23%)
Erythema †1	5/28 (17.86%)	2/62 (3.23%)
Macule †1	6/28 (21.43%)	1/62 (1.61%)
Petechiae †1	6/28 (21.43%)	9/62 (14.52%)
Pruritus †1	4/28 (14.29%)	5/62 (8.06%)
Purpura †1	5/28 (17.86%)	6/62 (9.68%)

Arm/Group Title	Chronic Lymphocytic Leukaemia	Non-Hodgkin's Lymphoma
Arm/Group Description	Participants with relapsed/refractory CLL received tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib study.	Participants with relapsed/refractory NHL receiv tirabrutinib until disease progression or until the participant entered into a possible future tirabrutinib stuc
Rash macular †1	3/28 (10.71%)	1/62 (1.61%)
Rash maculo-papular †1	2/28 (7.14%)	3/62 (4.84%)
Skin lesion †1	3/28 (10.71%)	2/62 (3.23%)
Swelling face †1	2/28 (7.14%)	1/62 (1.61%)
Vascular disorders		
Haematoma †1	7/28 (25.00%)	3/62 (4.84%)
Hypertension †1	0/28 (0.00%)	4/62 (6.45%)

† Indicates events were collected by systematic assessment

1 Term from vocabulary, MedDRA 18.1

Limitations and Caveats

[Not Specified]

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Gilead Sciences

Collaborators

- Ono Pharmaceutical Co. Ltd

Investigators

- Study Director: Gilead Study Director, Gilead Sciences

Publications

Study Results

These publications are provided voluntarily by the person who enters information about the study and are about the study results.

- Walter HS, Salles GA, Dyer MJ. New Agents to Treat Chronic Lymphocytic Leukemia. N Engl J Med. 2016 Jun 2;374(22):2185-6. doi: 10.1056/NEJMc1602674. No abstract available. (https://pubmed.ncbi.nlm.nih.gov/27248633)
- Walter HS, Rule SA, Dyer MJ, Karlin L, Jones C, Cazin B, Quittet P, Shah N, Hutchinson CV, Honda H, Duffy K, Birkett J, Jamieson V, Courtenay-Luck N, Yoshizawa T, Sharpe J, Ohno T, Abe S, Nishimura A, Cartron G, Morschhauser F, Fegan C, Salles G. A phase 1 clinical trial of the selective BTK inhibitor ONO/GS-4059 in relapsed and refractory mature B-cell malignancies. Blood. 2016 Jan 28;127(4):411-9. doi: 10.1182/blood-2015-08-664086. Epub 2015 Nov 5. (https://pubmed.ncbi.nlm.nih.gov/26542378)
- Fegan, C, Bagshawe J, Salles G, et al. The Bruton's tyrosine kinase (BTK) inhibitor ONO-4059: promising single agent activity and well tolerated in patients with high risk chronic lymphocytic leukaemia (CLL). Paper presented at: 56th American Society of Hematology Annual Meeting and Exposition; December 6-9, 2014; San Franscisco, CA.
- Morschhauser F, Terriou L, Dyer M, et al. The Bruton's tyrosine kinase (BTK) inhibitor ONO-4059: promising single agent activity in patients with relapsed and refractory NHL. Haematologica. 2014 Jun; 99: 150.

More Information

Record History

Certain Agreements

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed

After conclusion of the study and without prior written approval from Gilead, investigators in this study may communicate, orally present, or publish in scientific journals or other media only after the following conditions have been met:

- The results of the study in their entirety have been publicly disclosed by or with the consent of Gilead in an abstract, manuscript, or presentation form; or
- The study has been completed at all study sites for at least 2 years

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COMPLETED

Study to Evaluate the Safety and Tolerability of Tirabrutinib (ONO/GS-4059) Given as Monotherapy in Participants With Relapsed/Refractory NHL and CLL

ClinicalTrials.gov ID NCT01659255

Sponsor Gilead Sciences

Information provided by Gilead Sciences (Responsible Party)

Last Update Posted 2021-03-16

Record History Tab

Study Record Versions

- This table shows all the versions of this study record arranged in order by submitted date.
  - To view one version of the study record, click the submitted date.

	Version	Date submitted (YYYY-MM-DD)	Changes
☐	1	2012-08-06	• None (earliest version on record)
☐	2	2012-08-09	• Recruitment Status • Study Status

Feedback

	Version	Date submitted (YYYY-MM-DD)	Changes
			• Contacts/Locations • Study Identification • Outcome Measures
☐	3	2012-09-20	• Study Status • Contacts/Locations
☐	4	2012-10-16	• Study Status • Contacts/Locations
☐	5	2013-06-06	• Study Status
☐	6	2013-10-22	• Study Status • Study Description • Arms and Interventions • Outcome Measures • Contacts/Locations
☐	7	2014-07-09	• Study Status
			• Outcome Measures • Study Design
☐	8	2015-01-16	• Study Status • Study Description • Arms and Interventions
☐	9	2015-08-17	• Recruitment Status • Study Status • Outcome Measures • Study Description • Arms and Interventions
☐	10	2016-02-15	• Recruitment Status • Study Status

	Version	Date submitted (YYYY-MM-DD)	Changes
			• Study Design
☐	11	2016-03-25	• Study Identification • Study Status • Study Description • Arms and Interventions • Outcome Measures • Contacts/Locations • Sponsor/Collaborators
☐	12	2021-01-06	• Study Status • Outcome Measures • Study Identification • Oversight • Study Description • Study Design • Arms and Interventions • Eligibility • Contacts/Locations • References • Participant Flow • Baseline Characteristics • Adverse Events • More Information
☐	13	2021-02-22	• Study Status • Outcome Measures