Clinical trial results:
A phase Ib/II open-label, multicenter study evaluating the safety, efficacy, and pharmacokinetics of mosunetuzumab in combination with tiragolumab with or without atezolizumab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma

Summary

EudraCT number	2021-001060-23
Trial protocol	DE BE
Global end of trial date	19 July 2023

Results information

Result version number	v1 (current)
This version publication date	01 August 2024
First version publication date	01 August 2024

Trial information

Trial identification

Sponsor protocol code	CO43116

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05315713
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, 4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 July 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the safety, efficacy, and pharmacokinetics of mosunetuzumab in combination with tiragolumab, with or without atezolizumab, in participants with relapsed or refractory follicular lymphoma or diffuse large B-cell lymphoma.

Protection of trial subjects:

All participants were require to sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 May 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	8
EEA total number of subjects	5

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	3
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants with relapsed or refractory follicular lymphoma or with diffuse large B-cell lymphoma

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab

Arm description:

Participants received SC mosunetuzumab on Cycle (C) 1 Day (D) 1, C1D8, C1D15, and on the first day of each subsequent 21-day treatment cycle. Participants also received IV tiragolumab every 3 weeks (Q3W).

Arm type	Experimental
Investigational medicinal product name	Tiragolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 600 mg IV tiragolumab Q3W after administration of SC mosunetuzumab.

Investigational medicinal product name	Mosunetuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Mosunetuzumab was administered via SC injection 5 mg on Cycle (C) 1 Day (D) 1 (C1D1), 45 mg on C1D8, 45 mg on C1D15, and 45 mg on the first day of each subsequent 21-day treatment cycle

Number of subjects in period 1	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab
Started	8
Completed	0
Not completed	8
Adverse event, serious fatal	2
Consent withdrawn by subject	1
Death	3
Study terminated by sponsor	1

Progressive disease	1

Baseline characteristics

Reporting groups	
Reporting group title	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab

Reporting group description:

Participants received SC mosunetuzumab on Cycle (C) 1 Day (D) 1, C1D8, C1D15, and on the first day of each subsequent 21-day treatment cycle. Participants also received IV tiragolumab every 3 weeks (Q3W).

Reporting group values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
Adults (18-64 years)	3	3	
From 65-84 years	5	5	
Age Continuous Units: Years			
arithmetic mean	64.9		
standard deviation	± 12.8	-	
Sex: Female, Male Units: Participants			
Female	4	4	
Male	4	4	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	6	6	
More than one race	0	0	
Unknown or Not Reported	2	2	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	6	6	
Unknown or Not Reported	2	2	

End points

End points reporting groups

Reporting group title	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab

Reporting group description:

Participants received SC mosunetuzumab on Cycle (C) 1 Day (D) 1, C1D8, C1D15, and on the first day of each subsequent 21-day treatment cycle. Participants also received IV tiragolumab every 3 weeks (Q3W).

Primary: Percentage of Participants with Adverse Events - Phase 1b

End point title	Percentage of Participants with Adverse Events - Phase 1b[1]

End point description:

End point type	Primary

End point timeframe:

From the start of treatment until 90 days after the final dose of study treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no formal statistical analyses planned for this endpoint

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percentage of participants	100			

Statistical analyses

No statistical analyses for this end point

Primary: Best Objective Response Rate (ORR) as Determined by the Investigator Using Lugano 2014 Criteria - Phase 2

End point title	Best Objective Response Rate (ORR) as Determined by the Investigator Using Lugano 2014 Criteria - Phase 2[2]

End point description:

This endpoint was not evaluated due to early study termination (Phase 2 did not occur).

End point type	Primary

End point timeframe:

Up to Cycle 17 (cycle length = 21 days)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no formal statistical analyses planned for this endpoint

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: Percentage of participants				
number (not applicable)				

Notes:

[3] - This endpoint was not evaluated due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Mosunetuzumab - Phase 1b

End point title	Serum Concentration of Mosunetuzumab - Phase 1b

End point description:

-9999: Pre-dose serum concentrations were below the limit of quantification.
9999: There were insufficient data points above the limit of quantification to calculate the CV.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 - Cycle 8 Day 1 (cycle length = 21 days)

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
C1D1 pre-dose (n=8)	-9999 (± 9999)			
C1D1 3 hrs post-dose (n=8)	0.00983 (± 9999)			
C1D2 24 hrs post-dose (n=8)	0.0556 (± 109.6)			
C1D4 72 hrs post-dose (n=8)	0.164 (± 90.5)			
C1D8 pre-dose (n=8)	0.166 (± 83.2)			
C1D15 pre-dose (n=7)	2.18 (± 48.8)			
C2D1 pre-dose (n=7)	4.02 (± 86.3)			

C3D1 pre-dose (n=6)	2.90 (± 81.8)			
C4D1 pre-dose (n=5)	2.34 (± 49.0)			
C4D1 3 hrs post-dose (n=6)	2.10 (± 48.2)			
C5D1 pre-dose (n=4)	2.59 (± 25.7)			
C8D1 pre-dose (n=3)	2.97 (± 17.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Best ORR as Determined by the Investigator Using Lugano 2014 Criteria - Phase 1b

End point title	Best ORR as Determined by the Investigator Using Lugano 2014 Criteria - Phase 1b

End point description:

Best ORR is defined as the fraction of participants with complete response (CR) or partial response (PR) at any time as determined by the investigator using Lugano 2014 criteria.

End point type	Secondary

End point timeframe:

Assessed at screening and then every 3-6 months until disease progression, start of new anti-cancer therapy, or withdrawal (through Cycle 8; cycle length = 21 days)

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percentage of participants				
number (not applicable)	62.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Complete Response (CR) Rate as Determined by the Investigator Using Lugano 2014 Criteria - Phase 1b and Phase 2

End point title	Best Complete Response (CR) Rate as Determined by the Investigator Using Lugano 2014 Criteria - Phase 1b and Phase 2

End point description:

End point type	Secondary

End point timeframe:

Assessed at screening and then every 3-6 months until disease progression, start of new anti-cancer therapy, or withdrawal (through Cycle 8; cycle length = 21 days)

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Percentage of participants				
number (not applicable)	37.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Determined by the Investigator Using Lugano 2014 Criteria - Phase 1b and Phase 2

End point title	Duration of Response (DOR) as Determined by the Investigator Using Lugano 2014 Criteria - Phase 1b and Phase 2

End point description:

End point type	Secondary

End point timeframe:

From the first occurrence of a documented response (CR or partial response (PR)) to disease progression or relapse, or death from any cause, whichever occurs first (up to approximately 4 years)

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: Time				
number (not applicable)				

Notes:

[4] - This endpoint was not analyzed due to an insufficient number of participants with the event.

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS) as Determined by the Investigator Using Lugano 2014 Criteria - Phase 2

End point title	Event-Free Survival (EFS) as Determined by the Investigator Using Lugano 2014 Criteria - Phase 2

End point description:

End point type	Secondary

End point timeframe:

From the first study treatment to the first occurrence of disease progression or relapse, or death from any cause, whichever occurs first (up to approximately 4 years)

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	0[5]			
Units: Time				
number (not applicable)				

Notes:

[5] - This endpoint was not evaluated due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) - Phase 2

End point title	Overall Survival (OS) - Phase 2

End point description:

End point type	Secondary

End point timeframe:

From the time of first study treatment to death from any cause (up to approximately 4 years)

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Time				

number (not applicable)				

Notes:

[6] - This endpoint was not evaluated due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events - Phase 2

End point title	Percentage of Participants with Adverse Events - Phase 2

End point description:

End point type	Secondary

End point timeframe:

From the start of treatment until 90 days after the final dose of study treatment

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	0[7]			
Units: Percentage of participants				
number (not applicable)				

Notes:

[7] - This endpoint was not evaluated due to early study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) as Determined by the Investigator Using Lugano 2014 Criteria - Phase 2

End point title	Progression-Free Survival (PFS) as Determined by the Investigator Using Lugano 2014 Criteria - Phase 2

End point description:

End point type	Secondary

End point timeframe:

From the first study treatment to the first occurrence of disease progression or relapse, or death from any cause, whichever occurs first (up to approximately 4 years)

End point values	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: Time				
number (not applicable)				

Notes:

[8] - This endpoint was not evaluated due to early study termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the start of treatment until 90 days after the final dose of study treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab

Reporting group description:

Participants received SC mosunetuzumab on Cycle (C) 1 Day (D) 1, C1D8, C1D15, and on the first day of each subsequent 21-day treatment cycle. Participants also received IV tiragolumab every 3 weeks (Q3W).

Serious adverse events	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	2		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebellar haematoma			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			

subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Septic shock			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Subcutaneous (SC) Mosunetuzumab + Intravenous (IV) Tiragolumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		

Malaise subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Injection site reaction subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 4		
Fatigue subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Chills subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Asthenia subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2		
Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Upper-airway cough syndrome subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Dyspnoea subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 4		
Productive cough subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Rhinitis allergic subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Investigations Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) Blood creatinine increased subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Injury, poisoning and procedural complications Fractured sacrum subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 3 / 8 (37.50%) 4 2 / 8 (25.00%) 4		
Ear and labyrinth disorders			

Ear congestion subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Eye disorders Retinal detachment subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Gastrointestinal disorders Oral pain subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Malignant dysphagia subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1 2 / 8 (25.00%) 2 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1 2 / 8 (25.00%) 2 1 / 8 (12.50%) 1		
Skin and subcutaneous tissue disorders Rash maculo-papular subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2 1 / 8 (12.50%) 1		
Renal and urinary disorders Renal failure subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		

Musculoskeletal and connective tissue disorders			
Osteoporosis			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Arthralgia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	2		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Rhinovirus infection			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypophosphataemia			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Hypomagnesaemia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		

Hypokalaemia subjects affected / exposed occurrences (all)	2 / 8 (25.00%) 2		
Decreased appetite subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 2		
Cachexia subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 September 2021	Exclusion criteria modified to exclude participants with a history of Grade ≥ 3 immune mediated adverse events associated with prior immune checkpoint inhibitor therapy with fewer exceptions
20 February 2023	Removed ADA endpoints for mosunetuzumab, tiragolumab, atezolizumab, and tocilizumab

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Early termination led to small numbers of participants for analysis.

Notes: