Clinical trial results:
A Modular Phase II, Open-label, Multicentre Study to Assess AZD4573 Efficacy and Safety as Monotherapy or in Combination With Anti-cancer Agents in Subjects With Relapsed/Refractory Peripheral T-cell Lymphoma or Classical Hodgkin Lymphoma

Summary

EudraCT number	2021-002570-54
Trial protocol	FR IT
Global end of trial date	16 February 2024

Results information

Result version number	v1 (current)
This version publication date	20 February 2025
First version publication date	20 February 2025

Trial information

Trial identification

Sponsor protocol code	D8231C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05140382
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	AstraZeneca AB, 151 85, Södertälje, Sweden, 15185
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.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	30 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 August 2023
Global end of trial reached?	Yes
Global end of trial date	16 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of AZD4573 monotherapy by evaluation of objective response rate.

Protection of trial subjects:

The study was conducted in accordance with the protocol, with the consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines for Health-related Research Involving Humans and with the applicable International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, as well as for any applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2021
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: 12
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 8
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	United States: 13
Worldwide total number of subjects	52
EEA total number of subjects	15

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)	37
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted from 15 December 2021 (first subject visit) to 16 February 2024 (last subject last visit). The study was conducted at 27 sites in 7 countries worldwide (Australia, France, Italy, South Korea, Taiwan, United Kingdom and United States).

Pre-assignment

Screening details:

Subjects who met the inclusion criteria and none of the exclusion criteria were enrolled to the study. All study assessments were performed as per the schedule of assessment.

Period 1

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

Blinding implementation details:

Open-label study

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 Non NK PTCL

Arm description:

Subjects with non-natural killer peripheral T-cell lymphoma (non-NK PTCL) received 12 mg dose of AZD4573 once weekly until disease progression.

Arm type	Experimental
Investigational medicinal product name	AZD4573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 12 mg dose of AZD4573 once weekly until disease progression.

Arm title	Cohort 2 NK PTCL

Arm description:

Subjects with natural killer T-cell lymphoma (NK PTCL) received 12 mg dose of AZD4573 once weekly until disease progression.

Arm type	Experimental
Investigational medicinal product name	AZD4573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 12 mg dose of AZD4573 once weekly until disease progression.

Arm title	Cohort 3 cHL

Arm description:

Subjects with classical Hodgkins lymphoma (cHL) received 12 mg dose of AZD4573 once weekly until disease progression.

Arm type	Experimental

Investigational medicinal product name	AZD4573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received 12 mg dose of AZD4573 once weekly until disease progression.

Number of subjects in period 1	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL
Started	31	2	19
Completed	0	0	0
Not completed	31	2	19
Adverse event, serious fatal	3	-	-
Consent withdrawn by subject	1	-	4
Unknown at data cut-off	-	-	1
Investigator decision	1	-	-
Unspecified	4	-	1
Subjective disease progression	2	1	-
Withdrawal of consent	-	-	1
Progressive disease	20	1	12

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1 Non NK PTCL
Reporting group description:	
Subjects with non-natural killer peripheral T-cell lymphoma (non-NK PTCL) received 12 mg dose of AZD4573 once weekly until disease progression.	
Reporting group title	Cohort 2 NK PTCL
Reporting group description:	
Subjects with natural killer T-cell lymphoma (NK PTCL) received 12 mg dose of AZD4573 once weekly until disease progression.	
Reporting group title	Cohort 3 cHL
Reporting group description:	
Subjects with classical Hodgkins lymphoma (cHL) received 12 mg dose of AZD4573 once weekly until disease progression.	

Reporting group values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL
Number of subjects	31	2	19
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	19	1	17
From 65-84 years	12	1	2
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	60.1	61.0	46.5
standard deviation	± 12.2	± 8.5	± 14.7
Sex: Female, Male Units: Subjects			
Female	13	0	10
Male	18	2	9

Reporting group values	Total		
Number of subjects	52		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	37		
From 65-84 years	15		
85 years and over	0		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	23		
Male	29		

End points

End points reporting groups

Reporting group title	Cohort 1 Non NK PTCL
Reporting group description:	
Subjects with non-natural killer peripheral T-cell lymphoma (non-NK PTCL) received 12 mg dose of AZD4573 once weekly until disease progression.	
Reporting group title	Cohort 2 NK PTCL
Reporting group description:	
Subjects with natural killer T-cell lymphoma (NK PTCL) received 12 mg dose of AZD4573 once weekly until disease progression.	
Reporting group title	Cohort 3 cHL
Reporting group description:	
Subjects with classical Hodgkins lymphoma (cHL) received 12 mg dose of AZD4573 once weekly until disease progression.	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[1]
End point description:	
Objective response rate is defined as the proportion of subjects who have a tumour response of complete response [CR] or partial response [PR] according to the Lugano (2014) response criteria for malignant lymphoma. Response evaluable set included all dosed subjects who had measurable disease at baseline.	
End point type	Primary
End point timeframe:	
From Screening (Day -30 to Day-1) until disease progression or survival until end of study (26 months)	

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: No statistical analysis was performed.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	2	19	
Units: Percentage of subjects				
number (confidence interval 95%)	22.6 (9.59 to 41.10)	0 (0 to 84.19)	21.1 (6.05 to 45.57)	

Statistical analyses

No statistical analyses for this end point

Secondary: Complete response (CR) rate

End point title	Complete response (CR) rate
End point description:	
Complete response rate is defined as proportion of subjects who have a complete response according to the Lugano (2014) response criteria. Response evaluable set included all dosed subjects who had measurable disease at baseline.	

End point type	Secondary

End point timeframe:

From Screening (Day -30 to Day-1) until disease progression or survival until end of study (26 months).

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	2	19	
Units: Percentage of subjects				
number (not applicable)	19.4	0	15.8	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

Progression-free survival is defined as the time from the date of first dose to documented disease progression, or death from any cause, whichever occurs first.
The arbitrary value 99999 represents that data were not calculable due to low number of subjects.
Full analysis set included all subjects who received any amount of any study intervention.

End point type	Secondary

End point timeframe:

From Screening (Day -30 to Day-1) until disease progression or survival until end of study (26 months).

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	2	19	
Units: Months				
median (confidence interval 95%)	1.8 (1.51 to 2.17)	0.7 (0.66 to 99999)	1.9 (1.64 to 4.11)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DoR)

End point title	Duration of response (DoR)

End point description:

Duration of response is defined as the time from the first objective response to the time of documented disease progression or death due to any cause, whichever occurs first.

The arbitrary value 99999 in cohort 1 and cohort 3 represent that data were not calculable due to insufficient number of subjects with the event of interest (less than 50%) occurred in the study.
Response evaluable set included all dosed subjects who had measurable disease at baseline.

End point type	Secondary

End point timeframe:

From Screening (Day -30 to Day-1) until disease progression or survival until end of study (26 months).

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	0[2]	4	
Units: Months				
median (confidence interval 95%)	99999 (1.8 to 99999)	(to)	5.2 (1.9 to 99999)	

Notes:

[2] - Number of subjects analysed were 0 due to insufficient number of events of interest.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

Overall survival is defined as the time from the date of first dose to death from any cause.
The arbitrary value 99999 in cohort 2 represents that data were not calculable due to low number of subjects and in cohort 3 represents that data were not calculable due to less number of events of interest (less than 50%).
Full analysis set included all subjects who received any amount of any study intervention.

End point type	Secondary

End point timeframe:

From Screening (Day -30 to Day-1) until disease progression or survival until end of study (26 months).

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	2	19	
Units: Months				
median (confidence interval 95%)	8.6 (2.33 to 10.18)	99999 (0.66 to 99999)	99999 (10.05 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Adverse events (AE) and Serious AEs (SAE)

End point title	Number of subjects with Adverse events (AE) and Serious AEs (SAE)

End point description:

The safety and tolerability of AZD4573 was assessed.
Adverse Event - AE
Common Terminology Criteria for Adverse Events - CTCAE
IMP - Investigational Medicinal Product
Serious Adverse Event - SAE
CTCAE grade 3 ≥ AE = Any AE of CTCAE grade 3 or higher
Safety set included all subjects who received at least 1 dose of any study intervention.

End point type	Secondary

End point timeframe:

From treatment period (Cycle 1) to follow up visit (30 [± 7]) days from the last dose (upto 26 months).

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	2	19	
Units: Subjects				
Any AE	31	2	18	
IMP-related AEs	31	2	16	
CTCAE grade 3 ≥ AEs	29	2	15	
CTCAE grade 3 ≥ Treatment-related AEs	27	2	13	
Any AE with death outcome	2	1	0	
IMP-related AE with death outcome	2	0	0	
SAE (including death outcome)	21	2	11	
IMP-related SAE (including death outcome)	16	1	8	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed plasma (peak) drug concentration (Cmax)

End point title	Maximum observed plasma (peak) drug concentration (Cmax)

End point description:

The plasma PK of AZD4573 when administered in subjects was assessed.
Here, 'n' in each row represents the number of subjects analyzed for each timepoint in each cohort. The arbitrary value 99999 in cycle 1 week 1, cycle 1 week 2, cycle 1 week 3 represents that data were not calculable due to low number of subjects and in cycle 2 represents that data were not available as no subjects were analysed.
Pharmacokinetic (PK) set included all subjects who received any amount of study intervention with at least 1 reportable concentration.

End point type	Secondary

End point timeframe:

Cycle 1 (Cycle length is 35 days), Day 1 of Weeks 1-3 and Cycle 2 (Cycle length is 21 Days), Day 1.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	2	19	
Units: Nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 week 1 day 1 (n: 31, 2, 19)	159.9 (± 53.2)	99999 (± 99999)	201.8 (± 82.1)	
Cycle 1 week 2 day 1 (n: 25, 1, 15)	312.4 (± 84.5)	99999 (± 99999)	278.2 (± 73.8)	
Cycle 1 week 3 day 1 (n: 25, 1, 16)	265.5 (± 54.1)	99999 (± 99999)	376.3 (± 89.9)	
Cycle 2 day 1 (n: 16, 0, 14)	308.6 (± 65.9)	99999 (± 99999)	381.8 (± 82.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration curve from zero to the last quantifiable concentration (AUClast)

End point title	Area under the plasma concentration curve from zero to the last quantifiable concentration (AUClast)

End point description:

The plasma PK of AZD4573 when administered in subjects was assessed.
Here, 'n' in each row represents the number of subjects analyzed for each timepoint in each cohort. The arbitrary value 99999 in cycle 1 week 1, cycle 1 week 2, cycle 1 week 3 represents that data were not calculable due to low number of subjects and in cycle 2 represents that data were not available as no subjects were analysed.
PK set included all subjects who received any amount of study intervention with at least 1 reportable concentration.

End point type	Secondary

End point timeframe:

Cycle 1 (Cycle length is 35 days), Day 1 of Weeks 1-3 and Cycle 2 (Cycle length is 21 Days), Day 1.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	2	19	
Units: hours (h)*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 week 1 day 1 (n: 31, 2, 19)	913.3 (± 95.0)	99999 (± 99999)	1039 (± 113.5)	
Cycle 1 week 2 day 1 (n: 25, 1, 15)	1695 (± 102.3)	99999 (± 99999)	1646 (± 86.7)	
Cycle 1 week 3 day 1 (n: 25, 1, 16)	1651 (± 76.5)	99999 (± 99999)	2228 (± 75.0)	
Cycle 2 day 1 (n: 16, 0, 14)	1933 (± 81.2)	99999 (± 99999)	2083 (± 115.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area under plasma concentration time curve from zero to infinity (AUC0-inf) of AZD4573

End point title	Area under plasma concentration time curve from zero to infinity (AUC0-inf) of AZD4573

End point description:

The plasma PK of AZD4573 when administered in subjects was assessed.
Here, 'n' in each row represents the number of subjects analyzed for each timepoint in each cohort. The arbitrary value 99999 in cycle 1 week 2 and cycle 1 week 3 represents that data were not calculable due to low number of subjects and in cycle 1 week 1 and cycle 2 represents that data were not available as no subjects were analysed.
PK set included all subjects who received any amount of study intervention with at least 1 reportable concentration.

End point type	Secondary

End point timeframe:

Cycle 1 (Cycle length is 35 days), Day 1 of Weeks 1-3 and Cycle 2 (Cycle length is 21 Days), Day 1.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	1	12	
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 week 1 day 1 (n: 18, 0, 9)	1294 (± 82.9)	99999 (± 99999)	1872 (± 59.3)	
Cycle 1 week 2 day 1 (n: 17, 1, 9)	1711 (± 86.8)	99999 (± 99999)	1984 (± 62.9)	
Cycle 1 week 3 day 1 (n: 18, 1, 12)	1490 (± 71.5)	99999 (± 99999)	2643 (± 88.2)	
Cycle 2 day 1 (n: 14, 0, 7)	1885 (± 72.9)	99999 (± 99999)	1899 (± 89.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to reach peak observed concentration following drug administration (tmax)

End point title	Time to reach peak observed concentration following drug administration (tmax)

End point description:

The plasma PK of AZD4573 when administered in subjects was assessed.
Here, 'n' in each row represents the number of subjects analyzed for each timepoint in each cohort. The arbitrary value 99999 represents that data were not available as no subjects were analysed. The median values for cycle 1 week 1, cycle 1 week 2 and cycle 1 week 3 in cohort 2 were not calculable due to low number of subjects.
PK set included all subjects who received any amount of study intervention with at least 1 reportable concentration.

End point type	Secondary

End point timeframe:

Cycle 1 (Cycle length is 35 days), Day 1 of Weeks 1-3 and Cycle 2 (Cycle length is 21 Days), Day 1.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	2	19	
Units: Hour				
median (full range (min-max))				
Cycle 1 week 1 day 1 (n: 31, 2, 19)	2.000 (0.97 to 6.00)	2.15 (1.90 to 2.15)	2.083 (1.00 to 23.00)	
Cycle 1 week 2 day 1 (n: 25, 1, 15)	2.083 (1.87 to 6.08)	2.15 (2.15 to 2.15)	2.083 (1.87 to 6.00)	
Cycle 1 week 3 day 1 (n: 25, 1, 16)	2.083 (0.87 to 6.00)	2.25 (2.25 to 2.25)	2.133 (1.78 to 4.00)	
Cycle 2 day 1 (n: 16, 0, 14)	2.133 (1.00 to 3.58)	99999 (99999 to 99999)	2.083 (0.97 to 5.02)	

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life (t1/2) of AZD4573

End point title	Half-life (t1/2) of AZD4573

End point description:

The plasma PK of AZD4573 when administered in subjects was assessed.
Here, 'n' in each row represents the number of subjects analyzed for each timepoint in each cohort. The arbitrary value 99999 represents that data were not available as no subjects were analysed. The median values for cycle 1 week 2 and cycle 1 week 3 in cohort 2 were not calculable due to low number of subjects.
PK set included all subjects who received any amount of study intervention with at least 1 reportable concentration.

End point type	Secondary

End point timeframe:

Cycle 1 (Cycle length is 35 days), Day 1 of Weeks 1-3 and Cycle 2 (Cycle length is 21 Days), Day 1.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	1	12	
Units: Hour				
median (full range (min-max))				
Cycle 1 week 1 day 1 (n: 18, 0, 9)	5.772 (1.67 to 11.6)	99999 (99999 to 99999)	5.858 (3.68 to 7.90)	
Cycle 1 week 2 day 1 (n: 17, 1, 9)	5.448 (4.10 to 11.3)	6.80 (6.80 to 6.80)	5.250 (4.11 to 9.71)	
Cycle 1 week 3 day 1 (n: 18, 1, 12)	5.435 (1.15 to 10.5)	5.09 (5.09 to 5.09)	5.499 (3.93 to 23.5)	
Cycle 2 day 1 (n: 14, 0, 7)	6.669 (3.50 to 16.0)	99999 (99999 to 99999)	4.323 (3.56 to 14.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Systematic clearance (CL)

End point title	Systematic clearance (CL)

End point description:

The plasma PK of AZD4573 when administered in subjects was assessed.
Here, 'n' in each row represents the number of subjects analyzed for each timepoint in each cohort. The arbitrary value 99999 in cycle 1 week 2 and cycle 1 week 3 represents that data were not calculable due to low number of subjects and in cycle 1 week 1 and cycle 2 represents that data were not available as no subjects were analysed.
PK set included all subjects who received any amount of study intervention with at least 1 reportable concentration.

End point type	Secondary

End point timeframe:

Cycle 1 (Cycle length is 35 days), Day 1 of Weeks 1-3 and Cycle 2 (Cycle length is 21 Days), Day 1.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	1	11	
Units: Liter/hour				
geometric mean (geometric coefficient of variation)				
Cycle 1 week 1 day 1 (n: 18, 0, 9)	4.636 (± 82.9)	99999 (± 99999)	3.205 (± 59.3)	
Cycle 1 week 2 day 1 (n: 17, 1, 9)	5.137 (± 82.3)	99999 (± 99999)	4.537 (± 62.9)	
Cycle 1 week 3 day 1 (n: 18, 1, 11)	7.799 (± 69.5)	99999 (± 99999)	4.965 (± 74.7)	
Cycle 2 day 1 (n: 14, 0, 7)	6.367 (± 72.9)	99999 (± 99999)	6.064 (± 85.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of distribution at terminal phase (Vz)

End point title	Volume of distribution at terminal phase (Vz)

End point description:

The plasma PK of AZD4573 when administered in subjects was assessed.
Here, 'n' in each row represents the number of subjects analyzed for each timepoint in each cohort. The arbitrary value 99999 in cycle 1 week 2 and cycle 1 week 3 represents that data were not calculable due to low number of subjects and in cycle 1 week 1 and cycle 2 represents that data were not available as no subjects were analysed.
PK set included all subjects who received any amount of study intervention with at least 1 reportable concentration.

End point type	Secondary

End point timeframe:

Cycle 1 (Cycle length is 35 days), Day 1 of Weeks 1-3 and Cycle 2 (Cycle length is 21 Days), Day 1.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	1	11	
Units: Liter				
geometric mean (geometric coefficient of variation)				
Cycle 1 week 1 day 1 (N: 18, 0, 9)	38.59 (± 49.0)	99999 (± 99999)	26.45 (± 54.2)	
Cycle 1 week 2 day 1 (N: 17, 1, 9)	45.96 (± 53.8)	99999 (± 99999)	37.68 (± 37.5)	
Cycle 1 week 3 day 1 (N: 18, 1, 11)	58.92 (± 33.1)	99999 (± 99999)	44.34 (± 55.7)	
Cycle 2 day 1 (N: 14, 0, 7)	63.45 (± 41.6)	99999 (± 99999)	43.38 (± 59.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of distribution at steady state (Vss)

End point title	Volume of distribution at steady state (Vss)

End point description:

The plasma PK of AZD4573 when administered in subjects was assessed.
Here, 'n' in each row represents the number of subjects analyzed for each timepoint in each cohort. The arbitrary value 99999 in cycle 1 week 2 and cycle 1 week 3 represents that data were not calculable due to low number of subjects and in cycle 1 week 1 and cycle 2 represents that data were not available as no subjects were analysed.
PK set included all subjects who received any amount of study intervention with at least 1 reportable concentration.

End point type	Secondary

End point timeframe:

Cycle 1 (Cycle length is 35 days), Day 1 of Weeks 1-3 and Cycle 2 (Cycle length is 21 Days), Day 1.

End point values	Cohort 1 Non NK PTCL	Cohort 2 NK PTCL	Cohort 3 cHL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	1	11	
Units: Liter				
geometric mean (geometric coefficient of variation)				
Cycle 1 week 1 day 1 (n: 18, 0, 9)	35.80 (± 51.1)	99999 (± 99999)	24.20 (± 54.3)	
Cycle 1 week 2 day 1 (n: 17, 1, 9)	39.25 (± 51.3)	99999 (± 99999)	33.20 (± 36.9)	
Cycle 1 week 3 day 1 (n: 18, 1, 11)	50.32 (± 27.8)	99999 (± 99999)	37.99 (± 66.3)	
Cycle 2 day 1 (n: 14, 0, 7)	55.93 (± 36.8)	99999 (± 99999)	37.29 (± 54.6)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From treatment period (Cycle 1) to follow up visit (30 [± 7]) days from the last dose (upto 26 months).	
Adverse event reporting additional description:	
Safety set included all subjects who received at least 1 dose of any study intervention.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Cohort 1 Non-NK PTCL
Reporting group description:	
Subjects with non-NK PTCL received 12 mg dose of AZD4573 once weekly until disease progression.	
Reporting group title	Cohort 3 cHL
Reporting group description:	
Subjects with cHL received 12 mg dose of AZD4573 once weekly until disease progression.	
Reporting group title	Cohort 2 NK PTCL
Reporting group description:	
Subjects with NK PTCL received 12 mg dose of AZD4573 once weekly until disease progression.	

Serious adverse events	Cohort 1 Non-NK PTCL	Cohort 3 cHL	Cohort 2 NK PTCL
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 31 (67.74%)	11 / 19 (57.89%)	2 / 2 (100.00%)
number of deaths (all causes)	17	2	1
number of deaths resulting from adverse events	2	0	1
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			

subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 31 (9.68%)	1 / 19 (5.26%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 31 (9.68%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	9 / 9	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	2 / 31 (6.45%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

White blood cell count decreased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 19 (0.00%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 31 (0.00%)	0 / 19 (0.00%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			

subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	4 / 31 (12.90%)	3 / 19 (15.79%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	2 / 4	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Fanconi syndrome acquired			
subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Staphylococcal bacteraemia			

subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	4 / 31 (12.90%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Tumour lysis syndrome			

subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Cohort 1 Non-NK PTCL	Cohort 3 cHL	Cohort 2 NK PTCL
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 31 (100.00%)	18 / 19 (94.74%)	2 / 2 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 31 (6.45%)	2 / 19 (10.53%)	1 / 2 (50.00%)
occurrences (all)	2	2	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 31 (3.23%)	6 / 19 (31.58%)	0 / 2 (0.00%)
occurrences (all)	1	6	0
Catheter site thrombosis			
subjects affected / exposed	3 / 31 (9.68%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Chills			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	5 / 31 (16.13%)	3 / 19 (15.79%)	1 / 2 (50.00%)
occurrences (all)	16	5	1
Pain			

subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	3 / 31 (9.68%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	3	1	0
Non-cardiac chest pain			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 31 (0.00%)	0 / 19 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	2
Serum sickness			
subjects affected / exposed	0 / 31 (0.00%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal dryness			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 31 (6.45%)	4 / 19 (21.05%)	0 / 2 (0.00%)
occurrences (all)	2	4	0
Dyspnoea			
subjects affected / exposed	0 / 31 (0.00%)	3 / 19 (15.79%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Hiccups			

subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Investigations			
Amylase increased			
subjects affected / exposed	3 / 31 (9.68%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	6	2	0
Alanine aminotransferase increased			
subjects affected / exposed	19 / 31 (61.29%)	11 / 19 (57.89%)	1 / 2 (50.00%)
occurrences (all)	90	35	1
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 31 (67.74%)	11 / 19 (57.89%)	2 / 2 (100.00%)
occurrences (all)	101	42	3
Blood cholesterol increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	3	1	0
Blood calcium decreased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	4	1	0
Blood bilirubin increased			
subjects affected / exposed	14 / 31 (45.16%)	5 / 19 (26.32%)	2 / 2 (100.00%)
occurrences (all)	46	18	2
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 31 (9.68%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	5	5	0
Bilirubin conjugated increased			

subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Blood creatinine increased			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Blood fibrinogen increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Prothrombin time prolonged			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count decreased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Lipase increased			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	4	1	0
International normalised ratio increased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Blood phosphorus decreased			
subjects affected / exposed	3 / 31 (9.68%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Blood phosphorus increased			
subjects affected / exposed	4 / 31 (12.90%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	6	5	0
Blood potassium decreased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	5	0	0
Blood potassium increased			

subjects affected / exposed	3 / 31 (9.68%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Blood triglycerides increased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Blood urea increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Fibrin D dimer increased			
subjects affected / exposed	1 / 31 (3.23%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	1	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	10 / 31 (32.26%)	4 / 19 (21.05%)	0 / 2 (0.00%)
occurrences (all)	18	7	0
Serum ferritin increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 31 (0.00%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Troponin increased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
White blood cell count decreased			
subjects affected / exposed	6 / 31 (19.35%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	34	2	0
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Palpitations			

subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 31 (3.23%)	3 / 19 (15.79%)	0 / 2 (0.00%)
occurrences (all)	1	3	0
Headache			
subjects affected / exposed	2 / 31 (6.45%)	4 / 19 (21.05%)	0 / 2 (0.00%)
occurrences (all)	4	6	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	13 / 31 (41.94%)	4 / 19 (21.05%)	1 / 2 (50.00%)
occurrences (all)	43	9	1
Neutropenia			
subjects affected / exposed	24 / 31 (77.42%)	13 / 19 (68.42%)	1 / 2 (50.00%)
occurrences (all)	126	54	1
Lymph node pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	3 / 31 (9.68%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	4	7	0
Febrile neutropenia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Anaemia			
subjects affected / exposed	11 / 31 (35.48%)	10 / 19 (52.63%)	0 / 2 (0.00%)
occurrences (all)	21	15	0
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Eye pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dry eye			

subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 31 (9.68%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	4	0	0
Constipation			
subjects affected / exposed	6 / 31 (19.35%)	5 / 19 (26.32%)	0 / 2 (0.00%)
occurrences (all)	6	5	0
Diarrhoea			
subjects affected / exposed	12 / 31 (38.71%)	7 / 19 (36.84%)	0 / 2 (0.00%)
occurrences (all)	18	8	0
Mouth ulceration			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	10 / 31 (32.26%)	9 / 19 (47.37%)	1 / 2 (50.00%)
occurrences (all)	14	14	1
Stomatitis			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	1	2	0
Vomiting			
subjects affected / exposed	8 / 31 (25.81%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	10	2	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 31 (6.45%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	2	2	0
Skin weeping			

subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	4	1	0
Rash			
subjects affected / exposed	3 / 31 (9.68%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	3	3	0
Pruritus			
subjects affected / exposed	1 / 31 (3.23%)	3 / 19 (15.79%)	0 / 2 (0.00%)
occurrences (all)	1	3	0
Erythema			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Back pain			
subjects affected / exposed	3 / 31 (9.68%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	4	2	0
Arthralgia			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Muscle spasms			
subjects affected / exposed	4 / 31 (12.90%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	5	1	0
Infections and infestations			
Enterobacter bacteraemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Bacteraemia			

subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Catheter site infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Enterococcal infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 31 (3.23%)	3 / 19 (15.79%)	0 / 2 (0.00%)
occurrences (all)	1	3	0
Urinary tract infection			
subjects affected / exposed	2 / 31 (6.45%)	1 / 19 (5.26%)	1 / 2 (50.00%)
occurrences (all)	3	1	1
Influenza			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	4 / 31 (12.90%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	4	1	0
Streptococcal infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Vascular device infection			
subjects affected / exposed	1 / 31 (3.23%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0

Hyperphosphataemia			
subjects affected / exposed	5 / 31 (16.13%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	9	1	0
Hyperkalaemia			
subjects affected / exposed	2 / 31 (6.45%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	5	5	0
Hyperglycaemia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Decreased appetite			
subjects affected / exposed	2 / 31 (6.45%)	2 / 19 (10.53%)	1 / 2 (50.00%)
occurrences (all)	2	2	1
Hypervolaemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	11 / 31 (35.48%)	4 / 19 (21.05%)	1 / 2 (50.00%)
occurrences (all)	14	6	1
Hypomagnesaemia			
subjects affected / exposed	4 / 31 (12.90%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	5	0	0
Hyponatraemia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 19 (0.00%)	0 / 2 (0.00%)
occurrences (all)	3	0	0
Hypophosphataemia			
subjects affected / exposed	4 / 31 (12.90%)	2 / 19 (10.53%)	0 / 2 (0.00%)
occurrences (all)	8	3	0
Tumour lysis syndrome			
subjects affected / exposed	0 / 31 (0.00%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	8 / 31 (25.81%)	1 / 19 (5.26%)	0 / 2 (0.00%)
occurrences (all)	16	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2021	Amendment 1: Section 7.1 Discontinuation of Study Intervention - Text moved to new section 7.1.1. dedicated to study-wide stopping rules for safety. Section 7.1.1 Criteria for stopping or pausing the study recruitment - New section added to specify in greater detail study-wide stopping rules for safety that would trigger SRC evaluation and potential study pause. Section 10.1.2 Schedule of Activities, footnote c; Section 10.8.2.5 Clinical Safety Laboratory Assessments - Footnote was updated and Section 10.8.2.5 amended for clarification of the haematologic and chemistry criteria required to initiate each cycle of therapy. Section 10.4.1 Module 1 Design: AZD4573 monotherapy - Inclusion of a requirement for pooled safety monitoring assessments to be conducted at 3-monthly intervals. Section 10.6.1 Dose Modification - Update of Grade 3 or 4 non-haematological toxicities Table 11 to add the guidance of one dose level reduction in order to resume AZD4573 dosing after resolution of a Grade 4 non-haematological (excluding liver and TLS) AE to Grade 1, and guidance on discontinuation following a third occurrence.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported