Clinical trial results:
INTERNATIONAL COLLABORATIVE TREATMENT PROTOCOL FOR INFANTS UNDER ONE YEAR WITH ACUTE LYMPHOBLASTIC OR BIPHENOTYPIC LEUKEMIA

Summary

EudraCT number	2005-004599-19
Trial protocol	IT BE FR DE GB AT PT DK IE
Global end of trial date	01 January 2023

Results information

Result version number	v1 (current)
This version publication date	29 November 2024
First version publication date	29 November 2024

Trial information

Trial identification

Sponsor protocol code	INTERFANT-06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00550992
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	DCOG
Sponsor organisation address	Heidelberglaan 25, Utrecht, Netherlands, 3584 CS
Public contact	Prof. dr. R. Pieters, DCOG, +31 889727272, r.pieters@prinsesmaximacentrum.nl
Scientific contact	Prof. dr. R. Pieters, DCOG, +31 889727272, r.pieters@prinsesmaximacentrum.nl

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 May 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2017
Global end of trial reached?	Yes
Global end of trial date	01 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the role of an early intensification of two `AML` induction blocks versus protocol Ib directly after induction, in a randomized way in MR and HR patients

Protection of trial subjects:

Parents signed informed consent; trial conducted according to ICH GCP and declaration of Helsinki

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2006
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: 41
Country: Number of subjects enrolled	Portugal: 29
Country: Number of subjects enrolled	United Kingdom: 83
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Belgium: 64
Country: Number of subjects enrolled	Denmark: 26
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 78
Country: Number of subjects enrolled	Italy: 62
Country: Number of subjects enrolled	Netherlands: 35
Country: Number of subjects enrolled	Argentina: 52
Country: Number of subjects enrolled	Hong Kong: 16
Country: Number of subjects enrolled	Chile: 36
Country: Number of subjects enrolled	United States: 31
Country: Number of subjects enrolled	Poland: 55
Country: Number of subjects enrolled	Canada: 4
Worldwide total number of subjects	651
EEA total number of subjects	388

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	137
Infants and toddlers (28 days-23 months)	514
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were
recruited from February 2006 to July 2016. Individual study groups obtained ethics approval and physicians obtained informed consent from parents. Eligibility criteria were a diagnosis of ALL (except those with a mature B phenotype), age 365 days or younger, and no prior antileukemic therapy other than emergency treatment.

Pre-assignment

Screening details:

All infants diagnosed with ALL

Period 1

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

Blinding implementation details:

n.a.

Arms

Are arms mutually exclusive?	Yes
Arm title	Protocol 1b

Arm description:

Standard of Care

Arm type	SOC

No investigational medicinal product assigned in this arm

Arm title	ADE+MAE

Arm description:

experimental myeloid courses, namely araC, daunorubicin, etoposide (ADE) and mitoxantrone, araC, etoposide (MAE)

Arm type	Active comparator
Investigational medicinal product name	AraC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg/m2 BID IV for 10 days during ADE and MAE course

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

Dosage and administration details:

50 mg/m2 per day on days 1, 3 and 5 during ADE course

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

Dosage and administration details: 100 mg/m2 per day for 5 days during ADE and MAE course	
Investigational medicinal product name	mitoxantrone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 12 mg/m2 per day on day 1, 3 and 5 of MAE course	

Number of subjects in period 1[1]	Protocol 1b	ADE+MAE
Started	161	169
Completed	161	169

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Total number of registered patients is 651; number of patients eligible for randomization and randomized is 330

Baseline characteristics

Reporting groups	
Reporting group title	Protocol 1b
Reporting group description:	
Standard of Care	
Reporting group title	ADE+MAE
Reporting group description:	
experimental myeloid courses, namely araC, daunorubicin, etoposide (ADE) and mitoxantrone, araC, etoposide (MAE)	

Reporting group values	Protocol 1b	ADE+MAE	Total
Number of subjects	161	169	330
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	43	41	84
Infants and toddlers (28 days-23 months)	118	128	246
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	61	69	130
Male	100	100	200

End points

End points reporting groups

Reporting group title	Protocol 1b
Reporting group description:	
Standard of Care	
Reporting group title	ADE+MAE
Reporting group description:	
experimental myeloid courses, namely araC, daunorubicin, etoposide (ADE) and mitoxantrone, araC, etoposide (MAE)	

Primary: 3-year Disease Free Survival rate

End point title	3-year Disease Free Survival rate[1]

End point description:

DFS, the primary end point, was defined as time from random assignment to relapse, death in continuous complete remission from any cause, or second malignant neoplasm, whichever occurred first.

End point type	Primary

End point timeframe:

DFS, the primary end point, was defined as time from random assignment to relapse, death in continuous complete remission from any cause, or second malignant neoplasm, whichever occurred first.

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: Descriptive statistics

End point values	Protocol 1b	ADE+MAE		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	169		
Units: percentage	39	45		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 6-year follow-up	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups	
Reporting group title	Protocol 1b
Reporting group description: Standard of Care	
Reporting group title	ADE+MAE
Reporting group description: experimental myeloid courses, namely araC, daunorubicin, etoposide (ADE) and mitoxantrone, araC, etoposide (MAE)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: We refer to the article added in the section More Information

Serious adverse events	Protocol 1b	ADE+MAE	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 161 (8.07%)	17 / 169 (10.06%)	
number of deaths (all causes)	13	17	
number of deaths resulting from adverse events	13	17	
General disorders and administration site conditions			
Death			
subjects affected / exposed	13 / 161 (8.07%)	17 / 169 (10.06%)	
occurrences causally related to treatment / all	0 / 13	0 / 17	
deaths causally related to treatment / all	0 / 13	0 / 17	

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

Non-serious adverse events	Protocol 1b	ADE+MAE	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 161 (0.00%)	0 / 169 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/31283407