Sponsor

Novartis

Generic Drug Name

Ranibizumab

Trial Indications

Retinopathy of prematurity (ROP)

Protocol Number

CRFB002H2403

Protocol Title

A 24-week, Open-label, Prospective, Single-arm Study Evaluating the Effectiveness and Safety of Lucentis® (Ranibizumab) 0.2 mg in Retinopathy of Prematurity (ROP) Participants in China

Clinical Trial Phase

Not applicable

Phase of Drug Development

Not applicable

Study Start/End Dates

Study Start Date: 13 January 2023 (first patient first visit)

Study Completion Date: 10 July 2024 (last patient last visit)

Reason for Termination

Not applicable

Study Design/Methodology

This was a 24-week, multicenter, open-label, single-arm, observational, post-approval commitment study, which was designed to collect effectiveness, safety and other clinical information of intravitreal ranibizumab 0.2 mg for the treatment of ROP participants in a real-world clinical setting in mainland China.

Eligible participants treated according to local routine clinical practice were enrolled in the study upon signing an informed consent.

The study entry visit was used to assess eligibility, collect baseline characteristics, and administer the intravitreal ranibizumab for eligible participants and was considered Day 1 (Baseline) of the 24-week observation period. Participants were treated according to the approved label and standard of care as per investigator judgment. During the observational period, participants could receive post-baseline treatment (i.e., ranibizumab or laser therapy). End of study was defined as completion of the Week 24 visit or premature withdrawal visit.

Centers

Participants were enrolled at 6 centers in China.

Objectives:

Primary objectives

- To evaluate the real-world effectiveness of ranibizumab 0.2 mg in the treatment of ROP in Chinese premature infants over a 24-week observation period.

Secondary objectives

- To evaluate ocular and systemic safety for up to 24-weeks in premature infants diagnosed with ROP and treated with intravitreal ranibizumab 0.2 mg.
- To evaluate the real-world clinical outcomes of ranibizumab 0.2 mg in the treatment of ROP.
- To evaluate fundus features of ranibizumab 0.2 mg in the treatment of ROP.

Test Product, Dose, and Mode of Administration

Participants were receiving intravitreal ranibizumab 0.2 mg, per standard of care, in this observational study.

Statistical Methods

Descriptive statistics were presented for all endpoints at all of the time points assessed.

Unless otherwise specified in the statistical analysis plan (SAP), continuous data were summarized using descriptive statistics: number of non-missing values (n), mean, standard deviation, median, minimum and maximum.

Unless otherwise specified in the SAP, categorical data were summarized using descriptive statistics: number and percentages of participants. When appropriate, associated 95% Clopper-Pearson (exact) confidence intervals were provided. Unless otherwise specified in the statistical outputs, percentages were computed using the number of participants in a given analysis set as the denominator.

Kaplan-Meier plots were provided for time-to-event data.

The following analysis sets were part of this study:

- The full analysis set (FAS) comprised all participants to whom study treatment was assigned. The FAS was used for the demographic analysis, baseline characteristic analysis, primary analysis, and other effectiveness evaluations.
- The safety set consisted of all participants who received at least one administration of study treatment. The safety set was used for exposure, some safety evaluations, and to display prior and concomitant medications/procedures.

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria

- Signed informed consent from parent(s) or legal guardian(s), in compliance with local requirements.
- Male or female premature infants with a birth weight of less than 1500 g.
- Bilateral ROP with 1 of the following retinal findings in each eye:
  - Zone I, stage 1+, 2+, 3 or 3+ disease, or
  - Zone II, stage 3+ disease, or
  - A-ROP

Exclusion criteria

- Had a history of hypersensitivity (either the participant or the mother) to ranibizumab or any component of the ranibizumab formulation or to drugs of similar chemical classes.
- Had been previously exposed to any intravitreal or systemic anti-VEGF agent (either the participant or the mother during this child's pregnancy).
- Had used (either the participant or the mother) other investigational drugs as part of another clinical study (other than vitamins and minerals) within 30 days or within 5 half-lives of the other investigational drug, whichever was longer.
- Had received any previous surgical or nonsurgical treatment for ROP (e.g., ablative laser therapy or cryotherapy, vitrectomy).
- Participants who had contraindications according to locally approved ranibizumab label.

Participant Flow Table

Participant disposition (all participants)

Disposition Reason	Enrolled Participants N=62 n (%)
Informed Consent Form Signed	62
Participants meet Eligibility Criteria	62
Participants did not meet Eligibility Criteria	0
Completed	53 (85.5)
Discontinued	9 (14.5)
Primary reason for discontinuation [1]	
Participant's parent(s) or legal guardian(s) decision	7 (11.3)
Adverse Event	1 (1.6)
Lost to follow-up	1 (1.6)

[1] Only showing non-zero results.

Baseline Characteristics

Participant demographics (FAS)

Characteristic Categories/Statistics	Full Analysis Set N=61
Gender, n (%)	
Male	35 (57.4)
Female	26 (42.6)
Missing	0
Gestational Age (completed weeks)	
n	61
Mean (SD)	27.4 (2.18)
Median	27.0
Min, Max	23, 33
Missing	0
Gestational Age category, n (%)	
≤ 24 weeks	4 (6.6)
> 24 - < 27 weeks	18 (29.5)
≥ 27 weeks	39 (63.9)
Age (months)	
n	61
Mean (SD)	2.34 (0.778)
Median	2.30
Min, Max	1.0, 4.0
Missing	0

Characteristic Categories/Statistics	Full Analysis Set N=61
Race, n (%)	
Asian	61 (100)
Non - Asian	0 (0.0)
Missing	0
Ethnicity, n (%)	
Chinese	61 (100)
Non - Chinese	0 (0.0)
Missing	0

n: Number of participants meeting the criterion (for categorical variables); number of participants with non-missing assessment (for continuous variables).

Baseline ROP characteristics (FAS)

Characteristic Categories/Statistics	Right Eye N=61	Left Eye N=61	Best Eye at Baseline N=61	Worst Eye at Baseline N=61
ROP, n (%)				
Yes	61 (100)	61 (100)	61 (100)	61 (100)
No	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0	0
Zone, n (%)				
I	9 (14.8)	9 (14.8)	9 (14.8)	9 (14.8)
II	52 (85.2)	52 (85.2)	52 (85.2)	52 (85.2)
III	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unknown / Not Reported	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Not Applicable	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
A-ROP Status, n (%)				
*A-ROP	3 (4.9)	3 (4.9)	3 (4.9)	3 (4.9)

Characteristic Categories/Statistics	Right Eye N=61	Left Eye N=61	Best Eye at Baseline N=61	Worst Eye at Baseline N=61
*Non A-ROP	58 (95.1)	58 (95.1)	58 (95.1)	58 (95.1)
Missing	0	0	0	0
ROP disease, n (%)				
ZONE I AP-ROP	2 (3.3)	2 (3.3)	2 (3.3)	2 (3.3)
*ZONE II AP-ROP	1 (1.6)	1 (1.6)	1 (1.6)	1 (1.6)
ZONE I STAGE 3+	3 (4.9)	3 (4.9)	3 (4.9)	3 (4.9)
ZONE I STAGE 2+	1 (1.6)	1 (1.6)	1 (1.6)	1 (1.6)
ZONE I STAGE 1+	3 (4.9)	3 (4.9)	3 (4.9)	3 (4.9)
ZONE II STAGE 3+	50 (82.0)	50 (82.0)	50 (82.0)	50 (82.0)
*ZONE II STAGE 2+	1 (1.6)	1 (1.6)	1 (1.6)	1 (1.6)
Extra-retinal vessels and judged to be a sign of active ROP disease, n (%)				
Yes	51 (83.6)	51 (83.6)	51 (83.6)	51 (83.6)
No	10 (16.4)	10 (16.4)	10 (16.4)	10 (16.4)
Not assessed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Baseline was defined as the last non-missing measurement taken at or before the first day of administration the intravitreal ranibizumab.

*: For one of the participants, the baseline ROP stage for both eyes was confirmed by investigator as "A-ROP", not "2+" after database lock, which was not reflected in this table.

n: Number of participants meeting the criterion (for categorical variables).

Primary Outcome Results

Summary of ranibizumab effectiveness (FAS)

		FAS N=61
	n/M	Proportion (%) (exact 95% CI)[1] (asymptotic 95% CI)
Primary effectiveness endpoint [2]		
Success	48/53	90.6 (79.3, 96.9) (82.7, 98.4)
Failure	5/53	9.4 (3.1, 20.7) (1.6, 17.3)
Require other intervention for ROP at or before the 24-week assessment	5	9.4 (3.1, 20.7) (1.6, 17.3)
Have active ROP in either eye at the 24-week assessment	0	0.0 (0.0, 6.7) (0.0, 0.0)
Vessel dilatation of plus disease in at least 2 quadrants of the eye	0	0.0 (0.0, 6.7) (0.0, 0.0)
Extra-retinal vessels extending from the retina into the vitreous and judged to be a sign of active ROP disease	0	0.0 (0.0, 6.7) (0.0, 0.0)
Have unfavorable structural outcomes in either eye at or before the 24-week assessment	1	1.9 (0.0, 10.1) (0.0, 5.5)
Retrolental membrane obscuring the view of the posterior pole	0	0.0 (0.0, 6.7) (0.0, 0.0)
Substantial temporal retinal vessel dragging causing abnormal structural features/ macular ectopia	1	1.9 (0.0, 10.1) (0.0, 5.5)
Posterior retinal fold involving the macula	0	0.0 (0.0, 6.7) (0.0, 0.0)
Retinal detachment involving the macula	0	0.0 (0.0, 6.7) (0.0, 0.0)
Non-evaluable [3]	8	

		FAS N=61
	n/M	**Proportion (%) (exact 95% CI)[1] (asymptotic 95% CI)**

M = number of evaluable participants, who qualified for the evaluation of success or failure.

Percentage was based on evaluable participants from full analysis set.

[1] Exact 95% CI is obtained from Clopper-Pearson method.

[2] The primary effectiveness endpoint was the absence of requiring intervention other than ranibizumab for ROP, the absence of active ROP and absence of unfavorable structural outcomes in both eyes during the observational period of 24-weeks after starting treatment.

[3] Non-evaluable = participants with missing data to qualify for the evaluation of success or failure.

Secondary Outcome Results

Summary of ocular examinations (Safety Set)

	Safety Set N=61 n (%)		
	Baseline (N'=61)	Week 12 (N'=43)	Week 24 (N'=53)
Ocular Examination (OU) - Eye Structure			
Best eye at baseline - anterior chamber			
Normal	58 (95.1)	43 (100)	53 (100)
Abnormal	3 (4.9)	0 (0.0)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0
Worst eye at baseline - anterior chamber			
Normal	58 (95.1)	43 (100)	53 (100)
Abnormal	3 (4.9)	0 (0.0)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0
Best eye at baseline - lens			
Normal	61 (100)	43 (100)	53 (100)
Abnormal	0 (0.0)	0 (0.0)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0
Worst eye at baseline - lens			
Normal	61 (100)	43 (100)	53 (100)
Abnormal	0 (0.0)	0 (0.0)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0

	Safety Set N=61 n (%)		
	Baseline (N'=61)	Week 12 (N'=43)	Week 24 (N'=53)
Ocular Examination (OU) - Findings			
Best eye at baseline - lens status			
Phakic	61 (100)	43 (100)	53 (100)
Pseudophakic	0 (0.0)	0 (0.0)	0 (0.0)
Aphakic	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0
Best eye at baseline - evaluation result of lens status			
Normal	61 (100)	43 (100)	52 (98.1)
Abnormal	0 (0.0)	0 (0.0)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	1 (1.9)
Missing	0	0	0
Worst eye at baseline - lens status			
Phakic	61 (100)	43 (100)	53 (100)
Pseudophakic	0 (0.0)	0 (0.0)	0 (0.0)
Aphakic	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0
Worst eye at baseline - evaluation result of lens status			
Normal	61 (100)	43 (100)	52 (98.1)
Abnormal	0 (0.0)	0 (0.0)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	1 (1.9)
Missing	0	0	0

N': number of safety set participants performed a given visit.
The percentage would be based on N'. Missing = N' - sum (number of participants in each category).
Baseline is defined as the last non-missing measurement taken at or before the first day of administration of the intravitreal ranibizumab. Week 12 corresponds to Day 85 (±14 days) after first dose of ranibizumab. Week 24 corresponds to Day 169 (±14 days) after first dose of ranibizumab. The participant data collected out of recommended window (±14 days) of visit 3 were re-mapped to visit 3 (week 24).
ADS source: ADOE

Summary of fundus examinations (Safety Set)

	Safety Set N=61 n (%)		
	Baseline (N'=61)	Week 12 (N'=43)	Week 24 (N'=53)
Best eye at baseline - optic disc			
Normal	61 (100)	43 (100)	53 (100)
Abnormal	0 (0.0)	0 (0.0)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0
Worst eye at baseline - optic disc			
Normal	61 (100)	42 (97.7)	53 (100)
Abnormal	0 (0.0)	1 (2.3)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0
Best eye at baseline - macula			
Normal	59 (96.7)	42 (97.7)	53 (100)
Abnormal	2 (3.3)	1 (2.3)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0

	Safety Set N=61 n (%)		
	Baseline (N'=61)	Week 12 (N'=43)	Week 24 (N'=53)
Worst eye at baseline - macula			
Normal	59 (96.7)	41 (95.3)	53 (100)
Abnormal	2 (3.3)	2 (4.7)	0 (0.0)
Not Done	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0	0	0
Best eye at baseline - full retinal vascularization in 12 clock hours			
Yes	0 (0.0)	7 (16.3)	31 (58.5)
No	61 (100)	33 (76.7)	18 (34.0)
Not Assessed	0 (0.0)	3 (7.0)	4 (7.5)
Missing	0	0	0
Worst eye at baseline - full retinal vascularization in 12 clock hours			
Yes	0 (0.0)	8 (18.6)	33 (62.3)
No	61 (100)	32 (74.4)	16 (30.2)
Not Assessed	0 (0.0)	3 (7.0)	4 (7.5)
Missing	0	0	0

N': number of safety set participants performed a given visit.
The percentage would be based on N'. Missing = N' - sum (number of participants in each category).
Baseline is defined as the last non-missing measurement taken at or before the first day of administration of the intravitreal ranibizumab. Week 12 corresponds to Day 85 (±14 days) after first dose of ranibizumab. Week 24 corresponds to Day 169 (±14 days) after first dose of ranibizumab. The participant data collected out of recommended window (±14 days) of visit 3 were re-mapped to visit 3 (week 24).
ADS source: ADOE

Physical examinations by visits (Safety Set)

Assessment (Units) / Visits	Statistics	Results
Systolic Blood Pressure (mmHg)		
Baseline (N'=55)	n	44
	Mean (SD)	75.1 (15.59)
	Median	77.5
	Min, Max	41, 115
	Missing	11
Week 12 (N'=24)	n	23
	Mean (SD)	98.0 (29.59)
	Median	88.0
	Min, Max	70, 202
	Missing	1
Week 24 (N'=30)	n	27
	Mean (SD)	91.8 (20.42)
	Median	87.0
	Min, Max	64, 167
	Missing	3
Diastolic Blood Pressure (mmHg)		
Baseline (N'=55)	n	44
	Mean (SD)	43.3 (11.50)
	Median	45.0
	Min, Max	19, 68
	Missing	11
Week 12 (N'=24)	n	23
	Mean (SD)	62.1 (24.13)
	Median	54.0

Assessment (Units) / Visits	Statistics	Results
	Min, Max	35, 153
	Missing	1
Week 24 (N'=30)	n	27
	Mean (SD)	56.9 (14.11)
	Median	55.0
	Min, Max	41, 93
	Missing	3
Length (cm)		
Baseline (N'=55)	n	52
	Mean (SD)	46.17 (4.591)
	Median	46.00
	Min, Max	36.0, 58.0
	Missing	3
Week 12 (N'=24)	n	23
	Mean (SD)	58.64 (4.569)
	Median	58.00
	Min, Max	52.0, 70.0
	Missing	1
Week 24 (N'=30)	n	30
	Mean (SD)	65.40 (4.019)
	Median	65.55
	Min, Max	56.5, 75.0
	Missing	0
Weight (g)		
Baseline (N'=55)	n	53
	Mean (SD)	2684.4 (1111.33)

Assessment (Units) / Visits	Statistics	Results
	Median	2450.0
	Min, Max	1000, 6000
	Missing	2
Week 12 (N'=24)	n	24
	Mean (SD)	5845.0 (1513.90)
	Median	5850.0
	Min, Max	3010, 10000
	Missing	0
Week 24 (N'=30)	n	30
	Mean (SD)	7236.0 (1773.89)
	Median	7225.0
	Min, Max	1150, 11500
	Missing	0
Head Circumference (cm)		
Baseline (N'=55)	n	48
	Mean (SD)	32.17 (3.245)
	Median	32.15
	Min, Max	25.0, 40.0
	Missing	7
Week 12 (N'=24)	n	24
	Mean (SD)	38.35 (2.278)
	Median	39.00
	Min, Max	34.0, 42.0
	Missing	0
Week 24 (N'=30)	n	30
	Mean (SD)	41.70 (1.452)

Assessment (Units) / Visits	Statistics	Results
	Median	42.00
	Min, Max	38.8, 45.0
	Missing	0
Lower Leg Length (cm)		
Baseline (N'=55)	n	42
	Mean (SD)	9.79 (1.670)
	Median	10.00
	Min, Max	5.0, 14.0
	Missing	13
Week 12 (N'=24)	n	23
	Mean (SD)	12.06 (1.170)
	Median	12.00
	Min, Max	10.0, 15.0
	Missing	1
Week 24 (N'=30)	n	30
	Mean (SD)	14.00 (2.121)
	Median	14.25
	Min, Max	6.0, 18.0
	Missing	0

Max: maximum, Min: minimum, N': number of safety set participants performed at least one physical examination test in a given visit, SD: standard deviation.
Missing = N' - number of participants with non-missing values.
ADS source: ADVS

Time to intervention with a second modality for ROP or development of unfavorable structural outcome

Overall, throughout the observational period, the probability of treatment with second modality for ROP or development of unfavorable structural outcome was less than 10.0%.

Ranibizumab retreatment (Safety Set)

	Safety Set N=61
Number of ranibizumab administrations received for retreatment	
n'	4
Mean (SD)	2.0 (0.00)
Median	2.0
Min, Max	2, 2
Frequency, count (%)	
1	0 (0.0)
2	4 (6.6)
Number of participants receiving retreatment, count (%)	4 (6.6)
Which eye(s) has been treated with ranibizumab when retreatment, count (%) [1]	
n'	4
Left eye	4 (100)
Right eye	4 (100)
Best eye at Baseline	4 (100)
Worst eye at Baseline	4 (100)
Both eyes	4 (100)

	Safety Set N=61
Dosage when retreatment, count (%) [1]	
n'	4
0.2 mg	3 (75.0)
0.25 mg	1 (25.0)
Reason for retreatment, count (%) [1]	
n'	4
Disease progression	1 (25.0)
Physician decision	2 (50.0)
Other	1 (25.0)

n': number of non-missing records in a given category.
[1] one participant may have had more than one record. Percentage was based on n.'

Ranibizumab initial treatment (Safety Set)

	Safety Set N=61
Number of ranibizumab administrations received during initial treatment	
n'	61
Mean (SD)	2.0 (0.00)
Median	2.0
Min, Max	2, 2
Frequency, count (%)	
1	0 (0.0)
2	61 (100)
Which eye(s) has been treated with ranibizumab during initial treatment, count (%)	

	Safety Set N=61
n'	61
Left eye	61 (100)
Right eye	61 (100)
Best eye at Baseline	61 (100)
Worst eye at Baseline	61 (100)
Both eyes	61 (100)
Dosage - initial treatment	
n'	61
0.2 mg	60 (98.4)
0.25 mg	1 (1.6)

Percentage were based on n.'

Summary of full retinal vascularization in 12 clock hours (FAS)

	FAS N=61 n (%)		
	Baseline N'=61	Week 12 N'=43	Week 24 N'=53
Both eye - full retinal vascularization in 12 clock hours			
Yes*	0 (0.0)	7 (16.3)	30 (56.6)
No	61 (100)	33 (76.7)	19 (35.8)
Not Assessed	0 (0.0)	3 (7.0)	4 (7.5)
Missing	0	0	0

N': number of full analysis set performed a given visit.
The percentage was based on N.' Missing = N' – sum (number of participants in each category).
Baseline was defined as the last non-missing measurement taken at or before the first day of administration the intravitreal ranibizumab. Week 12 corresponded to Day 85 (±14 days) after first dose of ranibizumab. Week 24 corresponded to Day 169 [-14, +14] days after first dose of ranibizumab. The participant data collected out of recommended window (±14 days) of visit 3 were re-mapped to visit 3 (Week 24).
*Count participants with both eyes "yes" as "yes."

Ocular treatment-emergent adverse events regardless of study treatment or procedure relationship by primary system organ class and preferred term (Safety Set)

Primary system organ class Preferred term	Safety Set N=61 n (%)
Total	11 (18.0)
Eye disorders	9 (14.8)
*Retinal haemorrhage	6 (9.8)
*Vitreous haemorrhage	3 (4.9)
Conjunctival haemorrhage	1 (1.6)
Injury, poisoning and procedural complications	2 (3.3)
Overdose	2 (3.3)
Investigations	1 (1.6)
Intraocular pressure increased	1 (1.6)

AEs with start date on or after the date of first study treatment administration are counted.
Primary system organ classes are presented alphabetically; preferred terms are sorted within primary system organ class by descending frequency.

Primary system organ class Preferred term	Safety Set N=61 n (%)

A participant with multiple occurrences of an AE for a preferred term or system organ class is counted only once in each specific category.
*Under SOC “Eye disorders,” one AE “Retinal haemorrhage” for one of the participants was changed to “Vitreous haemorrhage” by the investigator in the source document after database lock, which is not reflected in this table.
MedDRA version 27.0 was used for reporting.

Non-ocular treatment-emergent adverse events regardless of study treatment or procedure relationship reported in ≥2 participants by primary system organ class and preferred term (Safety Set)

Primary system organ class Preferred term	Safety Set N=61 n (%)
Total	36 (59.0)
Blood and lymphatic system disorders	10 (16.4)
Anaemia	9 (14.8)
Coagulopathy	2 (3.3)
Leukopenia	2 (3.3)
Congenital, familial and genetic disorders	2 (3.3)
Patent ductus arteriosus	2 (3.3)
Gastrointestinal disorders	5 (8.2)

Primary system organ class Preferred term	Safety Set N=61 n (%)
Inguinal hernia	3 (4.9)
Necrotising enterocolitis neonatal	2 (3.3)
Hepatobiliary disorders	3 (4.9)
Hepatic function abnormal	3 (4.9)
Infections and infestations	24 (39.3)
Pneumonia	11 (18.0)
Neonatal infection	2 (3.3)
Pertussis	2 (3.3)
Upper respiratory tract infection	2 (3.3)
Urinary tract infection	2 (3.3)
Investigations	8 (13.1)
Globulins decreased	4 (6.6)
Blood bilirubin increased	2 (3.3)
Metabolism and nutrition disorders	11 (18.0)
Hypoproteinaemia	7 (11.5)
Electrolyte imbalance	3 (4.9)
Hyperglycaemia	2 (3.3)
Hyperlipidaemia	2 (3.3)
Respiratory, thoracic and mediastinal disorders	5 (8.2)
Bronchopulmonary dysplasia	3 (4.9)
Cough	2 (3.3)

Primary system organ class Preferred term	Safety Set N=61 n (%)
Pulmonary hypertension	2 (3.3)

AEs with start date on or after the date of first study treatment administration are counted.
Primary system organ classes are presented alphabetically; preferred terms are sorted within primary system organ class by descending frequency.
A participant with multiple occurrences of an AE for a preferred term or system organ class is counted only once in each specific category.
MedDRA version 27.0 was used for reporting.

Deaths, SAEs, or AEs leading to study discontinuation or study drug permanent discontinuation (Safety Set)

Deaths, SAEs, or AEs leading to study discontinuation or study drug permanent discontinuation	Safety Set N=61 n (%)
Deaths	1 (1.6)
SAEs	20 (32.8)
AEs leading to study discontinuation or study drug permanently discontinued	1 (1.6)

Numbers (n) represent counts of participants.

Serious non-ocular adverse events regardless of study treatment or procedure relationship reported in ≥2 participants by primary system organ class and preferred term (Safety Set)

Primary system organ class Preferred term	Safety Set N=61 n (%)
Total	19 (31.1)
Blood and lymphatic system disorders	2 (3.3)
Anaemia	2 (3.3)

Primary system organ class Preferred term	Safety Set N=61 n (%)
Infections and infestations	14 (23.0)
Pneumonia	9 (14.8)
Pertussis	2 (3.3)
Respiratory, thoracic, and mediastinal disorders	3 (4.9)
Bronchopulmonary dysplasia	3 (4.9)
Pulmonary hypertension	2 (3.3)

AEs with start date on or after the date of first study treatment administration are counted.
Primary system organ classes are presented alphabetically; preferred terms are sorted within primary system organ class by descending frequency.
A participant with multiple occurrences of an AE for a preferred term or system organ class is counted only once in each specific category.
MedDRA version 27.0 was used for reporting.

Safety Results

Safety was a secondary outcome measure; adverse events are reported in the Secondary Outcome Results section.

Adverse Events by System Organ Class

Please refer to the Secondary Outcome Results section.

Most Frequently Reported AEs Overall by Preferred Term n (%)

Please refer to the Secondary Outcome Results section.

Serious Adverse Events and Deaths

Please refer to the Secondary Outcome Results section.

Other Relevant Findings

Not applicable

Conclusion

This real-world, observational study demonstrated that ranibizumab 0.2 mg was an effective treatment for retinopathy of prematurity (ROP) in routine clinical practice in China, with the majority of participants achieving treatment success at Week 24. The safety and tolerability of ranibizumab 0.2 mg observed in this study is consistent with the known safety profile of ranibizumab, based on the global clinical data accumulated to date.

Date of Clinical Study Report

10 December 2024