Clinical trial results:
A Phase 2, Multicenter, Open-label, Single-arm Study of AL101 Monotherapy in Patients with Notch-activated Triple Negative Breast Cancer

Summary

EudraCT number	2020-001979-33
Trial protocol	GB FR
Global end of trial date	23 March 2022

Results information

Result version number	v1 (current)
This version publication date	15 February 2024
First version publication date	15 February 2024

Trial information

Trial identification

Sponsor protocol code	AL-TNBC-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04461600
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ayala Pharmaceuticals, Inc.
Sponsor organisation address	Oppenheimer 4, Rehovot, Israel, 7670104
Public contact	Clinical Trial Information, Ayala Pharmaceuticals, Inc., clinicaltrials@ayalapharma.com
Scientific contact	Clinical Trial Information, Ayala Pharmaceuticals, Inc., clinicaltrials@ayalapharma.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	09 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 March 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of AL101 monotherapy in subjects with Notch-activated recurrent or metastatic TNBC

Protection of trial subjects:

1. Hepatic function will be closely monitored throughout the study.
2. Signs and symptoms of colitis will be closely monitored.
3. In case of a Grade 3 or 4 allergic reaction, IP infusion will be stopped and infusion tubing from the subject will be disconnected. Glucocorticoids may be administered to treat infusion reactions and as premedication to prevent further reactions.
4. Subjects will be closely monitored for skin changes throughout the study. Subjects will be counseled to avoid excessive sun and UV exposure during the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	18
EEA total number of subjects	6

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)	16
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was conducted between January 2021 to March 2022 in 4 countries: Spain, Belgium, Israel and USA.

Pre-assignment

Screening details:

Patient must be at least 18 years old, have at least one measurable lesion, FFPE tissue available from a metastatic lesion, documented tumor progression following no more than 3 lines of therapy, histologically confirmed diagnosis of TNBC and documented Notch activation from tumor biopsy results from within the last 2 years

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	AL101 6mg

Arm description:

This is a lead-in cohort with 6 subjects to ascertain the safety of AL101, 6 mg weekly (QW) intravenously (IV).

Arm type	Experimental
Investigational medicinal product name	AL101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

6mg of AL101 was administered using an IV infusion pump over 60 minutes, once a week.

Arm title	AL101 4mg

Arm description:

AL101, 4 mg weekly (QW) intravenously (IV).

Arm type	Experimental
Investigational medicinal product name	AL101
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

4mg of AL101 was administered using an IV infusion pump over 60 minutes, once a week.

Number of subjects in period 1	AL101 6mg	AL101 4mg
Started	6	12
Completed	0	6
Not completed	6	6
Consent withdrawn by subject	1	-
Death	5	6

Baseline characteristics

Reporting groups	
Reporting group title	AL101 6mg
Reporting group description:	
This is a lead-in cohort with 6 subjects to ascertain the safety of AL101, 6 mg weekly (QW) intravenously (IV).	
Reporting group title	AL101 4mg
Reporting group description:	
AL101, 4 mg weekly (QW) intravenously (IV).	

Reporting group values	AL101 6mg	AL101 4mg	Total
Number of subjects	6	12	18
Age categorical Units: Subjects			
Adults (18-64 years)	6	11	17
From 65-84 years	0	0	0
Above 85	0	1	1
Age continuous Units: years			
median	45	48	
full range (min-max)	36 to 55	30 to 87	-
Gender categorical Units: Subjects			
Female	6	12	18
Male	0	0	0
Race Units: Subjects			
Asian	0	1	1
Black or African American	1	0	1
White	5	9	14
Unknown or Not Reported	0	2	2

End points

End points reporting groups

Reporting group title	AL101 6mg
Reporting group description:	
This is a lead-in cohort with 6 subjects to ascertain the safety of AL101, 6 mg weekly (QW) intravenously (IV).	
Reporting group title	AL101 4mg
Reporting group description:	
AL101, 4 mg weekly (QW) intravenously (IV).	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[1]
End point description:	
RR is defined as partial response (PR) + complete response (CR) as assessed by the investigator based on Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 for target lesions assessed by MRI. Complete Response (CR): Disappearance of all target lesions. Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.	
End point type	Primary
End point timeframe:	
12 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: The study was terminated prematurely and SAP was not finalized.

End point values	AL101 6mg	AL101 4mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	10		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Response Rate (CBR)

End point title	Clinical Benefit Response Rate (CBR)
End point description:	
Clinical benefit response rate (CBR) is defined as complete response (CR) + partial response (PR) + stable disease (SD) by investigator review based on RECIST v1.1 for target lesions assessed by MRI. Complete Response (CR): Disappearance of all target lesions. Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Stable Disease (SD): Neither sufficient shrinkage (at least 30%) to qualify for PR nor sufficient increase (more than 20%) to qualify for PD, taking as reference the smallest sum diameters.	
End point type	Secondary
End point timeframe:	
12 months	

End point values	AL101 6mg	AL101 4mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	10		
Units: Participants	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

End point type	Secondary

End point timeframe:

Duration of response (DOR) is defined as the time from randomization to disease progression or death in patients who achieve complete or partial response.

End point values	AL101 6mg	AL101 4mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: month				
number (not applicable)				

Notes:

[2] - Duration of response data was not collected as there were no patients with either CR or PR.

[3] - Duration of response data was not collected as there were no patients with either CR or PR.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
1 year and 3 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23

Reporting groups	
Reporting group title	AL101 6mg
Reporting group description:	
This is a lead-in cohort with 6 subjects to ascertain the safety of AL101, 6 mg weekly (QW) intravenously (IV).	
Reporting group title	AL101 4mg
Reporting group description:	
AL101, 4 mg weekly (QW) intravenously (IV).	

Serious adverse events	AL101 6mg	AL101 4mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	2 / 12 (16.67%)	
number of deaths (all causes)	5	6	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer metastatic			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Metastases to lung			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	AL101 6mg	AL101 4mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	12 / 12 (100.00%)	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	4 / 12 (33.33%)	
occurrences (all)	0	8	
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Device related thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)	5 / 12 (41.67%)	
occurrences (all)	2	9	
Gait disturbance			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	

Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Localised oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Mucosal dryness			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 6 (33.33%)	3 / 12 (25.00%)	
occurrences (all)	2	6	
Dry throat			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Dysphonia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Dyspnoea			

subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Lower respiratory tract congestion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Nasal dryness			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Pleural effusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Sneezing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

Insomnia			
subjects affected / exposed	2 / 6 (33.33%)	3 / 12 (25.00%)	
occurrences (all)	2	4	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	3	5	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	2	8	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	3	
Blood bilirubin increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood creatine increased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Blood phosphorus decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood potassium decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Blood triglycerides increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Lymphocyte count decreased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	4	
Neutrophil count decreased			

subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Platelet count decreased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Transaminases increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Anosmia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Cerebral haemorrhage			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	3	
Dysgeusia			
subjects affected / exposed	2 / 6 (33.33%)	6 / 12 (50.00%)	
occurrences (all)	4	8	
Dystonia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Headache			

subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Taste disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Lymph node pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Anaemia			
subjects affected / exposed	0 / 6 (0.00%)	3 / 12 (25.00%)	
occurrences (all)	0	4	
Eye disorders			
Photophobia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	4	
Abdominal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Abdominal pain upper			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	5 / 6 (83.33%)	5 / 12 (41.67%)	
occurrences (all)	10	8	
Dry mouth			

subjects affected / exposed	1 / 6 (16.67%)	3 / 12 (25.00%)	
occurrences (all)	1	4	
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Eructation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	3 / 6 (50.00%)	5 / 12 (41.67%)	
occurrences (all)	3	10	
Odynophagia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	2	
Stomatitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	3	2	
Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	3 / 12 (25.00%)	
occurrences (all)	5	3	
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	2	
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	1	2	
Rash maculo-papular			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Skin odour abnormal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Endocrine disorders			
Cushing's syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	2	5	
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	2 / 12 (16.67%)	
occurrences (all)	3	3	
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	3	
Musculoskeletal pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	2	

Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Oral candidiasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Sinusitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Sputum purulent			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 6 (16.67%)	3 / 12 (25.00%)	
occurrences (all)	3	4	
Dehydration			

subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	2	0	
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Hypocalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 12 (8.33%)	
occurrences (all)	2	1	
Hypokalaemia			
subjects affected / exposed	3 / 6 (50.00%)	1 / 12 (8.33%)	
occurrences (all)	4	1	
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	3 / 6 (50.00%)	3 / 12 (25.00%)	
occurrences (all)	4	3	
Vitamin D deficiency			
subjects affected / exposed	1 / 6 (16.67%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2020	1. Modify study population (delete Notch activated endocrine refractory breast cancer). Rationale: Per FDA suggestion, this population may be included in the future once there is sufficient data on the response of subjects with TNBC. 2. Add a lead-in cohort with 6 subjects at dose level 6 mg QW and modify sample size. Rationale: Per FDA request, as a safety precaution, to allow safety evaluation of 6 mg QW in 6 subjects before proceeding to enroll the rest of the subjects. 3. Add PK assessment per FDA request. 4.Replace triglyceride with complete lipid panel as a safety precaution.
12 August 2020	1. Delete reference to 'Early Discontinuation'. In this study end of study and early discontinuation are synonymous. 2. Update exclusion criterion 11f (creatinine) -creatinine clearance (CrCl) <50 mL/min (calculation of CrCl will be based on acceptable institution standard). Rationale: Allow inclusion based on normal creatinine values, as well as sufficient GFR, as AL101 is not expected to impact renal function. 3. Introduce change in regimen (2 weeks on / 1 week of) for first episode of Grade 2 or 3 diarrhea and Grade 2 Colitis before dose reduction on subsequent episodes. Rationale: To allow investigators to use a 2 weeks on 1 weeks off regime at 6 mg QW, before implementing dose reduction. The aim is to introduce a scheduled dose interruption to prevent recurrence of toxicity.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported