Clinical trial results:
A prospective, open, randomized, phase-II study of a therapeutic cancer vaccine (L-BLP25, Stimuvax®) in the pre-operative treatment of women with primary breast cancer

Summary

EudraCT number	2011-004822-85
Trial protocol	AT
Global end of trial date	10 April 2015

Results information

Result version number	v1 (current)
This version publication date	14 August 2021
First version publication date	14 August 2021

Trial information

Trial identification

Sponsor protocol code	ABCSG-34

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Code: EMR63325-603

Notes:

Sponsors

Sponsor organisation name	ABCSG (Austrian Breast & Colorectal Cancer Study Group)
Sponsor organisation address	Nußdorfer Platz 8/12, Vienna, Austria, 1190
Public contact	Hannes Fohler (Trial Office Director), ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsg.at
Scientific contact	Michael Gnant (ABCSG President and Trial Chair), ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsg.at

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	10 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2015
Global end of trial reached?	Yes
Global end of trial date	10 April 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare efficacy of pre-operative standard of care treatment with or without a therapeutic cancer vaccine (L-BLP25), measured by Residual Cancer Burden (RCB) at the time of surgery

Protection of trial subjects:

The study specific patient information and informed consent form included language to encourage study participants to reach out to the Study Doctor / Study Team in case they have any questions, concerns or doubts. Section 15 specifically referenced a 24/7 contact person to reach out to, the ICF furthermore contained a reference to the local ombudsman / patient advocacy and a study specific patient card was implemented and distributed, containing important information and contact details. A dedicated IDMC was established to ensure patient safety throughout the trial.

Background therapy:

Standard of care chemotherapy (Epirubicin, cyclophosphamide, docetaxel) irrespective of sequence.

Evidence for comparator:

No

Actual start date of recruitment	08 May 2012
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	Austria: 400
Worldwide total number of subjects	400
EEA total number of subjects	400

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)	312

From 65 to 84 years	88
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A careful check of inclusion and exclusion criteria had to be performed by the Investigators / Site Teams and a web based randomization system was subsequently used which assigned treatment arms electronically, i.e. randomized the participants into the previously described treatment arms.

Pre-assignment period milestones

Number of subjects started	400
Number of subjects completed	400

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Chemo conv with L-BLP25

Arm description:

Patients received SoC and tecemotide (L-BLP25). Neo-adjuvant chemotherapy conventional sequence (Chemo conv) was considered SoC.

Arm type	Experimental
Investigational medicinal product name	L-BLP25 (Stimuvax)
Investigational medicinal product code	EMD531444
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

4 x 0.5 ml reconstituted L-BLP25 (containing 918 mcg (total of 4 vials) of BLP25 lipopeptide) mg/l milligram(s)/litre

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Endoxana Injection 1g
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

300 mg/m2

Arm title	Chemo rev with L-BLP25

Arm description:

Patients received SoC and tecemotide (L-BLP25). Neo-adjuvant chemotherapy reverse sequence (Chemo rev) was considered SoC.

Arm type	Experimental

Investigational medicinal product name	L-BLP25 (Stimuvax)
Investigational medicinal product code	EMD531444
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

4 x 0.5 ml reconstituted L-BLP25 (containing 918 mcg (total of 4 vials) of BLP25 lipopeptide) mg/l milligram(s)/litre

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Endoxana Injection 1g
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

300 mg/m2

Arm title	AI with L-BLP25

Arm description:

Patients received SoC and tecemotide (L-BLP25). Preoperative endocrine therapy (AI) was considered SoC.

Arm type	Experimental
Investigational medicinal product name	L-BLP25 (Stimuvax)
Investigational medicinal product code	EMD531444
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

4 x 0.5 ml reconstituted L-BLP25 (containing 918 mcg (total of 4 vials) of BLP25 lipopeptide) mg/l milligram(s)/litre

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Endoxana Injection 1g
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

300 mg/m2

Investigational medicinal product name	Letrozol
Investigational medicinal product code	
Other name	Letrozol Sandoz
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg milligram(s)

Arm title	Chemo conv without L-BLP25

Arm description:

Patients received SoC only and no tecemotide (L-BLP25). Neo-adjuvant chemotherapy conventional sequence (Chemo conv) was considered SoC.

Arm type	SOC

No investigational medicinal product assigned in this arm

Arm title	Chemo rev without L-BLP25

Arm description:

Patients received SoC only and no tecemotide (L-BLP25). Neo-adjuvant chemotherapy reverse sequence (Chemo rev) was considered SoC.

Arm type	SOC
No investigational medicinal product assigned in this arm	
Arm title	AI without L-BLP25

Arm description:

Patients received SoC only and no tecemotide (L-BLP25). Preoperative endocrine therapy (AI) was considered SoC.

Arm type	Active comparator
Investigational medicinal product name	Letrozol
Investigational medicinal product code	
Other name	Letrozol Sandoz
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg milligram(s)

Number of subjects in period 1	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25
Started	78	79	43
Completed	73	73	41
Not completed	5	6	2
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	5	5	2
Other	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Chemo conv without L-BLP25	Chemo rev without L-BLP25	AI without L-BLP25
Started	76	78	46
Completed	74	76	44
Not completed	2	2	2
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	-	1
Other	2	-	1
Lost to follow-up	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Chemo conv with L-BLP25
Reporting group description:	
Patients received SoC and tecemotide (L-BLP25). Neo-adjuvant chemotherapy conventional sequence (Chemo conv) was considered SoC.	
Reporting group title	Chemo rev with L-BLP25
Reporting group description:	
Patients received SoC and tecemotide (L-BLP25). Neo-adjuvant chemotherapy reverse sequence (Chemo rev) was considered SoC.	
Reporting group title	AI with L-BLP25
Reporting group description:	
Patients received SoC and tecemotide (L-BLP25). Preoperative endocrine therapy (AI) was considered SoC.	
Reporting group title	Chemo conv without L-BLP25
Reporting group description:	
Patients received SoC only and no tecemotide (L-BLP25). Neo-adjuvant chemotherapy conventional sequence (Chemo conv) was considered SoC.	
Reporting group title	Chemo rev without L-BLP25
Reporting group description:	
Patients received SoC only and no tecemotide (L-BLP25). Neo-adjuvant chemotherapy reverse sequence (Chemo rev) was considered SoC.	
Reporting group title	AI without L-BLP25
Reporting group description:	
Patients received SoC only and no tecemotide (L-BLP25). Preoperative endocrine therapy (AI) was considered SoC.	

Reporting group values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25
Number of subjects	78	79	43
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)	73	73	19
From 65-84 years	5	6	24
85 years and over	0	0	0
Age continuous Units: years			
median	50	49	65
full range (min-max)	28 to 73	25 to 72	52 to 83
Gender categorical Units: Subjects			
Female	78	79	43
Male	0	0	0

Menopausal Status			
Units: Subjects			
perimenopausal	27	28	43
postmenopausal	5	0	0
premenopausal	45	48	0
missing	1	3	0
Tumor Size			
T-stage			
Units: Subjects			
T1	21	23	19
T2/Z3/T4	57	56	23
missing	0	0	1
Nodal Stage			
N-stage			
Units: Subjects			
negative	53	45	32
positive	24	30	11
missing	1	4	0
Estrogen Receptor			
ER			
Units: Subjects			
negative	31	41	0
positive	47	36	43
missing	0	2	0
Progesterone Receptor			
PR			
Units: Subjects			
negative	40	46	4
positive	38	32	39
missing	0	1	0
BMI			
Body Mass Index			
Units: score			
median	24.5	24.3	27.1
full range (min-max)	16.5 to 42.8	15.0 to 39.0	19.1 to 36.3
Ki67			
Units: score			
median	50	50	10
full range (min-max)	2 to 90	5 to 95	3 to 80

Reporting group values	Chemo conv without L-BLP25	Chemo rev without L-BLP25	AI without L-BLP25
Number of subjects	76	78	46
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)	69	64	14
From 65-84 years	7	14	32
85 years and over	0	0	0
Age continuous			
Units: years			
median	48	47	68.5
full range (min-max)	26 to 78	26 to 75	52 to 81
Gender categorical			
Units: Subjects			
Female	76	78	46
Male	0	0	0
Menopausal Status			
Units: Subjects			
perimenopausal	29	28	45
postmenopausal	3	3	0
premenopausal	44	47	1
missing	0	0	0
Tumor Size			
T-stage			
Units: Subjects			
T1	18	24	20
T2/Z3/T4	58	54	26
missing	0	0	0
Nodal Stage			
N-stage			
Units: Subjects			
negative	41	39	38
positive	33	39	8
missing	2	0	0
Estrogen Receptor			
ER			
Units: Subjects			
negative	37	35	0
positive	36	42	46
missing	3	1	0
Progesterone Receptor			
PR			
Units: Subjects			
negative	36	35	3
positive	37	42	42
missing	3	1	1
BMI			
Body Mass Index			
Units: score			
median	24.6	24.5	28.3
full range (min-max)	18.1 to 35.2	18.8 to 40.5	19.9 to 47.6
Ki67			
Units: score			
median	50	50	10
full range (min-max)	3 to 90	3 to 90	1 to 50

Reporting group values	Total		
Number of subjects	400		
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)	312		
From 65-84 years	88		
85 years and over	0		
Age continuous Units: years			
median			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	400		
Male	0		
Menopausal Status Units: Subjects			
perimenopausal	200		
postmenopausal	11		
premenopausal	185		
missing	4		
Tumor Size			
T-stage			
Units: Subjects			
T1	125		
T2/Z3/T4	274		
missing	1		
Nodal Stage			
N-stage			
Units: Subjects			
negative	248		
positive	145		
missing	7		
Estrogen Receptor			
ER			
Units: Subjects			
negative	144		
positive	250		
missing	6		
Progesterone Receptor			
PR			
Units: Subjects			
negative	164		
positive	230		

missing	6		

BMI			
Body Mass Index			
Units: score median full range (min-max)	 -		
Ki67 Units: score median full range (min-max)	 -		

End points

End points reporting groups

Reporting group title	Chemo conv with L-BLP25
Reporting group description:	
Patients received SoC and tecemotide (L-BLP25). Neo-adjuvant chemotherapy conventional sequence (Chemo conv) was considered SoC.	
Reporting group title	Chemo rev with L-BLP25
Reporting group description:	
Patients received SoC and tecemotide (L-BLP25). Neo-adjuvant chemotherapy reverse sequence (Chemo rev) was considered SoC.	
Reporting group title	AI with L-BLP25
Reporting group description:	
Patients received SoC and tecemotide (L-BLP25). Preoperative endocrine therapy (AI) was considered SoC.	
Reporting group title	Chemo conv without L-BLP25
Reporting group description:	
Patients received SoC only and no tecemotide (L-BLP25). Neo-adjuvant chemotherapy conventional sequence (Chemo conv) was considered SoC.	
Reporting group title	Chemo rev without L-BLP25
Reporting group description:	
Patients received SoC only and no tecemotide (L-BLP25). Neo-adjuvant chemotherapy reverse sequence (Chemo rev) was considered SoC.	
Reporting group title	AI without L-BLP25
Reporting group description:	
Patients received SoC only and no tecemotide (L-BLP25). Preoperative endocrine therapy (AI) was considered SoC.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Since the aim of this phase II study is to detect any effect of tecemotide, a pure intention-to-treat (ITT) analysis based on a conservative worst-case approach may underestimate the effect. Therefore the ITT analysis population includes all randomized patients who are evaluable at the time of final surgery. Patients are analysed according to the treatment to which they have been randomized.	
Subject analysis set title	Safety
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety population includes all randomized patients with at least one administration of study treatment (investigational and/or non-investigational medical product – IMP and/or NIMP). Patients are analysed according to the treatment they have actually received.	

Primary: Residual Cancer Burden (RCB)

End point title	Residual Cancer Burden (RCB)
End point description:	
The primary endpoint is histopathological response to pre-operative standard of care (SoC) treatment with or without L-BLP25 therapy when measured by Residual Cancer Burden (RCB) at the time of surgery and is defined by reaching RCB-0 or RCB-I (=RCB index ≤1.36) vs RCB-II or RCB-III (=RCB index >1.36).	
End point type	Primary
End point timeframe:	
at surgery	

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	72	40	70
Units: Subjects				
RCB 0/I	31	26	10	26
RCB II/III	41	46	30	44

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	45		
Units: Subjects				
RCB 0/I	28	6		
RCB II/III	45	39		

Statistical analyses

Statistical analysis title	Primary endpoint analysis

Statistical analysis description:

The proportions of patients exhibiting RCB-0/I are compared between the experimental group (with L-BLP25) and the control group (without L-BLP25) using the Cochran-Mantel-Haenszel test to take into account different prognoses for endocrine therapy (AI) and chemotherapy (chemo). Hence, conventional and reverse chemotherapy patients are considered within one group/arm for this analysis.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	372
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.4024
Method	Cochran-Mantel-Haenszel

Notes:

[1] - H0: proportion of patients with RCB-0 or RCB-I in the experimental group is equal to that in the control group
H1: proportion of patients with RCB-0 or RCB-I in the experimental group differs from that in the control group

Secondary: Pathological Complete Response (pCR)

End point title	Pathological Complete Response (pCR)

End point description:

This secondary endpoint describes the absence of invasive cancer cells in surgical specimen as pathological complete response (pCR) and is defined by pCR yes vs pCR no.

End point type	Secondary

End point timeframe:

at surgery

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	73	73	41	75
Units: Subjects				
pCR yes	19	21	2	17
pCR no	54	52	39	58

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	45		
Units: Subjects				
pCR yes	16	1		
pCR no	59	44		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - pCR

Statistical analysis description:

The proportions of patients exhibiting pCR (=absence of invasive cancer cells in surgical specimen) are compared between the experimental (with L-BLP25) and the control (without L-BLP25) arm using the Cochran-Mantel-Haenszel test to take into account different prognoses for endocrine therapy (AI) and chemotherapy (chemo). Hence, conventional and reverse chemotherapy patients are considered within one group/arm for this analysis.

Comparison groups	Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	382
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2312
Method	Cochran-Mantel-Haenszel

Secondary: Residual Cancer Burden (RCB) - conv vs rev

End point title	Residual Cancer Burden (RCB) - conv vs rev[2]

End point description:

This secondary endpoint describes the efficacy of reverse versus conventional sequence chemotherapy as measured by Residual Cancer Burden (RCB) at the time of surgery and is defined by reaching RCB-0 or RCB-I (=RCB index ≤1.36) vs RCB-II or RCB-III (=RCB index >1.36).

End point type	Secondary

End point timeframe:

at surgery

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This analysis was planned to not include all the arms - only chemotherapy arms are compared.

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	Chemo conv without L-BLP25	Chemo rev without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	72	72	70	73
Units: Subjects				
RCB 0/I	31	26	26	28
RCB II/III	41	46	44	45

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - RCB conv vs rev

Statistical analysis description:

Proportions of RCB (RCB-0/I versus RCB-II/III) are compared between chemotherapy conventional sequence and chemotherapy reverse sequence using Chi² test within the subset of patients receiving chemotherapy. Hence, with and without L-BLP25 patients are considered within one group/arm for this analysis.

Comparison groups	Chemo rev with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v Chemo conv with L-BLP25
Number of subjects included in analysis	287
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6141
Method	Chi-squared

Secondary: Tumor Associated Lymphocytes (TAL) - stromal BL

End point title	Tumor Associated Lymphocytes (TAL) - stromal BL

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by stromal tumor associated lymphocytes (TAL).

End point type	Secondary

End point timeframe:

at baseline

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	69	40	69
Units: Percentages				
median (full range (min-max))	5 (0 to 80)	5 (0 to 70)	0 (0 to 20)	5 (0 to 70)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	44		
Units: Percentages				
median (full range (min-max))	5 (0 to 60)	0 (0 to 30)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL stromal BL

Statistical analysis description:

Proportions of stromal TALs at baseline are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4664
Method	Wilcoxon (Mann-Whitney)

Secondary: Tumor Associated Lymphocytes (TAL) - stromal MT

End point title	Tumor Associated Lymphocytes (TAL) - stromal MT

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by stromal tumor associated lymphocytes (TAL).

End point type	Secondary

End point timeframe:

at mid-therapy

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	36	37	43
Units: Percentages				
median (full range (min-max))	1 (0 to 40)	5 (0 to 80)	0 (0 to 30)	5 (0 to 60)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: Percentages				
median (full range (min-max))	1 (0 to 50)	0 (0 to 10)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL stromal MT

Statistical analysis description:

Proportions of stromal TALs at mid-therapy are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	239
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5276
Method	Wilcoxon (Mann-Whitney)

Secondary: Tumor Associated Lymphocytes (TAL) - stromal SU

End point title	Tumor Associated Lymphocytes (TAL) - stromal SU

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by stromal tumor associated lymphocytes (TAL).

End point type	Secondary

End point timeframe:

at surgery

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	39	38	49
Units: Percentages				
median (full range (min-max))	1 (0 to 40)	1 (0 to 40)	1 (0 to 40)	1 (0 to 70)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	42		
Units: Percentages				
median (full range (min-max))	1 (0 to 50)	1 (0 to 30)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL stromal SU

Statistical analysis description:

Proportions of stromal TALs at surgery are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5601
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in Tumor Associated Lymphocytes (TAL) - stromal BL to MT

End point title	Change in Tumor Associated Lymphocytes (TAL) - stromal BL to MT

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by changes in stromal tumor associated lymphocytes (TAL) under tumor therapy.

End point type	Secondary

End point timeframe:

baseline to mid-therapy

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	31	35	39
Units: Percentages				
median (full range (min-max))	-4 (-60 to 35)	0 (-20 to 49)	0 (-10 to 25)	0 (-35 to 55)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	37		
Units: Percentages				
median (full range (min-max))	0 (-10 to 35)	0 (-29 to 5)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL stromal BL to MT

Statistical analysis description:

Changes of stromal TALs under tumor therapy (baseline to mid-therapy) are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	225
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4497
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in Tumor Associated Lymphocytes (TAL) - stromal BL to SU

End point title	Change in Tumor Associated Lymphocytes (TAL) - stromal BL to SU

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by changes in stromal tumor associated lymphocytes (TAL) under tumor therapy.

End point type	Secondary

End point timeframe:

baseline to surgery

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	37	37	46
Units: Percentages				
median (full range (min-max))	-4 (-39 to 35)	0 (-40 to 39)	0 (-20 to 39)	-0.5 (-40 to 39)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	41		
Units: Percentages				
median (full range (min-max))	-1 (-60 to 40)	0 (-25 to 29)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL stromal BL to SU

Statistical analysis description:

Changes of stromal TALs under tumor therapy (baseline to surgery) are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5251
Method	Wilcoxon (Mann-Whitney)

Secondary: Tumor Associated Lymphocytes (TAL) - intratumoral BL

End point title	Tumor Associated Lymphocytes (TAL) - intratumoral BL

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by intratumoral tumor associated lymphocytes (TAL).

End point type	Secondary

End point timeframe:

at baseline

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	68	40	68
Units: Percentages				
median (full range (min-max))	5 (0 to 80)	5 (0 to 70)	0 (0 to 40)	5 (0 to 60)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	70	44		
Units: Percentages				
median (full range (min-max))	5 (0 to 70)	0 (0 to 30)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL intratumoral BL

Statistical analysis description:

Proportions of intratumoral TALs at baseline are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	364
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6096
Method	Wilcoxon (Mann-Whitney)

Secondary: Tumor Associated Lymphocytes (TAL) - intratumoral MT

End point title	Tumor Associated Lymphocytes (TAL) - intratumoral MT

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by intratumoral tumor associated lymphocytes (TAL).

End point type	Secondary

End point timeframe:

at mid-therapy

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	37	37	43
Units: Percentages				
median (full range (min-max))	0 (0 to 30)	1 (0 to 80)	0 (0 to 30)	1 (0 to 80)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	38		
Units: Percentages				
median (full range (min-max))	1 (0 to 60)	0 (0 to 10)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL intratumoral MT

Statistical analysis description:

Proportions of intratumoral TALs at mid-therapy are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	240
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7715
Method	Wilcoxon (Mann-Whitney)

Secondary: Tumor Associated Lymphocytes (TAL) - intratumoral SU

End point title	Tumor Associated Lymphocytes (TAL) - intratumoral SU

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by intratumoral tumor associated lymphocytes (TAL).

End point type	Secondary

End point timeframe:

at surgery

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	39	38	49
Units: Percentages				
median (full range (min-max))	1 (0 to 80)	1 (0 to 50)	0 (0 to 40)	0 (0 to 70)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	42		
Units: Percentages				
median (full range (min-max))	0 (0 to 70)	0 (0 to 20)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL intratumoral SU

Statistical analysis description:

Proportions of intratumoral TALs at surgery are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	257
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5959
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in Tumor Associated Lymphocytes (TAL) - intratumoral BL to MT

End point title	Change in Tumor Associated Lymphocytes (TAL) - intratumoral BL to MT

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by changes in intratumoral tumor associated lymphocytes (TAL) under tumor therapy.

End point type	Secondary

End point timeframe:

baseline to mid-therapy

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	32	35	39
Units: Percentages				
median (full range (min-max))	-4 (-60 to 20)	0 (-30 to 79)	0 (-40 to 25)	-1 (-30 to 60)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	37		
Units: Percentages				
median (full range (min-max))	0 (-50 to 20)	0 (-25 to 5)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL intra BL to MT

Statistical analysis description:

Changes of intratumoral TALs under tumor therapy (baseline to mid-therapy) are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	226
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7325
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in Tumor Associated Lymphocytes (TAL) - intratumoral BL to SU

End point title	Change in Tumor Associated Lymphocytes (TAL) - intratumoral BL to SU

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by changes in intratumoral tumor associated lymphocytes (TAL) under tumor therapy.

End point type	Secondary

End point timeframe:

baseline to surgery

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	41	37	37	46
Units: Percentages				
median (full range (min-max))	-4 (-50 to 70)	0 (-60 to 35)	0 (-40 to 39)	0 (-55 to 50)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	41		
Units: Percentages				
median (full range (min-max))	-2.5 (-70 to 60)	0 (-29 to 19)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - TAL intra BL to SU

Statistical analysis description:

Changes of intratumoral TALs under tumor therapy (baseline to surgery) are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	246
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.888
Method	Wilcoxon (Mann-Whitney)

Secondary: Ki67 tumor status (MIB1) - BL

End point title	Ki67 tumor status (MIB1) - BL

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by Ki67 tumor status (MIB1).

End point type	Secondary

End point timeframe:

at baseline

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	72	42	71
Units: Percentages				
median (full range (min-max))	55 (5 to 90)	55 (10 to 90)	20 (5 to 70)	50 (5 to 90)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	44		
Units: Percentages				
median (full range (min-max))	50 (1 to 80)	20 (5 to 70)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - Ki67 BL

Statistical analysis description:

Proportions of Ki67 tumor status (MIB1) at baseline are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo rev with L-BLP25 v Chemo conv with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	375
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.649
Method	Wilcoxon (Mann-Whitney)

Secondary: Ki67 tumor status (MIB1) - MT

End point title	Ki67 tumor status (MIB1) - MT

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by Ki67 tumor status (MIB1).

End point type	Secondary

End point timeframe:

at mid-therapy

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	34	36	44
Units: Percentages				
median (full range (min-max))	20 (1 to 90)	25 (1 to 90)	3 (1 to 10)	15 (1 to 90)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	36		
Units: Percentages				
median (full range (min-max))	15 (1 to 90)	1 (1 to 30)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - Ki67 MT

Statistical analysis description:

Proportions of Ki67 tumor status (MIB1) at mid-therapy are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	237
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6418
Method	Wilcoxon (Mann-Whitney)

Secondary: Ki67 tumor status (MIB1) - SU

End point title	Ki67 tumor status (MIB1) - SU

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by Ki67 tumor status (MIB1).

End point type	Secondary

End point timeframe:

at surgery

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	40	38	48
Units: Percentages				
median (full range (min-max))	10 (1 to 80)	30 (1 to 90)	5 (0 to 40)	7.5 (0 to 90)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	42		
Units: Percentages				
median (full range (min-max))	10 (0 to 80)	1 (0 to 70)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - Ki67 SU
Statistical analysis description:	
Proportions of Ki67 tumor status (MIB1) at surgery are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.	
Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	262
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1601
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in Ki67 tumor status (MIB1) - BL to MT

End point title	Change in Ki67 tumor status (MIB1) - BL to MT
End point description:	
This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by changes in Ki67 tumor status (MIB1) under tumor therapy.	
End point type	Secondary
End point timeframe:	
baseline to mid-therapy	

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	31	36	42
Units: Percentages				
median (full range (min-max))	-10 (-75 to 20)	-10 (-60 to 40)	-15 (-50 to -4)	-20 (-75 to 20)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	35		
Units: Percentages				
median (full range (min-max))	-15 (-69 to 40)	-10 (-69 to 0)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - Ki67 BL to MT

Statistical analysis description:

Changes of Ki67 tumor status (MIB1) under tumor therapy (baseline to mid-therapy) are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	229
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5818
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in Ki67 tumor status (MIB1) - BL to SU

End point title	Change in Ki67 tumor status (MIB1) - BL to SU

End point description:

This secondary endpoint describes the proportion of patients with “lymphocyte-predominant” breast cancer as measured by changes in Ki67 tumor status (MIB1) under tumor therapy.

End point type	Secondary

End point timeframe:

baseline to surgery

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	44	38	38	47
Units: Percentages				
median (full range (min-max))	-19.5 (-79 to 20)	-10 (-70 to 40)	-9 (-50 to 10)	-25 (-79 to 60)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	41		
Units: Percentages				
median (full range (min-max))	-10 (-70 to 20)	-10 (-65 to 65)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - Ki67 BL to SU

Statistical analysis description:

Changes of Ki67 tumor status (MIB1) under tumor therapy (baseline to surgery) are described descriptively (median, range) per treatment arm. Due to the skewed distribution of parameters, differences in parameters between treatment arms (with and without L-BLP25) are analysed using Wilcoxon tests. Tests schould not be considered conclusive, but as additional description.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6003
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in Quality of Life (QoL) - BL to SU

End point title	Change in Quality of Life (QoL) - BL to SU

End point description:

This secondary endpoint describes the change in Quality of Life (QoL) from baseline to surgery based on the standardized Quality of Life questionnaires from EORTC, QLQ-C30 (Version 3.0) and QLQ-BR23 (Version 1.0) - example shows the global health score.

End point type	Secondary

End point timeframe:

baseline to surgery

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	62	31	58
Units: value				
arithmetic mean (standard deviation)	-0.30 (± 1.52)	-0.44 (± 1.52)	0.15 (± 1.16)	-0.41 (± 1.73)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	58	32		
Units: value				
arithmetic mean (standard deviation)	-0.59 (± 1.40)	0.03 (± 1.55)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - QoL BL to SU

Statistical analysis description:

Changes of quality of life (QoL) under tumor therapy (baseline to surgery) are described descriptively (mean, standrad deviation) per treatment arm - example shows the global health score. A pre-post comparison is done using the Wilcoxon signed-rank test for paired samples.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	300
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0001
Method	Wilcoxon signed rank

Secondary: Change in Quality of Life (QoL) - BL to EOS

End point title	Change in Quality of Life (QoL) - BL to EOS

End point description:

This secondary endpoint describes the change in Quality of Life (QoL) from baseline to end of study (EOS) visit based on the standardized Quality of Life questionnaires from EORTC, QLQ-C30 (Version 3.0) and QLQ-BR23 (Version 1.0) - example shows the global health score.

End point type	Secondary

End point timeframe:

baseline to end of study (EOS) visit

End point values	Chemo conv with L-BLP25	Chemo rev with L-BLP25	AI with L-BLP25	Chemo conv without L-BLP25
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	52	57	26	53
Units: value				
arithmetic mean (standard deviation)	-0.38 (± 1.83)	-0.21 (± 1.47)	-0.17 (± 1.33)	-0.31 (± 1.53)

End point values	Chemo rev without L-BLP25	AI without L-BLP25		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	56	28		
Units: value				
arithmetic mean (standard deviation)	-0.59 (± 1.63)	0.09 (± 1.69)		

Statistical analyses

Statistical analysis title	Secondary endpoint analysis - QoL BL to EOS

Statistical analysis description:

Changes of quality of life (QoL) under tumor therapy (baseline to end of study (EOS) visit) are described descriptively (mean, standrad deviation) per treatment arm - example shows the global health score. A pre-post comparison is done using the Wilcoxon signed-rank test for paired samples.

Comparison groups	Chemo conv with L-BLP25 v Chemo rev with L-BLP25 v AI with L-BLP25 v Chemo conv without L-BLP25 v Chemo rev without L-BLP25 v AI without L-BLP25
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0025
Method	Wilcoxon signed rank

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All SAEs occurring after the patient had signed the Informed Consent until the End of Study Visit must be reported to ABCSG within above mentioned timelines.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Chemotherapy conventional sequence with L-BLP25
Reporting group description: -	
Reporting group title	Chemotherapy conventional sequence without L-BLP25
Reporting group description: -	
Reporting group title	Chemotherapy reverse sequence with L-BLP25
Reporting group description: -	
Reporting group title	Chemotherapy reverse sequence without L-BLP25
Reporting group description: -	
Reporting group title	Endocrine Aromatase inhibitor therapy with L-BLP25
Reporting group description: -	
Reporting group title	Endocrine Aromatase inhibitor therapy without L-BLP25

Reporting group description: -

Serious adverse events	Chemotherapy conventional sequence with L-BLP25	Chemotherapy conventional sequence without L-BLP25	Chemotherapy reverse sequence with L-BLP25
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 77 (28.57%)	19 / 77 (24.68%)	30 / 77 (38.96%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges	Additional description: Metastases to meninges		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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

Flushing	Additional description: Flushing		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hot flush	Additional description: Hot flush		
subjects affected / exposed	1 / 77 (1.30%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension	Additional description: Hypotension		
subjects affected / exposed	1 / 77 (1.30%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian vein thrombosis	Additional description: Subclavian vein thrombosis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis	Additional description: Thrombophlebitis		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Thrombosis	Additional description: Thrombosis		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Venous thrombosis	Additional description: Venous thrombosis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort	Additional description: Chest discomfort		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chest pain	Additional description: Chest pain		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Extravasation	Additional description: Extravasation		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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

Fatigue	Additional description: Fatigue		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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

General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	1 / 77 (1.30%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Generalised oedema	Additional description: Generalised oedema		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Impaired healing	Additional description: Impaired healing		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Implant site extravasation	Additional description: Implant site extravasation		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Medical device complication	Additional description: Medical device complication		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Necrosis	Additional description: Necrosis

subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	2 / 77 (2.60%)	2 / 77 (2.60%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Sarcoidosis	Additional description: Sarcoidosis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal oedema	Additional description: Pharyngeal oedema		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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 glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
C-reactive protein increased	Additional description: C-reactive protein increased		
subjects affected / exposed	1 / 77 (1.30%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	2 / 77 (2.60%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fractured sacrum	Additional description: Fractured sacrum		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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
Joint injury	Additional description: Joint injury		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus lesion	Additional description: Meniscus lesion		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture	Additional description: Pubis fracture		

subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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
Seroma	Additional description: Seroma		
subjects affected / exposed	0 / 77 (0.00%)	2 / 77 (2.60%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence	Additional description: Wound dehiscence		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Epidermolysis	Additional description: Epidermolysis		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sebaceous naevus	Additional description: Sebaceous naevus		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Nervous system disorders			
Balance disorder	Additional description: Balance disorder		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cerebral infarction	Additional description: Cerebral infarction		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Headache	Additional description: Headache		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness	Additional description: Loss of consciousness		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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
Sciatica	Additional description: Sciatica		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Speech disorder	Additional description: Speech disorder		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	1 / 77 (1.30%)	1 / 77 (1.30%)	6 / 77 (7.79%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia	Additional description: Leukopenia		

subjects affected / exposed	3 / 77 (3.90%)	1 / 77 (1.30%)	4 / 77 (5.19%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy	Additional description: Lymphadenopathy		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	4 / 77 (5.19%)	0 / 77 (0.00%)	3 / 77 (3.90%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia	Additional description: Pancytopenia		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Ear and labyrinth disorders			
Vertigo	Additional description: Vertigo		
subjects affected / exposed	3 / 77 (3.90%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	2 / 77 (2.60%)	0 / 77 (0.00%)	0 / 77 (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
Anal fissure	Additional description: Anal fissure		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Colitis	Additional description: Colitis		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	2 / 77 (2.60%)	3 / 77 (3.90%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 2	0 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diverticulum intestinal haemorrhagic	Additional description: Diverticulum intestinal haemorrhagic		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Duodenal ulcer haemorrhage	Additional description: Duodenal ulcer haemorrhage		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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

Enteritis	Additional description: Enteritis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Faecaloma	Additional description: Faecaloma		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastritis erosive	Additional description: Gastritis erosive

subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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
Glossitis	Additional description: Glossitis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	1 / 77 (1.30%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema	Additional description: Eczema		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurodermatitis	Additional description: Neurodermatitis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling face	Additional description: Swelling face		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Urticaria	Additional description: Urticaria		

subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute	Additional description: Renal failure acute		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain	Additional description: Bone pain		
subjects affected / exposed	1 / 77 (1.30%)	1 / 77 (1.30%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis	Additional description: Osteonecrosis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess	Additional description: Abdominal abscess		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute tonsillitis	Additional description: Acute tonsillitis		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Appendicitis	Additional description: Appendicitis		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Bartholin's abscess	Additional description: Bartholin's abscess		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Bronchopneumonia	Additional description: Bronchopneumonia		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Device related infection	Additional description: Device related infection		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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

Device related sepsis	Additional description: Device related sepsis		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Febrile infection	Additional description: Febrile infection		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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

Gastrointestinal infection	Additional description: Gastrointestinal infection		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Implant site abscess	Additional description: Implant site abscess

subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	0 / 77 (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
Infection	Additional description: Infection		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Localised infection	Additional description: Localised infection		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	2 / 77 (2.60%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection	Additional description: Postoperative wound infection		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection	Additional description: Urinary tract infection		

subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection	Additional description: Viral infection		
subjects affected / exposed	0 / 77 (0.00%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Electrolyte imbalance	Additional description: Electrolyte imbalance		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	0 / 77 (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

Serious adverse events	Chemotherapy reverse sequence without L-BLP25	Endocrine Aromatase inhibitor therapy with L-BLP25	Endocrine Aromatase inhibitor therapy without L-BLP25
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 78 (30.77%)	5 / 41 (12.20%)	5 / 46 (10.87%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges	Additional description: Metastases to meninges		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis	Additional description: Deep vein thrombosis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flushing	Additional description: Flushing		

subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hot flush	Additional description: Hot flush		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian vein thrombosis	Additional description: Subclavian vein thrombosis		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Thrombophlebitis	Additional description: Thrombophlebitis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis	Additional description: Thrombosis		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Venous thrombosis	Additional description: Venous thrombosis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort	Additional description: Chest discomfort		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain	Additional description: Chest pain		

subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Extravasation	Additional description: Extravasation		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
General physical health deterioration	Additional description: General physical health deterioration		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema	Additional description: Generalised oedema		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing	Additional description: Impaired healing		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site extravasation	Additional description: Implant site extravasation		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device complication	Additional description: Medical device complication		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrosis	Additional description: Necrosis		

subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Sarcoidosis	Additional description: Sarcoidosis		
subjects affected / exposed	0 / 78 (0.00%)	1 / 41 (2.44%)	0 / 46 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal oedema	Additional description: Pharyngeal oedema		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax	Additional description: Pneumothorax		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (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
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood glucose increased	Additional description: Blood glucose increased		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased	Additional description: C-reactive protein increased		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fractured sacrum	Additional description: Fractured sacrum		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint injury	Additional description: Joint injury		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus lesion	Additional description: Meniscus lesion		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture	Additional description: Pubis fracture		

subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma	Additional description: Seroma		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence	Additional description: Wound dehiscence		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Congenital, familial and genetic disorders			
Epidermolysis	Additional description: Epidermolysis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sebaceous naevus	Additional description: Sebaceous naevus		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 78 (0.00%)	1 / 41 (2.44%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Balance disorder	Additional description: Balance disorder		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cerebral infarction	Additional description: Cerebral infarction		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache	Additional description: Headache		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Loss of consciousness	Additional description: Loss of consciousness		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica	Additional description: Sciatica		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Speech disorder	Additional description: Speech disorder		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	6 / 78 (7.69%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia	Additional description: Leukopenia		

subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy	Additional description: Lymphadenopathy		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Pancytopenia	Additional description: Pancytopenia		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo	Additional description: Vertigo		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure	Additional description: Anal fissure		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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

Colitis	Additional description: Colitis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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

Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (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

Diverticulum intestinal haemorrhagic	Additional description: Diverticulum intestinal haemorrhagic		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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

Duodenal ulcer haemorrhage	Additional description: Duodenal ulcer haemorrhage		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Enteritis	Additional description: Enteritis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Faecaloma	Additional description: Faecaloma		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastritis erosive	Additional description: Gastritis erosive

subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glossitis	Additional description: Glossitis		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (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
Skin and subcutaneous tissue disorders			
Eczema	Additional description: Eczema		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Neurodermatitis	Additional description: Neurodermatitis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling face	Additional description: Swelling face		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria	Additional description: Urticaria		

subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute	Additional description: Renal failure acute		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 78 (0.00%)	1 / 41 (2.44%)	0 / 46 (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
Bone pain	Additional description: Bone pain		
subjects affected / exposed	3 / 78 (3.85%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis	Additional description: Osteonecrosis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess	Additional description: Abdominal abscess		
subjects affected / exposed	0 / 78 (0.00%)	1 / 41 (2.44%)	0 / 46 (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
Acute tonsillitis	Additional description: Acute tonsillitis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Appendicitis	Additional description: Appendicitis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bartholin's abscess	Additional description: Bartholin's abscess		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchopneumonia	Additional description: Bronchopneumonia		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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

Device related infection	Additional description: Device related infection		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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

Device related sepsis	Additional description: Device related sepsis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Febrile infection	Additional description: Febrile infection		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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

Gastrointestinal infection	Additional description: Gastrointestinal infection		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Implant site abscess	Additional description: Implant site abscess

subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection	Additional description: Infection		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Localised infection	Additional description: Localised infection		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Postoperative wound infection	Additional description: Postoperative wound infection		
subjects affected / exposed	1 / 78 (1.28%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (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
Sepsis	Additional description: Sepsis		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection	Additional description: Urinary tract infection		

subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection	Additional description: Viral infection		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Electrolyte imbalance	Additional description: Electrolyte imbalance		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	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	Chemotherapy conventional sequence with L-BLP25	Chemotherapy conventional sequence without L-BLP25	Chemotherapy reverse sequence with L-BLP25
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 77 (100.00%)	77 / 77 (100.00%)	76 / 77 (98.70%)
Vascular disorders			
Flushing	Additional description: Flushing		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	5 / 77 (6.49%)
occurrences (all)	0	1	7
Hot flush	Additional description: Hot flush		
subjects affected / exposed	14 / 77 (18.18%)	13 / 77 (16.88%)	18 / 77 (23.38%)
occurrences (all)	18	16	22
Thrombophlebitis	Additional description: Thrombophlebitis		
subjects affected / exposed	10 / 77 (12.99%)	4 / 77 (5.19%)	5 / 77 (6.49%)
occurrences (all)	13	4	5
General disorders and administration site conditions			

Asthenia	Additional description: Asthenia		
subjects affected / exposed	3 / 77 (3.90%)	7 / 77 (9.09%)	7 / 77 (9.09%)
occurrences (all)	4	11	8
Axillary pain	Additional description: Axillary pain		
subjects affected / exposed	4 / 77 (5.19%)	2 / 77 (2.60%)	3 / 77 (3.90%)
occurrences (all)	4	2	3
Chest pain	Additional description: Chest pain		
subjects affected / exposed	3 / 77 (3.90%)	2 / 77 (2.60%)	3 / 77 (3.90%)
occurrences (all)	3	2	3
Fatigue	Additional description: Fatigue		
subjects affected / exposed	54 / 77 (70.13%)	49 / 77 (63.64%)	45 / 77 (58.44%)
occurrences (all)	132	127	97
Injection site erythema	Additional description: Injection site erythema		
subjects affected / exposed	4 / 77 (5.19%)	0 / 77 (0.00%)	9 / 77 (11.69%)
occurrences (all)	8	0	12
Mucosal dryness	Additional description: Mucosal dryness		
subjects affected / exposed	9 / 77 (11.69%)	6 / 77 (7.79%)	8 / 77 (10.39%)
occurrences (all)	10	9	8
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	4 / 77 (5.19%)	6 / 77 (7.79%)	6 / 77 (7.79%)
occurrences (all)	7	12	9
Oedema	Additional description: Oedema		
subjects affected / exposed	0 / 77 (0.00%)	2 / 77 (2.60%)	6 / 77 (7.79%)
occurrences (all)	0	3	7
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	19 / 77 (24.68%)	14 / 77 (18.18%)	20 / 77 (25.97%)
occurrences (all)	22	17	32
Pain	Additional description: Pain		
subjects affected / exposed	10 / 77 (12.99%)	12 / 77 (15.58%)	7 / 77 (9.09%)
occurrences (all)	16	20	10
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	17 / 77 (22.08%)	6 / 77 (7.79%)	7 / 77 (9.09%)
occurrences (all)	21	6	8
Reproductive system and breast disorders			

Breast pain	Additional description: Breast pain		
subjects affected / exposed	3 / 77 (3.90%)	4 / 77 (5.19%)	5 / 77 (6.49%)
occurrences (all)	4	5	6
Menstruation irregular	Additional description: Menstruation irregular		
subjects affected / exposed	0 / 77 (0.00%)	4 / 77 (5.19%)	1 / 77 (1.30%)
occurrences (all)	0	4	1
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Cough		
subjects affected / exposed	15 / 77 (19.48%)	10 / 77 (12.99%)	8 / 77 (10.39%)
occurrences (all)	18	10	9
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	5 / 77 (6.49%)	9 / 77 (11.69%)	7 / 77 (9.09%)
occurrences (all)	6	11	12
Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	0 / 77 (0.00%)	1 / 77 (1.30%)	2 / 77 (2.60%)
occurrences (all)	0	1	3
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	4 / 77 (5.19%)	3 / 77 (3.90%)	9 / 77 (11.69%)
occurrences (all)	5	4	12
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	14 / 77 (18.18%)	7 / 77 (9.09%)	12 / 77 (15.58%)
occurrences (all)	19	7	20
Psychiatric disorders			
Insomnia	Additional description: Insomnia		
subjects affected / exposed	4 / 77 (5.19%)	7 / 77 (9.09%)	9 / 77 (11.69%)
occurrences (all)	5	10	10
Sleep disorder	Additional description: Sleep disorder		
subjects affected / exposed	8 / 77 (10.39%)	10 / 77 (12.99%)	11 / 77 (14.29%)
occurrences (all)	9	10	11
Investigations			
Body temperature increased	Additional description: Body temperature increased		
subjects affected / exposed	4 / 77 (5.19%)	1 / 77 (1.30%)	5 / 77 (6.49%)
occurrences (all)	6	1	6
Injury, poisoning and procedural complications			
Procedural pain	Additional description: Procedural pain		

subjects affected / exposed	2 / 77 (2.60%)	4 / 77 (5.19%)	3 / 77 (3.90%)
occurrences (all)	2	5	3
Seroma	Additional description: Seroma		
subjects affected / exposed	3 / 77 (3.90%)	5 / 77 (6.49%)	3 / 77 (3.90%)
occurrences (all)	3	5	3
Cardiac disorders			
Cardiovascular disorder	Additional description: Cardiovascular disorder		
subjects affected / exposed	4 / 77 (5.19%)	3 / 77 (3.90%)	2 / 77 (2.60%)
occurrences (all)	4	3	2
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	5 / 77 (6.49%)	5 / 77 (6.49%)	6 / 77 (7.79%)
occurrences (all)	7	9	9
Nervous system disorders			
Ageusia	Additional description: Ageusia		
subjects affected / exposed	2 / 77 (2.60%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	2	0	1
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	19 / 77 (24.68%)	23 / 77 (29.87%)	25 / 77 (32.47%)
occurrences (all)	24	27	35
Headache	Additional description: Headache		
subjects affected / exposed	22 / 77 (28.57%)	18 / 77 (23.38%)	23 / 77 (29.87%)
occurrences (all)	29	23	30
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	3 / 77 (3.90%)	2 / 77 (2.60%)	7 / 77 (9.09%)
occurrences (all)	3	2	12
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	5 / 77 (6.49%)	8 / 77 (10.39%)	5 / 77 (6.49%)
occurrences (all)	7	10	8
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	10 / 77 (12.99%)	9 / 77 (11.69%)	9 / 77 (11.69%)
occurrences (all)	16	13	17
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	5 / 77 (6.49%)	3 / 77 (3.90%)	3 / 77 (3.90%)
occurrences (all)	6	3	4
Polyneuropathy	Additional description: Polyneuropathy		

subjects affected / exposed	19 / 77 (24.68%)	20 / 77 (25.97%)	17 / 77 (22.08%)
occurrences (all)	28	26	31
Tremor	Additional description: Tremor		
subjects affected / exposed	5 / 77 (6.49%)	1 / 77 (1.30%)	1 / 77 (1.30%)
occurrences (all)	5	2	2
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	9 / 77 (11.69%)	17 / 77 (22.08%)	9 / 77 (11.69%)
occurrences (all)	17	35	17
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	23 / 77 (29.87%)	25 / 77 (32.47%)	17 / 77 (22.08%)
occurrences (all)	128	139	86
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	24 / 77 (31.17%)	24 / 77 (31.17%)	24 / 77 (31.17%)
occurrences (all)	92	103	69
Ear and labyrinth disorders			
Tinnitus	Additional description: Tinnitus		
subjects affected / exposed	2 / 77 (2.60%)	0 / 77 (0.00%)	4 / 77 (5.19%)
occurrences (all)	2	0	5
Vertigo	Additional description: Vertigo		
subjects affected / exposed	12 / 77 (15.58%)	10 / 77 (12.99%)	17 / 77 (22.08%)
occurrences (all)	20	14	27
Eye disorders			
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	2 / 77 (2.60%)	1 / 77 (1.30%)	4 / 77 (5.19%)
occurrences (all)	3	2	6
Dry eye	Additional description: Dry eye		
subjects affected / exposed	5 / 77 (6.49%)	3 / 77 (3.90%)	5 / 77 (6.49%)
occurrences (all)	5	4	5
Lacrimation increased	Additional description: Lacrimation increased		
subjects affected / exposed	8 / 77 (10.39%)	17 / 77 (22.08%)	18 / 77 (23.38%)
occurrences (all)	9	21	21
Visual acuity reduced	Additional description: Visual acuity reduced		
subjects affected / exposed	1 / 77 (1.30%)	5 / 77 (6.49%)	0 / 77 (0.00%)
occurrences (all)	1	5	0
Gastrointestinal disorders			

Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	3 / 77 (3.90%)	0 / 77 (0.00%)	5 / 77 (6.49%)
occurrences (all)	4	0	6
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	4 / 77 (5.19%)	2 / 77 (2.60%)	5 / 77 (6.49%)
occurrences (all)	5	4	5
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	5 / 77 (6.49%)	7 / 77 (9.09%)	8 / 77 (10.39%)
occurrences (all)	6	7	9
Constipation	Additional description: Constipation		
subjects affected / exposed	27 / 77 (35.06%)	27 / 77 (35.06%)	27 / 77 (35.06%)
occurrences (all)	46	46	47
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	16 / 77 (20.78%)	21 / 77 (27.27%)	29 / 77 (37.66%)
occurrences (all)	28	35	48
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	6 / 77 (7.79%)	6 / 77 (7.79%)	2 / 77 (2.60%)
occurrences (all)	6	6	2
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	6 / 77 (7.79%)	6 / 77 (7.79%)	7 / 77 (9.09%)
occurrences (all)	6	9	9
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	1 / 77 (1.30%)	3 / 77 (3.90%)	4 / 77 (5.19%)
occurrences (all)	1	4	4
Flatulence	Additional description: Flatulence		
subjects affected / exposed	2 / 77 (2.60%)	4 / 77 (5.19%)	0 / 77 (0.00%)
occurrences (all)	2	4	0
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	6 / 77 (7.79%)	5 / 77 (6.49%)	3 / 77 (3.90%)
occurrences (all)	6	8	3
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	4 / 77 (5.19%)	1 / 77 (1.30%)	2 / 77 (2.60%)
occurrences (all)	4	1	2
Nausea	Additional description: Nausea		
subjects affected / exposed	57 / 77 (74.03%)	51 / 77 (66.23%)	50 / 77 (64.94%)
occurrences (all)	114	101	108

Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	24 / 77 (31.17%)	15 / 77 (19.48%)	16 / 77 (20.78%)
occurrences (all)	41	29	40
Vomiting	Additional description: Vomiting		
subjects affected / exposed	16 / 77 (20.78%)	14 / 77 (18.18%)	6 / 77 (7.79%)
occurrences (all)	23	16	8
Skin and subcutaneous tissue disorders			
Acne	Additional description: Acne		
subjects affected / exposed	1 / 77 (1.30%)	0 / 77 (0.00%)	4 / 77 (5.19%)
occurrences (all)	2	0	5
Alopecia	Additional description: Alopecia		
subjects affected / exposed	33 / 77 (42.86%)	38 / 77 (49.35%)	32 / 77 (41.56%)
occurrences (all)	38	41	35
Dry skin	Additional description: Dry skin		
subjects affected / exposed	7 / 77 (9.09%)	9 / 77 (11.69%)	14 / 77 (18.18%)
occurrences (all)	8	9	15
Erythema	Additional description: Erythema		
subjects affected / exposed	5 / 77 (6.49%)	6 / 77 (7.79%)	11 / 77 (14.29%)
occurrences (all)	6	11	14
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	5 / 77 (6.49%)	5 / 77 (6.49%)	4 / 77 (5.19%)
occurrences (all)	6	5	4
Nail discolouration	Additional description: Nail discolouration		
subjects affected / exposed	6 / 77 (7.79%)	2 / 77 (2.60%)	2 / 77 (2.60%)
occurrences (all)	6	2	2
Nail disorder	Additional description: Nail disorder		
subjects affected / exposed	9 / 77 (11.69%)	6 / 77 (7.79%)	14 / 77 (18.18%)
occurrences (all)	9	7	17
Nail dystrophy	Additional description: Nail dystrophy		
subjects affected / exposed	6 / 77 (7.79%)	3 / 77 (3.90%)	5 / 77 (6.49%)
occurrences (all)	7	3	5
Onychalgia	Additional description: Onychalgia		
subjects affected / exposed	2 / 77 (2.60%)	1 / 77 (1.30%)	2 / 77 (2.60%)
occurrences (all)	2	1	3
Onychoclasis	Additional description: Onychoclasis		

subjects affected / exposed	3 / 77 (3.90%)	4 / 77 (5.19%)	10 / 77 (12.99%)
occurrences (all)	3	4	10
Palmar-plantar erythrodysaesthesia syndrome	Additional description: Palmar-plantar erythrodysaesthesia syndrome		
subjects affected / exposed	2 / 77 (2.60%)	6 / 77 (7.79%)	4 / 77 (5.19%)
occurrences (all)	4	12	4
Pruritus	Additional description: Pruritus		
subjects affected / exposed	3 / 77 (3.90%)	3 / 77 (3.90%)	8 / 77 (10.39%)
occurrences (all)	3	3	9
Rash	Additional description: Rash		
subjects affected / exposed	4 / 77 (5.19%)	4 / 77 (5.19%)	18 / 77 (23.38%)
occurrences (all)	5	4	23
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	9 / 77 (11.69%)	16 / 77 (20.78%)	11 / 77 (14.29%)
occurrences (all)	14	20	13
Back pain	Additional description: Back pain		
subjects affected / exposed	4 / 77 (5.19%)	1 / 77 (1.30%)	3 / 77 (3.90%)
occurrences (all)	4	1	3
Bone pain	Additional description: Bone pain		
subjects affected / exposed	24 / 77 (31.17%)	24 / 77 (31.17%)	19 / 77 (24.68%)
occurrences (all)	37	40	32
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	1 / 77 (1.30%)	4 / 77 (5.19%)	1 / 77 (1.30%)
occurrences (all)	1	4	1
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	4 / 77 (5.19%)	2 / 77 (2.60%)	4 / 77 (5.19%)
occurrences (all)	4	2	4
Myalgia	Additional description: Myalgia		
subjects affected / exposed	17 / 77 (22.08%)	18 / 77 (23.38%)	21 / 77 (27.27%)
occurrences (all)	28	23	35
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	17 / 77 (22.08%)	16 / 77 (20.78%)	17 / 77 (22.08%)
occurrences (all)	27	22	27
Infections and infestations			

Infection	Additional description: Infection		
subjects affected / exposed	5 / 77 (6.49%)	1 / 77 (1.30%)	3 / 77 (3.90%)
occurrences (all)	6	1	3
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	16 / 77 (20.78%)	13 / 77 (16.88%)	8 / 77 (10.39%)
occurrences (all)	17	15	9
Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	7 / 77 (9.09%)	8 / 77 (10.39%)	10 / 77 (12.99%)
occurrences (all)	16	13	17
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	8 / 77 (10.39%)	4 / 77 (5.19%)	2 / 77 (2.60%)
occurrences (all)	8	4	2
Pharyngitis	Additional description: Pharyngitis		
subjects affected / exposed	2 / 77 (2.60%)	3 / 77 (3.90%)	2 / 77 (2.60%)
occurrences (all)	2	3	2
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	5 / 77 (6.49%)	6 / 77 (7.79%)	4 / 77 (5.19%)
occurrences (all)	5	6	5
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	5 / 77 (6.49%)	8 / 77 (10.39%)	8 / 77 (10.39%)
occurrences (all)	7	9	8
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	7 / 77 (9.09%)	7 / 77 (9.09%)	5 / 77 (6.49%)
occurrences (all)	11	7	8
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	7 / 77 (9.09%)	13 / 77 (16.88%)	14 / 77 (18.18%)
occurrences (all)	7	16	16
Increased appetite	Additional description: Increased appetite		
subjects affected / exposed	4 / 77 (5.19%)	0 / 77 (0.00%)	1 / 77 (1.30%)
occurrences (all)	4	0	1

Non-serious adverse events	Chemotherapy reverse sequence without L-BLP25	Endocrine Aromatase inhibitor therapy with L-BLP25	Endocrine Aromatase inhibitor therapy without L-BLP25
Total subjects affected by non-serious adverse events			
subjects affected / exposed	78 / 78 (100.00%)	25 / 41 (60.98%)	25 / 46 (54.35%)

Vascular disorders			
Flushing	Additional description: Flushing		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	2	0	0
Hot flush	Additional description: Hot flush		
subjects affected / exposed	15 / 78 (19.23%)	5 / 41 (12.20%)	6 / 46 (13.04%)
occurrences (all)	19	6	6
Thrombophlebitis	Additional description: Thrombophlebitis		
subjects affected / exposed	3 / 78 (3.85%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	5	0	0
General disorders and administration site conditions			
Asthenia	Additional description: Asthenia		
subjects affected / exposed	3 / 78 (3.85%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences (all)	7	0	1
Axillary pain	Additional description: Axillary pain		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Chest pain	Additional description: Chest pain		
subjects affected / exposed	1 / 78 (1.28%)	3 / 41 (7.32%)	0 / 46 (0.00%)
occurrences (all)	2	3	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	47 / 78 (60.26%)	6 / 41 (14.63%)	5 / 46 (10.87%)
occurrences (all)	110	7	5
Injection site erythema	Additional description: Injection site erythema		
subjects affected / exposed	0 / 78 (0.00%)	4 / 41 (9.76%)	0 / 46 (0.00%)
occurrences (all)	0	5	0
Mucosal dryness	Additional description: Mucosal dryness		
subjects affected / exposed	2 / 78 (2.56%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences (all)	3	1	0
Mucosal inflammation	Additional description: Mucosal inflammation		
subjects affected / exposed	7 / 78 (8.97%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	9	0	0
Oedema	Additional description: Oedema		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral	Additional description: Oedema peripheral		

subjects affected / exposed	24 / 78 (30.77%)	1 / 41 (2.44%)	1 / 46 (2.17%)
occurrences (all)	29	1	1
Pain	Additional description: Pain		
subjects affected / exposed	3 / 78 (3.85%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	4	0	0
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	11 / 78 (14.10%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences (all)	14	0	1
Reproductive system and breast disorders			
Breast pain	Additional description: Breast pain		
subjects affected / exposed	3 / 78 (3.85%)	2 / 41 (4.88%)	1 / 46 (2.17%)
occurrences (all)	5	2	1
Menstruation irregular	Additional description: Menstruation irregular		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Cough		
subjects affected / exposed	5 / 78 (6.41%)	2 / 41 (4.88%)	3 / 46 (6.52%)
occurrences (all)	5	3	5
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	7 / 78 (8.97%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	12	0	0
Dyspnoea exertional	Additional description: Dyspnoea exertional		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	5	0	0
Epistaxis	Additional description: Epistaxis		
subjects affected / exposed	5 / 78 (6.41%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	5	0	0
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	8 / 78 (10.26%)	0 / 41 (0.00%)	2 / 46 (4.35%)
occurrences (all)	10	0	2
Psychiatric disorders			
Insomnia	Additional description: Insomnia		
subjects affected / exposed	8 / 78 (10.26%)	1 / 41 (2.44%)	3 / 46 (6.52%)
occurrences (all)	11	1	3
Sleep disorder	Additional description: Sleep disorder		

subjects affected / exposed	12 / 78 (15.38%)	6 / 41 (14.63%)	4 / 46 (8.70%)
occurrences (all)	13	6	4
Investigations			
Body temperature increased	Additional description: Body temperature increased		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	5	0	0
Injury, poisoning and procedural complications			
Procedural pain	Additional description: Procedural pain		
subjects affected / exposed	4 / 78 (5.13%)	2 / 41 (4.88%)	1 / 46 (2.17%)
occurrences (all)	4	2	1
Seroma	Additional description: Seroma		
subjects affected / exposed	5 / 78 (6.41%)	1 / 41 (2.44%)	1 / 46 (2.17%)
occurrences (all)	5	1	1
Cardiac disorders			
Cardiovascular disorder	Additional description: Cardiovascular disorder		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Tachycardia	Additional description: Tachycardia		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	5	0	0
Nervous system disorders			
Ageusia	Additional description: Ageusia		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	7	0	0
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	30 / 78 (38.46%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences (all)	45	1	0
Headache	Additional description: Headache		
subjects affected / exposed	13 / 78 (16.67%)	4 / 41 (9.76%)	3 / 46 (6.52%)
occurrences (all)	20	4	4
Hypoaesthesia	Additional description: Hypoaesthesia		
subjects affected / exposed	6 / 78 (7.69%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	9	0	0
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences (all)	6	0	1

Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	15 / 78 (19.23%)	1 / 41 (2.44%)	1 / 46 (2.17%)
occurrences (all)	23	1	1
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	3	0	0
Polyneuropathy	Additional description: Polyneuropathy		
subjects affected / exposed	14 / 78 (17.95%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	18	0	0
Tremor	Additional description: Tremor		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	13 / 78 (16.67%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	27	0	0
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	15 / 78 (19.23%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	90	0	0
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	17 / 78 (21.79%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	87	0	0
Ear and labyrinth disorders			
Tinnitus	Additional description: Tinnitus		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Vertigo	Additional description: Vertigo		
subjects affected / exposed	7 / 78 (8.97%)	2 / 41 (4.88%)	1 / 46 (2.17%)
occurrences (all)	7	2	1
Eye disorders			
Conjunctivitis	Additional description: Conjunctivitis		
subjects affected / exposed	2 / 78 (2.56%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences (all)	4	1	0
Dry eye	Additional description: Dry eye		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	4	0	0
Lacrimation increased	Additional description: Lacrimation increased		

subjects affected / exposed	15 / 78 (19.23%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	17	0	0
Visual acuity reduced	Additional description: Visual acuity reduced		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort	Additional description: Abdominal discomfort		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences (all)	6	0	1
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	4	0	0
Abdominal pain upper	Additional description: Abdominal pain upper		
subjects affected / exposed	6 / 78 (7.69%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	6	0	0
Constipation	Additional description: Constipation		
subjects affected / exposed	30 / 78 (38.46%)	2 / 41 (4.88%)	2 / 46 (4.35%)
occurrences (all)	51	2	2
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	29 / 78 (37.18%)	4 / 41 (9.76%)	0 / 46 (0.00%)
occurrences (all)	39	5	0
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences (all)	1	0	1
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	5 / 78 (6.41%)	1 / 41 (2.44%)	1 / 46 (2.17%)
occurrences (all)	5	1	1
Dysphagia	Additional description: Dysphagia		
subjects affected / exposed	0 / 78 (0.00%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	0	0	0
Flatulence	Additional description: Flatulence		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease	Additional description: Gastrooesophageal reflux disease		
subjects affected / exposed	3 / 78 (3.85%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	3	0	0

Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	1 / 78 (1.28%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences (all)	1	1	0
Nausea	Additional description: Nausea		
subjects affected / exposed	41 / 78 (52.56%)	6 / 41 (14.63%)	0 / 46 (0.00%)
occurrences (all)	71	7	0
Stomatitis	Additional description: Stomatitis		
subjects affected / exposed	18 / 78 (23.08%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	29	0	0
Vomiting	Additional description: Vomiting		
subjects affected / exposed	9 / 78 (11.54%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences (all)	10	1	0
Skin and subcutaneous tissue disorders			
Acne	Additional description: Acne		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	2	0	0
Alopecia	Additional description: Alopecia		
subjects affected / exposed	31 / 78 (39.74%)	1 / 41 (2.44%)	3 / 46 (6.52%)
occurrences (all)	34	1	3
Dry skin	Additional description: Dry skin		
subjects affected / exposed	8 / 78 (10.26%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences (all)	9	0	1
Erythema	Additional description: Erythema		
subjects affected / exposed	5 / 78 (6.41%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences (all)	5	1	0
Hyperhidrosis	Additional description: Hyperhidrosis		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	2	0	0
Nail discolouration	Additional description: Nail discolouration		
subjects affected / exposed	5 / 78 (6.41%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	5	0	0
Nail disorder	Additional description: Nail disorder		
subjects affected / exposed	13 / 78 (16.67%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	13	0	0
Nail dystrophy	Additional description: Nail dystrophy		

subjects affected / exposed	3 / 78 (3.85%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	3	0	0
Onychalgia	Additional description: Onychalgia		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	5	0	0
Onychoclasis	Additional description: Onychoclasis		
subjects affected / exposed	7 / 78 (8.97%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	7	0	0
Palmar-plantar erythrodysaesthesia syndrome	Additional description: Palmar-plantar erythrodysaesthesia syndrome		
subjects affected / exposed	3 / 78 (3.85%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	3	0	0
Pruritus	Additional description: Pruritus		
subjects affected / exposed	5 / 78 (6.41%)	2 / 41 (4.88%)	1 / 46 (2.17%)
occurrences (all)	5	2	2
Rash	Additional description: Rash		
subjects affected / exposed	14 / 78 (17.95%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences (all)	15	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	17 / 78 (21.79%)	6 / 41 (14.63%)	9 / 46 (19.57%)
occurrences (all)	23	7	11
Back pain	Additional description: Back pain		
subjects affected / exposed	4 / 78 (5.13%)	1 / 41 (2.44%)	2 / 46 (4.35%)
occurrences (all)	7	1	2
Bone pain	Additional description: Bone pain		
subjects affected / exposed	28 / 78 (35.90%)	1 / 41 (2.44%)	1 / 46 (2.17%)
occurrences (all)	58	1	2
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	1 / 78 (1.28%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences (all)	1	0	1
Musculoskeletal pain	Additional description: Musculoskeletal pain		
subjects affected / exposed	5 / 78 (6.41%)	4 / 41 (9.76%)	1 / 46 (2.17%)
occurrences (all)	9	4	2
Myalgia	Additional description: Myalgia		

subjects affected / exposed	17 / 78 (21.79%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	23	0	0
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	18 / 78 (23.08%)	0 / 41 (0.00%)	1 / 46 (2.17%)
occurrences (all)	25	0	1
Infections and infestations			
Infection	Additional description: Infection		
subjects affected / exposed	0 / 78 (0.00%)	1 / 41 (2.44%)	0 / 46 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis	Additional description: Nasopharyngitis		
subjects affected / exposed	10 / 78 (12.82%)	2 / 41 (4.88%)	2 / 46 (4.35%)
occurrences (all)	13	2	2
Oral candidiasis	Additional description: Oral candidiasis		
subjects affected / exposed	9 / 78 (11.54%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	14	0	0
Oral herpes	Additional description: Oral herpes		
subjects affected / exposed	2 / 78 (2.56%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	2	0	0
Pharyngitis	Additional description: Pharyngitis		
subjects affected / exposed	6 / 78 (7.69%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	6	0	0
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	4 / 78 (5.13%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	4	0	0
Rhinitis	Additional description: Rhinitis		
subjects affected / exposed	7 / 78 (8.97%)	0 / 41 (0.00%)	0 / 46 (0.00%)
occurrences (all)	7	0	0
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	5 / 78 (6.41%)	3 / 41 (7.32%)	4 / 46 (8.70%)
occurrences (all)	7	4	4
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	12 / 78 (15.38%)	3 / 41 (7.32%)	0 / 46 (0.00%)
occurrences (all)	14	3	0
Increased appetite	Additional description: Increased appetite		

subjects affected / exposed occurrences (all)	0 / 78 (0.00%) 0	0 / 41 (0.00%) 0	0 / 46 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2013	Main changes included updates on subset of patients for safety run in phase, on parameters for early stopping rule, estimated treatment and study duration, details for L-BLP25 treatment and non-investigational medicinal products, requirements for DMC requests, definition of time windows for study assessments, and definition of interim analysis

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported