Available online at www.sciencedirect.com
SciVerse ScienceDirect
EJSO 38 (2012) 902–909
EJSO the Journal of Cancer Surgery
www.ejso.com

Lanreotide autogel 90 mg and lymphorrhea prevention after axillary node dissection in breast cancer: A phase III double blind, randomized, placebo-controlled trial

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Accepted 21 May 2012
Available online 15 June 2012

Abstract

Aim: The aim of this study was to assess the efficacy of Lanreotide Autogel 90 mg PR to prevent lymphorrhea after axillary dissection in breast cancer.
Methods: A Phase III double-blind, randomized, placebo-controlled trial was performed between April 1st, 2008, and December 31st, 2010. The primary endpoint was the lymphorrhea volume (ml) in the axillary drain during the first four postoperative days. The secondary end points were the number of days until axillary drain removal, hospital stay duration (days), lymphorrhea volume (ml) up to days 15, 30 and 180, number of cases with seroma aspiration and number of seroma aspirations, evaluation of wound, arm pain and mobility on days 15, 30 and 180.
Results: A total of 148 patients were recruited for the study. Altogether 145 patients were randomized and analysed on an intention-to-treat basis. On the day before surgery 73 patients received the placebo and 72 patients received lanreotide. At four postoperative days, there was a tendency towards a reduction of the lymphorrhea volume in the lanreotide group (median 292 ml, range 1–965 ml) as compared to the placebo group (median 337 ml, range 0–1230 ml), although it was not statistically significant ($p = 0.18$). There was no significant difference for the secondary end points. In the group with axillary dissection performed alone ($n = 24$), the lymphorrhea volume was shown to be significantly reduced in the lanreotide group, ($p = 0.035$) as compared to the placebo group.
Conclusion: Our study did not identify any overall significant reduction of lymphorrhea on lanreotide.

Keywords: Lanreotide; Somatostatin; Lymphorrhea; Seroma; Breast cancer; Axillary dissection

Introduction

In spite of the increased use of sentinel node biopsy,[1] axillary lymph node dissection is still an integral part of breast carcinoma staging and therapy. Lymphorrhea and seroma formation are the most common early complications. Lymphorrhea refers to fluid production following breast and axillary surgery. The fluid is a combination of lymph resulting from the dissection of lymph vessels and exsudate. Fluid buildup leads to seroma formation in up to 90% of cases.[2] Lymphorrhea can lead to prolonged hospital stays. Seroma can contribute to discomfort, pain, slow wound healing, infection and potentially delayed adjuvant treatment. The pathogenesis of seroma formation is multifactorial and not yet fully understood. It includes lymphorrhea from the damaged lymph vessels, local inflammation increasing the permeability of the lymphatic capillaries, a surgically created dead space filled with serous fluid and anticoagulant administration.[2–4] Many attempts have been made to prevent seroma formation, including suction drains, external compressive dressings, shoulder immobilisation, fibrin glue, careful

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doi:10.1016/j.ejso.2012.05.009

haemostasis and lymphostasis and axillary padding.[5–10] Despite all these measures, lymphorrhea and seroma formation still cannot be avoided.

Somatostatin could be an option. It is a tetradecapeptide hormone which can inhibit gastrointestinal endocrine and exocrine secretion and motility, as well as hepatic and splanchnic blood flow. The inhibitory action on splanchnic blood flow and triglyceride absorption is believed to be the main explanation of reduced lymph production. There may also be direct effects on the lymphatic system through somatostatin receptors.[11] Synthetic somatostatin analogues have a higher affinity for somatostatin receptors and a higher potency than the natural peptide. Octreotide, a synthetic somatostatin analogue, has been used in the treatment of chylous ascites and thoracic duct injuries for the first time.[12–14] After axillary dissection (AD) in breast cancer, a randomized study has shown a significant decrease in lymphorrhea with a five-day course of octreotide 0.1 mg 3 times a day, starting on the first postoperative day.[11] More recently, a non-randomized urological study has shown the potential efficacy of octreotide for the management of lymphorrhea after pelvic lymph node dissection in radical prostatectomy.[15] But iterative octreotide injections are uncomfortable and the efficacy of somatostin analogues needs to be confirmed. Lanreotide is an octapeptide somatostatin analogue. The Autogel form is composed of lanreotide acetate and water which form a supersaturated injectable solution of the peptide. Prolonged release of the peptide occurs thanks to the physical nature of the supersatured solution. The terminal half-life is approximately 28 days.

In the current study, we assessed the effect of prolonged release (PR) lanreotide Autogel 90 mg (Somatuline®, Ipsen Pharma Boulogne Billancourt, France) on lymphorrhea after axillary lymphadenectomy in breast cancer.

Patients and methods

This prospective double-blind randomized, placebo-controlled, trial was conducted at the breast institute of the University Hospital of Limoges (France) from April 1st, 2008, to December 31st, 2010. This study was supported by the University Hospital of Limoges.

Patients and treatment

Eligibility criteria: the patients included were over-18-year-old women with breast cancer who had to undergo axillary lymph node dissection (AD) either alone or with either lumpectomy or mastectomy. Exclusion criteria were diabetes mellitus with insulinotherapy, cyclosporin treatment, kidney failure and pregnancy. The study protocol was approved by the local ethics committee. Written informed consent was obtained preoperatively in accordance with the ethical standards of the Helsinki declaration. On the day before surgery, patients were enrolled and randomized to either the lanreotide or the control group. Randomization was stratified according to the surgical method (AD alone, AD with lumpectomy and AD with mastectomy) and performed using a 1:1 ratio. On the day before surgery, around 10:00 P.M., the treatment group received one deep subcutaneous (sc) 0.3 ml injection of Lanreotide Autogel 90 mg PR (Somatuline®, Ipsen Pharma Boulogne Billancourt, France) and the control group received one sc injection of 0.3 ml saline preparation using the same protocol. This was a double-blind study. Because lanreotide and placebo look different, only the nurse who gave the injection knew what was injected. This nurse was excluded from both patient follow up and data measurements.

Surgery

Axillary dissections were performed in case of sentinel lymph node involvement or palpable axillary nodes. We routinely remove the sentinel lymph node under local anaesthesia, thus avoiding frozen tissue examination.[16] In case of sentinel lymph node involvement, axillary dissection is performed first and breast surgery (lumpectomy or mastectomy) is performed under general anaesthesia the week after. Sometimes up to the surgeon's choice, sentinel lymph node dissection can be performed at the same time as breast surgery under general anaesthesia. In case of sentinel lymph node involvement, axillary dissection is performed alone later. In this study surgery was performed by four experienced breast surgeons who were blinded to the treatment arm. Berg level I and II lymph node dissections were performed routinely. The long thoracic and thoracodorsal neurovascular bundles were preserved in all cases. Haemostasis and lymphostasis were performed with clips and electrocautery. A closed suction drain was placed in the axillary fossa in all cases. In case of concomitant mastectomy, another suction drain was placed under the skin in the mastectomy space. The mastectomy drain was removed on the first postoperative day whereas the axillary fossa drain was left in place at least until postoperative day 4. From the fourth day postoperatively, the drain was removed when the total fluid discharge had been $<$50 ml over the previous 24 h.

In our institute, it is uncommon to perform immediate breast reconstruction concomitantly with axillary dissection.

Follow-up and end points

Objective measurements were performed by different physicians who were blinded to the treatment arm of the patient. During hospitalisation, data concerning the volume of lymph in the axillary drain, weight (Kg), pain assessment – with a visual analogue scale – and adverse events were collected each day. The following data were also collected: patient age, cancer histology, number

of patients with sentinel lymph node biopsy, number of non-sentinel lymph nodes removed, number of cases with non-sentinel lymph node involvement and time between injection and drainage (min). Patients were scheduled for assessment after 15, 30 and 180 postoperative days to objectively evaluate seroma aspiration, wound complications, arm pain and mobility. Information about seroma aspiration performed in an emergency between follow-ups was also collected. Data concerninglymphorrhea volume (ml) up to days 15, 30 and 180 were collected. *Lymphorrhea at day 15* was defined as total lymph volume in drain + volume of seroma aspirate between hospital discharge and day 14 + volume of seroma aspirate on day 15. *Lymphorrhea at day 30* was defined as lymphorrhea volume at day 15 + volume of seroma aspirate between days 16 and 29 + volume of seroma aspirate on day 30. *Lymphorrhea at day 180* was defined as lymphorrhea volume at day 30 + volume of seroma aspirate between days 31 and 179 + volume of seroma aspirate on day 180. The primary endpoint was to compare the lymphorrhea volume (ml) in the axillary drain during the first four postoperative days between the lanreotide group and the placebo group. The secondary end points were the number of days until axillary drain removal, hospital stay duration (days), number of patients requiring seroma aspiration on days 15, 30 and 180, total number of cases with seroma aspiration, lymphorrhea volume (ml) at days 15, 30 and 180 and evaluation of wound, arm pain and mobility on days 15, 30 and 180.

Statistical methods

Sample size

Based on a retrospective analysis made by our team, the mean lymphorrhea volume in the placebo group was estimated to be 211 ml ± 129 ml four days after surgery. To detect a clinically relevant 30% reduction of this volume in the lanreotide group (i.e. an expected mean volume of 147 ml in subjects treated with lanreotide) with 5% significance and 80%, power the sample size had to be at least 132 subjects overall (66 in each group), which was increased by 10% to account for potentially non-evaluable data, which led to the inclusion of 148 subjects.

Statistical analysis

Quantitative variables are systematically described using median and range (we also present mean and standard deviation (SD) for the primary endpoint only because sample size calculation was based on mean, difference between mean and expected standard deviation). Qualitative variables are described using frequency and percentage. Intention-to-treat analysis was performed. The comparisons of the quantitative variables between the two groups were performed using the Student t test or the Mann Whitney U test, depending on the variable distribution. The Shapiro–Wilk test was used to assess distribution normality. Percentages were compared using the Chi2 test or Fisher's exact test. P value lower than 0.05 was considered as statistically significant. A sub analysis was planned to analyse the primary for each type of breast surgery. Analyses were performed and are presented in accordance with the Consort statement.[17]

Results

Patients

A total of 148 patients were recruited for the study (Fig. 1). But one refused to participate before randomization and two between randomization and injection. A total of 145 patients were finally randomized. Among the 145 patients who received the injection, eight (four in each group) presented protocol deviations (in seven patients the axillary drain was removed on the 3rd postoperative day and one was transferred to intensive care on the 3rd postoperative day because of respiratory distress). None of the 145 randomized patients was excluded from analysis so that 73 patients received placebo and 72 patients received lanreotide. Nineteen patients (9 in the placebo group and 10 in the lanreotide group) were lost to follow up, four between the 4th and the 15th postoperative days, two between the 15th and the 30th postoperative days and 13 between the 30th and the 180th postoperative days. One patient in the placebo group died of causes unrelated to cancer between the 30th and the 180th postoperative days. At baseline the patients' characteristics were homogeneous in the two groups (Table 1).

Primary endpoint (Table 2)

At postoperative day 4, the lymphorrhea volume tended to decrease in the lanreotide group (median and range: 292 (1–965), mean ± sd: 330 ± 182 ml) as compared to the placebo group (median and range: 337 (0–1230), mean ± sd: 383 ± 230 ml), although it was not statistically significant ($p = 0.18$).

Secondary end points (Table 2)

There was no significant difference between the lymphorrhea volumes at postoperative days 15, 30 and 180. No statistically significant difference was found in the duration of drainage, number of cases with drainage >4 days, length of hospital stay, number of cases with seroma aspiration, pain, wound complication and arm mobility (Table 2). Treatment-induced side effects were minimal. Gastrointestinal disorders (abdominal pain, nausea and diarrhoea) were observed in 13.7% of the placebo group and 23.6% of the lanreotide group ($p = 0.12$).

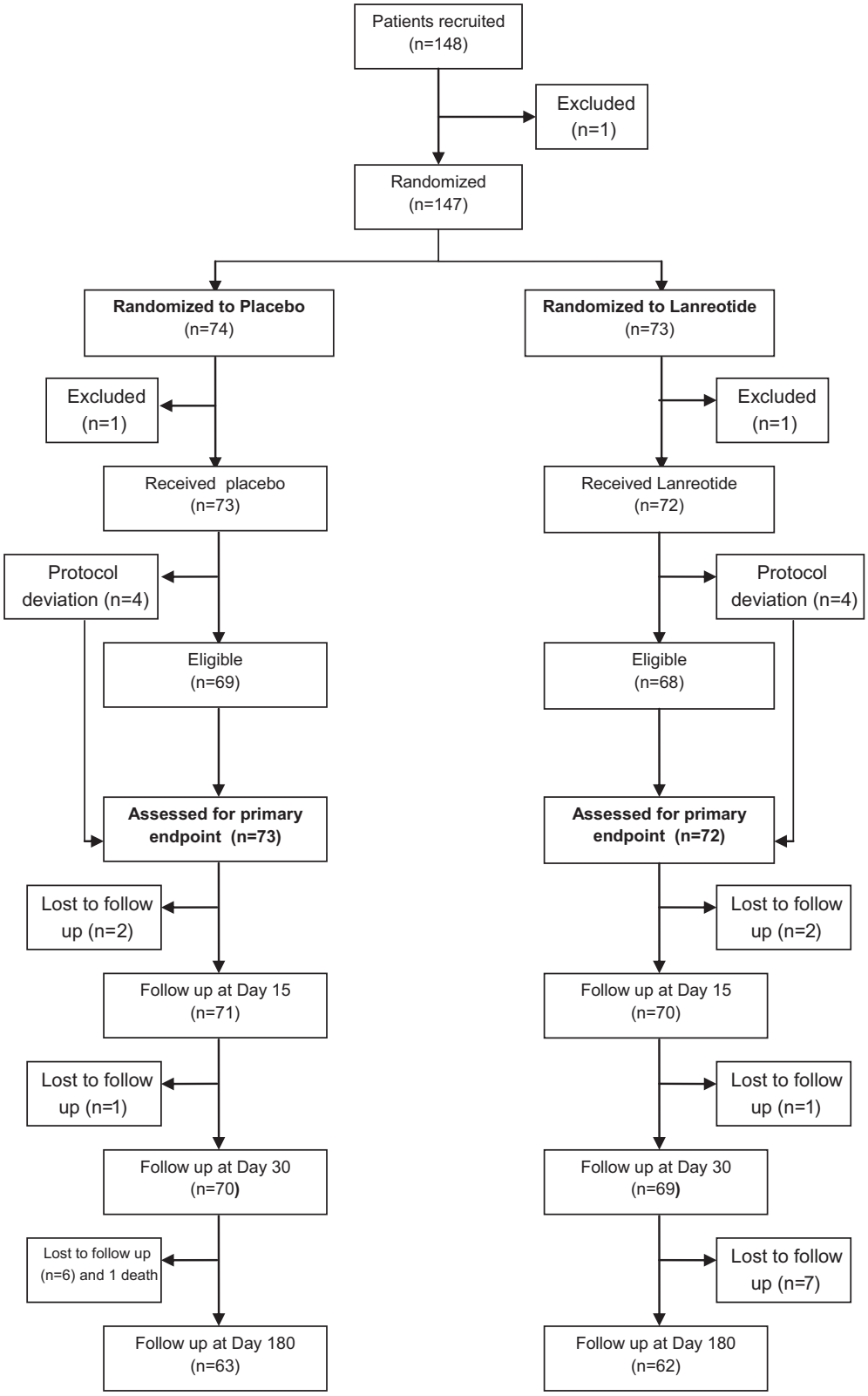

Figure 1. Flowchart of the trial.

Table 1
Patient characteristics at baseline.

	Placebo ($n = 73$)	Lanreotide ($n = 72$)	p-value
Median Age (years)	59 (21–89)	56 (32–87)	0.40[a]
Median BMI (kg/m^2)	27 (18–45)	25 (17–44)	0.41[b]
Tumour pathology			0.19[c]
Invasive ductal	56	60	
Invasive lobular	9	10	
Invasive mixt	4	2	
Other	4	0	
Number of patients with sentinel lymph node biopsy	38	38	0.93[d]
Median number of non sentinel lymph nodes removed	13 (1–27)	13 (2–28)	0.52[b]
Case with non-sentinel lymph node involvement	31	33	0.68[d]
Median time between injection and drainage (hours)	15 (11–20)	14 (10–20)	0.11[a]
Type of surgery			0.87[d]
Mastectomy + AD	25	25	
Lumpectomy + AD	37	34	
AD alone	11	13	
Chemotherapy	64	66	0.43[d]
Neoadjuvant chemotherapy	20	15	0.36[d]
Radiotherapy	66	64	0.76[d]
Hormonotherapy	60	56	0.51[d]

Results are expressed as median (range) or number.
AD: axillary dissection.
[a] Student t test.
[b] Mann Whitney test.
[c] Fisher's exact test.
[d] Chi2 test.

Subgroup analysis (Table 3)

In the subgroup with axillary dissection performed alone ($n = 24$), the lymphorrhea volume on post-operative day 4 was significantly reduced in the lanreotide group, ($p = 0.035$) as compared to the placebo group. In the subgroup on lanreotide with AD alone or AD combined with lumpectomy, the drain was left in place for a significantly shorter time ($p = 0.02$).

Discussion

In this phase III double-blind, randomized, placebo-controlled trial, we did not show any significant efficacy of lanreotide in the prevention of lymphorrhea and seroma formation. We showed only a trend towards a reduction when lanreotide was used compared to placebo. All the risk factors for developing seroma formation like body weight, radical mastectomy, age and number of lymph nodes removed[2] were controlled through randomization. The possible impact of the type of surgery was controlled through stratification. The rate of seroma aspiration was close to 40%, which corresponds to the mean found in the literature.[2,5,18]

Somatostatin analogue and lymphorrhea

Lanreotide has the advantage of requiring only one injection contrary to octreotide, another synthetic somatostatin analogue. However, two studies have shown a significant action of octreotide. In breast cancer, Carcoforo et al. demonstrated a significant reduction of lymphorrhea and hospital stay with a five-day course of octreotide 0.1 mg 3 times a day.[11] But blinding was difficult to confirm to since this prospective randomized study was not placebo-controlled and the schedule for drain removal and lymphorrhea measurement was unclear. However, the strength of the study was its population including 261 patients, 125 in the octreotide group and 136 in the control group. Our statistical hypothesis hoped for a 65 ml difference in the lymphorrhea volume between the two groups at day 4, with 129 ml as the standard deviation used for sample size calculation. In the study the mean difference of volume observed between the groups was smaller (53 ml) and the variability higher (230 and 182 ml for the standard deviation in the placebo and lanreotide arms respectively). Besides, we had to use a non-parametric test to compare lymphorrhea distribution (Mann Whitney test) instead of the Student t test, which reduced the power of our analysis. As a result the power of our study was 32%. Nevertheless, this reduction is lower than the clinically relevant effect considered when the investigators were writing the protocol. A number of 260 subjects per group would have been necessary to achieve 80% power with these data. Octreotide has also been described in urology in a prospective non-randomized study, in case of patients with a high lymphorrhea volume at postoperative day 3, after pelvic lymph node dissection in radical prostatectomy.[15]

Table 2
Results of primary and secondary end points in the placebo and lanreotide groups.

Variable	Placebo ($n = 73$)	Lanreotide ($n = 72$)	p-value
Volume of lymphorrhea on postoperative day 4 (ml)	337 (0–1230)	292 (1–965)	0.18[a]
Duration of drain (days)	4 (2–15)	4 (2–9)	0.10[a]
Drain > 4 days	31	22	$p = 0.16$[b]
Length of hospitalisation (days)	4.5 (3–14)	4 (2–9)	$p = 0.33$[a]
Total number of cases with seroma aspiration	28	25	$p = 0.20$[b]
Volume of lymphorrhea (ml)			
On postoperative day 15	407 (80–2320) ($n_p = 71$†)	317.5 (1–1635) ($n_l = 70$†)	$p = 0.26$[a]
On postoperative day 30	407 (80–2340) ($n_p = 69$†)	327.5 (1–2015) ($n_l = 68$†)	$p = 0.26$[a]
On postoperative day 180	403 (91–2340) ($n_p = 63$†)	317.5 (1–2015) ($n_l = 62$†)	$p = 0.20$[a]
Seroma aspiration			
On postoperative day 15	29 ($n_p = 71$†)	23 ($n_l = 70$†)	$p = 0.38$[b]
On postoperative day 30	10 ($n_p = 69$†)	13 ($n_l = 67$†)	$p = 0.49$[b]
On postoperative day 180	1 ($n_p = 63$†)	1 ($n_l = 60$†)	$p = 1.00$[b]
Pain visual analogue scale			
On postoperative day 15	2 (0–9) ($n_p = 67$†)	3 (0–7) ($n_l = 68$†)	$p = 0.29$[a]
On postoperative day 30	1.5 (0–7) ($n_p = 68$†)	1 (0–7) ($n_l = 60$†)	$p = 0.97$[a]
On postoperative day 180	0 (0–7) ($n_p = 58$†)	0 (0–7) ($n_l = 56$†)	$p = 0.26$[a]
Wound complications			
On postoperative day 15	9 ($n_p = 70$†)	5 ($n_l = 69$†)	$p = 0.39$[b]
On postoperative day 30	4 ($n_p = 67$†)	6 ($n_l = 67$†)	$p = 0.74$[b]
On postoperative day 180	0 ($n_p = 63$†)	0 ($n_l = 61$†)	nc
Arm mobility on postoperative day 15	$n_p = 69$†	$n_l = 68$†	$p = 0.39$[b]
Normal	18	18	
Moderately reduced	45	39	
Severely reduced	6	11	
Arm mobility on postoperative day 30	$n_p = 68$†	$n_l = 66$†	$p = 0.80$[b]
Normal	28	32	
Moderately reduced	38	32	
Severely reduced	2	2	
Arm mobility on postoperative day 180	$n_p = 62$†	$n_l = 60$†	$p = 0.16$
Normal	53	43	
Moderately reduced	8	15	
Severely reduced	1	2	

Results are expressed as median (range) or number.
Numbers of subjects in analysis can vary due to drop out at day 15, 30 or 180 or by sub-group analysis (†); these numbers are expressed as: n_p = number of subjects in the placebo group; n_l = number of subjects in the lanreotide group.
nc: not calculated.
† due to missing data.
[a] Mann Whitney test.
[b] Fisher's exact test.

This 89 patient study (45 untreated and 44 treated) showed a significant reduction of both lymphorrhea and length of hospital stay. However, in addition to the lack of randomization, results need to be cautiously analysed since the origins of lymphorrhea might be different in the axillary and the abdominal areas. Indeed the peritoneum has absorption properties.[19] Moreover the impact of the created dead space should be less important than in breast surgery.

Weaknesses of the study

The multifactorial origin of seroma formation may explain our disappointing results.[2] In a subgroup analysis, we showed significant lymphorrhea reduction on postoperative day 4 in case of AD performed alone in the lanreotide group (median 235, range (110–405), $n_l = 13$) as compared to the placebo group (median 405, range (180–680), $n_p = 11$), ($p = 0.035$). In the subgroup on lanreotide with AD alone or AD combined with lumpectomy, the drain was removed significantly earlier ($p = 0.02$) and lymphorrhea reduction was close to significance ($p = 0.09$). In these situations, the impact of the created dead space is lower as opposed to what happens in case of mastectomy. Furthermore, there is usually no large skin dissection, i.e. no non-adherent skin flap leading to prolonged primary wound healing and blood and lymphatic fluid oozing as the patients resume moving their arms.[20–22] Lanreotide may have no effect on this mechanism of seroma formation. Moreover, a drawback of our study was to have left the drain in place for at least four days. Indeed the drain acts as a foreign body[19] which triggers an inflammatory reaction and contributes to serous fluid production, which can potentially decrease the effect of lanreotide. A future study on lanreotide use with and without a drain could be interesting. This is the first phase III double-blind, randomized, placebo-controlled trial to evaluate the

Table 3
Subgroup analysis according to surgery.

Variable		Placebo ($n = 73$)	Lanreotide ($n = 72$)	p-value
Volume of lymphorrhea on postoperative day 4 per sub-group	AD with mastectomy	400 (91–1230) ($n_p = 25$)	335 (62–965) ($n_l = 25$)	0.79[a]
	AD with lumpectomy	315 (0–880) ($n_p = 37$)	267 (1–940) ($n_l = 34$)	0.44[a]
	AD alone	405 (180–680) ($n_p = 11$)	235 (110–405) ($n_l = 13$)	**0.035**[a]
	AD alone + AD with lumpectomy	320 (0–880) ($n_p = 48$)	265 (1–940) ($n_l = 47$)	0.09[a]
Volume of lymphorrhea (ml) on postoperative day 15 per sub	AD with mastectomy	485 (91–2320) ($n_p = 24$†)	465 (62–1635) ($n_l = 25$)	0.92[a]
	AD with lumpectomy	337.5 (80–1344) ($n_p = 36$†)	280 (1–1050) ($n_l = 32$†)	0.48[a]
	AD alone	435 (180–1020) ($n_p = 11$)	281 (110–795) ($n_l = 13$)	0.08[a]
	AD alone + AD with lumpectomy	370 (80–1344) ($n_p = 48$)	280 (1–1050) ($n_l = 47$)	0.12[a]
Volume of lymphorrhea (ml) on postoperative day 30 per subgroup	AD with mastectomy	500 (91–2340) ($n_p = 23$†)	470 (67–2015) ($n_l = 25$)	0.95[a]
	AD with lumpectomy	345 (80–1344) ($n_p = 35$†)	280 (1–1050) ($n_l = 31$†)	0.26[a]
	AD alone	435 (180–1020) ($n_p = 11$)	290 (110–955) ($n_l = 13$)	0.19[a]
	AD alone + AD with lumpectomy	370 (80–1344) ($n_p = 46$†)	280 (1–1050) ($n_l = 43$†)	0.08[a]
Volume of lymphorrhea (ml) on postoperative day 180 per subgroup	AD with mastectomy	453.5 (91–2340) ($n_p = 18$†)	470 (67–2015) ($n_l = 23$†)	0.75[a]
	AD with lumpectomy	370 (120–1990) ($n_p = 33$†)	270 (1–1050) ($n_l = 25$†)	0.06[a]
	AD alone	435 (180–1020) ($n_p = 11$)	290 (110–955) ($n_l = 13$)	0.19[a]
	AD alone + AD with lumpectomy	375 (120–1990) ($n_p = 44$†)	280 (1–1050) ($n_l = 37$†)	**0.015**[a]
Duration of drain (days) per subgroup	AD with mastectomy	4 (3–15) ($n_p = 23$†)	4.5 (4–8) ($n_p = 24$†)	0.85[a]
	AD with lumpectomy	4 (2–11) ($n_p = 37$)	4 (2-9 ($n_l = 34$)	0.09[a]
	AD alone	4 (4–8) ($n_p = 10$†)	4 (2–7) ($n_l = 13$)	0.10[a]
	AD alone + AD with lumpectomy	4 (2–11) ($n_p = 47$†)	4 (2–9) ($n_l = 47$)	**0.02**[a]
Seroma aspiration on postoperative day 15 by subgroup	AD with mastectomy	16 ($n_p = 23$†)	15 ($n_p = 25$†)	0.48[c]
	AD with lumpectomy	9 ($n_p = 36$†)	5 ($n_l = 32$†)	0.33[c]
	AD alone	4 ($n_p = 11$†)	4 ($n_l = 13$†)	1[b]
	AD alone + AD with lumpectomy	13 ($n_p = 47$†)	8 ($n_l = 45$†)	0.25[c]
Seroma aspiration on postoperative day 30 by subgroup	AD with mastectomy	8 ($n_p = 23$†)	11 ($n_p = 24$†)	0.44[c]
	AD with lumpectomy	1($n_p = 35$†)	1 ($n_l = 31$†)	1[b]
	AD alone	1($n_p = 11$†)	2 ($n_l = 13$†)	1[b]
	AD alone + AD with lumpectomy	2 ($n_p = 46$†)	2 ($n_l = 43$†)	1[b]
Seroma aspiration on postoperative day 180 by subgroup	AD with mastectomy	1 ($n_p = 18$†)	1 ($n_l = 24$†)	1[b]
	AD with lumpectomy	0 ($n_p = 34$†)	0 ($n_l = 24$†)	nc
	AD alone	0 ($n_p = 11$†)	0 ($n_l = 12$†)	nc
	AD alone + AD with lumpectomy	0 ($n_p = 45$†)	0 ($n_l = 36$†)	nc

Results are expressed as median (range) or number.
AD = axillary dissection.
Numbers of subjects in analysis can vary due to drop out at day 15, 30 or 180 or by sub-group analysis (†); these numbers are expressed as: n_p = number of subjects in the placebo group; n_l = number of subjects in the lanreotide group. Bold values represent significant results are in bold.
nc: not calculated.
† due to missing data.
[a] Mann Whitney test.
[b] Fisher's exact test.
[c] Chi 2 test.

properties of lanreotide, a prolonged release synthetic somatostatin analogue, in breast cancer surgery. Given our results and its expensive price, it is not possible to currently recommend lanreotide in the prevention of lymphorrhea and seroma formation in breast cancer. However, its potential efficacy in subgroups undergoing AD performed alone or with lumpectomy away from AD needs to be confirmed.

Funding

This study was funded by Ipsen Pharma. Ipsen Pharma was involved in the design of the study and provided logistical support during the trial. Analyses were performed independently and in a blinded manner at the Unité Fonctionnelle de Recherche Clinique et de Biostatistique of the Limoges teaching hospital. Ipsen Pharma was allowed to review the manuscript and to suggest changes, but the final decision on content was exclusively made by the authors.

Conflicts of interest

None.

Acknowledgements

The authors wish thank Julie Grenier and the team of Unité Fonctionnelle de Recherche Clinique et Biostatistique, for managing and analysing the data; the authors also thank the team of DRRCI (Delegation Regionale à la Recherche Clinique et à l'Innovation du Limousin) and of DRI (Direction de la Recherche Clinique et de l'Innovation du CHU de Limoges).

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