Drug Substance Goserelin Study Code NIS-OHU-ZOL-2009/1 Date	**SYNOPSIS**	

PROstaTE Cancer Treatment and Obesity in Zoladex-Astrazeneca patients Non Interventional Study

Study dates
First subject enrolled 26 November 2009
Last subject completed 25 March 2013

Phase of development
Phase IV prospective observational

Objectives

Primary
To define the incidence of biochemical and/or clinical recurrence during the investigation period in obese and normal weight patients treated with goserelin with or without previous curative (RP or RT) treatment.

Secondary
To assess the recurrence rate in normal and overweight patients during goserelin treatment in 3 subsets based on primary curative therapy.
subset 1.: no curative treatment
subset 2.: radical prostatectomy
subset 3.: radiotherapy

Changes in body weight of patients and to assess its impact on the incidence of recurrence.

Assessment of quality of life among obese and normal weight patients using overall satisfaction scale adapted to prostate cancer.

Study design
Prospective, observational, cohort non-interventional study to compare biochemical and clinical recurrence rates of obese versus normal weight prostate cancer patients treated with goserelin.

Target population and sample size
1500 patients with histologically confirmed prostate cancer who:

- undergone curative treatment and being on adjuvant goserelin therapy for at least 1 month
- had not received curative treatment and being goserelin therapy for at least 1 month

Investigational product: dosage, mode of administration
Subcutaneous abdominal injection of goserelin (3.6 mg, once per 28 days or 10.8 mg, once per 3 months)

Duration of treatment
33 months or until progression

Variables
BMI, degree of obesity, clinical recurrence, biochemical recurrence, scale of general satisfaction, change of bodyweight

Statistical methods
Fisher test was used to determine the p-value of the comparative statistical analyses, and Mann-Whitney test to assess the quality of life questionnaires and the change of the bodyweight

Subject population
A total of 1376 patients were enrolled. Out of 1376 involved patients 1198 attended each (12) visits and completed the study.

The mean age of patients was 71.25 (49-98) years. The average body weight was 82.3 (53-115) kg and mean BMI was 27.72 (18-41.4).

Patients were categorized into 2 groups in terms of BMI: non obese (< 25 kg/m^2) patients represented 16.35%, overweight (≥ 25 kg/m^2) patients represented 83.65 % of study population.

Average Total Gleason score was 5.58 (2-10), mean PSA after the primary therapy was 1.61ng/ml and serum testosterone was 14.26 ng/dl.
Majority of enrolled patients had T2 and T3 stage prostate cancer (see Table 1).

Table 1 Clinical classification

Value	N	%
T0	37	2.69
T1	160	11.64
T2	678	49.31
T3	447	32.51
T4	53	3.85
N/A	1	

60.1% of patients had not undergone primary curative treatment (see Table 2).

Table 2 Primary therapy

Value	N	%
Radical prostatectomy	17	1.24
Radiotherapy	325	23.62
Did not occur	839	60.97
No data	195	14.17

Summary of results

Clinical recurrence rate in the full cohort based on physicians written assessment was 1.53% (see Table 3).

Table 3 Clinical recurrence rate

Value	N	%
No	1355	98.47
Yes	21	1.53

Biochemical recurrence rate (defined as difference from NADIR is ≥2 ng/ml) rate in the full cohort was 3.42% (see Table 4).

Table 4 Biochemical recurrence rate

Value	N	%
No	1329	96.58
Yes	47	3.42

Primary endpoint

Overweight patients were significantly less likely to experience clinical and biochemical recurrence (p=0.0133 and p=0.0002 respectively) (see Table 5 and Table 6).

Table 5 Clinical recurrence rate in normal and obese patients

BMI Group	Value	N	%
<25 kg/m^2	No	217	96.44
	Yes	8	3.56
≥ 25 kg/m^2	No	1138	98.87
	Yes	13	1.13

Odds Ratio: 0.3102 (CI 95%: [0.1176, 0.8743]).
The difference between the two groups is significant (p=0.0133)

Table 6 Biochemical recurrence rate in normal and obese patients

Group	Value	N	%
<25 kg/m2	No	207	92
	Yes	18	8
≥25 kg/m2	No	1122	97.48
	Yes	29	2.52

Odds Ratio: 0.2976 (CI 95%: [0.1564, 0.5803]).
The difference between the two groups is significant (p=0.0002).

Secondary endpoints

In radical prostatectomy subgroup there was no significant difference in clinical or biochemical recurrence rate between normal and overweight patients. Although the very small number of patients limits the validity of the result (see Table 2).

In patient group with primary radiotherapy clinical and biochemical recurrence rate was significantly lower in obese men (p=0.0126 and p=0.0242 respectively).

In previously untreated patients clinical recurrence did not differ significantly in normal and overweight groups (p=0.4703), but in terms of biochemical relapse there was significantly lower rate in the higher BMI group (p=0.0021).

In parallel, patients who had clinical or biochemical progression experienced significantly greater weight loss during the study (p=0.0116, p<0.0001 respectively) (see Table 7 and Table 8).

Table 7 Change of bodyweight from baseline to recurrence/final visit (kg)

Clinical recurrence	N	Average	SD	Minimum	Median	Maximum
No	1355	2.85	5.56	−20	4	36
Yes	21	0.67	6.27	−8	0	18

The difference between the two groups is significant (p=0.0116).

Table 8 Change of bodyweight from baseline to recurrence/final visit (kg)

Biochemical recurrence	N	Average	SD	Minimum	Median	Maximum
No	1329	2.94	5.52	−20	4	36
Yes	47	−0.51	6.07	−20	0	18

The difference between the two groups is significant ($p<0.0001$).

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Patients overall satisfaction and quality of life were assessed by validated questionnaires on each visit. Significant difference was demonstrated between normal and obese patient groups favouring obese men in terms of daily activities ($p=0.0137$), general health status ($p<0.0001$) and satisfaction with the current treatment ($p=0.0246$).

Summary of safety results (not applicable)

During the study period side effects have been reported by physicians according to the local rules, however collection of safety data was not the objective of the study.

All patients provided written informed consent, and the study was approved by Hungarian Ministry of Health ETT TUKEB (Scientific and Research Ethics Committee) in accordance with the international standards of good clinical practice.