3 REPORT SUMMARY

3.1 Sponsor identification

IPSEN PHARMA, S.A.
Torre Realia – Plaza Europa 41-43, Planta 7
08908 L'Hospitalet de Llobregat (Barcelona)
PPD

3.2 Title

Post-approval observational prospective study to evaluate the prevalence of the metabolic syndrome in prostate cancer patients both before and after a 12-month treatment with quarterly LHRH analogue formulation (ANAMET Study)

3.3 Code

IPS-TRI-2008-01

3.4 Principal investigator

Dr. Juan Morote
Hospital Vall d'Hebron
Passeig de la Vall d'Hebron 119-129
08035- Barcelona

3.5 Centres

The study was conducted in 48 sites of Spain.

3.6 Ethics Committees

Hospital Vall d'Hebron's ECCR

3.7 Objectives

The objective of this study was to assess the prevalence of the metabolic syndrome in accordance with the NCEP ATP III Panel definition in patients with prostate cancer both before and after 12-month treatment with quarterly LHRH analogue formulations.

3.8 Design

ANAMET was a post-approval observational, prospective, multicentre and open study to assess the prevalence of the metabolic syndrome in patients with prostate cancer both before and after 12-month treatment with quarterly LHRH analogue formulations.

3.9 Disease or disorder under study

Male prostate cancer patients.

3.10 Medicinal product

The patients included in the study received treatment with LHRH quarterly analogues.

The LHRH analogues commercialised in our country are:

- buserelin (9.45 mg quarterly implant; SC injection)
- goserelin (10.8 mg quarterly implant; SC injection)
- leuprorelin (22.5 mg quarterly injection; SC injection)
- leuprorelin (22.5 mg quarterly injection; IM injection)
- triptorelin (11.25 mg quarterly injection; IM injection)

3.11 Study Population and Sample Size

Patients diagnosed with prostate cancer and scheduled to receive a long-term (12 months) treatment with LHRH quarterly analogues.

Patients should give their written informed consent (personally signed and dated) before starting with any study-related procedures, 18 years old or over; should have a histology-confirmed prostate cancer diagnosis, and be eligible for either continuous androgen deprivation therapy or treatment with LHRH analogues in accordance with the specifications of the relevant data sheets for a period of at least 12 months. They also should have an estimated survival expectance of at least 12 months in the investigator's opinion.

Any patient who was having or had previously received androgen deprivation therapy were not eligible for the study.

It was planned to recruit a total of 556 subjects from some 60 Spanish centres.

3.12 Study Calendar

The inclusion of the first patient was foreseen to take place on the first quarter of 2009, and treatment completion by the last patient was foreseen to occur on the first quarter of 2011

The statistical analysis and final study report was ready by the fourth quarter of 2012.

3.13 Financial Source of the Study

As the sponsor of the study, IPSEN PHARMA, S.A met all expenses originated by the same.

3.14 Summary -Conclusions

Results

The study screened 539 patients from 10 December 2008 to 20 October 2009. Out of them 19 (3.5%) did not take any LHRH analogue and accordingly the study / safety population included 520 patients. At the end of the study 452 (83.8% of screened population) patients completed the study, but 310 (59.6% of study / safety population) patients were part of the completer population (patients who completed the study and had all evaluations). Median age of patients was 72 years old (range between 45 and 87).

Mean time from diagnosis to the inclusion was 0.68 years (SD 1.91). A total of 322 (61.9%) presented a Gleason Score between 5 and 7 points, and a 60.2% (313) patients had a TNM classification between T1-2 N0 M0.

Conclusions

In the completer population (patients who completed the study and had all the evaluations) metabolic syndrome was detected in 71 (22.9%) patients at baseline. After 12 months of study treatment, the absolute increased rate of metabolic syndrome from baseline was of 3.9% (12 patients). The prevalence of waist circumference > 102 cm, ST > 150 mg/dL and FPG > 110 mg/dL increased from baseline at 12 months (52.3% to 56.5%, 23.6% to 31.0% and 36.8% to 40.0% respectively), and the prevalence of HDL <40 mg/dL and BP > 130/85 mmHg decreased (16.1% to 13.9% and 33.2% to 31.3% respectively).

After 6 months of study treatment, the absolute increased rate of metabolic syndrome from baseline was of 2.6% (8 patients). The prevalence of waist circumference > 102 cm, ST > 150 mg/dL, FPG > 110 mg/dL and BP >130/85 mmHg increased from baseline at 6 months (52.3% to 52.9%, 23.6% to 28.7%, 36.8% to 42.6% and 33.2% to 33.6% respectively), and the prevalence of HDL <40 mg/dL decreased (16.1% to 9.4%).

In the study / safety and completer populations, patients seemed to show an increase in BMI, weight and abdominal perimeter (mean in the completer population 28.17 kg/m^2 to 28.83 kg/m^2, 78.54 kg to 80.02 kg, and 103.46 cm to 104.67 cm, respectively) (however patients with metabolic syndrome at baseline had a decrease in abdominal perimeter [mean in the completer population 110.69 cm to 109.60 cm]); nevertheless, they seemed to have decreases in the systolic and diastolic blood pressure (mean in the completer population 147.53 mmHg to 146.98 mmHg, and 80.93 mmHg to 79.76 mmHg, respectively).

Regarding laboratory tests for the study / safety population, patients seemed to show a decrease after 6 and 12 months in PSA and total testosterone. Additionally, they seemed to have decreases after 12 months in TSH and C - reactive protein.

Only two patients (0.4%), having metabolic syndrome at baseline experienced LHRH analogue related adverse events during the study, one who took Triptorelin and the other one who took Leuprorelin,. These two Adverse Events were pruritus (1 patient, 0.2%) and pruritus generalized (1 patient, 0.2%) that were serious adverse events and led to withdrawal of the patient.

A total of 14 patients died during treatment, but none of these deaths were considered related to LHRH analogue.

Some metabolic syndrome increase under ADT therapy with GnRH agonists for 1 year, has been observed in this open observational study. The prevalence of metabolic syndrome was high at baseline in this ADT-naïve population, suggesting that other measures unrelated to prostate cancer therapy (such as weight control) are important for reducing the risk of metabolic syndrome in this population. More long-term observational data are needed to elucidate the impact of ADT on metabolic syndrome.

Date of report

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