Clinical Trial Results Summary
Study 303

Study Number: 303

Title of Study: Phase IV, Multicenter, Open-Label Study to Collect Vantas® Implant Retrieval Data from Patients with Advanced Prostate Cancer and Difficult to Remove Implants

Principal Investigator: There is one principal investigator per investigational center.

Study center(s): Planned per protocol in up to 50 U.S. study sites. Actual sites enrolling at least 1 patient: 7 study sites.

Publications (reference): Not applicable

Studied period (weeks):	**Phase of development:** Phase IV
Date first patient enrolled (screening date): July 6, 2006 Data last patient enrolled (screening date): May 8, 2007 Date of last patient completing: June 6, 2007	

Objectives:

The main study objective was to collect implant retrieval information in 10 patients using Vantas®, the 50 mg histrelin implant. Patients who had been identified as having a difficult to locate or non-palpable implant were to have been enrolled. Sites were to adhere to the instructions in the Package Insert, which included specialized investigations such as ultrasound, CT, and MRI, to be used for the location and removal of implants.

Methodology:

Up to 50 centers using Vantas, the recently approved histrelin implant as part of their urology practice for treating patients with advanced prostate cancer, were to be identified for participation in this Phase IV post-marketing trial. Up to 10 patients who had been implanted with Vantas at these participating centers, and who had difficult to locate or non-palpable implants at the time of removal, were to be enrolled in this trial. A Screening Visit was to be conducted to consent the patient and to collect basic medical and safety information for patient participation. Upon patient enrollment, up to 3 subsequent visits (Visits 1, 2, and 3) were to be conducted (within 2 weeks of the Screening Visit). The investigator was to locate and remove the implant by following the instructions provided in the protocol. Methods for location of the implant included ultrasound, CT, or MRI procedures. The visit at which the implant was successfully located and removed was to be the final study visit for the patient. Upon successful retrieval of the implant or a determination that, per Study Instructions, the implant cannot be located/removed, the study was completed for the patient. No information was to be collected on re-implantation of a new implant. Safety was to be monitored throughout the two week study. Blood samples for testosterone and PSA were only collected at the Screening Visit. The implants removed from the patients were to be returned to the Sponsor for analysis.

Number of patients (planned): 10 patients

Number of patients (actual): 12 patients

Diagnosis and main criteria for inclusion:

The study was planned to include approximately 10 patients with locally advanced or metastatic prostate cancer who satisfied the inclusion and exclusion criteria, as follows:

Inclusion Criteria:

Patients were eligible to participate in the study if they:

- Were male patients with adenocarcinoma of the prostate;
- Were age 45 years or older;

- Had received a Vantas implant;
- Had difficult to locate or non-palpable implant at time of implant retrieval;
- Had the ability to undergo ultrasound, and/or CT, and/or MRI within two weeks of Screening Visit;
- Voluntarily provided Informed Consent prior to the performance of any study-specific procedures.

Exclusion Criteria:

Patients were to be excluded from the study if they had:

- Major medical or psychiatric illness that would interfere with return visits; patient not suitable (e.g., noncompliance history) for study in opinion of the Investigator or Sponsor;
- Participated in a clinical trial for an investigational agent within 30 days prior to the Screening Visit (unless enrolled in Protocol 301 Extension).

Test product, dose and mode of administration, batch number: Not applicable

Duration of treatment: 2 weeks (from screening through implant removal)

Reference therapy, dose and mode of administration, batch number: Not applicable

Criteria for evaluation:

Efficacy:

The key presentation of data was to take the form of a series of by-patient narratives. For each patient, a Safety Narrative was written that describes the medical procedures used to locate and retrieve the difficult to locate or non-palpable implant. Each patient's outcome has been classified as "implant successfully retrieved" or "implant not successfully retrieved"; a tabulation of the rate of successful retrievals is presented, as well as an overall summary of the methods used for the successful location of the implants.

Safety:

The following safety determinations were obtained at specified visits:

- Brief physical examination with vital signs
- Clinical laboratory (for testosterone and PSA parameters) assessments
- Ultrasound (as required)
- CT (as required)
- MRI (as required)
- Adverse events, evaluated between Screening Visit and Final Visit (Visit 1 or 2)

Statistical methods: Data were generally presented in by-domain data listings; a medical and statistical review of the data listings was performed.

Baseline Characteristics and Exposure

Descriptive methods used to present these data.

Efficacy

The number (and percent) of successfully located and removed implants was tabulated. By-patient narratives were written that described the methods used to locate and explant the Vantas implants.

Other data were presented in by-domain data listings.

Safety

Safety data were presented in by-domain data listings. As there were only 3 AEs reported in this study, no tabulation of incidence rates was performed. Rather, a brief narrative was written for each AE.

SUMMARY

EFFICACY RESULTS:

For those patients who had the implant *in situ* at enrollment (Patient 010 had his implant expelled prior to enrollment into the study), the number (and percent) of patients with their implant successfully located, retrieved, and for those with the implant successfully located, the method used, is tabulated in Table 1.

Table 1: Number (Percent) of Patients Enrolled *Who Had Implant In situ at Enrollment* with Implant Successfully Located, Retrieved, and Method Used to Locate Implant Prior to Removal – Implant *In situ* Patient Sample (Study 303)

		Patients with Implant *In situ* at Enrollment
		N=11
Implant Successfully Located	Yes	11 (100.0)
	No	0 (0.0)
Implant Successfully Retrieved[1]	Yes	9 (81.8)
	No	2 (18.2)
Method used to *successfully* locate implant (% of Implants Successfully Located)	Ultrasound	11 (100.0)
	CT	0 (0.0)
	MRI	0 (0.0)

[1] Patient 003 was judged by the investigator to be too frail for the implant to be explanted; however, the implant was visualized *in situ.* The implant in Patient 012 was also successfully located; however, the patient chose not to have the implant removed because he felt the removal procedure was too painful. Thus, the implant was not retrieved from this patient.

Thus, all patients in whom the implant was in situ at study entry had their implant successfully located, and all patients who were judged by the investigator to be healthy enough or who could tolerate the explant procedure had their implant extracted successfully. Further, the use of ultrasound was found to be the best prescribed method to locate the implant for removal.

SAFETY RESULTS:

The study was not designed to collect safety on the histrelin implant, but rather to gather implant retrieval information in difficult to locate or non-palpable implants. As part of this evaluation, while patients were enrolled in the study, selected safety information was collected, and included:

- AEs
- Clinical laboratory tests (testosterone and PSA only)
- Brief physical examination with vital signs.

There were 3 AEs reported during this study (all reported for the same patient); mild left renal colic, a urinary tract infection, and a gastrointestinal hemorrhage. None of these events were judged as at least possibly related to the Vantas implant or to the explant procedure. There was 1 SAE (unrelated to study treatment) in this study, and there were no deaths.