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Prescribing decisions should be made based on the approved package insert in the country of prescription.

Sponsor/Company: sanofi-aventis **Drug substance**: XRP6976, previously RP56976 (docetaxel,Taxotere®)	**Study Identifier**: NCT00723086 **Study code**: ARD6563 (XRP6976J-2102)
Title of the study: An extension multicenter phase II open label non-comparative trial of RP56976 administered every three weeks in combination with daily prednisolone for metastatic hormone refractory prostate cancer.	
Study centers: Multicenter study with 19 centers in Japan.	
Study period: Date first patient enrolled: 09-May-2005 Date last patient completed: 18-Sep-2008	
Phase of development: Phase 2	
Objectives: To evaluate the safety of docetaxel administered every three weeks repeatedly for more than 10 cycles in combination with daily prednisolone for metastatic hormone refractory prostate cancer (HRPC).	
Methodology: This was a multicenter, non-comparative, open label phase II study, an extension of the ARD6562 (XRP6976-2102) study and only subjects who completed 10 cycles of treatment were qualified to enter this trial.	
Number of patients: Planned: 42 (actually enrolled 16) Randomized: Not applicable Treated: 15 Efficacy: Not applicable Safety: 15	
Diagnosis and criteria for inclusion: Subjects with hormone refractory prostate cancer who had no alternative therapy who completed 10 cycles of docetaxel administrations in the ARD6562 study and in the opinion of the investigator continued administration of docetaxel was beneficial were included.	
Investigational product: -Docetaxel	
Dose: The same dose at Cycle 10 of the ARD6562-study (i.e. either 70, 60, or 50 mg/m^2) or a dose reduction of 10 mg/m^2 except for the lowest dose of 50 mg/m^2. Dose reductions were made in case of study medication related toxicities (hemorrhage/bleeding, neuropathy, hematological toxicity, other toxicities).	
Administration: Docetaxel was intravenously administered in 60 minutes or longer infusions on Day 1. The administration was repeated every 3 weeks until the subject met the withdrawal criteria defined in the protocol (subject request, investigator decision, life-threatening/toxicity conditions, and/or disease progression).	
Reference therapy: Not applicable	
Dose: Not applicable	
Administration: Not applicable	

Duration of treatment:

Until the subject met the withdrawal criteria.

Duration of observation:

The earliest day among followings 6 weeks (Day 43) from last infusion of docetaxel or start of other anti-cancer HRPC except corticosteroids. Documented date of lost to follow-up.

Criteria for evaluation:

Efficacy:

Not applicable

Safety:

Incidence rate of adverse events on each grade evaluated by National Cancer Institute Common Toxicity Criteria (NCI-CTC) Version 2.0.

Statistical methods:

Efficacy:

Not applicable

Safety:

Safety analysis included frequency of treatment-emergent adverse events (TEAEs) considering the worst grade and was calculated for the safety population, subjects who enrolled in this study and were administered docetaxel. Toxicity grading was decided according to NCI-CTC Version 2.0.

Summary:

Efficacy results:

Not applicable

Safety results:

Treatment-emergent adverse events regardless of relationship to study drug with high incidence ≥ 50% were alopecia (93.3%, 14/15), followed by neutrophils/granulocytes reduction (73.3%, 11/15), leukocytes reduction (73.3%, 11/15), fatigue (73.3%, 11/15), sensory neuropathy (66.7%, 10/15), lymphocyte reduction (60.0%, 9/15), edema (60.0%, 9/15), anorexia (60.0%, 9/15), blood lactate dehydrogenase (LDH) increases (60.0%, 9/15), nail change (53.3%, 8/15), weight gain (53.3%, 8/15), and white blood cell count increases (53.3%, 8/15). Grade ≥3 TEAEs occurred in 2 or more subjects with neutrophils/granulocytes reduction (73.3%, 11/14), leukocytes reduction (53.3%, 8/15), lymphocyte reduction (40.0%, 6/15), infection with grade 3 or 4 neutrophil decrease (20.0%, 3/11), new onset of diabetes mellitus (13.3%, 2/15), and hyponatremia (13.3%, 2/15).

No subjects died during the study.

Serious adverse events (SAEs) were reported in 6 subjects (8 events). In 5 subjects, 5 SAEs were reported (3 infections with grade 3 or 4 neutropenia, 1 febrile neutropenia, and 1 edema) in which a causal relationship with docetaxel could not be ruled out. Unexpected SAEs were reported in 2 subjects (colonic polyp, and compression fracture). In both cases, the causal relationship with study drug was ruled out. The last event was arthritis and the relationship to docetaxel was denied.

There were 4 subjects who discontinued study treatment due to TEAEs. Two of these were discontinued for SAEs, and 1 subject had pneumonitis/pulmonary infiltrates concurrently with SAE and this event was also reported as TEAE leading to study discontinuation. In the other 2 subjects, the TEAEs that caused discontinuation of study treatment were sensory neuropathy (1 subject) and neutrophils/granulocytes reduction (1 subject).

In this study, pneumonitis or pulmonary infiltrates were observed in 26.7% (4/15) of subjects and 1 subject discontinued study treatment due to this adverse event. However, these events were grade 1 or 2, and none of these were reported as SAEs.

In 3 subjects, the dose of docetaxel was reduced. Treatment-emergent adverse events that caused dose reduction were infection with grade 3 or 4 neutrophil reduction, febrile neutrophil reduction, and sensory neuropathy.

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