ZYTIGA® (abiraterone acetate)
Use of ZYTIGA in Patients with Renal Impairment

SUMMARY

- The pharmacokinetics of abiraterone were examined in patients with end-stage renal disease (ESRD) on a stable hemodialysis schedule (N=8) and in matched control subjects with normal renal function (N=8). In the ESRD cohort of the trial, a single 1,000 mg ZYTIGA dose was given under fasting conditions 1 hour after dialysis, and samples for pharmacokinetic (PK) analysis were collected up to 96 hours post dose. Systemic exposure to abiraterone after a single oral 1,000 mg dose did not increase in subjects with end-stage renal disease on dialysis, compared to subjects with normal renal function.[1,2]
- An analysis of the Prostate Cancer Registry (PCR), a prospective, real-world, observational study in patients with metastatic castration-resistant prostate cancer (mCRPC), reported time to progression (TTP) and overall survival (OS) data for 1583 patients receiving initial therapy with either ZYTIGA plus prednisone, enzalutamide, or docetaxel. There were 52 patients with renal impairment receiving ZYTIGA plus prednisone however results were not delineated for this patient population.[3]

CLINICAL DATA

Phase 1 and Pharmacokinetic Study

Marbury et al (2014)[1] evaluated the pharmacokinetics and safety of ZYTIGA in male patients with ESRD on stable hemodialysis and male subjects with normal renal function (N=16).

Study Design/Methods

- Phase 1, open-label, single-dose study
- ZYTIGA 1,000 mg was administered orally after a 6-hour fast; participants maintained fasting for 4 hours after dosing.
- **Study endpoints**: PK parameters, safety and tolerability, clinical laboratory tests, electrocardiogram results, vital signs, and physical examination
- Healthy control subjects with normal renal function were matched to patients with impairment for age and body mass index.
- **Exclusion criteria**: Significant medical history other than renal impairment, acute or exacerbating renal disease, fluctuating or rapidly deteriorating renal function, hypertension (systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥95 mm Hg), or clinically significant laboratory findings except those related to renal impairment

Results

Patient Characteristics

- Men with ESRD (n=8) and matched control men with normal renal function (n=8) were included.
- Mean age in ESRD group: 51 years; mean age in control group: 47 years
- More participants in the ESRD group (n=6) than in the control group (n=2) were black or African American, but otherwise the groups were well matched.

Pharmacokinetics

- No PK analysis was conducted for abiraterone acetate since the plasma concentrations for abiraterone acetate were below the limit for quantification.
- In the PK analysis of abiraterone, 1 patient in the normal renal function group had maximum plasma concentration (C_{max}, 407 ng/mL), area under the curve from the time of dosing to the last measurable concentration ($AUC_{0\text{-last}}$, 1731 ng•h/mL), and area under the curve from the time of dosing extrapolated to infinity ($AUC_{0\text{-}\infty}$, 1768 ng•h/mL) values that were 5-6 times higher than the average values for the remaining 7 subjects with normal renal function.[2]
    - There were no protocol deviations that could account for the elevated systemic exposure to abiraterone in this patient.
- When the data for this patient were excluded, there were no differences in C_{max}, $AUC_{0\text{-last}}$, or $AUC_{0\text{-}\infty}$ between the ESRD and normal renal function groups. See Table: Pharmacokinetic Parameters for Abiraterone in Patients with ESRD or Subjects with Normal Renal Function.

Pharmacokinetic Parameters for Abiraterone in Patients with ESRD or Subjects with Normal Renal Function[1]

Parameter	Mean (SD) Plasma Pharmacokinetic Parameters for Abiraterone	
	ESRD (n=8)	Normal Renal Function (n=7)[a]
C_{max} (ng/mL)	50.2 (37.7)	60.6 (23.5)
T_{max}[b] (hours)	3.0 (1.0, 6.0)	1.50 (1.0, 4.0)
$AUC_{0\text{-last}}$ (ng•h/mL)	305 (267)	307 (108)
$AUC_{0\text{-}\infty}$ (ng•h/mL)	315 (265)	315 (108)
$t_{1/2}$ (hours)	16.0 (2.0)	18.2 (3.7)
CL/F (L/h)	5060 (3034)	3539 (1357)
Vd/F (L)	118,926 (74,377)	88,952 (23,453)

Abbreviations: $AUC_{0\text{-}\infty}$, area under the curve from the time of dosing extrapolated to infinity; $AUC_{0\text{-last}}$, area under the curve from the time of dosing to the last measurable concentration; CL/F, oral clearance; C_{max}, maximum plasma concentration; ESRD, end-stage renal disease; SD, standard deviation; $t_{1/2}$, terminal half-life; T_{max}, time to maximum plasma concentration; Vd/F, apparent volume of distribution.
[a]One patient was excluded from the analysis because of C_{max}, $AUC_{0\text{-last}}$, and $AUC_{0\text{-}\infty}$ values that were 5-6 times higher than the average values for the remaining 7 patients.
[b]Median (minimum, maximum).

- Systemic exposure to abiraterone as assessed by C_{max} appeared to be slightly lower in patients with ESRD than healthy controls with normal renal function. The ratio of the geometric mean estimates for the ESRD group (n=8) compared with the healthy control group (n=8) was 53.1% for C_{max}, 62.8% for $AUC_{0\text{–last}}$, and 65% for $AUC_{0\text{–}\infty}$.[1]

Safety

- There was 1 treatment-emergent adverse event (TEAE) reported in the ESRD group (rhinorrhea).
- No patients discontinued treatment because of TEAEs, and there were no clinically significant changes in hematologic or clinical chemistry laboratory tests, vital sign assessments, or electrocardiograms.
- There were no deaths, life-threatening adverse events (AEs), or serious AEs reported.

Prospective Study

Chowdhury et al (2020)[3] evaluated the outcomes of patients with mCRPC, including those with baseline comorbidities such as renal impairment, receiving initial therapy with either ZYTIGA plus prednisone, enzalutamide, or docetaxel utilizing the PCR (n=1583).

Study Design/Methods

- Prospective, international, multicenter, real-world, observational study of 3003 patients with mCRPC and a history of progression despite testosterone <50 ng/dL, androgen deprivation therapy, and/or history of orchiectomy in routine clinical practice (NCT02236637).
- This analysis of the PCR evaluated patients treated with ZYTIGA plus prednisone or prednisolone, enzalutamide, docetaxel, other chemotherapy, or radium-223 as initial therapy for mCRPC.
- **Outcome measures:** TTP and OS

Results

Patient Characteristics

- Patients treated with other chemotherapy or radium-223 were excluded because the number of patients were too low.
- Select baseline characteristics for the patients who had not received previous mCRPC treatment at baseline and patients treated with first-line ZYTIGA plus prednisone are reported below in Table: Patient Characteristics.

Patient Characteristics[3]

	Patients who had not Received Previous mCRPC Treatment at Baseline (n=1874)	Patients treated with First-Line ZYTIGA plus Prednisone (n=754)
Mean age, years (SD)	73.1 (8.58)	75.3 (8.20)
Gleason score 8-10[a], n (%)	949 (55.4)	344 (51.0)
ECOG performance status ≥2, n (%)	189 (10.9)	57 (8.0)
Bone metastases ≥5, n (%)	548 (39.3)	203 (36.9)
Select Baseline Comorbidities Requiring Treatment, n (%)		
Renal	143 (7.6)	52 (6.9)
Chronic renal disease	82 (4.4)	31 (4.1)
Other renal	62 (3.3)	21 (2.8)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; mCRPC, metastatic castration-resistant prostate cancer; SD, standard deviation.
[a]At initial diagnosis.

Efficacy and Safety

- The median treatment duration was 11.2 months (95% CI, 9.8-12.2) and 11.5 months (95% CI, 9.1-16.1) in all patients receiving ZYTIGA plus prednisone.
- Outcomes for the total population included in the registry receiving ZYTIGA plus prednisone are reported below in Table: Efficacy Outcomes for Patients with mCRPC that Received ZYTIGA plus Prednisone.
- Safety data were not reported.

Efficacy Outcomes for Patients with mCRPC that Received ZYTIGA plus Prednisone[3]

	All Patients Receiving ZYTIGA plus Prednisone (n=754)
Median TTP, months (95% CI)	9.6 (8.4-10.8)
Median OS, months (95% CI)	27.1 (25.3-28.9)

Abbreviations: CI, confidence interval; OS, overall survival; TTP, time to progression.

Case Reports

A case report describes the use of ZYTIGA plus prednisone in 2 patients with mCRPC previously treated with chemotherapy and concurrent chronic kidney disease.[4]

The use of ZYTIGA plus prednisone in a patient on hemodialysis with mCRPC and chronic renal failure is presented in a case report.[5]

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 05 March 2025.

REFERENCES

1. Marbury T, Lawitz E, Stonerock R, et al. Single-dose pharmacokinetic studies of abiraterone acetate in men with hepatic or renal impairment. *J Clin Pharmacol*. 2014;54(7):732-741.

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3. Chowdhury S, Bjartell A, Lumen N, et al. Real-world outcomes in first-line treatment of metastatic castration-resistant prostate cancer: the prostate cancer registry. *Target Oncol*. 2020;15(3):301-315.

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