YONDELIS® (trabectedin)
Use of YONDELIS in Patients with Renal Impairment

SUMMARY

- Mild to moderate renal impairment is not associated with a clinically significant effect on the pharmacokinetics (PK) of YONDELIS.[1]
- No dose adjustment is recommended in patients with mild (creatinine clearance [CL_{cr}] of 60 to 89 mL/min) or moderate (CL_{cr} of 30 to 59 mL/min) renal impairment.[1] In a meta-analysis of 5 phase 1 and 9 phase 2 studies involving 603 cancer patients, mild to moderate (CL_{cr} of 30 to 89 mL/min) renal impairment did not influence YONDELIS PK.[1,2]
- The PK of YONDELIS has not been evaluated in patients with severe renal impairment (CL_{cr} <30 mL/min) or end stage renal disease. The effects of severe renal impairment or end stage renal disease on YONDELIS exposure are unknown.[1]
- Hemodialysis is not expected to enhance the elimination of YONDELIS because it is highly bound to plasma proteins (97%) and not significantly renally excreted.[1]
- In a case report involving a cancer patient on hemodialysis, a standard dose of YONDELIS (1.5 mg/m^2) was associated with approximately double the median values of maximum plasma concentration (C_{max}) and exposure (ie, area under the plasma concentration [AUC]) and half the total body clearance of a person without renal impairment.[3]
- Please refer to the WARNINGS AND PRECAUTIONS, USE IN SPECIFIC POPULATIONS, OVERDOSAGE, and CLINICAL PHARMACOLOGY sections of the full Prescribing Information.[1]

CLINICAL DATA

Meta-Analysis

In a meta-analysis of 5 phase-1 and 9 phase-2 studies involving 603 cancer patients, CL_{cr} was not statistically related to YONDELIS PK parameters.[2]

Case Report

A 59-year old woman with retroperitoneal myxoid liposarcoma and chemotherapy-related kidney failure (CL_{cr} of 6 mL/min and 450 mL/day residual diuresis) was treated with a standard dose of YONDELIS 1.5 mg/m^2 as a 24-hour infusion every 3 weeks and was pretreated with intravenous dexamethasone 20 mg. PK analysis of dialysate samples in the patient showed a higher C_{max}, lower elimination half-life, and lower volume of distribution compared with published PK data from a patient population with normal renal function (ie, control population). In addition, the AUC of the patient was twice that of the median value of the control population. Her total body clearance was half that of the median value of the control group. Results from the dialyzer indicated that levels of YONDELIS were below the limit for quantification, indicating a very low ability to extract YONDELIS from the blood.[3]

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, Derwent Drug File (and/or other resources, including internal/external databases) was conducted on 18 September 2024.

REFERENCES

1. YONDELIS (trabectedin) [Prescribing Information]. Horsham, PA: Janssen Products, LP;https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/YONDELIS-pi.pdf.

2. Perez-Ruixo JJ, Zannikos P, Hirankam S, et al. Population pharmacokinetic meta-analysis of trabectedin (ET-743, Yondelis) in cancer patients. *Clin Pharmacokinet*. 2007;46(10):867-884.

3. Thariat J, Etienne-Grimaldi MC, Launay-Vacher V, et al. Pharmacokinetics of trabectedin on hemodialysis: an application for the management of cancer patients with end-stage renal disease. *Cancer Chemother Pharmacol*. 2011;68(5):1363-1367.