# Pharmacokinetics of Oxaliplatin in a Hemodialyzed Patient: Chemotherapy Dose Adjustment and Timing of Dialysis

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## Clinical Practice Points

- There are no data on the optimal dose adjustment of oxaliplatin and timing of dialysis session when treating colorectal cancer patients who require hemodialysis.
- We report pharmacokinetics of oxaliplatin in a colorectal cancer patient who received the FLOX (5-fluorouracil, leucovorin, and oxaliplatin) regimen while hemodialysis-dependent. Oxaliplatin was administered with a dose reduction of 50% and a dialysis session was started 1.5 hours after the end of the oxaliplatin infusion. With these measures we observed a clinically meaningful exposure to the drug with no relevant toxicity and no need for dose delays.
- Based on our data, for colorectal cancer patients who are hemodialysis-dependent we suggest a 50% reduction of biweekly oxaliplatin, keeping the standard 2-week interval between infusions and performing a dialysis session on the same day of the oxaliplatin administration.

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## Introduction

In colorectal cancer the combination of oxaliplatin with a fluoropyrimidine represents the standard adjuvant treatment and is also a widely used chemotherapy backbone for the addition of biologic drugs in the metastatic setting.[1]

Oxaliplatin is mainly eliminated through the kidneys and its pharmacokinetic profile is altered in patients with renal insufficiency, with a strong correlation between glomerular filtration rate (GFR) and drug clearance and also between GFR and oxaliplatin area under the curve (AUC) in patients with different degrees of impaired renal function.[2] However, only limited data are available on oxaliplatin pharmacokinetics, efficacy, and safety in cancer patients who are dependent on hemodialysis.[3-5] Therefore, it is still unclear if oxaliplatin can be safely prescribed and if a dose reduction is necessary in hemodialysis patients.[6]

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## Case Report

We report the oxaliplatin pharmacokinetic profile from a 55-year-old male patient with a pelvic recurrence of colorectal adenocarcinoma that caused bilateral ureteral obstruction and consequent chronic renal failure despite percutaneous nephrostomies, with necessity of hemodialysis 3 times a week. In September 2013, the FLOX (5-fluorouracil 500 mg/m$^2$ intravenous [I.V.] bolus and leucovorin 500 mg/m$^2$ I.V. over 2 hours weekly for 6 weeks every 8 weeks, with oxaliplatin 85 mg/m$^2$ over 2 hours in weeks 1, 3, and 5 of each 8-week cycle) regimen was started for the patient, with an oxaliplatin dose reduction of 50% (ie, 42.5 mg/m$^2$) corresponding to an oxaliplatin total dose of 85 mg. On the same day of oxaliplatin administration, 1.5 hour after the end of drug infusion the patient received a 3.5-hour dialysis session with an acrylonitrile and sodium methallyl sulfonate copolymer membrane (Nephral 300, Gambro-Lund-Sweden). The blood flow rate was 220 mL/min and the bicarbonate-buffered dialysate flow rate was 500 mL/min.

Pharmacokinetics blood samples were collected on the day of the second administration of oxaliplatin, at the following times: before the beginning and at the end of drug infusion, 15, 30, and 90 minutes, 3, 5, 24, and 48 hours after the end of the infusion. Total and ultrafilterable platinum (free-Pt) plasma concentrations were analyzed using inductively coupled plasma mass spectrometry.


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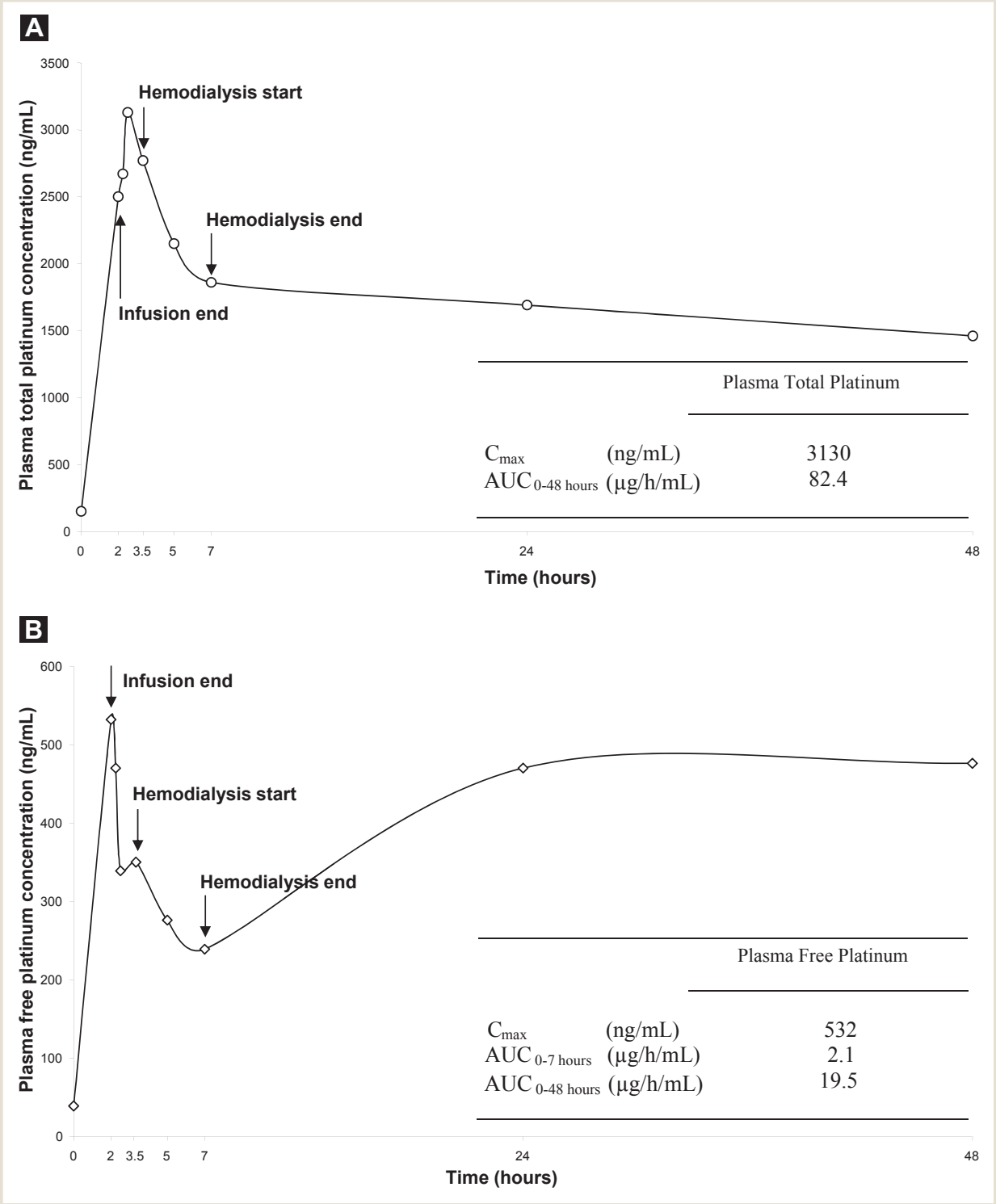
Free-Pt concentration reached a maximum concentration ($C_{max}$) of 532 ng/mL at the end of the infusion (Figure 1) and quickly declined during the next 30 minutes. Afterward, the concentration remained stable until hemodialysis was started, decreased during hemodialysis, and increased again after the end of the dialysis session.

**Figure 1** (A) Plasma Total Platinum Concentration Time Curve, and (B) Plasma Free Platinum Concentration Time Curve




Abbreviations: AUC = Area Under the Curve; $C_{max}$ = Maximum Concentration.