



• Serious allergic reactions. See "What is the most important information I should know about Oxaliplatin for injection?"
• Confusion or a change in the way you think
• Seizures
• Vision problems, such as blurriness or vision loss. You should not drive, operate heavy machinery, or engage in dangerous activities if you have vision problems while receiving Oxaliplatin for injection.

Table 14 - Adverse Hepatic - Clinical Chemistry Abnormalities in Previously Treated Patients (≥5% of patients)
Table with columns: Clinical Chemistry, 5-FU/FLU (N=142), Oxaliplatin for Injection + 5-FU/FLU (N=152). Rows include ALT (SGPT-ALAT), AST (SGOT-ASAT), Total Bilirubin.

6.2 Postmarketing Experience
The following adverse reactions have been identified during post-approval use of Oxaliplatin for Injection...
6.3 Immune-mediated Adverse Reactions
6.4 Renal Impairment
6.5 Reproductive Toxicity

≥65 years of age receiving the Oxaliplatin for Injection combination therapy experienced more Grade 3-4 granulocytopenia than patients <65 years of age (45% versus 39%).
In the previously untreated for advanced colorectal cancer randomized clinical trial (see Clinical Studies (14)) of Oxaliplatin for Injection, 163 patients treated with Oxaliplatin for Injection and 5-fluorouracil/leucovorin were <65 years and 99 patients were ≥65 years...

8.6 Patients with Renal Impairment
The exposure (AUC) of unbound platinum in plasma ultrafiltrate tends to increase in renal impaired patients (see Pharmacokinetics (12.3)). Caution and close monitoring should be exercised when Oxaliplatin for Injection is administered to patients with renal impairment.

10 OVERDOSSAGE
There is no known antidote for Oxaliplatin for Injection overdose. In addition to thrombocytopenia, the anticipated complications of an Oxaliplatin for Injection overdose include hypersensitivity reaction, myelosuppression, nausea, vomiting, diarrhea and neurotoxicity.

Testicular damage, characterized by degeneration, hypoplasia, and atrophy, was observed in dogs administered oxaliplatin at 0.75 mg/kg/day x 5 days every 28 days for three cycles. A no effect level was not identified. This daily dose is approximately one-sixth of the recommended human dose on a body surface area basis.

14.1 Combination Adjuvant Therapy with Oxaliplatin for Injection and Infusional 5-Fluorouracil/Leucovorin in Patients with Colon Cancer
An international, multicenter, randomized study compared the efficacy and evaluated the safety of Oxaliplatin for Injection in combination with an infusional schedule of 5-fluorouracil/leucovorin to infusional 5-fluorouracil/leucovorin alone, in patients with Stage II (Dukes' B2) or III (Dukes' C) colon cancer who had undergone complete resection of the primary tumor...

Table 15 - Dosing Regimens in Adjuvant Therapy Study
Table with columns: Treatment Arm, Dose, Regimen. Rows include Oxaliplatin for Injection + 5-FU/FLU (N=1123), 5-FU/FLU (N=1123).

The following tables show the baseline characteristics and dosing of the patient population entered into this study. The baseline characteristics were well balanced between arms.

Table 16 - Patient Characteristics in Adjuvant Therapy Study
Table with columns: Oxaliplatin for Injection + infusional 5-FU/FLU (N=1123), Infusional 5-FU/FLU (N=1123). Rows include Sex: Male (%), Female (%), Median age (years), etc.

Table 17 - Dosing in Adjuvant Therapy Study
Table with columns: Oxaliplatin for Injection + Infusional 5-FU/FLU (N=1108), Infusional 5-FU/FLU (N=1111). Rows include Median Relative Dose Intensity (%), 5-FU, Oxaliplatin for Injection, etc.

Table 18 - Summary of DFS analysis - ITT analysis
Table with columns: Oxaliplatin for Injection + Infusional 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Overall, Stage III (Dukes' C), Stage II (Dukes' B2).

Table 19 - Summary of OS analysis - ITT analysis
Table with columns: Oxaliplatin for Injection + Infusional 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Overall, Stage III (Dukes' C), Stage II (Dukes' B2).

Table 20 - Dosing Regimens in Refractory and Relapsed Colorectal Cancer Clinical Trial
Table with columns: Treatment Arm, Dose, Regimen. Rows include Oxaliplatin for Injection + 5-FU/FLU (N=152), 5-FU/FLU (N=151), Oxaliplatin for Injection (N=150).

Table 21 - Patient Demographics in Patients Previously Untreated for Advanced Colorectal Cancer Clinical Trial
Table with columns: Oxaliplatin for Injection + 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Sex: Male (%), Female (%), Median age (years), etc.

Table 22 - Summary of DFS analysis - ITT analysis
Table with columns: Oxaliplatin for Injection + Infusional 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Overall, Stage III (Dukes' C), Stage II (Dukes' B2).

Table 23 - Summary of OS analysis - ITT analysis
Table with columns: Oxaliplatin for Injection + Infusional 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Overall, Stage III (Dukes' C), Stage II (Dukes' B2).

Disease-free survival at 5 years
A hazard ratio of less than 1.00 favors Oxaliplatin for Injection + Infusional 5-Fluorouracil/Leucovorin

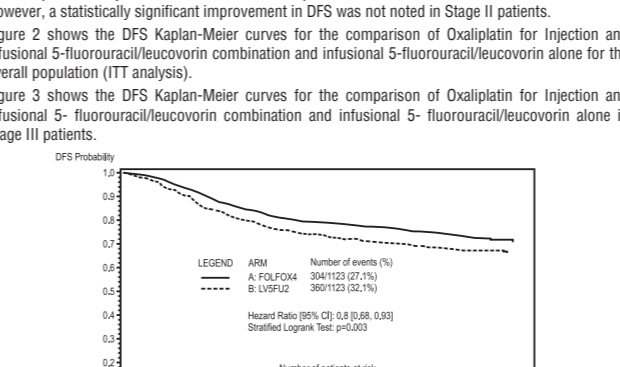


Figure 2 - DFS Kaplan-Meier curves by treatment arm (cutoff: 1 June 2006) - ITT population

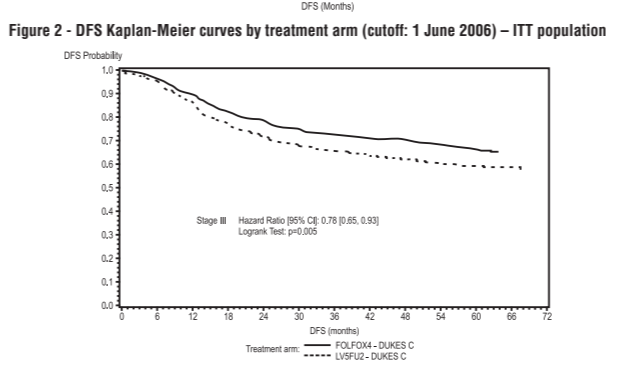


Figure 3 - DFS Kaplan-Meier curves by treatment arm (cutoff: 1 June 2006) - ITT population

The following table summarizes the overall survival (OS) results in the overall randomized population and in patients with Stage II and III disease, based on the ITT analysis.

Table 24 - Patient Demographics in Refractory and Relapsed Colorectal Cancer Clinical Trial
Table with columns: Oxaliplatin for Injection + 5-FU/FLU (N=151), Oxaliplatin for Injection (N=150). Rows include Sex: Male (%), Female (%), Median age (years), etc.

4.1.2 Combination Therapy with Oxaliplatin for Injection and 5-Fluorouracil/Leucovorin in Patients Previously Untreated for Advanced Colorectal Cancer
A North American, multicenter, open-label, randomized controlled study was sponsored by the National Cancer Institute (NCI) as an intergroup study led by the North Central Cancer Treatment Group (NCCTG).

Table 25 - Dosing Regimens in Patients Previously Untreated for Advanced Colorectal Cancer Clinical Trial
Table with columns: Treatment Arm, Dose, Regimen. Rows include Oxaliplatin for Injection + 5-FU/FLU (N=152), 5-FU/FLU (N=151), Oxaliplatin for Injection (N=150).

Table 26 - Patient Demographics in Patients Previously Untreated for Advanced Colorectal Cancer Clinical Trial
Table with columns: Oxaliplatin for Injection + 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Sex: Male (%), Female (%), Median age (years), etc.

Table 27 - Summary of DFS analysis - ITT analysis
Table with columns: Oxaliplatin for Injection + Infusional 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Overall, Stage III (Dukes' C), Stage II (Dukes' B2).

Table 28 - Summary of OS analysis - ITT analysis
Table with columns: Oxaliplatin for Injection + Infusional 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Overall, Stage III (Dukes' C), Stage II (Dukes' B2).

Table with columns: Parameter, Oxaliplatin for Injection + 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Prior surgery (%), Prior adjuvant (%).

Table 22 - Summary of Efficacy
Table with columns: Oxaliplatin for Injection + 5-FU/FLU (N=267), Irinotecan + 5-FU/FLU (N=264), Oxaliplatin for Injection + Irinotecan (N=264). Rows include Survival (ITT), Median survival (months), Hazard Ratio and (95% confidence interval), etc.

Table 23 - Dosing Regimens in Refractory and Relapsed Colorectal Cancer Clinical Trial
Table with columns: Treatment Arm, Dose, Regimen. Rows include Oxaliplatin for Injection + 5-FU/FLU (N=152), 5-FU/FLU (N=151), Oxaliplatin for Injection (N=150).

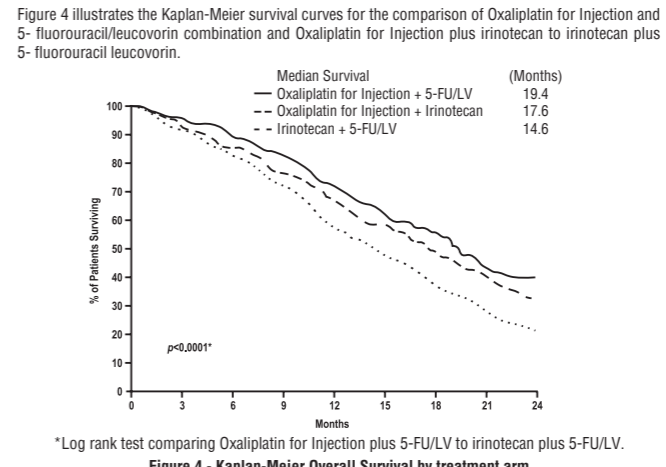


Figure 4 - Kaplan-Meier Overall Survival by treatment arm

4.1.3 Combination Therapy with Oxaliplatin for Injection and 5-Fluorouracil/Leucovorin in Previously Treated Patients with Advanced Colorectal Cancer
A multicenter, open-label, randomized, three-arm controlled study was conducted in the US and Canada comparing the efficacy and safety of Oxaliplatin for Injection in combination with infusional 5-fluorouracil/leucovorin to irinotecan plus 5-fluorouracil/leucovorin.

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Table with columns: Parameter, Oxaliplatin for Injection + 5-FU/FLU (N=151), Oxaliplatin for Injection (N=150). Rows include ≥2 Liver involvement (%), Liver only, Liver + other.

Table 25 - Response Rates (ITT Analysis)
Table with columns: Best Response, 5-FU/FLU (N=151), Oxaliplatin for Injection (N=150), Oxaliplatin for Injection + 5-FU/FLU (N=152). Rows include CR, PR, p-value, 95% CI.

Table 26 - Summary of Radiographic Time to Progression\*
Table with columns: Arm, 5-FU/FLU (N=151), Oxaliplatin for Injection (N=150), Oxaliplatin for Injection + 5-FU/FLU (N=152). Rows include No. of Progressors, No. of patients with no radiological evaluation beyond baseline, Median TTP (months), 95% CI.

\* This is not an ITT analysis. Events were limited to radiographic disease progression documented by independent review of radiographs. Clinical progression was not included in this analysis, and 18% of patients were excluded from the analysis based on unavailability of the radiographs for independent review.

11.1 NCIHS Alert: Preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings. 2004. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165.

16 HOW SUPPLIED/STORAGE AND HANDLING
Oxaliplatin for Injection, USP is supplied in clear, glass, single-use vials with gray elastomeric stoppers and aluminum flip-off seals containing 50 mg or 100 mg of oxaliplatin as a sterile, preservative-free lyophilized powder for reconstitution. Lactose monohydrate is also present as an inactive ingredient.

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16.2 Storage
Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

16.3 Handling and Disposal
As with other potentially toxic anticancer agents, care should be exercised in the handling and preparation of intrusions solutions prepared from Oxaliplatin for Injection. The use of gloves is recommended.

17 PATIENT COUNSELING INFORMATION
17.1 Information for Patients
Patients and patients' caregivers should be informed of the expected side effects of Oxaliplatin for Injection, particularly its neurologic effects, both the acute, reversible effects and the persistent neurosensory toxicity.

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