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#### *YERVOY with nivolumab:*

When YERVOY 1 mg/kg was administered in combination with nivolumab 3 mg/kg every 3 weeks, the CL of ipilimumab was unchanged compared to when YERVOY was administered alone.

When YERVOY 1 mg/kg every 6 weeks was administered in combination with nivolumab 3 mg/kg every 2 weeks, the CL of ipilimumab increased by 30% compared to YERVOY administered alone and the CL of nivolumab was unchanged compared to nivolumab administered alone.

When administered in combination, the CL of ipilimumab was unchanged in the presence of anti-ipilimumab antibodies and the CL of nivolumab increased by 20% in the presence of anti-nivolumab antibodies.

#### **Specific Populations**

The effects of various covariates on the PK of ipilimumab were assessed in population PK analyses. The CL of ipilimumab increased with increasing body weight supporting the recommended body weight (mg/kg) based dosing. The following factors had no clinically important effect on the CL of ipilimumab: age (range: 23 to 88 years), sex, performance status, renal impairment, mild hepatic impairment, previous cancer therapy, and baseline lactate dehydrogenase (LDH) levels. The effect of race was not examined due to limited data available in non-Caucasian ethnic groups.

*Renal Impairment:* The effect of renal impairment on the CL of ipilimumab was evaluated in patients with mild (GFR  $<90$  and  $\geq 60$  mL/min/1.73 m<sup>2</sup>; n=349), moderate (GFR  $<60$  and  $\geq 30$  mL/min/1.73 m<sup>2</sup>; n=82), or severe (GFR  $<30$  and  $\geq 15$  mL/min/1.73 m<sup>2</sup>; n=4) renal impairment compared to patients with normal renal function (GFR  $\geq 90$  mL/min/1.73 m<sup>2</sup>; n=350) in population PK analyses. No clinically important differences in the CL of ipilimumab were found between patients with renal impairment and patients with normal renal function [see *Use in Specific Populations (8.6)*].

*Hepatic Impairment:* The effect of hepatic impairment on the CL of ipilimumab was evaluated in patients with mild hepatic impairment (n=76) compared to patients with normal hepatic function (n=708) in the population PK analyses, and no clinically important differences in the CL of ipilimumab were found. YERVOY has not been studied in patients with moderate or severe hepatic impairment [see *Use in Specific Populations (8.7)*].

*Pediatric Population:* [see *Use in Specific Populations (8.4)*].



































