

Hematologic Toxicity of Valganciclovir Prophylaxis in Solid Organ Transplant Recipients As a Function of Weight-adjusted Ganciclovir Exposure

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BACKGROUND:

- Valganciclovir (VGC), an orally bioavailable prodrug of ganciclovir (GCV), is the preferred agent for cytomegalovirus (CMV) prophylaxis in solid organ transplant (SOT) recipients
- Manufacturer-recommended VGC dosing includes adjustments for CrCl but not weight (wt)
- Patients exposed to excess GCV by not wt-adjusting VGC doses may be at increased risk of toxicity

METHODS:

Study Design: Retrospective Cohort Study at three large academic medical centers

Inclusion Criteria: Adult SOT patients receiving CMV prophylaxis with valganciclovir (8/1/2016-9/30/2019)

Exclusion Criteria: Dialysis-dependence, ganciclovir exposure (>5 consecutive days), active CMV infection

Primary Outcome: Time to first occurrence of neutropenia (ANC <1.5 K/mm³) within 6 months post-transplant

Secondary Outcome: Time to first occurrence of leukopenia (WBC <3.0 K/mm³) within 6 months post-transplant

RESULTS

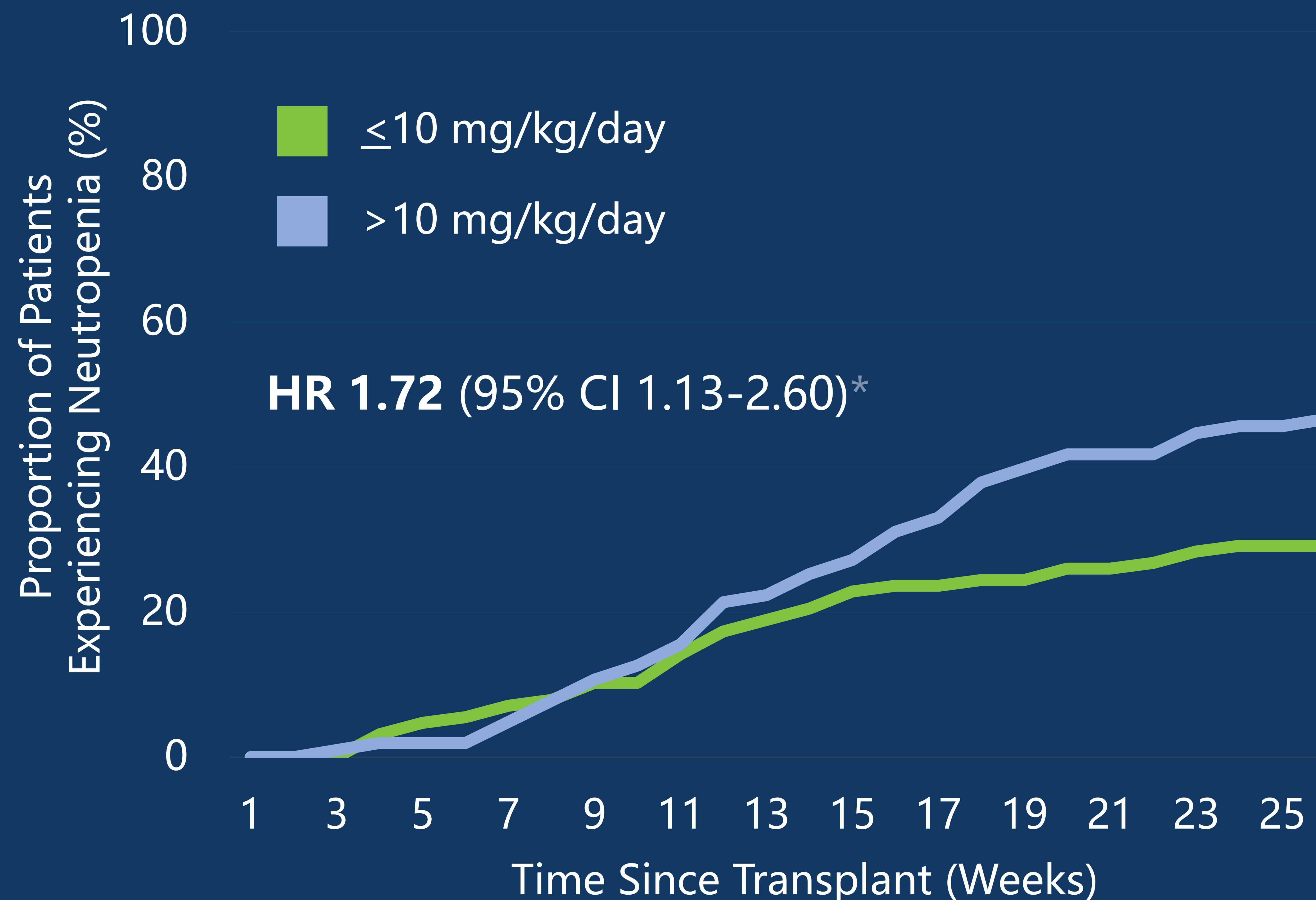
Cox proportional hazard analysis of weight-adjusted valganciclovir exposure (>10 mg/kg vs ≤10 mg/kg)

All Patients	HR	95% CI	P-Value
Neutropenia	1.72	1.13-2.60	0.01

Sub-groups	HR	95% CI	P-Value
Kidney Only	3.66	1.59-8.42	<0.001
Non-Kidney Only	1.09	0.64-1.86	0.75
Lung Only	0.66	0.34-1.30	0.237
Non-Lung Only	3.21	1.89-5.45	<0.001

Higher weight-adjusted valganciclovir exposure was associated with an increased risk of neutropenia in solid organ transplant patients receiving CMV prophylaxis.

Time to First Neutropenia Post-Transplant



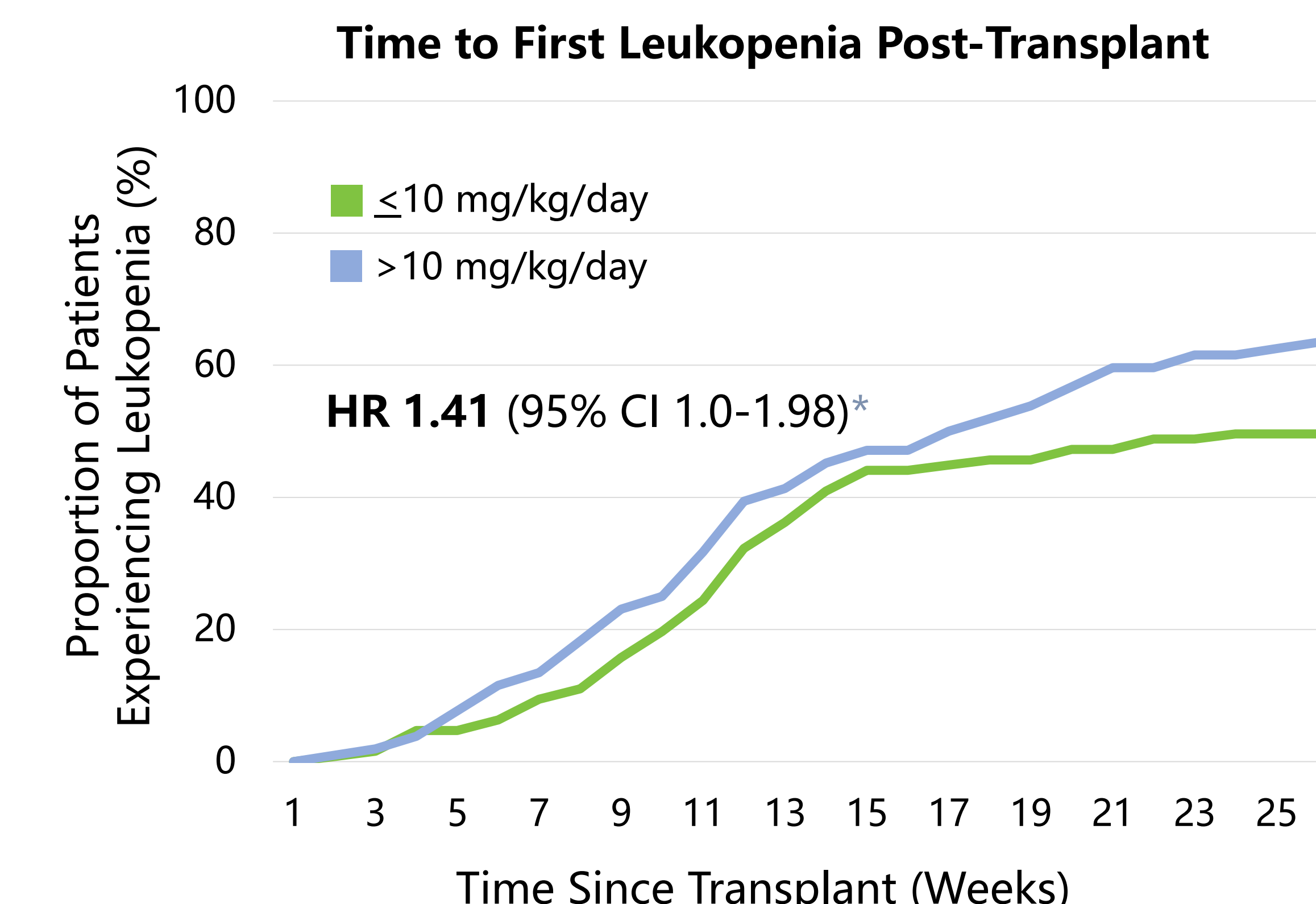
*Cox proportional hazard analysis of weight-adjusted valganciclovir exposure (≤10 mg/kg) associated with time to first occurrence of neutropenia (P=0.01)

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SECONDARY OUTCOME:



*Cox proportional hazard analysis of weight-adjusted valganciclovir exposure (≤10 mg/kg) associated with time to first occurrence of leukopenia (P=0.049)

POPULATION DEMOGRAPHICS:

	VGC ≤10 mg/kg/d N=127	VGC >10 mg/kg/d N=104
Age (median)	61 years	59.7 years
Sex (% Male)	67.7%	50.0%
UCSF	5.5%	23.1%
UC Davis	15.8%	27.9%
Temple	78.7%	49.0%
Initial CrCl (median)	36.3 mL/min	61.9 mL/min
VGC dose (median)	5.7 mg/kg/d	12.2 mg/kg/d
VGC dose (median)	450 mg/d	900 mg/d
Weight (median)	90 kg	73.8 kg
Lung	27.6%	51%
Kidney	18.1%	36.5%
Heart-Lung	37%	1.0%
Heart	8.7%	2.9%
Other	8.7%	8.6%

P-values <0.05 for all categories other than Age (p=0.06)