

Supplementary Information

Half-dose Glucarpidase as Efficient Rescue for Toxic Methotrexate Levels in Patients with Acute Kidney Injury Cancer Chemotherapy and Pharmacology

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Supplemental Table 1: Folinic Acid Rescue in HDMTX ($\geq 0.1 \text{ g/m}^2$ to $\leq 4 \text{ g/m}^2$ and ≤ 4 hours infusion time), warning signs and indicators for glucarpidase treatment

Time from start of MTX infusion [h]	Blood sampling (MTX level, creatinine)	Folinic acid administration	MTX level [$\mu\text{mol/L}$]	Folinic acid dose [#]	Warning signs for potentially protracted MTX clearance	Strong indicators for treatment with glucarpidase (modified from [8])
24	X	X		15 mg/m ²	MTX > 10 $\mu\text{mol/L}$ or increase in creatinine >25% from baseline	MTX > 30 $\mu\text{mol/L}$ \pm creatinine > 25% from baseline
30		X	<10 >10	15 mg/m ² 100 mg/m ²		MTX > 10 $\mu\text{mol/L}$ or increase in creatinine >50% from baseline
36		X				
42	X	X				MTX > 10 $\mu\text{mol/L}$ \pm creatinine > 50% from baseline
48	X	X	<0.1 ≥ 0.1 to <1.0 ≥ 1.0 to ≤ 5.0 >5.0	Stop rescue 15 mg/m ² 100 mg/m ² MTX level x bodyweight [kg]	MTX > 1 $\mu\text{mol/L}$ or increase in creatinine >50% from baseline	MTX > 5 $\mu\text{mol/L}$ \pm creatinine > 50% from baseline
54		X				
60		X				
66		X				
72	X	X				
78		X	<0.1 ≥ 0.1 to <0.4 ≥ 0.4 to ≤ 5.0 >5.0	Stop rescue 15 mg/m ² 100 mg/m ² MTX level x bodyweight [kg]	MTX > 0.1 $\mu\text{mol/L}$ or increase in creatinine >50% from baseline	
84		X				
90		X				
96	X	X				
102		X				
108		X				

Continue blood sampling (MTX level and serum creatinine once a day) and folinic acid rescue every 6 hours as per time point t = 96 h until MTX <0.1 $\mu\text{mol/L}$

[#] In the event of glucarpidase treatment, the dose of folinic acid should be reduced to 100 mg/m² after glucarpidase injection as LC/MS results are not available for dose calculation at short notice.

Supplemental Table 2: Folinic Acid Rescue in HDMTX ($\geq 0.5 \text{ g/m}^2$ to $\leq 1.5 \text{ g/m}^2$ and 24 hours infusion time)^a, warning signs and indicators for glucarpidase treatment

Time from start of MTX infusion [h]	Blood sampling: MTX level	Blood sampling: creatinine	MTX level [$\mu\text{mol/L}$]	Folinic acid dose #	Warning signs for potentially protracted MTX clearance	Strong indicators for treatment with glucarpidase (modified from [8])
24	X	X	<150	-	MTX $\geq 150 \mu\text{mol/L}$ or increase in creatinine >25% from baseline	
			≥ 150	-		
36	X		<3	0 mg/m^2	MTX $\geq 3 \mu\text{mol/L}$	MTX > 30 $\mu\text{mol/L}$ \pm creatinine > 50% from baseline
			≥ 3	30 mg/m^2		
42	X		<1	30 mg/m^2	MTX $\geq 2 \mu\text{mol/L}$	MTX > 10 $\mu\text{mol/L}$ \pm creatinine > 50% from baseline
			≥ 1 to <2	30 mg/m^2		
			≥ 2 to <3	45 mg/m^2		
			≥ 3 to <4	60 mg/m^2		
			≥ 4 to <5	75 mg/m^2		
48	X	X	<0.4	15 mg/m^2	MTX $\geq 1 \mu\text{mol/L}$ or increase in creatinine >25% from baseline	MTX > 5 $\mu\text{mol/L}$ \pm creatinine > 50% from baseline
			≥ 0.4 to <1	15 mg/m^2		
			≥ 1 to <2	30 mg/m^2		
			≥ 2 to <3	45 mg/m^2		
			≥ 3 to <4	60 mg/m^2		
			≥ 4 to <5	75 mg/m^2		
54	X		<0.25	15 mg/m^2 , then stop rescue	MTX $\geq 0.25 \mu\text{mol/L}$	
			≥ 0.25 to <1	15 mg/m^2		
			≥ 1 to <2	30 mg/m^2		
			≥ 2 to <3	45 mg/m^2		
			≥ 3 to <4	60 mg/m^2		
			≥ 4 to <5	75 mg/m^2		
			≥ 5	MTX level x bodyweight [kg]		

Continue blood sampling (MTX level every 6 hours, serum creatinine once a day) and folinic acid rescue every 6 hours as per time point t=54 h until MTX <0.25 $\mu\text{mol/L}$

In the event of glucarpidase treatment, the dose of folinic acid should be reduced to 100 mg/m^2 after glucarpidase injection as LC/MS results are not available for dose calculation at short notice.

^a GMALL 08/2013 trial (EudraCT 2013-003466-13)