Supplemental Tables

Table 1 Criteria for dose modifications of RUXOLITINIB due to study drug-related toxicity after Cycle 1 for Phase I and Phase II

Worst Toxicity CTCAE Grade* unless otherwise specified (Value)		Time point	Dose Modification Guidelines
HEMATOLOGICAL TOXICITIES			
Thrombocytopenia	< 20 x 10^9/L	Cycles 2-6	No dose modification allowed
		After cycle 6	Option to Interrupt study treatment dosing until resolved to ≥ 20 x 109/L, then restart study treatment at reduced level
	> 20 x 10^9/L + grade 3 bleed	Cycles 2-3	No dose modification allowed
		After cycle 3	Interrupt study treatment dosing until bleeding is resolved and platelet count is at level before bleed was noted, then resume study treatment at reduced level
Neutropenia (ANC)	Grade 4 (ANC < 0.5 x 10^9/L)	Cycles 2-6	No dose modification allowed
		After cycle 6	Option to interrupt study treatment dosing until resolved to ≤ grade 2, or baseline, then: • If resolved within 7 days then restart study treatment at an unchanged dose level • If resolved in more than 7 days then restart study treatment at reduced level
	Febrile neutropenia (ANC < 1.0 x 10^9/L, fever ≥ 38.5°C)	Cycles 2-3	No dose modification allowed
		After cycle 3	Interrupt study treatment dosing until fever resolved and ANC ≤ grade 2, then restart study treatment at reduced level
Anemia only requires dose reductions after cycle 6	Doubling of transfusion frequency from baseline# or requiring 2 units per week x 4 consecutive weeks	Cycles 2-6	No dose modification allowed
		After Cycle 6	Interrupt study treatment, if hemoglobin (or transfusion frequency) returns to baseline within 28 days restart ruxolitinib at same dose, if this recurs again then reduce dose

Worst Toxicity CTCAE Grade* unless otherwise specified (Value)		Time point	Dose Modification Guidelines
NON-HEMATOLOGICAL TOXICITIES			
GASTROINTESTINAL			
Diarrhea	Grade 2 (4-6 stools/day over baseline, etc.) despite the use of optimal antidiarrheal medications	Cycles 2-3	No dose modification allowed
		After Cycle 3	Hold ruxolitinib dosing until resolved to ≤ grade 1, or baseline, then restart at unchanged dose level
	Grade 3 (≥ 7 stools/day over baseline, etc.) despite the use of optimal antidiarrheal medications	Cycles 2-3	No dose modification allowed
		After Cycle 3	Hold ruxolitinib dosing until resolved to ≤ grade 1, or baseline, then restart study treatment at reduced level
	Grade 4 (life-threatening consequences, hemodynamic collapse, etc.) despite the use of optimal antidiarrheal medications	After Cycle 1	Permanently discontinue study treatment dosing
Vomiting/Nausea**	Grade 1 & 2 not requiring treatment **or** controlled using standard anti-emetics	Cycles 2-3	No dose modification allowed
		After Cycle 3	Interrupt study treatment dosing until resolved to ≤ grade 1, or baseline, then restart study treatment at same dose level
	Grade 3 or 4 vomiting or Grade 3 nausea that cannot be controlled despite the use of standard anti-emetics	Cycles 2-3	Interrupt study treatment dosing until resolved to ≤ grade 1, or baseline, then restart study treatment at same dose level
		After Cycle 3	Interrupt study treatment dosing until resolved to ≤ grade 1, or baseline, then restart study treatment at reduced level

Worst Toxicity CTCAE Grade* unless otherwise specified (Value)		Time point	Dose Modification Guidelines
HEPATIC			
Total Bilirubin	Grade 3 or 4	Cycles 2-3	Interrupt study treatment dosing until resolved to ≤ grade 1, or baseline, then restart study treatment at same dose level
		After Cycle 3	Interrupt study treatment dosing until resolved to ≤ grade 2, or baseline, then restart study treatment at reduced level
	Note: If Grade 3 or Grade 4 hyperbilirubinemia is due to the indirect component only, and hemolysis as the etiology has been ruled out as per institutional guidelines (e.g., review of peripheral blood smear and haptoglobin determination), then reduction of one dose level and continuation of treatment is at the discretion of the Investigator.		
AST/SGOT, ALT/SGPT	> 5-10 x ULN	After Cycle 1	Interrupt study treatment dosing until resolved to ≤ grade 1 (or ≤ grade 2 if liver infiltration with tumor is present), or baseline, then: • If resolved within 7 days, then restart study treatment at unchanged dose level • If resolved in more than 7 days, then restart study treatment at reduced level
	> 10 x ULN	After Cycle 1	Interrupt study treatment dosing until resolved to ≤ grade 1, or baseline, then: • restart study treatment at reduced level
	Note: All dose modifications should be based on the worst preceding toxicity.		

\# Only applies to patients requiring at least 2 units of packed red blood cells every three weeks at baseline

* Common Terminology Criteria for Adverse Events (CTCAE Version 4.0)

** See also concomitant medication section

Table 2 Criteria for dose modifications (treatment delays and interruptions) of Decitabine due to study drug-related toxicity after Cycle 1 for Phase I and Phase II

Worst Toxicity CTCAE Grade* unless otherwise specified (Value)		Time Point	Dose Modification Guidelines
HEMATOLOGICAL TOXICITIES			
Thrombocytopenia	< 20 x 10^9/L	Cycles 2-6	No dose delay or interruption required
		After Cycle 6	Option to delay Decitabine dosing until resolved to ≥ 20 x 10^9/L, then restart study treatment
	> 20 x 10^9/L + grade 3 bleed	Cycles 2-3	No dose delay or interruption required
		After Cycle 3	Interrupt and/or delay Decitabine dosing until bleeding is resolved and platelet count is at level before bleed was noted, then resume study treatment
Neutropenia (ANC)	Grade 4 (ANC < 0.5 x 10^9/L)	After Cycle 1	No dose delay or interruption required
	Febrile neutropenia (ANC < 1.0 x 10^9/L, fever ≥ 38.5°C)	Cycles 2-3	No dose delay or interruption required
		After Cycle 3	Option to interrupt and/or delay Decitabine dosing until source of infection identified and treatment initiated then restart study treatment. If fever is determined due to MPN, continue treatment.

Worst Toxicity CTCAE Grade* unless otherwise specified (Value)		Time Point	Dose Modification Guidelines
NON-HEMATOLOGICAL TOXICITIES			
GASTROINTESTINAL			
Diarrhea	Grade 3 (≥ 7 stools/day over baseline, etc.) despite the use of optimal antidiarrheal medications	After Cycle 1	Interrupt and/or delay Decitabine dosing until resolved to ≤ grade 1, or baseline, then restart study treatment
	Grade 4 (life-threatening consequences, hemodynamic collapse, etc.) despite the use of optimal antidiarrheal medications	After Cycle 1	Permanently discontinue study treatment dosing
Vomiting/Nausea* **	Grade 1 & 2 not requiring treatment **or** controlled using standard anti-emetics	After Cycle 1	No dose delay or interruption required
	Grade 3 or 4 vomiting or Grade 3 nausea that cannot be controlled despite the use of standard anti-emetics	After Cycle 1	Interrupt and/or delay Decitabine dosing until resolved to ≤ grade 1, or baseline, then restart study treatment

Worst Toxicity CTCAE Grade* unless otherwise specified (Value)		Time Point	Dose Modification Guidelines
HEPATIC			
Total Bilirubin	Grade 3 or 4	Cycles 2-3	Interrupt and/or delay Decitabine dosing until resolved to ≤ grade 2, or baseline, then restart study treatment
		After Cycle 3	Interrupt and/or delay Decitabine dosing until resolved to ≤ grade 2, or baseline, then restart study treatment at 20% dose reduction
	Note: If Grade 3 or Grade 4 hyperbilirubinemia is due to the indirect component only, and hemolysis as the etiology has been ruled out as per institutional guidelines (e.g., review of peripheral blood smear and haptoglobin determination), continuation of treatment is at the discretion of the Investigator at a 20% reduction in Decitabine dosing.		
AST/SGOT, ALT/SGPT	> 5-10 x ULN	After Cycle 1	Interrupt and/or delay Decitabine dosing until resolved to ≤ grade 1 (or ≤ grade 2 if liver infiltration with tumor is present), or baseline, then restart treatment
	> 10 x ULN	Cycles 2-3	Interrupt and/or delay Decitabine dosing until resolved to ≤ grade 1, or baseline, then restart treatment
		After Cycle 3	Interrupt and/or delay Decitabine dosing until resolved to ≤ grade 1, or baseline, then restart at 20% dose reduction
	Note: All dose modifications should be based on the worst preceding toxicity.		

* Common Terminology Criteria for Adverse Events (CTCAE Version 4.0)

*** See also concomitant medication section

Supplemental Figure Legends

Supplemental Figure 1 A) Heatmap of evaluated cytokines for MPN-AP/BP baseline and MF controls. Each row constitutes one cytokine, with the data for individual patients organized in columns. Green and red denote markers that are present at lower and higher levels, respectively. **B) Log2 fold changes shown for evaluated cytokines**. Comparisons consisted of baseline MPN-AP/BP versus MF controls.

Supplemental Figure 1

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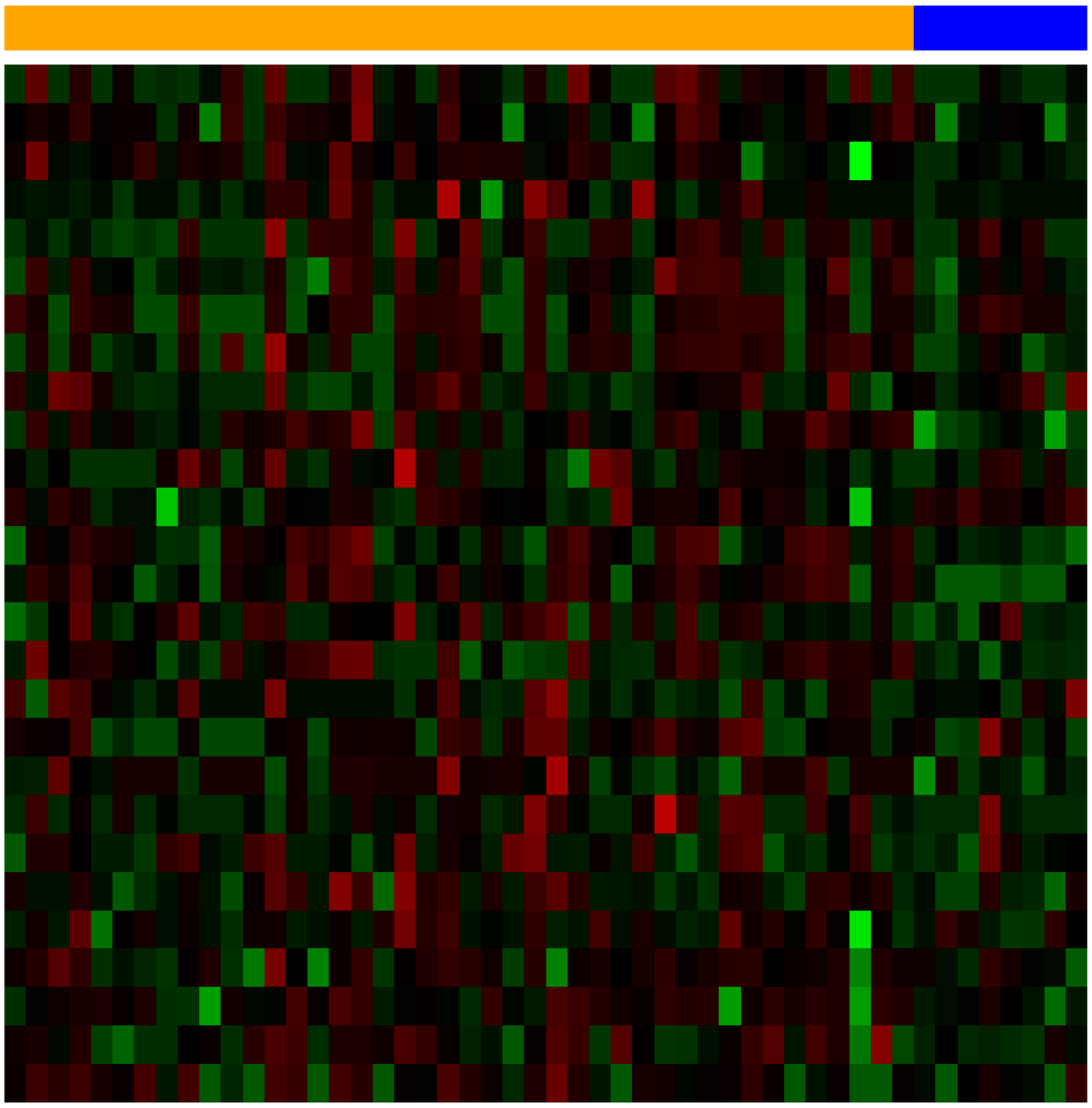

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