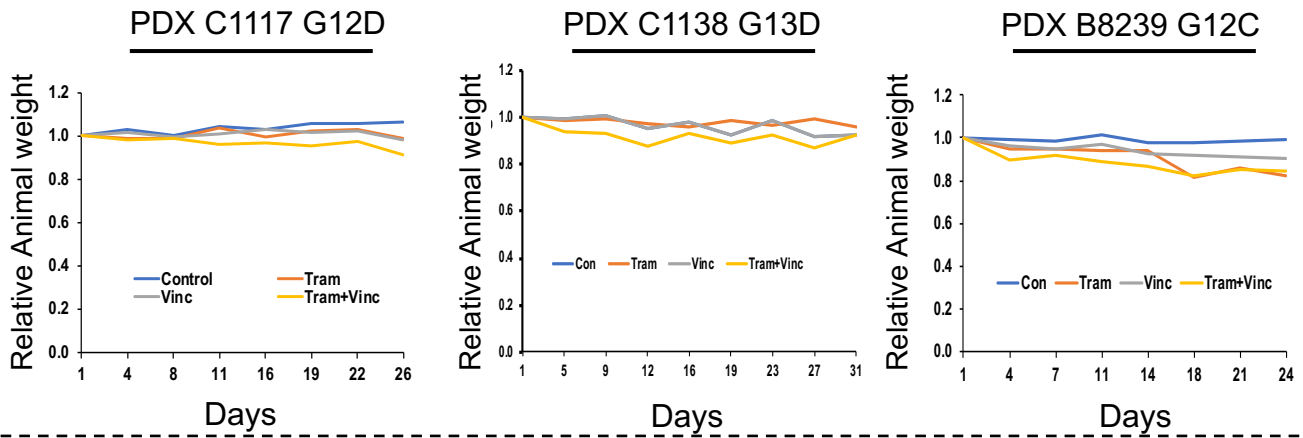


A**B**

HISTOPATHOLOGY REPORT AND DIAGNOSIS					
Species		Mouse	Mouse	Mouse	Mouse
Treatment Group		CONTROL	CONTROL	CONTROL	CONTROL
Organ		Lesion	Lesion	Lesion	Lesion
Block No.	Morphologic Diagnosis	Grade	Grade	Grade	Grade
1	LUNG	Hemorrhage,minimal,mf	N	N	N
2	LIVER	N	Infiltration,mononuclear, minimal	N	N
3	KIDNEY	N	N	N	N
4	SPLEEN	N	N	N	N
5	INTESTINE	N	N	N	N
Treatment Group		TRAM	TRAM	TRAM	TRAM
1	LUNG	Hemorrhage,minimal,mf	N	N	N
2	LIVER	N	N	N	N
3	KIDNEY	N	N	N	N
4	SPLEEN	N	N	N	N
5	INTESTINE	N	N	N	N
Treatment Group		VINC	VINC	VINC	VINC
1	LUNG	N	N	N	N
2	LIVER	N	Infiltration,mononuclear, minimal	N	N
3	KIDNEY	N	N	N	N
4	SPLEEN	N	N	N	N
5	INTESTINE	N	N	N	N
Treatment Group		TRAM+VINC	TRAM+VINC	TRAM+VINC	TRAM+VINC
1	LUNG	N	N	N	N
2	LIVER	N	N	N	N
3	KIDNEY	N	N	N	N
4	SPLEEN	N	N	N	N
5	INTESTINE	N	N	N	N

LEGEND
N = Normal tissue or No significant lesion observed
A = Abnormal tissue (Lesion present)
P = The lesion is present, but not graded
S = Suspected/Presumptive diagnosis (needs more tests to confirm the Dx.)
MF-Multifocal
WNL=Within normal Limits

Supplementary Figure 4: Combination of trametinib and vincristine is well tolerated by mice. (A) Changes in body weight of mice following treatment with vehicle (C), trametinib (Tram), vincristine (Vinc), or the combination (Tram+Vinc) over time. (B) Summary of histopathological reports showing organs examined and lesion grade.