

Supplemental Figures/Tables:

Figure S1: Mean ruxolitinib concentration profile for 18 evaluable patients during single agent ruxolitinib run-in and during combination ruxolitinib and decitabine phase of treatment.

Table S1: Response criteria utilized for this study. Responses were assessed based on peripheral blood counts and blast percentages, as the majority of patients did not have an aspirable bone marrow.

Table S2: Clinical characteristics of enrolled patients, including MPN history, thrombotic history, and baseline hematologic parameters.

Table S3: Baseline molecular and cytogenetic findings.

Table S4: Adverse events (Grade 3 or greater) observed during cycle 1 of therapy, regardless of attribution, divided by disease subtype (accelerated phase versus blast phase).

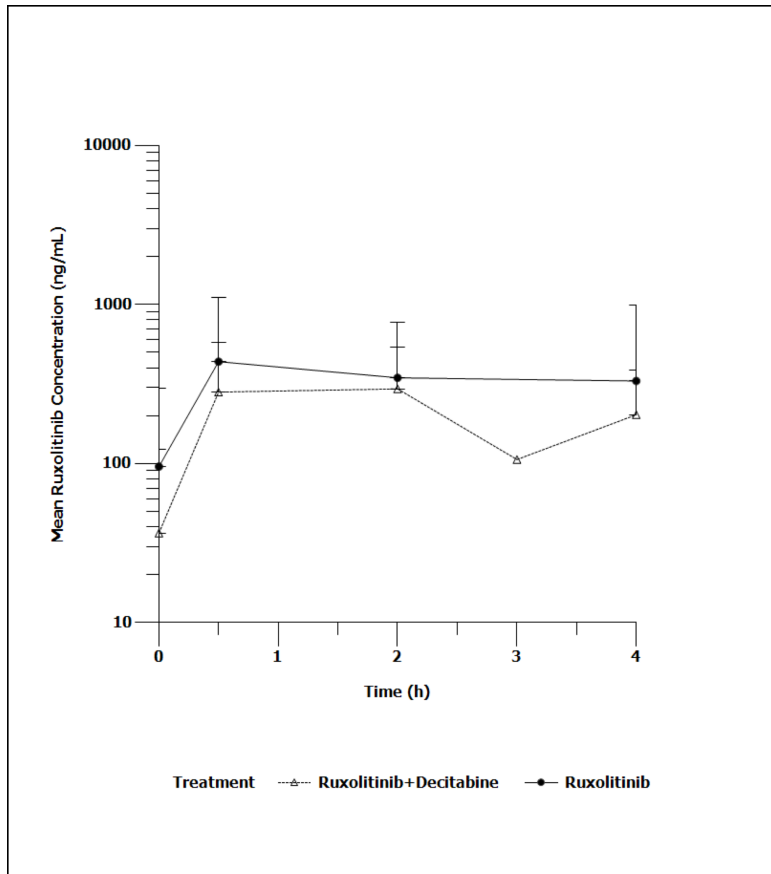
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Supplemental Figure 1



Supplemental Table 1

Response Designation	Criteria
Complete Response (CR)	0% peripheral blood blasts, WBC $\geq 4 \times 10^9/L$, hemoglobin $\geq 10g/L$, and platelets $\geq 100 \times 10^9/L$
Complete Response with incomplete count recovery (CRi)	0% peripheral blood blasts with incomplete count recovery
Partial Response (PR)	$\geq 50\%$ decrease in peripheral blood blasts regardless of blood counts.
No Response (NR)	None of the above

Supplemental Table 2

	10mg BID (N=6)	15mg BID (N=3)	25mg BID (N=6)	50mg BID (N=6)	Total (N=21)
Initial Diagnosis					
Accelerated Phase MPN	0 (0.0%)	0 (0.0%)	3 (50.0%)	0 (0.0%)	3 (14.3%)
Acute Myeloid Leukemia	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.8%)
ET related Myelofibrosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (33.3%)	2 (9.5%)
Essential Thrombocythemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	1 (4.8%)
PV related Myelofibrosis	1 (16.7%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	2 (9.5%)
Polycythemia Vera	3 (50.0%)	2 (66.7%)	2 (33.3%)	1 (16.7%)	8 (38.1%)
Primary Myelofibrosis	1 (16.7%)	1 (33.3%)	1 (16.7%)	1 (16.7%)	4 (19.0%)
Thrombotic events last 12 months	1 (16.7%)	0 (0.0%)	1 (16.7%)	1 (16.7%)	3 (14.3%)
Hemorrhagic events last 12 months	1 (16.7%)	0 (0.0%)	0 (0.0%)	2 (33.3%)	3 (14.3%)
History of Splenectomy	1 (16.7%)	0 (0.0%)	1 (16.7%)	0 (0.0%)	2 (9.5%)
White blood cell count, x10 ⁹ /L (median, range)	14.6 (2.7-21.8)	4.1(3.4-4.8)	3.8(2.7-65.1)	11.7(2.3-54.1)	6.9(2.3-65.1)
Hematocrit, % (median, range)	32.7(26.2-35.4)	27.3(22.9-32.8)	22.1(21.1-28.4)	29.1(23.0-39.8)	28.3(21.1-39.8)
Platelet count, x10 ⁹ /L (median, range)	135(55.0-556.0)	25(13.0-51.0)	191.5(10.0-458.0)	96.5(11.0-776.0)	92.0(10.0-776.0)
Lactate Dehydrogenase u/L (median, range)	640(247.0-1255.0)	359(189.0-1117.0)	278.5(195.0-1385.0)	448.5(11.0-1058.0)	511.0(11.0-1385.0)

Supplemental Table 3

Subject	Baseline Molecular Genetic Profile	Normal Karyotype (Y/N)	Karyotype Clone 1	Number of Cells	Karyotype Clone 2	Number of Cells	Notes
1	JAK2p.V617F, TET2p.I1873T		46,XX,der(1)t(1;7)(p22;q21.1)del(7)(q21.2),der(7)del(7)(q21.2)t(1;7)(p22;q21.1),del(20)(q11.2q13.1)[12]	12	47,XX,der(1)t(1;7)(p22;q21.1)del(7)(q21.2),der(7)del(7)(q21.2)t(1;7)(p22;q21.1),+8,del(20)(q11.2q13.1)[3]	3	
2	JAK2p.V617F		43,XY,-5,-7,add(16)(p12),-17,-19,+mar[2]	2			FISH for deletion of TP53 was observed in 64% of interphase cells
3	TP53p.E343fs*2		46,XX,+1,der(1;18)(q10;q10)[15]	15	44,XX,-12,-17,add(20)(q12)[2]	2	
4	MPLp.R592*, SF3B1 P.K666N	Y (46,XY)					
5	JAK2p.V617F,SRSF2p.95H, IDH1p.R132C, RUNX1p.G165V, RUNX1p.H105Y, TET2p.I1859T	Y (46,XY)					
6	JAK2p.V617F,TP53p.L257R, BCORp.R63K	Y (46,XX)					
7	CALRp.K374fs*48, RUNX1p.F163V,U2AF1p.Q157P,MPLp.H624D						
8	JAK2p.V617F RUNX1p.Q335fs*25						Technically Inadequate
9	JAK2V617F, DNMT3A p.C586Y		39-40,XY,-3,-5,-7,del(10)(q22q24),add(11)(p11.2),-12,-13,-15,add(16)(p?12),-17,-18,		add(19)(q13.1),del(20)(q?11.2q?13.1),+mar1,+mar2,inc[c p12]/46,XY	2	
10	JAK2p.V617F,TP53p.R248V,NOTCH1p.T1344M, FLT3p.T167A	46,XY					
11	JAK2p.V617F, TET2p.E711*, KRASp.G13D		45,XX,-3,del(5)(q13q33),-7,add(9)(p24),-14,add(18)(p11.2),+2mar	18	46,XX,-3,del(5)(q13q33),-7,add(9)(p24),add(18)(p11.2),+2mar	2	
12	SETBP1p.G870C,U2AF1p.S34Y,CCND2p.281R, DNMT3Ap.R882C	46,XY		20			
13	KRASp.G12C,PTPN11p.A72T,IKZF1p.N159S,SU Z12p.D605A,RAD21p.M489L, ASXL1p.T848fs*19		47,XY,+8	18	46,XY,del(20)(q11.2q13.1)	2	
14	MPLp.W515G, MPLp.W515S,ASXL1p.R693*,ASXL1p.E635fs*15	Y (46,XY)					
15	MPLp.S505C,KMT2Dp.E5211K		45,XX,del(5)(q31q35),del(14)(q11.2q13),-17,der(19)t(17;19)(q11.2;p13.1)t(5;17)(q31;q25)[9]	9	46,XX,t(4;14;19)(q21;q11.2;q13)[3]	3	
16	JAK2p.V617F,SRSF2p.P95A,SF3B1p.K666N,STA G2p.R614*, ASXL1p.Q748*,ASXL1p.G646fs*58,EZH2p.N263fs*8	Y (46,XY)					
17	JAK2p.V617F,EZH2p.D664V	Y (46,XX)					
18	JAK2p.V617F,U2AF1p.Q157P,NOTCH1p.R1598H, RUNX1p.Q335fs*255,ASXL1p.E635fs*15	Y (46,XY)					
19	JAK2p.V617F, CEBPAp.A167T, TP53p.P128f*42		45,XY,add(1)(p13),-13,-15,-19,add(21)(q22),+mar1,+mar2	17	46,XY	3	
20	JAK2p.V617F,PTPN11p.G503V,RUNX1p.R201Q, EZH2p.E645fs*10		45,XY,-7				
21	JAK2p.V617F,TET2p.N1387S, TET2p.V218fs*32, NOTCH2p.L2408H	Y		20	46,idem,+mar	20	

Supplemental Table 4

	Accelerated Phase (n=8)	Blast Phase (n=13)	Total (n=21)
Hematologic			
Neutropenia	4 (50.0%)	3 (23.1%)	7 (33.3%)
Grade 3	3	3	6
Grade 4	1		1
Febrile neutropenia	3 (37.5%)	4 (30.8%)	7 (33.3%)
Grade 3	3	4	7
Lymphocytopenia	2 (25.0%)	2 (15.4%)	4 (19.0%)
Grade 3	2	2	4
Thrombocytopenia	1 (12.5%)	3 (23.1%)	4 (19.0%)
Grade 3	1	1	2
Grade 4		2	2
Anemia	1 (12.5%)	3 (23.1%)	3 (14.3%)
Grade 3	1	2	3
Non-hematologic			
Pneumonia	2 (25.0%)	3 (23.1%)	6 (28.6%)
Grade 3	2	4	6
Respiratory failure	1 (12.5%)	1 (7.7%)	2 (9.5%)
Grade 3	1		1
Grade 4		1	1
Sepsis	2 (25.0%)	1 (7.7%)	3 (14.3%)
Grade 3			
Grade 4	2	1	3
Squamous cell carcinoma	2 (25.0%)		2 (9.5%)
Grade 3	2		2
Cellulitis		2 (15.4%)	2 (9.5%)
Grade 3		2	2
Gastrointestinal bleeding	1 (12.5%)	1 (7.7%)	2 (9.5%)
Grade 3	1		1
Grade 4		1	1
Hypertension	2 (25.0%)		2 (9.5%)
Grade 3	2		2

Supplemental Table 5

Patient response	Dose level (mg)	Genomic Alterations	Baseline Spleen size (cm)	MPN-AP/BP
CR-I	10 mg	JAK2p.V617F, TET2p.I1873T	19	MPN-BP
PR	10 mg	MPLp.R592*, SF3B1 P.K666N	17	MPN-AP
PR	15 mg	CALRp.K374fs*48, RUNX1p.F163V,U2AF1 p.Q157P,MPLp.H624D	N/A	MPN-BP
PR	15 mg	JAK2p.V617F RUNX1p.Q335fs*25	6	MPN-BP
CR-I	25 mg	MPLp.W515G,MPLp.W 515S,ASXL1p.R693*,ASXL1p.E635fs*15	15	MPN-AP
CR-I	50 mg	JAK2p.V617F,SRSF2p.P95A,SF3B1p.K666N,S TAG2p.R614*,ASXL1p.Q748*,ASXL1p.G646fs*58,EZH2p.N263fs*8	0	MPN-AP
PR	50 mg	JAK2p.V617F, EZH2p.D664V	0	MPN-AP
CR-I	50 mg	JAK2p.V617F, CEBPAp.A167T, TP53p.P128f*42	0	MPN-BP
PR	50 mg	JAK2p.V617F,TET2p.N1387S,TET2p.V218fs*32,NOTCH2p.L2408H	0	MPN-BP

Supplemental Table 6

Mutation Type	CR-I/PR	NR
Splicing Factor	3	3
<i>RUNX1</i>	2	2
<i>TP53</i>	1	0
<i>TET2/IDH1/2</i>	1	2
<i>ASXL1</i>	2	2
≤ 3 mutations	5	2
≥ 3 mutations	4	6