Supplemental table 1. Phase I or phase I/II trials with new drugs in myeloproliferative neoplasms

Author (year)	Study phase	Drug	Disease	N. of patients	Population	Primary endpoint
Verstovsek et al., Leuk Res, 2013[1]	Phase I	XL019	MF	30	In need of therapy with <20% blasts in BM. Pts. with pre-existing peripheral neuropathy excluded (by animal toxicity studies)	Safety; PK; Response
Mascarenhas et al., BJH, 2013[2]	Phase I/II	Panobinostat	MF	18	High-or intermediate-risk patients (Lille score)	DLT; MTD; Adverse events; Response
Pardanani et al., Leukemia, 2013[3]	Phase I/II	CYT387	MF	60	High- or intermediate II-risk (IWG) or intermediate-1 with either hepatosplenomegaly or unresponsiveness to therapies	Safety and tolerability; therapeutic dose; PK; Response
Foran et al., Clin Lymphoma, Myeloma Leuk., 2013[4]	Phase I	AT9283	ALL, AML, CML, MF	48 (MF=9)	Advanced MF patients	DLT; MTD; PK; Response
Pardanani et al., JCO, 2011[5]	Phase I	TG101348	MF	59	High- or intermediate-risk patients (IWG)	Safety and tolerability; DLT; MTD; PK; Response
Barosi et al., Am J Hematol,	Phase 1-2	Bortezomib	MF	20	High- or intermediate-risk patients (IWG score)	Safety; DLT; MTD; Response

2010[6]						
Verstovsek et al., NEJM 2010[7]	Phase I/II	Ruxolitinib	MF	153	Patients requiring therapy, had had a relapse or had severe side effects from therapy or disease that was refractory to previous therapy. If newly diagnosed disease: intermediate or high risk disease; symptomatic splenomegaly (10 cm below the LCM)	Safety; tolerability; DLT; MTD; Response
Guglielmelli et al., Blood, 2011[8]	Phase I/II	Everolimus	MF	39	High or intermediate risk (Lille score), or low-risk with splenomegaly >10 cm from LCM	MTD; Response (EUMNET response criteria)

Legend: IWG = International Working Group; MF = myelofibrosis; PK = pharmacokinetics; DLT = Dose limiting toxicity; MTD = maximum tolerated dose

Supplemental table 2: Phase II trials with new drugs in myeloproliferative neoplasms

Author (year)	Study phase	Drug	Disease	N. of Patients	Population	Primary endpoint
Andersen et al., BJH, 2013[9]	Phase II	Vorinostat	PV and ET	63	In need of cytoreductive therapy or intolerant to other therapies	Response (ELN)
Finazzi et al., BJH, 2013[10]	Phase II	Givinostat plus hydroxycarbamide	PV	44	Unresponsive to hydroxycarbamide monotherapy	Response (ELN)
De Angelo et al., BJH, 2013[11]	Phase II	Panobinostat	MF	35	Intermediate II or high risk disease	Response (IWG-MRT)
Talpaz et al., J Hematol Oncol, 2013[12]	Phase II	Ruxolitinib	MF (with low platelets)	34	Symptoms (MFSAF 1>5 or 2>3); Platelet count 50-100 x10^9/L; Hb >65 g/L; PB blast count <5%; DIPSS score >1	Response on splenomegaly by imaging (MRI) Response on symptoms (MFSAF)
Verstovsek et al., Cancer, 2013[13]	Phase II	Ruxolitinib	PV	34	Refractory to treatment with HU or for whom HU was contraindicated	Response rate (ELN)
Mesa et al., Haematologica, 2013[14]	Phase II (2 stage)	Bevacizumab	MF	13	Symptomatic; relapsed/refractory; Intermediate- or high-risk patients	Response rate (complete and major best response by 6 months) according IWG-MRT
Quintas-Cardama et al., Leuk Res, 2012[15]	Phase II	Pracinostat	MF	22	Intermediate 1, intermediate 2 or high-risk disease or with low risk and symptomatic	Response (IWG-MRT)

					splenomegaly	
Bejanyan et al., Cancer, 2012[16]	Phase II	TADA	Myelododysplastic/myeloproliferative, MF	28 (MF=5)	Performance status from 0 to 2	Response (IWG)
Apostolidou et al., Cl Lymphoma Myeloma Leuk, 2010[17]	Phase II	Sunitinib	MF	14	If patients required therapy, had had a relapse or had severe side effects from therapy or disease that was refractory to previous therapy. If newly diagnosed disease: intermediate- or high-risk disease; symptomatic splenomegaly (10 cm below the LCM)	Response (IWG)
Parikh et al., Cl Lymphoma Myeloma Leuk, 2010[18]	Phase II	Obatoclax mesylate	MF	22	ECOG<=2	PK; Response (IWG)
Santos et al., Blood, 2010[19]	Phase II	CEP-701	MF	22	Requiting therapy, including previously treated who were relapsed, intolerant or refractory	Response (IWG)
Rambaldi et al., BJH, 2010[20]	Phase II	Givinostat	PV, ET, MF	29	In need of cytoreductive therapy; intolerant or refractory to hydroxycarbamide	Response (ELN/EUMNET)

Legend: LCM = left costal margin; PV = polycythemia vrea; ET = essential thrombocythemia; IWG = International Working Group; PK = pharmacodynamics

Supplemental table 3. Phase III trials with new drugs in myeloproliferative neoplasms

Author (year)	Study phase	Disease	Design	N. of patients	Population	Primary Endpoint
Harrison, NEJM, 2012[21]	Phase III	MF	Ruxo vs. BAT	219	Palpable spleen 5 cm or more below the costal margin Intermediate2- or high-risk IPSS; Peripheral blasts less than 10%; Platelet count of 100 $x10^9$/L or more	R**e**duction of 35% or more in spleen volume from baseline at week 48 (MRI or CT).
Verstovsek, NEJM, 2012[22]	Phase III	MF	Ruxo vs.placebo	309	Intermediate2- or high-risk IPSS; Peripheral blasts less than 10%; An absolute peripheral blood CD34+ cell count of more than 20x 10^6/L ; Platelet count of 100 $x10^9$/L or more; Palpable spleen 5 cm or more below the LCM	Proportion of patients with a reduction of 35% or more in spleen volume from baseline to week 24, measured by means of MRI or CT.

Legend: BAT = best available therapy; LCM = left costal margin;

Supplemental references

1. Verstovsek S, Tam CS, Wadleigh M, et al. Phase I evaluation of XL019, an oral, potent, and selective JAK2 inhibitor. Leuk Res 2014;38:316-322.

2. Mascarenhas J, Lu M, Li T, et al. A phase I study of panobinostat (LBH589) in patients with primary myelofibrosis (PMF) and post-polycythaemia vera/essential thrombocythaemia myelofibrosis (post-PV/ET MF). Br J Haematol 2013;161:68-75.

3. Pardanani A, Laborde RR, Lasho TL, et al. Safety and efficacy of CYT387, a JAK1 and JAK2 inhibitor, in myelofibrosis. Leukemia 2013;27:1322-1327.

4. Foran J, Ravandi F, Wierda W et al. A Phase I and Pharmacodynamic Study of AT9283, a Small-Molecule Inhibitor of Aurora Kinases in Patients With Relapsed/Refractory Leukemia or Myelofibrosis. Clin Lymphoma Myeloma Leuk. Nov. 2013

5. Pardanani A, Gotlib JR, Jamieson C, et al. Safety and efficacy of TG101348, a selective JAK2 inhibitor, in myelofibrosis. J Clin Oncol 2011;29:789-796.

6. Barosi G, Gattoni E, Guglielmelli P, et al. Phase I/II study of single-agent bortezomib for the treatment of patients with myelofibrosis. Clinical and biological effects of proteasome inhibition. Am J Hematol 2010;85:616-619.

7. Verstovsek S, Kantarjian H, Mesa RA, et al. Safety and efficacy of INCB018424, a JAK1 and JAK2 inhibitor, in myelofibrosis. N Engl J Med 2010;363:1117-127.

8. Guglielmelli P, Barosi G, Rambaldi A, et al. Safety and efficacy of everolimus, a mTOR inhibitor, as single agent in a phase 1/2 study in patients with myelofibrosis. Blood 2011;118:2069-2076.

9. Andersen CL, McMullin MF, Ejerblad E, et al. A phase II study of vorinostat (MK-0683) in patients with polycythaemia vera and essential thrombocythaemia. Br J Haematol 2013;162:498-508.

10. Finazzi G, Vannucchi AM, Martinelli V, et al. A phase II study of Givinostat in combination with hydroxycarbamide in patients with polycythaemia vera unresponsive to hydroxycarbamide monotherapy. Br J Haematol 2013;161:688-694.

11. DeAngelo DJ, Mesa RA, Fiskus W, et al. Phase II trial of panobinostat, an oral pan-deacetylase inhibitor in patients with primary myelofibrosis, post-essential thrombocythaemia, and post-polycythaemia vera myelofibrosis. Br J Haematol 2013;162:326-335.

12. Talpaz M, Paquette R, Afrin L, et al. Interim analysis of safety and efficacy of ruxolitinib in patients with myelofibrosis and low platelet counts. J Hematol Oncol 2013;6:81.

13. Verstovsek S, Passamonti F, Rambaldi A, et al. A phase 2 study of ruxolitinib, an oral JAK1 and JAK2 Inhibitor, in patients with advanced polycythemia vera who are refractory or intolerant to hydroxyurea. Cancer 2014;120:513-520.

14. Mesa RA, Silver RT, Verstovsek S, et al. Single agent bevacizumab for myelofibrosis: results of the Myeloproliferative Disorders Research Consortium Trial. Haematologica 2013;98:1421-1423.

15. Quintás-Cardama A, Kantarjian H, Estrov Z, et al. Therapy with the histone deacetylase inhibitor pracinostat for patients with myelofibrosis. Leuk Res 2012;36:1124-1127.

16. Bejanyan N, Tiu RV, Raza A, et al. A phase 2 trial of combination therapy with thalidomide, arsenic trioxide, dexamethasone, and ascorbic acid

(TADA) in patients with overlap myelodysplastic/myeloproliferative neoplasms (MDS/MPN) or primary myelofibrosis (PMF). Cancer 2012;118:3968-3976.

17. Apostolidou E, Kantarjian H, Thomas D, et al. Phase II study of sunitinib in patients with primary or post-polycythemia vera/essential thrombocythemia myelofibrosis. Clin Lymphoma Myeloma Leuk 2010;10:281-284.

18. Parikh SA, Kantarjian H, Schimmer A, et al. Phase II study of obatoclax mesylate (GX15-070), a small-molecule BCL-2 family antagonist, for patients with myelofibrosis. Clin Lymphoma Myeloma Leuk 2010;10:285-289.

19. Santos FP, Kantarjian HM, Jain N, et al. Phase 2 study of CEP-701, an orally available JAK2 inhibitor, in patients with primary or post-polycythemia vera/essential thrombocythemia myelofibrosis. Blood 2010;115:1131-1136.

20. Rambaldi A, Dellacasa CM, Finazzi G, et al. A pilot study of the Histone-Deacetylase inhibitor Givinostat in patients with JAK2V617F positive chronic myeloproliferative neoplasms. Br J Haematol 2010;150:446-455.

21. Verstovsek S, Mesa RA, Gotlib J, et al: A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. N Engl J Med 2012;366:799-807.

22. Harrison C, Kiladjian JJ, Al-Ali HK, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med 2012;366:787-798.