Published in final edited form as:

Leuk Res. 2015 August ; 39(8): 822–827. doi:10.1016/j.leukres.2015.05.002.

Association of Lymphoid Malignancies and Philadelphia-Chromosome Negative Myeloproliferative Neoplasms: Clinical Characteristics, Therapy and Outcome

Lucia Masarova[1], **Kate J. Newberry**[1], **Sherry A. Pierce**[1], **Zeev Estrov**[1], **Jorge E. Cortes**[1], **Hagop M. Kantarjian**[1], and **Srdan Verstovsek**[1]

[1]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Abstract

The co-occurrence of myeloproliferative and lymphoproliferative neoplasms (MPN/LPN) has been reported, mostly in case reports. The aim of this study was to assess the characteristics and clinical course of the coexistent diseases. Among 9866 patients who presented to our institution from 1960 to 2014, 34 (0.3%) were diagnosed with MPN/LPN. LPN was diagnosed first in 16 patients, second in 15, and at the same time in 3. The time to secondary malignancy was longer when LPN was diagnosed first (119 vs 98 months). Myelofibrosis (41%), polycythemia vera (24%), and essential thrombocythemia (18%) were the most common MPNs, and non-Hodgkin lymphoma (50%) and chronic lymphocytic leukemia (32%) were the most common LPNs. Seventy-three percent of patients treated for MPN and 72% of those treated for LPN achieved a complete response. After a median follow-up from MPN diagnosis of 84 months, 16 patients are alive and 18 died (4 related to MPN and 2 LPN). Coexistent MPN/LPN is a rare event that does not appear to predict worse outcomes. Treatment choice is generally oriented towards controlling the prevalent disease; the other malignancy may influence treatment strategies in selected cases.

Keywords

Myeloproliferative neoplasm; lymphoproliferative neoplasm; concurrent; clinical course

Introduction

Myeloproliferative neoplasms (MPN) are a group of heterogeneous, relatively indolent neoplastic disorders, encompassing essential thrombocythemia (ET), polycythemia vera (PV), and myelofibrosis (MF). Patients with ET and PV have life expectancies that are comparable with that of age-matched healthy individuals. The clinical course of MF is more aggressive, with a median survival of 5–7 years[1]. Patients with ET and PV have an increased risk of vascular events, as well as increased risk of transformation into myelodysplastic syndrome or MF. All 3 MPNs (ET, PV, MF) may develop into acute leukemia[2] or more rarely the patients may develop a second solid or hematologic malignancy. Studies suggest

Corresponding Author: Srdan Verstovsek, MD, PhD, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 428, Houston, TX 77030, USA, Ph.: 713-745-3429, Fax: 713-745-0930, sverstov@mdanderson.org.

that the incidence of second tumor of the hematopoietic system is higher in patients with MPN[3,4] however, the coexistence of an MPN and a lymphoproliferative neoplasm (LPN) is still believed to be a rare finding, reported sporadically in the literature. Moreover, very few retrospective studies of the clinical behavior of these coexistent disorders have been published. A report by Palandri et al. described only non-Hodgkin lymphoma (NHL) in the context of MPN,[5] and Laurenti et al. described the coexistence of CLL and an MPN.[6] Both authors concluded that the coexistence of an LPN and an MPN is an uncommon, occasional event and in most cases, the coexistent diseases have a fairly indolent clinical behavior. In a review of the literature through December 2014, we found over 200 cases describing various subtypes of coexistent LPN and MPN (LPN/MPN), most of which were single case reports. In this study, we aimed to define the prevalence of MPN/LPN, the clinicobiological characteristics and clinical course of both diseases, as well as the possible influence of treatment on the course of the second disease.

Design and Methods

We reviewed the entire MPN (n= 1475) and CLL (n=8391) databases of patients referred to MD Anderson Cancer Center between 1960 and 2014. We identified 34 patients diagnosed with both MPN and LPN during their lifetime. We retrospectively collected and analyzed all relevant demographic, clinical, and therapeutic data by reviewing the patients' medical records, with special attention given to the LPN diagnosis and its timing with respect to the MPN diagnosis. For each patient, the follow up time was defined as the date of MPN diagnosis to the date of death or last follow-up, whichever came first. The observational time was defined as the date of first diagnosis (MPN or LPN) to the date of death or last follow-up.

Results

Between 1960 and 2014, 9,866 patients diagnosed with MPN (n=1475) or CLL (n=8391) presented to our institution. MF was the most common diagnosis (n=871), followed by PV (n=178) and ET (n=265). Among these, 34 (0.3%) were also diagnosed with a lymphoid neoplasm during their lifetime (23 from the MPN database and 11 from the CLL database). A similar percentage of patients were diagnosed with the LPN either before (47%) or after (44%) the MPN diagnosis. LPN was diagnosed most often in patients with MF (n= 14; 4%), and NHL was the most common lymphoid malignancy (n=17; 50%). Demographic and clinicobiological characteristics of all patients at the time of presentation to our institution are summarized in Table 1, and detailed information about patients' treatment and clinical outcome are included in Table 2. Male to female ratio was 1.4:1, and the median age at diagnosis for each disease (LPN or MPN) was the same (56 years). The median follow-up time from the date of MPN diagnosis was longer than the median follow-up time from presentation to our institution (84 vs 37 months, respectively). When divided by MPN subtype or timing of LPN diagnosis, demographic (gender, age), clinical characteristics (JAK2, karyotype, PS, splenomegaly) and primary therapeutic interventions were similar. The only significant clinical differences were that 100% of PV patients harbored the JAK2 V617F mutation, and symptomatic splenomegaly was more common in patients with MF. Most of the patients with NHL had an aggressive histology (70%) and more than half of them presented with an advanced stage of their disease, whereas the majority of CLLs, HLs and multiple myeloma cases presented in the early stages.

The majority of patients received treatment for their first disease, whether MPN or LPN (73 vs 94%), with monotherapy being the most common. Detailed data are shown in Table 2 and summarized in Table 3. The median time between the beginning of treatment for the first disease and diagnosis of the second disease was longer for those first diagnosed with an MPN (11 vs 9 years); however, only 6 patients with a primary diagnosis of LPN received treatment within 3 months of their MPN diagnosis. Overall, eleven out of 15 patients with primary MPN required treatment for their MPN after the LPN diagnosis, 3 of these patients had not been treated for MPN prior to diagnosis of the LPN. Reasons for MPN treatment after LPN diagnosis were evolution of the initial MPN to secondary myelofibrosis (PPV MF) or blastic phase (2 patients) and coexistence of MF with T-NHL, which was diagnosed during splenectomy, in one patient. Treatments for LPN were standard first line approaches with chemotherapy, surgery or radiation, except for 4 patients with primary and 2 with secondary LPN who had relapsed or refractory, progressive disease. Seventy three percent of patients treated for MPN and 72% of those treated for LPN achieved a good response to therapy (complete response (MPNs) or remission). Three patients treated for MPN (13%) and 3 patients treated for LPN (18.7%) failed treatment. Nine patients experienced evolution of their MPN to MF or blastic phase, and five of these patients did not receive any treatment for it for various reasons (2 PET MF, 1 PPV MF, and 2 MF in the blastic phase). One patient, who developed PPV MF 18 years after the initial PV diagnosis, was still being observed at the time of last follow up with stable MF and LPN in CR for 5 years. Overall, the clinical behavior of the coexistent diseases was benign: the first disease did not progress after diagnosis of the second disease or the disease responded very well to chemotherapy in more than 92% of LPNs and 86% of MPNs. None of the MPNs that coexisted with a progressive LPN progressed or was influenced by LPN treatment.

After a median follow up of 84 months, 16 patients are still alive. Eighteen patients have died, with MPN/LPN related deaths equally distributed regardless of whether the LPN was diagnosed first or second. All 16 patients who are still alive are in CR for the LPN or are being observed (CLLs). Of these, 8 patients' MPN are stable on therapy (3 on hydroxyurea, 3 on JAK2 inhibitor, 2 on pegylated interferon), 5 are in CR following treatment including stem cell transplantation, and 3 are being observed.

Because the frequency of MPN/LPN subtypes in our series were different from those previously published, we performed sub analyses of patients stratified by timing of LPN (Table 1, PART II and III) and outcomes of different MPN/LPN subtypes (data not shown). The majority of patients with LPN as a primary diagnosis were in long-term remission before they were diagnosed with an MPN (Figure 1). Even when divided based on the most common MPN/LPN subtypes (PV, MF, NHL, CLL) or timing of LPN diagnosis, there were no significant differences in the disease behavior, treatment needed, or response and overall outcome. Even though some patients had evolution of their MPNs (2 ET, 3 PV, 4 MF) to MF or AML or progression of LPNs (3 NHL, 1 CLL) which required more aggressive treatment, it did not seem to have any influence on the coexistent disease or its outcome, as all coexistent disorders remained stable during or after the other one had progressed. The latency period before evolution of MPN to MF or the blastic phase was similar to what has been reported in the literature. The longest latency period was for ET and PV evolving to MF (20 and 18 years, respectively) and the shortest was for MF evolving to the blastic phase (4.5 years). Furthermore, the latency period between MF and the blastic phase was shorter for patients with secondary MF than for those with primary MF (3 and 8 years, respectively). We also had 2 unique cases of secondary hypereosinophilic syndrome (HES): one in a patient with a primary diagnosis of CLL and one with a primary diagnosis of HL. The patient with HL was diagnosed with HES after being in complete remission for 12 years. The patient did not respond to the treatment given for HES, but the HES remained stable for the rest of the follow-up period. The other patient was diagnosed with HES after being on treatment for CLL for 5 years. The HES also did not respond to initial therapy, but a complete remission was achieved with ongoing treatment for CLL.

Discussion

The association of a Philadelphia chromosome–negative MPN and LPN in the same patient is a relatively uncommon event, described mostly sporadically in the literature. To the best of our knowledge, the series described in this report, is the most complex one reported to date. We also report the largest number of MF patients with a coexistent LPN, representing 41% of MPN/LPN cases. However, MF was also the most common MPN diagnosis in our database. We also report the largest number of NHLs co-occurring with an MPN, which was more common than CLL and an MPN. Different from previous reports of NHL co-occurring with MPN, which were mostly indolent with good prognosis[5], the patients with NHL in our database had more aggressive disease. On the other hand, the co-occurring CLLs had benign clinical behavior with overall favorable prognoses.[5,6] Table 4 summarizes the data from the literature along with our own results. In our series, MPN followed the development of LPN in the majority of the cases (47%), with MF being the most common subtype, which is in contrast to published data (Table 4) and Rumi's hypothesis that the more aggressive behavior of LPN precludes people from developing MPN later over their life time.[3] Unique features of our series include the coexistence of more NHLs after a prior PV diagnosis, Hodgkin's lymphoma exclusively preceding a later MPN, and the coexistence of HES with MPN. The majority of patients required treatment for their MPN or LPN during their lifetime and generally had a good treatment response without an impact on the clinical behavior of the second disease. Progression or evolution of the LPN or MPN does not seem to influence or worsen the clinical course of the second disorder, and is mostly an expression of the natural behavior of the disease than due to its coexistence with another malignancy; however, the presence of first disease could have impact on treatment strategies in selected cases. A history of either disorder does not seem to influence the treatment outcome.

In conclusion, our study shows that the co-occurrence of MPN and LPN is a relatively rare event and the LPN can be diagnosed before, at the same time as or subsequent to the diagnosis of an MPN. Treatment is generally oriented to control the prevalent disease, the other malignancy presence may have impact on treatment choice in selected cases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Cervantes F, Passamonti F, Barsi G. Life expectancy and prognostic factors in the classic BCR-ABL-negative myeloproliferative disorders. Leukemia. 2008; 22(5):905–914. [PubMed: 18385755]
2. Campbell PJ, Green AR. The myeloproliferative disorders. N Engl J Med. 2006; 355:2452–2466. [PubMed: 17151367]
3. Rumi E, Passamonti F, Elena C, et al. Increased risk of lymphoid neoplasm in patients with MPN: A study of 1915 patients. Haematologica. 2011; 96:454–458. [PubMed: 21109692]
4. Vannuchi AM, Masala G, Antonioli E, et al. Increased risk of lymphoid neoplasms in patients with Ph chromosome-negative MPN. Cancer Epidemiol Biomarkers Prev. 2009; 18:2068–2073. [PubMed: 19531676]
5. Palandri F, Derenzini E, Ottaviani E. Association of essential thrombocythemia and non-Hodgkin lymphoma: a single-centre experience. Leukemia and Lymphoma. 2009 Mar; 50(3):481–484. [PubMed: 19241208]
6. Laurenti L, Tarnani L, Nichele I, et al. The coexistence of chronic lymphocytic leukemia and MPN: A retrospective multicentric GIMEMA experience. Am. J. Hematol. 2011; 86:1007–1021. [PubMed: 21953617]
7. Melikian AL, Kolosheinova TI, Goriacheva SR, et al. Synchronous and metachronous myeloid and lymphoid tumors. Terapevticheskiiarkhiv. 2014; 86(7):37–44.
8. Frederiksen H, Farkas DK, Christiansen CF, Hasselbalch HC, Sorensen HT. Chronic myeloproliferative neoplasms and subsequent cancer risk: a Danish population- based cohort study. Blood. 2011; 118:6515–6520. [PubMed: 22039256]

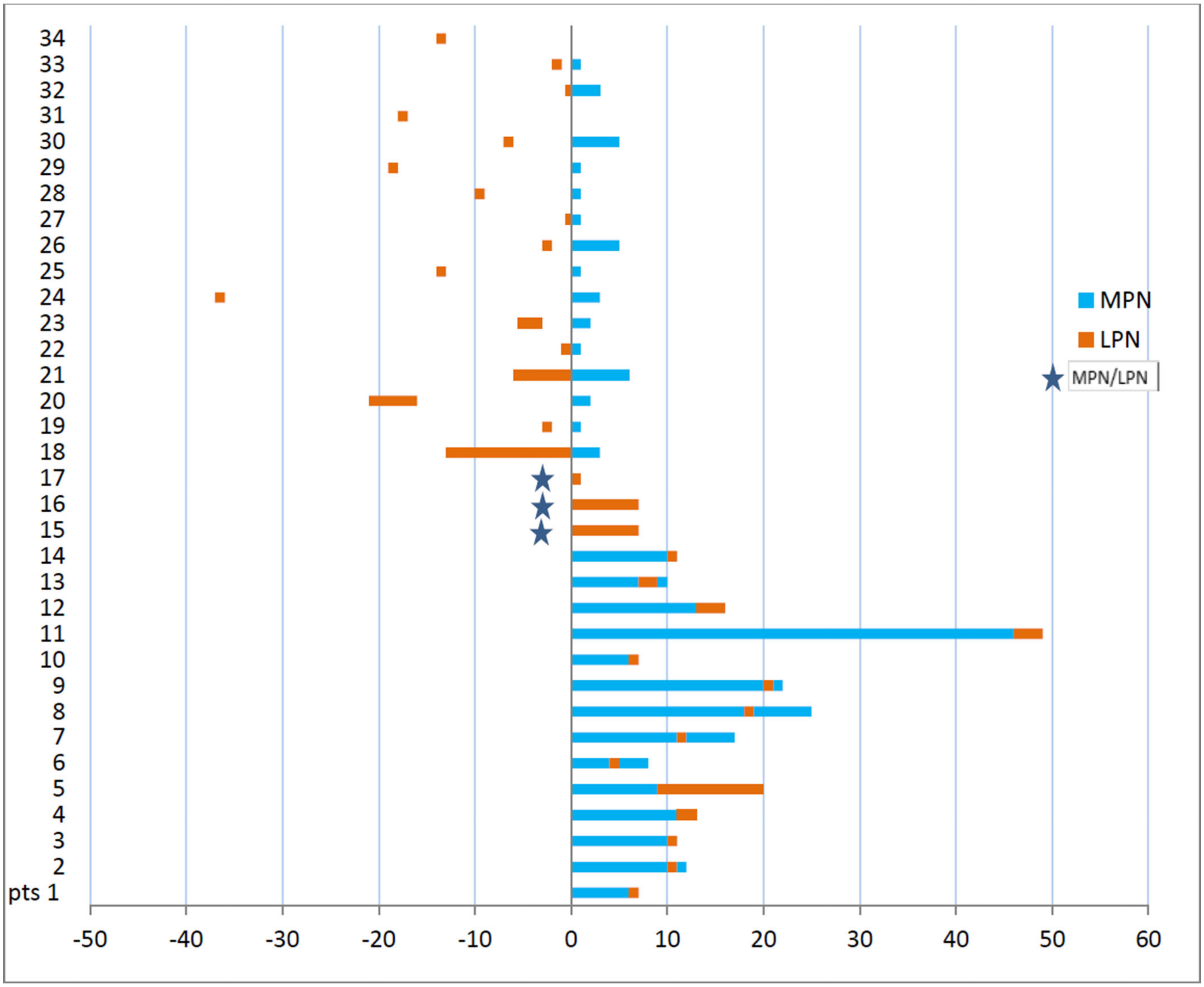

Figure 1.

Order of LPN/MPN diagnosis and disease duration during the observation period for all patients (0 year value represents the time of MPN diagnosis).

Table 1

Clinicobiological characteristics of all patients with MPN/LPN: stratified by MPN subtype (PART I.), and LPN timing (PART II. + III.)

PART I.	**TOTAL**	**ET**	**PV**	**MF**	**MPN-U**	**HES**
MPN & CLL database, n	1475 & 8391	265	178	871	72	89
MPN/LPN n, (%)	34 (0.3)	6 (1)	8 (3)	14 (2)	4 (6)	2 (2)
LPN type, n, (%)						
Non-Hodgkin's lymphoma (NHL)	17 (50)	4 (66)	5 (63)	6 (43)	2 (50)	0
Chronic lymphocytic leukemia (CLL)	11 (33)	2 (33)	2 (25)	5 (36)	1 (25)	1 (50)
Hodgkin's lymphoma (HL)	3 (9)	0	1 (12)	1 (7)	0	1 (50)
Multiple myeloma (MM)	3 (9)	0	0	2 (14)	1 (25)	0
LPN timing, n (%)						
First dx	16 (49)	0	2 (25)	9 (64)	3 (75)	2 (100)
Second dx	15 (42)	5 (83)	6 (75)	3 (21)	1 (25)	0
Simultaneous dx	3 (9)	1 (17)	0	2 (14)	0	0
Sex, n (%)						
Male	20 (59)	4 (67)	5 (63)	7 (50)	3 (75)	1 (50)
Female	14 (41)	2 (33)	3 (37)	7 (50)	1 (25)	1 (50)
Race, n (%)						
Caucasian (Cauc)	31 (91)	6 (100)	7 (88)	12 (86)	4 (100)	2 (100)
Black (Bl)	2 (6)	0	1 (12)	1 (7)	0	0
Hispanic (Hisp)	1 (3)	0	0	1 (7)	0	0
Median age at MPN dx, [range] months	56 [16–79]	46.5 [16–60]	60 [45–71]	62 [34–79]	53 [31–55]	64 [62–66]
PS, n (%)						
0–1	32 (94)	6 (100)	8(100)	14 (100)	2 (50)	2 (100)
2	2 (6)	0	0	0	2 (50)	0
Splenomegaly, n (%)	13 (33)	2 (33)	3 (38)	8 (57)	2 (50)	1 (50)
JAK2 positive, n (%)	14/24 (42)	1/3 (17)	8/8 (100)	3/10 (21)	2/3 (50)	1/1 (100)
Abnormal karyotype, n (%)	15 (47)	2 (33)	5 (63)	6 (46)	1 (25)	1 (50)
PART II.	**LPN Prior to MPN, n=16 (47%)**		**LPN After MPN, n=15 (44%)**		**Simultan. LPN & MPN, n=3 (9%)**	

LPN type, n, (%)	6 NHL, 5 CLL, 3 HL, 2 MM	1 NHL, 4 CLL, 1 MM	1 NHL, 2 CLL
MPN type, n, (%)	2 PV, 9 MF, 3 MPN, 2 HES	5 ET, 6 PV, 3 MF, 1 MPN	1 ET, 2 MF
Male/Female Ratio	1.0 (8/8)	2.0 (10/5)	2.0 (2/1)
Race, n (%)	15 Cauc, 1 Bl	13 Cauc, 1 Bl, 1 Hisp	3 Cauc
Median age at MPN dx, [range] months	51.5 (34–77)	67 (22–84)	59 (56–72)
Median age at LPN dx, [range] months	51 (8–76)	53 (16–71)	59 (56–72)
PS 2, n (%)	0	2 (13)	0
Splenomegaly, n (%)	5 (31)	6 (40)	1 (33)
JAK2 positive, n (%)	6/10 (60)	8/11 (72)	1/2 (50)
Abnormal karyotype, n (%)	6/15 (40)	8/15 (53)	1/3 (33)
PART III.	**LPN Prior to MPN, n=16 (47%)**	**LPN After MPN, n=15 (44%)**	**Simultan. LPN & MPN, n=3 (9%)**
Median time to 2nd DX, months (range)	98 (4.7–439)	119 (1–552)	NA
Median follow up [MPN], months, (range)	34 (0.5–180)	151 (91–585)	87 (6.8–88)
Median follow up [presentation], months (range)	36 (1–204)	44 (2–125)	31.8 (5.8–86)
Median observation time [1st DX], months (range)	150 (12–470)	151 (91–585)	87 (6.8–88)
Median OS [MPN], months (range)	42 (1.7–181)	132 (78–585)	6.8
Median OS [LPN], months (range)	144 (12–422)	26 (9.4–128)	6.8
Overall status - Alive/Death, n (%)	8/8 (50/50)	6/9 (40/60)	2/1 (67–33)

Table 2

Treatments and clinical outcomes of all MPN/LPN patients (n=34)

LPN prior MPN, patients # 1–16											
LPN-MPN type	*Time between LPN-MPN*[a]	*LPN status at time of MPN*	*LPN treatment type Initial (I)/ After 2nd DX (II)*		*MPN treatment type*	*Treatment response LPN (II RX)/ MPN*		*DX status at LFU LPN/ MPN*		*Overall outcome*	*Cause of death*
NHL-MPN	14	CR	cht, NOS	investigational	--	UNK	UNK	UNK	UNK	Died	UNK
NHL-MPN	3	CR	CHOP	--	--	CR	UNK	CR	UNK	Alive	
NHL-MF	7 months	CR	R-CHOP+ HD MTX	--	OBS.	CR	SD	CR	SD	Alive	
NHL-MF	17	CR	COP-BLEO, XRT	--	INT., THAL., HU, Imatinib, 6-MP	CR	PD	CR	PD	Died	MF-AML
NHL-MF	6	CR	CHOP, XRT	--	HU, AlloSCT	CR	CR	CR	CR	Alive	
NHL-PV	18	CR	CHOP	--	PEG.	CR	CR	CR	CR	Alive	
MM-MF	10	CR	VAD, THAL.	--	HU, THAL.	CR	CR	CR	PD	Died	MF-AML
MM-MPN	1	ON therapy	VTD	ASCT	ASCT	CR	CR	CR	CR	Alive	
HL-MF	3	CR	NOVP, XRT	--	AlloSCT	CR	CR	CR	CR	Died	AlloSCT compl.
HL-HES	12	CR	MOPP, XRT	--	Imatinib	CR	NR	CR	SD	Died	Heart Failure
HL-PV	37	CR	cht, XRT - NOS	--	PEG.	CR	CR	CR	CR	Alive	
CLL-MF	3	PD	CHLOR, ALEMT.	hCVAD, AlloSCT	LEN, AlloSCT	CR	CR	CR	CR	Died	AlloSCT compl.
CLL-MF	16	CR	FCR	--	Ruxolitinib	CR	CR	CR	CR	Alive	
CLL-HES	6	CR	FCR	FCAR, Dasatinib, FCR +Bev., BR	Imatinib	PD	NR	PD	CR	Died	CLL PD
CLL-MF	16	SD	OBS.	--	OBS.	SD	SD	SD	SD	Alive	
CLL-MF	1	CR	BR	--	OBS.	CR	SD	CR	SD	Died	UNK
MPN prior LPN, patients # 1–15											
MPN-LPN type	*Time between MPN-LPN*[a]	*MPN status at time of LPN*	*MPN treatment type Initial (I)/ After 2nd DX (II)*		*LPN treatment type*	*Treatment response MPN (II RX)/ LPN*		*DX status at LFU MPN/ LPN*		*Overall outcome*	*Cause of death*
ET-NHL	6	CR	HU, PEG., HU	HU	R-EPOCH	CR	CR	CR	CR	Alive	
MF-NHL	10	CR	HU	Induction + consolidation cht	surgery	PD	CR	PD	CR	Died	MF-AML

PV-NHL	4	CR	OBS	THAL, Imatinib	XRT	SD	CR	PD*	CR	Died	UNK
ET-NHL	11	CR	INF., HU, ANAG.	OBS	CHOP, ESHAP, VTEPA, IFO, R-HyperCVAD,	UNK	PD	UNK	PD	Died	NHL PD
ET-NHL	9	SD	OBS	OBS	COPP, CHOPx3, BU, FLU, XRT, HU	SD	PD	UNK*	PD	Died	UNK
PV-NHL	11	CR	Inf, HU	Ruxolitinib	HyperCVAD	CR	CR	CR*	CR	Alive	
PV-NHL	19	CR	HU	HU	R-CHOP	CR	CR	CR	CR	Alive	
ET-NHL	20	SD	OBS	Induction cht, LEN	CHOP, XRT	PD	CR	PD*	CR	Died	UNK
MF-MM	6	SD	LEN	OBS	VCD	SD	CR	PD	CR	Died	MF-AML
MPN-CLL	46	CR	HU, ANAG.	HU	OBS.	CR	CR	CR	CR	Died	UNK
PV-CLL	13	SD	OBS	OBS	cht, NOS	SD	CR	SD*	CR	Alive	
ET-CLL	7	CR	HU	HU	BU	CR	CR	CR	CR	Died	Mts sarcoma
PV-CLL	10	CR	HU	HU	BR	CR	CR	CR	UNK	Died	IM
PV-NHL	10	CR	ANAG, PEG.	AlloSCT	R-CHOP, R-ICE, alloSCT	CR	CR	CR	CR	Alive	
MF-NHL	1 month	PD	splenectomy	AlloSCT	splenectomy, AlloSCT	CR	CR	CR	CR	Alive	
MPN concomitant with LPN, patients # 1–3											
MPN-LPN type	*Time between MPN-LPN*[a]	*MPN status at time of LPN*	*MPN treatment type Initial (I)/ After 2nd DX (II)*		*LPN treatment type*	*Treatment response MPN (II RX)/ LPN*		*DX status at LFU MPN/ LPN*		*Overall outcome*	*Cause of death*
MF-NHL	--	--	--	HU, THAL., Ruxolitinib	Rituximab	CR	CR	CR	CR	Alive	
ET-CLL	--	--	--	HU	OBS.	SD	CR	SD	CR	Alive	
MF-CLL	--	--	--	OBS	OBS.	SD	SD	SD	SD	Died	UNK

[a]Time between MPN and LPN in years, unless otherwise specified,

*PET or PPV myelofibrosis

Abbr.: cht = chemotherapy; NOS = not otherwise specified; OBS.= observation; XRT = radiotherapy; THAL.= thalidomide; LEN = lenalidomide; CLOR = chlorambucil; ALEMT.= alemtuzumab; HU = hydroxyurea; ANAG.= anagrelide; INF. = interferon alfa; PEG.= pegylated interferon; 6-MP = 6 - mercaptopurine; Bev.= bevacizumab, FLU = fludarabine, AlloSCT = allogeneic stem cell transplantation, ASCT = autologous stem cell transplantation, CR = complete remission, SD = stable disease, UNK = unknown, PD = progression, NR = no response

Table 3

Summary of disease course, treatment and outcomes for MPN/LPN patients stratified by LPN timing

Treatment characteristics	**LPN Prior to MPN, n=16 (47%)**	**LPN After MPN, n=15 (44%)**	**Simultan. MPN & LPN n=3 (9%)**
1st DX initial treatment (I), n (%)	15 (94)	11 (73)	NA
1st DX treatment after 2nd DX (II), n (%)	4 (25)	11 (73)	MPN treatment - 2 (67)
1st DX treatment (II) response	2 CR, 1 PD, 1 UNK	12 CR/SD, 2PD, 1 UNK	2 CR
2nd DX treatment, n (%)	11 (69)	14 (93)	LNP treatment - 1 (33)
2nd DX treatment response	8 CR, 1 PD, 2 NR	12 CR, 2 PD, 1 UNK	1 CR
Stem Cell Transplantation, n (%)	4 (25)	2 (13)	0
Disease status at last follow up			
LPN	14 CR/SD, 1 PD, 1 UNK	12 CR, 2 PD, 1 UNK	3 CR
MPN	12 CR/SD, 2 PD, 2 UNK	10 CR, 4 PD, 1 UNK	3 CR
Evolution to MF or blastic phase, n (%)	2 MF (12.5)	2 ET, 3 PV*, 2 MF (47)	0
Overall status at last follow up			
Alive, n (%)	8 (50)	6 (40)	2 (67)
Death, n (%)	8 (50)	9 (60)	1 (33)
Cause of death	2 MPN; 1 LPN, 2 alloSCTcompl., 1 UNR, 2 UNK	2 MF, 1 LPN, 2 UNR, 4 UNK	UNK

Table 4

Comparison of previously published data with data from our series

	MPN type	Number, (%)	MPN prior LPN, n (%)	MPN after LPN, n (%)	MPN-LPN simultaneously, n (%)
Literature review	**TOTAL**	233	109 (47)	41 (18)	83 (36)
	ET	82 (35)	49 (45)[3,4,6]	10 (24)[6]	23 (28)
	PV	108 (46)	45 (41)[6,7,8]	15 (37)[6,7,8]	48 (58)[3,4]
	MF	31 (13)	15 (14)	11 (27)	5 (6)[6]
	MPN	11 (4.7)	0	5 (12)	6 (7)
	HES	1 (0.4)	0	0	1 (1)
Our own results	**TOTAL**	34	15 (44)	16 (47)	3 (9)
	ET	6 (18)	5 (33)	0	1 (33)
	PV	8 (23)	6 (40)	2 (12)	0
	MF	14 (41)	3 (20)	9 (56)	2 (66)
	MPN	4 (12)	1 (7)	3 (19)	0
	HES	2 (6)	0	2 (12)	0

* comments: citations include publications reporting more than 3 MPNs of the same type; the rest of literature represent mostly single case reports

** complete list of reviewed literature is in an online supplement at: