Sindromi Mieloproliferative Croniche Ph -

Confronto real Word e Studi registrativi

San Giovanni Rotondo 8 Novembre 2018

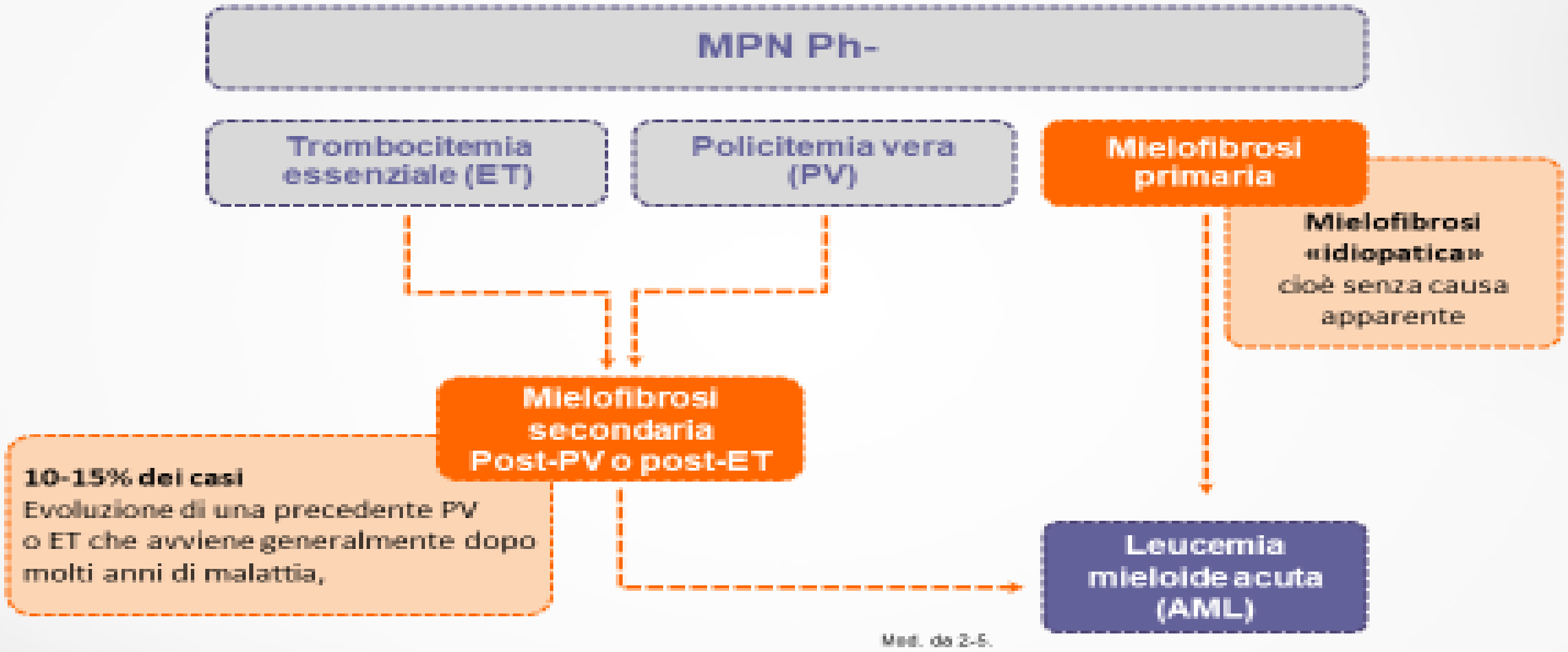
Dott. Patrizio Mazza

Myeloproliferative Neoplasms (MPN): WHO 2016

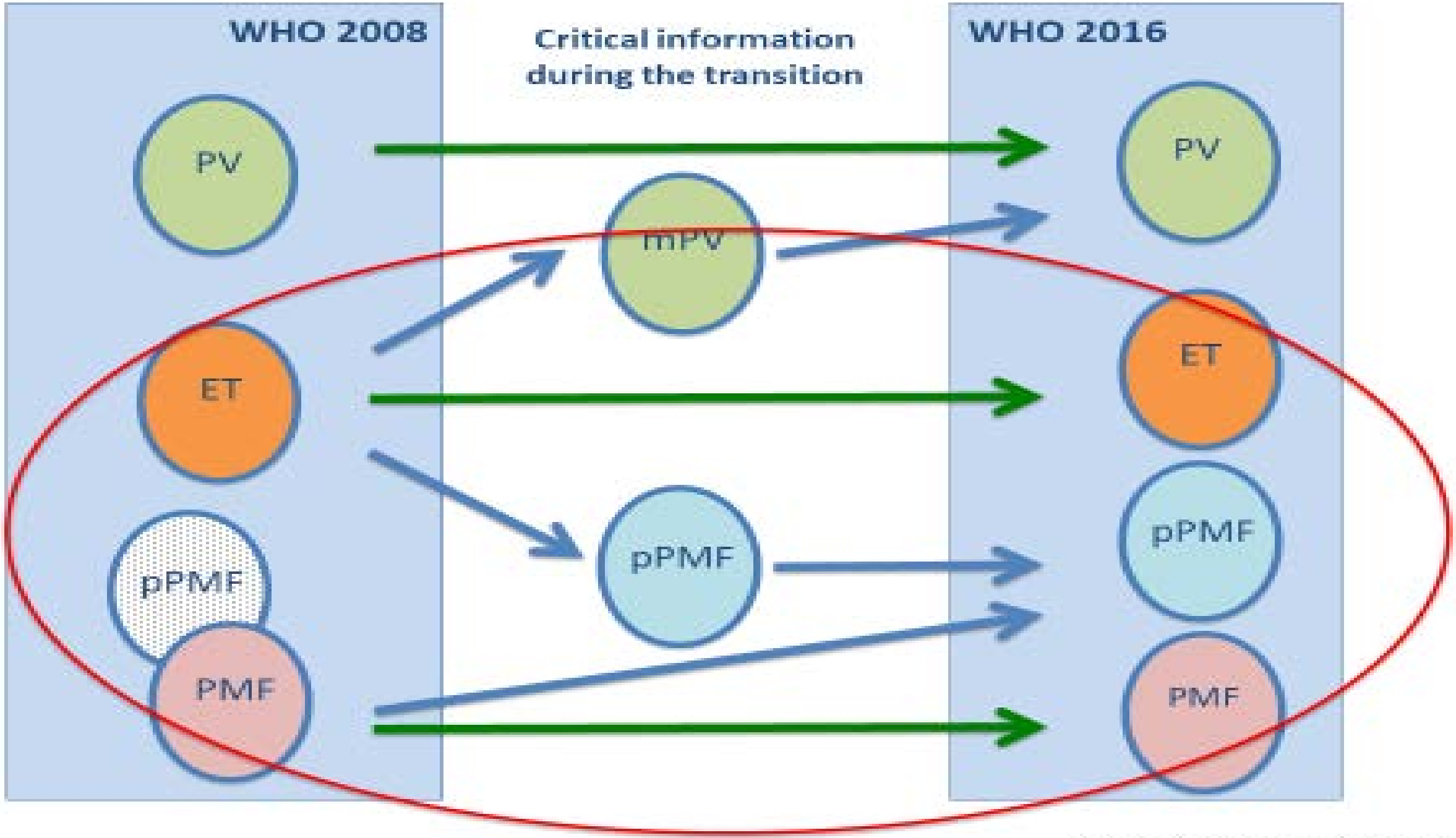
- Chronic myeloid leukemia (CML), BCR-ABL1[1]
- Chronic neutrophilic leukemia (CNL)
- **Polycythemia vera (PV)**
- **Primary myelofibrosis (PMF)**
  - PMF, prefibrotic/early stage
  - PMF, overt fibrotic stage
- **Essential Thrombocythemia (ET)**
- Chronic eosinophilic leukemia, not otherwise specified (NOS)
- MPN, unclassifiable

Arber A et al, Blood 2016; 12:2391-2405

MIELOFIBROSI PRIMARIA E SECONDARIA



1. Kornokji RS, et al. Cancer Control 2012; **2.** Vardiman JW, et al. Blood 2009; 114(5): 937-51; **3.** Abdel-Wahab O, et al. Ann Rev Med 2009; 60: 233-45; **4.** Moulard O, et al. Eur J Haematol 2013 Dec 24. doi: 10.1111/ejh.12256. [Epub ahead of print]; **5.** Barosi G, et al. Leukemia 2008; 22: 437-8.



Passamonti F, ASH 2016

DIAGNOSTIC CRITERIA OF PMF

- **WHO2016**

Pre-PMF	Overt PMF
Major criteria 1. BM biopsy with Mk proliferation and atypia, w/o reticulin fibrosis >G1; with incr. cellularity, granulocytic prolifer. and often decreased erythropoiesis 2. Not meeting WHO criteria for other myeloid neoplasms **3. Presence of *JAK2V617F*, *CALR* or *MPL* mutation, or in the absence of these mutations, presence of another clonal marker,** or absence of minor reactive BM reticulin **Minor criteria** 1. Anemia 2. Leucocytosis >$11x10^9$/L 3. Palpable splenomegaly 4. Increased LDH	**Major criteria** 1. BM biopsy with Mk proliferation and atypia with either reticulin fibrosis G2-3 and/or collagen 2. Not meeting WHO criteria for other myeloid neoplasms **4. Presence of *JAK2V617F*, *CALR* or *MPL* mutation, or in the absence of these mutations, presence of another clonal marker,** or absence of reactive myelofibrosis **Minor criteria** 1. Anemia 2. Leucocytosis >$11x10^9$/L 3. Palpable splenomegaly 4. Increased LDH 5. Leukoerythroblastosis
3 major + ≥1 minor	**3 major + ≥1 minor**

In the absence of any of the 3 major clonal mutations, the search for the most frequent accompanying mutations (eg. ***ASXL1, EZH2, TET2, IDH1/IDH2, SRSF2, SF3B1***) are of help in determining the clonal nature of the disease.

Arber DA et al. Blood 2016; 127:2391-405

Reproducibility of WHO criteria for prePMF

Studies with formal assessment of concordance between pathologists

Study	Consensus	n
Barbui, T et al., 2011 J Clin Oncol, 29:3179-84	81 %	1,104
Thiele, J et al., 2011 Blood, 117:5710-5718	88 %	295
Gisslinger, H et al., 2013 Blood, 121:1720-1728	83 %	259
Madelung, AB et al., 2013 Am J Hematol, 88:1012-1016	83 %	272
Gianelli U, et al., 2013 Mod Pathol, PMID: 24201120	76 %	103
Overall consensus	**82 %**	**2,033**

Study	Consensus	n
Wilkens, BS et al., 2008 Blood, 111:60-70	53 %	370
Brousseau, M et al., 2010 Histopathology, 56:758-767	65 %	127
Koopmans SM, et al., 2011 Am J Clin Pathol, 136:618-624	70 %	56
Buhr T, et al., 2012 Haematologica, 97:360-365	62 %	102
Overall consensus	**63 %**	**655**

Additional studies supporting validity of the WHO criteria (n=736)

Study	n
Florena, AM et al., 2004, Haematologica, 89:911-919	142
Kreft, A et al., 2005, Acta Haematol., 113: 137-143	275
Gianelli, U et al., 2006, Leuk. Lymphoma, 47:1774-1781	116
Gianelli, U et al., 2008, Am. J. Clin. Pathol., 130:336-342	50
Vener, C et al., 2008, Blood, 111:1862-1865	113
Ejerblad E et al., 2013, Hematology, 18:8-13	40

EPIDEMIOLOGIA - GENERALITÀ

Chi si ammala? Quando ci si ammala? È una malattia frequente?

- Lo studio della frequenza e della distribuzione di una malattia a livello di popolazione si definisce "epidemiologia".

- La frequenza di una malattia si può misurare in due modi: statico e dinamico

Misura statica: **PREVALENZA**

tutti i casi esistenti
in un certo momento
e in una certa popolazione

quanti sono **oggi**
i casi di mielofibrosi per ogni
100.000 persone?

Misura dinamica: **INCIDENZA**

numero di **nuovi casi** che si verificano
in una certa popolazione
in un certo intervallo di tempo

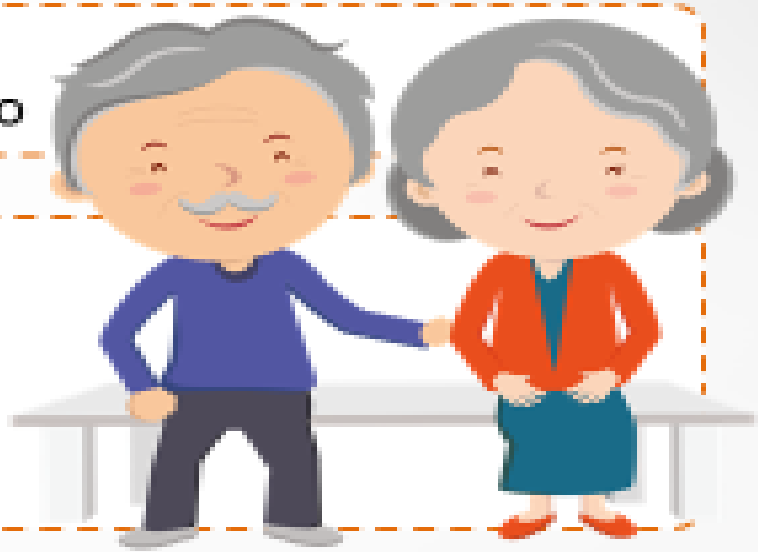
nell'arco di un anno, quanti sono
i **nuovi casi** di mielofibrosi
per ogni 100.00 persone?

EPIDEMIOLOGIA - DATI ATTUALI

Epidemiologia

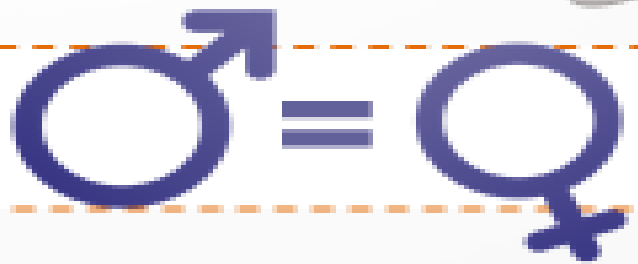
Prevalenza:
Da **1** a **9** casi su 100.000

Incidenza:
Da **0,5** a **1,5** nuovi casi su 100.000 soggetti all'anno



Età alla diagnosi:
nella maggior parte dei casi colpisce pazienti tra i **60** e i **70 anni** di età. Nel 15% dei casi può interessare persone con meno di 55 anni, mentre i casi pediatrici sono rarissimi

Sesso:
Non vi è prevalenza di sesso



AIL. Mielofibrosi. Conosciamola meglio. 2013.

Study Design

Seven international centers

Inclusion criteria:

local **ET diagnosis** (from 1975 to 2008)

and **pre-treatment Bone Marrow biopsy** obtained at time of diagnosis (or within 1 year of diagnosis in untreated patients)

1,104 ET patients

WHO 2008 review by

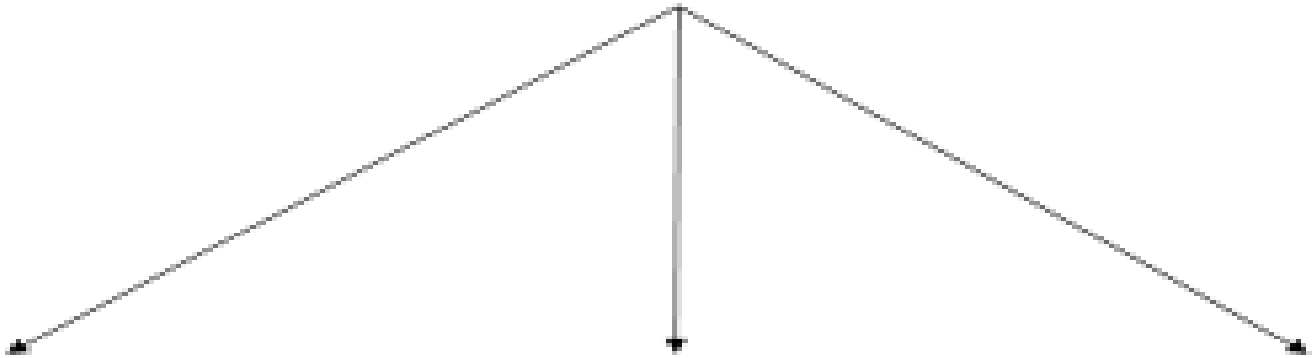
WHO author (JT)

completely blinded to outcome data

***True* ET** ***Early* MF**

Barbui T et al, JCO 2011; 29:3179-84.

FINAL ASSIGNMENT IN 1104 PATIENTS PRESENTING WITH ET



ET cases
891 (81%)

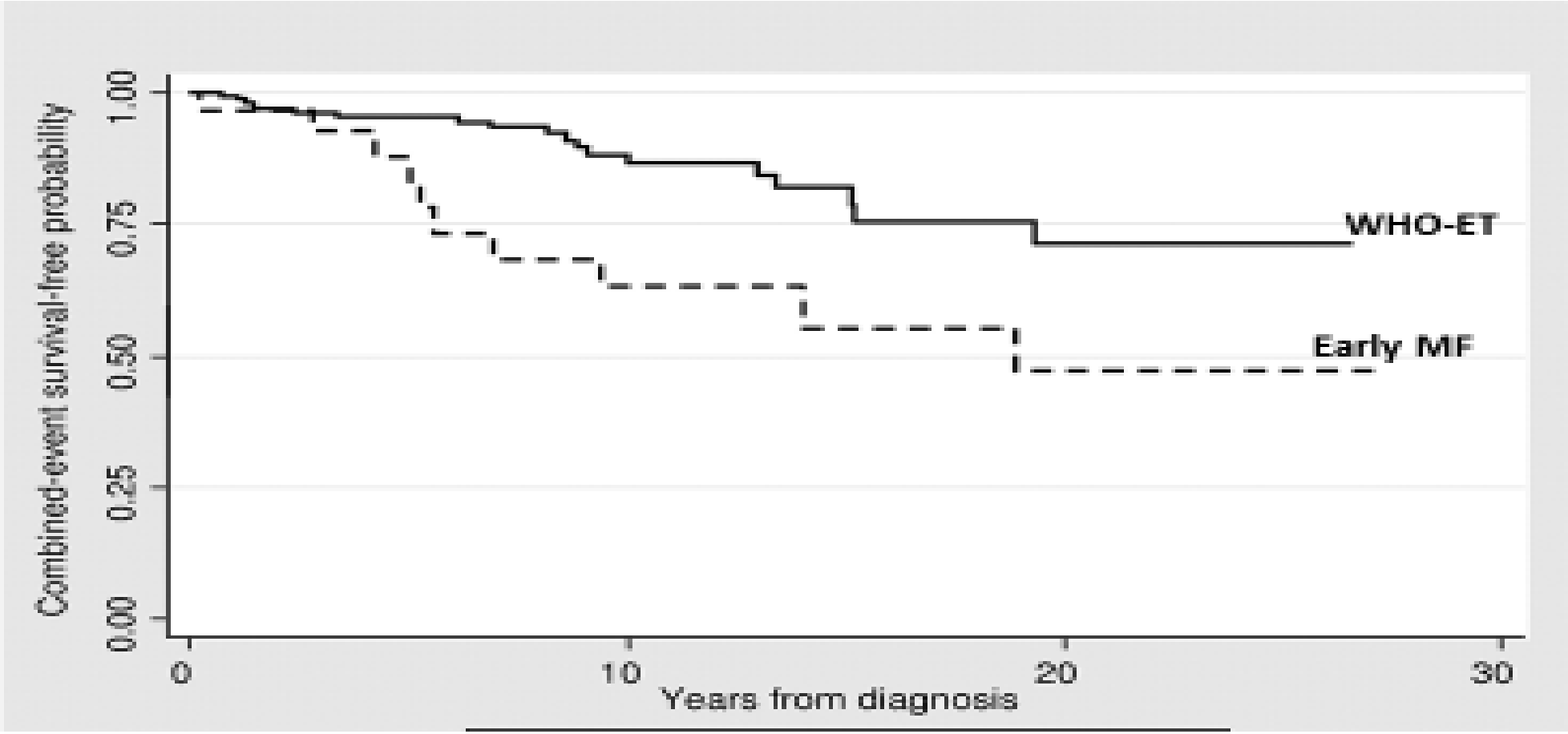
Early MF cases
180 (16%)

Others*
33 (3%)

*(were inadequate or reactive cases)

Agreement between pathologists was **83%** for discriminating ET from early/prefibrotic PMF

Clinical Outcome in Young Adults with ET *versus* Early/prefibrotic Myelofibrosis

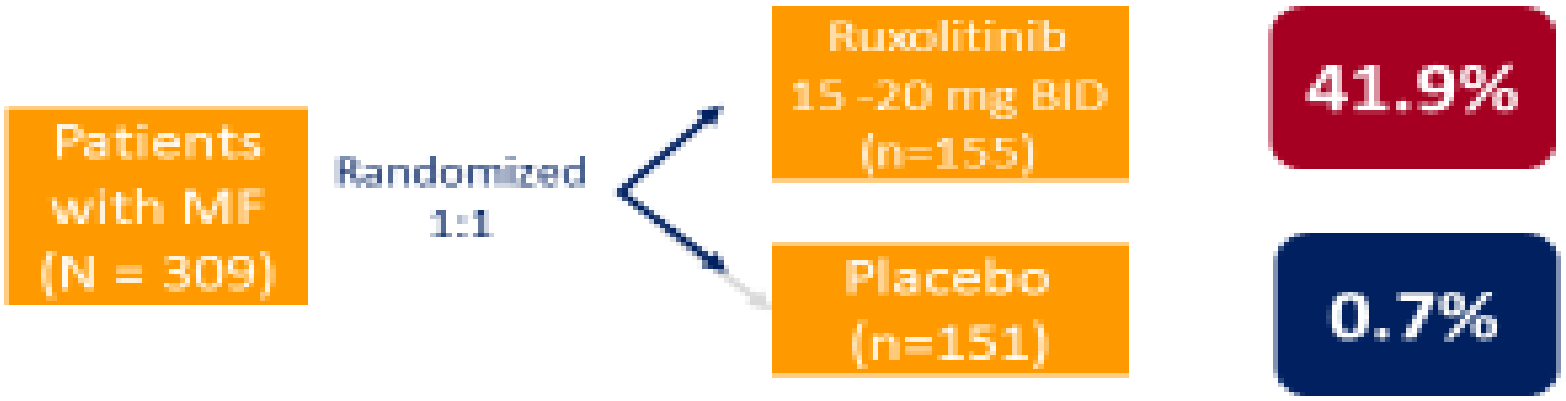


The rates of composite outcomes (thrombosis, bleeding, and evolution to overt MF) were significantly higher in early PMF than in WHO-ET patients (3.43% vs 1.29% of patients/year, respectively).

Barbui T et al. Blood 2012;120:569-571

COMFORT Trials (5-yrs follow up)

COMFORT-I



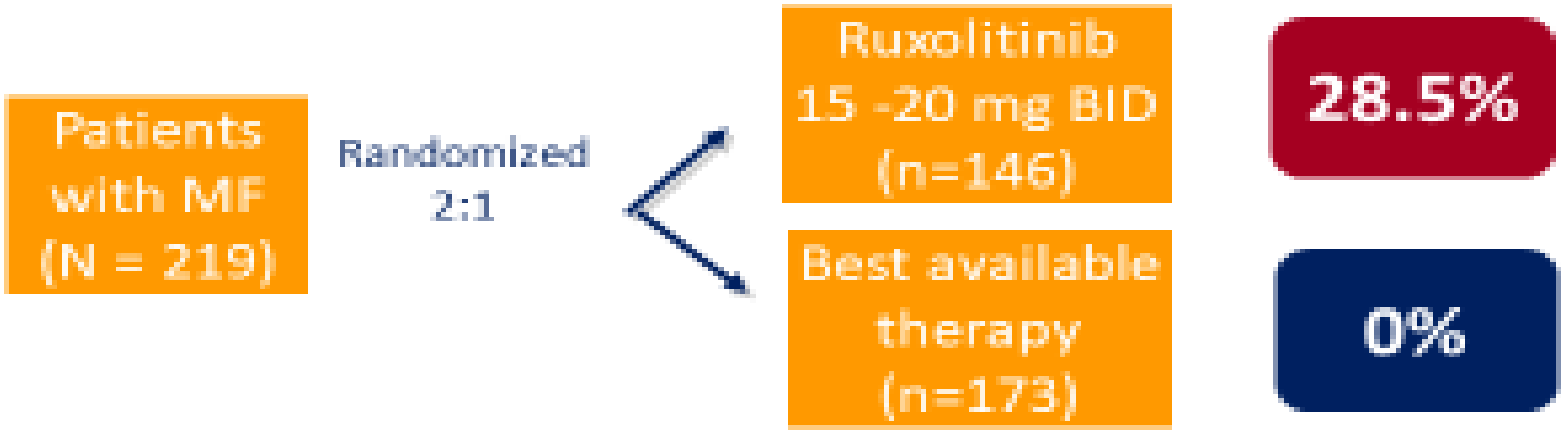
Primary Endpoint

- Subjects achieving ≥35% reduction in spleen volume from baseline to week 24

Secondary Endpoint

- Proportion of patients with ≥50% reduction in Total Symptom Score (mod. MFSAF v2.0)

COMFORT-II



Primary Endpoint

- Subjects achieving ≥35% reduction in spleen volume from baseline to week 48

Secondary/Exploratory endpoints

- Changes in functioning and symptoms

Verstovsek et al, NEJM 2012;366:799-807; Harrison C et al, NEJM 2012;366:787-98

Current status: ruxolitinib in MF

- A highly effective drug benefitting many patients (53% of spleen response at any time in COMFORT-II)
- Consolidated data from 2233 patients in the JUMP trial
- Anemia (gr 3-4:22%) and especially thrombocytopenia (gr 3-4:15%) may limit effective dosing

Studio di fase 2 per valutare l'efficacia e la sicurezza di Ruxolitinib in pazienti con mielofibrosi ed anemia (studio REALISE)

PMF,
PPV-MF,
PET-MF

1. Anemia Hb<10g/dl
2. PLT>50x10^9/L
3. Milza palpabile >5cm
4. Blasti SP ≤ 10%

12 settimane

16 settimane

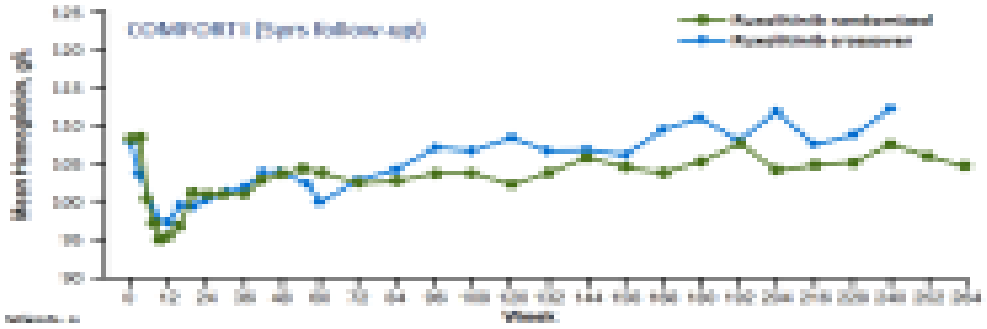
Ruxolitinib 10mg x2/die

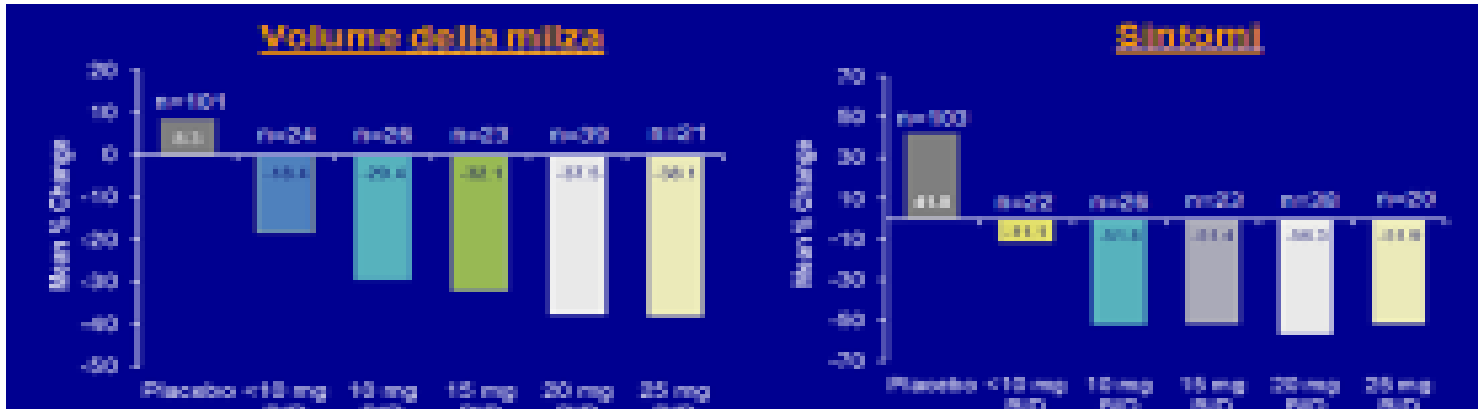
Riduzione del 50% della milza

SI

PLT 100-200 x10^9/L — Ruxolitinib 15 mg x2/die

PLT >200 x10^9/L — Ruxolitinib 20 mg x2/die

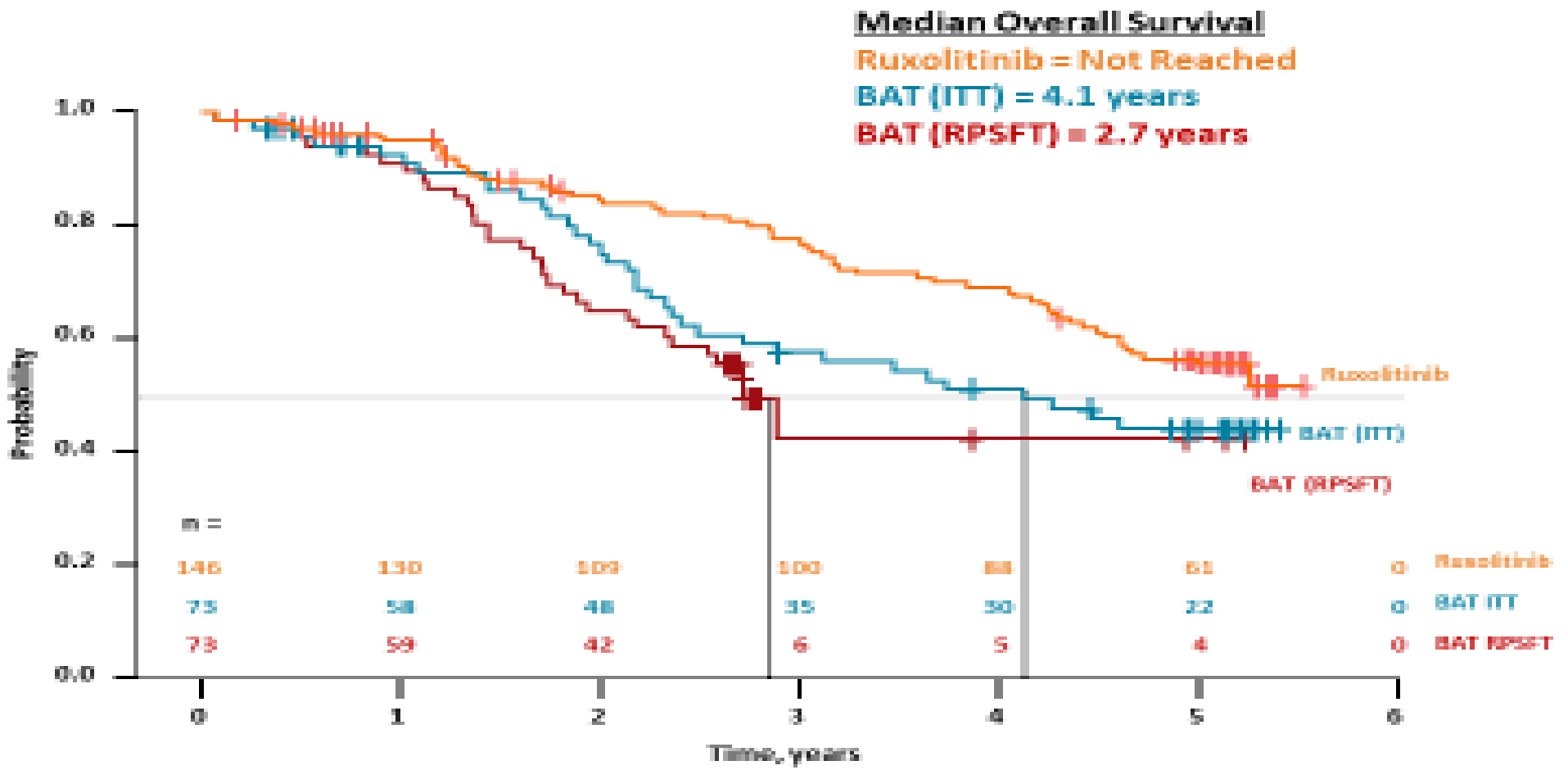




Current status: ruxolitinib in MF

- A highly effective drug benefitting many patients (53% of spleen response at any time in COMFORT-II)
- Consolidated data from 2233 patients in the JUMP trial
- Anemia (gr 3-4:22%) and especially thrombocytopenia (gr 3-4:15%) may limit effective dosing
- Infections are more frequent
- Lack of current evidence of benefit from early disease with aim of disease moderation
- Definition of failure variable in clinical trials, unclear in clinical practice

Ruxolitinib and OS: results from COMFORT-II

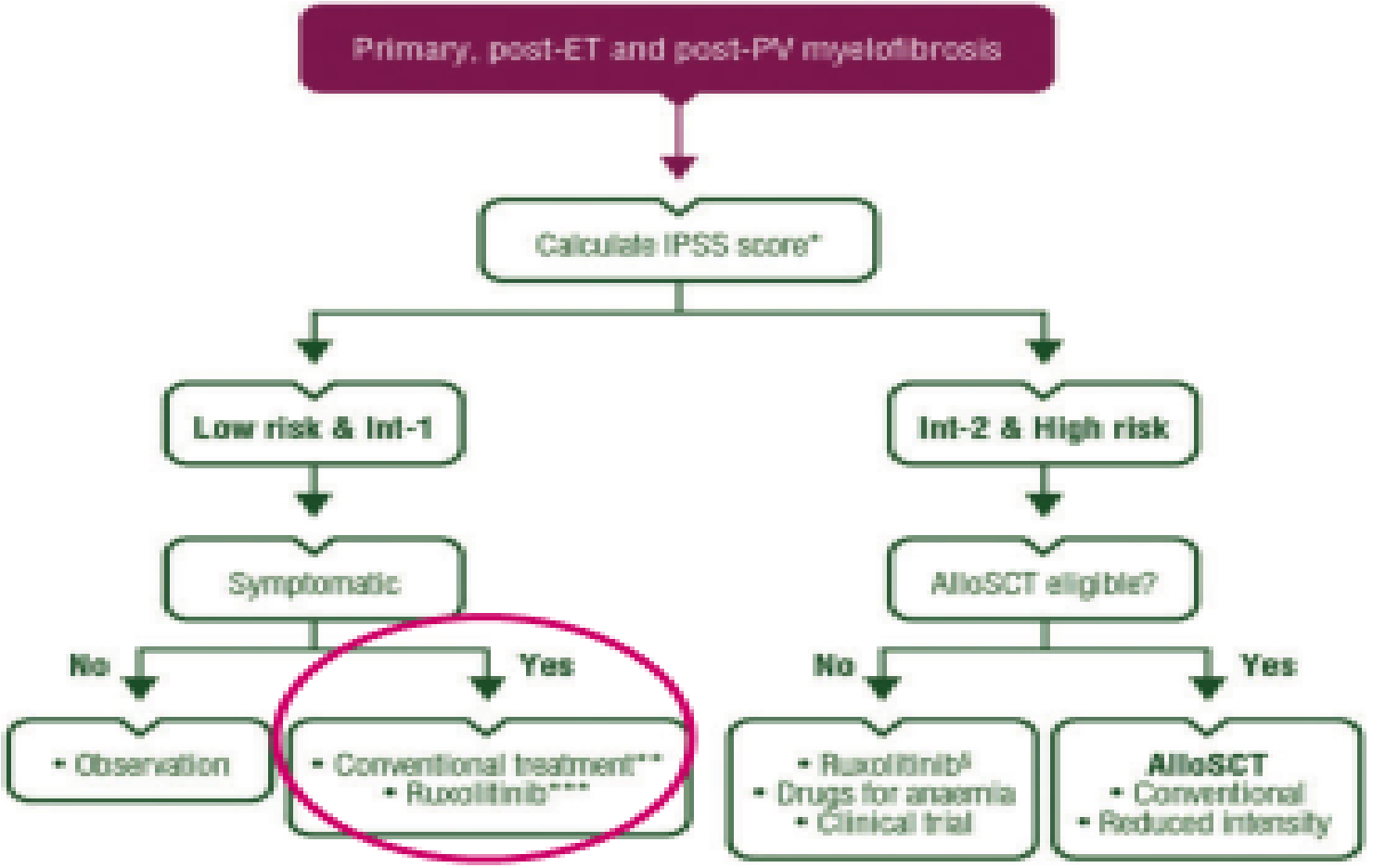


K-M estimated probability of OS at 5 yrs: 56% with Ruxolitinib and 44% with BAT

Harrison CN et al; Leukemia 2016;30;1701-7

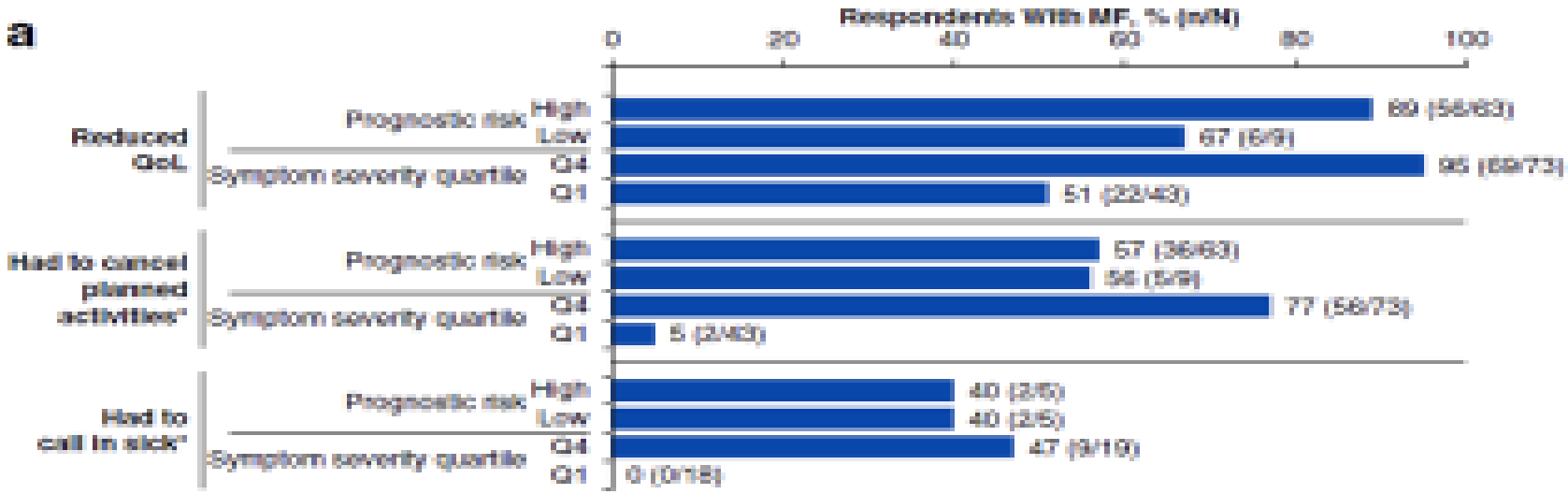
MF treatment algorithm

ESMO 2015 guidelines



Vannucchi et al, 2015, ESMO guidelines

IPSS low/Int-1 patients may have burdensome symptoms with impact on QoL



Lower DIPSS patients may be symptomatic in 44% of cases

QoL, work and social impairment is similar in lower and higher risk categories

Total Symptom Score is significantly associated with spleen length

A single MPN10 symptom value >5/10 has been suggested as predictive for higher DIPSS and for patients who could benefit from treatment

Mesa R, et al. *BMC Cancer* 2016;16:167

ELN/SIE evidence based recommendations

- **Ruxolitinib is recommended for improving splenomegaly in:**

- Patients with int2-high risk and either symptomatic or severe splenomegaly (*strong recommendation*)

- Patients with int1 risk and either symptomatic or severe splenomegaly not responsive or intolerant to HU or IFN (*weak recommendation*)

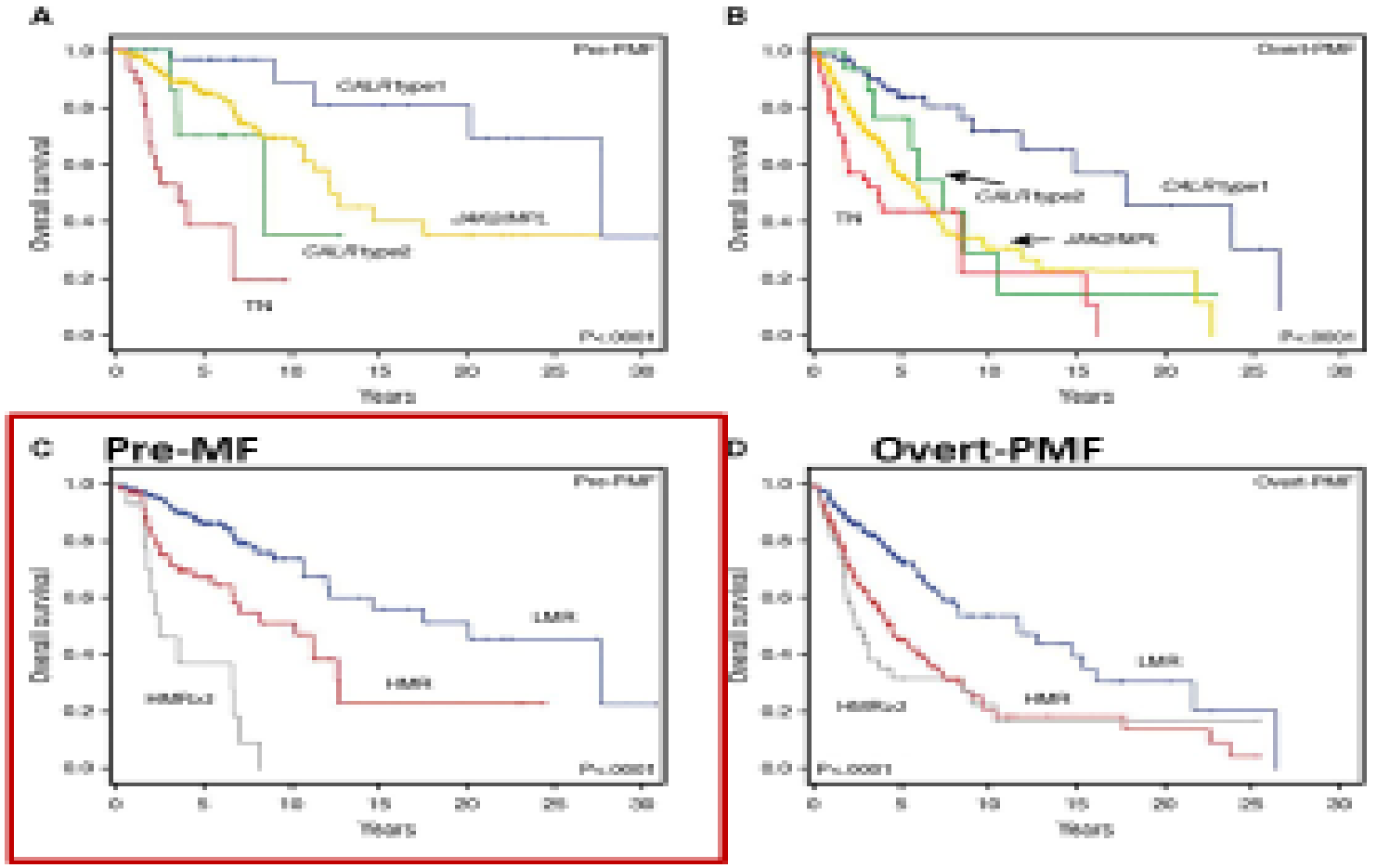
- Patients with int1 risk and both symptomatic or severe splenomegaly not previously treated with any cytoreductive agent (*weak recommendation*)

- **Ruxolitinib is recommended for improving symptoms in:**

- Patients with a MPN10 score > 44 or refractory itching (score >6) or unintended weight loss (>10% in the past 6 months) not attributable to other causes or unexplained fever (*strong recommendation*)

Marchetti et al, Leukemia 2016

Even the early stages may have prognostically unfavourable mutations



- Approximately 40% of intermediate-1 risk patients are at high molecular risk (HMR),[1] associated with poor prognosis[2]
- These are patients who may require early intervention

Guglielmelli et al. Blood 2017;129:3227-3236

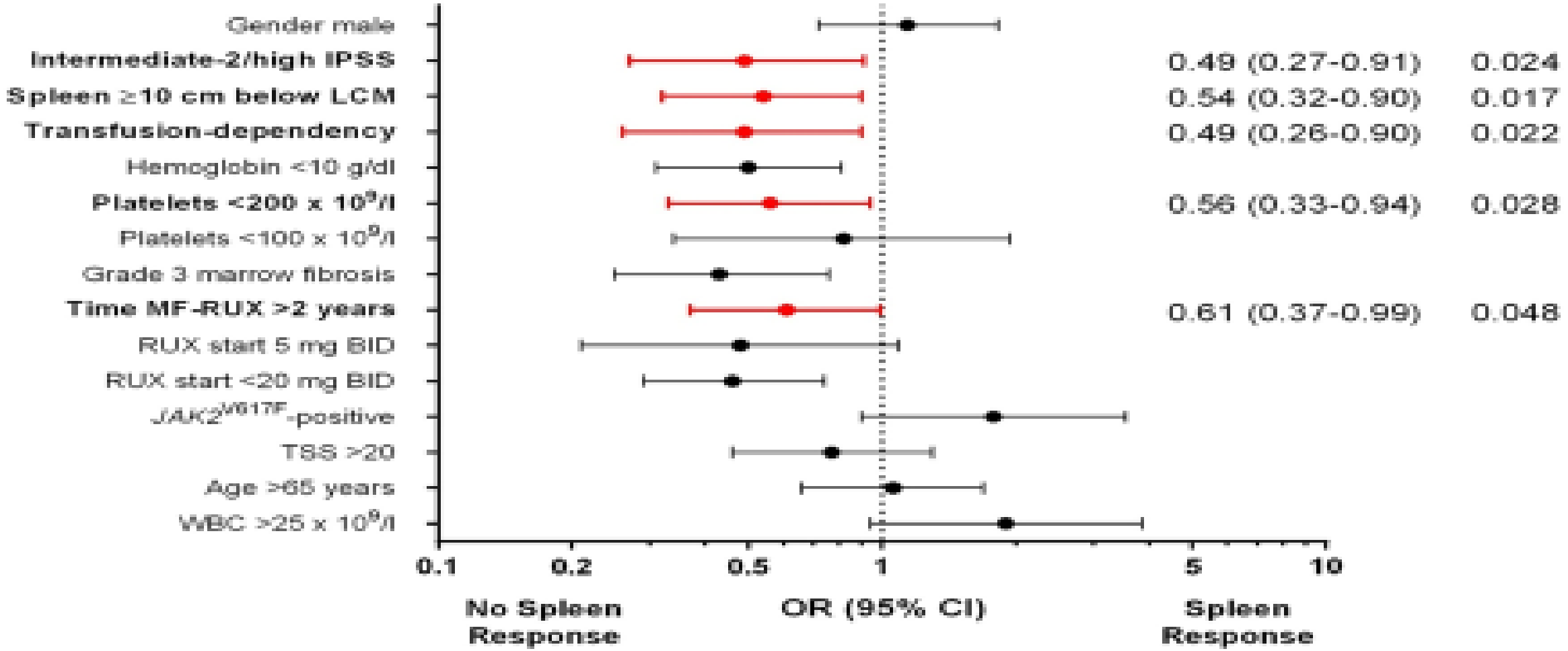
Italian multicentric study on 408 patients

Caratteristiche	Pazienti (n. 408)
Sesso maschile, no. (%)	230 (56.4%)
Mielofibrosi primaria, no (%)	222 (54.4%)
Età >65 anni, no (%)	259 (63.5%)
IPSS intermedio-2/alto, no (%)	344 (84.3%)
Emoglobina g/dl (range)	10.7 (7-16.7)
Anemia trasfusione dipendente	114 (27.9%)
Piastrine, x10^9/l (range)	257 (50-1887)
Sintomi costituzionali, no (%)	220 (53.9%)
Total symptoms score (TSS)	20 (12-70)
Milza palpabile, no (%)	394 (96.6%)
Milza ≥ 10 cm dal MCS	262 (64.2%)
JAK2^{V617F} mutation, no (% su 347)	281 (81.0%)
Cariotipo sfavorevole, no (% su 212)	17 (8.0%)
Fibrosi midollare grado 3 , no (% su 378)	108 (28.6%)
Tempo MF-inizio ruxo >2 anni, no (%)	185 (45.3%)
Dose iniziale di ruxolitinib	
5 mg BID	49 (12.0%)
10 mg BID	30 (7.3%)
15 mg BID	108 (26.5%)
20 mg BID	221 (54.2%)

- ✓ Caratteristiche principali all'inizio del trattamento con ruxolitinib :
  - Rischio IPSS Intermedio 2/alto (84.3%)
  - Sintomi costituzionali (53.9%)
  - Splenomegalia> 10 cm (64.2%)
- ✓ 27.9% anemia trasfusione dipendente
- ✓ Dose iniziale media=20 mg BID (7.3% 10 mg BID)
- ✓ Tempo mediano, tra diagnosi di MF e inizio ruxolitinib, 18 mesi (1-344)
- ✓ Follow-up mediano dalla diagnosi di MF, 3.8 anni (0.3-29.2)
- ✓ Mediana di esposizione a ruxolitinib, 20 mesi (3-56.2)

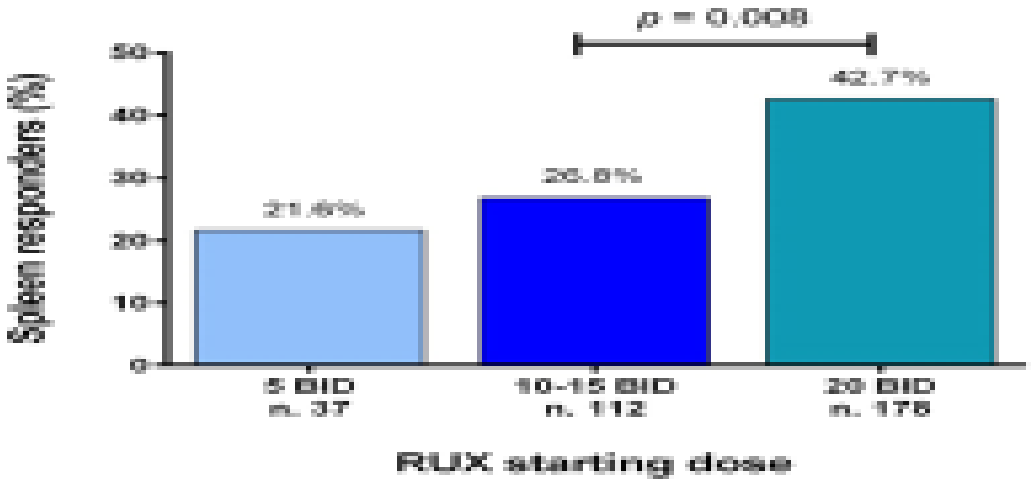
Palandri F *et al*, Oncotarget 2017

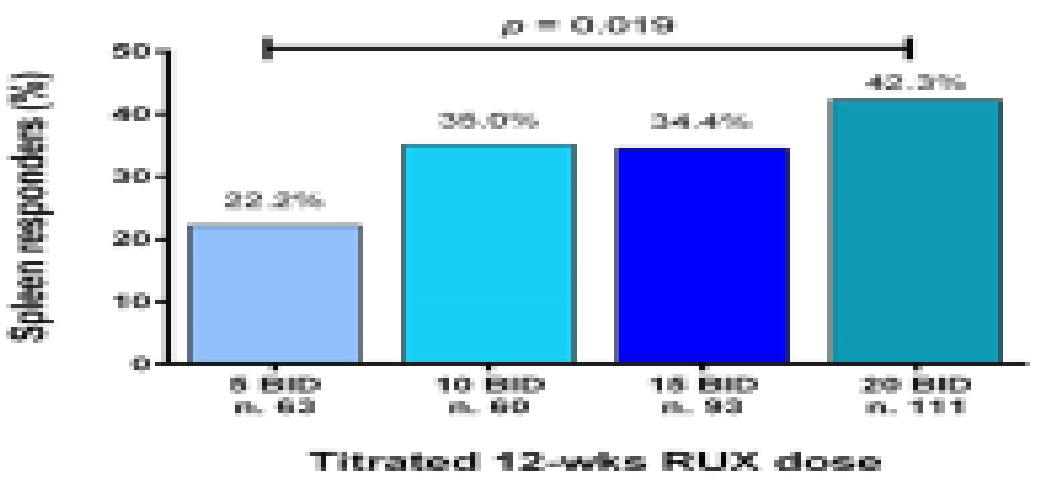
Time to ruxolitinib impacts on response

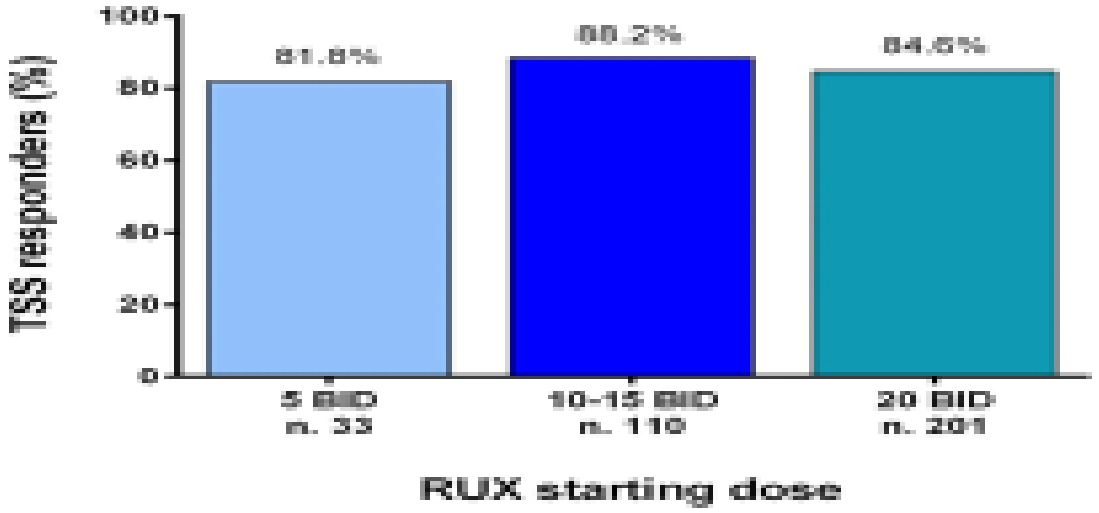


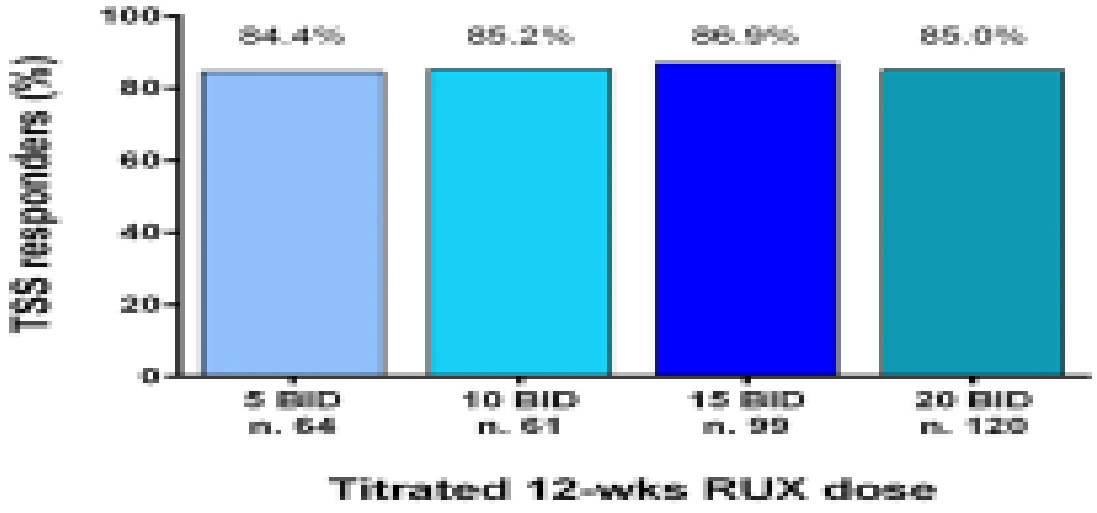
The probability of spleen response was significantly inferior in patients with a more advanced MF and in patients who started ruxolitinib later

Spleen and TSS response with dosage





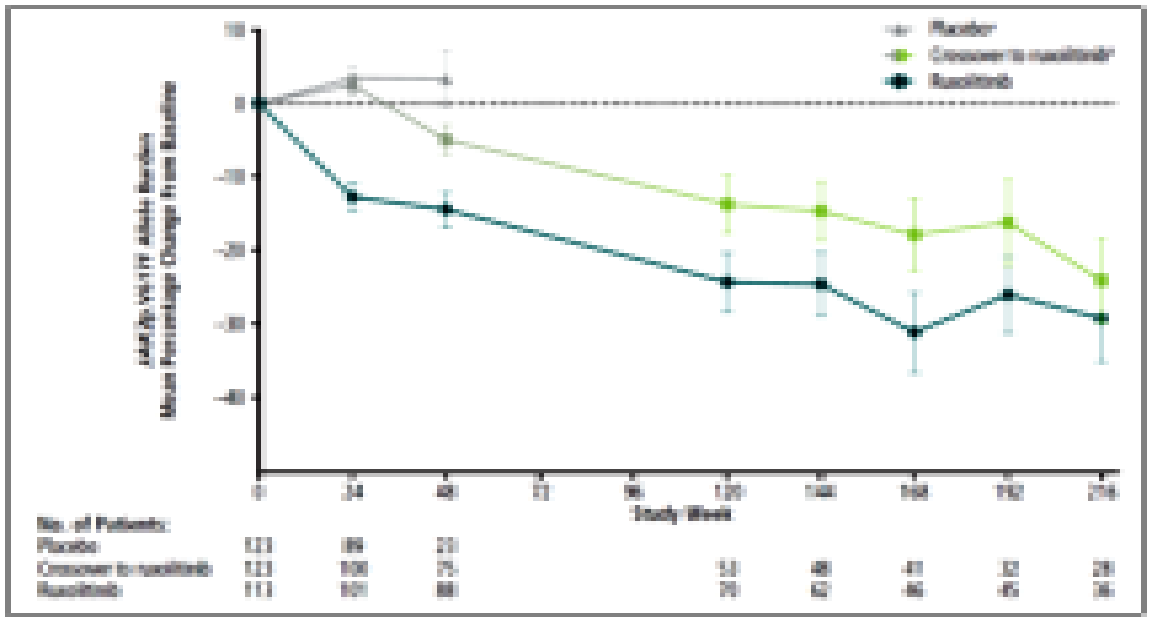




Palandri F et al. Oncotarget 2017

Can Ruxolitinib modify the pathogenesis of the disease?

- Modification of allele burden in the COMFORT studies especially in patients that have a short time from the diagnosis



- BM fibrosis modification due to a probable effect on the medullary microenvironment

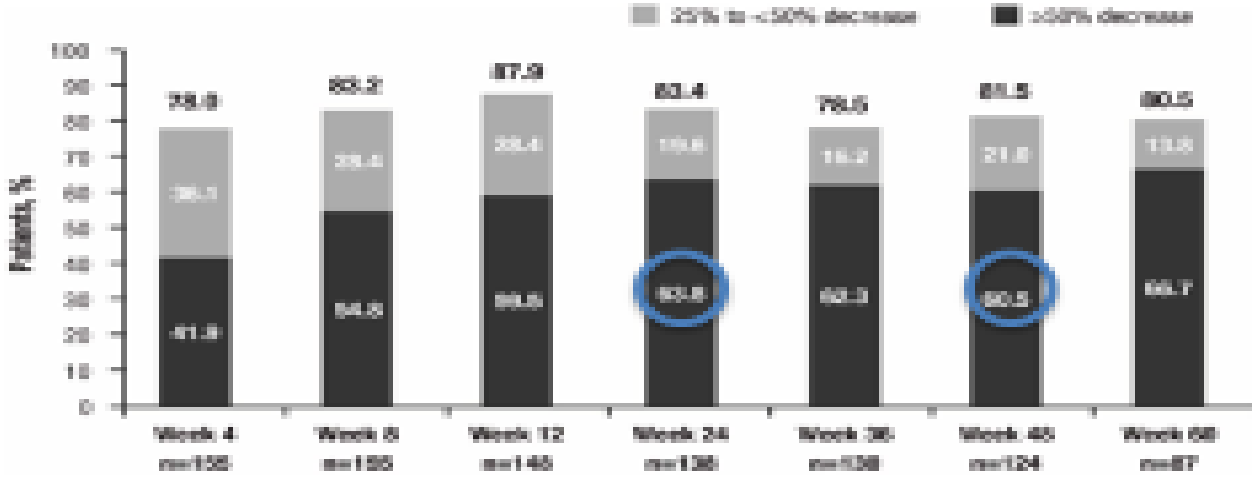
Last available postbaseline fibrosis grade	Ruxolitinib (n = 146)				
	Baseline Fibrosis Grade, n (%)				
	0	1	2	3	Missing
0	1 (0.7)	1 (0.7)	2 (1.4)	1 (0.7)	2 (1.4)
1	0	10 (6.8)	9 (6.2)	2 (1.4)	0
2	0	2 (1.4)	8 (5.5)	8 (5.5)	1 (0.7)
3	0	6 (4.1)	19 (13.0)	28 (19.2)	2 (1.4)
Missing	2 (1.4)	2 (1.4)	17 (11.6)	20 (13.7)	3 (2.1)

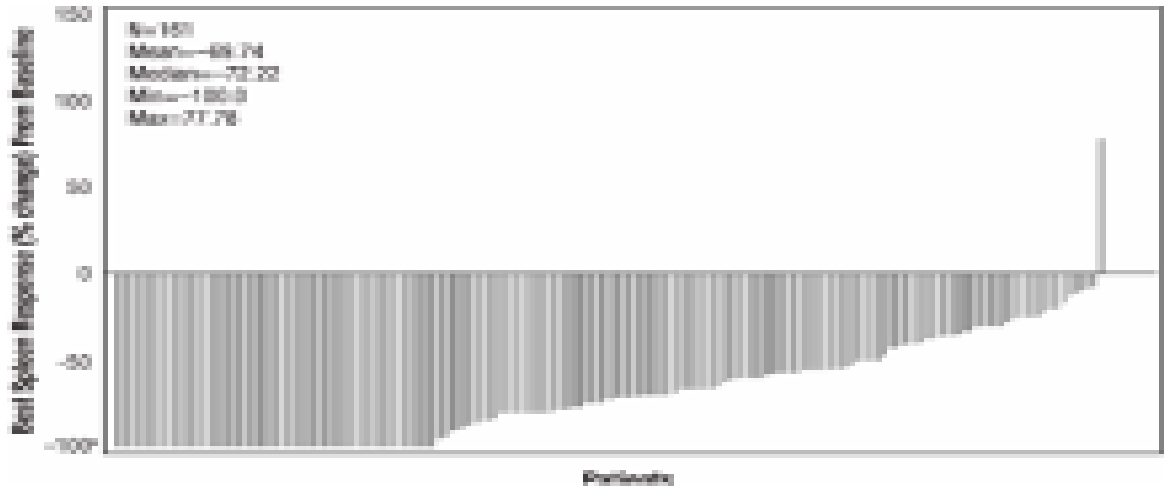
Improvement No change Worsening

Deininger M, et al. Blood. 2015 Jul 30; Harrison et al, ASH 2015 Abstract #59
Kvasnicka H, et al. Oral presentation at EHA Annual Congress; June 13-16, 2013. Abstract S591.
Hu K, et al. Blood 2014; 124(21): 2930
Kvasnicka H, et al. Blood 2014; 124(21): 4578

JUMP study: treatment for intermediate-1 risk pts

- 163 interm-1 risk pts (median age 62 years, range 25-79)
- Median time form diagnosis 17.9 mos (range 0.2-276 mos)
- 76% of pts remained on treatment, 65% with 20 mg BID
- 64% pts modified the dose
- Similar toxicity profile as to interm2/high risk (anemia 54% all grades, 24.5% grade 3/4, thrombocytopenia 40.5% all grades, 11% grade 3/4

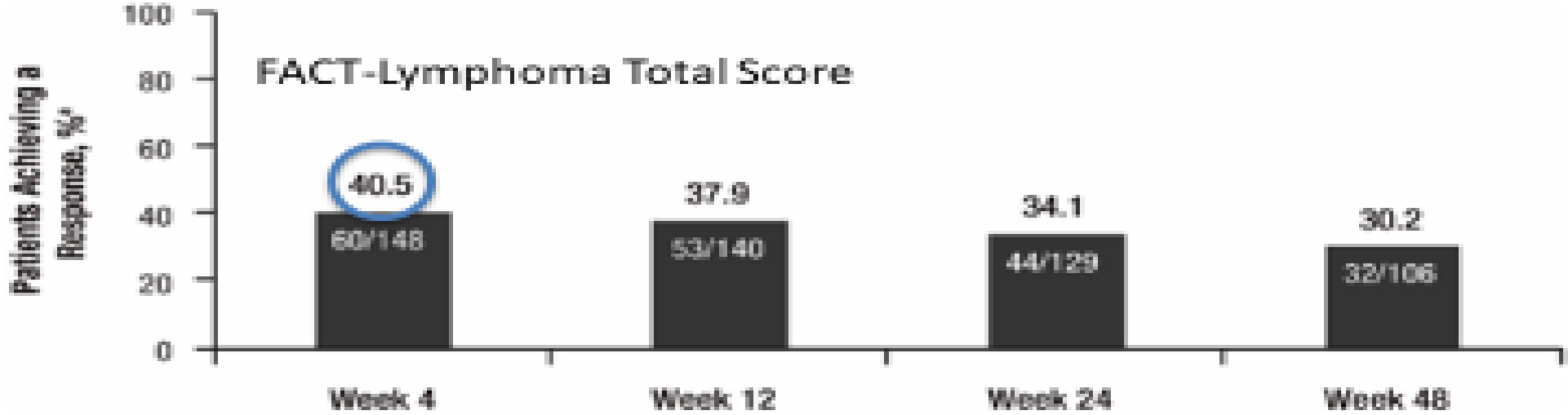


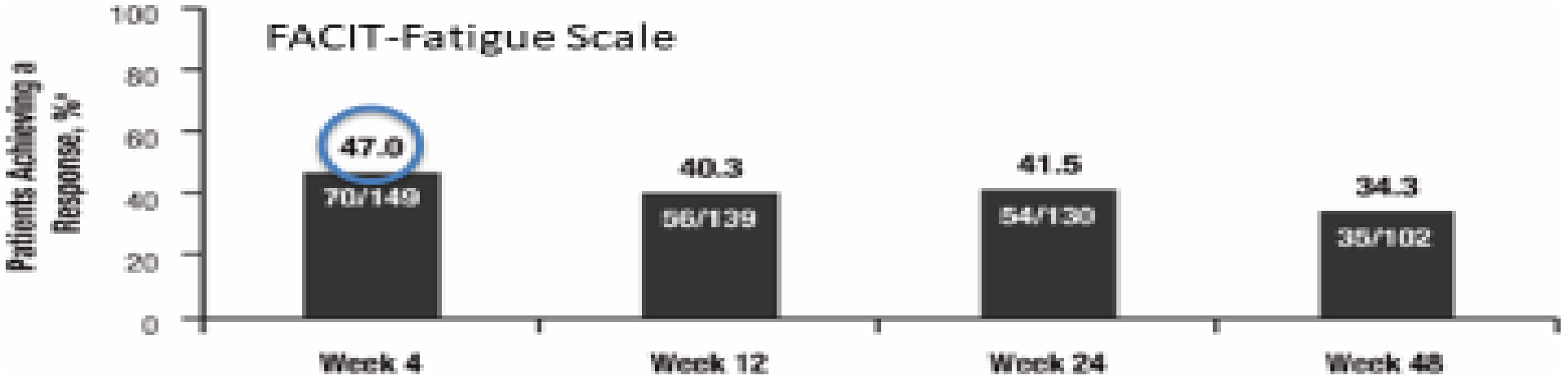


- At 72 weeks, 77.6% pts ha reduced > 50% of splenomegaly with 21% of CR.
- No differences of efficacy between 20 mg and 15 mg BID

Al-Ali et al, Haematologica 2016

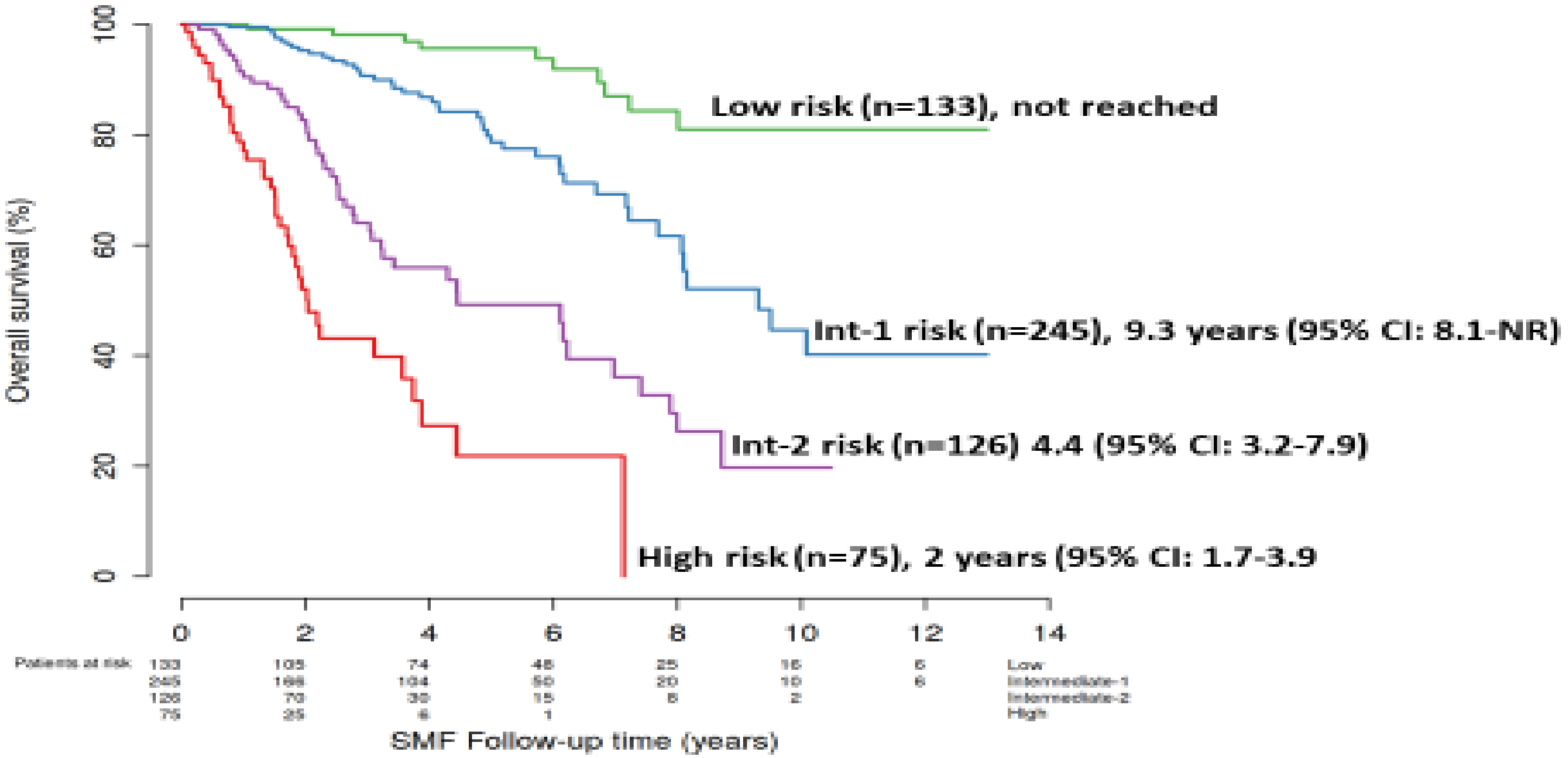
JUMP: improvement of symptoms in int-1 risk pts





Al-Ali et al, Haematologica 2016

The MYSEC-PM estimate of survival in SMF



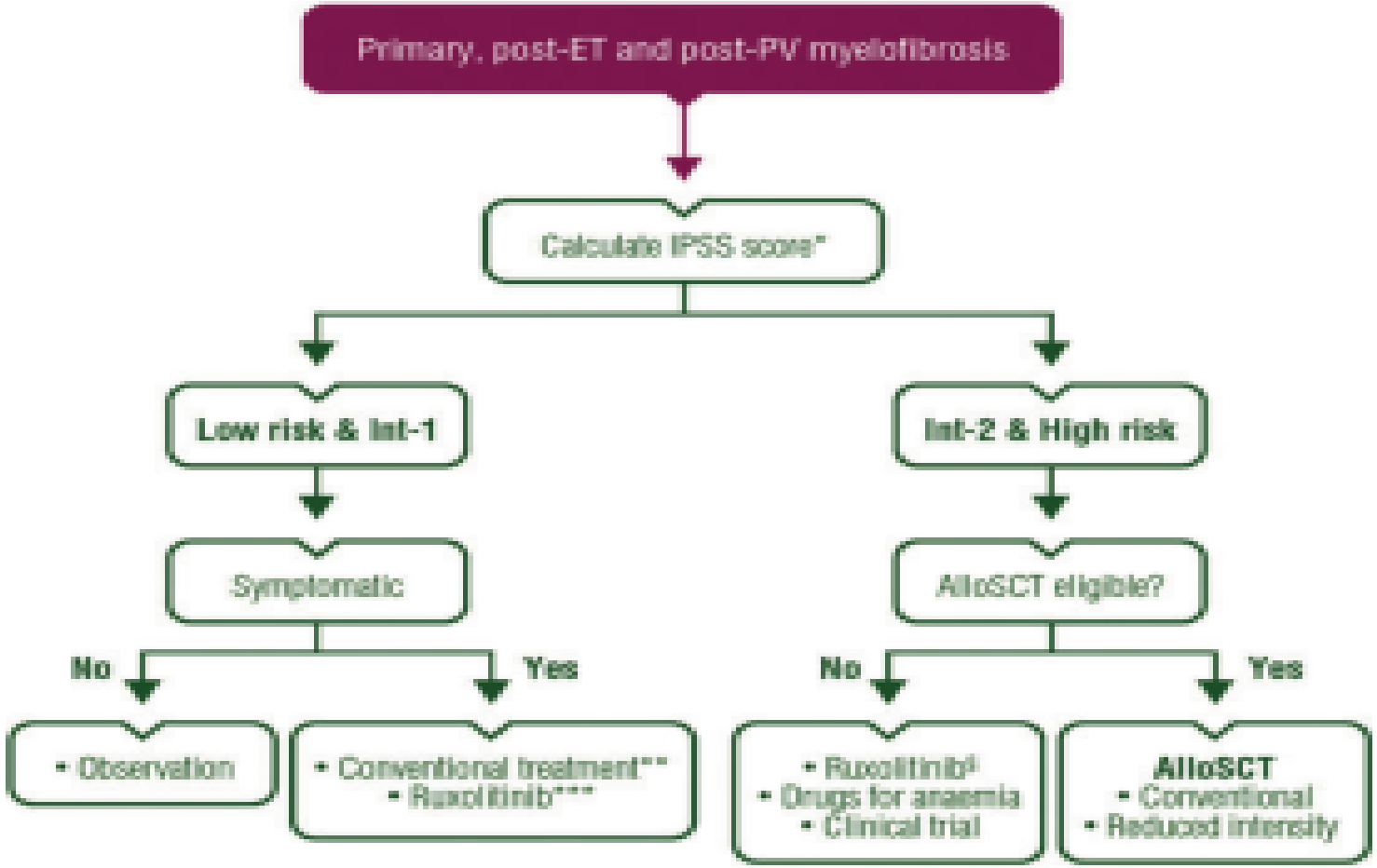
Passamonti et al. Leukemia. 2017 Dec;31(12):2726-2731.

Treatment of MF – general overview

- **All patients are very different**: the treatment needs to be tailored to an individual patient's symptoms and circumstances
- Some patients **may not need treatment** for several years, others are very unwell at diagnosis and **need treatment straight away**
- **Stem cell transplantation** is the only potentially *curative* strategy – but only a small minority of patients are suitable
- **For all other patients – the primary aim of current drug treatments are symptom control and improving quality of life**

MF treatment algorithm

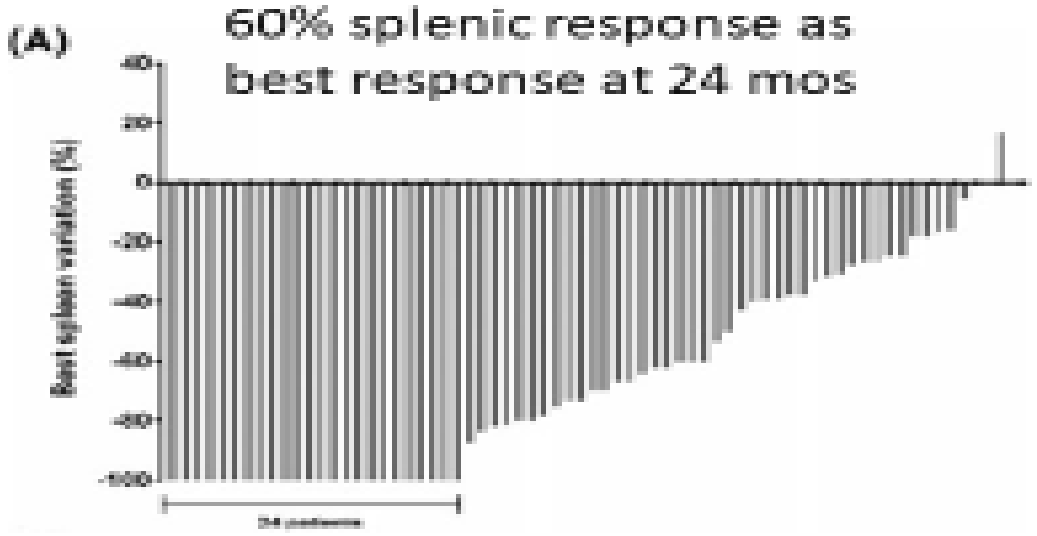
ESMO 2015 guidelines

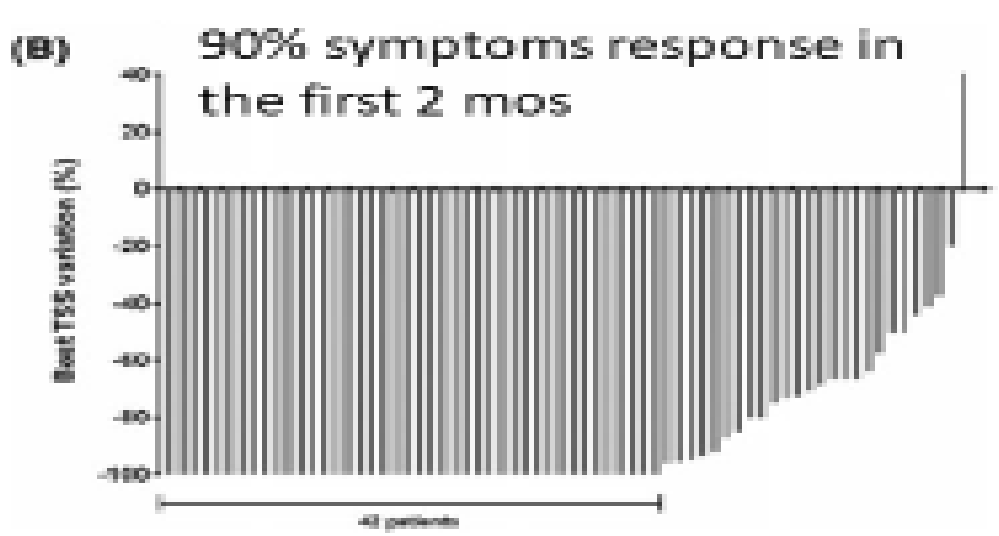


Vannucchi et al, 2015, ESMO guidelines

Cooperative Italian study for interm-1 risk (II)

- + 3 mos responses: 41% splenic responses, 72.5% symptoms response
- +6 mos: 54.7% splenic responses, 80% symptoms response
- After a median FU of 27 mos, 39% of pts maintained the response
- 80.6% of pts maintained the dose > 15 mg BID





Palandri et al, Hematol Oncol 2017

2018 ELN Recommendations on the Management of Myelofibrosis

Asymptomatic patients with low- or intermediate-I risk disease:

- Observation alone for IPSS/DIPSS/DIPSS-plus low- or intermediate-1 MF risk patients who lack significant symptoms, and who do not display significant anemia, splenomegaly, leukocytosis, or marked thrombocytosis.
- If cytoreductive treatment for the reduction of leukocytosis or thrombocytosis is indicated, the first-line drug of choice is hydroxyurea

Treatment of MF-associated anemia

- The choice of a specific drug for MF-associated anemia should be based on overall toxicity profile and its expected risk in the individual patient (Androgen, Thalidomide)
- In patients with transfusion dependency, a low rate of response to epoetins is expected, therefore the risk/benefit of a therapeutic use with epoetins is questionable.
- Lenalidomide use is justified in cases with the presence of del(5q31).
- There is currently not enough evidence to recommend combination therapy for MF-associated anemia, other than the addition of a short course of prednisone therapy to treatment with thalidomide.

Barbui T et al. Leukemia, 2018 Feb 27. doi: 10.1038/s41375-018-0077-1.

2018 ELN Recommendations on the Management of Myelofibrosis

Treatment of MF-associated splenomegaly

Ruxolitinib is recommended as first-line approach for MF-associated splenomegaly in patients with intermediate-2 or high-risk disease. In patients with intermediate-1 risk disease and highly symptomatic splenomegaly, first-line therapy is ruxolitinib.
In other patients with intermediate-1 risk disease, and in those with low-risk disease in need of therapy for MF-associated splenomegaly, hydroxyurea is recommended as first-line therapy.
Ruxolitinib is also recommended for reducing splenomegaly in patients with splenomegaly not responding or intolerant to hydroxyurea

Splenectomy

Splenectomy remains a viable palliative treatment option for drug-refractory symptomatic splenomegaly and may be considered when drug-induced anemia hampers the effective use of hydroxyurea or ruxolitinib.

Barbui T et al. Leukemia. 2018 Feb 27. doi: 10.1038/s41375-018-0077-1.

2018 ELN Recommendations on the Management of Myelofibrosis

Allogeneic stem cell transplantation

We recommend considering allogeneic stem cell transplant for all transplant-eligible patients with IPSS/DIPSS/DIPSS-plus high or intermediate-2 risk.
The Panel also recommended consideration of allogeneic stem cell transplantation for transplant eligible patients with IPSS/DIPSS/DIPSS Plus intermediate-1 risk score who present with either refractory, transfusion-dependent anemia, or a percentage of blasts in peripheral blood >2% in at least two repeated manual measurements, or adverse cytogenetics, or high-risk mutations.,
In this situation, the transplant procedure should be performed in a controlled setting (registries, clinical trial).

Barbui T et al. Leukemia. 2018 Feb 27. doi: 10.1038/s41375-018-0077-1.

Fin qui abbiamo

- Ruxolitinib è meglio che niente
- Ruxolitinib è meglio che qualsiasi altra terapia
- Ruxolitinib ha un’efficacia maggiore in stadi più precoci malattia
- Ruxolitinib è entrato nella terapia ormai consolidata del paziente ad alto rischio e si inserisce ormai sempre più frequentemente come terapia del paziente a rischio intermedio o basso e anche come preparazione al trapianto

Ma quale il limite nella vita reale

- Il problema dell’anemia
- Il problema della leucocitosi
- Il problema della piastrinopenia
- L’efficacia nelle mielofibrosi non splenomegaliche

Studio Romei

- Real-World Management of Myelofibrosis with Ruxolitinib: Initial Analysis of an Italian Observational Study (ROMEI)
- Massimo Breccia1, Paola Guglielmelli2, Alessandra Malato3, Francesco Mendicino4, Giuseppe Palumbo5, Carmine Selleri6, Daniela Cilloni7, Patrizio Mazza8, Sergio Siragusa9 Elisabetta Abruzzese10,Robin Foa11, Monica Crugnola12, Domenico Pastore13, Serena Rupoli14, Umberto Vitolo15, Mara Morelli16, Francesca Palandri17 and Francesco Passamonti18.

RoMEI

- ROMEI (CINC424AIT04 Ruxolitinib Observational study in Myelofibrosis treated patiEnts in Italy) is a prospective observational study that aims to bridge the knowledge gap between the clinical experience of registration trials and routine patient management by following roughly 200 myelofibrosis (MF) patients (pts) treated with ruxolitinib in everyday clinical practice. Enrollment began in April 2017 and ended in May 2018.

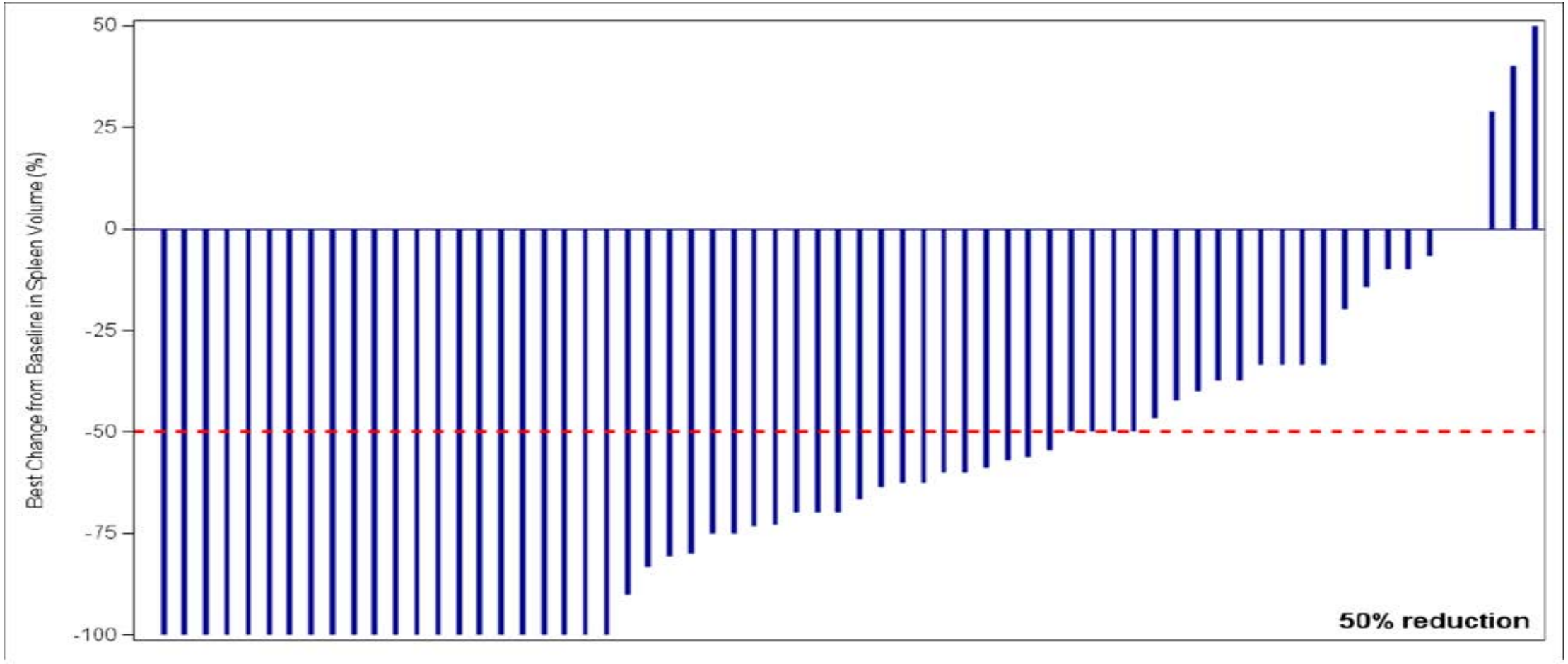
ROMEI

- The primary endpoint is to evaluate changes in symptoms and quality of life during treatment with ruxolitinib through the Myeloproliferative Neoplasm 10 (MPN-10) disease-specific questionnaire and EuroQoL-5D-5L (EQ-5D-5L) general health questionnaire. Secondary endpoints: spleen length (change from baseline in palpable spleen length from left costal margin), effects on bone marrow fibrosis, changes in patient-reported outcome (Myelofibrosis 7-Items Symptom Scale), overall survival (OS), adherence to treatment, safety and tolerability, and changes in work and productivity impairment. This first interim analysis evaluated only the primary endpoint, spleen length, OS and safety of the first pts with at least 24 weeks of exposure to ruxolitinib.

Risultati

- Mean spleen length decreased from 9.78 ± 5.65 cm (range 0 - 24) at baseline to 4.97 ± 5.91 cm (range 0 - 24) at Visit 5, corresponding to a mean absolute change of -5.82 cm (95% CI: -7.23; -4.41 cm) and a percentage change of -58.56% (95% CI: -69.55; -47.57%). The proportion of patients with a > 50% reduction in palpable spleen length increased at each visit: 0.36 (95% CI: 0.24; 0.48) at Visit 2, 0.52 (95% CI: 0.39; 0.65) at Visit 3, 0.62 (95% CI: 0.50; 0.75) at Visit 4 and 0.64 (95% CI: 0.51; 0.77) at Visit 5. Best changes from baseline in spleen volume % in evaluable pts is show in Figure 1b.

Riduzione della milza



ROMEI

- Preliminary data of the ROMEI study confirm the efficacy of ruxolitinib in everyday clinical practice in terms of symptom relief assessed through the MPN-10 and spleen response. The improvement from baseline observed in MPN 10 total score and the slight early improvement in EQ-5D-5L score at Week 24 may be partially related to the shorter median time from diagnosis to start of treatment (only 4 months) compared to that of pivotal or phase IIIb clinical trials.

Che cosa manca per la vita reale?

- Paziente di 70 anni con una storia di mielofibrosi primaria da 7 anni con milza all'ombelicale trasversa ed epatomegalia con varici esofagee saltuariamente sanguinanti, piastrinopenia (<60x10^3/uL), leucopenia e blasti circolanti 5%
- Trasfusioni o EPO in alternativa
- Ruxolitinib?

Che cosa manca per la vita reale?

- Paziente di 66 anni con alle spalle una storia di malattia di 5 anni con splenomegalia all'ombelicale trasversa, PLT 700x10^3/uL, WBC 25x10^3/uL, Hb 10.2.
- WBC in crescita
- Oncocarbide
- Ruxolitinib?

Cosa manca per la vita reale?

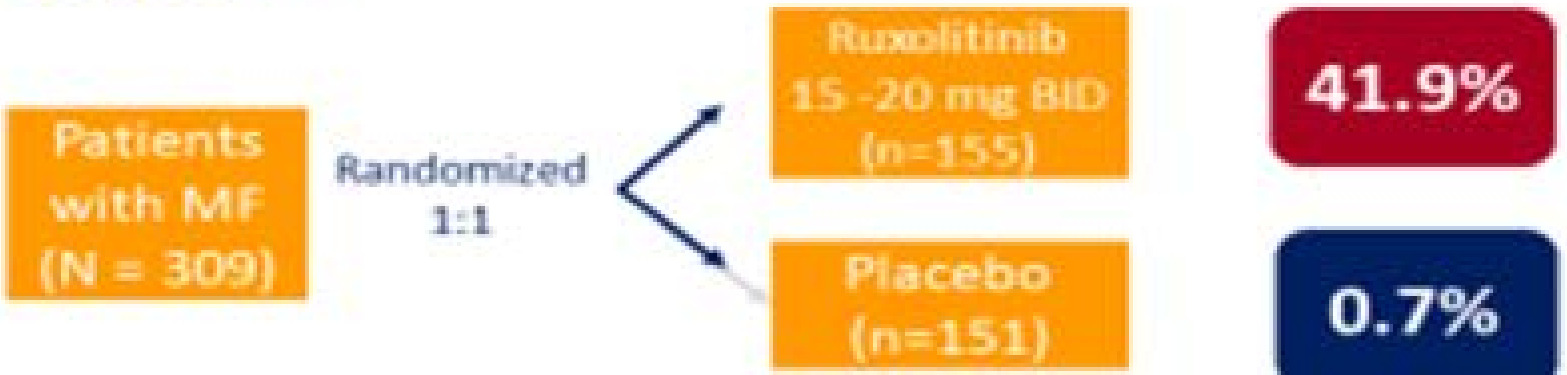
- Paziente di 73 anni testimone di Geova, Hb 6,7gr/dL, splenomegalia all'ombelicale trasversa, PLT 130x10^3/uL, WBC 3,2x10^3/uL
- Eritropoietina + bilancio del ferro
- Ruxolitinib?

Cosa manca per la vita reale?

- Quando è il timing corretto per le terapie di cui si dispone
- La miglior terapia va utilizzata all'inizio o alla fine?
- Fino a quando possiamo spingere con la terapia con Ruxolitinib?
- Quanto possono essere utili le combinazioni con oncocarbide o altro
- Eritropoietina e Ruxolitinib

COMFORT Trials (5-yrs follow up)

COMFORT-I



Primary Endpoint

- Subjects achieving ≥35% reduction in spleen volume from baseline to week 24

Secondary Endpoint

- Proportion of patients with ≥50% reduction in Total Symptom Score (mod. MFSAF v2.0)

COMFORT-II

Primary Endpoint

- Subjects achieving ≥35% reduction in spleen volume from baseline to week 48

Secondary/Exploratory endpoints

- Changes in functioning and symptoms

Verstovsek *et al*, NEJM 2012;366:799-807; Harrison C *et al*, NEJM 2012;366:787-98

Considerazioni

- Paziente con mielofibrosi già con una storia di malattia e terapia ha il 41% di possibilità di sopravvivenza a 5 anni con Ruxolitinib e pressochè 0 chances senza farmaco
- Se somministriamo Ruxolitinib fin dalla prima diagnosi cosa succede?
- Il vero quesito ora è di sapere quanto è il tempo medio di perdita della risposta nei pazienti che hanno iniziato Ruxolitinib alla prima diagnosi