# El resurgir del Interferón

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THE LANCET, AUGUST 13, 1988

# RECOMBINANT INTERFERON-ALPHA FOR TREATMENT OF POLYCYTHAEMIA VERA

## HAEMATOLOGICAL FINDINGS IN THREE PATENTS WITH POLYCYTHAEMIA VERA BEFORE (A) AND DURING (B) PHLEBOTOMY AND 1 YEAR AFTER START OF rIFN-α (C)

| — | Patient 1 (64, F) | | | Patient 2 (52, M) | | | Patient 3 (46, M) | | |
|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | A | B | C | A | B | C |
| RBC | 8·0 | 5·1 | 4·6 | 6·5 | 7·1 | 5·6 | 6·7 | 5·5 | 6·7 |
| Hct | 72 | 47 | 36 | 58 | 49 | 37 | 59 | 51 | 49 |
| WBC | 13·5 | 7·7 | 7·5 | 18·2 | 12·7 | 10·3 | 8·1 | 6·6 | 4·0 |
| Plt | 276 | 300 | 225 | 305 | 350 | 450 | 654 | 425 | 400 |
| Spl | 2·0 | . . | 0·5 | 15·0 | . . | 8·0 | 4·0 | . . | tip |

For A and B results are medians.
RBC = red blood-cells ($10^6$/μl); Hct = haematocrit (%); WBC = white blood-cells ($10^6$/μl); Plt = platelets (1000s/μl); Spl = spleen size (cm below left costal margin).

Silver, Lancet 1988;2(8607):403

# Practice Patterns in the Diagnosis and Treatment of Polycythemia Vera in the Post–*JAK2* V617F Discovery Era

Elizabeth M. Kander, MD[a]; Alison R. Moliterno, MD[b]; Alfred Rademaker, PhD[a]; Michael B. Streiff, MD[b]; Jerry L. Spivak, MD[b]; and Brady L. Stein, MD, MHS[a]

Journal of the National Comprehensive Cancer Network 2016;14:1238

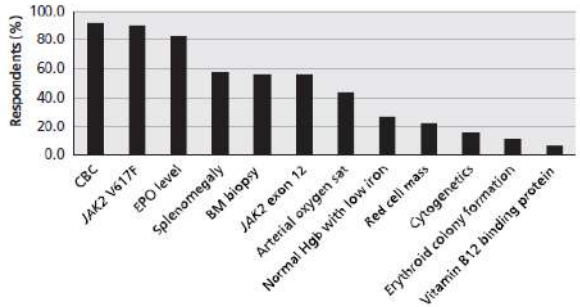


**Figure 2.** Diagnostic testing reported most useful to diagnose polycythemia vera.
Abbreviations: BM, bone marrow; CBC, complete blood count; EPO, erythropoietin; Hgb, hemoglobin; sat, saturation.

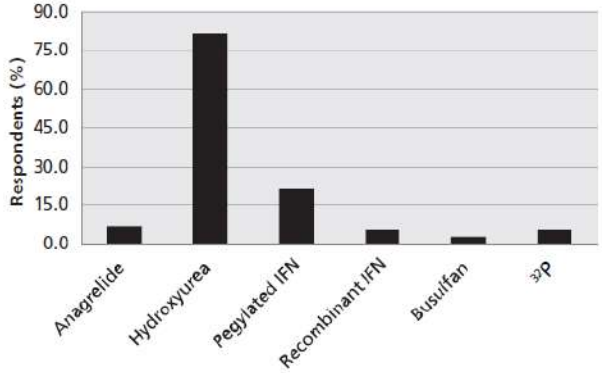


**Figure 5.** Preferred cytoreductive therapy in polycythemia vera.
Abbreviation: IFN, interferon.

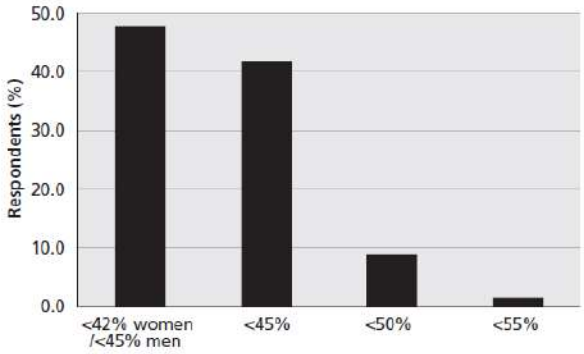


**Figure 3.** Target hematocrit in polycythemia vera.

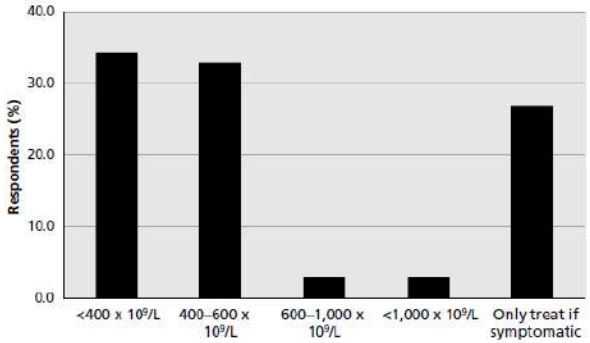


**Figure 4.** Target platelet count in polycythemia vera.

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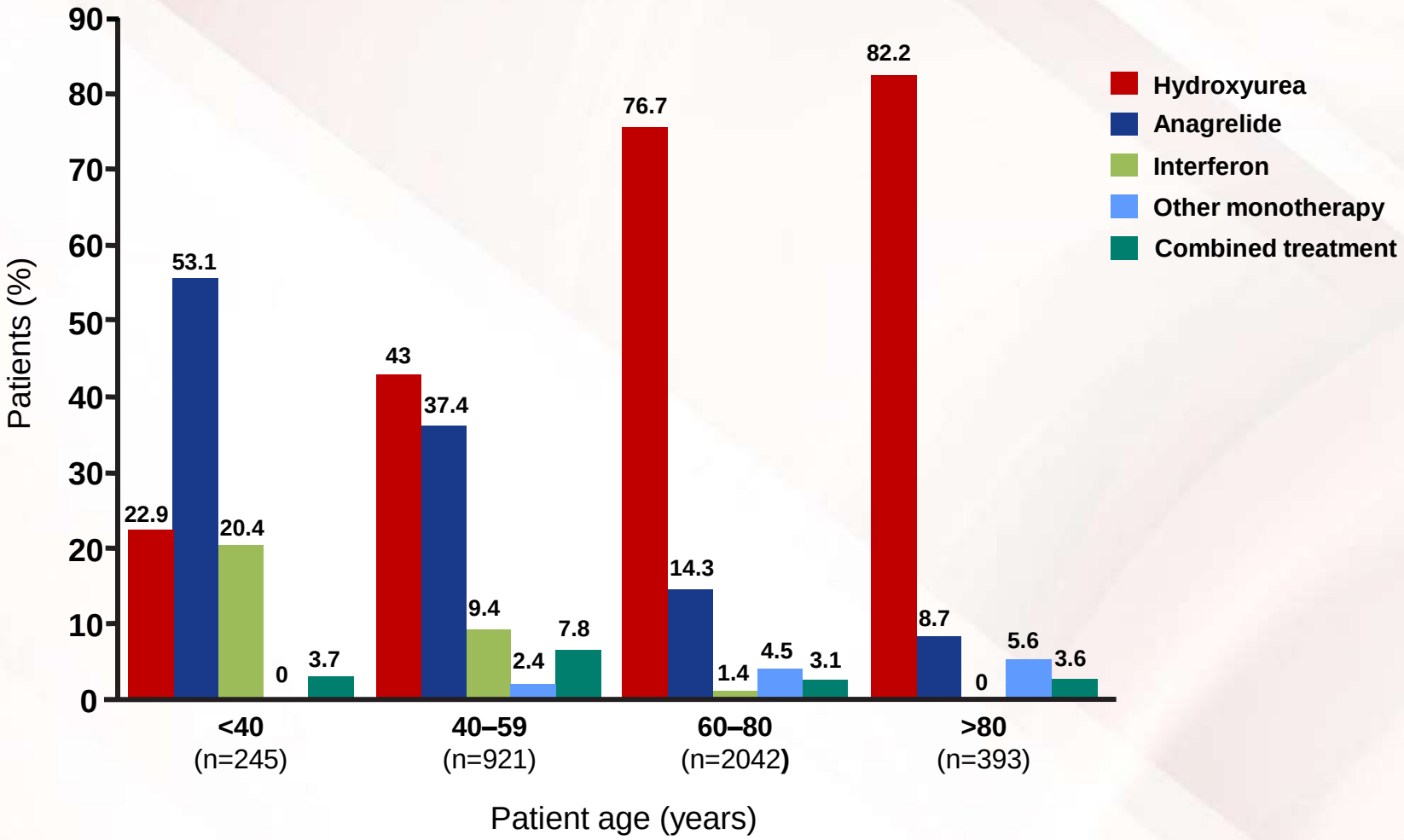
# EXELS Study: 3643 High-Risk ET Patients

## Type of cytoreductive treatment at study inclusion according to patient age




Besses *et al*, Leuk Res 2013;37:162

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# Interferon Treatment in MPN

| Advantages | Disadvantages |
| --- | --- |
| • Biological compound<br>• Non-leukemogenic<br>• Selective elimination of the neoplastic clone<br>• Cytogenetic remissions reported<br>• Reduction of *JAK2*V617F & *CALR*-mutated allelic burden<br>• Potential disease-modifying effect<br>• Sustained long-term benefit | • Frequent side-effects<br>• Flu-like symptoms<br>• Aggravation of mood disorders<br>• Induction of autoimmunity<br>• Subcutaneous application not yet licensed for MPN |

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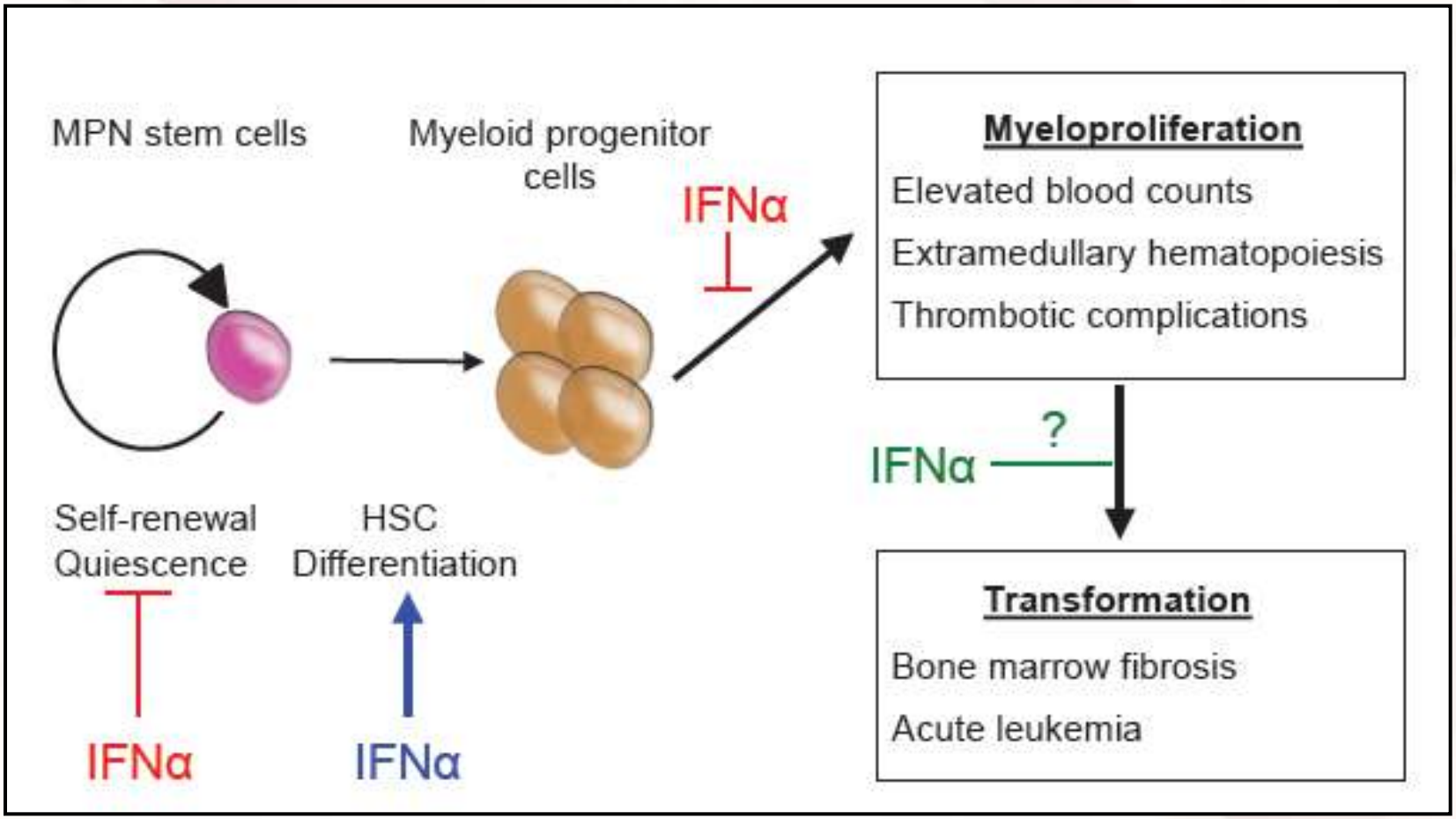
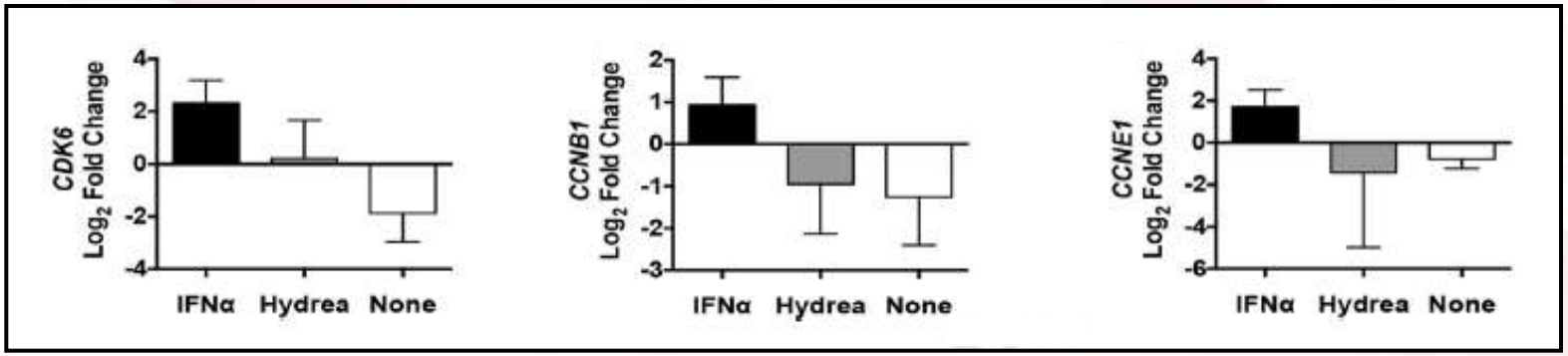
# Mechanisms of Action of IFN in MPN Stem Cells

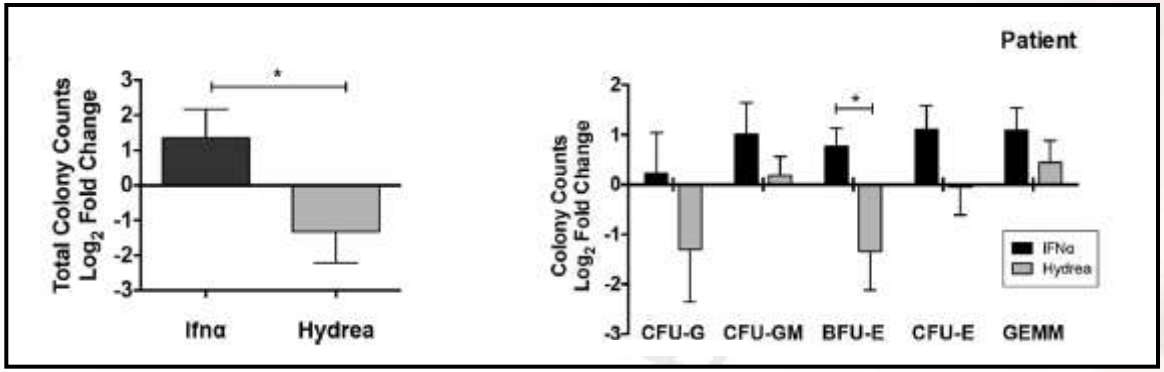



Lane & Mullally, Oncotarget 2013;4(4):500

# RNA Expression Levels of Cell Cycle-regulated Genes in CD34 cells from Untreated and Treated PV and ET Patients with IFNα and HU




# Change in Total Colony Number and Colony Type Formation by IFNα and HU




King *et al*, Exp Hematol 2015;43:912

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# Clinical Trials of Pegylated IFN in PV

## Hematological Response

| | **PVN-1** (n=40) | **MD Anderson** (n=40) | **Peginvera** (n=51)[1] |
|---|---|---|---|
| **CR** | 91% | 70% | 53% |
| **PR** | 9% | 10% | 45% |
| **NR** | 0% | 20% | 2% |
| Follow-up (median) | 2.6 yrs | 1.8 yrs | 1.4 yrs |
| Discontinuation by AEs | 24% | 10% | 20% |

[1] 47 evaluable

CR: Normalization of Hct (<45%), WBC and platelet counts, and spleen size without phlebotomies
PR: At least ≥50% reduction in phlebotomy requirements or spleen size ± elevated (>400x$10^9$/L) platelet count
NR: Any response not fulbilling CR or PR criteria
AE: Adverse events

Kiladjian *et al*, Blood 2008;112:3065
Quintas-Cardama *et al*, J Clin Oncol 2009;27:5418
Them *et al*, Am J Hematol 2015;90:288

# Clinical Trials of Pegylated IFN in PV

## Molecular Response

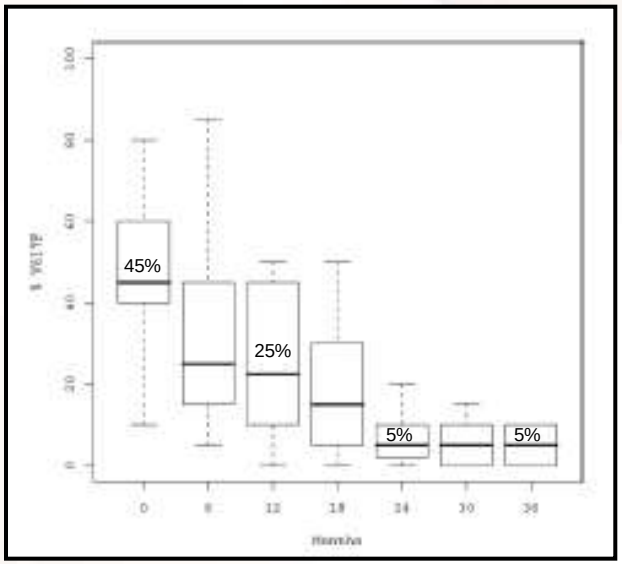
| | **PVN-1** (n=29)[1] | **MD Anderson** (n=35)[1] | **Peginvera** (n=35)[1] |
|---|---|---|---|
| **CR** (undetectable) | 24% | 14% | 6% |
| **PR** (↓ ≥50%) | 48% | 31% | 46% |
| **minor MR** (↓ 20-49%) | 17% | 9% | |
| **no MR** (↓ <20%) | 11% | 46% | 49% (↓ <50%) |
| Follow-up (median) | 2.6 yrs | 1.8 yrs | 1.6 yrs |

[1] number of evaluable patients

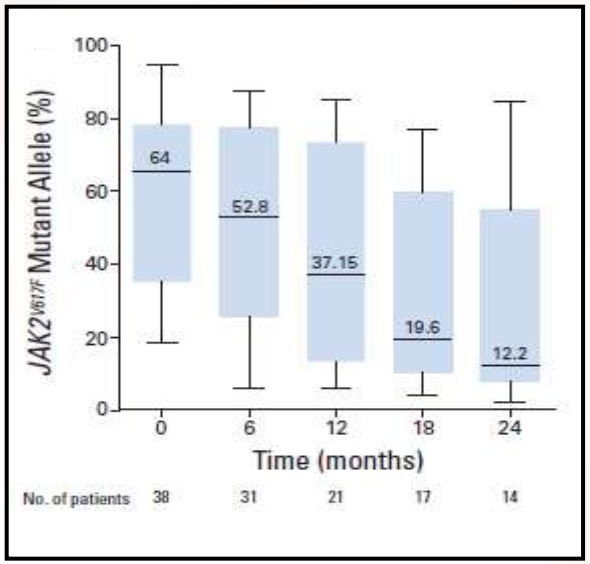
Kiladjian *et al*, Blood 2008;112:3065
Quintas-Cardama *et al*, J Clin Oncol 2009;27:5418
Them *et al*, Am J Hematol 2015;90:288

# Clinical Trials of Pegylated IFNs in PV

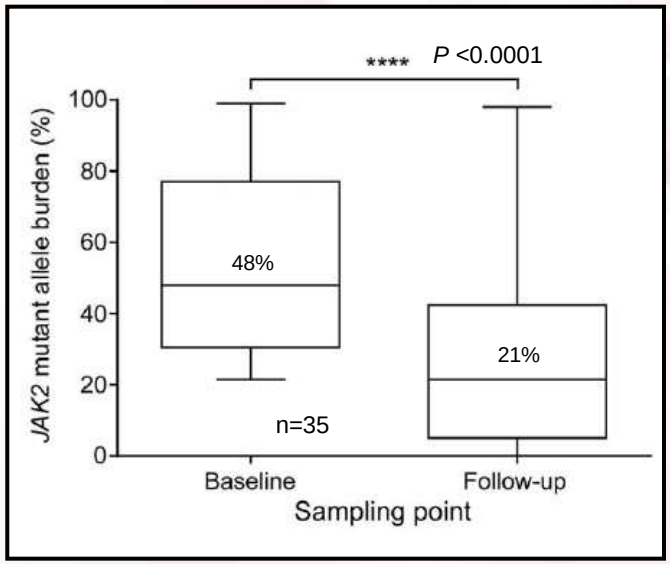
## Dynamics of *JAK2*V617F allele burden




Kiladjian *et al*, 2008




Quintas-Cardama *et al*, 2009




Them *et al*, 2015


Kiladjian *et al*, Blood 2008;112:3065
Quintas-Cardama *et al*, J Clin Oncol 2009;27:5418
Them *et al*, Am J Hematol 2015;90:288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# PVN-1 Long-term Analyses of Peg-IFNα-2a

- Cumulative incidence of molecular CR:
  - 14% at 2 years
  - 30% at 4 years
- Clinical remissions without cytoreductive therapy
  - 27% of patients could stop Peg-IFNα-2a and remained in hematological CR without cytoreductive treatment for a median time of 31 + months (up to 66+ months)
- Additional findings:
  - No vascular events reported (expected: 6-10)
  - In some patients histological complete remission was observed

courtesy of JJ Kiladjian; EHA 2015

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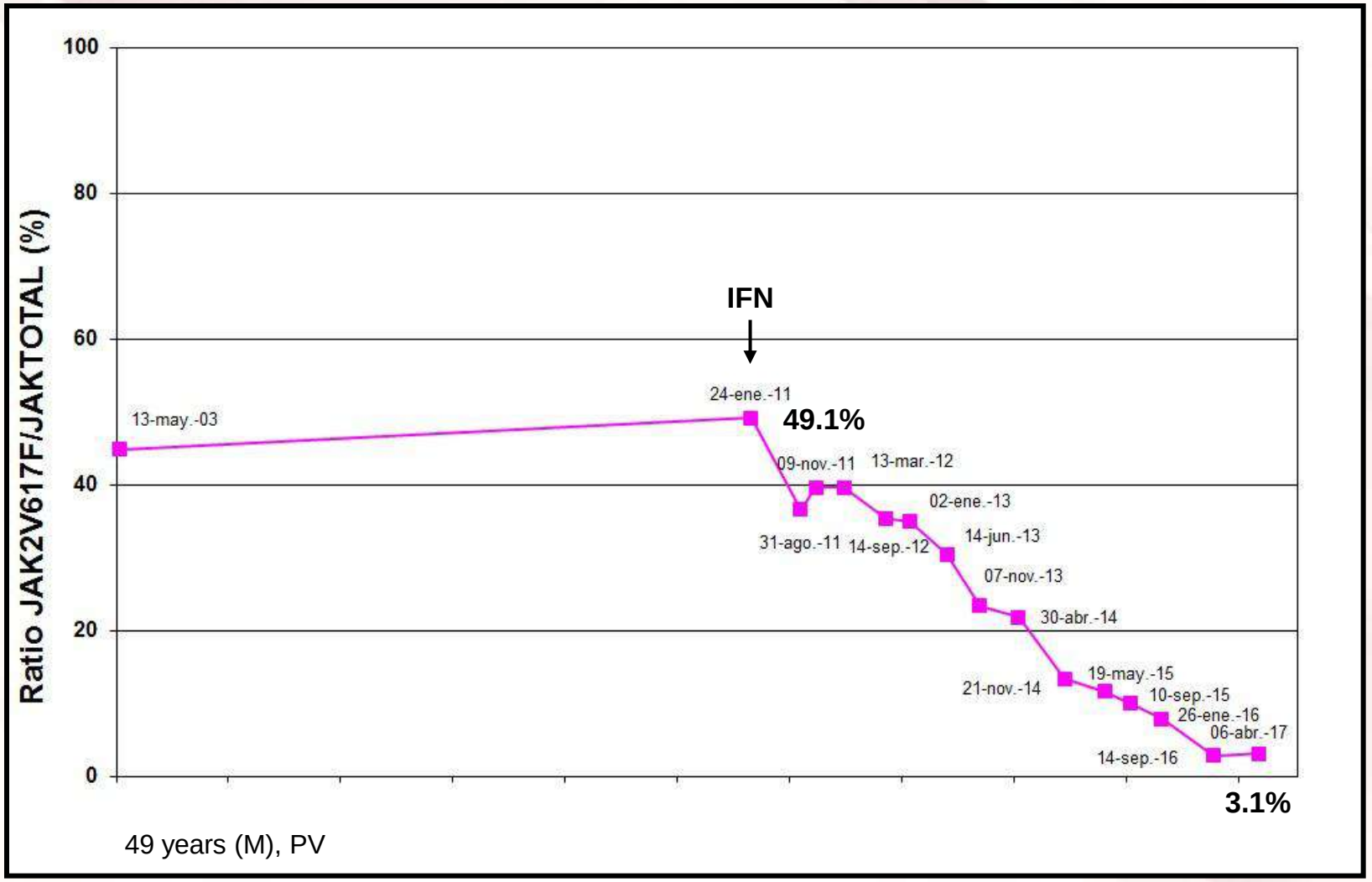
# Dynamics of *JAK2*V617F Allele Burden During Pegylated Interferon Treatment



# PEG-IFN-α2a in PV and ET Patients

## MD Anderson experience

- **83 patients** (43 PV, 40 ET)
- 7 year median follow-up
- Patients **on study**: 32 **(39%)**
  Patients **off study**: 51 **(61%)**

| Therapy Discontinuation | |
|---|---|
| **Reason** | **No. (%)** |
| Toxicity G1-2<br>G3-4 | 8 (10)<br>10 (12) |
| Vascular events | 7 (14) |
| Progression to MF/AML | 7 (14) |
| Loss of response/NR | 3 (6) |
| Others* | 16 (32) |

* Including death, other malignancy, financial

Masarova *et al*, Lancet Haematol 2017;4:165

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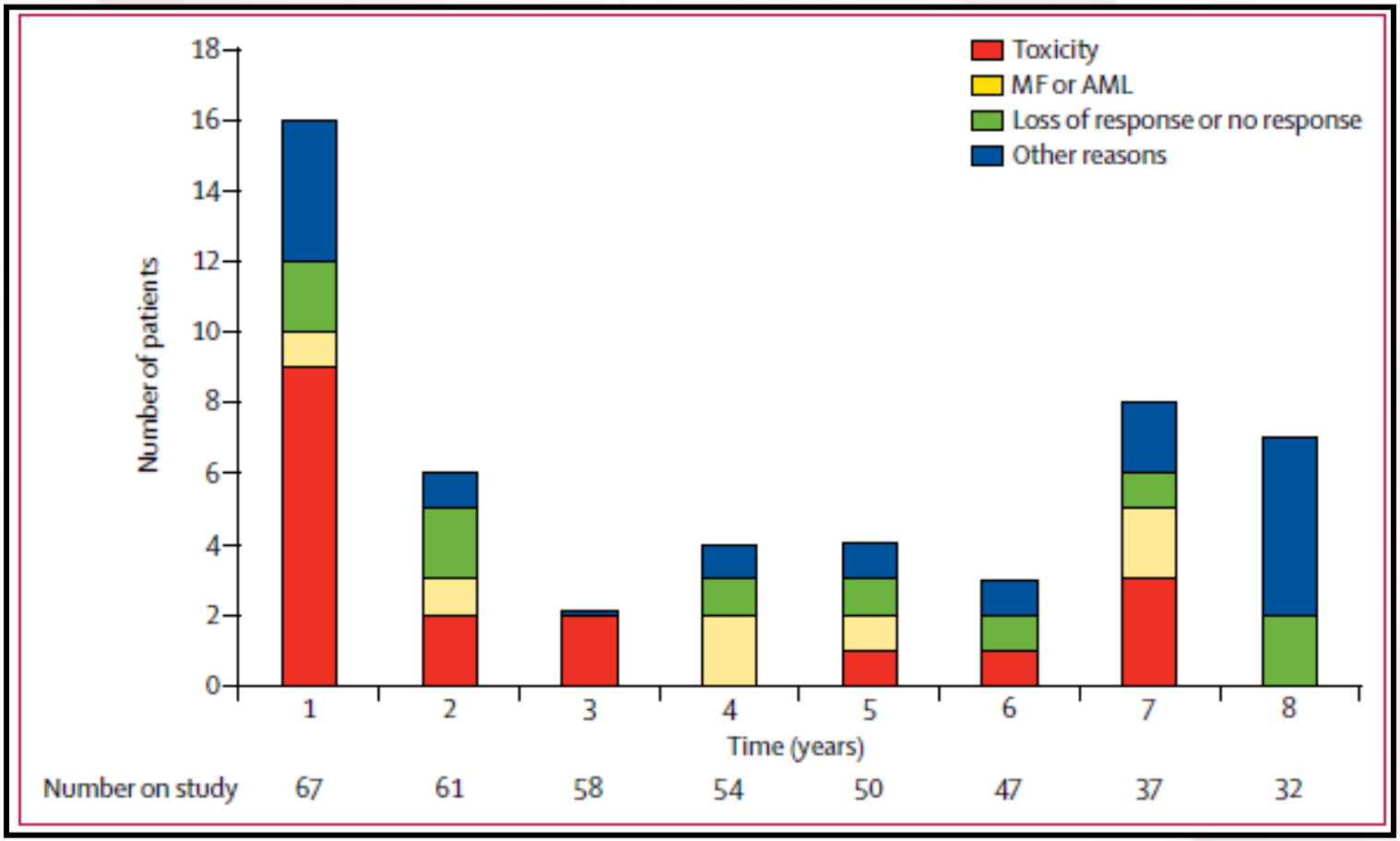
# MD Anderson Experience

## Proportion of the 43 PV and 40 ET Patients Treated with Peg-IFN alfa-2a who Discontinued by Year and Reasons for Treatment Discontinuation




Median FU: 83 months

*Most common adverse events: fatigue (75%), muscle pain (52%), GI toxicity (44%), depression (31%)*

Masarova *et al*, Lancet Haematol 2017;4:165

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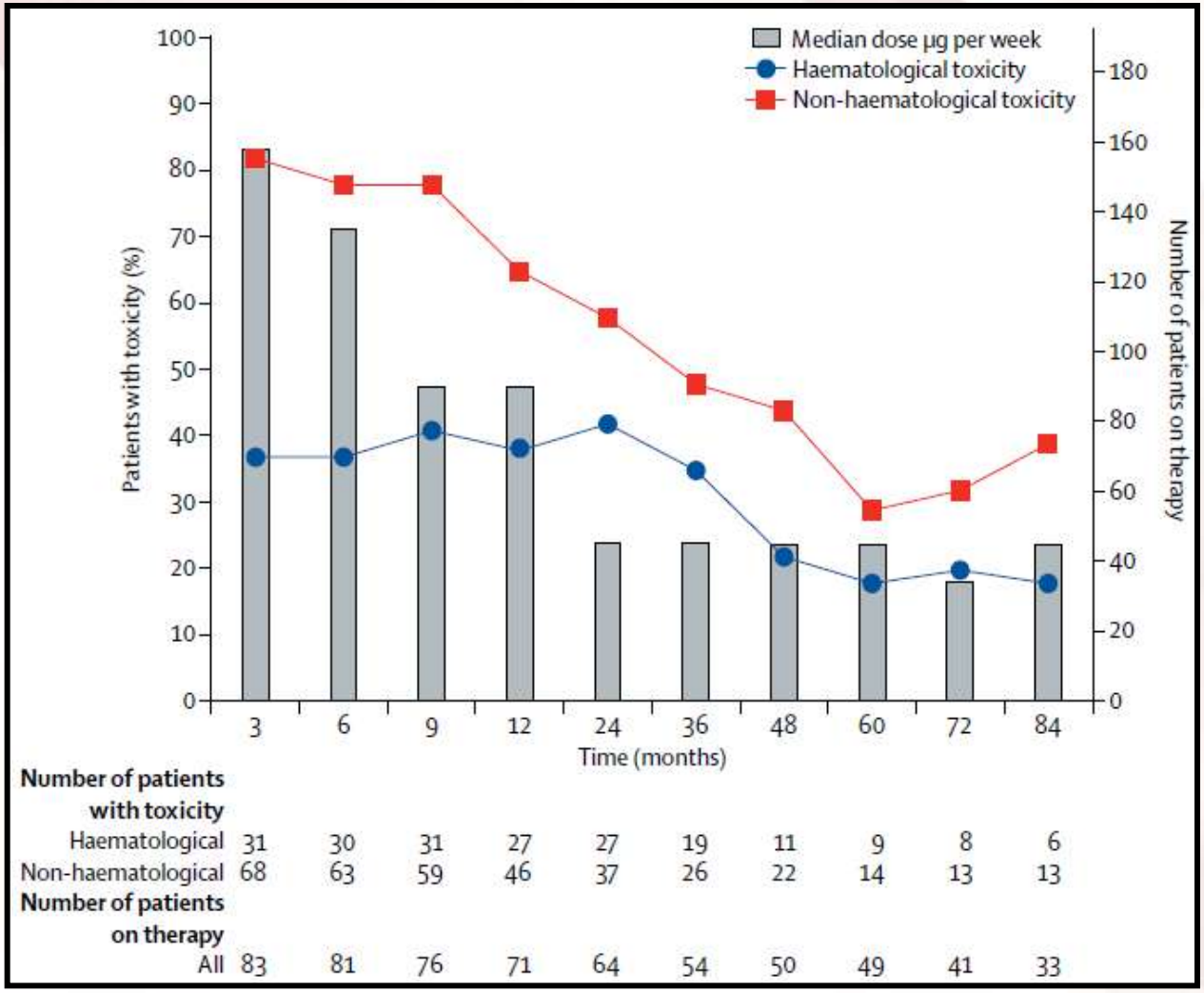
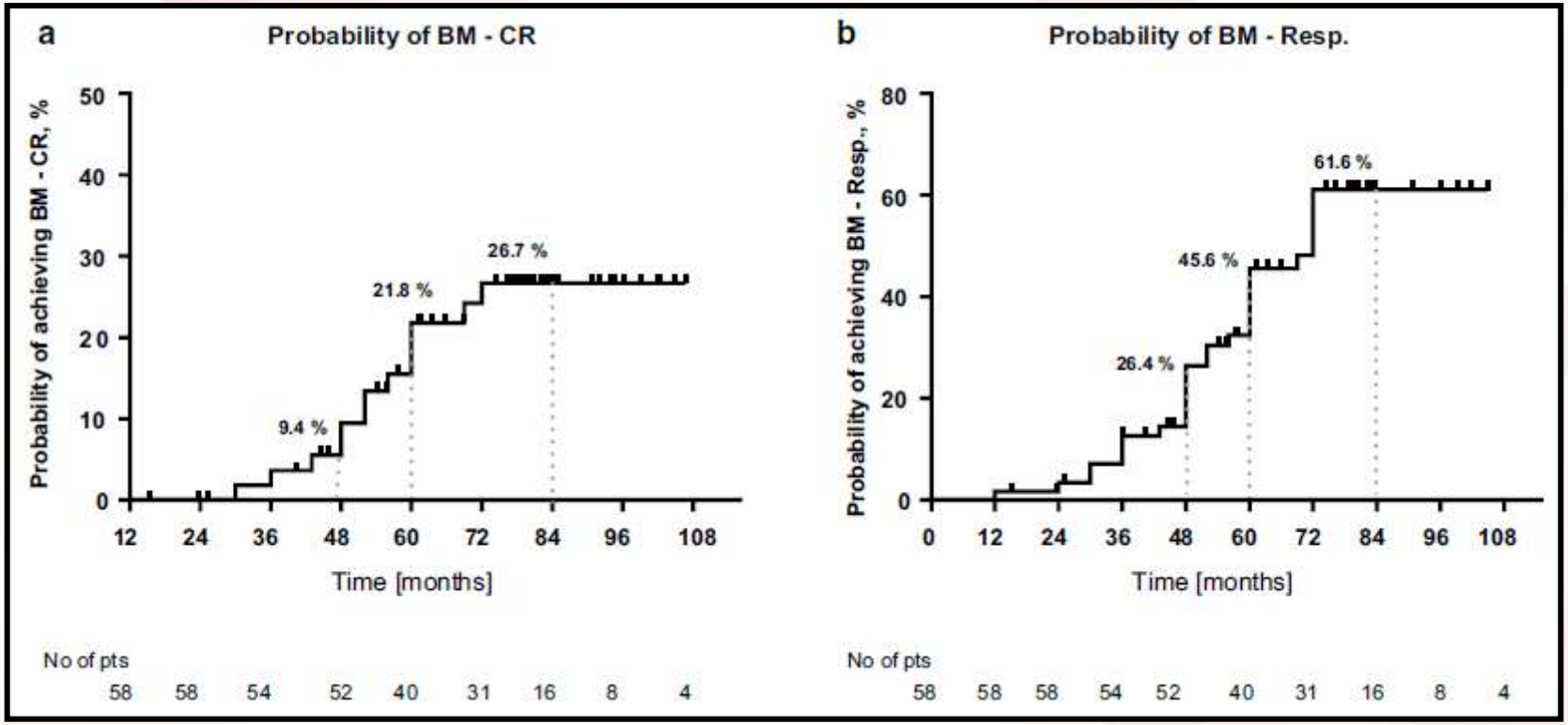
# Correlation of Toxicities with Time and Dose of PEG-IFNα2a




| Number of patients with toxicity | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Haematological | 31 | 30 | 31 | 27 | 27 | 19 | 11 | 9 | 8 | 6 |
| Non-haematological | 68 | 63 | 59 | 46 | 37 | 26 | 22 | 14 | 13 | 13 |
| **Number of patients on therapy** | | | | | | | | | | |
| All | 83 | 81 | 76 | 71 | 64 | 54 | 50 | 49 | 41 | 33 |

Masarova *et al*, Lancet Hematol 2017;4:e165

# Probability of Achieving a Bone Marrow Response in 25 PV and 31 ET Patients Treated with PEG-INF-α-2a (MD Anderson Cohort)




BM-CR: Absence of more than grade 1 reticulin fibrosis and disappearance of megakaryocyte hyperplasia in ET *or* trilinear hyperplasia with age-adjusted normocellularity in PV

BM-PR: Fibrosis grading that had improved by at least one grade level on at least 2 consecutive samples taken ≥12 months apart, but with persistent morphological features of ET or PV

Masarova *et al*, Exp Hematol Oncol 2017;6:30

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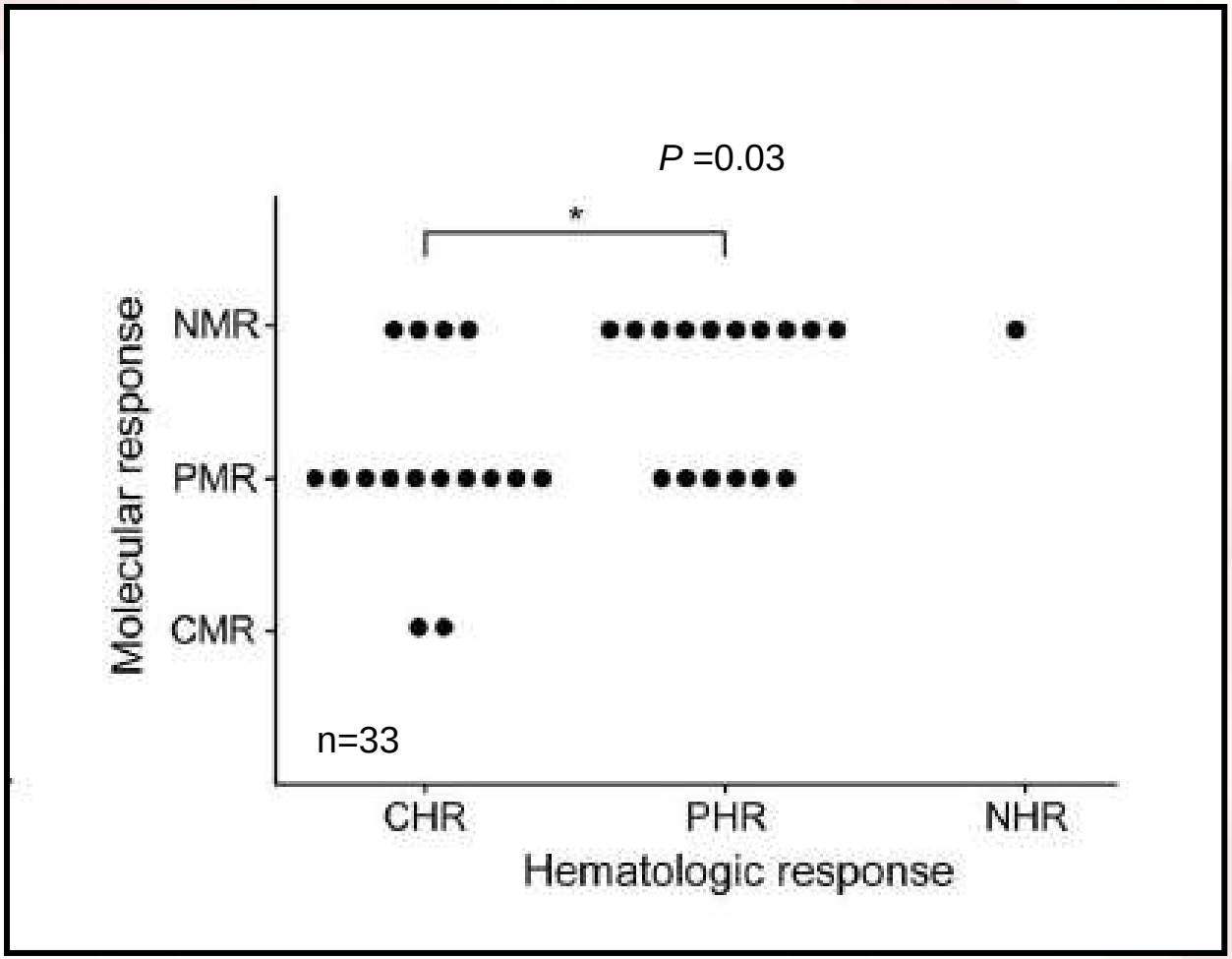
# Hematological and Molecular Responses to Peg-proline-IFNα-2b in 51 PV Patients




Median follow-up: 19 months

Them *et al*, Am J Hematol 2015;90:288

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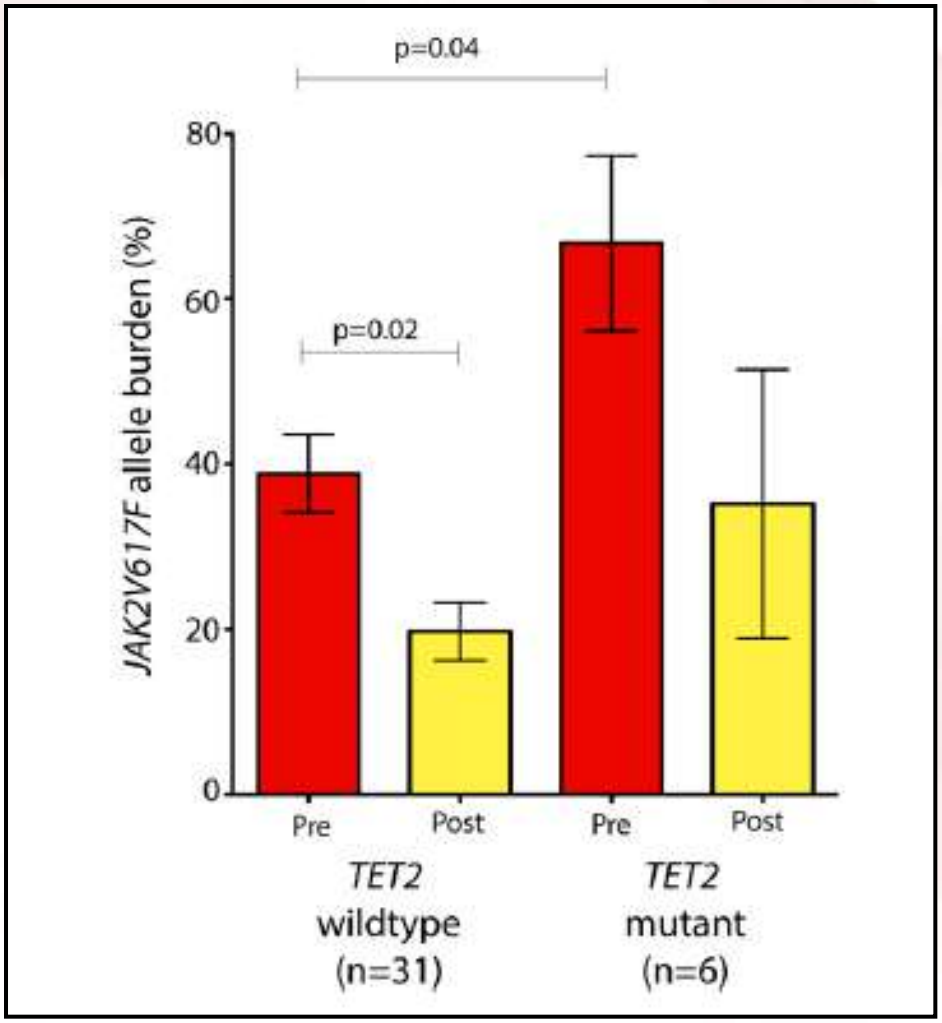
# *JAK2*V617F Allele Burden Prior and During PEG-IFNα-2a Therapy Based on *TET2* Mutational Status




Quintas-Cardama *et al*, Blood 2013;122:893

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# Serial Mutational Analysis of Genes Outside of *JAK2* During Therapy with PEG-IFNα-2a

| *JAK2V617F* response | Patient | Days between serial samples | *JAK2V617F* allele-burden Initial | *JAK2V617F* allele-burden Serial[1] | *TET2* | *DNMT3A* | *ASXL1* | *IDH1/2* | *EZH2* |
|---|---|---|---|---|---|---|---|---|---|
| CMR | 1 | 577 | 82.4% | 0.01% | | | | | |
| | 2 | 524 | 63.4% | 2.5% | | | | | |
| | 3 | 885 | 58.7% | 0% | Mutation lost | | | | Mutation lost |
| | 4 | 1,292 | 68.4% | 0.01% | | | | | |
| | 5 | 550 | 5.8% | 0.01% | | Mutation lost | | | |
| | 6 | 356 | 45.8% | 0.01% | | | | | |
| | 7 | 723 | 11.8% | 0% | | | Mutation lost | | |
| | 8 | 259 | 9.1% | 0.02% | | | | | |
| | 9 | 2,554 | 8.1% | 0.02% | | | | | |
| PMR | 10 | 1,084 | 82.1% | 19.8% | Mutation acquired | | | | |
| | 11 | 1,462 | 86.1% | 23.8% | | Mutation retained | | | |
| | 12 | 1,462 | 45.4% | 14.1% | | | | | |
| | 13 | 1,462 | 41.9% | 14.7% | Mutation retained | | | | |
| | 14 | 1,462 | 98.8% | 25.9% | | Mutation acquired | | | |
| | 15 | 564 | 89.6% | 7.0% | | | | | |
| | 16 | 363 | 71.8% | 55% | | | | | |
| | 17 | 1,462 | 77.7% | 18.5% | Mutation acquired | | | | |
| mMR | 18 | 373 | 92.6% | 89.8% | | | | | |
| | 19 | 1,857 | 87.7% | 71.4% | Mutation acquired | Mutation acquired | Mutation acquired | Mutation lost | |
| No response | 20 | 366 | 83.0% | 79.2% | | Mutation acquired | | | |
| | 21 | 749 | 68.2% | 78% | | Mutation acquired | | | |
| | 22 | 400 | 52.4% | 82.3% | Mutation acquired | Mutation acquired | Mutation acquired | | |
| | 23 | 780 | 99.2% | 94.6% | | | | | |

[1] All CMR patients found to have sustained undetectable quantitative *JAK2V617F* allele burden coicident or following these values

Mutation lost in serial sample

Mutation acquired in serial sample

Mutation retained in serial sample

No mutation in genes sequenced (other than possibly *JAK2*)

Quintas-Cardama *et al*, Blood 2013;122:893

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## Characteristics of 31 CALR-Mutated ET Patients Treated with PEG-IFNα

| | |
|---|---|
| Number of patients | 31 |
| Female, no. (%) | 20 (65%) |
| Age at diagnosis (mean) | 39 years |
| Splenomegaly, no. (%) | 5 (16) |
| Treatment duration (mean, months) | 34 |
| Still treated* | 19 (61%) |
| Stopped treatment* | |
| by toxicity | 6 (19%) |
| by HR | 6 (19%) |
| Hematological response | 31 (100%) |
| CHR | 24 (77%) |
| PHR | 7 (23%) |

* At last follow-up

HR: hematological response
CHR: complete hematological response
PHR: partial hematological response

Verger *et al*, Blood 2015;126:2585

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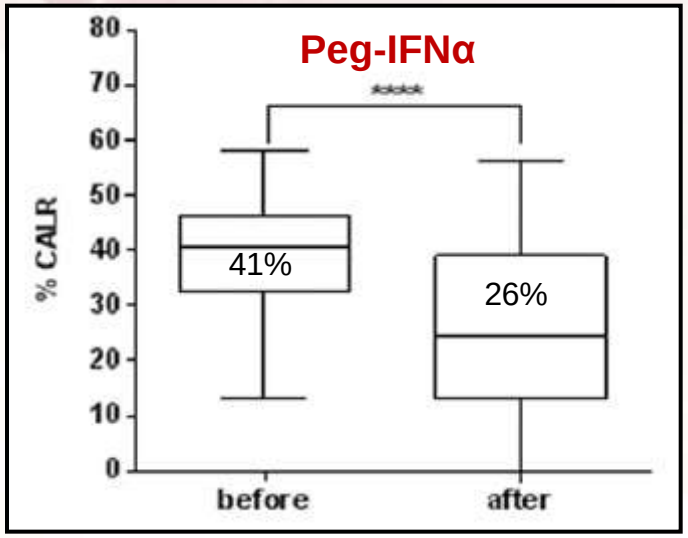
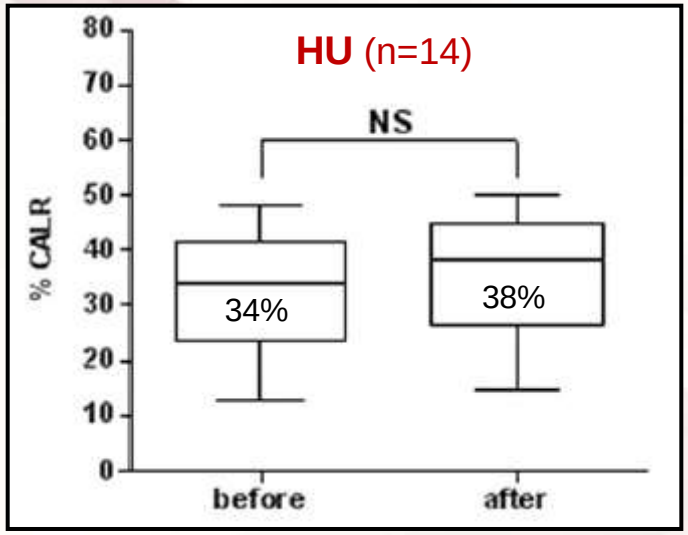
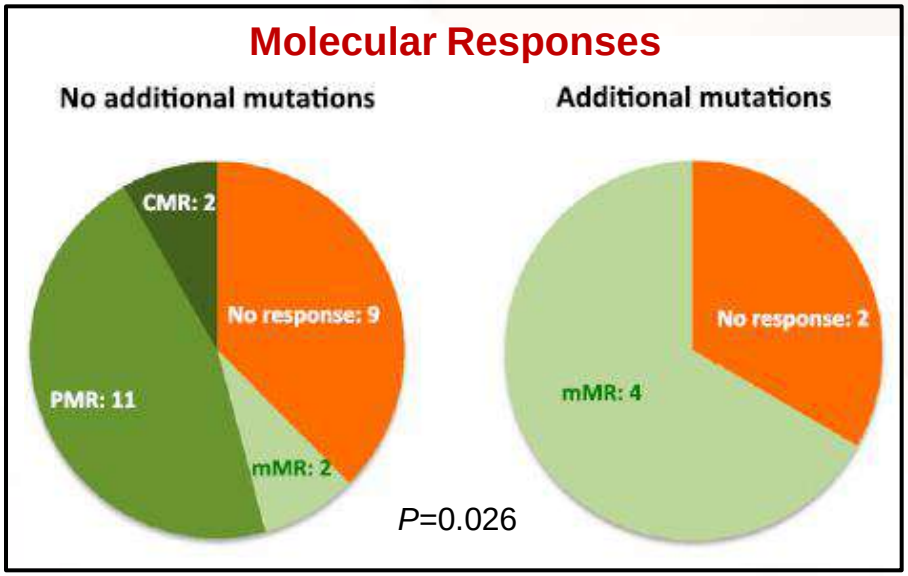
# Evolution of *CALR* Mutant Allele Burden with Time




CMR: undetectable
PMR: ⇓ allele burden >50%
mMR: ⇓ allele burden 25% to 49%

Verger et al, Blood 2015;126:2585

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# Interim Analysis of the MPD-RC Phase III Trial of Front Line PEG-INF2a *vs.* HU in High-Risk PV & ET

## Primary Objective

CHR by ELN 2009 after 12 months of therapy

## Secondary Objectives

- To evaluate the toxicity and tolerability of therapy
- The ability of therapy to achieve a CR or PR by ELN criteria
- Survival and clonal transformation
- Incidence of major cardiovascular events
- To measure the impact of therapy on key biomarkers

CHR: complete hematologic response

Mascarenhas *et al*, Blood 2016;128(22):479

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# Interim Analysis of the MPD-RC Phase III Trial of Front Line PEG-INF2a *vs.* HU in High-Risk PV & ET

| | HU (n=39) | PEG-INF2a (n=36) | *P* |
|---|---|---|---|
| Age, years, median (range) | 66 (28-85) | 56 (20-71) | <0.001 |
| Gender, female | 19 (49%) | 16 (44%) | 0.71 |
| MPN subtype, ET/PV | 16 (41%), 23 (59%) | 15 (42%), 21 (58%) | 0.95 |
| *JAK2*V617F | 36 (92%) | 32 (89%) | 0.51 |
| Age >60 years | 27 (69%) | 15 (42%) | 0.02 |
| History of venous thrombosis | 6 (15%) | 5 (14%) | 0.86 |
| History of arterial thrombosis | 4 (10%) | 9 (25%) | 0.09 |
| Cardiovascular risk factors | 25 (64%) | 16 (44%) | 0.09 |
| Palpable spleen | 10 (26%) | 7 (19%) | 0.52 |
| Hemoglobin (g/dL) | 14.1 (12.1-22.4) | 14.4 (11.3-16.6) | 0.17 |
| Hematocrit (%) | 45.7 (36.2-70.2) | 43.9 (33.5-60.7) | 0.33 |
| Leukocytes ($x10^9$/L) | 10.3 (4.8-20) | 8.1 (4-23.4) | 0.43 |
| Platelets ($x10^9$/L) | 615 (142-1444) | 538 (112-1382) | 0.24 |

Mascarenhas *et al*, Blood 2016;128(22):479

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# Interim Analysis of the MPD-RC Phase III Trial of Front Line PEG-INF2a *vs.* HU in High-Risk PV & ET

## Overall Response Rates at 12 Months by Treatment Arm

| | **HU** (n=39) | | | **PEG-INF2a** (n=36) | | | *P* value |
|---|---|---|---|---|---|---|---|
| | ORR n (%) | PR n (%) | CR n (%) | ORR n (%) | PR n (%) | CR n (%) | |
| **Entire cohort (n=75)** | 27 (69) | 14 (36) | 13 (33) | 29 (81) | 19 (53) | 10 (28) | 0.6 |
| **ET (n=31)** | 11/16 (69) | 4/16 (25) | 7/16 (44) | 12/15 (80) | 6/15 (40) | 6/15 (40) | 0.8 |
| **PV (n=44)** | 16/23 (70) | 10/23 (44) | 6/23 (26) | 17/21 (62) | 13/21 (62) | 4/21 (19) | 0.6 |

Mascarenhas *et al*, Blood 2016;128(22):479

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# Interim Analysis of the MPD-RC Phase III Trial of Front Line PEG-INF2a *vs.* HU in High-Risk PV & ET

| Adverse Event | HU (n=36) | PEG-INF2a (n=36) | *P* |
|---|---|---|---|
| Abdominal pain | 2 (6%) | 7 (19%) | 0.07 |
| Anemia | 6 (17%) | 7 (19%) | 0.76 |
| Depression | - | 10 (28%) | <0.001 |
| Diarrhea | 5 (14%) | 7 (19%) | 0.53 |
| Dyspnea | 1 (3%) | 7 (19%) | 0.02 |
| Fatigue | 10 (28%) | 18 (50%) | 0.05 |
| Flu-like symptoms | 1 (3%) | 12 (33%) | <0.001 |
| Headache | 4 (11%) | 7 (19%) | 0.33 |
| Injection site reaction | - | 9 (25%) | 0.001 |
| Leukopenia | 3 (8%) | 8 (22%) | 0.10 |
| Nausea | 7 (19%) | 7 (19%) | 0.99 |
| Pain | 9 (25%) | 11 (31%) | 0.60 |
| Pruritus | 3 (8%) | 10 (28%) | 0.03 |
| Thrombocytopenia | 7 (19%) | 6 (17%) | 0.76 |
| Overall (grade 1+) | 32 (89%) | 36 (100%) | 0.04 |
| Overall (grade 3+) | 5 (14%) | 17 (47%) | 0.002 |

Mascarenhas *et al*, Blood 2016(22):479

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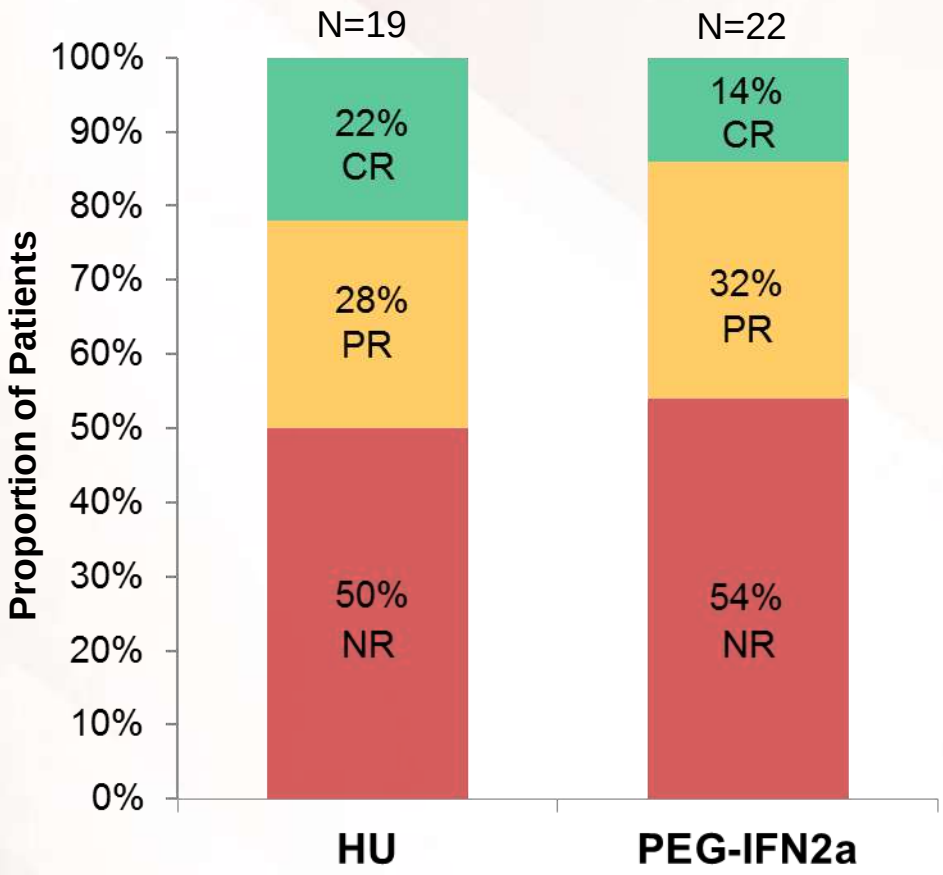
# Interim Analysis of the MPD-RC Phase III Trial of Front Line PEG-INF2a *vs.* HU in High-Risk PV & ET

## 2009 ELN Molecular Response Category




| VAF | HU | PEG-IFN2a |
|---|---|---|
| Baseline | 19.7% | 18.8% |
| 12 months | 8.3% | 8.4% |

VAF: variant allele frequency

Mascarenhas *et al*, Blood 2016;128:479

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# Interim Analysis of the MPD-RC Phase III Trial of Front Line PEG-INF2a *vs.* HU in High-Risk PV & ET

| Complete Histopathologic Bone Marrow Response at 12 Months | | |
|---|---|---|
| | **HU** | **PEG-INF2a** |
| **ET + PV** | 8/22 | 2/24 |
| **ET** | 5/10 | 2/10 |
| **PV** | 3/12 | 0/14 |

Criteria for response:

- Normalized BM cellularity
- Reticulin fibrosis <MF2
- ET: disappearance of megakaryocyte hyperplasia, and abnormal megakaryocyte histotopography
- PV: disappearance of trilineage hyperplasia

Mascarenhas *et al*, Blood 2016(22):479

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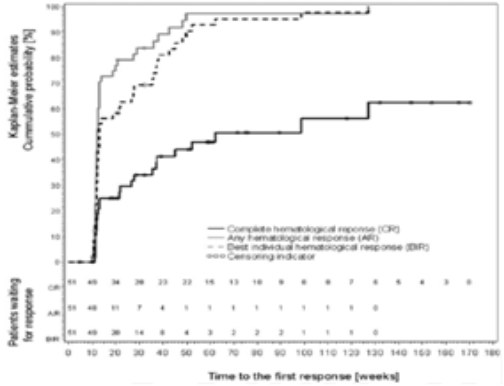
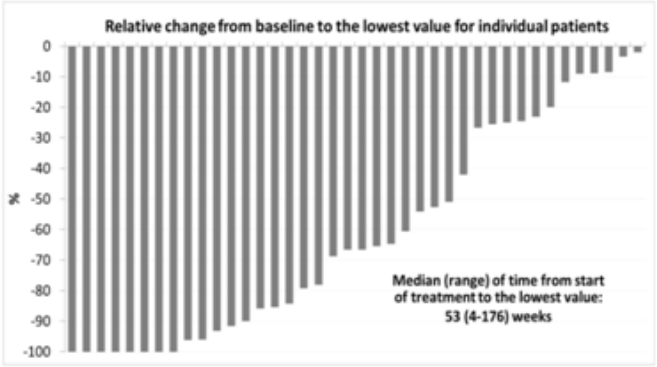
# Ropeginterferon alfa-2b (AOP2014)

- **Novel monopegylated Interferon alfa-2b**
  single isoform due to innovative pegylation technology
- **Administration frequency once every 14 days**
  (once monthly in long-term maintenance)
- **Phase II** trial PEGINVERA (up to 5 years follow-up)

Hematologic response




Molecular-genetic response




Gisslinger *et al*, ASH 2015

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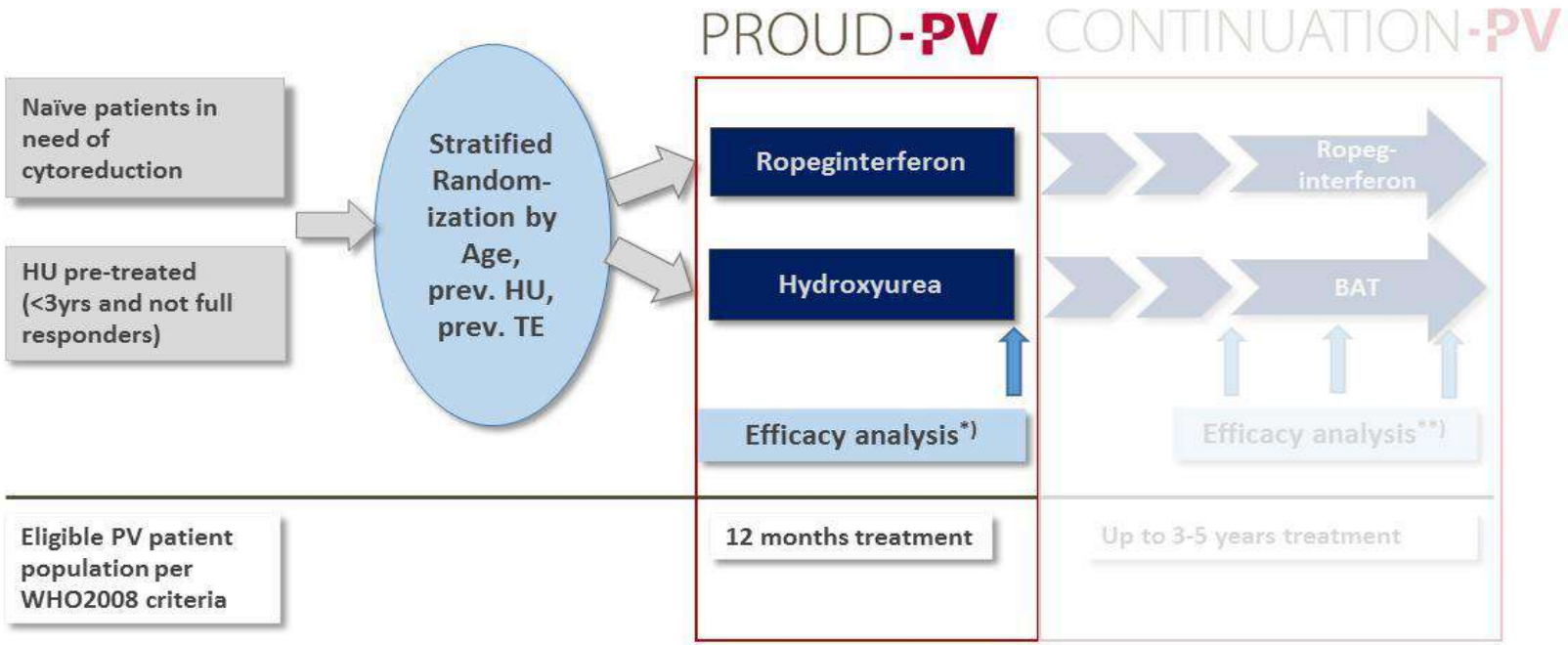
# Ropeginterferon alfa-2b phase III development: PROUD/CONTI-PV




Expected outcome: *) non-inferiority: Hematologic Response

**) benefit: durable Hematologic Response, PFS, PV symptom relief

Gisslinger *et al*, ASH 2016

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# Patient baseline demographics

| | AOP2014 (n=127) | HU (n=127) |
|---|---|---|
| Caucasian | 100% | 100% |
| WHO2008 PV *) | 100% | 100% |
| Female | 53.5% | 52.8% |
| Age (median, range) | 60 (30-85) | 60 (21-81) |
| Disease duration (median, range) | 1.9 month (0-146) | 3.6 month (0-126) |
| HU pretreated | 47 (37%) | 47 (37%) |
| Hematocrit (mean, SD) | 49.5% (±5.4) | 49.8% (±5.5) |
| Spleen length (median, range) | 13.1 cm (7.0-25.0) | 13.0 cm (7.5-24.5) |
| Spleen normal/slightly enlarged **) | 90.6% | 88.2% |
| Spleen length >17cm/>22cm | 9.4%/2.4% | 11.8%/3.9% |
| Mean JAK2V617F burden | 42% | 43% |

*) confirmed by bone marrow biopsy

**) slightly enlarged >12/13cm (f/m) – 17cm

Gisslinger *et al*, ASH 2016

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# Complete Hematologic Response at 12 months

| | AOP2014 | HU | Difference % (95% CI) | P-value *) |
|---|---|---|---|---|
| Complete hematologic response rate (ITT) | 43.1% | 45.6% | -2.5 (-14.9 to 9.9) | 0.0028 |
| Responding patients/n | 53/123 | 57/125 | | |
| Complete hematologic response rate (PP) | 44.3% | 46.5% | -2.2 (-15.2 to 10.7) | 0.0036 |
| Responding patients/n | 50/113 | 53/114 | | |

→ non-inferiority is demonstrated, p=0.0028

*) Non-inferiority margin 20.0%

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# All grade AEs in >10% of patients in either treatment arm

| Adverse Event | AOP2014 (n=127) n (%) | HU (n=127) n (%) | P-value* |
|---|---|---|---|
| Anaemia | 8 (6.3%) | 31 (24.4%) | p<0.01 |
| Leukopenia | 11 (8.7%) | 27 (21.3%) | p<0.01 |
| Thrombocytopenia | 19 (15.0%) | 36 (28.3%) | p<0.01 |
| Nausea | 3 (2.4%) | 15 (11.8%) | p<0.01 |
| Fatigue | 16 (12.6%) | 17 (13.4%) | n.s. (p>0.05) |
| GGT increased | 18 (14.2%) | 1 (0.8%) | p<0.01 |

Number of patients with any treatment-emergent event regardless of relationship to study drug and intensity

* Fisher's exact test
n.s. not significant

Gisslinger *et al*, ASH 2016

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# Adverse Events of Special Interest

| AESI | AOP2014 (n=127) n (%) | HU (n=127) n (%) | P-value* |
|---|---|---|---|
| Endocrine disorders* | 4 (3.1%) | 1 (0.8%) | n.s. |
| Psychiatric disorders** | 2 (1.6%) | 0 (0.0%) | n.s. |
| Cardiac/Vascular disorders*** | 4 (3.1%) | 2 (1.6%) | n.s. |
| Tissue disorders**** | 2 (1.6%) | 0 (0.0%) | n.s. |

* Fisher's exact test
s. significant
n.s. not significant (p>0.05)

* Autoimmune thyroiditis, Hypo-/Hyperthyroidism
** Anxiety, Depression, Mood altered
*** Major cardio-vascular events within different System organ classes (cardiac failure, thrombotic event, stroke)
**** Rheumatoid arthritis, psoriasis

Gisslinger *et al*, ASH 2016

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# Two-Year Results of Ropeginterferon Alfa-2b of Phase III Continuation-PV Study

| | **RopegIFN** n=88 | | **HU/BAT** n=73 |
|---|---|---|---|
| CHR | 70% | *p*=0.01 | 49% |
| CHR plus symptom improvement and splenomegaly | 49% | *p*=0.12 | 36% |
| Partial molecular response | 69% | *p*=0.004 | 28% |
| Treatment-related adverse events | 70% | | 77% |

CHR: complete hematologic response

Gisslinger *et al*, ASH 2017

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# Interferon in Myelofibrosis

- Retrospective studies (primary & secondary MF; all IPSS scores)
- Variable degrees of clinical response (IWG-MRT criteria)
- Mild toxicity (grade 1-2)
- Decrease in *JAK2*V617F allele burden
- Better response if:
  - BM fibrosis ≤ MF2
  - Spleen size <4 cm, <6 cm
- Lower response if:
  - HMR mutations
  - Clonal complexity
- Survival benefit?

Silver *et al*, Blood 2011;117:6669
Ianotto *et al*, Br J Haematol 2013;162:783
Silver *et al*, Cancer 2017;123:2680
Ianotto *et al*; Haematologica 2018;103:438

# Conclusions

- IFN achieves high hematological response rates either in newly diagnosed or previously treated PV and ET patients outside or inside clinical trials
- IFN attains molecular responses regardless of *JAK2* or *CALR* mutational status although presence of additional somatic mutations may compromise molecular response rates
- Discontinuation rate of 20%-40% according to different cohorts/clinical trials; tolerability is improved when using low doses at initiation
- New IFN formulations allow a more prolonged administration (clinical benefit!)
- Some patients may achieve sustained hematologic and molecular responses even after discontinuation of therapy
- Preliminary analysis of RCT suggest non-inferiority of Peg-INF compared to HU although more mature follow-up is needed prior to drawing conclusions
- The role of INF in MF is still uncertain and its clinical use in this setting should be individualized