

# Pipeline for ET and MF

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# Conflict of Interest Disclosures

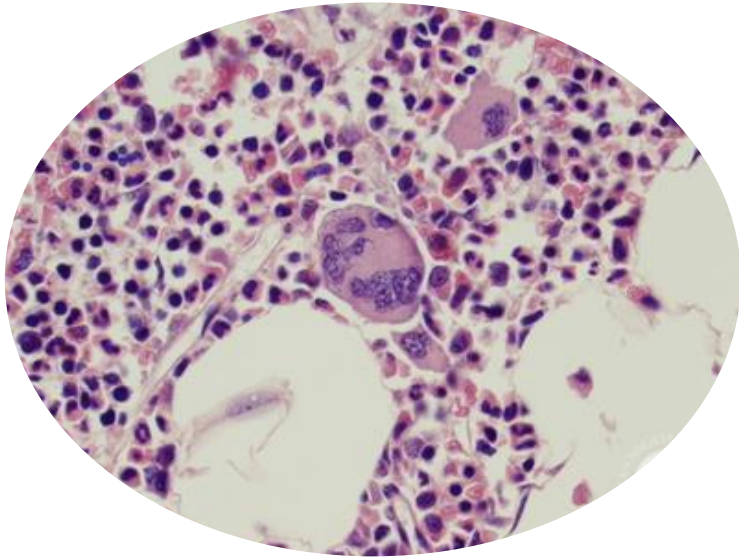
## **Research funding:**

Celgene, Constellation, Novartis

## **Advisory role:**

AbbVie, AOP, BMS, Celgene, CTI, IMAGO, Novartis, Galacteo, Geron, Gilead, GSK, Janssen, Keros, Promedior, Roche, Shire.

# ET: simple yet also complex and confusing:



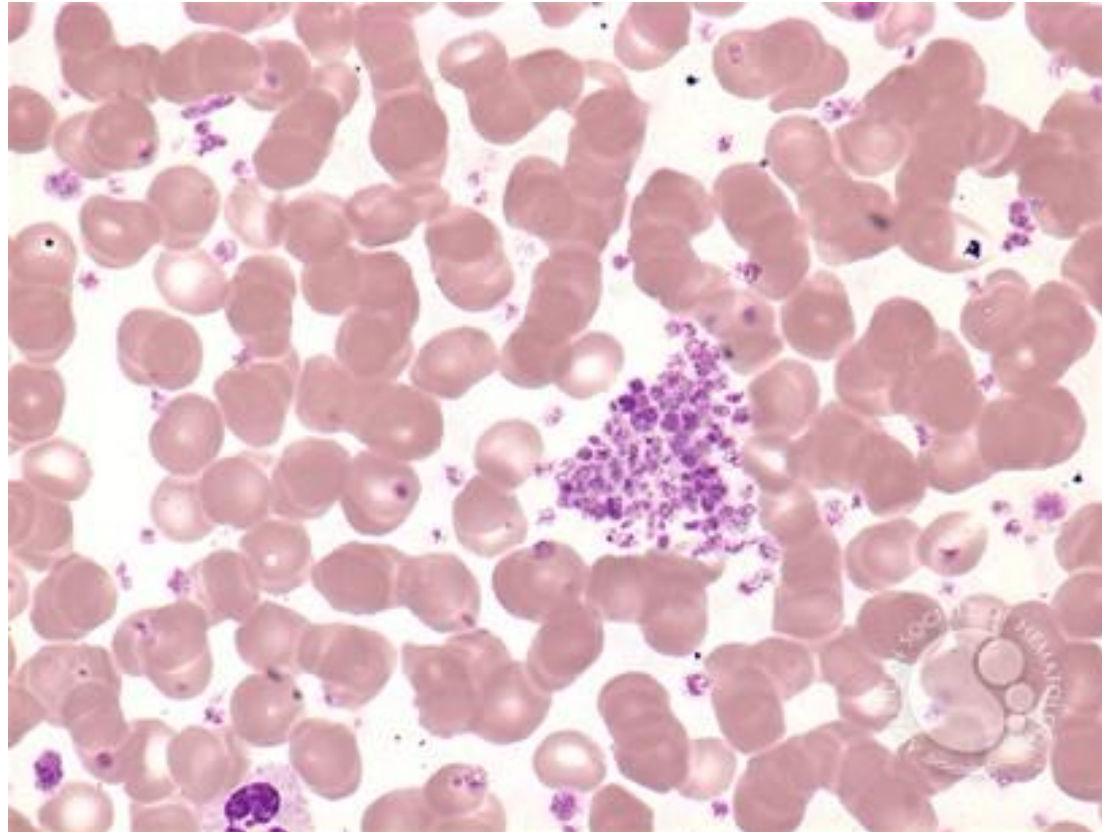
Message even re simple therapy (aspirin) is confused !

Should *CALR*-ET, triple negative ET be treated the same as *JAK2*- or *cMPL*-ET?

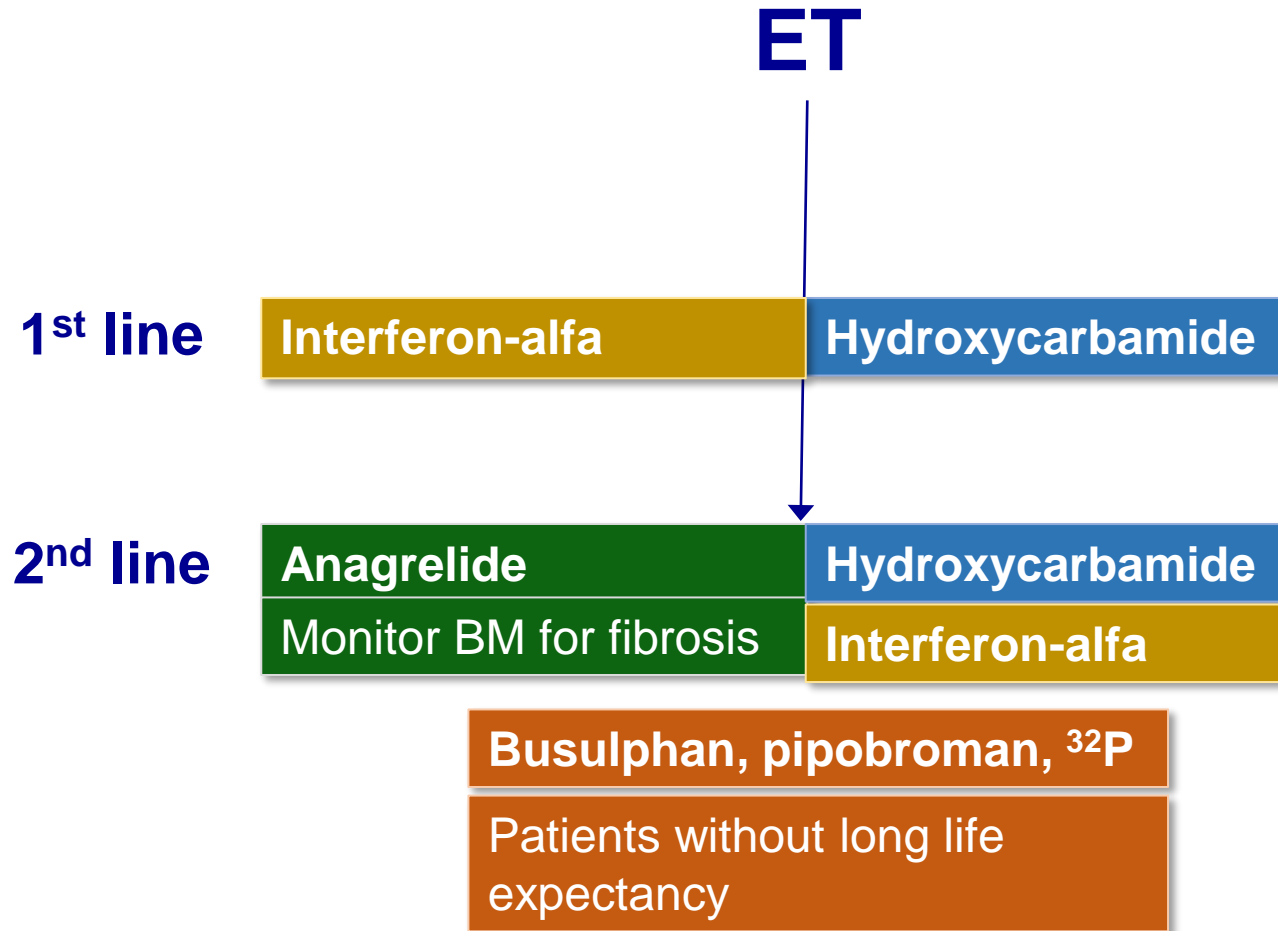
Should *JAK2*-ET be managed as PV?

Should we treat triple negative ET at all?

# Essential thrombocythaemia:



# Cytoreduction in high-risk ET simple but confusing:



## In addition:

Currently unclear if we should really treat CALR-ET and triple negative ET in the same way as JAK2- or cMPL-ET

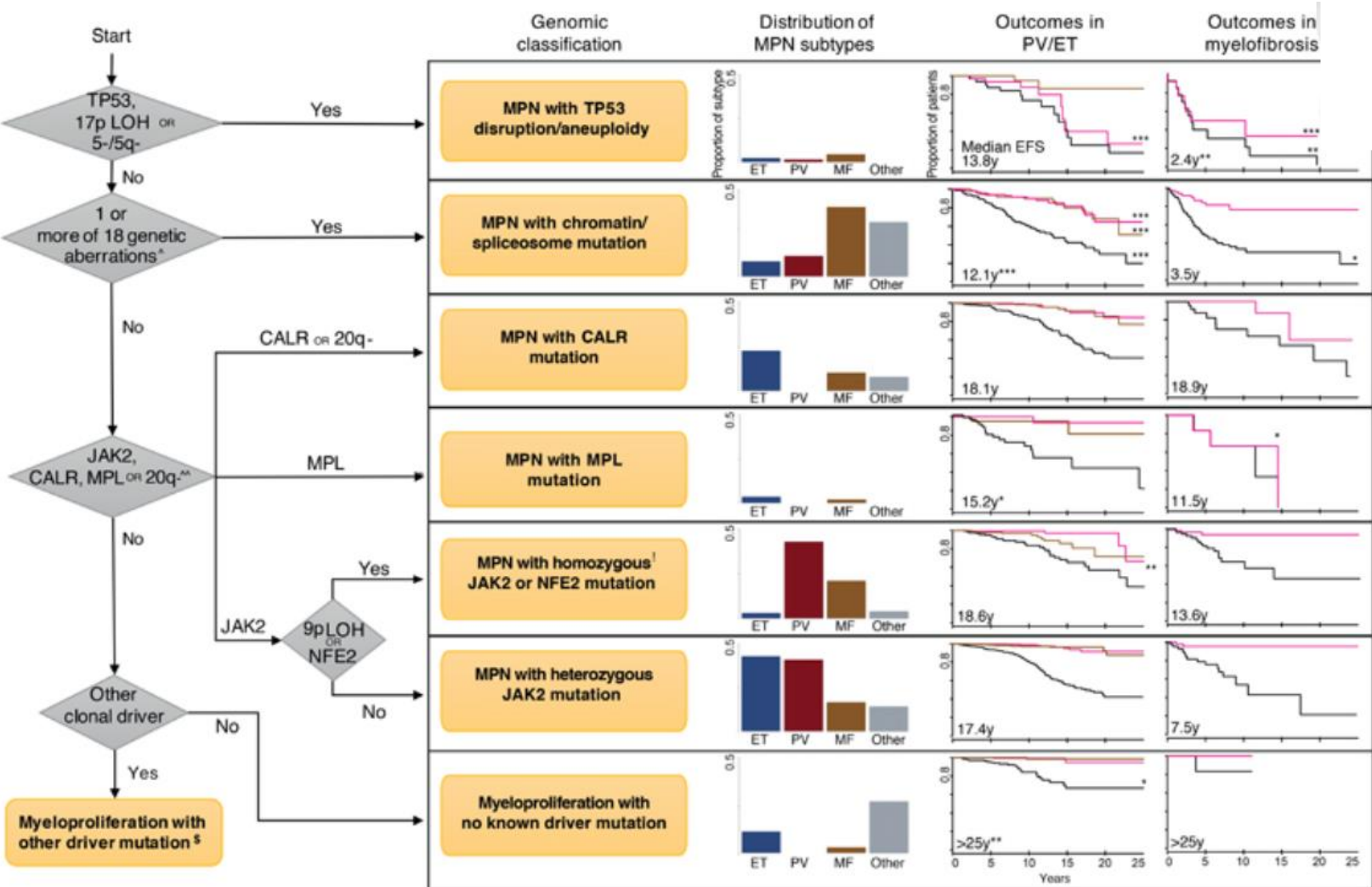
IPSET score defines most JAK negative ET as intermediate risk despite count and age

Should JAK2-ET be managed as PV?

ORIGINAL ARTICLE

# Classification and Personalized Prognosis in Myeloproliferative Neoplasms

J. Grinfeld, J. Nangalia, E.J. Baxter, D.C. Wedge, N. Angelopoulos, R. Cantrill, A.L. Godfrey, E. Papaemmanuil, G. Gundem, C. MacLean, J. Cook, L. O'Neil, S. O'Meara, J.W. Teague, A.P. Butler, C.E. Massie, N. Williams, F.L. Nice, C.L. Andersen, H.C. Hasselbalch, P. Guglielmelli, M.F. McMullin, A.M. Vannucchi, C.N. Harrison, M. Gerstung, A.R. Green, and P.J. Campbell




<sup>A</sup> EZH2, IDH1/2, ASXL1, PHF6, CUX1, ZRSR2, SRSF2, U2AF1, KRAS, NRAS, GNAS, CBL, 7/7q LOH, 4q LOH, RUNX1, STAG2, BCOR

AML transformation (pink line), MF transformation (orange line), Overall survival (black line).  
\*p<0.05, \*\*p<0.01, \*\*\*p<0.001 for outcome difference compared with MPN with heterozygous JAK2 mutation



# New options in ET?

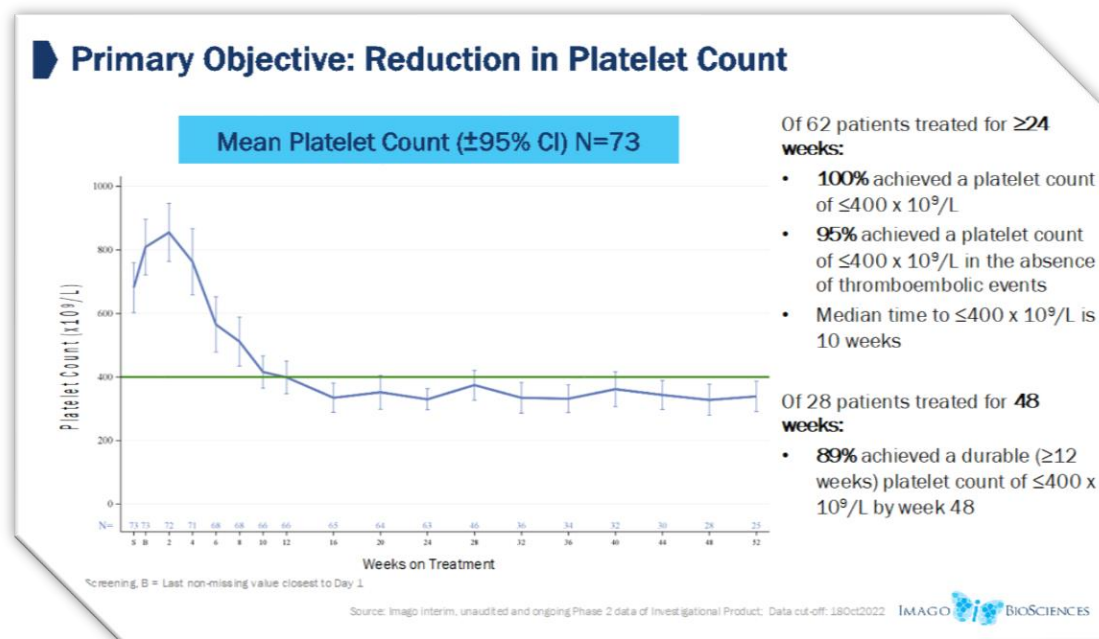
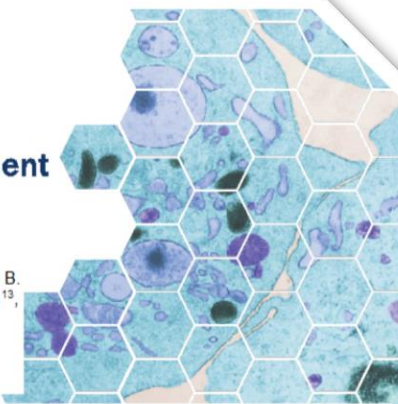
- Clinical trials with the **LSD1 inhibitor bomedemstat** – ALSO BEING EVALUATED IN PV, upfront and second line ET trials have begun

IMAGO  BIOSCIENCES

**Phase 2 Study of the LSD1 Inhibitor Bomedemstat (IMG-7289) for the Treatment of Essential Thrombocythemia (ET)**

Harinder Gill<sup>1</sup>, Francesca Palandri<sup>2</sup>, David M. Ross<sup>3</sup>, Tara Cochrane<sup>4</sup>, Courtney Tate<sup>5</sup>, Steven W. Lane<sup>6</sup>, Stephen R. Larsen<sup>7</sup>, Aaron T. Gerds<sup>8</sup>, Anna B. Halpern<sup>9</sup>, Jake Shortt<sup>10</sup>, James M. Rossetti<sup>11</sup>, Kristen M. Pettit<sup>12</sup>, James Liang<sup>13</sup>, Adam Mead<sup>14</sup>, Monia Marchetti<sup>15</sup>, Alessandro Vannucchi<sup>16</sup>, Andrew Wilson<sup>17</sup>, Joachim R. Göthert<sup>18</sup>, Merit Hanna<sup>19</sup>, Francesco Passamonti<sup>20</sup>, William S. Stevenson<sup>21</sup>, Claire N. Harrison<sup>22</sup>, Moshe Talpaz<sup>23</sup>, Nicola Vianelli<sup>24</sup>, Hugh Young Rienhoff Jr.<sup>25</sup>

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- Effective regardless of driver mutation

# Response in the Initial 24 Week Treatment Period

	Bomedemstat N = 72 <sup>a</sup>		Bomedemstat N = 72 <sup>a</sup>
<b>Week 4</b>		<b>Week 16</b>	
Patients with assessment results at visit, n	71	Patients with assessment results at visit, n	65
Responders, n (%) [95% CI]	8 (11) [5.0-21.0]	Responders, n (%) [95% CI]	49 (75) [63.1-85.2]
<b>Week 8</b>		<b>Week 20</b>	
Patients with assessment results at visit, n	68	Patients with assessment results at visit, n	63
Responders, n (%) [95% CI]	28 (41) [29.4-53.8]	Responders, n (%) [95% CI]	41 (65) [52.0-76.7]
<b>Week 12</b>		<b>Week 24</b>	
Patients with assessment results at visit, n	68	Patients with assessment results at visit, n	64
Responders, n (%) [95% CI]	40 (59) [46.2-70.6]	Responders, n (%) [95% CI]	49 (77) [64.3-86.2]
		<i>P</i> value	<0.0001

**At week 24, 77% of patients had a response**, defined as a reduction in platelet count to  $\leq 400 \times 10^9/L$  with no new thromboembolic events

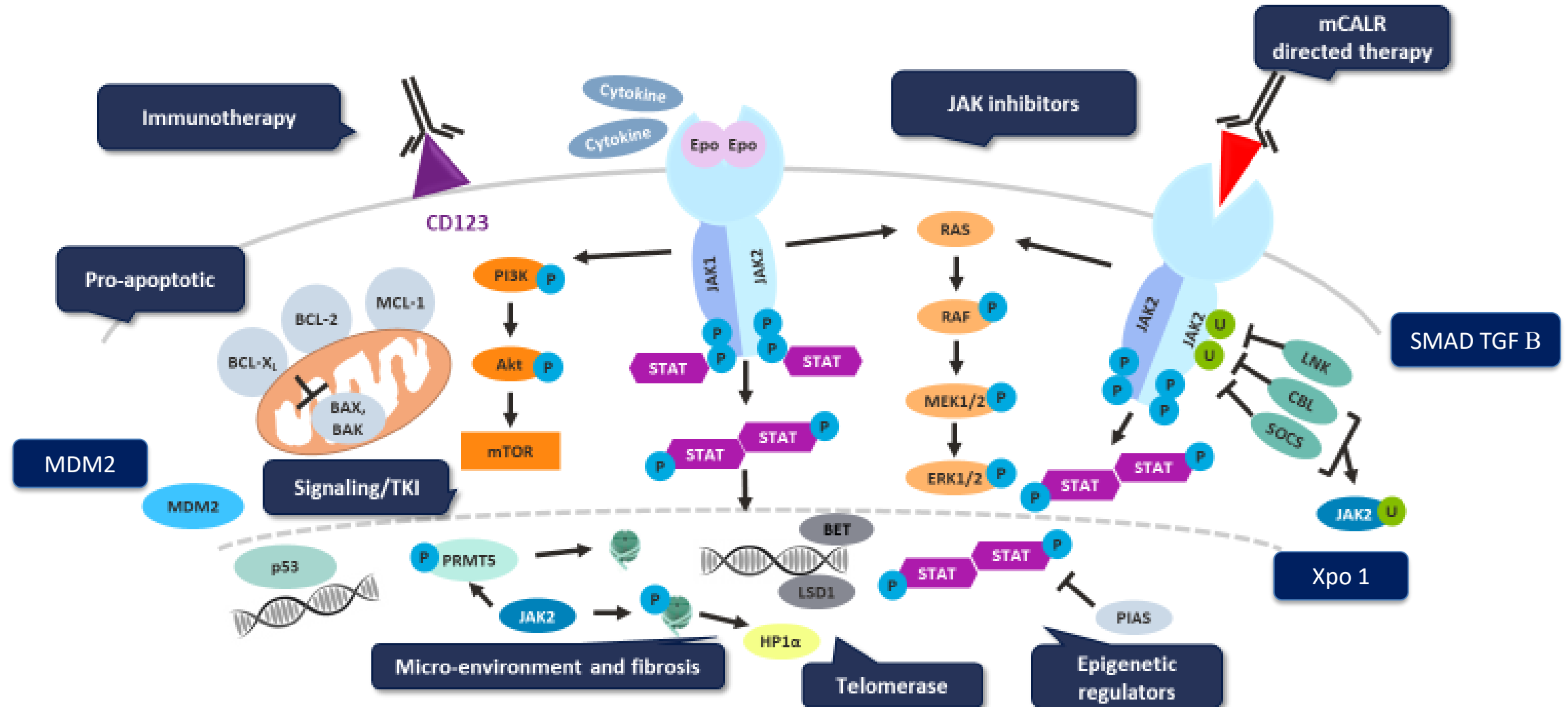


# Pelabresib (CPI-0610) Monotherapy in Patients With High-Risk Essential Thrombocythemia Refractory or Intolerant to Hydroxyurea: Preliminary Results From the MANIFEST Study

**Francesco Passamonti,<sup>1</sup> Andrea Patriarca,<sup>2</sup> Steven Knapper,<sup>3</sup> Candido Rivera,<sup>4</sup> Joseph M Scandura,<sup>5</sup> Timothy Devos,<sup>6</sup> Nikki Granacher,<sup>7</sup> Adam Mead,<sup>8</sup> Stephen Oh,<sup>9</sup> Jeanne Palmer,<sup>10</sup> Raajit K Rampal,<sup>11</sup> Lino Teichmann,<sup>12</sup> Qing Li,<sup>13</sup> Jean-Pierre Eliane,<sup>13</sup> Tzuu-Wang Chang,<sup>13</sup> Sandra Klein,<sup>13</sup> Gozde Colak,<sup>13</sup> Claire Harrison<sup>14</sup>, *on behalf of the MANIFEST study investigators***

<sup>1</sup>Università degli Studi di Milano; Fondazione I.R.C.C.S. Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy; <sup>2</sup>Hematology Unit, Department of Translational Medicine, University of Eastern Piedmont and AOU Maggiore della Carità, Novara, Italy; <sup>3</sup>Department of Haematology, Division of Cancer and Genetics, School of Medicine, Cardiff University, Cardiff, Wales, UK; <sup>4</sup>Mayo Clinic Florida, Jacksonville, FL, USA; <sup>5</sup>The Richard T. Silver, M.D. Myeloproliferative Neoplasms Center, Division of Hematology and Oncology, Cornell Medicine, New York, NY, USA; <sup>6</sup>Department of Hematology, University Hospitals Leuven and Laboratory of Molecular Immunology (Rega Institute), KU Leuven, Leuven, Belgium; <sup>7</sup>Ziekenhuis Netwerk Antwerpen, Antwerp, Belgium; <sup>8</sup>MRC Molecular Haematology Unit, MRC Weatherall Institute of Molecular Medicine, University of Oxford, John Radcliffe Hospital, Oxford, UK; <sup>9</sup>Washington University School of Medicine in St. Louis, St. Louis, MO, USA; <sup>10</sup>Mayo Clinic Arizona, Phoenix, AZ, USA; <sup>11</sup>Memorial Sloan Kettering Cancer Center, New York, NY, USA; <sup>12</sup>Universitätsklinikum Bonn, Bonn, Germany; <sup>13</sup>Constellation Pharmaceuticals, Inc., a MorphoSys Company, Boston, MA, USA; <sup>14</sup>Guy's and St Thomas' NHS Foundation Trust, London, UK.

# Future perspectives in the treatment of MF..



TKI, tyrosine kinase inhibitor.

Adapted from: Dayer N & Assi R. *Oncol Hematol Rev* 2016; 12:71–74; McLarnan DP & Harrison CN. *Br J Haematol* 2020; 191:121–36;

Schleiber M, et al. *Blood Cancer J* 2019; 9:74; Tremblay D & Mascarenhas J. *Cells* 2021; 10:1034.