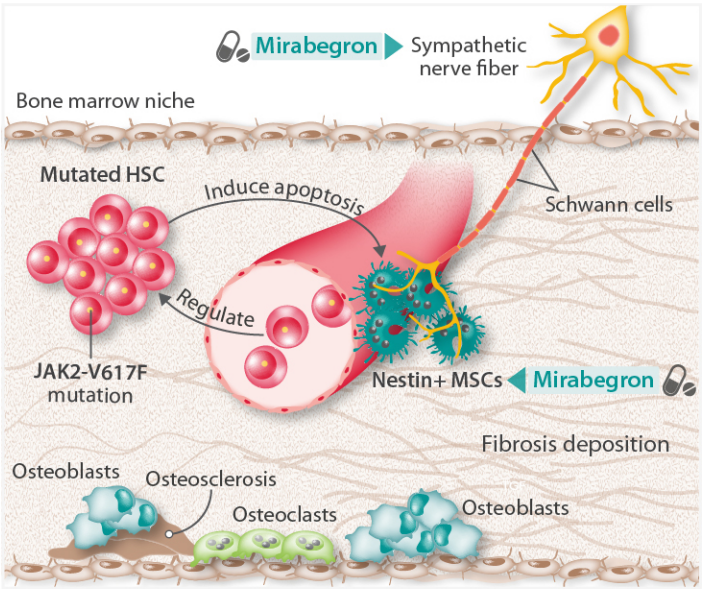
Testing the efficacy of mirabegron, a β3-adrenoceptor agonist, in patients with JAK2-V617F positive myeloproliferative neoplasms



Myeloproliferative neoplasms (MPN)
are initiated and maintained from an acquired mutation in JAK2 (JAK2-V617F) in hematopoietic stem cells (HSCs)

Nestin-positive mesenchymal stem cells (Nestin+ MSCs)
- are innervated by sympathetic nerve fibers
- are important in regulating normal HSCs
- are reduced in bone marrow from patients with MPN
- depletion of nestin+ MSCs accelerated MPN progression

A multicenter, prospective, single-arm, single-stage and open phase II trial

39 JAK2-V617F positive patients with MPN and a mutant allele burden >20%

Mirabegron (50ng/day) for 24 weeks

Treatment completion	82% (32/39)
Treatment interruption	13% (5/39)
Adverse events	85% (33/39)

- **Primary endpoint** of a ≥ 50% reduction of JAK2-V617F allele burden — not reached (0/39)
- **Secondary endpoint** of a ≥ 25% reduction of JAK2-V617F allele burden — 1/39

- Decrease in reticulin fiber content from a median grade of 1.0 (IQR 0-3) to 0.5 (IQR 0-2) (p=0.01)
- Increase in the nestin+ MSCs from a median of 1.09/mm2 (IQR 0.38-3.27) to 3.95/mm2 (IQR 1.98-8.79) (p<0.0001)

Drexler *et al.*, Haematologica, 2019