

# Pregnancy in MPN



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# Pregnancy in MPN

## Why is this an important issue?

- MPN is diagnosed earlier today.  
(molecular diagnosis, better attention/awareness of MPN etc.)
- This means that we increasingly have younger MPN patients.
- On the other hand, the age of pregnant women is getting higher and higher.
- We know more and more about "MPN and pregnancy".
- Our treatment strategies are getting better and better (IFN etc.)

# Pregnancy in MPN

- Data available for ET > PV > PMF.
- No standard treatment.
- Randomised studies not possible.
- Mostly retrospective data and case series.

*M Griesshammer et al. Blood Rev. 2008, M Griesshammer et al. Exp Rev Hematol 2018, SE Robinson & CN Harrison Br J Haematol 2020*

# Pregnancy in MPN

## ➤ Background complication rate in “normal” pregnancies

- Spontaneous abortion ( $\leq$  20<sup>th</sup> week) 11 %
- Stillbirth ( $>$  20<sup>th</sup> week) 0.43 %
- Pre-term delivery (24-37<sup>th</sup> week &  $<$  2,5kg) 9 %
- Thrombosis 1 out of 1000
- “Success rate”  $\sim$  80%

*M Griesshammer et al. Blood Rev. 2008, M Griesshammer et al. Exp Rev Hematol 2018, SE Robinson & CN Harrison Br J Haematol 2020*

# Pregnancy in MPN

Fertility and effects of MPN therapy on the child

## I. Fertility

- Sperm need 72 days to mature (10 weeks)

## II. Potential effects of therapy

- Malformations
- Premature birth or intrauterine growth retardation

## III. Risk depends on

- Organ formation (3rd to 8th week of development)
- Duration of medication, dose...
- Hydroxyurea > Anagrelide > Interferon

# Pregnancy in MPN

## Influence of pregnancy on clinical course

### Thrombosis ↑

- ✓ Normal pregnancy: risk of thrombosis -> 1 out of 1000
- ✓ Risk of thrombosis in age group: **2% (ET) or 3,8% (PV) per patient year**

### Hemorrhage ↑

- ✓ Acquired Von Willebrand`s disease, platelet dysfunction
- ✓ Influenced by aspirin or LMWH

### Natural course of MPN

- ✓ No significant influence

## Essential thrombocythemia and pregnancy - Obstetrical outcome -

EXPERT REVIEW OF HEMATOLOGY  
2018, VOL. 11, NO. 9, 697–706  
<https://doi.org/10.1080/17474086.2018.1506325>



REVIEW



### Contemporary management of patients with *BCR-ABL1*-negative myeloproliferative neoplasms during pregnancy

Martin Griesshammer, Parvis Sadjadian and Kai Wille

University Clinic for Haematology, Oncology, Hemostaseology and Palliative Care, Johannes Wesling Medical Center Minden, UKRUB, University of Bochum, Minden, Germany

- 793 pregnancies in 492 ET patients
- Success rate 68,5% (normal > 80%)
- Miscarriages 31,5%

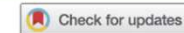
*M. Griesshammer et al. Exp Rev Hematol 2018*

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- 1.8% thromboses in ET patients
- 2.4% major bleeding
- No maternal deaths!

*M. Griesshammer et al. Exp Rev Hematol 2018*



## Pregnancy in MPN



- High risk ET pregnancy -> IFN alpha recommended
- Until now < 80 cases in the literature!
- In this series success rate of 74% without significant side effects!

*L. Schrickel et al. Journal Cancer Res and Clin Oncol 2020*

# Interferon alpha for essential thrombocythemia during 34 high-risk pregnancies: outcome and safety

Lukas Schrickel, Florian H. Heidel<sup>2</sup>, Parvis Sadjadian, Tatjana Becker, Vera Kolatzki, Andreas Hochhaus, Martin Griesshammer, Kai Wille for the German Study Group MPN, GSG-MPN

- Reasons defining high-risk ET pregnancy in all 23 patients were:
  - Thrombosis ( $n = 9$ ) or severe hemorrhage ( $n = 2$ ) in history, or
  - Platelet count  $\geq 1500 \times 10^3/\mu\text{l}$  ( $n = 8$ ), or
  - Severe microcirculatory disturbances not completely responding to ASA ( $n = 4$ )
- 18 / 23 patients were already on cytoreduction prior to pregnancy.
- Without IFN, live birth rate was 60% (6/10), however, after the use of IFN live birth rate increased to 73.5% (25/34 pregnancies).
- 9 pregnancies ended in miscarriages (9/34; 26.5%); all of them spontaneous abortions.

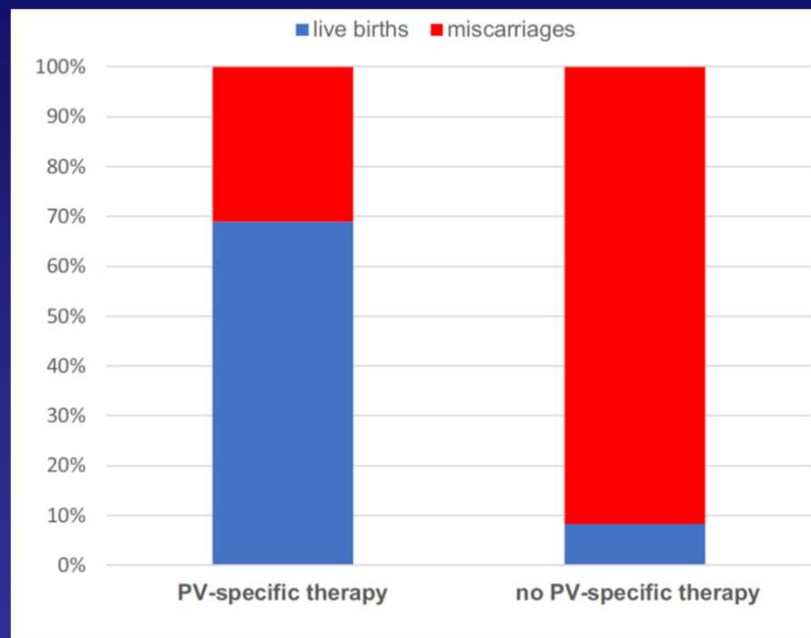
*L. Schrickel et al. J Cancer Res Clin Oncol. 2020 Nov 2.*

# Pregnancy in PV

- ✓ Compared with ET (~1000 pregs.) fewer preg. reported (< 200 preg.)
- ✓ Low dose aspirin advantageous
- ✓ Low molecular heparin in addition to aspirin in high risk patients
- ✓ Tight control of hematocrit by venesection - Caveat: Fe<sup>2+</sup> supplementation
- ✓ Interferon alpha in PV pts. with
  - a disease-related prior reason for cytoreduction
  - or in high-risk pregnancies

*C Harrison et al. Br J Haematol. 2005, M. Griesshammer et al. Exp Rev Hematol 2018, SE Robinson & CN Harrison Br J Haematol 2020*

## The management, outcome, and postpartum disease course of 41 pregnancies in 20 women with polycythemia vera



Pregnancy outcome according to the use of PV-specific therapy. PV-specific therapy during pregnancy included acetylsalicylic acid, low molecular weight heparin and interferon-alpha. The difference in live birth rates (69% of pregnancies with PV-specific therapy vs. 8.3% with no PV-specific therapy) was statistically significant ( $P < .001$ ).

## HOW I TREAT A PV PATIENT: The challenge of pregnancy

### - Conclusions -

- Polycythemia vera (PV)
  - Success rate 53-66 %
  - Thrombosis rate ~ 2,6 %, major bleeding ~ 5 %
- PV-specific therapy improved the live birth rate
- Aspirin + LMWH ↑ live birth rate, PEG IFN in high risk pregnancy
- Significantly more complicated postpartum PV courses were observed after miscarriages

## Association of Treatments for Myeloproliferative Neoplasms During Pregnancy With Birth Rates and Maternal Outcomes - A Systematic Review and Meta-analysis

- Systematic review and meta-analysis of 22 studies, reporting on 1210 pregnancies.
- Most studies reported on pregnancy with ET (n=815) – PV (n=159).
- The live birth rate was 71.3%.
- Most common adverse maternal event was preeclampsia, with 3.1% (95%CI, 1.7%-4.5%).
- Use of aspirin and interferon, but not heparin, associated with higher odds of live birth.

*D. Maze et al. JAMA Network Open 2019*

# Pregnancy Management in MPN

## Preconception

- **Counsel**
- Risk assessment
- Optimise haematocrit & platelet count
- Address cardiovascular risk factors
- Pre-existing indication cytoreduction: Switch to Interferon alpha

## Pregnancy all

- **Offer low dose aspirin**
- Venesection (PV)
- Offer low molecular weight heparin in the presence of one additional thrombosis risk factor
- Anomaly scan & Uterine artery Doppler 20/40
- Serial growth scans
- Avoid dehydration & immobility (hyperemesis and labour)

## Pregnancy high risk

- Offer Interferon alpha
- Offer low molecular weight heparin if prior thrombosis
- **Consider** low molecular weight heparin if prior poor pregnancy outcome
- Increased fetal monitoring

## Post delivery

- **Low molecular weight heparin for 6 weeks**
- Continue aspirin according to management MPN prior to pregnancy
- Individual breast feeding plan
- Discuss contraception options