

REGIONE VENETO
AZIENDA U.L.S.S. n. 9 di Treviso

Con il patrocinio di



SIE - Società Italiana di Ematologia

Unità Operativa di Ematologia
Responsabile Dott. F. Gherlinzoni

HIGHLIGHTS IN EMATOLOGIA

17-18 NOVEMBRE 2017 - TREVISO
Sala Convegni - Ospedale Ca' Foncello

Sessione III: emopatie e gravidanza

Le piastrinopenie immuni

Marco Ruggeri
UOC Ematologia
Vicenza

REGIONE DEL VENETO



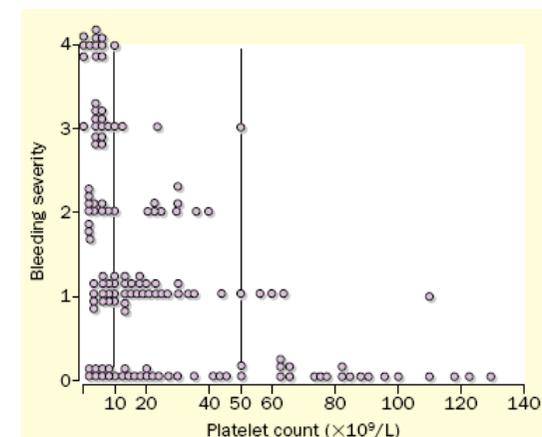
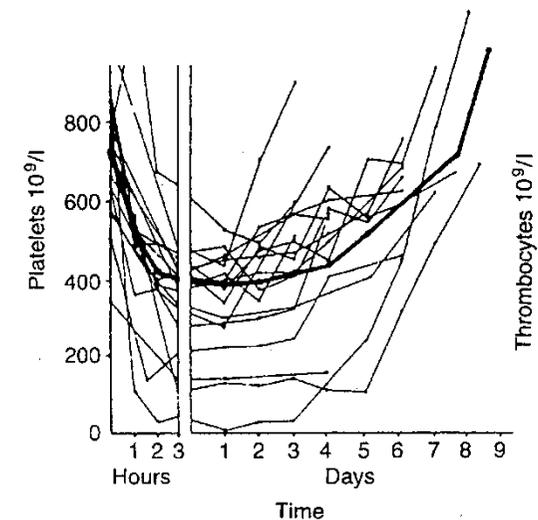
Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group

Francesco Rodeghiero, Roberto Stasi, Terry Gernsheimer, Marc Michel, Drew Provan, Donald M. Arnold, James B. Bussel, Douglas B. Cines, Beng H. Chong, Nichola Cooper, Bertrand Godeau, Klaus Lechner, Maria Gabriella Mazzucconi, Robert McMillan, Miguel A. Sanz, Paul Imbach, Victor Blanchette, Thomas Kühne, Marco Ruggeri and James N. George

Primary Immune ThrombocytoPenia

(no longer Idiopathic Thrombocytopenic Purpura)

- Primary = absence of any initiating/underlying disease (opposed to *Idiopathic*)
- Immune = immune-mediated pathogenesis
- Avoid Purpura: a minority of patients present bleeding at the onset of the disease
- ThrombocytoPenia: to save acronym ITP (utility in electronic database search)



Incidence of Adult Chronic ITP

- **58-66 new cases/1.000.000 per year**

(Mc Millan 1997)

- **Affects mainly women in childbearing age,
Female:Male ratio = 3:1**

(Waters 1992)

- **ITP occurs in 1 per 1000 to 1 per 10.000
pregnancies**

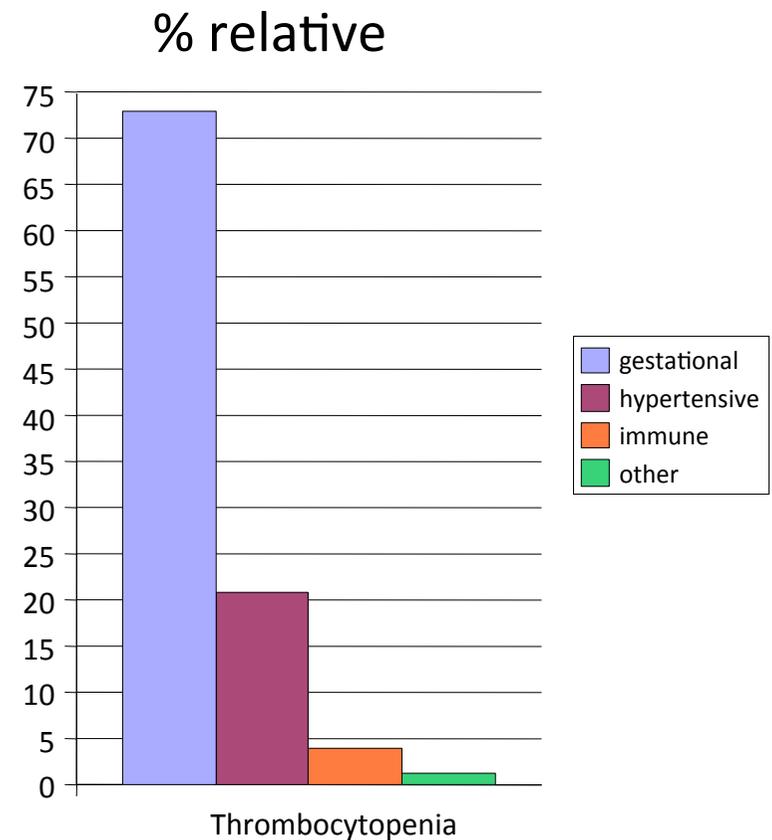
(Gill & Kelton 2000)

Rate of maternal low platelet count-associated diseases during pregnancy

(Burrows and Kelton, NEJM 1993)

Platelet < $150 \times 10^3/\mu\text{L}$
at partum

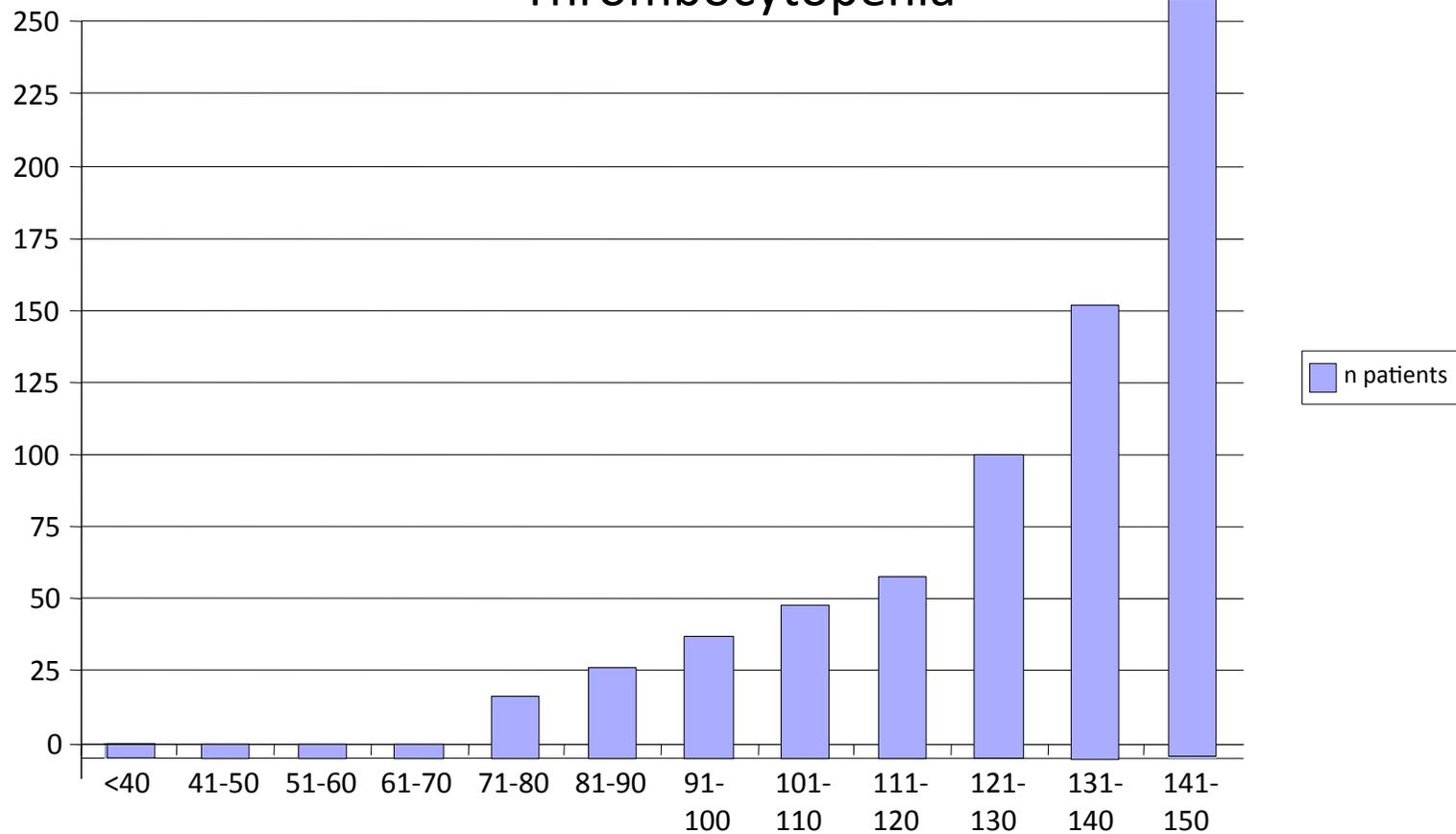
| Type of disease | n. | % rel. | % ass. |
|-----------------|------------|--------|--------|
| Gestational | 756 | 73 | 4.8 |
| Hypertensive | 216 | 21 | 1.4 |
| ITP | 31 | 3 | 0.25 |
| LES | 8 | 0.8 | 0.005 |
| Other | 13 | 1.2 | 0.08 |
| Total: | 1027/15471 | | 6.6 |



Maternal platelet count in 756 gestational thrombocytopenia

(Burrows and Kelton, 1993)

Frequency of platelet count in mothers with gestational Thrombocytopenia



| Cause of thrombocytopenia | Time of the most common onset | Grade of thrombocytopenia | Biochemical abnormalities | Clinical symptoms |
|---------------------------|-------------------------------|---------------------------|--|----------------------------|
| Gestational | III trimester | mild | no | no |
| ITP | I-II trimester | mild to severe | no | bleeding in severe cases |
| Eclampsia | III trimester | mild to severe | DIC ⁽⁴⁾ proteinuria | hypertension |
| HELLP ⁽¹⁾ | III trimester | mild to severe | DIC, hemolytic anemia ↑ AST/ALT | no or complex presentation |
| TTP ⁽²⁾ | II trimester | mild | hemolytic anemia | fever, CNS ⁽⁵⁾ |
| HUS ⁽³⁾ | Post - partum | mild | hemolytic anemia | fever, renal failure |
| AFL ⁽⁶⁾ | III trimester | mild | DIC, hemolytic anemia, hypoglycemia | complex presentation |

ITP in Pregnancy: Maternal Outcome

(Webert et al, Blood 2003)

Retrospective study, patients from 2 hospitals: 92 ITP, 123 newborns, 119 pregnancies

Bleeding symptoms during 116 pregnancies:

- 76 (65.5%) no symptoms
- 15 (12.9%) mild (purpura)
- 21 (18.1%) moderate (epistaxis, post-trauma hemorrhage, muco-cutaneous bleeding)
- 4 (3.4%) severe (2 hematuria, 1 gastrointestinal hemorrhage); platelet count: 3 - 117 x10⁹/L

ITP in Pregnancy: Maternal Outcome

(Webert et al, Blood 2003)

Need of therapy during 119 pregnancies:

- 82 (69 %) no treatment (plt 32-521 x 10⁹/L)
- 37 (31 %) therapy to increase platelet count (response in **46%** cases) :
 - 20 Ig i.v.
 - 8 Steroids
 - 7 Ig i.v,+ Steroids
 - 1 anti-D Ig + Steroids
 - 1 Ig i.v.+ anti-D + Steroids

ITP in Pregnancy: Maternal Outcome

(Webert et al, Blood 2003)

Delivery outcomes (119):

- 98 (82 %) vaginal 21 (18 %) cesarean section
Plt: 88 x10⁹/L Plt: 75 x10⁹/L (p=0.16)
- Bleeding at partum: 4 women with blood loss > 1 L, no relationship with platelet count (54-321 x10⁹/L)
(17 cases, 15% with plt < 50x10⁹/L at partum)
- Bleeding post-partum (74 cases):
 - 2 hemorrhages, no need of transfusion
 - 1 with plt 119x10⁹/L, vaginal
 - 1 with plt 39x10⁹/L, cesarean section

ITP in Pregnancy: Neonatal Outcome

- Real incidence of thrombocytopenia not clearly established (ranging from 16% to 56%)
 - No consensus on the level of platelet count required to define severe thrombocytopenia (<20, < 30, < 50 /10⁹/L)
 - Variability in the timing of platelet count assessment
- Severe bleeding complications ~ 1% (?)



blood[®]

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doi:10.1182/blood-2016-04-710285 originally published
online July 11, 2016

Corticosteroids compared with intravenous immunoglobulin for the treatment of immune thrombocytopenia in pregnancy

Dongmei Sun, Nadine Shehata, Xiang Y. Ye, Sandra Gregorovich, Bryon De France, Donald M. Arnold, Prakesh S. Shah and Ann Kinga Malinowski

| | No Treatment (n 137) | IVIg (n = 47) | Steroids (n = 51) |
|---|-------------------------|------------------|----------------------|
| Maternal age mean (SD) | 32.7 (4.1) | 31.1 (4.8) | 30.5 (5.1) |
| Age at ITP diagnosis mean (SD) | 24.9 (7.2) | 27.2 (6.5) | 26.7 (6.0) |
| Maternal pre- treatment platelet count ($\times 10^9/L$) mean (SD) | NA | 49 (25) | 50 (22) |

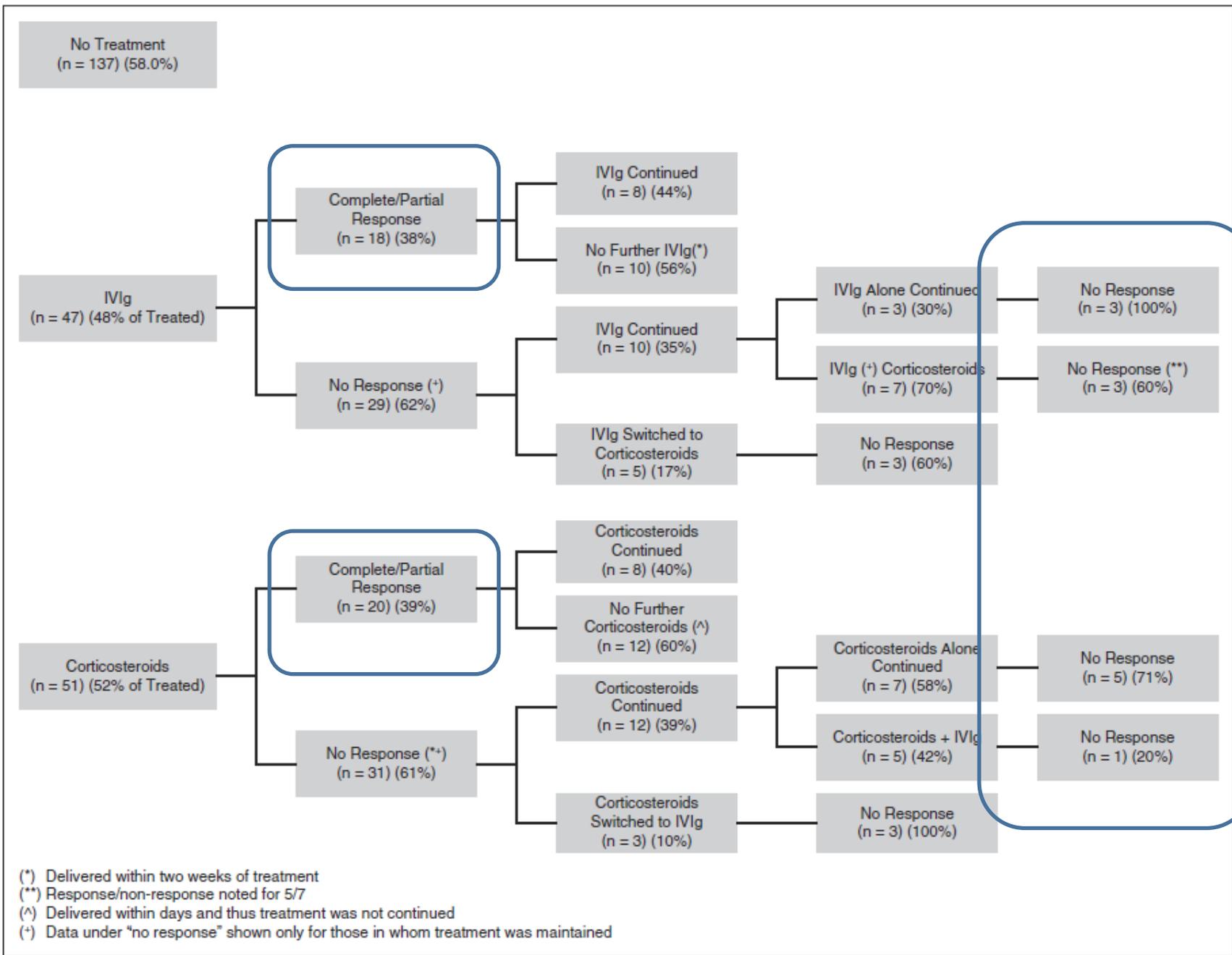


Table 2. Maternal and neonatal outcomes according to treatment strategy

| Outcomes | No treatment (n = 137) | IVIg (n = 47) | Corticosteroids (n = 51) | P value | |
|--|------------------------|---------------|--------------------------|------------|-------------------------|
| | | | | All groups | IVIg vs corticosteroids |
| Maternal response to initial treatment (n), (%) | N/A | 18 (38) | 20 (39) | — | .85 |
| Maternal platelet count at delivery ($\times 10^9/L$), mean (SD) | 103.2 (1.8) | 68.7 (1.8) | 77.3 (1.6) | <.0001 | .71 |
| Antepartum hemorrhage (n), (%) | 2 (1.5) | 5 (10.6) | 3 (5.9) | .08 | .39 |
| Postpartum hemorrhage (n), (%) | 6 (4.4) | 9 (19.2) | 6 (11.8) | <.03 | .33 |
| Pre-delivery platelet transfusion (n), (%) | 1 (0.7) | 6 (12.8) | 3 (5.9) | <.02 | .25 |
| Peripartum transfusion: any blood product (n), (%) | 2 (1.5) | 9 (19.2) | 3 (5.9) | .01 | .05 |
| Haemoglobin drop >30 g/L after delivery (n/N), (%) | 9/106 (8.5) | 12/47 (25.5) | 9/47 (19.2) | .02 | .39 |
| Stillbirth (n), (%) | 2 (1.5) | 0 | 2 (3.9) | .37 | .49 |
| Preterm birth <37 wk (n), (%) | 16 (11.7) | 4 (8.5) | 5 (9.8) | .81 | .99 |
| Preterm birth <34 wk (n), (%) | 7 (5.1) | 2 (4.3) | 1 (2.0) | .63 | .61 |
| Birth weight (g), mean (SD) | 3309 (637) | 3193 (769) | 3308 (521) | .54 | .38 |
| Small for gestational age (n/N), (%) | 6/136 (4.4) | 6/47 (12.8) | 5/51 (9.8) | .12 | .64 |
| Apgar score <7 at 5 min (n), (%) | 5 (3.7) | 2 (4.3) | 3 (5.9) | .80 | .99 |
| Maternal composite outcome (n), (%) | 14 (10.2) | 22 (46.8) | 12 (23.5) | <.0001 | .02 |
| Fetal/neonatal composite outcome (n), (%) | 13 (9.5) | 9 (19.2) | 9 (17.7) | .17 | .87 |

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Splenectomized patients
21/235 (9%)
16/137 (12%) no treated

| | |
|-------------------------------------|----------------------------------|
| Mean platelet count at delivery | 243 x 10 ⁹ /L (±128) |
| Mean platelet count nadir | 197 x 10 ⁹ /L (±135) |
| Mean neonatal platelet count nadir | 189 x 10 ⁹ /L (±106) |
| Neonates < 150 x 10 ⁹ /L | 5 (28%) |

Partum management

| | No treatment | IVIg | Steroids |
|----------------------------|--------------|------------|------------|
| Operative vaginal delivery | 9/106 (8.5) | 1/35 (2.9) | 1/43(2.3) |
| Cesarean section | 53 (38.7) | 20 (42.6) | 15 (29.4) |

Neonatal outcomes

| | Treated pregnancies | Untreated pregnancies |
|------------------------------------|----------------------------------|---------------------------------|
| Mean neonatal platelet count nadir | 182 x 10 ⁹ /L (±104) | 205 x 10 ⁹ /L (±74) |

Cranial ultrasound in 25 neonates (45%)

2 with intracranial hemorrhage (one with a platelet count of 135 x10⁹/L; one with a cord platelet count of 186 x 10⁹/L and 18 x 10⁹/L 3 days after

Case n° 1: Elisa

- June 1994
 - female patient, 11-years old
 - platelet count: $2 \times 10^9/L$
 - bleeding symptoms
 - ITP diagnosis
 - no response to PDN/Ig
- December 1994
 - splenectomy: CR

- December 2010
 - bleeding symptoms
 - platelet count $10 \times 10^9/L$
 - diagnosis of relapse of ITP
- Weak response to PDN/Ig
- After 3 months (PDN 10 mg/day)
 - platelet count $\sim 10-15 \times 10^9/L$
 - WBC $24.000/\mu L$
 - no bleeding symptoms
- Therapy “on demand”

- September 2011
 - bleeding symptoms
 - platelet count $10 \times 10^9/L$
 - start therapy with Eltrombopag
- June 2012
 - bleeding symptoms
 - platelet count $10 \times 10^9/L$
 - stop Eltrombopag
- August 2012
 - platelet count $\sim 10-15 \times 10^9/L$
 - start therapy with Romiplostim

- April 2014
 - platelet count $90 \times 10^9/L$
 - stop Romiplostim (pregnancy planned)
 - relapse of ITP
 - “on demand” treatment with Ig (transient response, side effects after infusions)
- February 2015
 - start pregnancy
 - platelet count $16 \times 10^9/L$
 - moderate bleeding symptoms

WHICH TREATMENT DURING PREGNANCY ?

Recommendations for the treatment of ITP in pregnancy

Target platelet counts for treatment:

- Throughout the first 2 trimesters, treatment is initiated when:
 - the patient is symptomatic
 - platelet counts fall below 20 to 30 x 10⁹/L
- Platelet count assessed monthly until 34 w

Recommendations for the treatment of ITP in pregnancy

- Oral corticosteroids or IVIg are considered first-line treatment (Grade C recommendation)
- Management options for pregnant ITP failing first line treatment:
 - Combining first-line therapies
 - IVIg + azathioprine for patients refractory to corticosteroids
- Splenectomy is rarely performed in pregnancy, but is best performed in the second trimester if absolutely necessary (Grade C recommendation)

Table 4. Therapeutic options for ITP in pregnancy

| | Intravenous gammaglobulin (IVIg) oral corticosteroids |
|--|---|
| First-line therapy | |
| Second line* | Combination therapy with corticosteroids and IVIg Splenectomy (second trimester) |
| Other therapeutic options† | |
| Relatively contraindicated | Anti-D immunoglobulin [C] Azathioprine [D] |
| Not recommended but use in pregnancy described | Cyclosporine A [C] Dapsone [C] Thrombopoietin receptor agonists [C]‡ Campath-1H [C] Rituximab [C] |
| Contraindicated | Mycophenolate mofetil [C] Cyclophosphamide [D] Vinca alkaloids [D] Danazol [X] |

Lupus. 2012 Dec;21(14):1571-4.

Successful treatment of severe thrombocytopenia with romiplostim in **a pregnant patient** with systemic lupus erythematosus.

Alkaabi JK1, et al.

We present a case of a pregnant woman at 27 weeks of gestation with systemic lupus erythematosus who developed severe thrombocytopenia presenting with melena, epistaxis, gum bleeding and frank hematuria. She was resistant to most treatment modalities, including steroids, intravenous immunoglobulins (IVIG), rituximab, IV cyclophosphamide and eltrombopag. She responded to romiplostim with normalization of her platelet count, which enabled her to be delivered safely at 34 weeks of gestation.

Obstet Gynecol. 2014 Aug;124(2 Pt 2 Suppl 1)

Rescue therapy with romiplostim for refractory primary immune thrombocytopenia during pregnancy.

Decroocq J1, et al.

BACKGROUND: Primary immune thrombocytopenia is not a rare event during pregnancy, and it must be carefully managed to avoid hemorrhagic complications for the mother. After failure of first-line treatments, the teratogenicity and toxicity of other therapeutic agents limit the available options and treatment.

CASES: We describe the cases of **two pregnant patients** with corticosteroid-refractory immune thrombocytopenia who were successfully treated by romiplostim, a thrombopoietin receptor agonist, without any fetal or maternal complications.

CONCLUSION: Romiplostim may represent an important alternative treatment choice during pregnancy for immune thrombocytopenia cases refractory to first-line therapy, especially because of its speed of action and high efficacy



blood[®]

2017 130: 1097-1103

doi:10.1182/blood-2017-01-761262 originally published
online June 19, 2017

A novel recombinant human thrombopoietin therapy for the management of immune thrombocytopenia in pregnancy

Zhangyuan Kong, Ping Qin, Shan Xiao, Hai Zhou, Hong Li, Renchi Yang, Xiaofan Liu, Jianmin Luo, Zhichun Li, Guochao Ji, Zhongguang Cui, Yusheng Bai, Yuxia Wu, Linlin Shao, Jun Peng, Jun Ma and Ming Hou

Multicenter, open-labeled, single arm study, aimed to determine the safety and efficacy on rhTPO in patients with steroids/IVIg – resistant ITP in pregnancy

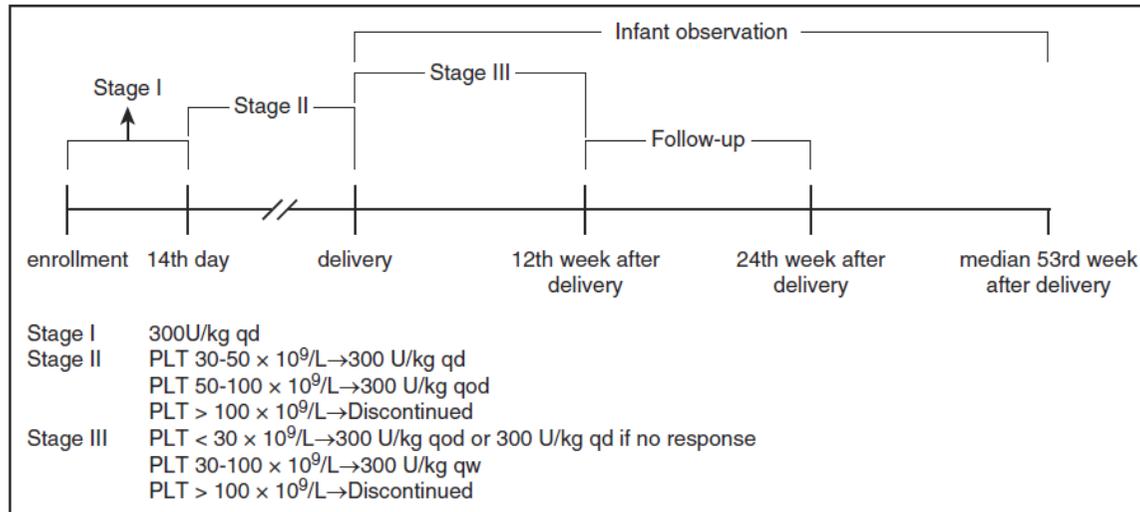
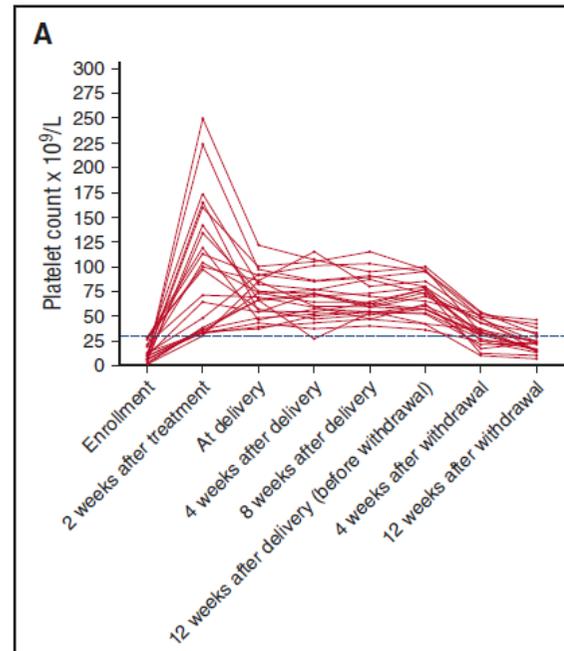
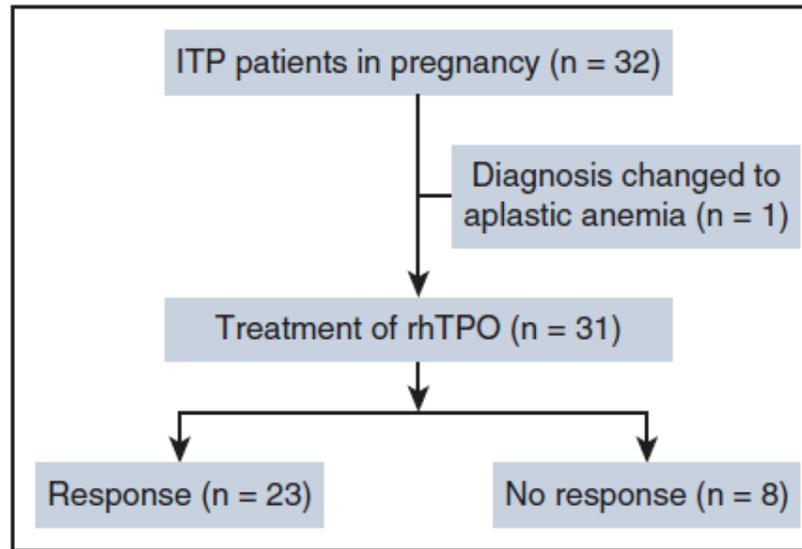


Figure 1. Dose scheme of rhTPO. PLT, platelet; qd, daily; qod, every other day; qw, every week.

| Characteristic | All patients (n = 31) |
|--|-----------------------|
| Age, median (IQR), y | 26 (24-33) |
| Age of gestation, median (IQR), wk | 24 (16-27) |
| 13-17 wk, n (%) | 11 (35.5) |
| 18-22 wk, n (%) | 5 (16.1) |
| 23-27 wk, n (%) | 8 (25.8) |
| 28-32 wk, n (%) | 4 (12.9) |
| ≥ 33 wk, n (%) | 3 (9.7) |
| Platelet count on enrollment, median (IQR), $\times 10^9/L$ | 10 (6-12) |
| Primigravida, n (%) | 29 (93.5) |
| Underlying disease, n (%) | |
| Hypertension | 3 (9.7) |
| Diabetes | 4 (12.9) |
| Diagnosis of ITP, n (%) | |
| Before pregnancy | 23 (74.2) |
| In pregnancy | 8 (25.8) |
| Prior therapies, n (%) | |
| Dex+PLT transfusion | 7 (22.6) |
| Pred+PLT transfusion | 8 (25.8) |
| IVIG+PLT transfusion | 9 (29.0) |
| Dex+IVIG+PLT transfusion | 2 (6.5) |
| Pred+IVIG+PLT transfusion | 4 (12.9) |
| Dex+Pred+IVIG+PLT transfusion | 1 (3.2) |
| Peak platelet count during previous treatments, n (%) | |
| $< 30 \times 10^9/L$ | 31 (100) |
| $\geq 30 \times 10^9/L$ | 0 (0) |
| Total amount of platelets transfused per patient (unit)*, median (IQR) | 10 (6-17) |
| Platelet transfusion refractoriness, n (%) | 31 (100) |
| Patients on stable dose (15-30 mg/d) of Pred upon enrollment, n (%) | 10 (32.3) |



| Adverse events | n (%) |
|--------------------------|--------------|
| Patients (n = 31) | |
| Dizziness | 1 (3.2) |
| Fatigue | 1 (3.2) |
| Pain at injection site | 1 (3.2) |
| Newborns (n = 31) | |
| Thrombocytopenia | 9 (29.0) |
| Abdominal distension | 1 (3.2) |

| Perinatal outcome | All newborns (n = 31) |
|---|------------------------------|
| Live birth, n (%) | 31(100) |
| Stillbirth, n (%) | 0 (0) |
| Age of gestation, median (IQR), wk | 39 (37-40) |
| Preterm births (before 37th wk), n (%) | 3 (9.7) |
| Birth weight, median (IQR), kg | 3.1 (2.9-3.5) |
| Birth weight <2.5 kg, n (%) | 2 (6.5) |
| Birth length, median (IQR), cm | 50.2 (48.4-51.3) |
| Birth head circumference, median (IQR), cm | 34.3 (33.6-35.2) |
| Birth chest circumference, median (IQR), cm | 33.1 (31.9-34.5) |
| Birth abdominal circumference, median (IQR), cm | 33.0 (32.0-34.3) |
| Platelet count at birth, n (%) | |
| <50 × 10 ⁹ /L | 0 (0) |
| 50-100 × 10 ⁹ /L | 9 (29.0) |
| Hemorrhagic complications, n (%) | 0 (0) |
| Neonatal death, n (%) | 0 (0) |

Case n° 2: Monica

- December 2014
 - female patient, 40-years old
 - platelet count: $25 \times 10^9/L$
 - mild bleeding symptoms
 - ITP diagnosis
 - transient response to PDN/Ig

- January 2015
 - start pregnancy
 - platelet count $25 \times 10^9/L$
 - moderate bleeding symptoms

 - low dose prednisone (12.5 mg/day)
 - PLT 30-40 $\times 10^9/L$ during pregnancy
- Last WBC before partum: PLT $37 \times 10^9/L$

WHICH TREATMENT before DELIVERY ?

Recommendations for the treatment of ITP in pregnancy

Target platelet counts for treatment before partum:

- PLT count assessed weekly at 34 w
- $\geq 50 \times 10^9/L$ (uncomplicated vaginal delivery with $20-25 \times 10^9/L$, but risk of cesarean section conversion possible)
- $\geq 75 \times 10^9/L$ for spinal or epidural anesthesia

Recommendations for the treatment of ITP in pregnancy

Therapies

- Prednisone, 1 mg/Kg b.w./day
- Intravenous Ig high dose (1 g/Kg b.w.) single infusion
- Combinations of IVIG, corticosteroids and **platelet transfusions** can be used
- The use of platelet transfusions before delivery in pregnant women with ITP has been reported in 5%-18.9% of cases

Case n° 3: Rosanna

- October 2009
 - female patient, 32-years old
 - platelet count: $15 \times 10^9/L$
 - mild bleeding symptoms
 - ITP diagnosis
 - partial response to PDN/Ig

- March 2013
 - start pregnancy
 - platelet count $25 \times 10^9/L$
 - moderate bleeding symptoms

 - low dose prednisone (12.5 mg/day)
 - PLT $50-70 \times 10^9/L$ during pregnancy
- Last PLT before partum: $75 \times 10^9/L$
 - caesarian section for fetal distress
 - cord platelet count : $9 \times 10^9/L$

Mode of delivery ?

WHICH neonatal TREATMENT ?

Management of delivery

- Mortality rate of babies <1%
- Incidence thrombocytopenia ($< 50 \times 10^9/L$): 9%- 14.%
- ICH: 0% - 1.5%

- There is no evidence that cesarean section is safer than **uncomplicated** vaginal delivery
- Most hemorrhagic events occur 24 to 48 hours after delivery at the nadir of the platelet count



The mode of delivery in ITP patients should be determined by purely obstetric indication

Management of delivery

- Procedures during labor that may be associated with increased hemorrhagic risk to the fetus should be avoided
- The American College of Obstetricians and Gynecologists recommends against operative vaginal delivery in a fetus with a known or suspected bleeding disorder
- However, "ad hoc" studies are lacking
- These recommendations must be balanced against risk of maternal and neonatal morbidity of cesarean section in the second stage of labor (elevation of impacted fetal head)

Neonatal management

- After delivery, platelet count assayed by venopuncture of a cord vessel
- Avoid intramuscular injections
- Transcranial ultrasonography performed on neonates with platelet count $< 50 \times 10^9/L$
- In thrombocytopenic neonate a daily platelet count could be performed (nadir after 2-5 days)
- Treat (IVIg) neonates with bleeding or with platelet count $< 20 \times 10^9/L$

PLATELETS AND THROMBOPOIESIS

Persistent neonatal thrombocytopenia can be caused by IgA antiplatelet antibodies in breast milk of immune thrombocytopenic mothers

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Key Points

- Persistent thrombocytopenia was observed in breastfed neonates of ITP women.
- Breast milk of ITP women may contain immunoglobulin A antiplatelet antibodies, which target $\alpha_{IIb}\beta_3$ integrin.

Immune thrombocytopenia (ITP) in pregnant women can cause neonatal thrombocytopenia by transport of antiplatelet autoantibodies across the placenta. Usually, an infant's platelet count normalizes within 2 months. We observed neonatal thrombocytopenia that persisted more than 4 months and disappeared following discontinuation of breastfeeding. The aim of our study was to discern whether breast milk of ITP mothers contained antiplatelet antibodies causing persistent thrombocytopenia. We collected milk samples from 3 groups of women: ITP group, 7 women who had ITP during pregnancy; R-ITP group, 6 women who recovered from ITP before pregnancy; and 9 healthy controls. We found increased levels of antiplatelet antibodies of the immunoglobulin A type in the milk of ITP patients compared with the other 2 groups. Similar increase was demonstrated for antibodies binding to $\alpha_{IIb}\beta_3$ expressed in cultured cells. Thus, transfer of antiplatelet antibodies from ITP mothers by breastfeeding can be associated with persistent neonatal thrombocytopenia.

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Effect of pregnancy on the course of immune thrombocytopenia: a retrospective study of 118 pregnancies in 82 women

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Summary

In women with pre-existing immune thrombocytopenic purpura (ITP), the effect of pregnancy on the course of the disease is poorly known. We performed a dual-centre retrospective cohort study of 118 pregnancies in 82 women with primary ITP. In early pregnancy, the platelet count was $<100 \times 10^9/l$ in 35.6% of pregnancies. During pregnancy the median platelet count nadir was $66 \times 10^9/l$ (25th–75th percentile: 42–117), with platelet count $<30 \times 10^9/l$ for 26 pregnancies (22%). In 49% of pregnancies, a significant decrease of the platelet count required treatment at least transiently in preparation for delivery. At the time of delivery, the median platelet count was $110 \times 10^9/l$ (77–155). Compared to before pregnancy, at 3 months post-partum, only 11% of pregnancies [95% confidence interval (95% CI): 6.8–20.2] showed disease worsening. Previous splenectomy was the only factor significantly associated with ITP worsening after pregnancy (53.9% vs. 10.3%, $P < 0.001$). For 8.3% of the pregnancies (95% CI: 3.8–15.1), neonatal thrombocytopenia required treatment, especially in case of previous maternal splenectomy (adjusted odds ratio 16.7, 95% CI: 2.61–106). The overall risk of exacerbation of ITP and severe thrombocytopenia during pregnancy is acceptable.

Keywords: immune thrombocytopenia, pregnancy, neonatal thrombocytopenia.

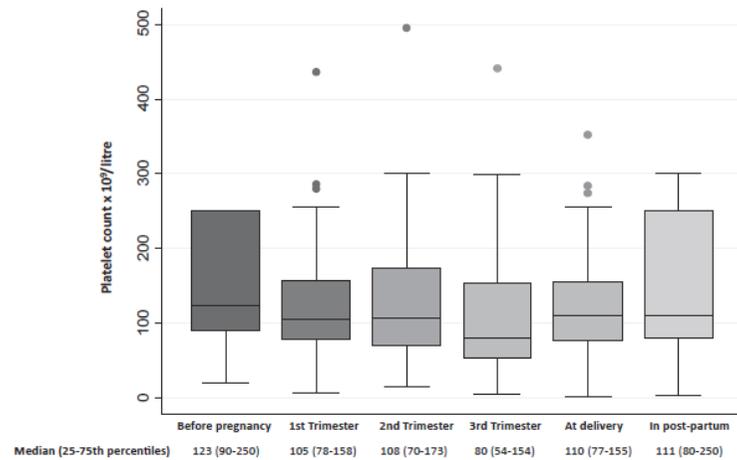


Fig 1. Fluctuations of platelet count during pregnancy and in the post-partum period.

Table II. Factors associated with immune thrombocytopenia (ITP) worsening in the mother after *versus* before pregnancy for 118 pregnancies in 82 women.

| | ITP worsening after pregnancy (n = 13) | Stable ITP status after pregnancy (n = 105) | P value* |
|--|---|--|----------|
| Age at ITP diagnosis, years, median (25th–75th percentile) | 28.3 (21.8–32.2) | 25.2 (20–28.8) | 0.61 |
| Positive antinuclear antibodies | 4 (30.8) | 44 (49.4) | 0.22 |
| Age at pregnancy diagnosis, years, median (25th–75th percentile) | 32.9 (29.5–34.1) | 30 (26.8) | 0.50 |
| Delay ITP/pregnancy, years, median (25th–75th percentile) | 1.3 (1–8.5) | 4.0 (2–8.2) | 0.94 |
| Previous splenectomy | 7 (53.9) | 10 (10.3) | <0.001 |
| Previous treatment with rituximab | 1 (8.3) | 5 (4.8) | 0.6 |
| ITP phase in early pregnancy | | | |
| Newly diagnosed | 0 (0.0) | 3 (2.9) | 0.31 |
| Persistent | 4 (30.8) | 10 (9.5) | |
| Chronic | 9 (69.2) | 88 (83.8) | |
| Previous history of transient ITP in complete remission | 0 (0.0) | 4 (3.8) | |
| Platelet count in early pregnancy | | | |
| <30 × 10 ⁹ /l | 0 (0.0) | 3 (2.9) | 0.50 |
| 30–100 × 10 ⁹ /l | 4 (30.8) | 35 (33.3) | |
| >100 × 10 ⁹ /l | 9 (69.2) | 67 (63.8) | |

Data are number (%) unless indicated

*Hierarchical logistic model with the pregnancy at level one and the women at level two.

Table III. Maternal factors associated with neonatal thrombocytopenia in 109 newborns.

| | Neonatal thrombocytopenia with treatment (<i>n</i> = 9) | No or moderate neonatal thrombocytopenia (<i>n</i> = 100) | <i>P</i> value* |
|---|---|---|-----------------|
| Age at ITP diagnosis, years, median (25th–75th percentile) | 26.2 (14.3–26.4) | 25.8 (20.3–30) | 0.26 |
| Age at pregnancy diagnosis, years, median (25th–75th percentile) | 31.7 (24.7–33) | 30.6 (27.4–34.6) | 0.27 |
| Previous splenectomy | 7 (77.8) | 10 (10.5) | <0.001 |
| Platelet count nadir during pregnancy, $\times 10^9/l$ | 45 (27–69) | 67 (43–126) | 0.43 |
| ITP worsening during pregnancy | 7 (77.8) | 54 (54) | 0.19 |
| Need for ITP treatment during pregnancy | 7 (77.8) | 48 (46.6) | 0.11 |
| Platelet count at delivery, $\times 10^9/l$, median (25th–75th percentile) | 123 (85.5–211) | 110 (77–156) | 0.07 |
| Previous history of neonatal thrombocytopenia (available in <i>n</i> = 79) | 1 (16.7) | 5 (7.7) | 0.47 |

Data are number (%) unless indicated.

*Hierarchical logistic model with the pregnancy at level one and the women at level two or logistic regression with robust variance (in case of nonconvergence of the hierarchical model for platelet count nadir and ITP worsening).



Grazie!