

**PLATELETS AND THROMBOPOIESIS**

# Use of thrombopoietin receptor agonists for immune thrombocytopenia in pregnancy: results from a multicenter study

Marc Michel,<sup>1</sup> Marco Ruggeri,<sup>2</sup> Tomas Jose Gonzalez-Lopez,<sup>3</sup> Salam Alkindi,<sup>4</sup> Stéphane Cheze,<sup>5</sup> Waleed Ghanima,<sup>6,7</sup> Tor Henrik Anderson Tvedt,<sup>8</sup> Mikael Ebbo,<sup>9</sup> Louis Terriou,<sup>10</sup> James B. Bussel,<sup>11</sup> and Bertrand Godeau<sup>1</sup>

<sup>1</sup>Department of Internal Medicine, National Reference Center for Immune Cytopenias, Henri Mondor University Hospital, Assistance Publique–Hôpitaux de Paris, Université Paris-Est Créteil, Créteil, France; <sup>2</sup>Department of Haematology, S. Bortolo Hospital, Vicenza, Italy; <sup>3</sup>Department of Hematology, Hospital Universitario de Burgos, Burgos, Spain; <sup>4</sup>Department of Haematology, Sultan Qaboos University, Muscat, Oman; <sup>5</sup>Institut d'Hématologie de Basse-Normandie, Centre Hospitalier Universitaire de Caen Normandie, Caen, France; <sup>6</sup>Department of Research, Østfold Hospital Trust, Sarpsborg, Norway; <sup>7</sup>Department of Hematology, Institute of Clinical Medicine, University of Oslo, Oslo, Norway; <sup>8</sup>Section for Hematology, Department of Medicine, Haukeland University Hospital, Bergen, Norway; <sup>9</sup>Department of Internal Medicine, La Timone University Hospital, Assistance Publique–Hôpitaux de Marseille, Aix Marseille Université, Marseille, France; <sup>10</sup>Immuno-Hematology, Hôpital Claude Huriez, Lille, France; and <sup>11</sup>Weill Cornell Medicine, New York, NY

**KEY POINTS**

- Transient use of Tpo-RAs for refractory ITP in pregnancy seems relatively safe and effective for mother and fetus.

**Management of immune thrombocytopenia (ITP) during pregnancy can be challenging because treatment choices are limited. Thrombopoietin receptor agonists (Tpo-RAs), which likely cross the placenta, are not recommended during pregnancy. To better assess the safety and efficacy of off-label use of Tpo-RAs during pregnancy, a multicenter observational and retrospective study was conducted. Results from 15 pregnant women with ITP (pregnancies, n = 17; neonates, n = 18) treated with either eltrombopag (n = 8) or romiplostim (n = 7) during pregnancy, including 2 patients with secondary ITP, were analyzed. Median time of Tpo-RA exposure during pregnancy was 4.4 weeks (range, 1-39 weeks); the indication for starting Tpo-RAs was preparation for delivery in 10 (58%) of 17 pregnancies, whereas 4 had chronic refractory symptomatic ITP and 3 were receiving eltrombopag when pregnancy started. Regarding safety, neither thromboembolic events among mothers nor Tpo-RA-related fetal or neonatal complications were observed, except for 1 case of neonatal thrombocytosis. Response to Tpo-RAs was achieved in 77% of cases, mostly in combination with concomitant ITP therapy (70% of responders). On the basis of these preliminary findings, temporary off-label use of Tpo-RAs for severe and/or refractory ITP during pregnancy seems safe for both mother and neonate and is likely to be helpful, especially before delivery. (*Blood*. 2020;136(26):3056-3061)**

## Introduction

Immune thrombocytopenia (ITP) occurs in 1 to 2 per 1000 pregnancies<sup>1</sup>; it may precede pregnancy or be newly diagnosed during pregnancy.<sup>2,3</sup> Except for preparation for delivery, indications for treating ITP during pregnancy are comparable to those of ITP outside pregnancy; on average, at least one-third of pregnant women with chronic ITP will require treatment during pregnancy.<sup>2,4,5</sup> The use of corticosteroids, alone or in combination with IV immunoglobulin, is safe for both mother and fetus, and they can be used as maintenance and/or rescue treatment at any time, especially in preparation for delivery.<sup>2,4,6</sup> Conversely, many treatments for ITP are either not recommended during pregnancy (rituximab)<sup>7</sup> or truly contraindicated (mycophenolate mofetil, vinca alkaloid).<sup>6</sup> Other immunosuppressors are not teratogenic, but either slow mode of action (azathioprine) or risk of hypertension (cyclosporin) limits their use.<sup>2</sup> Lastly, data on the safety and efficacy of splenectomy during pregnancy are limited.<sup>8,9</sup> Therefore, management of women with ITP during pregnancy with

poor response to corticosteroids and IV immunoglobulin is challenging. A study from China reported the efficacy and safety of recombinant thrombopoietin (Tpo) for treating ITP in 31 pregnancies.<sup>10,11</sup> However, the Tpo administered in this study is neither approved for ITP nor widely available outside China. Tpo receptor agonists (Tpo-RAs) eltrombopag and romiplostim, which were approved for adult ITP >10 years ago, are not recommended during pregnancy, because they are likely to cross the placenta, and their safety is not established.<sup>12</sup> To better assess the efficacy and safety of Tpo-RAs for ITP during pregnancy, we performed a retrospective multicenter observational study.

## Study design

This was an observational multicenter international study established by the French reference center for adult immune cytopenias extended to a group of international ITP experts. To be included, patients had to fulfill the following criteria: pregnant

**Table 1. ITP characteristics and outcomes**

Patient n	Patient age, y	ITP phase	N of prior treatment lines for ITP	Tpo-RA (maximal dose during pregnancy)	Gestation at Tpo-RA initiation, wk (treatment duration during pregnancy, wk)	Platelet count nadir during pregnancy/ platelet count before Tpo-RA/ platelet count at time of delivery, × 10 <sup>9</sup> /L	Bleeding manifestations/main reason for using Tpo-RA	Pattern of initial platelet response (concomitant ITP therapy, yes or no)*
1	33	Chronic	4 (splenectomy)	Eltrombopag (50 mg)	36 (4)	10/10/110	No/in preparation for delivery	CR (no)
1†	35	Chronic	4 (splenectomy)	Eltrombopag (25 mg)	38 (2)	9/15/94	No/in preparation for delivery	CR (no)
2	30	Chronic	3	Eltrombopag (50 mg)	8‡ (12)	1/2/123	Yes (skin + mucosa)/unexpected pregnancy on eltrombopag	R (yes)
3	36	Chronic	2	Eltrombopag (50 mg)	4‡ (9)	4/4/114	Yes (skin)/unexpected pregnancy on eltrombopag	CR (yes)
4	29	Chronic	2	Eltrombopag (50 mg)	33 (7)	7/14/169	Yes (skin + mucosa)/in preparation for delivery	CR (no)
5	21	Chronic	7 (splenectomy)	Eltrombopag (75 mg)	8‡ (12)	50/10‡/68	No/chronic refractory ITP, unexpected pregnancy on eltrombopag	R (no)
6	29	Chronic	2	Eltrombopag (75 mg)	34 (5)	8/13/23	Yes (skin)/in preparation for delivery	NR (no)
7	32	Newly diagnosed	2	Eltrombopag (50 mg)	27 (10)	4/4/64	Yes (skin)/insufficient response to steroids + IV immunoglobulin	R (no)
8	32	Persistent secondary ITPs	4	Eltrombopag (100 mg)	30 (4)	1/6/136	Yes (skin + mucosa)/refractory ITP	R (yes)
9	33	Chronic	4 (splenectomy)	Romiplostim (10 µg/kg)	39 (1)	1/1/6	Yes (skin)/in preparation for delivery	NR (yes)

CR, complete response; GI, gastrointestinal; NR, no response; R, response.

\*Includes mostly corticosteroids and/or IV immunoglobulin ± platelet transfusion.

†Second pregnancy occurred in same patient.

‡Weeks before pregnancy (patient already receiving ELT when unplanned pregnancy occurred).

§Sjögren syndrome-associated ITP.

||Systemic lupus erythematosus-associated ITP with positive lupus anticoagulant, immunoglobulin G anticardiolipin antibody, and anti-β<sub>2</sub>-glycoprotein 1.

**Table 1. (continued)**

Patient n	Patient age, y	ITP phase	N of prior treatment lines for ITP	Tpo-RA (maximal dose during pregnancy)	Gestation at Tpo-RA initiation, wk (treatment duration during pregnancy, wk)	Platelet count nadir during pregnancy/ platelet count before Tpo-RA/ platelet count at time of delivery, × 10 <sup>9</sup> /L	Bleeding manifestations/main reason for using Tpo-RA	Pattern of initial platelet response (concomitant ITP therapy, yes or no)*
10	24	Chronic	5 (splenectomy)	Romiplostim (10 µg/kg)	34 (6)	12/12/250	Yes (skin)/in preparation for delivery	CR (yes)
11	19	Chronic	4	Romiplostim (10 µg/kg)	32 (1)	2/15/7	Yes (skin, mucosa)/in preparation for delivery	NR (yes)
12	36	Newly diagnosed	2	Romiplostim (7.5 µg/kg)	37 (1)	5/10/40	Yes (skin + mucosa)/in preparation for delivery	CR (yes)
13	38	Chronic	3 (splenectomy)	Romiplostim (3 µg/kg)	36 (1)	5/19/120	Yes (skin + mucosa)/in preparation for delivery	CR (yes)
14	29	Newly diagnosed	2	Romiplostim (4 µg/kg)	37 (1)	17/20/21	Yes (skin)/in preparation for delivery	CR (yes)
15	34	Newly diagnosed secondary ITPII	7	Romiplostim (500 µg)	31 (3)	3/4/367	Yes (skin, active GI tract bleeding, hematuria)/severe refractory ITP	R (yes)
15†	37	Chronic secondary ITPII	7	Eltrombopag (50 mg)	36‡ (39)	44/55/249	No/chronic refractory secondary ITP	R (yes)

CR, complete response; GI, gastrointestinal; NR, no response; R, response.

\*Includes mostly corticosteroids and/or IV immunoglobulin ± platelet transfusion.

†Second pregnancy occurred in same patient.

‡Weeks before pregnancy (patient already receiving ELT when unplanned pregnancy occurred).

§§Ögren syndrome-associated ITP.

||Systemic lupus erythematosus-associated ITP with positive lupus anticoagulant, immunoglobulin G anticardiolipin antibody, and anti-β2-glycoprotein 1.

**Table 2. Neonatal complications**

Case n (mother n)	Gestation at Tpo-RA initiation, wk (treatment duration during pregnancy, wk)	Type of event in neonate	Outcome (intervention)	Causal relationship with Tpo-RA exposure in mother (yes or no)/ comment
1 (1)	36 (4)	Neonatal thrombocytopenia; platelet count, $6 \times 10^9/L$	Recovery (IV immunoglobulin + platelet transfusion)	No
2 (1)	36 (2)	Neonatal thrombocytopenia; platelet count, $8 \times 10^9/L$	Recovery (no treatment)	No
3* (1)	36 (2)	Neonatal thrombocytopenia; platelet count, $34 \times 10^9/L$	Recovery (IV immunoglobulin + platelet transfusion)	No
4 (4)	33 (7)	Neonatal thrombocytopenia; platelet count, $20 \times 10^9/L$	Recovery (IV immunoglobulin)	No
5 (11)	32 (1)	Neonatal thrombocytopenia; platelet count, $4 \times 10^9/L$	Recovery (IV immunoglobulin + platelet transfusion)	No
6 (13)	36 (1)	Neonatal thrombocytopenia; platelet count, $20 \times 10^9/L$	Recovery (IV immunoglobulin)	
7 (9)	36 (1)	Trisomy 8 (undetected preterm)	Died on day 7	No/only 1-wk exposure to romiplostim in preparation for delivery
8 (14)	37 (1)	Pulmonary artery stenosis diagnosed during pregnancy	Favorable outcome after surgery at 2 wk of life	No/only 1-wk exposure to eltrombopag in preparation for delivery
9 (8)	30 (4)	Grade 1 intraventricular hemorrhage at birth (cranial ultrasound)	Favorable outcome without any sequela (no intervention)	Very unlikely, prematurity, favorable outcome
10 (8)	30 (4)	Neonatal thrombocytosis; platelet count, $555 \times 10^9/L$	Persistent thrombocytosis for few wk (breastfeeding on eltrombopag)	Possible

\*Twin of case 2.

woman, age  $\geq 18$  years, diagnosis of either primary or secondary ITP,<sup>4,5</sup> treatment with eltrombopag or romiplostim for at least 1 week for ITP during pregnancy, and at least 1 month of follow-up after Tpo-RA initiation. Women who became pregnant while on Tpo-RAs could be included as long as sufficient data on pregnancy outcome were available. All available clinical and biological data from the mothers and neonates were collected and analyzed. Treatment response was defined as complete response or response, according to standard definitions.<sup>4,5</sup> Data are presented as mean  $\pm$  standard deviation (SD) or median (interquartile range) for continuous variables, depending on distribution. Categorical variables are presented as number (percentage).

The study was performed in accordance with the ethical standards of the Helsinki Declaration and approved by our local institutional review board.

## Results and discussion

In total, data from 15 women, 17 pregnancies, and 18 neonates (1 twin pregnancy) were analyzed (Table 1). Ten of 15 patients had preexisting chronic ITP (mean duration,  $9.3 \pm 3.2$  years), including 2 cases of secondary ITP; 1 patient had persistent ITP at pregnancy onset; and ITP was diagnosed during pregnancy in 4 cases (Table 1). Median number of treatment lines before the

use of Tpo-RAs was 3.0 (range, 2-7 lines), including splenectomy for 5 patients. Patients were exposed during pregnancy to either eltrombopag ( $n = 8$ ; mean maximal daily dose, 60 mg [SD,  $\pm 24.4$  mg]; median dose, 50 mg [range, 25-100 mg]) or romiplostim ( $n = 7$ ; mean maximal weekly dose, 7.28  $\mu\text{g}/\text{kg}$  [SD,  $\pm 2.97$   $\mu\text{g}/\text{kg}$ ]; median dose, 7  $\mu\text{g}/\text{kg}$  [range, 3-10  $\mu\text{g}/\text{kg}$ ]). Patient 15, who had severe chronic refractory ITP, was successively treated with romiplostim during a first pregnancy<sup>13</sup> and was receiving eltrombopag when a second unexpected pregnancy occurred; eltrombopag was continued for 39 weeks until delivery and beyond, because she refused to interrupt the pregnancy. She gave birth at term to a healthy baby (weight, 2.7 kg). Median time of exposure to Tpo-RAs during pregnancy was 4.4 weeks (range, 1-39 weeks). At time of Tpo-RA initiation, ITP was symptomatic in 13 (76%) of 17 pregnancies, with mucosal bleeding in 6 cases and life-threatening gastrointestinal bleeding in 1 case (Table 1). Tpo-RAs were started beyond week 32 of gestation in preparation for delivery, because platelet count was  $\leq 20 \times 10^9/L$  in 10 (58%) of 17 pregnancies; in 4 cases, patients with chronic ITP were receiving Tpo-RAs when they became pregnant, and in 3 cases, Tpo-RAs were started early in the third trimester for symptomatic ITP not responding to standard therapy.

Two patients receiving Tpo-RAs reported mild headache, but no serious adverse events, especially no clinically symptomatic

thromboembolic events, were observed. No patient was receiving thromboprophylaxis, including patient 15, who was triple positive for lupus anticoagulant, anticardiolipin, and anti- $\beta_2$ -glycoprotein 1 antibodies.

No fetal loss occurred; delivery occurred preterm (between 34 and 38 weeks of gestation) in 5 (29%) of 17 pregnancies. Mode of delivery was vaginal in 11 cases and caesarean section in 6 (all for obstetrical reasons). Platelet counts were available at birth for 14 of 18 neonates, and neonatal thrombocytopenia was found in 6, 3 of whom were neonates, including twins from 1 mother. One case of neonatal thrombocytosis (platelet count at  $558 \times 10^9/L$ ) was observed. Birth data were available for all neonates; 2 severe neonatal complications (trisomy 8,  $n = 1$ ; pulmonary artery stenosis,  $n = 1$ ) leading to 1 death and 1 grade 1 intraventricular hemorrhage occurred. None of these events were directly attributable to Tpo-RA exposure in the mother (Table 2).

Median platelet count at time of Tpo-RA initiation was  $10 \times 10^9/L$  (range,  $1 \times 10^9/L$  to  $20 \times 10^9/L$ ), and an initial response was achieved in 10 (77%; complete response,  $n = 6$ ; response,  $n = 4$ ), whereas no response was seen in 3 patients with longstanding chronic ITP, including 2 splenectomized patients. Seven of 10 responders received concomitant ITP medication, mostly corticosteroids. Median platelet count at delivery was  $94 \times 10^9/L$  (range,  $6 \times 10^9/L$  to  $250 \times 10^9/L$ ), with a count  $< 50 \times 10^9/L$  in only 5 (29%) of 17 and no case of severe maternal bleeding.

Although reassuring case reports on the use of romiplostim or eltrombopag for ITP during pregnancy have been published,<sup>13-21</sup> Tpo-RAs are not recommended in pregnancy, and experience is very limited.<sup>2,12</sup> On the basis of the 15 patients reported here, it is reassuring that no severe adverse events and no thrombosis occurred. However, placental infarction has been previously reported,<sup>16</sup> and Tpo-RAs during pregnancy should be used with particular caution in patients with lupus and/or antiphospholipid antibody syndrome-associated ITP.<sup>22</sup> Interestingly, exposure to Tpo-RAs at the end of pregnancy does not seem to have a major impact on fetal thrombopoiesis, because thrombocytosis was observed in only 1 neonate, in keeping with recombinant Tpo.<sup>10</sup> Conversely, severe neonatal thrombocytopenia occurred in 6 neonates, but 3 were from the same mother, who had previously undergone splenectomy.<sup>3,23</sup> No correlation was found between platelet response or treatment duration in the mother and platelet count in the neonate (data not shown).

Neonatal serious complications, including 1 death, occurred in 2 of 18 neonates, neither of which could be related to Tpo-RA treatment. Efficacy of Tpo-RAs administered either alone or often in combination with another ITP therapy was in keeping with expectations, taking into account that patients had experienced failure of a median of 3 previous ITP treatment lines, including splenectomy for 5 patients. There were no obvious

differences between eltrombopag and romiplostim. Limitations of this study are its uncontrolled retrospective design; the relatively small number of cases, with possible recruitment bias; and potential underestimation of placental thrombosis.

In conclusion, transient use of eltrombopag or romiplostim for pregnant women with ITP who are refractory to at least corticosteroids and IV immunoglobulin and need treatment because of bleeding manifestations, because of profound thrombocytopenia, and/or in preparation for delivery seems safe for the mother and the fetus/neonate. However, a prospective international registry is needed to monitor whether, with more widespread use of these treatments in the future, any maternal or neonatal complications may emerge, especially in the neonatal and postneonatal periods.

## Authorship

Contribution: M.M. coordinated the study, included patients, and wrote the manuscript; M.R., T.J.G.-L., S.A., S.C., W.G., T.H.A.T., M.E., L.T., and J.B.B. included patients and read the manuscript; B.G. participated in the coordination of the study; and M.M., B.G., and J.B.B. participated in the writing of the manuscript.

Conflict-of-interest disclosure: M.M. has received honoraria for consultancy from Amgen, Novartis, Alexion Pharmaceuticals, Rigel, and Sanofi/Bioerativ. W.G. has received lecture fees and honoraria for participation in advisory board meetings from Novartis and Amgen. T.H.A.T. has participated in advisory boards for Alexion Pharmaceuticals, Inc., Novartis, and Ablynx. L.T. has received lecture fees and honoraria for participation in advisory board meetings from Novartis. T.J.G.-L. has received advisory board honoraria from Novartis, Amgen, and Momenta and speaker's honoraria and research support from Novartis and Amgen. M.E. has received honoraria for participation in advisory boards from Amgen, Grifols, GlaxoSmithKline, and Novartis. S.C. has participated in advisory boards for Novartis and Amgen. J.B.B. has served on advisory boards and/or consulted for Amgen, Novartis, Dova, Rigel, UCB, Argenx, Momenta, Regeneron, RallyBio, and CSL-Behring. B.G. has served as an expert for Amgen, Novartis, Grifols, LFB, and Roche and received a research grant from Amgen. The remaining authors declare no competing financial interests.

ORCID profiles: S.A., 0000-0001-6863-5748; W.G., 0000-0003-2225-6165.

Correspondence: Marc Michel, Hôpital Henri Mondor, 51 av. du Mal de Lattre de Tassigny, Créteil, 94010, France; e-mail: marc.michel2@aphp.fr.

## Footnotes

Submitted 10 June 2020; accepted 4 August 2020; prepublished online on *Blood* First Edition 19 August 2020. DOI 10.1182/blood.2020007594.

The first pregnancy of patient 15 has been reported previously in Alkaabi et al.<sup>13</sup>

There is a *Blood* Commentary on this article in this issue.

The publication costs of this article were defrayed in part by page charge payment. Therefore, and solely to indicate this fact, this article is hereby marked "advertisement" in accordance with 18 USC section 1734.

## REFERENCES

1. McCrae KR. Thrombocytopenia in pregnancy. *Hematology Am Soc Hematol Educ Program*. 2010;2010:397-402.
2. Gernsheimer T, James AH, Stasi R. How I treat thrombocytopenia in pregnancy. *Blood*. 2013; 121(1):38-47.
3. Loustau V, Debouverie O, Canoui-Poitrine F, et al. Effect of pregnancy on the course of immune thrombocytopenia: a retrospective study of 118 pregnancies in 82 women. *Br J Haematol*. 2014;166(6):929-935.
4. Rodeghiero F, Stasi R, Gernsheimer T, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113(11):2386-2393.
5. Provan D, Arnold DM, Bussell JB, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Adv*. 2019; 3(22):3780-3817.

6. Sun D, Shehata N, Ye XY, et al. Corticosteroids compared with intravenous immunoglobulin for the treatment of immune thrombocytopenia in pregnancy. *Blood*. 2016;128(10):1329-1335.
7. Chakravarty EF, Murray ER, Kelman A, Farmer P. Pregnancy outcomes after maternal exposure to rituximab. *Blood*. 2011;117(5):1499-1506.
8. Bleau N, Czuzoj-Shulman N, Spence AR, Abenheim HA. Safety of splenectomy during pregnancy. *J Matern Fetal Neonatal Med*. 2017;30(14):1671-1675.
9. Mahey R, Kaur SD, Chumber S, Kriplani A, Bhatla N. Splenectomy during pregnancy: treatment of refractory immune thrombocytopenic purpura. *BMJ Case Rep*. 2013;2013:bcr2013201778.
10. Kong Z, Qin P, Xiao S, et al. A novel recombinant human thrombopoietin therapy for the management of immune thrombocytopenia in pregnancy. *Blood*. 2017;130(9):1097-1103.
11. Liu Y, Wang R, Han P, et al. Effect of recombinant human thrombopoietin on immune thrombocytopenia in pregnancy in a murine model. *Int Immunopharmacol*. 2019;67:287-293.
12. Ghanima W, Cooper N, Rodeghiero F, Godeau B, Bussel JB. Thrombopoietin receptor agonists: ten years later. *Haematologica*. 2019;104(6):1112-1123.
13. Alkaabi JK, Alkindi S, Riyami NA, Zia F, Balla LM, Balla SM. Successful treatment of severe thrombocytopenia with romiplostim in a pregnant patient with systemic lupus erythematosus. *Lupus*. 2012;21(14):1571-1574.
14. Purushothaman J, Puthumana KJ, Kumar A, Innah SJ, Gilvaz S. A case of refractory immune thrombocytopenia in pregnancy managed with eltrombopag. *Asian J Transfus Sci*. 2016;10(2):155-158.
15. Decroocq J, Marcellin L, Le Ray C, Willems L. Rescue therapy with romiplostim for refractory primary immune thrombocytopenia during pregnancy. *Obstet Gynecol*. 2014;124(2 Pt 2 suppl 1):481-483.
16. Patil AS, Dotters-Katz SK, Metjian AD, James AH, Swamy GK. Use of a thrombopoietin mimetic for chronic immune thrombocytopenic purpura in pregnancy. *Obstet Gynecol*. 2013;122(2 Pt 2):483-485.
17. Suzuki N, Hiraga J, Hariyama Y, et al. A low birth weight infant with no malformations delivered by a primary immune thrombocytopenia patient treated with eltrombopag. *Int J Hematol*. 2018;108(1):109-111.
18. Rodrigues-Nunes RM, Rubio Lacambra L, Palomo Bravo A, Langenhorst Baniandres L. Use of romiplostim during pregnancy as a rescue therapy in primary immune thrombocytopenia: literature review and case description. *Platelets*. 2020;31(3):403-406.
19. Ferreira IJMCF, Sousa F, Vasco EM, et al. Severe immune thrombocytopenia in pregnancy treated with eltrombopag - a case report. *J Gynecol Obstet Hum Reprod*. 2018;47(8):405-408.
20. Chon AH, Chan R, Lee RH, Kwong K, Wertheimer FB, Weitz IC. Multidrug therapy for refractory immune thrombocytopenia in pregnancy. *Obstet Gynecol*. 2020;135(3):723-727.
21. Favier R, De Carne C, Elefant E, Lapsuaneu R, Gkalea V, Rigouzzo A. Eltrombopag to treat thrombocytopenia during last month of pregnancy in a woman with MYH9-related disease: a case report. *A A Pract*. 2018;10(1):10-12.
22. Guitton Z, Terriou L, Lega JC, et al. Risk of thrombosis with anti-phospholipid syndrome in systemic lupus erythematosus treated with thrombopoietin-receptor agonists. *Rheumatology (Oxford)*. 2018;57(8):1432-1438.
23. Webert KE, Mittal R, Sigouin C, Heddle NM, Kelton JG. A retrospective 11-year analysis of obstetric patients with idiopathic thrombocytopenic purpura. *Blood*. 2003;102(13):4306-4311.