# THE OCCURANCE OF THROMBOSIS IN ITP PATIENTS ON TPO-RAS IN ROYAL UNITED HOSPITAL, BATH, UK

B. Bentil-Tumi[1], S. Punnialingam[2], S. Wexler[3], D. Gange[4]
b.bentiltumi@nhs.net , sinthiya.punnialingam2@nhs.net, sarahwexler@nhs.net, danielle.gagne@nhs.net

## BACKGROUND

Immune Thrombocytopenic Purpura (ITP) is a condition known to increase the risk of bleeding and paradoxically, the incidence of thromboembolic events. Consequently, management challenges include reducing the bleeding and prothrombotic risk.

Patients with refractory or chronic ITP have previously failed either steroids or rituximab. Therefore, their second line involves thrombopoietin receptor agonists (TPO-RA). TPO-RAs initiate platelet proliferation as noted in Figure 1 (van Dijk et al., 2021). These proliferative properties have created uncertainty on the risks TPO-RAs can have on thromboembolic events.

While Moulis et al., (2018), suggested a higher incidence in venous clots for cohorts on TPO-RAs, with a 2- 6% overall incidence of both venous and arterial, Tjepkema et al., (2022) and Dong et al., (2023) displayed no significant precedence in thrombosis.

## OBJECTIVES

This review assesses all patients receiving TPO-RAs in Royal United Hospital, Bath, UK. The aim is to evaluate the incidence of thromboembolic events among these patients.

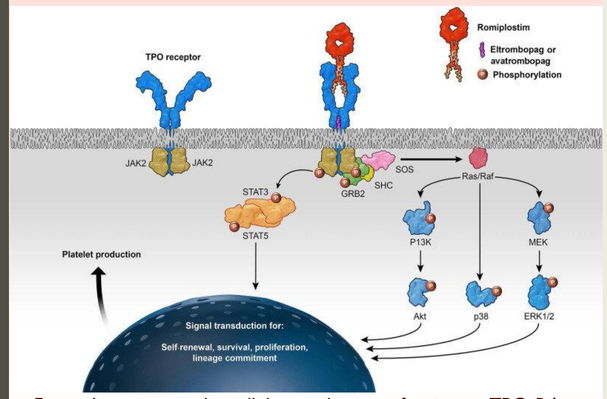


Figure 1 represents the cellular mechanism of action on TPO-RAs (Bussel et al., 2021).

## METHODS

A comprehensive study of all patients on TPO-RAs at Bath Hospital between November 2014 and May 2024 was undertaken. Pharmacy records, clinical letters, electronic information including were extracted using Citrix Millenium and Integrated Care Records (ICR). Study included 47 patients and 67 encounters. Each TPO-RA use was counted as a different encounter, accounting for patients who had multiple TPO-RAs.

Table 1: The exclusion and inclusion criteria of the patient's selection.

| Inclusion criteria | Exclusion criteria |
|---|---|
| Diagnosis of Immune Thrombocytopenia confirmed by Haematologist | Age less than 18 |
| Patient who have previously failed first line therapy (steroids, MMF, rituximab) | Pregnancy |
| TPO-RAs used: Eltrombopag, Avatrombopag and Romiplostim | Platelet level over 50 when starting TPO-RA |

## RESULTS

In a study of four thrombus incidents, three were arterial and one venous, as illustrated in Figure 2. No correlation with the platelet levels was established, although all four exhibited some degree of increased platelet counts without any adjustments in the TPO-RAs. Romiplostim, which constituted 42.5% of the cohort, did not result in thromboembolic events. In contrast, Avatrombopag (13% ) was associated with two clot occurrences, while Eltrombopag (56.7% ) was also linked to two thrombotic events.

The underlying causes of three incidents could not be attributed solely to TPO-RAs; as infections, co-morbidities and concurrent steroid use were also influential . Interestingly, two of the three arterial clots defied expectations, given that they occurred in scenarios typically associated with thrombus . Notably, the one incident that had a clear correlation with eltrombopag was also an arterial clot.

Table 2:A table showing the profiles of the 4 patients who had clots in the study.

| Age , Gender | 53, M | 54, F | 46, F | 77, M |
|---|---|---|---|---|
| TPORA | Avatrombopag | Avatrombopag | Eltrombopag | Eltrombopag |
| Plt count before | 36 | 5 | 245 | 87 |
| Plt count at time of clot | 64 | 330 | 229 | 121 |
| Steroid | No | Yes | No | Yes |
| Venous or arterial? | Arterial | Arterial | Venous | Arterial |
| Further clots | No | Yes | No | Yes |
| Co-morbidities | Prediabetic, high BMI | High BMI | PAH, Antiphospholipid syndrome (APS) | Prev CVA with carotid artery stenosis |
| Suggested reason for clot | Abscess just before clot | Avatrombopag+ steroid started a week before clot | Co-morbidities | Eltrombopag |

**A chart showing the variation in platelet counts in the 4 inidividuals with clot incidences. Red represent arterial (3) and green, venous clot.**


## CONCLUSIONS

In this study, the incidence of clots was 6.15%, lower than the rates reported in current literature for licensed TPO-RAs. Remarkably, our findings revealed a higher incidence of arterial clots, and a lower occurrence of venous clots compared to published data. Our results indicate anti-phospholipid syndrome (APS) is a contributing factor. However, further research is needed to evaluate the role of APS and cardiovascular co-morbidities in the overall burden of thrombosis associated with TPO-RAs.

## REFERENCES


- van Dijk, W.E.M. *et al.* (2021) 'Hemostatic changes by thrombopoietin-receptor agonists in immune thrombocytopenia patients', *Blood Reviews*, 47, p. 100774. doi:10.1016/j.blre.2020.100774.
- Tjepkema, M., Amini, S. and Schipperus, M. (2022) 'Risk of thrombosis with thrombopoietin receptor agonists for ITP patients: A systematic review and meta-analysis', *Critical Reviews in Oncology/Hematology*, 171, p. 103581. doi:10.1016/j.critrevonc.2022.103581.
- Dong, Y. *et al.* (2023) 'Risk of thrombotic events in immune thrombocytopenia patients treated with THROMBOPOIETIC agents: A systematic review and meta-analysis', *Thrombosis Journal*, 21(1). doi:10.1186/s12959-023-00509-z.
- Moulis, G. *et al.* (2018) 'Risk factors of thrombosis in adults with primary immune thrombocytopenia. A French nationwide cohort study', *Blood*, 132(Supplement 1), pp. 3745–3745. doi:10.1182/blood-2018-99-112506.
- Bussel, J.B. *et al.* (2021) 'A review of Romiplostim Mechanism of action and clinical applicability', *Drug Design, Development and Therapy*, Volume 15, pp. 2243–2268. doi:10.2147/dddt.s299591.