

## Comment on "Drug-Induced Thrombocytopenia: An Updated Systematic Review"

We have read with great interest the letter published by Dr Swisher and colleagues<sup>[1]</sup> on drug-induced thrombocytopenia. The same group have previously published similar letters to update their initial review article published in 1998.<sup>[2]</sup> However, their previous publications on drug-induced thrombocytopenia (DIT) and thrombotic thrombocytopenic purpura have failed to recognize that fluoroquinolones, a class of commonly used antimicrobials in clinical practice, can cause DIT. We recently described a patient in whom ciprofloxacin-dependent platelet-reactive IgG antibodies against glycoprotein (GP) IIb/IIIa were found.<sup>[3]</sup> A literature search identified a total of 82 cases of thrombocytopenia related to fluoroquinolone exposure. In our case report we isolated ciprofloxacin-dependent antibodies by flow cytometry and subsequently demonstrated their specificity for GPIIa/IIIb by monoclonal antibody immobilization of platelet antibodies. This suggests immune-mediated, drug-dependent destruction. Fluoroquinolones have a structural similarity with quinine, a well documented cause of DIT,<sup>[4]</sup> and we postulate that fluoroquinolones induce antibodies that bind reversibly to platelet glycoproteins such as IIb/IIIa, allowing complement-mediated opsonization and destruction of platelets in a similar manner to quinine. Fluoroquinolones have also been described to cause haemolytic anaemia, pancytopenia and hemolytic-uremic syndrome and thrombotic thrombocytopenic purpura (HUS-TTP), the exact mechanism still unknown.

All detailed reviews on DIT published in the last 20 years<sup>[1,2,5]</sup> have overlooked fluoroquinolones as a cause and we feel it necessary to highlight this potentially fatal complication as fluoroquinolones are still widely used in clinical practice.

In almost 50% of all cases of DIT associated with fluoroquinolone use that have been published, patients have developed some form of symptomatic bleeding secondary to their low platelet count, with ecchymoses and purpura being the most common. The incidence is not that low and ciprofloxacin-induced thrombocytopenia has been estimated by some to be around 50–500 per million patients<sup>[6-8]</sup> in comparison with only 25 per million patients for fluoroquinine-induced thrombocytopenia,<sup>[9]</sup> a not insignificant finding.

Therefore, for the completeness of this review, we conclude that fluoroquinolone-induced thrombocytopenia is an uncommon but often unrecognized entity that when undiagnosed can cause bleeding, bone marrow suppression, HUS-TTP and even death.

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### Acknowledgements

No sources of funding were used to assist in the preparation of this letter. The authors have no conflicts of interest that are directly relevant to the content of this letter.

### References

1. Swisher KK, Li X, Vesely SK, et al. Drug-induced thrombocytopenia: an updated systematic review. *Drug Saf* 2009; 32 (1): 85-6
2. George JN, Raskob GE, Shah SR, et al. Drug-induced thrombocytopenia: a systematic review of published case reports. *Ann Intern Med* 1998; 129 (11 Pt 1): 886-90
3. Cheah C, De Keulenaer B, Leary M. Fluoroquinolone induced immune thrombocytopenia: a case report and review. *IMJ*. In press
4. Burgess JJK, Lopez JJA, Berndt MMC, et al. Quinine-dependent antibodies bind a restricted set of epitopes on the glycoprotein Ib-IX complex: characterization of the epitopes. *Blood* 1998; 92 (7): 2366-73
5. Aster RH, Bougie DW. Drug-induced immune thrombocytopenia. *N Engl J Med* 2007; 357 (6): 580-7
6. Davis RR, Markham AA, Balfour JJA. Ciprofloxacin: an updated review of its pharmacology, therapeutic efficacy and tolerability. *Drugs* 1996; 51 (6): 1019-74
7. Schacht PP, Arcieri GG, Hullmann RR. Safety of oral ciprofloxacin: an update based on clinical trial results. *Am J Med* 1989; 87 (5A): 98-102S
8. Jick SSS, Jick HH, Dean AAD. A follow-up safety study of ciprofloxacin users. *Pharmacotherapy* 1993; 13 (5): 461-4
9. Kaufman DDW, Kelly JJP, Johannes CCB, et al. Acute thrombocytopenic purpura in relation to the use of drugs. *Blood* 1993; 82 (9): 2714-8