

# Drug-Induced Thrombocytopenia An Updated Systematic Review, 2008

Using methodology initially established 10 years ago,<sup>[1]</sup> we have systematically reviewed all English-language reports on drug-induced thrombocytopenia and published updates every 2 years, most recently through 20 October 2006.<sup>[2-5]</sup> Our goal for these updates is to provide an accessible resource for standardized analysis of all published reports of drug-induced thrombocytopenia, describing the level of evidence for a causal role of the drug in each report.<sup>[6]</sup> This letter presents the results of our current literature search.

Using our previously described MEDLINE literature search strategy on 6 October 2008<sup>[1]</sup> we retrieved 56 articles. Using our evaluation criteria,<sup>[1]</sup> each article was reviewed independently by three of the authors to assess the level of evidence for a causal role of the drug for the thrombocytopenia; disagreements were resolved by consensus. Thirteen articles were excluded from further analysis because they were review articles or experimental studies with no primary patient data, or they reported heparin-associated thrombocytopenia, a topic excluded from our reviews.<sup>[1]</sup> Ten articles reported group data; in five articles a causal role for the drug could not be assessed because the study met one or more of our six exclusion criteria.<sup>[1]</sup> The remaining five articles reported data on four drugs: two had level 1 (definite) evidence, two had level 2 (probable) evidence and one had level 3 (possible) evidence. Thirty-three articles reported data on 46 individual patients who had thrombocytopenia associated with 27 different drugs. Twenty-two patient reports were excluded because they met one or more of our six exclusion criteria.<sup>[1]</sup> The remaining 24 patient reports described thrombocytopenia associated with 16 drugs; one reported level 1 data, 15 reported level 2 data, five reported level 3 data and three reported level 4 data. From both the reports of group data and the individual

**Table 1.** Drugs causing thrombocytopenia that had not been documented in previous reviews<sup>[1-5]</sup> as causing thrombocytopenia

Drug <sup>a</sup>	Reports (no.)	
	level 1 evidence	level 2 evidence
<b>Individual patient data</b>		
Trastuzumab	0	2
<b>Group data</b>		
Orbifiban	1	0
Linezolid	0	2

a These three drugs were not reported in our previous systematic reviews<sup>[1-5]</sup> as having evidence supporting a causal relation to thrombocytopenia, defined by at least one report with level 1 (definite) evidence or two reports with level 2 (probable) evidence. For individual patient data, definite evidence (level 1) required re-exposure to the drug causing a repeated episode of thrombocytopenia. Probable evidence requires all criteria except re-exposure to the drug; therefore, two reports with probable evidence are accepted as establishing a causal relation to thrombocytopenia. For group patient data, definite evidence (level 1) was defined as a significantly increased rate of thrombocytopenia associated with the drug as compared with a control group in a randomized clinical trial; probable evidence (level 2) was defined as a significantly increased rate of thrombocytopenia associated with the drug compared with a control group in a non-randomized study.

patient data, three drugs were identified as having evidence supporting a causal relation to thrombocytopenia, defined by at least one report with level 1 (definite) evidence or two reports with level 2 (probable) evidence, that had not been documented in our previous systematic literature reviews (table I). The complete database of all articles from this literature search together with our previous literature search, including the definitions of levels of evidence, exclusion criteria, complete citations, and demographics and clinical outcomes of the individual patients, is available at <http://www.ouhsc.edu/platelets>.<sup>[6]</sup>

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