

Supplement Table S2. Criteria for assessing reports of drug-induced TMA and levels of evidence for determining an association of the suspected drug and TMA

A. Reports of individual patients with suspected immune-mediated drug-induced TMA

Criteria for evaluation of reports	
1. Clinical or pathologic diagnostic criteria for TMA were present	
2. Clinically apparent causes of clinical/pathologic criteria other than TMA, and causes of TMA other than drug toxicity were excluded and the suspected drug was the only drug taken or other drugs were continued or restarted and if the suspected drug had been taken daily, systemic symptoms occurred within 21 days of starting the drug, or if the suspected drug had been taken intermittently, systemic symptoms began suddenly, within 24 hours of drug exposure	
3. Previous or subsequent drug exposure associated with systemic symptoms or TMA	
4. Drug-dependent antibodies were documented, reactive with platelets or other cells	
5. The suspected drug had been taken daily for more than one year, or subsequent drug exposure did not result in systemic symptoms or TMA, or TMA persisted or recurred without subsequent drug exposure (kidney injury may persist)	
Levels of evidence for an association of the suspected drug with TMA	
Evidence level	Criteria met
Level 1 Definite	1 and 2 plus 3 or 4
Level 2 Probable	1 and 2
Level 3 Possible	1
Level 4 Unlikely	1 and 5
Level 5 Excluded from Review (reason[s] for exclusion [check all])	
1. No individual patient data reported	
2. Insufficient patient data to assess report	
3. Diagnostic criteria for TMA (Criterion 1) not met	
4. Inappropriate drug dose or non-therapeutic use (e.g., suicide)	
5. Drug etiology neither proposed nor discussed	
6. Combination drug etiology proposed	

B. Reports of individual patients with suspected drug-induced TMA caused by acute or chronic dose-dependent toxicity

Criteria for evaluation of reports	
1. Clinical or pathologic diagnostic criteria for TMA were present	
2. Clinically apparent causes of clinical/pathologic criteria other than TMA and causes of TMA other than drug toxicity were excluded and the suspected drug was the only drug taken or other drugs were continued or restarted	
3. TMA resolved or improved when suspected drug stopped or dose reduced (kidney injury may persist)	
4. TMA worsened after suspected drug discontinued or TMA recurred without subsequent drug exposure	
Levels of evidence for an association of the suspected drug with TMA	
Evidence level	Criteria met
Level 1 Definite	1, 2 and 3
Level 2 Probable	1 and 2
Level 3 Possible	1
Level 4 Unlikely	1 and 4
Level 5 Excluded from Review (reason[s] for exclusion [check all])	
1. No individual patient data reported	
2. Insufficient patient data to assess report	
3. Diagnostic criteria for TMA (Criterion 1) not met	
4. Inappropriate drug dose or non-therapeutic use (e.g., suicide)	
5. Drug etiology neither proposed nor discussed	
6. Combination drug etiology proposed	

C. Reports of group data for patients with suspected drug-induced TMA, either immune-mediated or dose-dependent toxicity

Criteria for evaluation of reports: study design	
1. Clinical or pathologic diagnostic criteria for TMA were present	
2. Randomized controlled trial with significantly greater frequency of TMA in patients treated with the suspected drug compared to patients not treated with the suspected drug	
3. Non-randomized controlled trial with significantly greater frequency of TMA in patients treated with the suspected drug compared to patients not treated with the suspected drug	
4. Case series without controls	
5. There was no significant difference in the frequency of TMA in patients treated with the suspected drug compared to patients not treated with the suspected drug	
Levels of evidence for an association of the suspected drug with TMA	
Evidence level	Criteria met
Level 1 Definite	1 and 2
Level 2 Probable	1 and 3
Level 3 Possible	1 and 4
Level 4 Unlikely	1 and 5
Level 5 Excluded	Criteria for exclusion
1. No relevant data reported	
2. Insufficient data to assess report	
3. Diagnostic criteria for TMA (Criterion 1) not met	
4. Drug etiology neither proposed nor discussed	
5. Combination drug etiology proposed	