HETEROGENEITY OF TERMINOLOGY AND CLINICAL DEFINITIONS IN ADULT IDIOPATHIC THROMBOCYTOPENIC PURPURA : A CRITICAL APPRAISAL FROM A SYSTEMATIC REVIEW OF THE LITERATURE

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Supplementary appendix

Table 1.

Definition of ITP, based on platelet count(§) (x 10^9/L) (10 papers)			**Grade of severity, based on platelet count** (x 10^9/L) (22 papers)		
	N	%	N	N	N
< 150 (ref: 5, 15, 17, 18, 20)	5	50			
≤ 120 (ref:13)	1	10			
≤ 100 (ref:14, 16, 19, 21)	4	40			
			Severe		
≤ 100 (ref: 36)			1		
≤ 50 (ref: 30)			1		
≤ 30 (ref: 5, 14, 27-29, 38, 39, 48)			8		
≤ 20 (ref:17, 22, 26, 35, 40)			5		
≤ 10 (ref: 9, 23, 31-33)			5		
≤ 5 (ref: 37)			1	Moderate	
≥ 30 ≤ 100 (ref:14, 22)				2	
≥ 30 (ref:26)				1	
					Mild
≥ 30 (ref:26)					1
≥ 80 (ref:32)					1
40-90 (ref:19)					1

§ variable time intervals from the first platelet count to definitive diagnosis: 2 consecutive platelet assays; from 2 to 6 months; ITP acute ≤ 2 months, sub-acute between 2 and 6 months. (ref: 1,15,17, 18, 20-25)

Table 2.

FIRST LINE THERAPY: PLATELET LEVEL (x 10^9/L) **TO START TREATMENT** (23 papers)	N	%
≤ 10 (ref: 23)	1	4
≤ 20 (ref: 7, 11, 18, 35, 44)	5	22
≤ 30 (ref: 1, 5, 6, 17, 19, 26, 27, 30, 32, 34, 41, 43, 45, 46)	14	60
≤ 50 (ref: 13, 15, 42)	3	14

Table 3.

FIRST LINE THERAPY: PLATELET COUNT (x 10^9/L) **TO DEFINE RESPONSE**

	CR (18 papers)		PR (18 papers)		NR (19 papers)		"Response" (9 papers)
	N	%	N	%	N	%	N
≥ 150 (ref: 17, 18, 20, 34, 35, 50-54)	10	56					
≥ 120 x 10^9/L (ref: 13)	1	5					
≥ 100 x 10^9/L (ref: 14, 36, 41, 47, 49)	5	28					
to "normal values" (ref: 24, 27)	2	11					
< 100 (ref: 47)			1	6			
≥ 50 ≤ 100 (ref: 36, 49, 50)			3	15			
≥ 50 ≤ 120 (ref: 13)			1	6			
≥ 50 ≤ 150 (ref: 34, 35, 51-54)			6	33			
≥ 50 ≤ 150 or doubling initial values (ref: 18, 20)			2	10			
≥ 50 ≤ 150 x 10^9/L or increase ≥ 30 (ref: 17)			1	6			
≥ 50 <"normal limit" (ref: 24)			1	6			
≥ 30 < "normal limit" (ref: 27)			1	6			
≥ 30 ≤ 50 (ref: 41)			1	6			
≥ 30 ≤ 100 (ref: 14)			1	6			
≤ 50 (ref: 13, 18, 20, 24, 34, 36, 50, 51, 53, 54)					10	53	
≤ 30 (ref: 14, 27, 47)					3	17	
≤ 30 or no doubling initial values or relapse during tapering (ref: 56)					1	5	
≤ 20 (ref: 35)					1	5	
≤ 30 o ≤ 50 after 10 days (re: 44)					1	5	
≤ 20 within 2 weeks or ≤ 50 within 4 weeks (ref: 49)					1	5	
≤ 50 o ≤ 30 to initial values (ref: 17)					1	5	
Worsening score (ref: 11)					1	5	
≥ 20 (ref: 30)							1
≥ 20-30 (ref: 41)							1
≥ 30 (ref: 7)							1
≥ 50 (ref: 50)							1
≥ 30 or doubling initial values (ref: 56)							1
≥ 50 or doubling initial value (ref: 15)							1
≥ 50 within 10 days or ≥ 30 and stop bleeding (ref: 44)							1
≥ 80 x 10^9/L or doubling initial value (ref: 42)							1
improve bleeding score (ref: 11)							1

CR: complete response
PR: partial response
NR: no response

Other definitions not included:
minimal response: between 20 and 50 x 10^9/L or doubling basis value[35]
incomplete response: 100-150 x 10^9/L[50]
good response: ≥ 50 x 10^9/L; poor response: ≤ 50 x 10^9/L[57]

Table 4.

FIRST LINE THERAPY					
Timing to assess response (13 papers)			**Time required to define a response as durable** (14 papers)		
	N	%			%
3-7 days (ref: 11, 35, 41, 42, 51)	5	38	3 weeks (ref: 11)	1	7
At 6 months (ref: 24, 44)	2	15	4 weeks (ref: 13, 20, 34, 54)	4	29
At 6-9 months (ref: 36)	1		2 months (ref: 14, 49)	2	14
At last control (ref: 47)	1		3 months (ref: 24, 27, 36)	3	21
At stop therapy (ref: 7)	1		6 months (ref: 41)	1	7
At 5 days (IVIg) or at 6 weeks (steroid) (ref: 56)	1		Persistent:12 months (ref: 35)	1	7
“Immediate” at 2 ws “Retarded “ at 6 ms (re: 53)	1		Sustained: 6 months (ref: 13, 44)	2	15
“Transient” at 4 ws “Defined” at 6 ws (ref: 54)	1				

Table 5.

DEFINITION OF CHRONIC ITP: PLATELET THRESHOLD (x 10^9/L) **AND DURATION FROM INITIAL THERAPY**					
Platelet threshold (11 papers)			**Duration** (25 papers)		
	N	%		N	%
≤ 50 (ref: 7, 15, 25, 47, 58)	5	45	≥ 3 months (ref: 9, 51, 58, 63)	4	16
≤ 100 (ref: 45, 60)	2		≥ 6 months (ref: 1, 13, 15, 17, 22-25, 42, 45, 47, 54, 57, 59, 60, 62, 64-66)	19	76
≤ 150 (ref: 17, 51)	2		"many" months (ref: 32)	1	
≤ "normal value" (ref: 59, 61)	2		"Years" (not specified) (ref: 29)	1	

Table 6.

Minimal platelet count (x 10^9/L) **required to perform splenectomy safely** (7 papers)	N
≥ 30 (ref: 5)	1
≥ 50 (ref: 1, 23)	2
≥80 (ref: 48)	1
≥ 100 (ref: 68)	1
"Sufficient" (ref : 6*, 50)	2

* If platelet count < 20 x 10^9/L, treatment with IVIg[6]

Table 7.

INDICATION TO SPLENECTOMY (15 papers)		
Main indication	Clinical conditions	N
4-6 weeks after initial treatment (ref: 23, 26)	Refractory to steroids	2
6 weeks after initial treatment if severe form, after 3 months if moderate (ref: 6,14, 34)	Refractory/relapsing to steroids	3
3 months after initial treatment (ref:65)	Chronic	1
6 months after initial treatment (ref: 40)	Chronic	1
3-6 months after initial treatment (ref: 1, 7)	Chronic	2
"Many" months after initial treatment (ref: 69)	Chronic	1
"When necessary" (ref: 47)	Chronic	1
After 4 weeks if <50 x 10^9/L; "Postpone" after 6-8 weeks if < "normal value" o relapse during tapering (ref: 31)	Chronic	1
Within 14 days "Postpone" after 4 weeks if <30 x 10^9/L (ref: 27,43,50)	Refractory to steroids/IVIg	3

Table 8.

SPLENECTOMY: PLATELET COUNT (x 10^9/L) **TO DEFINE RESPONSE**						
	CR (24 papers)		PR (20 papers)		NR (16 papers)	
	N	%	N	%	N	%
≥ 150 (ref: 8, 17, 18, 20, 21, 34, 51, 52, 54, 55, 67, 68, 70)	13	54				
≥ 100 (ref: 12, 14, 16, 47, 56, 72)	6	25				
≥ 100 - 150 (ref: 23)	1	4				
To "normal values" (ref: 24, 26, 46)	3	13				
≥ 50 x 10^9/L (ref : 71)	1	4				
≥30 ≤ 100 (ref: 14, 56, 72)			3	15		
≥ 100 ≤ 150 (ref: 68)			1	5		
≥ 50 ≤ 100 (ref: 16, 61)			2	10		
≤ 100 (ref: 47)			1	5		
≥ 50 ≤ 150 (ref: 8, 21, 24, 34, 51, 52, 54, 55, 70)			9	45		
≥ 50 ≤ 150 or doubling initial value (ref: 18, 20)			2	10		
≥ 50 ≤ 150 or increase ≥ 30 (ref: 17)			1	5		
≥ 30 to "normal value" (ref: 69)			1	5		
≤ 50 (ref: 8, 16, 18, 20, 21, 24, 34, 51, 54, 55, 70)					11	70
≤ 30 (re: 14, 17, 56, 69)					5	30

CR: complete response
PR: partial response
NR: no response

Other definitions:**:**
"response**"** is a count ≥100 x 10^9/L [22]
"good**"** response is ≥ 50 x 10^9/L; "poor**"** response is ≤ 50 x 10^9/L [57]

Table 9.

SPLENECTOMY: TIMING FOR THE ASSESSMENT OF THE RESPONSE					
Time to assess response (11 papers)			**Time required to define a response as durable** (13 papers)		
	N	%		N	%
At 3 days/at last control (ref: 68)	1	9	1 month (8, 20, 34, 54, 55)	5	38.
At 3-7 days (ref: 51)	1	9	2 months (14, 69)	2	15
At 30 days (ref: 8, 55)	2	18	3 months (24, 26, 46)	3	23
At 1 months (ref: 56)	1	9	12 months (57)	1	7
At 3 months (ref: 22)	1	9	During follow-up (56)	1	7
At 6 months (ref: 24)	1	9	Stable: 10 years (72)	1	7
At last control (ref: 47)	1	9			
During and after therapy (ref: 69)	1	9			
Any time after surgery (ref: 54)	1	9			
5-60 days (ref 67)	1	9			

Table 10.

PLATELET COUNT (x 10^9/L) **USED IN THE DEFINITION OF REFRACTORY ITP** (7 papers)		
	N	%
≤ 20 (ref: 7, 57, 65)	3	43
≤ 30 (ref: 62, 69)	2	29
≤ 50 (ref: 22)	1	
≤ 100 (ref: 12)	1	

Table 11.

SECOND LINE THERAPY: PLATELET COUNT (x 10^9/L) **TO START TREATMENT** (24 papers)		
Platelet count	N	%
≤ 10 (ref: 26)	1	
≤ 20 (ref: 1, 9, 39, 65, 66, 75, 77)	7	29
≤ 30 (ref: 6, 17, 29, 31, 32, 45, 48, 58, 62, 74, 76)	11	45
≤ 35 (ref: 22)	1	
≤ 50 (ref: 64)	1	
≤ 50 in two separate plt counts (ref: 63)	1	
≤ 60 (ref: 38)	1	
≤ 90 (ref: 78)	1	

Table 12.

SECOND LINE THERAPY: CRITERIA TO DEFINE RESPONSE (PLATELET COUNT x 10^9/L)							
	CR (31 papers)		PR (27 papers)		MR (4 papers)	NR (25 papers)	
	N	%	N	%	N	N	%
≥ 180 (ref: 83)	1						
≥ 150 (ref: 9, 17-20, 38, 58, 63, 65, 74, 81, 82)	12	39					
≥ 120-200 (ref: 80)	1						
≥ 110 (ref: 62)	1						
≥ 100 (ref: 25, 37, 45, 64, 66, 73, 75)	7	23					
≥ 100 or doubling initial value (ref: 59)	1						
≥ 100 – 150 (ref: 60)	1						
≥ "normal values" (ref: 24, 29, 39, 48, 69, 77, 79)	7	23					
≥ 80 ≤ 120 (ref:29, 48)			2				
≥ 50 ≤ 100 (ref: 25, 37, 60, 75, 82)			5	16			
≥ 50 ≤ 150 (ref: 19, 58, 74, 81)			4	13			
≥ 50 ≤ 180 (ref: 83)			1				
≥ 50 ≤ 150 or doubling initial value (ref: 18, 20, 38, 63)			4	13			
≥ 50 ≤ 150 or increase ≥ 30 (ref: 17)			1				
≥ 50 ≤ 100 or doubling initial value (ref: 59, 64)			2				
≥ 50 to "normal values" (ref: 24, 79)			2				
≥ 50 (ref: 66, 73, 80)			3				
≥ 40 (ref: 62)			1				
≥ 30 ≤ 100 (ref: 45)			1				
≥ 30 ≤ 150 (ref: 77)			1				
≥ 30 to "normal values" (ref: 69)			1				
≥10 x (ref: 9)			1				
“No clinical response” (ref: 39)			1				
>30 <50 (ref: 82)					1		
> 30 (ref: 77)					1		
< 50 (ref: 73, 75)					2		
≤10 (ref: 9)						1	
≤ 50 (ref: 18-20, 24, 25 37, 53, 58, 64, 83)						10	40
≤ 40 (ref: 29, 48, 62)						3	
≤ 30 (ref: 69, 77, 82)						3	
≤ 20 (ref: 65)						1	
no increase (ref: 73)						1	
no increase or ≤ 50 (ref: 60, 75, 80)						3	
≤ 50 or increase ≤ 30 (ref: 17)						1	
≤ 50 or increase ≤ 20 (ref: 59)						1	
Bleeding symptoms (ref: 38)						1	

Other definitions:
“Significant response” [38]: increase of platelet count ≥ 50 x 10^9/L or doubling initial value
“Response”: doubling the initial count, ≥ 20 ≤ 50 x 10^9/L [59]; ≥ 20 x 10^9/L without therapy[65]; ≥ 50 x 10^9/L or doubling initial value [38] ; “Transient” : ≥ 40 x 10^9/L in 2-4 weeks [62]; “Maintained”: platelet count stable during therapy [48] ; “Good “: ≥ 30 x 10^9/L and stable level[39] ;“Adequate”: ≥ 100 x 10^9/L [76] ; “Relapse” : < 50 or < 30 x10^9/L after initial response [54, 56]

Table 13.

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SECOND LINE THERAPY (TIME PARAMETERS)			
Time to assess response (11 papers)		**Time required to define a response as durable** (13 papers)	
	N		N
At 2 weeks (ref: 82)	1	Permanent (without therapy) (80)	1
At 1 month (ref: 62, 75)	2	6 weeks (ref: 63, 66)	2
At 12 weeks (ref: 59)	1	1 month (ref: 20, 77)	2
"Transient" at 2 months "Long lasting" 2 months (ref: 64)	1	2 months (ref: 58)	1
At 3 months (ref: 38, 48)	2	3 months (ref: 9, 24, 29, 65)	4
At 6 months (ref: 24, 60)	2	6 months (ref: 25, 45, 75)	3
At last control (ref: 79)	1		
"Temporary" while on therapy (ref: 80)	1		