

Is splenectomy an outdated treatment for ITP?

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Splenectomy is a long-standing procedure

- Splenectomy utilised for ‘idiopathic purpura’ since 1916¹
 - No rigorous testing of procedures at that time
- Dr Harrington first described pathology of disease in 1950²
- ‘First-line, gold standard procedure’ until the 1960s with the advent of corticosteroids³
 - Since then, many medical therapies have been introduced
- Splenectomy can be considered as ‘removal of a healthy organ’
 - Many educated patients often refuse splenectomy on this basis



Paul Kaznelson
Medical Student



Dr William J Harrington

Splenectomy is considered curative in those who respond

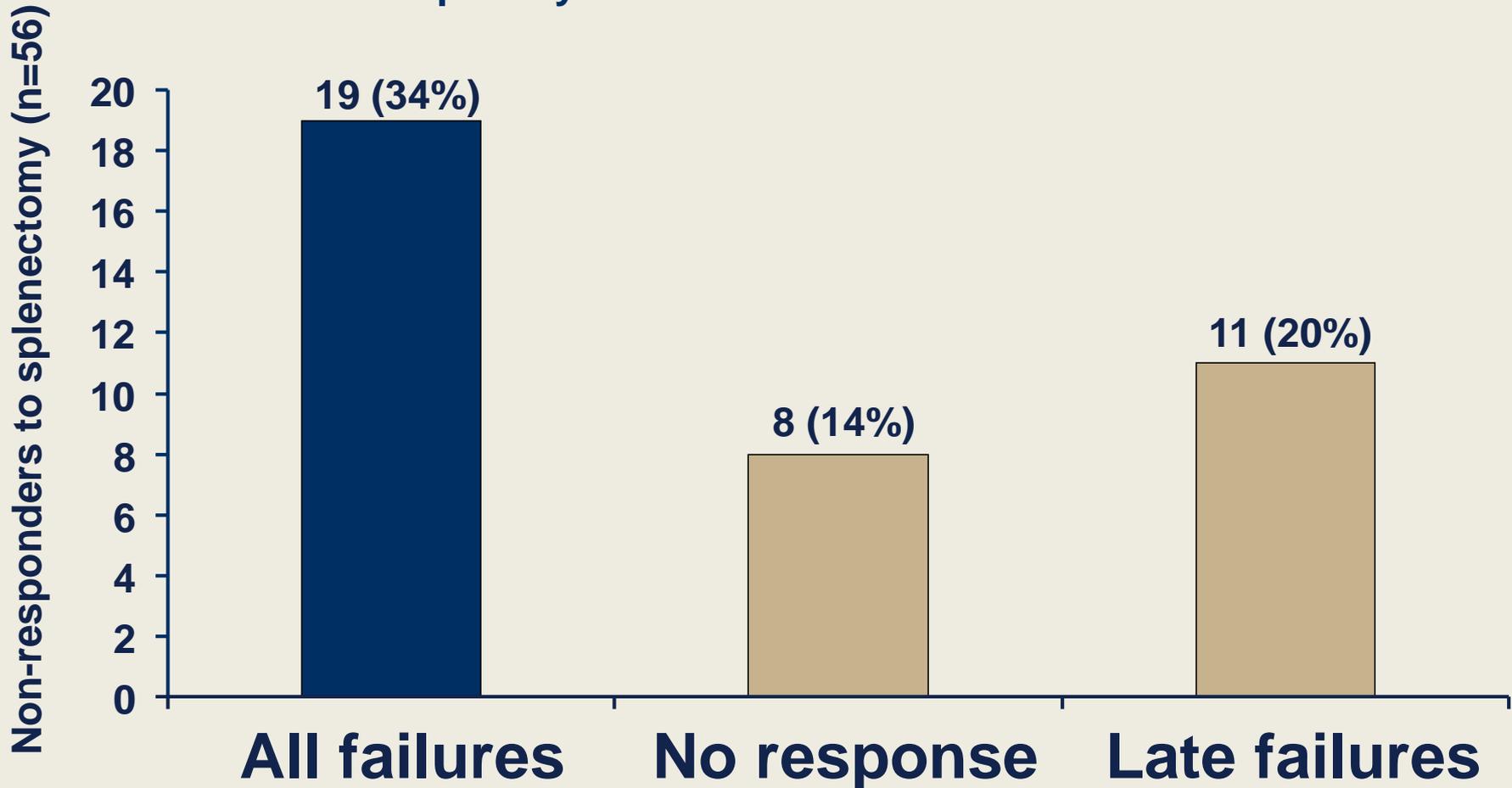
Systematic analysis of 135 splenectomy case series, 1966–2004¹

All adult case series	
No. of case series	47
No. of patients with complete response/ total no. of evaluable patients	1731/2623 (66%)
Adult case series with at least 5 years follow-up	
No. of case series	14
No. of patients with complete response/total no. of evaluable patients	456/707 (64%)

No other treatment has the overall success rate of splenectomy, with two-thirds of patients developing normal platelet counts and requiring no further therapy^{2,3}

Splenectomy is ineffective in one-third of patients with ITP

Median follow-up: 7.5 years

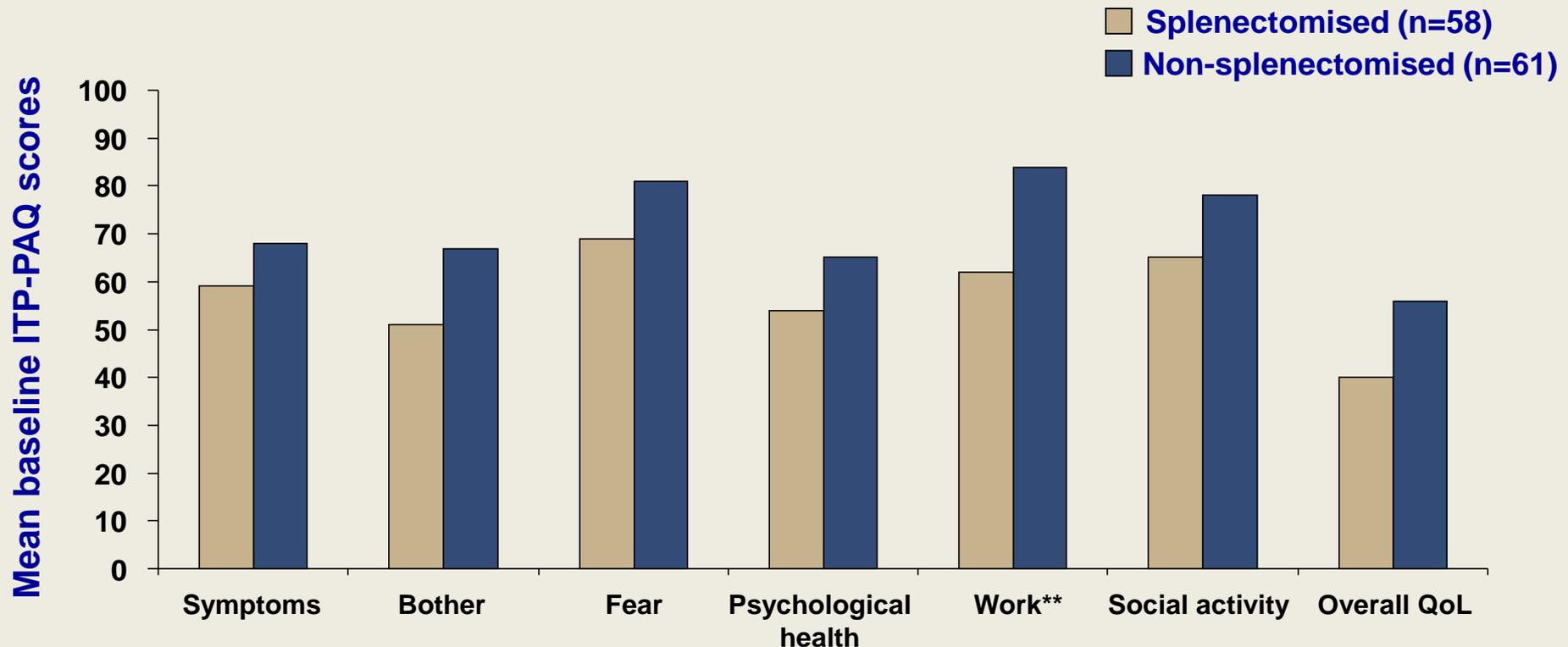


Mortality in refractory ITP

Author	Haemorrhage-related deaths		Deaths due to infection
Shatner et al, 1994	1/480–120	(0.2-0.8%)	2/480–120 (0.4-1.6%)
George et al, 1996	35/465	(5%)	NR
Cohen et al, 2000	49/1817	(2.6%)	NR
Vianelli et al, 2001	1/33	(3%)	0/33
Portielje et al, 2001	1/12	(8.3%)	1/12
McMillan et al, 2001	3/13	(23%)	2/13
Bourgeois et al, 2003	3/47	(6%)	NR
TOTAL	83/2507	(3.3%)	5/178 (2.8%)

Non-responders to splenectomy have worse QoL compared with non-splenectomised patients

Splenectomised patients with similar baseline platelet counts to non-splenectomised patients had significantly lower baseline ITP-PAQ scores for 7 of 10 ITP-PAQ scores*



All ITP-PAQ scales shown are statistically significant

**work: splenectomised, n=24, non-splenectomised, n=32

Long-term complications of splenectomy

- Long-term complications include:
 - Thrombosis: ITP and splenectomy both associated with thromboembolic risks^{1,2}
 - Overwhelming post-splenectomy infection (OPSI [sepsis])³ rare (~0.5 case per 100 person-years) but 50% mortality rate, unpredictable and lifelong risk *Staphylococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Capnocytophaga canimorsus*, and increased risk of severe malaria among travellers
 - Potential increase in atherosclerotic events⁴
 - Chronic thromboembolic hypotension⁵
 - Arterial complications⁶

1. Aledort LM et al. *Am.J Hematol* 2004;76:205-213; 2. McMillan R & Durette C.

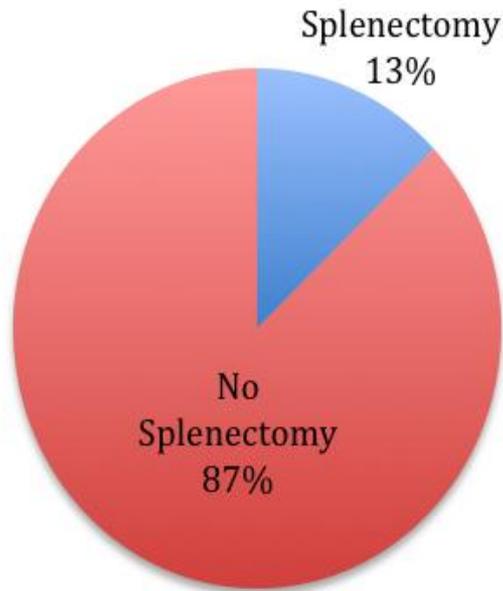
Blood 2004;104:956-960; 3. Portielje JE et al. *Blood* 97;2549-2554;

4. Schilling RF. *Lancet* 1997;350:1677-1678; 5. Jaïs X. *Thorax* 2005;60:1031-1034;

6. Robinette CD & Fraumeni JF Jr. *Lancet* 1977;2:127-129

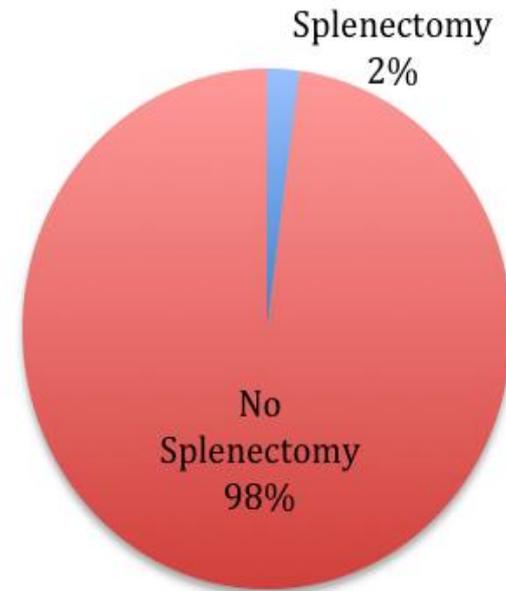
Splenectomy percentage pre and post Consensus document¹

Diagnosed Pre-guidelines



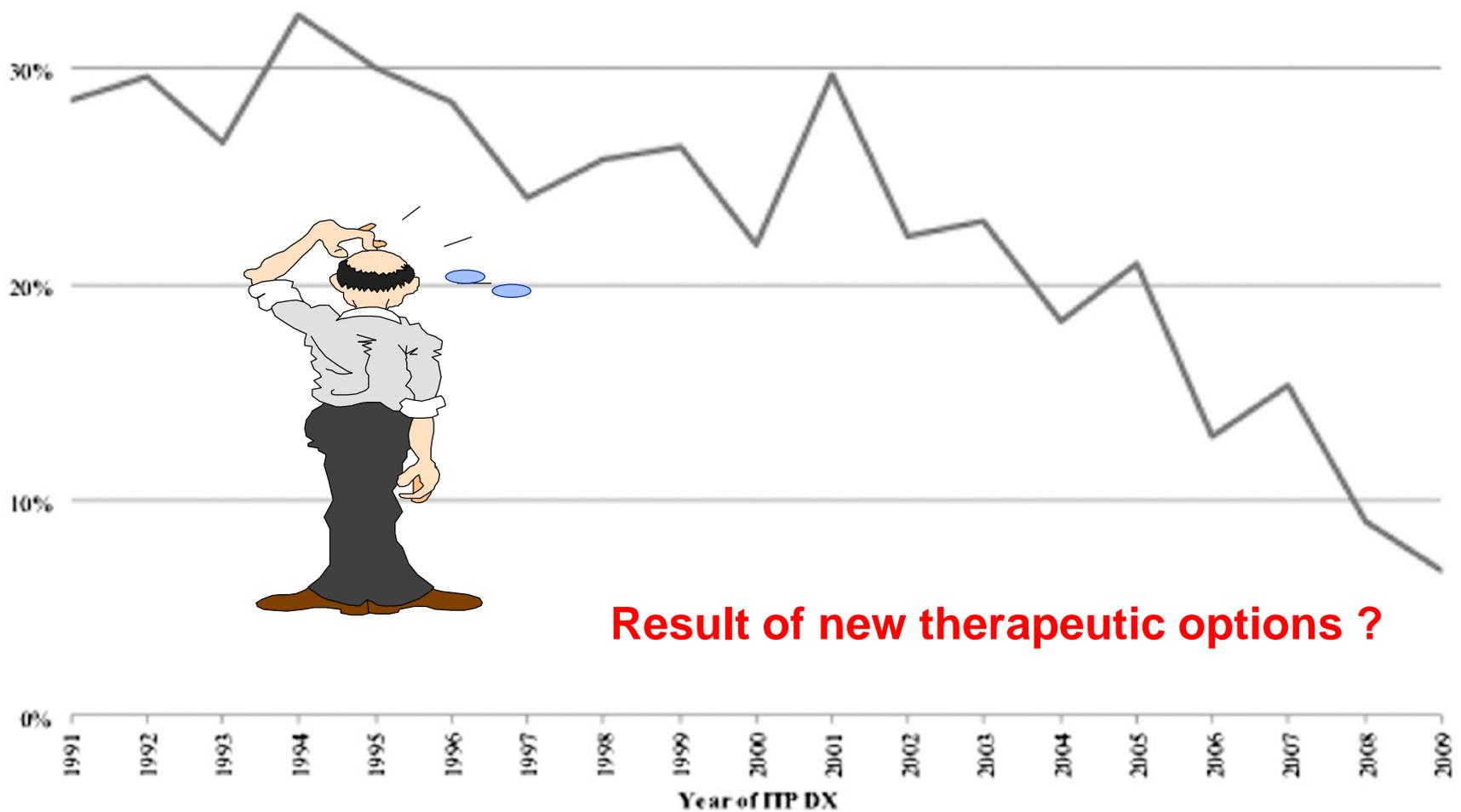
N = 168

Diagnosed Post-Guidelines



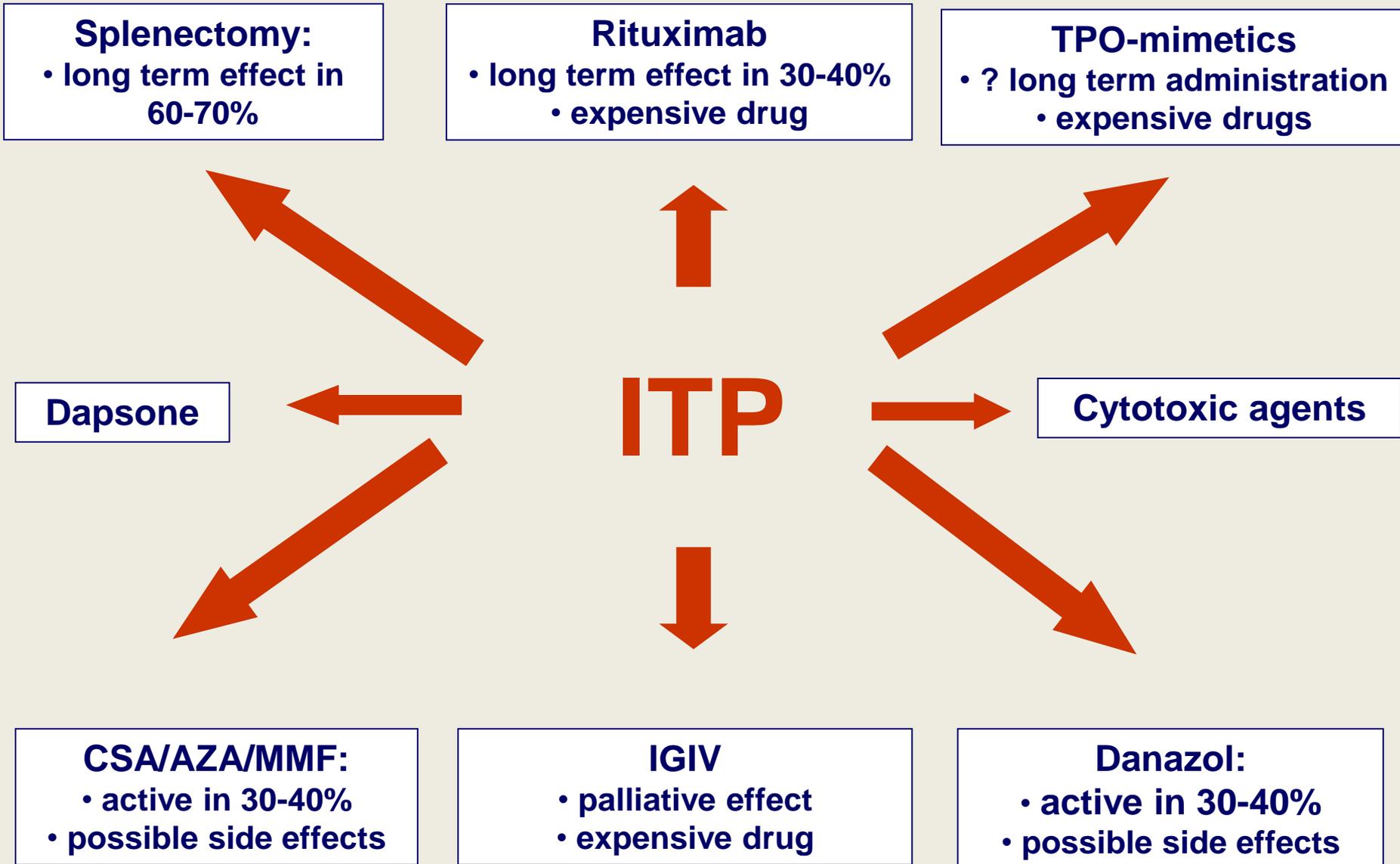
N = 857

Decline in the rate of splenectomy over time



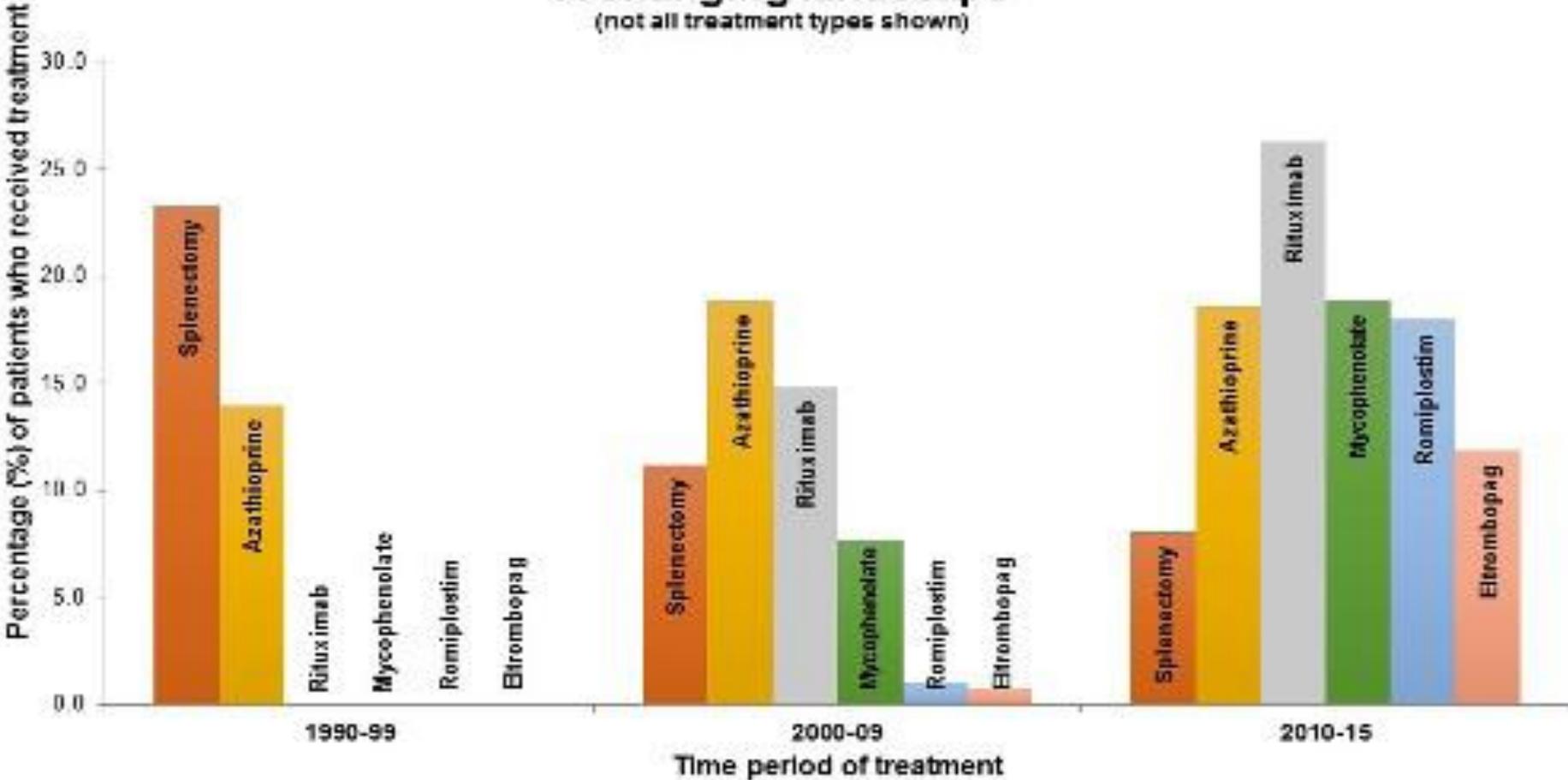
Result of new therapeutic options ?

Rescue therapies in ITP



Changing trends in treatment of cITP

Figure. Second line treatment options in ITP
A changing landscape
(not all treatment types shown)



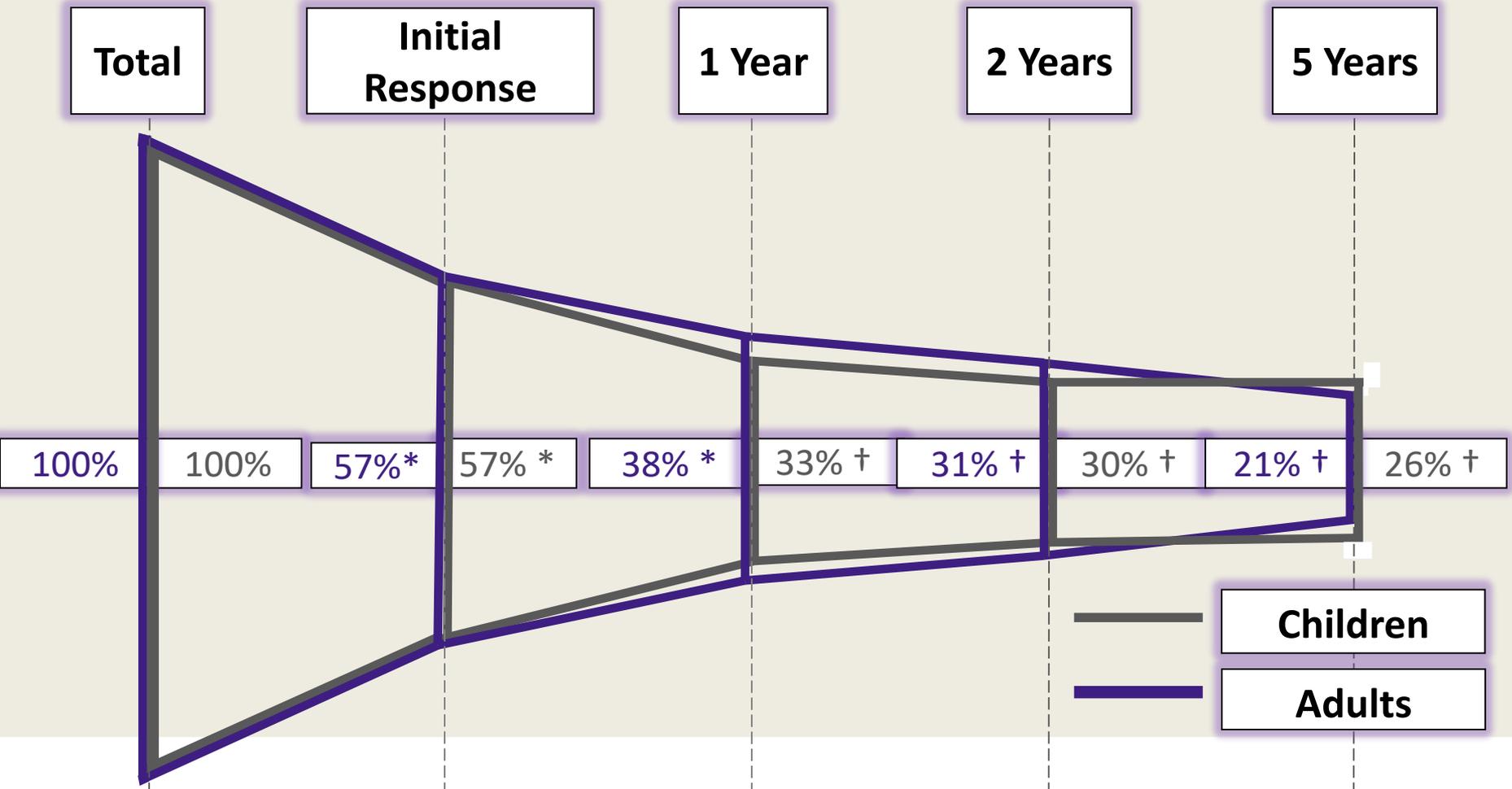
Newland – personal communication: UK ITP Registry

Is rituximab efficacious in ITP patients?

	Outcome	Contributing reports, (n)
Overall platelet count response (>50 x 10 ⁹ /L), % (95% CI)	62.5 (52.6–72.5)	19 (313)
Complete platelet count response (>150 x 10 ⁹ /L), % (95% CI)	46.3 (29.5–57.5)	13 (191)
Partial platelet count response (50–150 x 10 ⁹ /L), % (95% CI)	24.0 (15.2–32.7)	16 (284)
Time to response, median weeks	5.5	6 (123)
Response duration, median month	10.5	16 (252)
Follow-up, median month	9.5	10 (187)

Data from descriptive and comparative studies, no randomised controlled trials reported (insufficient risk:benefit profile)

Summary of response to rituximab in children and adults with ITP



* Derived from published reports

† Long-term follow up data acquired in this study

Patel VL, et al. *Blood* 2010; 116: Abstract 72; Patel VL, et al. *Blood* 2012; 119: 5989–95

Sustained remission after cessation of TPO-RAs: Retrospective data

TPO-RAs: Rates of sustained remission

Romiplostim:

11/46 (24%) (FU 33 months)¹

8/20 (40%) (FU 13.5 months)²

9/31 (29%) (FU ≥3 months)³

Eltrombopag:

26/80 (33%) (FU 9 months)⁴

1. Cervinek L. Int J Hematol. 2015;102(1):7-11; 2. Mathevas M et al. Br J Haematol. 2014;165(6):865-9; 3. Ghadaki B et al. Transfusion. 2013;53(11):2807-12; 4. Gonzales-Lopez TJ et al. Am J Hematol. 2015 ;90(3):E40-3.

Can we make the response to splenectomy more predictable¹⁻⁵

- ¹¹¹Indium-labelled autologous platelet scanning appears a sensitive indicator of response (pure or predominant splenic sequestration)
- If scanning reveals splenic platelet destruction, ~90% respond to splenectomy¹
 - Conversely, if platelet destruction was hepatic or diffuse: failure observed in ~90% of patients
 - Highly significant correlation has been noticed between splenectomy result and platelet sequestration site ($p < 0.01$)²
- **But low availability** is a true limit and the test is difficult to perform in patients with profound thrombocytopenia ($< 20 \times 10^9/L$)
- Responses to IVIg may be indicative of good splenectomy response⁶

1. Najean Y et al. *Br.J Haematol* 1997;97:547–550; 2. Sarpatwari A et al . *BJH* 2010; 151, 477–487

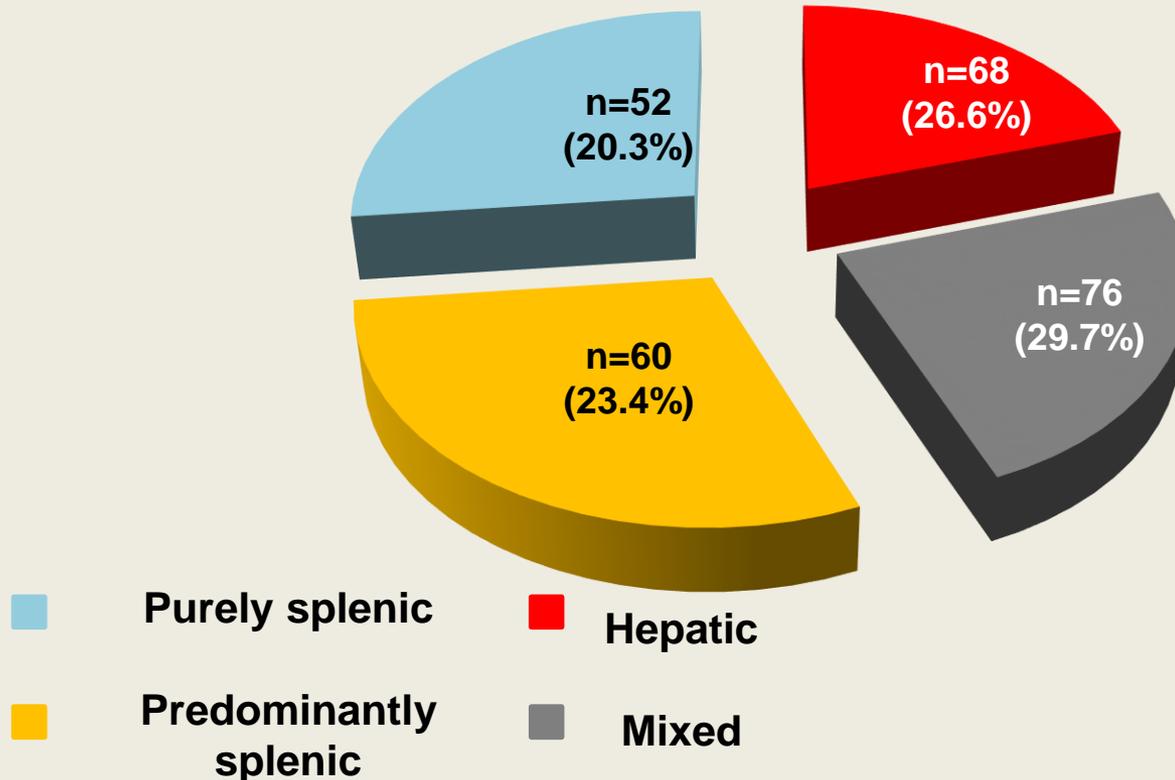
3. Todorovic-Tirnanic M et al. *Glas Srp Akad Nauka [Med]* 2005;48:119–135; 4. Pampin C et al. *J Pediatr.Hematol Oncol* 2000;22:256–258; 5. Roca M et al , *Am J Hematol.* 2011; 86: 909-913

6. Law C et al. *N.Engl.J Med* 1997;336:1494–1498

Pre-surgical indicators of splenectomy outcome

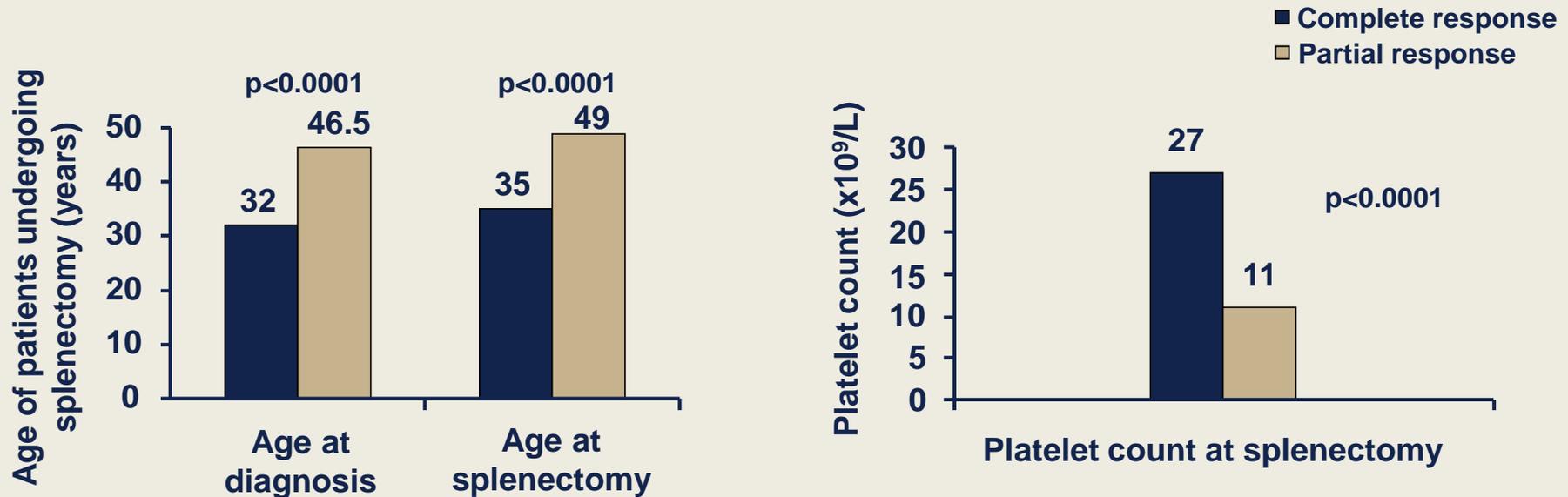
- Platelet sequestration pattern

Scanned primary ITP patients
(N=256)



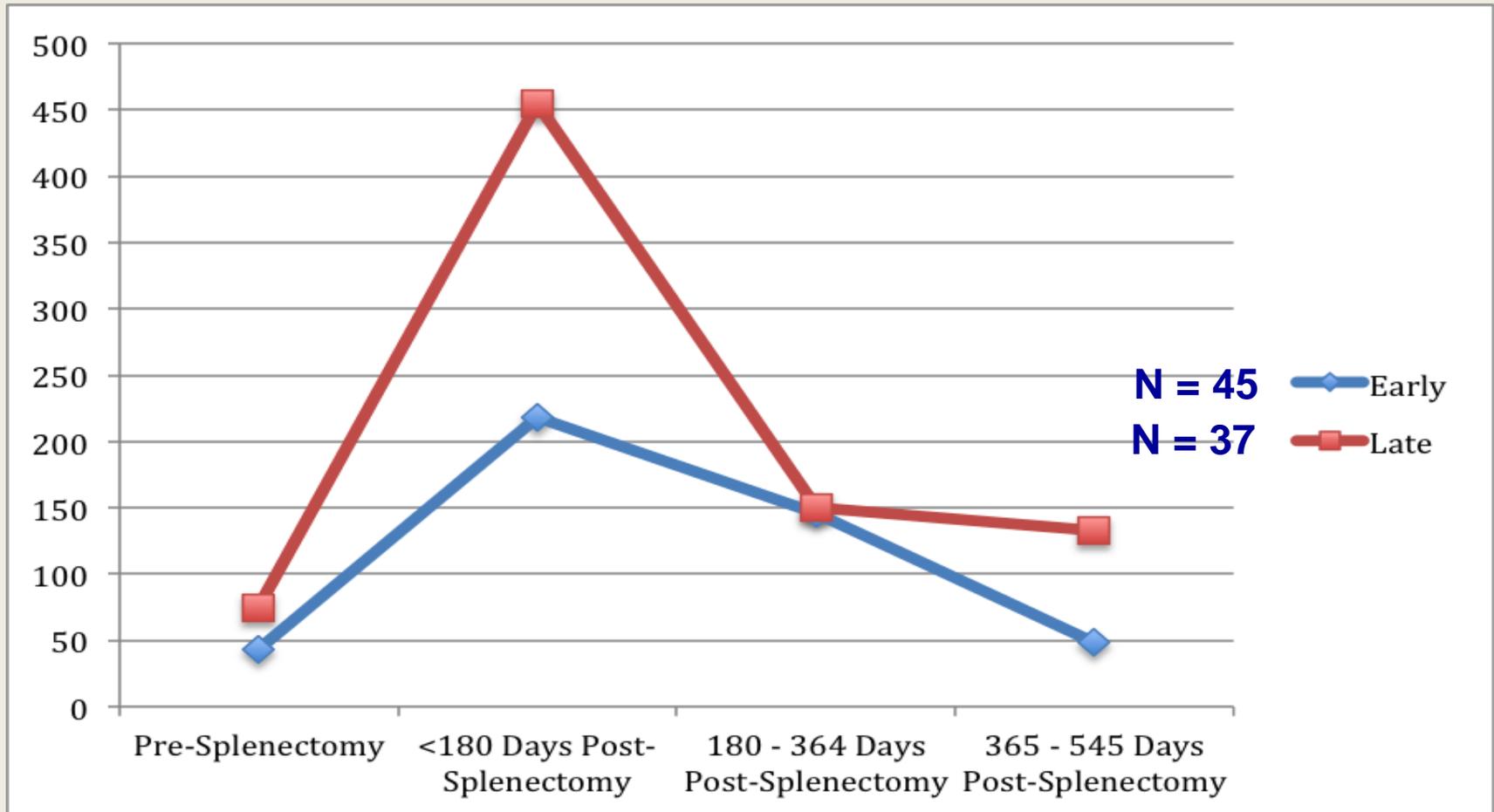
Treatments shown here may not be licensed in all countries for the indication as listed

Monitoring additional factors may increase the success rate of splenectomy



- Predictive of favourable response to splenectomy:
 - Younger age ($p < 0.0001$)
 - Higher platelet count at splenectomy ($p < 0.0001$)
 - Number of former therapies ($p < 0.01$)

Does it harm to delay splenectomy: Results depending on time of surgery



Mean time to surgery – 365 days

UK ITP Registry data

Splenectomy should be delayed in case of spontaneous remissions

- Spontaneous remissions of ~10% occur in adult patients with ITP even up to a year post-diagnosis¹
 - No data have proven preferable outcomes if splenectomy is performed early on in the disease course
- Sustained platelet responses have been reported with and without medical treatment
 - In one cohort of 152 patients, at 2 years after diagnosis, over two-thirds of patients had attained a platelet count $>30 \times 10^9/L$ after first-line therapy had ceased²

What is the place of Splenectomy?

Thrombopoietin

- Elderly
- Contra-indication to splenectomy
 - *Severe comorbidities*
- Liver sequestration on isotopic study
- Reluctant?

Splenectomy

- Young patients
- Splenic or predominantly splenic sequestration on isotopic study
- Delay until at least 1 year post-diagnosis

