ITP and Drug Induced Thrombocytopenias

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DISCLOSURES

Financial Relationships with Relevant Commercial Interests
• CVS/Caremark….Consulting on their formulary

Research Support
• Janssen
• Celegene
• Bristol Myer Squibb
• Medivation
• Incyte
ITP DEFINITION

- Thrombocytopenia with otherwise normal CBC & smear
- No congenital disorders
- No drugs, MDS or carcinomatosis
- No viral infection (including HIV)
- No SLE or other autoimmune disease
- No lymphoproliferative disease
**Age and sex distribution of ITP**  
Age and sex distribution of patients with idiopathic thrombocytopenic purpura (ITP) derived from reported case series. In children, the peak age is two to four years and girls and boys are equally affected. A female preponderance begins in adolescence and continues into adulthood. Among adults, 70 percent are women and 72 percent of women are less than 40 years of age. (Data from Beutler, E, Lichtman, MA, Coller, BS, et al, Williams Hematology, 5th ed, McGraw-Hill, New York, 1995.)
ITP BACKGROUND

IMPORTANT FINDINGS

• 1951 Harrington found anti-platelet factor in the plasma of ITP patients
• 1965 Shulman identified the anti-platelet factor in the 7S gamma region
• 1968 Karpatkin identified platelet associated Ig
• 1975 Rosse quantitated PAIg: His findings were reproduced in other labs
Effect of infusing 250 ml of plasma from patients with chronic idiopathic thrombocytopenic purpura (ITP) on platelet levels in normal recipients. On each of eight occasions, a significant decrease in platelet levels was observed. Average change is denoted by the heavy line. High initial platelet concentrations are due to use of an indirect counting technique.

* Harrington WJ, J Lab Clin Med 1951;38:1
OVERVIEW

- Autoantibodies to Platelet Membrane Antigens

- Chronic ITP is typically seen in adults
  - Acute ITP is typically seen in children

- Prevalence: 9.5 to 23.6/100,000 (UK health registry)
  - Lower in US

- Most common in females 20-45 years

- Possible trend: older patients female to male ratio 1

- Biggest risk - Intracranial bleed

- Spleen is normal size!
IMMUNE THROMBOCYTOPENIA

FINDINGS

- Thrombocytopenia
- Increased megakaryocytes
- Increased PAIgG
- Increased platelet destruction
- Decreased platelet production
FIGURE 117-8  Bleeding manifestations in relation to the platelet count in patients with ITP. Bleeding criteria are designated: 0, no bleeding; 1, minimal bleeding after trauma; 2, spontaneous but self-limited bleeding; 3, spontaneous bleeding requiring special attention, such as nasal packs for epistaxis; and 4, severe, life-threatening bleeding. (Reproduced from Lacy and Penner with permission.)
IMMUNE THROMBOCYTOPENIA
MAJOR SECTIONS

- PATHOPHYSIOLOGY
- MAKING THE DIAGNOSIS
- TREATMENT & TREATMENT GUIDELINES
ITP PATHOPHYSIOLOGY
PLATELET ASSOCIATED AB

- Increased in 90% of ITP patients
- Non-specific finding in other disorders
- Auto antibodies to Membrane glycoproteins:
  - GP IIb/IIIa
  - GP Ib/IX
ITP PATHOPHYSIOLOGY
IMPAIRED IMMUNE REGULATION

- Rapid platelet destruction
- Antibodies to platelet antigens
- Suppression of thrombopoiesis
- Antibodies to megakaryocyte Antigens
- Altered T Cell function
- Requires an intact RE system
HETEROGENEITY OF PLATELET TURNOVER
Indium Studies in the 1980s

SIEGEL, BLOOD 1982;50:191a
GROSSI, SCAN J HAEM 1983;31:206
SCHMIDT, SCAN J HAEM 1985;34:47
STOLL, BLOOD 1985;65:584
HEYNS, BLOOD 1986;67:86
BALLEM, JCI 1987;80:33
ITP Plasma & Monoclonal Ab inhibit Megakaryopoiesis in vitro

- Umbilical cord mononuclear cells, 10% plasma from ITP patients and normal individuals were incubated with TPO
- Megakaryopoiesis was diminished
- Conclusion: This is additional evidence that GP IIb/IIIa and GP Ib binds to megakaryocyte membranes and reduces platelet production

* Chang M et al, Blood 2003;102:887-895
T Cell Abnormalities

- Increase in T helper (Th) type 1 (proinflammatory) response seen in organ specific autoimmune disease
- Increase in Th1/Th2 ratio
- T cells stimulate Ab synthesis after exposure to GP IIb/IIIa

Semple et al., Blood 1996;87(10)4245-4254
Stasi et al., Blood 2007;110(8)2924-2930
Kuwana et al., J Clin Invest 1998;102(7)1393-1402
ITP PATHOPHYSIOLOGY

- Complement and immune complexes usually are not involved.
- The sensitizing event is obscure in adults.
- Platelet count is a dynamic equilibrium between production & destruction rates.
Causes of Secondary ITP

- Antiphospholipid syndrome
- Autoimmune thrombocytopenia (eg Evans syndrome)
- Common variable immune deficiency
- Drug administration side effect
- Infection with cytomegalovirus, *Helicobacter pylori*, hepatitis C, human immunodeficiency virus, varicella zoster
- Lymphoproliferative disorders
- Bone marrow transplantation side effect
- Vaccination side effect
- Systemic lupus erythematosus

*Blood 2011,117;16:4190-4207*
Estimated fraction of the various forms of secondary ITP based on clinical experience of the authors.

## ACUTE AND CHRONIC ITP

<table>
<thead>
<tr>
<th></th>
<th>ACUTE</th>
<th>CHRONIC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PEAK AGE</strong></td>
<td>2-6 yrs</td>
<td>20-40 yrs</td>
</tr>
<tr>
<td><strong>SEX PREDILECTION</strong></td>
<td>None</td>
<td>Women 3:1</td>
</tr>
<tr>
<td><strong>PRIOR INFECTION</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>ONSET</strong></td>
<td>Abrupt</td>
<td>Insidious</td>
</tr>
<tr>
<td><strong>PLATELET COUNT</strong></td>
<td>&lt;20,000</td>
<td>20-80,000</td>
</tr>
<tr>
<td><strong>DURATION</strong></td>
<td>6-8 weeks</td>
<td>Chronic</td>
</tr>
<tr>
<td><strong>SPONT REMISSION</strong></td>
<td>Usual</td>
<td>Unusual</td>
</tr>
</tbody>
</table>
Physiology of Thrombopoietin (TPO)

- A constant amount is produced by the liver

- Binds to TPO receptors of
  - megakaryocyte precursors
  - megakaryocytes
  - platelets
PHYSIOLOGY OF THROMBOPOIETIN (TPO)

- **Effect on megakaryocyte precursors**
  - Increases megakaryocyte production

- **Effect on megakaryocytes**
  - Causes more platelet production

- **TPO binds to platelets and is internalized**
  - Platelet numbers determine plasma TPO level
IMMUNE THROMBOCYTOPENIA

MAJOR SECTIONS

- PATHOPHYSIOLOGY
- MAKING THE DIAGNOSIS
- TREATMENT & TREATMENT GUIDELINES
International Working Group (IWG) Consensus Panel Recommendations

ITP DIAGNOSIS BASED ON:

- History and Physical Exam
- CBC and Peripheral Smear exam
- HIV, HCV Testing for patients at Risk
- Blood Group (Rh)
- Bone Marrow Bx not needed in any age group for pts with classic ITP

Blood 2011, 117:16:4190-4207
International Working Group (IWG) Consensus Panel Recommendations

Blood 2011, 117; 16: 4190-4207

NOT NECESSARY OR APPROPRIATE

• PAIgG
• Bleeding Time

George J N et al, Blood 1996; 88: 3-40
IMMUNE THROMBOCYTOPENIA
MAJOR SECTIONS

• PATHOPHYSIOLOGY

• MAKING THE DIAGNOSIS

• TREATMENT & TREATMENT GUIDELINES
TREATMENT GOALS IN AITP

- MAINTAIN HEMOSTASIS
- MINIMIZE TOXICITY
# RECOMMENDATIONS FOR SURGERY

<table>
<thead>
<tr>
<th>SURGERY</th>
<th>RECOMMENDED PLATELET COUNT</th>
</tr>
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<tbody>
<tr>
<td>Dental Prophylaxis (Cleaning/Scaling)</td>
<td>&gt;20-30,000</td>
</tr>
<tr>
<td>Simple Dental Extraction</td>
<td>&gt;30,000</td>
</tr>
<tr>
<td>Complex Dental Extraction</td>
<td>&gt;50,000</td>
</tr>
<tr>
<td>Minor Surgery</td>
<td>&gt;50,000</td>
</tr>
<tr>
<td>Major Surgery</td>
<td>&gt;80,000</td>
</tr>
<tr>
<td>Major Neurosurgery</td>
<td>&gt;100,000</td>
</tr>
</tbody>
</table>

_Cuker A and Cines DB Hematology 2010; p377-384_  
(adapted from Proven et al Blood 2010;115:168-186)
IMMUNE THROMBOCYTOPENIA EMERGENCY THERAPY

- Platelet transfusion
- IVIg
- Corticosteroids
PRACTICE GUIDELINES – ADULTS

- Tx given when platelet count less than 30,000 (2C)
- Longer steroid courses are better than shorter courses (2B)
- Use IVIg with steroids when rapid response is needed (2B)
- Either IVIg or anti-D used first line, if steroids are contraindicated (2C)
- If IVIg is used, initial infusion: 1 gm/kg as a one time dose...it may be repeated if necessary (2B)

Blood 2011,117;16:4190-4207
Treatment of ITP IWG –

Tx of unresponsive / relapsed patients after initial steroids

RECOMMENDATIONS:

- Splenectomy for patients who have failed corticosteroid therapy (1B)

- Thrombopoietin Receptor Agonists (TRA) for patients who relapse after splenectomy OR have a contraindication to splenectomy OR have failed at least one other therapy (1B)

Blood 2011,117;16:4190-4207
Treatment of ITP IWG –
Tx of unresponsive / relapsed patients after initial steroids

SUGGESTIONS:

- Thrombopoietin receptor agonists for patients at risk of bleeding who have failed one line of therapy such as corticosteroids or IVIg and who have not had splenectomy (2C)

- Rituximab for patients at risk of bleeding who have failed one line of therapy such as corticosteroids, IVIg, or splenectomy (2C)

Blood 2011,117;16:4190-4207
Treatment of ITP IWG –
Laparoscopic versus open splenectomy

RECOMMENDATIONS:
• For medically suitable patients, both laparoscopic and open splenectomy offer similar efficacy (1C)

Tx of ITP after splenectomy

RECOMMENDATIONS:
• No further treatment in asymptomatic patients with platelet counts greater than 30,000 (1C)

Blood 2011,117;16:4190-4207
Treatment of ITP IWG – Management of secondary ITP, HCV-associated

SUGGESTIONS:

- Antiviral therapy should be considered in the absence of contraindications (2C). However, platelet count should be closely monitored due to risk of worsening thrombocytopenia attributable to medications.

- If treatment for ITP is required, initial treatment should be IVIg (2C).

Blood 2011,117;16:4190-4207
Treatment of ITP IWG –
Management of secondary ITP, HCV-associated

RECOMMENDATIONS:

• Antiviral therapy should be considered before other treatment options unless the patient has clinically significant bleeding complications (1A)

• If treatment for ITP is required, initial treatment should consist of corticosteroids, IVIg, or anti-D (2C) and splenectomy in preference to other agents in symptomatic patients who fail corticosteroids, IVIg, or anti-D (2C)

Blood 2011,117;16:4190-4207
Treatment of ITP IWG –
Management of secondary ITP, *H pylori*-associated

**RECOMMENDATIONS:**
- Eradication therapy be administered in patients who are found to have *H pylori* infection (based on urea breath tests, stool antigen tests, or endoscopic biopsies) (1B)

**SUGGESTIONS:**
- Screening for *H pylori* be considered in patients with ITP in whom eradication therapy would be used if testing is positive (2C)
TREATMENT WITH STEROID IS INDICATED:

- When platelets < 20-30,000
- When platelets < 50,000 and there are significant mucous membrane bleeding Major Risk Factors (HT, PUD)

HOSPITALIZATION IS INDICATED:

- In patients with platelets < 20,000 & significant mucous membrane bleeding or in non-compliant patients

George J N et al, Blood 1996;88:3-4
IMMUNE THROMBOCYTOPENIA PRACTICE GUIDELINES - ADULTS

SPLENECTOMY IS NOT INDICATED:

- When plts > 50,000, Dx > 6 mos, no bleeding
- As initial therapy in patients without bleeding, minor purpura, or major bleeding risks

SPLENECTOMY IS INDICATED:

- Bleeding, plts< 30,000, after med Tx 4-6 wks

PRE-OP THERAPY BEFORE SPLENECTOMY:

- IVIg or steroids, if platelets < 50,000
- Transfusions only if platelets < 10,000
IMMUNE THROMBOCYTOPENIA
PREDNISONE THERAPY

- 1 mg/kg qD at diagnosis
- Improvement usually within 3 days
- Maximal improvement within 2 weeks
- Allows increased platelet production
- Reduces rate of platelet destruction
INITIAL THERAPY IN ITP
HIGH DOSE DEXAMETHASONE

125 pts with mean plt count = 12,000/m³
Initial Tx: Dexamethasone 40 mg qd X 4

RESULTS:
Good response in 106/125 (85%)
Mean platelet count 101, 400 (50-260 k) at 7 d
50% had a sustained response
Platelets < 90,000 on day 10 = high relapse
risk, most within 3 months
Well tolerated.....Splenectomy or other tx = 36%

Cheng Y et al, NEJM 2003;349:831-6
IVIg IN ITP

MECHANISM:
Reticuloendothelial blockade
Anti-idiotypic antibodies

ADVANTAGES:
Low toxicity
Effective (Pre-op)

DISADVANTAGES:
Temporary effect
Expensive
Expected Therapeutic Response

PLATELET COUNT

- 150,000
- 100,000
- 50,000

DAYS

- 1
- 2
- 3
- 4
- 5
- 3 weeks

IVIG + Pred
INTRAVENOUS Anti-D THERAPY

- Minimal toxicity
- Anti-D is effective only in Rh + patients with intact spleens
- Ig binds to erythrocyte D Ag
- Immune clearance of sensitized RBCs occupies the Fc receptors in the RE system
- Minimizes removal of Ab coated platelets
- Potential for hemolytic anemia after multiple treatments
- Do not use in pts with Pos Coombs or Hgb < 10
SPLENECTOMY
DEFINITIVE THERAPY FOR ITP

- REMEMBER IMMUNIZATIONS FOR pneumococcus, H. Flu and N. Meningiitis
- Utilized when more than low dose prednisone is needed for maintenance
- Removes: Predominant site of platelet destruction anti-platelet antibody production
  
  Karpatkin Br J Haem 1972;23:67
  McMillan NEJM 1972;286:681
- Decreased PAIg after splenectomy
  
IMMUNE THROMBOCYTOPENIA
SPLENECTOMY

Postpone in children until after 6 yo

Remission is most likely in patients with:

- Short platelet survival
- High platelet turnover
- Post-op platelet count > 500,000 plts/ul
- Good response to corticosteroids
- Good response to IVIg
- Patients < 60 yo
USE OF IVIg AND RESPONSE TO SPLENECTOMY

- Retrospective study of 30 patients who received IVIg, then had splenectomy
- 9 had poor response to IVIg and splenectomy
- 19/21 had good/excellent response to IVIg also had good/excellent response to splenectomy

Law et al., NEJM 1997;336:1494-8
LAPAROSCOPIC SPLENECTOMY

- Longer Procedure Time
- Earlier Tolerance of Fluids
- Diminished Need for Narcotics
- Shortened Hospital Stay
- Open Procedure if Necessary
Fig. 1. Kaplan–Meier curve of remission rate (CR+PR) in 56 adults with ITP following splenectomy.
### TABLE II. Response to Splenectomy

<table>
<thead>
<tr>
<th></th>
<th>Immediate post-operative</th>
<th>Long-term follow-up</th>
<th>Therapy post-operative</th>
<th>No therapy post-operative</th>
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</thead>
<tbody>
<tr>
<td>Complete remission</td>
<td>43 (77%)</td>
<td>32 (57%)</td>
<td>—</td>
<td>32 (57%)</td>
</tr>
<tr>
<td>Partial remission</td>
<td>5 (9%)</td>
<td>5 (9%)</td>
<td>—</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>Failure</td>
<td>8 (14%)</td>
<td>19 (34%)</td>
<td>19 (34%)</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>56</td>
<td>19 (34%)</td>
<td>37 (66%)</td>
</tr>
</tbody>
</table>
IMMUNE THROMBOCYTOPENIA
REFRACTORY PATIENTS

- Patients who do not respond to splenectomy
- Patients who recur after remission from splenectomy
VINCA ALKALOIDS
AFTER SPLENECTOMY

- VINCRISTINE 0.02 mg/kg
- VINBLASTINE 0.1 mg/kg

- Platelet count rises 5-10 days later
- Series of 3 infusions
- Mechanism unknown, ? Macrophage inhibitor
- Infusion better than bolus

Ahn, Ann Int Med 1984;100:192
DANAZOL

DOSE 50mg qD TO 800mg qD

- DECREASES NUMBER OF MONOCYTE RECEPTORS
- ALTERS CLEARANCE OF Ig COATED PLATELETS

Ahn NEJM 1983;308:1396
Schreiber NEJM 1987;316:503
Yeon Ann Int Med 1987;107:197
DANAZOL
DOSE RELATED PROBLEMS

- Expensive
- Voice change
- Weight
- Increased LFTs
- Other androgenic consequences
IMMUNE THROMBOCYTOPENIA
ACCESSORY SPLEENS

- Seen in 3/6 patients with good response to splenectomy
- In refractory patients approximately 50% will respond to accessory splenectomy
Venous Thromboembolism

post chest

Lt.
IMMUNE THROMBOCYTOPENIA
HIGH DOSE DEXAMETHASONE

10 Refractory ITP Patients
All had Received > 2 prior Tx

Dexamethasone 40 mg qd X 4 days q month
Regimen used for 6 cycles

Mean pre-tx Platelet Count - 12,000
Mean post-tx Platelet Count - 248,000

Minimal Toxicity

Andersen JC, NEJM 1994;330:1560-4
11 Older ITP patients with AITP studied
8 pts with secondary ITP studied
All pts given XRT 1-6 Weeks (Dose 75-1370 cGy)

Of 11 pts with ITP, 8 Responded, 3 for >52 weeks
4 Additional pts had plt ct increase for 8-25 weeks
2 of 8 pts with secondary ITP responded

CONCLUSION:
Splenic XRT can be a safe means for raising the platelet count in patients with steroid resistant AITP

CYTOTOXIC AGENTS

- CYCLOPHOSPHAMIDE (CYTOXAN)
  AZOTHIAPRINE (IMURAN)

- ADVANTAGES:
  SALVAGE THERAPY
  USUALLY NO ACUTE TOXICITY

- DISADVANTAGES:
  UP TO 2 MONTH LAG PERIOD
  POSSIBLE LEUKEMIA
20 Refractory AITP Patients
Patients had Received 2-8 (mean 4.8) prior Tx

Cytoxan 1.0 - 1.5g/m² (1-4 doses, mean 2.0)

13/20 (65%) Complete Response
  8 in remission median 2.5 years later
  Of 5 that relapsed, 2 were successfully retreated

4/20 (20%) Partial Response
  2 remain in PR 10 mos & 4 years later

3/20 (15%) No Response

Reiner et al, Blood 1996;85:351-58
RITUXIMAB THERAPY IN REFRACTORY ITP PATIENTS

- Rituximab: anti CD-20 chimeric monoclonal Ab
- FDA Approved for treating NHL
- CD-20: transmembrane protein on B cells (excluding plasma cells)
- Results in marked reduction of all B Cells
- Study: 57 adult chronic ITP patients received Rituximab, 4 weekly doses of 375mg/m2

- Response Rate was 54%
  - CR = 18 patients
  - PR = 13 patients
  - 29/31 responded within 8 weeks

Complete response to Rituximab as a function of duration of ITP

Cooper N, Stasi R, Russel JB, British Journal of Hematology 2004;125(2)232-239
HIV RELATED THROMBOCYTOPENIA

• Pathophysiology
  • Accelerated peripheral destruction
  • Decreased platelet production

• HAART therapy
  • Increase platelet production
  • Sustained increase in platelet count

• Spleen size normal or slightly increased
HIV RELATED THROMBOCYTOPENIA

• OTHER CAUSES
  • Myelodysplasia
  • AFB disease
  • Other granulomatous diseases
  • Drug induced
    • Decreased production
    • More rapid destruction
HIV RELATED THROMBOCYTOPENIA

- Steroids
- IVIg
- Anti-D (WinRho)

- Splenectomy
  - Effective
  - No difference in CD4 decline
MORBIDITY & MORTALITY in ADULTS with ITP

132 ITP patients were followed for 10.5 yrs

Splenectomy had a long term success rate of 66%

114 (85%) maintained platelet counts > 30,000/ul after all tx

These patients had mortality risk equal to general population

Portielje JEA et al, Blood 2001;97:2549-2554
12 patients (9%) had refractory thrombocytopenia
  • mortality risk of 4.2 relative to general population

Death equally caused by bleeding and infection

8 patients (6%) had platelet count > 30,000/ul
  • on maintenance therapy.

Portielje JEA et al, Blood 2001;97:2549-2554
THROMBOPOIETIN MIMETICS:

IN ITP
AMG 531, a Thrombopoiesis-Stimulating Protein, for Chronic ITP

James B. Bussel, M.D., David J. Kuter, M.D., D.Phil., James N. George, M.D.,
Robert McMillan, M.D., Louis M. Aledort, M.D., George T. Conklin, M.D.,
Alan E. Lichtin, M.D., Roger M. Lyons, M.D., Jorge Nieva, M.D.,
Jeffrey S. Wasser, M.D., Israel Wiznitzer, M.D., Reggie Kelly, B.S.,
Chien-Feng Chen, Ph.D., and Janet L. Nichol, M.S.
Eltrombopag for the Treatment of Chronic Idiopathic Thrombocytopenic Purpura

James B. Bussel, M.D., Gregory Cheng, M.D., Mansoor N. Saleh, M.D., Bethan Psaila, M.D., Lidia Kovaleva, M.D., Balkis Meddeb, M.D., Janusz Kloczko, M.D., Habib Hassani, Ph.D., Bhabita Mayer, M.Sc., Nicole L. Stone, Ph.D., Michael Arning, M.D., Drew Provan, M.D., and Julian M. Jenkins, M.Sc.*
THROMBOPOIETIN MIMETICS

- Romiplostim (N-plate) Peptide memetic FDA approved 8/08 for ITP
  - Dose 1-10 mcg/kg/wk (in a 70 kg patient)
  - Extrapolated cost: $5100/4 weeks* x 13 = $66,300
  - Risks of reversible marrow fibrosis, HA, dizziness, myalgia
  - No neutralizing Ab

- Eltrombopag (Primacta) Oral non-peptide memetic, FDA approved 11/08
  - Dose 50 mg qd, 25 mg in East Asian pts/ those with hepatic insuff
  - Extrapolated cost: $3960/4 weeks* x 13 = $51,480
  - Risk of mild headaches, increased ALT, bili, reversible fibrosis
  - No neutralizing Ab

- Both have a 60-85% response rate

Medical Letter 2009:51;1-2
POSSIBLE ADVERSE EFFECTS

- Thrombocytosis
- Thrombosis
- Tumor/leukemia cell growth
- Interaction with other cytokines
- Formation of neutralizing antibodies cross-reactive with native thrombopoietin
- Stem cell depletion
- Platelet activation and acceleration of pathophysiologic process
- Increased bone marrow reticulin or collagen deposition
- Rebound thrombocytopenia below baseline upon sudden Cessation of therapy
Romiplostim or Standard of Care in Patients with Immune Thrombocytopenia

- 234 adult ITP patients were randomized to standard of care (77 pts) v weekly SQ Romiplostim (157 pts)
  - One or more types of therapy for ITP
  - Had not undergone splenectomy
  - Pre-tx platelet count < 50,000
  - No cancer, stem cell disorder, current pregnancy

- Patients in Romiplostim group had:
  - Higher rate of platelet response (2.3 x)
  - Lower incidence of treatment failure and splenectomy
  - Less bleeding and fewer blood transfusions
  - A higher quality of life

Kuter DJ et al, NEJM 2010;363: 1889:1899
Drug-Induced Thrombocytopenia

- Frequency is uncertain
- Frequency of medication use increases with age
- Frequency of alternative medicine use is increasing at all ages
Drug-Induced Thrombocytopenia

- Usually first diagnosed as ITP

- Correct diagnosis is essential to:
  - avoid inappropriate treatment
  - prevent recurrence
Drug-Induced Thrombocytopenia
Initial Diagnosis as ITP

- 343 patients registered as ITP, 1993-1999
- 28 (8%) excluded because of subsequent diagnosis of drug-induced thrombocytopenia
- Quinine most common cause (13 of 28, 46%)

Neylon, Br J Haem 2003; 122:966
CONCLUSIONS

- Think of drug-induced thrombocytopenia
- Do not allow treatment of ITP to be worse than the disease
- Splenectomy provides durable complete remissions in 2/3 patients
- Role of other treatments uncertain
- Thrombopoietic agents are FDA approved and in use