Immune Cytopenias: Controversies in ITP

Michelle Sholzberg MDCM, MSc, FRCPC
Hematologist & Medical Director of Coagulation Laboratory
St. Michael’s Hospital, Toronto, Canada
Objectives

- Review controversies in adult immune thrombocytopenia (ITP)
- Focus on new data and a practical approach
Disclosures

• Honoraria from Amgen and Novartis

• Unrestricted research funding from Amgen and Novartis
ITP Basics
Immune Thrombocytopenia (ITP)

- 1:10,000 adults

- Primary versus secondary

- Clinical diagnosis:
  - Platelet count <100
  - Diagnosis of exclusion

The most compelling evidence for the presence of ITP is response to standard therapy

Rodeghiro et al., Blood 2009; Cuker and Neunert, Blood 2016
ITP: Overview of Pathology

ITP is caused by:

- **Increased platelet destruction**: mediated by platelet-reactive autoantibodies
- **Impaired platelet production**: endogenous thrombopoietin (TPO) levels are inadequate for the degree of thrombocytopenia in ITP

ITP: Bleeding and Clotting
Rate of Bleeding-related Episodes in Adult Patients with Primary ITP?

- Retrospective cohort study, 2008-2012
- Large administrative medical claims database in the US, N=6652

- Bleeding-related episode (BREs) = composite endpoint
  - bleeding and/or rescue therapy use (IVIG, IV steroids, platelet transfusion)

- 57% experienced >1 BRE (1.08 BRE per patient-year, 95% CI 1.06-1.10)
  - 58% of BREs consisted of rescue therapy use only

- Newly diagnosed and splenectomized patients had elevated BRE rates

- Common bleeding types: GI and GU bleeding, ecchymosis, epistaxis
- ICH reported in 74 patients (1%)
Is ITP a Thrombophilic Disorder?

• Slightly increased risk of VTE
  – Particularly post-splenectomy

• Patients over age 60 with additional risk factors it is important to counsel regarding risk modification
  – Post-splenectomy
  – Prolonged corticosteroid use
  – Vascular risk factors
  – Lupus anticoagulant positivity

Rodeghiero et al., AJH, 2016; Doobaree et al. EJH, 2016; Moulis et al., Autoimmunity Reviews, 2015.
Is ITP a Thrombophilic Disorder?

<table>
<thead>
<tr>
<th>Study</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TEE</strong></td>
<td></td>
</tr>
<tr>
<td>Enger et al</td>
<td>1.70 (1.41, 2.05)</td>
</tr>
<tr>
<td>Sarpatwari et al</td>
<td>1.41 (1.04, 1.91)</td>
</tr>
<tr>
<td>Subtotal (I-squared = 9.7%, P = 0.293)</td>
<td>1.60 (1.34, 1.86)</td>
</tr>
<tr>
<td><strong>ATE</strong></td>
<td></td>
</tr>
<tr>
<td>Enger et al</td>
<td>1.58 (1.29, 1.94)</td>
</tr>
<tr>
<td>Sarpatwari et al</td>
<td>1.37 (0.94, 2.00)</td>
</tr>
<tr>
<td>Subtotal (I-squared = 0.0%, P = 0.508)</td>
<td>1.52 (1.25, 1.80)</td>
</tr>
<tr>
<td><strong>VTE</strong></td>
<td></td>
</tr>
<tr>
<td>Enger et al</td>
<td>2.89 (1.33, 6.29)</td>
</tr>
<tr>
<td>Sarpatwari et al</td>
<td>1.58 (0.94, 2.48)</td>
</tr>
<tr>
<td>Subtotal (I-squared = 0.0%, P = 0.323)</td>
<td>1.70 (0.96, 2.43)</td>
</tr>
</tbody>
</table>

ATE Arterial thromboembolism  ITP Immune thrombocytopenia
TEE any thromboembolism  VTE Venous thromboembolism

Doobaree et al., EJH, 2016.
Platelet Function in Adult ITP Patients

• Platelet activity tested by flow cytometric measurement of agonist induced P-selectin expression

• 23 adult ITP patients
• 22 healthy volunteers

Middelburg et al., Hematology, 2016
Increased platelet activity was associated with decreased bleeding risk in patients with counts <30.
ITP: Immune Function and Risk of Infection
The principal mechanisms of innate and adaptive immunity.

**Innate immunity**
- Microbes
- Epithelial barriers
- Phagocytes
- Platelets
- Complement
- NK cells

**Adaptive immunity**
- B lymphocytes
- Antibodies
- T lymphocytes
- Effector T cells

**Time after infection**
- Hours: 0, 6, 12
- Days: 1, 3, 5

W.B. Saunders Company items and derived items copyright © 2002 by W.B. Saunders Company.
Platelets and the immune continuum

John W. Semple*†‡, Joseph E. Italiano Jr†§ and John Freedman*‡

Abstract | Platelets are anucleate cells that are crucial mediators of haemostasis. Most immunologists probably don’t think about platelets every day, and may even consider these cells to be ‘nuisances’ in certain in vitro studies. However, it is becoming increasingly clear that platelets have inflammatory functions and can influence both innate and adaptive immune responses. Here, we discuss the mechanisms by which platelets contribute to immunity: these small cells are more immunologically savvy than we once thought.

NATURE REVIEWS | IMMUNOLOGY | VOLUME 11 | APRIL 2011 | 271

Platelets are immune cells

- Activated platelets promote DC activation, which increases antigen presentation to T cells
- Activated platelets produce cytokines and chemokines and promote neutrophil activation
- Neutrophil activation
- Platelet-expressed selectins promote neutrophil tethering
- Damaged endothelium
- Selectin ligand
- Selectin
- Fibrin
- Cytokines and chemokines
- Neutrophil
- CD154
- CD40
- Bacterial destruction
- Trapping of bacteria by platelets
- Thrombocidins
- Bacteria
- TLR4
- Platelet

Activation of adaptive immune responses

DC
- MHC
- TCR
- T cell
Increased Susceptibility to Infections

- Infections after the diagnosis of ITP have mostly been connected to immunosuppressive therapy
- Swedish patient registry
- 1087 adult patients with primary chronic ITP
- Increased risk of infection (candida, viral infection) requiring inpatient or outpatient care within 5 years before the development and diagnosis of ITP
  - Standardized incidence ratio 8.74 (85% CI 7.47-10.18)

Ekstrand et al. Platelets, 2015
Corticosteroid Associated Risk of Severe Infection in Primary ITP

- Nested case-control study
- French national health insurance database
- N=1805 from 2009-2012

- Cases defined as infection as the primary diagnosis code during hospitalization
- 161 cases occurred during the study period - 9 opportunistic

- Corticosteroid doses were converted in prednisone equivalent (PEQ)
- Highest risk in the month preceding the date of risk measure

Corticosteroid Associated Risk of Severe Infection in Primary ITP

- Dose-effect relation showed that the risk existed from averaged daily doses of \( \geq 5 \text{ mg PEQ} \) (vs. \(<5 \text{ mg PEQ}: 2.09, 95\% \text{ CI 1.17-3.71} \))
  - Not \( >20 \text{ mg PEQ} \)
  - Past exposure prior to the month preceding the date of infection and past cumulative dose does not seem to play a major role

- Increased risk of infection in the 6 months following Rituximab

Table 4. Multivariate model\* assessing the dose-effect relation between exposure to corticosteroids during the month before the index date and occurrence of severe infection.

<table>
<thead>
<tr>
<th>Average daily dose of corticosteroids in the month before the index date ( \dagger ), mg PEQ</th>
<th>OR [95% CI]</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>1.63 [1.11–2.40]</td>
<td>0.01</td>
</tr>
<tr>
<td>Average daily dose of corticosteroids in the month before the index date ( \dagger ), mg PEQ</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>(&lt;5)</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>([5–10])</td>
<td>2.09 [1.17–3.71]</td>
<td>0.01</td>
</tr>
<tr>
<td>(\geq 10)</td>
<td>1.99 [1.26–3.17]</td>
<td>0.003</td>
</tr>
</tbody>
</table>

ITP: Adherence to Guidelines?
Diagnosis and Management
Real-life Management of Primary ITP in Adults and Adherence to Guidelines

• Retrospective review of 101 patients from 2011-2012
• Only included patients requiring treatment
• 75.2% symptomatic

• Significant diagnostic discrepancies from guidelines:
  – Failure to perform PB film review in 22.8% of patients
  – 50.5% had bone marrow evaluations
  – 54.8% unjustified use of IVIG (no bleeding symptoms)
  – Splenectomy not being deferred until 6-12 months (median 161 days (~5 months))
  – Trend toward early use of Tpo-RAs in patients refractory to first line therapy

Lozano et al., Annals of Hematology, 2016
Does Intensification of Up-front Therapy Impact Long-term Outcomes?
Does Intensification of Up-front Therapy Impact Long-term Outcomes?

- **Prednisone 1mg/kg/day** has long been the standard first-line therapy
  - Most respond
  - Relapse is common after steroids are tapered
  - Depending on the definition 40-60% of patients maintain a response at 6 months
  - 20-30% beyond 1-2 years

- **High dose dexamethasone (HDD)** 40 mg (267 mg PEQ) x 4 days
  - Repeated cycles q2-4 weeks
  - 1-2 cycles of HDD result in a greater initial response and shorter time to response but do not improve long-term response rates
  - ≥ 3 cycles may enhance long-term response rates (RCT currently recruiting)

- **Addition of Rituximab up front** revealed higher response rates but
- **Data on use of Tpo-RAs in newly diagnosed ITP** are limited
- **Extended follow-up needed**
  - ?greater cure rates or merely delayed relapse?

Does Intensification of Up-front Therapy Impact Long-term Outcomes?

Current evidence does not support routine use of intensified up-front therapy in newly diagnosed ITP outside of a clinical trial

Cuker et al., Curr Opin Hematol, 2016
What is the Optimal Second-Line Therapy for ITP? Splenectomy or Not?
Have Splenectomy Rates and ITP Outcomes Changed?

Treatment Strategies According to the Years of Diagnosis

- Retrospective study N=557 ITP patients in Italy from 1980-2015
- Over the decades – splenectomy was delayed from 2\textsuperscript{nd} to 3\textsuperscript{rd} line
  - Steadily used in 15-25\% patients
- Rituximab emerged as 2\textsuperscript{nd} line therapy
- TPO-RAs emerged as 3\textsuperscript{rd} line therapy

---

**Figure 1a: Second Line**

---

**Figure 1b: Third Line**

Palandri et al., AJH, 2016.
Have Splenectomy Rates and ITP Outcomes Changed?

- Overall responses were similar over time
- >97% achieving a response in all time-periods
- Risk of infection remained stable
- Cumulative risk of bleeding decreased

Palandri et al., AJH, 2016.
Is Splenectomy still the Treatment of Choice for Second-Line Therapy?

• **Factors that contribute the decline in splenectomy:**
  – Surgical mortality (<1%)
  – Splenic or portal vein thrombosis (0.1-4/100 patient years)
  – 5-30X increased risk of infection in 1st 90 days
  – 1-3X life-long increased risk of infection or sepsis
    • absolute risk 1.2 vs. 0.7/100 patient years
  – >30X increased risk of VTE compared to the general population
    • AR 0.63% for DVT and 0.73% for PE
    • 1-5X long term increased risk

• **Few studies stratify on splenectomy-associated M&M for ITP as an indication**
  – Even fewer include the non-splenectomized ITP cohort for comparison

There is No Clear Second Line Therapy Winner

Individualize care
- Optimal second line treatment is uncertain

Studies that directly compare efficacy, safety, impact on HR-QOL and cost-effectiveness are needed

Cuker et al., Curr Opin Hematol 2016.
Quality Improvement in the Care of Patients with Asplenia

<table>
<thead>
<tr>
<th>Vaccination</th>
<th>Date of Last Dose MM/DD/YYYY</th>
<th>Date Next Dose Due MM/DD/YYYY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningococcal conjugate A,C,Y,W-135 (Menactra®, Menveo®)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal conjugate C (Menjugate®, Meningitec®, NeisVac-C®)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal polysaccharide A,C,Y,W-135 (Menomune®)*</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Meningococcal serogroup B (Bexsero®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus B conjugate (Act-HIB)</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal conjugate 13-valent (Prevnar® 13)</td>
<td>Not applicable</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal polysaccharide polyvalent (Pneumovax® 23, Pneumo® 23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Not all listed meningococcal vaccines are given to every patient. Please see the back of the card for details.

What to do if you have a fever
If your temperature is 38°Celsius or higher, immediately go to the nearest Emergency Department for treatment.
If you cannot get to a hospital within 2 hours of when your fever started, take a single dose of (Name of prescribed antibiotic) and go to the nearest Emergency Department.

Physician Name
Physician Signature Date

primum non nocere
What is the Optimal Therapy for Refractory ITP?

Post-splenectomy or Splenectomy contraindicated
Management of Refractory ITP

• Majority of evidence is limited to case reports and uncontrolled case series

• Non-responsiveness to treatment should prompt \textbf{reassessment of the diagnosis}
  – Ensure manual platelet counts are performed
    • automated cell counters misclassify large and agglutinated platelets
  – R/O non-immune thrombocytopenia
  – R/O secondary ITP

Cuker and Neunert, Blood, 2016
Three Tiered Approach to Treatment

• Goal is not a perfect platelet count
• Goal is a safe platelet count

• 3 tiered approach based on efficacy, safety and quality of evidence
  – No direct comparisons of treatment options within a given tier
  – Exhaust each tier before moving to the next
• Individualize choice of treatment based on age, comorbidities, drug availability, cost and patient preference

• When a durable platelet count cannot be attained with monotherapy → consider combining agents with different mechanisms of action

# Tier 1 Treatment Options

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Response rate¹</th>
<th>Time to response</th>
<th>Selected toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-dose prednisone</td>
<td>≤ 5 mg PO daily</td>
<td>&lt; 10%</td>
<td>N/A²</td>
<td>Weight gain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Osteoporosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cataracts</td>
</tr>
<tr>
<td>Rituximab</td>
<td>375 mg/m² IV weekly × 4 (lower doses may be effective)</td>
<td>60% overall 40% complete 20-25% at 5 years</td>
<td>1-8 weeks</td>
<td>Infusion reactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Serum sickness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HBV reactivation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PML (rare)</td>
</tr>
<tr>
<td>Romiplostim</td>
<td>1-10 μg/kg SC weekly</td>
<td>80% overall 40-50% persistent</td>
<td>1-4 weeks</td>
<td>Reticulin fibrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rebound thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thrombosis</td>
</tr>
<tr>
<td>Eltrombopag</td>
<td>25-75 mg PO daily</td>
<td>80% overall 40-50% persistent</td>
<td>1-2 weeks</td>
<td>Reticulin fibrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rebound thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Thrombosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hepatotoxicity</td>
</tr>
</tbody>
</table>

¹Response rate is based on the percentage of patients responding to treatment.
²N/A: Not applicable.

Cuker and Neunert, Blood, 2016
## Tier 2 Treatment Options

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Response rate</th>
<th>Time to response</th>
<th>Selected toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-mercaptopurine</td>
<td>50-75 mg/m² PO QD</td>
<td>83%</td>
<td>Not reported</td>
<td>Hepatotoxicity, Neutropenia, Infection, Pancreatitis</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>1-2 mg/kg PO QD (maximum 150 mg/day)</td>
<td>40%-60%</td>
<td>3-6 months</td>
<td>Hepatotoxicity, Neutropenia, Infection, Pancreatitis</td>
</tr>
<tr>
<td>Cyclosporin A</td>
<td>5-6 mg/kg/day PO divided twice daily (titrate to blood levels of 100-200 ng/mL)</td>
<td>30%-60%</td>
<td>3-4 weeks</td>
<td>Nephrotoxicity, Hypertension, Tremor, Parathesias, Gingival hyperplasia</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>0.3-1.0 g/m² IV repeated every 2-4 weeks × 1-3 doses</td>
<td>24%-85%</td>
<td>1-16 weeks</td>
<td>Neutropenia, Nausea/Vomiting, Infertility, Secondary malignancy</td>
</tr>
<tr>
<td>Danazol</td>
<td>50-800 mg/day PO divided 2-4 times daily</td>
<td>10%-70%</td>
<td>3-6 months</td>
<td>Hepatotoxicity, Virilization, Amenorrhea</td>
</tr>
<tr>
<td>Dapsone</td>
<td>75-100 mg PO QD</td>
<td>40%-75%</td>
<td>3 weeks</td>
<td>Hemolysis (in patients with G6PD deficiency), Rash, Nausea, Methemoglobinemia</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>250-1000 mg PO BID</td>
<td>11%-80%</td>
<td>4-6 weeks</td>
<td>Headache, Diarrhea, Nausea, Anorexia, Infection</td>
</tr>
<tr>
<td>Vinca alkaloids</td>
<td>Vincristine: 1-2 mg IV weekly × 3 weeks Vinblastine: 10 mg IV weekly × 3 weeks</td>
<td>10%-75%</td>
<td>5-7 days</td>
<td>Peripheral neuropathy, Vesication at infusion site, Constipation, Fever, Neutropenia</td>
</tr>
</tbody>
</table>
## Tier 3 Treatment Options

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>Response rate</th>
<th>Selected toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATRA(^{86})</td>
<td>10 mg PO TID</td>
<td>29%</td>
<td>Retinoic Acid Syndrome&lt;br&gt;Flu-like Symptoms&lt;br&gt;Musculoskeletal pain&lt;br&gt;Nausea/Vomiting&lt;br&gt;Peripheral neuropathy</td>
</tr>
<tr>
<td>Autologous HSCT(^{87})</td>
<td>Cyclophosphamide 50 mg/kg IV QD × 4 days (conditioning)</td>
<td>43%</td>
<td>Neutropenic fever&lt;br&gt;Infection</td>
</tr>
<tr>
<td>Colchicine(^{88})</td>
<td>1.2 grams PO QD</td>
<td>21%</td>
<td>Agranulocytosis&lt;br&gt;Neutropenia&lt;br&gt;Diarrhea&lt;br&gt;Nausea/Vomiting</td>
</tr>
<tr>
<td>Interferon α(^{89–92})</td>
<td>Various</td>
<td>0-36%</td>
<td>Neutropenia&lt;br&gt;Fever&lt;br&gt;Influenza-like symptoms&lt;br&gt;Hepatotoxicity</td>
</tr>
<tr>
<td>Plasma exchange(^{93–95})</td>
<td>One plasma volume exchange QD × 1-8 days</td>
<td>29-80%</td>
<td>Hypocalcemia&lt;br&gt;Anaphylactoid reactions</td>
</tr>
<tr>
<td>Protein A immunoadsorption(^{96})</td>
<td>Average of 6 treatments (0.25 to 2.0 L plasma per treatment) over 2-3 weeks</td>
<td>21%</td>
<td>Hyper-sensitivity reactions&lt;br&gt;Pain&lt;br&gt;Nausea/Vomiting&lt;br/Cardiopulmonary complications</td>
</tr>
<tr>
<td>Vitamin C(^{97–100})</td>
<td>2 grams PO QD</td>
<td>0-82%</td>
<td>Dyspepsia&lt;br&gt;Nausea/Vomiting</td>
</tr>
</tbody>
</table>
Tolerability of Tpo-RAs

- **Reticulin Fibrosis:**
  - Pooled analysis of 14 trials of adults with ITP treated with romiplostim → Bone marrow reticulin was observed in 17/921 (1.8%) patients
  - **Eltrombopag** extension study → 2/117 (1.7%) moderate-marked bone marrow reticulin fibrosis

- **Thromboembolism:**
  - May increase incidence of thromboembolism in some populations
  - Meta-analysis suggested that they do not increase thrombosis in patients with ITP vs. placebo

- **Rebound thrombocytopenia**
  - Platelet count may temporarily fall below baseline once TRAs discontinued

- **Hepatotoxicity** with eltrombopag

- **Prolonged responsiveness after discontinuation has been described.....?**
  
Tpo-RAs Multitask in ITP

• Directly stimulate thrombopoiesis
  – Increase platelet production

• Immunomodulatory
  – May lower platelet destruction
  – Some studies have shown a sustained platelet count response after Tpo-RA discontinuation

• ITP patients on Tpo-RA
  – Improved Treg activity
  – Decreased effector T cell function
  – Correction of B regulatory cell number and function
  – Restoration of FcγR balance on monocytes

Yazdanbakhshm, Platelets and Thrombopoiesis, 2016
What about ITP in Pregnancy? Evidence?
ITP in Pregnancy

- Treatment options are limited
- Evidence to guide management decisions are lacking

- *Retrospective study*
  - N=195; 235 pregnancies
  - 137 pregnancies (58%) did not require treatment
  - 91 required treatment – ~50:50 IVIG:corticosteroids

- Mean maternal platelet counts at birth
- Proportion of those who achieved a response
- Neonatal outcomes


did not differ between the 2 groups

Sun et al., Blood, 2016.
Neonatal and Maternal Platelet Count Nadir – Lack of Relationship Between Variables

Sun et al., Blood, 2016.
ITP in Pregnancy: Outcomes

Neonates:
- 56 (28%) had a birth platelet count <150
- 18 (9%) had platelet counts <50
- Nadir platelet counts for most affected neonates occurred at birth
  - for some, nadir platelet counts occurred up to 6 days postnatally
- Intracranial hemorrhage was noted in two neonates
  - nadir platelet counts were 135 and 18, respectively
- There were no neonatal deaths

- Prospective studies warranted
  - To characterize safety of treatments
  - Determine optimal dose of steroids
  - Identify risk factors for neonatal thrombocytopenia

Sun et al., Blood, 2016.
Extrapolation from evidence in inherited bleeding disorders

Multidisciplinary care makes intuitive sense
Summary: Key Points

- Bleeding is more common than thrombosis in ITP - related to platelet function
- Risk of infection pre- and post-diagnosis of ITP
- Lack of adherence to current guidelines
- No evidence for up-front therapeutic intensification
- Tiered approach to advanced line therapy
- Expert opinion-based and individualized care
Objectives Revisited

- Review controversies in adult immune thrombocytopenia (ITP)
- Focus on new data and a practical approach
Thank you

Questions?

sholzbergm@smh.ca