

Management of Primary Immune Thrombocytopenia, 2012: A Survey of Oklahoma Hematologists-Oncologists

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Abstract: *Background:* Management options for patients with primary immune thrombocytopenia (ITP) have increased, and treatment of patients with ITP has changed during the past 10 years. *Methods:* To document current practice and to determine how current practice is related to recommendations of 2 recent practice guidelines for ITP, an International Consensus report and an American Society of Hematology (ASH) guideline, the authors surveyed practicing hematologists-oncologists in Oklahoma. Surveys were specific for children or adults. Each survey had 3 questions describing patients with a new diagnosis and patients who had not achieved remission with initial treatment. Questions were adapted from the clinical scenarios of the ASH guideline. *Results:* Twelve (92%) Oklahoma pediatric hematologists-oncologists responded; 82 (81%) Oklahoma adult hematologists-oncologists responded. For a child with a new diagnosis of ITP, a platelet count of 8000/ μ L and minor bleeding, 5 (42%) hematologists-oncologists selected observation without drug treatment (recommended by both guidelines). For an adult with a platelet count of 9000/ μ L who had failed to respond to initial treatment with corticosteroids and IVIg, 32 (39%) selected splenectomy (recommended by the ASH guideline); 30 (37%) selected rituximab and 13 (16%) selected thrombopoietin-receptor agonists (both recommended by the International Consensus report). Hematologists-oncologists who had more years in practice were more likely to select splenectomy ($P = 0.047$). *Conclusions:* In a time of changing management for patients with ITP, these data document reported current management in Oklahoma and provide a basis for serial comparisons across time and for comparisons with other regions and comparison of management with patient outcomes.

Key Indexing Terms: Immune thrombocytopenic purpura; ITP; Practice guidelines; Splenectomy; Thrombopoietin-receptor agonists. [*Am J Med Sci* 2014;347(3):190–194.]

With the availability of multiple new agents, management of patients with primary immune thrombocytopenia (ITP) has changed substantially since the initial practice guideline for ITP was developed by American Society of Hematology (ASH), 1994 to 1995.¹ Anti-(Rh)D was approved by the FDA for treatment of ITP in 1995 and has become a common initial treatment

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for children with ITP.² Rituximab was first used for ITP in 1999³ and is now frequently used for patients who do not respond to initial treatment,^{4,5} although it has never been approved by the FDA for treatment of ITP. Two thrombopoietin (TPO)-receptor agonists, romiplostim and eltrombopag, were approved by the FDA for treatment of ITP in 2008; they have been extensively studied in randomized clinical trials, actively marketed and increasingly used.^{5–7} Two recently published clinical practice guidelines, an International Consensus report (ICR) published in 2010⁸ and an updated practice guideline developed by ASH published in 2011,⁹ have made recommendations for management of ITP in children and adults. To document reported current clinical management and to determine how reported current management is related to the recommendations of these guidelines, we surveyed practicing hematologists-oncologists in Oklahoma.

METHODS

Surveys

The ASH clinical practice guideline for ITP⁹ based its systematic literature review and recommendations on focused clinical questions to describe management issues for children and adults. We used these clinical questions as the basis for our survey questions, to better compare physician responses with guideline recommendations. Although the ICR⁸ did not use the format of focused clinical questions, the clinical indications for its recommendations were similar.

Separate surveys were developed for children and adults. Each survey had 3 clinical scenarios; each clinical scenario had 5 to 7 management choices (see complete surveys, Supplemental Digital Contents 1 and 2, <http://links.lww.com/MAJ/A24> and <http://links.lww.com/MAJ/A25>). Hematologists-oncologists were instructed to select only 1 management choice. Data were collected from each respondent for (1) their number of years in practice; (2) the site of their practice, described as University of Oklahoma Medical Center (OUMC) or community; and (3) the estimated number of patients with ITP they see each year. In addition, whether community hematologists-oncologists had trained at OUMC and whether the hematologists-oncologists practicing at OUMC were faculty or fellows in training were determined from records of the OUMC Hematology-Oncology Divisions. There is no fellowship training program in pediatric hematology-oncology program at OUMC.

To determine if the clinical scenarios and management choices were clear and appropriate, the surveys were pilot tested by 5 pediatric hematologists-oncologists (Carolyn Bennett, Atlanta, GA; George Buchanan, Dallas, TX; Alan Cohen, Philadelphia, PA; Shelley Crary, Little Rock, AR; Cindy Neunert, Augusta, GA) and 6 adult hematologist-oncologists (Mark Crowther, Hamilton, Ontario, Canada; Mehrdad Jafari and Kiarash Kojouri, Mt. Vernon, WA; Mujahid Rizvi, Medford, OR; Lawrence Solberg Jr, Jacksonville, FL). Their comments were incorporated into the final version of the surveys. The surveys were approved by the Institutional Review Board of the University of Oklahoma Health Sciences Center.

Identification of Hematologists-Oncologists

Hematologists-oncologists were identified by searching the Oklahoma Board of Medical Licensure and the Oklahoma Osteopathic Association Web sites for all physicians certified in hematology/oncology, hematology, oncology or pediatric hematology/oncology. Hematologists-oncologists were included if they had an active Oklahoma license and were currently treating hematology-oncology patients in Oklahoma as of December 31, 2011. Current practice was determined by contacting the hematologists-oncologists' offices. Exclusion criteria included physicians who were radiation oncologists, gynecologic oncologists, surgical oncologists and pathologists, whose careers were devoted to full-time research or administration, who did not have an active Oklahoma license or who were not currently treating hematology-oncology patients in Oklahoma. In addition, hematologists-oncologists had to report seeing at least 1 ITP patient per year on the survey.

Data Collection

Surveys were initially sent to each physician by e-mail or fax on January 30, 2012. If there was no response within 2 weeks, then the hematologist-oncologist or the office nurse was contacted to remind them. To achieve the maximum response, some hematologists-oncologists were contacted multiple times by one of the authors (J.N.G.). The last surveys were returned on March 15, 2012.

Statistical Analysis

Descriptive statistics were used to describe the characteristics of the respondents and their responses, stratified by pediatric and adult hematologists-oncologists. Because of the small number of pediatric hematologists-oncologists, no comparison of their responses to their characteristics (years in practice, site of practice and number of patients seen each year) was performed. For the adult hematologists-oncologists, comparison of the number of years in practice with the responses was selected *a priori* because it was hypothesized that hematologists-oncologists with fewer years in practice may more readily accept newer treatments whereas hematologists-oncologists with more years in practice may prefer more traditional management. Chi-square or Fisher's exact test were used to determine if treatment responses differed by number of years in practice. SAS version 9.2 was used; alpha was set at 0.05.

Only the stronger grades of recommendations by the ICR and ASH guidelines were used for comparison with the hematologists-oncologists' responses. For the ICR, grade A (based on evidence from randomized clinical trials) or grade B (based on well-designed clinical studies) recommendations were used (not grade C).⁸ For the ASH guideline, grade 1 recommendations were used (not grade 2).⁹

RESULTS

Pediatric Hematologists' Treatment of ITP in Children

All 13 pediatric hematologists-oncologists returned their surveys. One survey was not eligible because there was no response to the question of how many ITP patients were seen each year. Characteristics of the respondents included 8 OUMC faculty and 4 community pediatric hematologists-oncologists. None of the 4 community pediatric hematologists-oncologists had trained at OUMC. Two (17%) hematologists-oncologists had been in practice for less than 5 years, 6 (50%) for 5 to 20 years, and 4 (33%) for more than 20 years. Three (25%) reported seeing 1 to 5 ITP patients per year and 9 (75%) more than 5 per year.

TABLE 1. A child with a new diagnosis of ITP and minor bleeding symptoms

| Management choice | Responses |
|---|-----------|
| Anti-D (Win-Rho) | 2 |
| Corticosteroids | 3 |
| IVIg | 2 |
| Observation with no drug treatment (watchful waiting) ^{a,b} | 5 |
| Thrombopoietin-receptor agonists (Nplate [romiplostim], Promacta [eltrombopag]) (if approved and available for use in children) | 0 |
| Other (describe): _____ | 0 |

Survey question 1: A 3-year-old boy presents with a 24-hour history of bruising and petechiae. He has a few areas of scattered petechiae and several small bruises on his arms and legs. His platelet count is 8000/ μ L. His complete blood count and smear review are otherwise normal, and his blood group is A+. What is your management choice?

^a Management recommended by the ICR: grade B.⁸

^b Management recommended by the ASH guideline: grade 1B.⁹

For a 3-year-old boy with a new diagnosis of ITP, a platelet count of 8000/ μ L and only minor bleeding, 5 (42%) pediatric hematologists-oncologists selected observation without drug treatment (watchful waiting); all 5 report seeing more than 5 ITP patients per year (Table 1). This was the management option recommended by both the ICR and ASH guidelines.

For a 3-year-old boy with a new diagnosis of ITP, a platelet count of 8000/ μ L and active bleeding, 6 (50%) pediatric hematologists-oncologists selected treatment with corticosteroids or IVIg (Table 2). These treatments were recommended by both guidelines. The ICR guideline also recommended treatment with anti-D, which was selected by 5 (42%) pediatric hematologists-oncologists.

For a 6-year-old girl with chronic symptomatic ITP for 12 months and a platelet count of 8000/ μ L, 7 (58%) pediatric hematologists-oncologists selected treatment with rituximab; 1 selected splenectomy (Table 3). The ICR guideline recommended

TABLE 2. A child with a new diagnosis of ITP and more severe bleeding symptoms

| Management choice | Responses |
|---|-----------|
| Anti-D (Win-Rho) ^a | 5 |
| Corticosteroids ^{a,b} | 1 |
| IVIg ^{a,b} | 5 |
| Observation with no drug treatment (watchful waiting) | 1 |
| Thrombopoietin-receptor agonists (Nplate [romiplostim], Promacta [eltrombopag]) (if approved and available for use in children) | 0 |
| Other (describe): _____ | 0 |

Survey question 2: A 3-year-old boy presents with a 24-hour history of bruising and petechiae. He has a few areas of scattered petechiae and several small bruises on his arms and legs. When in your office, he develops epistaxis that lasts about 15 minutes. His platelet count is 8000/ μ L. His complete blood count and smear review are otherwise normal, and his blood group is A+. What is your management choice?

^a Management recommended by the ICR: grade A.⁸

^b Management recommended by the ASH guideline: grade 1B.⁹

TABLE 3. A child with chronic, symptomatic ITP

| Management choice | Responses |
|--|----------------|
| Anti-D (Win-Rho) | 0 |
| Corticosteroids (daily oral prednisone) | 0 |
| Corticosteroids (intermittent high-dose dexamethasone) | 0 |
| IVIg | 0 |
| Observation with no drug treatment (watchful waiting) | 0 |
| Rituximab ^a | 7 |
| Splenectomy ^{a,b} | 1 |
| Thrombopoietin-receptor agonists (Nplate [romiplostim], Promacta [eltrombopag] (if approved and available for use in children) | 3 |
| Other (describe): _____ | 1 ^c |

Survey question 3. A 6-year-old girl was diagnosed with ITP 12 months ago and continues to have a platelet count of 8000/μL. During these 12 months, she had only transient responses to IVIg and anti-D and recently has had a decline in response to periodic courses of corticosteroids. She has recurrent epistaxis that often requires her to be sent home from school. Her complete blood count and smear review are otherwise normal, and her blood group is A+. What is your management choice?

^a Management recommended by the ICR: grade B.⁸

^b Management recommended by ASH guideline: grade 1B.⁹

^c Other: "IVIg or Win-Rho with steroid burst. If this fails, follow with rituximab."

either rituximab or splenectomy; the ASH guideline recommended only splenectomy.

Adult Hematologists Treatment of ITP in Adults

Eighty-three (82%) of the 101 hematologists-oncologists for adults returned their surveys; 1 survey was not eligible because the respondent saw no ITP patients. Characteristics of the respondents included 21 (26%) at OUMC (11 faculty, 10 fellows) and 61 community hematologists-oncologists. Of the 61 community hematologists-oncologists, 24 (39%) had trained at OUMC, 1975–2009. Twenty-four (29%) respondents had been in practice for less than 5 years, 30 (37%) for 5 to 20 years, and 28 (34%) for more than 20 years. Fifty-five (68%) respondents reported seeing 1 to 5 ITP patients per year and 27 (32%) more than 5 per year.

For a 28-year-old woman who was incidentally discovered to have ITP with a platelet count of 40,000/μL, 77 (94%) hematologists-oncologists selected observation without drug treatment (Table 4). Although this was consistent with statements in the text of both guidelines, neither had a strong recommendation for management of a patient with this clinical presentation. There was not a statistically significant difference between the number of years in practice for 77 hematologists-oncologists who selected observation versus the 5 who selected corticosteroid treatment ($P = 0.618$).

For a 28-year-old woman with a new diagnosis of ITP, a platelet count of 9000/μL and moderate bleeding symptoms, 62 (76%) hematologists-oncologists selected treatment with daily oral prednisone (Table 5). Neither guideline had a strong recommendation for management of a patient with this clinical presentation. There was not a statistically significant difference between the number of years in practice for the 62 hematologists-oncologists who selected daily oral prednisone versus those who chose other treatment options (high-dose dexamethasone, 17; IVIg, 3) ($P = 0.598$).

For a 28-year-old woman who had persistent severe and symptomatic thrombocytopenia with a platelet count of 9000/μL after failing 3 months of treatment with corticosteroids and IVIg, 32 (39%) of hematologists-oncologists selected splenectomy (recommended by the ASH guideline but not by the ICR), 30 (37%) selected rituximab and 13 (16%) selected TPO-receptor agonists (both treatments recommended by the ICR but not by the ASH guideline). Hematologists-oncologists who had been in practice for more than 20 years selected splenectomy more often than other treatment options, and they selected splenectomy more often than hematologists-oncologists who had been in practice for 20 years or less. There was a significant difference between the number of years in practice for those who selected splenectomy versus all other treatment options ($P = 0.047$) (Table 6).

DISCUSSION

Management of patients with ITP is changing with the availability of new treatments and new concepts of when treatment is appropriate. These changes stimulated the development of new clinical practice guidelines for ITP that were published in 2010 and 2011.^{8,9} Although clinical practice guidelines provide evidence-based recommendations, they may have limited influence on physicians' practice.^{10–13} To document how physicians describe their management of ITP in Oklahoma, we

TABLE 4. An adult with incidentally discovered asymptomatic thrombocytopenia

| Management choice | Responses | Years in practice | | |
|---|-----------|-------------------|------|-----|
| | | <5 | 5–20 | >20 |
| Anti-D (Win-Rho) | 0 | 0 | 0 | 0 |
| Corticosteroids (daily oral prednisone) | 5 | 1 | 3 | 1 |
| Corticosteroids (intermittent high-dose dexamethasone) | 0 | 0 | 0 | 0 |
| IVIg | 0 | 0 | 0 | 0 |
| Observation with no drug treatment (watchful waiting) | 77 | 23 | 27 | 27 |
| Rituximab | 0 | 0 | 0 | 0 |
| Thrombopoietin-receptor agonists (Nplate [romiplostim], Promacta [eltrombopag]) | 0 | 0 | 0 | 0 |
| Other (describe): _____ | 0 | 0 | 0 | 0 |

Survey question 1. An active healthy, nonpregnant 28-year-old woman is discovered on a routine evaluation to have a platelet count of 40,000/μL. She has no symptoms of bruising, and her menstrual periods have been normal. Her complete blood count and smear review are otherwise normal, and her blood group is A+. What is your management choice?

No strong recommendations by either the ICR⁸ or the ASH⁹ guideline.

TABLE 5. An adult with a new diagnosis of ITP and moderate bleeding symptoms

| Management choice | Responses | Years in practice | | |
|---|-----------|-------------------|------|-----|
| | | <5 | 5–20 | >20 |
| Anti-D (Win-Rho) | 0 | 0 | 0 | 0 |
| Corticosteroids (daily oral prednisone) | 62 | 17 | 22 | 23 |
| Corticosteroids (intermittent high-dose dexamethasone) | 17 | 6 | 6 | 5 |
| IVIg | 3 | 1 | 2 | 0 |
| Observation with no drug treatment (watchful waiting) | 0 | 0 | 0 | 0 |
| Rituximab | 0 | 0 | 0 | 0 |
| Thrombopoietin-receptor agonists (Nplate [romiplostim], Promacta [eltrombopag]) | 0 | 0 | 0 | 0 |
| Other (describe): _____ | 0 | 0 | 0 | 0 |

Survey question 2. An active healthy, nonpregnant 28-year-old woman presents with spontaneous minor bruising and moderately prolonged menses for 2 months. She has a few areas of scattered petechiae and several small bruises on her arms and legs. Her platelet count is 9000/ μ L. Her complete blood count and smear review are otherwise normal, and her blood group is A+. What is your management choice?

No strong recommendations by either the ICR⁸ or the ASH⁹ guideline.

sent surveys to all hematologists-oncologists in Oklahoma. The response rates were high: 92% of the 13 pediatric hematologists-oncologists and 81% of the 101 adult hematologists-oncologists returned their surveys. We then compared the hematologists-oncologists' reported management to the recommendations of the 2 recent clinical practice guidelines.^{8,9}

An important issue for the management of children with a new diagnosis of ITP is whether observation with no drug treatment is appropriate for children with only minor purpura, regardless of the platelet count. Both recent guidelines recommended this management.^{8,9} In our survey, 5 (42%) pediatric hematologists-oncologists selected observation with no drug treatment for a child with a new diagnosis of ITP, a platelet count of 8000/ μ L and only minor bleeding. Although this result may suggest a shift from a previous survey of U.S. practice in which only 16% of pediatric hematologists-oncologists managed these children with observation with no drug treatment,^{2,14} it remains less than management of ITP in the United Kingdom, where 84% of children are

managed by pediatric hematologists with observation.¹⁵ The difference between our survey responses and guideline recommendations reflects the strong opinions regarding management of these children by observation alone versus drug treatment. An analysis of pediatric hematologists' opinions regarding observation alone versus drug treatment for a child presenting with only minor purpura concluded that their opinions would not be influenced by any practical clinical trial.¹⁶

Although splenectomy was recommended by the ASH guideline for a child with symptomatic chronic ITP, rituximab and TPO-receptor agonists were the treatments selected by 10 (83%) pediatric hematologists-oncologists. Rituximab and splenectomy was recommended by the ICR.⁸ Because TPO-receptor agonists are not currently approved by the FDA for use in children, they were not addressed by the guidelines. In our survey, this option was qualified by the statement, "if approved and available for use in children." The selection of TPO-receptor agonists by 4 (33%) pediatric hematologists-oncologists suggests that the use of these agents may be readily accepted after approval.

TABLE 6. An adult with symptomatic ITP who has failed to achieve a durable response with corticosteroids and IVIg

| Management choice | Responses | Years in practice | | |
|--|----------------|-------------------|------|-----|
| | | <5 | 5–20 | >20 |
| Anti-D (Win-Rho) | 6 | 1 | 3 | 2 |
| Corticosteroids (intermittent high-dose dexamethasone) | 0 | 0 | 0 | 0 |
| IVIg | 0 | 0 | 0 | 0 |
| Observation with no drug treatment (watchful waiting) | 0 | 0 | 0 | 0 |
| Rituximab ^a | 30 | 11 | 12 | 7 |
| Splenectomy ^b | 32 | 8 | 8 | 16 |
| Thrombopoietin-receptor agonists (Nplate [romiplostim], Promacta [eltrombopag]) ^c | 13 | 4 | 7 | 2 |
| Other (describe): _____ | 1 ^d | 0 | 0 | 1 |

Survey question 3. An active healthy, nonpregnant 28-year-old woman initially presented with a platelet count of 9,000/ μ L, which increased to 170,000/ μ L with corticosteroid treatment, which was then tapered and discontinued. When corticosteroid treatment was stopped 3 months later, epistaxis and mucosal bleeding developed associated with a platelet count of 9,000/ μ L. She was treated with corticosteroids and IVIg. She is uncomfortable with the side effects of corticosteroids. Although IVIg was effective for short times, it failed to maintain her platelet count at a level that controlled bleeding. Her complete blood count and smear review are otherwise normal, and her blood group is A+. What is your management choice?

^a Management recommended by the ICR: grade B.⁸

^b Management recommended by ASH guideline: grade 1B.⁹

^c Management recommended by the ICR: grade A.⁸

^d Other response: "I offer both splenectomy and a TPO agent and discuss the options with the patient."

The decision for initiating treatment for adults with a new diagnosis of ITP is typically based on the platelet count. Although neither current ITP guideline made a strong recommendation for initial treatment of adults, the hematologists-oncologists' responses were consistent with their text statements.^{8,9}

The availability of rituximab and the approval of the TPO-receptor agonists have substantially changed the management of adults who require treatment following the failure of initial corticosteroid treatment to establish a durable remission.⁵ The 2 current practice guidelines have different recommendations for second-line treatment: the ICR recommends TPO-receptor agonists and rituximab but not splenectomy; the ASH guideline recommends splenectomy but not TPO-receptor agonists or rituximab. For the clinical scenario addressing this issue in our survey, 39% of hematologists-oncologists selected splenectomy, 37% selected rituximab and 16% selected TPO-receptor agonists. The different treatment choices of the Oklahoma hematologists-oncologists and the different recommendations by the 2 current practice guidelines reflect the changing clinical practice. Hematologists-oncologists who had been in practice for more than 20 years were more likely to select splenectomy. This may be consistent with greater acceptance of newer treatments by younger hematologists-oncologists.

There are multiple limitations for these data. 1) The number of hematologists-oncologists was small, especially for pediatric hematologists-oncologists. 2) Oklahoma has a small population (3,791,508 in July 2011) and 1 university medical center, which may limit the diversity of clinical practice. The diversity of clinical practice may also have been limited by the large fraction of hematologists-oncologists who practice at OUMC and the many adult community hematologists-oncologists who had trained at OUMC. 3) Survey data of physicians' clinical practice decisions have inherent limitations compared with actual audits of physicians' records.^{10,13} In this survey, hematologists-oncologists may have considered which treatment option was "correct" and which option they commonly select in their practice. The concern for the correct response may have been increased because one of the authors (J.N.G.) has been influential in Oklahoma regarding management of ITP. 4) Finally, these data may not be generalizable because there are many examples of geographic variations of clinical practice across the United States.¹⁷

However, the strength of these observations is that it provides for the first time an estimate of actual current clinical management of patients with ITP. Although these data may not be generalizable, the high survey response rate provides confidence that these data accurately reflect the judgment, if not the actual practice, of Oklahoma hematologists-oncologists. These data are novel because they provide insight into the judgment and practice of hematologists-oncologists who are caring for patients with ITP at a time when practice patterns are changing because of the availability of new agents, because of extensive marketing of the TPO-receptor agonists and because of changes in the U.S. health care system. These data are important because they provide the first objective measure of the reported practice of most hematologists-oncologists within a defined geographic region. They provide a basis for serial surveys to document evolution of treatment patterns across time and a basis for surveys of hematologists-oncologists across different regions of the United States and other countries with different health care systems.

These data also provide a basis for comparing practice patterns with patient outcomes.

REFERENCES

1. **George JN, Woolf SH, Raskob GE, et al.** Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. *Blood* 1996;88:3–40.
2. **Vesely SK, Buchanan GR, Adix L, et al.** Self-reported initial management for childhood idiopathic thrombocytopenic purpura: results of a survey of members of the American Society of Pediatric Hematology/Oncology-2001. *J Pediatr Hematol/Oncol* 2003;25:130–133.
3. **Arnold DM, Dentali F, Crowther MA, et al.** Systematic review: efficacy and safety of rituximab for adults with idiopathic thrombocytopenic purpura. *Ann Intern Med* 2007;146:25–33.
4. **Patel VL, Mahévas M, Lee SY, et al.** Outcomes 5 years after response to rituximab therapy in children and adults with immune thrombocytopenia. *Blood* 2012;119:5989–5995.
5. **Ghanima W, Godeau B, Cines DB, et al.** How I treat immune thrombocytopenia: the choice between splenectomy or a medical therapy as a second-line treatment. *Blood* 2012;120:960–969.
6. **Kuter DJ, Rummel M, Boccia R, et al.** Romiplostim or standard care in patients with immune thrombocytopenia. *N Eng J Med* 2010;363:1889–1899.
7. **Cheng G, Saleh MN, Marcher C, et al.** Eltrombopag for management of chronic immune thrombocytopenia (RAISE): a 6-month, randomized, phase 3 study. *Lancet* 2011;377:393–402.
8. **Provan D, Stasi R, Newland AC, et al.** International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood* 2010;115:168–186.
9. **Neunert CE, Lim W, Crowther MA, et al.** The American Society of Hematology 2011 evidenced-based practice guideline for immune thrombocytopenia. *Blood* 2011;117:4190–4207.
10. **Leaf DA, Neighbor WE, Schaad D, et al.** A comparison of self-report and chart audit in studying resident physician assessment of cardiac risk factors. *J Gen Intern Med* 1995;10:194–198.
11. **Rätsep A, Kalda R, Oja I, et al.** Family doctors' knowledge and self-reported care of type 2 diabetes patients in comparison to the clinical practice guideline: cross-sectional study. *BMC Fam Pract* 2006;7:36–43.
12. **Prior M, Guerin M, Grimmer-Somers K.** The effectiveness of clinical guideline implementation strategies—a synthesis of systematic review findings. *J Eval Clin Pract* 2008;14:888–897.
13. **Seymann GB, Francesco LD, Sharpe B, et al.** The HCAP gap: differences between self-reported practice patterns and published guidelines for health care-associated pneumonia. *Clin Infect Dis* 2009;49:1868–1876.
14. **Vesely SK, Buchanan GR, George JN, et al.** Self-reported diagnostic and management strategies in childhood idiopathic thrombocytopenic purpura: Results of a survey of practicing pediatric hematology/oncology specialists. *J Pediatr Hematol Oncol* 2000;22:55–61.
15. **Grainger JD, Rees JL, Reeves M, et al.** Changing trends in the UK management of childhood ITP. *Arch Dis Child* 2012;97:8–11.
16. **Lehmann HP, Dambita N, Buchanan GR, et al.** ITP Decision Group of the TMH Pediatric Subcommittee. Decision modeling of disagreements: pediatric hematologists' management of idiopathic thrombocytopenic purpura. *Med Decis Making* 2011;31:805–815.
17. **Zuckerman S, Waidmann T, Berenson R, et al.** Clarifying sources of geographic differences in medicare spending. *N Eng J Med* 2010;363:54–62.