ONKOLOGIE

Original Article · Originalarbeit

Onkologie 2012;35:342–348
DOI: 10.1159/000338935

Published online: May 22, 2012

A Retrospective Observational Single-Centre Study on the Burden of Immune Thrombocytopenia (ITP)

Matthaeus Bauer[a] Anja Baumann[b] Karin Berger[c] Birgit Ackermann[d]
Rita Shlaen[d] Dorothee Schopohl[c] Helmut Ostermann[b]

[a]Dept. of Medical Management,
[b]Dept. of Haematology/Oncology,
[c]Dept. of Transfusion Medicine and Haemostasis, University Hospital of Munich,
[d]IMS Health, Health Economics and Outcomes Research, Munich, Germany

Keywords

Adult patients · Costs · Immune thrombocytopenia · ITP · Resource consumption · Treatment

Summary

Background: German data on economic consequences of immune thrombocytopenia (ITP) are limited. **Patients and Methods:** A retrospective, observational study based on chart review of adult patients with a confirmed diagnosis of ITP was conducted at a German university hospital. Costs are presented from the hospital perspective. **Results:** Of 50 eligible patients, 45 could be classified by disease duration: 19 patients < 3 months (38%, newly diagnosed ITP), 12 patients ≥ 3 to < 12 months (24%, persistent ITP), 19 patients ≥ 12 months (38%, chronic ITP). Complications included 85 bleeding events in 43 patients, including 3 intracranial haemorrhages. Documented were 955 outpatient visits in 43 patients (86%) and 92 inpatient hospital admissions in 45 patients (90%). Of the 46 patients (92%) treated, all received corticosteroids, 25 (50%) intravenous immunoglobulin, and 7 (14%) further therapies. 12 patients (24%) underwent splenectomy. Average total direct medical costs (mean (standard deviation)) were €17,091 (€18,859) per patient, €12,749 (€11,663) in 17 newly diagnosed ITP patients with a 0.88-month (0.65 months) average disease duration, and €29,868 (€29,397) in 13 chronic ITP patients with a 33.5-month (16.8 months) average disease duration. Inpatient stays were the main cost drivers. **Conclusion:** These data concerning current healthcare provision for ITP patients in Germany indicate considerable resource consumption and the need for more effective treatment options in individual patients.

Schlüsselwörter

Erwachsene Patienten · Kosten · Immunthrombozytopenie · ITP · Ressourcenverbrauch · Behandlung

Zusammenfassung

Hintergrund: Deutsche Daten zu den ökonomischen Konsequenzen der Immunthrombozytopenie (ITP) fehlen weitgehend. **Patienten und Methoden:** Eine retrospektive Beobachtungsstudie anhand der Krankenakten erwachsener Patienten mit gesicherter ITP-Diagnose wurde an einer deutschen Universitätsklinik durchgeführt. Die Kostendarstellung erfolgte aus der Krankenhausperspektive. **Ergebnisse:** Von 50 auswertbaren Patienten konnten 45 nach der Krankheitsdauer klassifiziert werden: 19 Patienten < 3 Monate (38%, neu diagnostizierte ITP), 7 Patienten ≥ 3 bis < 12 Monate (14% persistierende ITP), 19 Patienten ≥ 12 Monate (38%, chronische ITP). Komplikationen umfassten 85 Blutungsereignisse bei 43 Patienten, einschließlich dreier intrakranieller Blutungen. Dokumentiert wurden 955 ambulante Arztbesuche bei 43 (86%) und 92 Krankenhauseinweisungen bei 45 Patienten (90%). Von 46 behandelten Patienten (92%) erhielten alle Kortikosteroide, 25 (50%) intravenöse Immunglobuline und 7 (14%) weitere Therapien. 12 Patienten (24%) wurden splenektomiert. Die durchschnittlichen direkten medizinischen Gesamtkosten (Mittelwert (Standardabweichung)) betrugen € 17 091 (€ 18 859) pro Patient, € 12 749 (€ 11 663) bei 17 neu diagnostizierten ITP-Patienten mit 0,88 Monaten (0,65 Monate) durchschnittlicher Krankheitsdauer und € 29 868 (€29 397) bei 13 Patienten mit chronischer ITP mit 33,5 Monaten (16,8 Monate) durchschnittlicher Krankheitsdauer. Hauptkostentreiber waren Krankenhausaufenthalte. **Schlussfolgerungen:** Diese Daten über die gegenwärtige Gesundheitsversorgung von ITP-Patienten in Deutschland zeigen einen erheblichen Ressourcenverbrauch und unterstreichen daher die Notwendigkeit effektiverer Behandlungsoptionen für einzelne Patienten.

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Prof. Dr. Helmut Ostermann
Klinikum der Universität München
Medizinische Klinik und Poliklinik III
Marchioninistraße 15, 81377 München, Germany
Tel. +49 89 7095603-8, Fax -9
Helmut.Ostermann@med.uni-muenchen.de

Introduction

Immune thrombocytopenia (ITP) is characterized by a reduced number of platelets in the circulating blood (platelet count less than 100×10^9/l) [1–3]. The diagnosis of ITP can be established only after other causes of thrombocytopenia, such as leukaemia, myelodysplasia, aplastic anaemia, infections including human immunodeficiency virus (HIV), hepatitis C or *Helicobacter pylori*, and drug-induced immune reactions have been ruled out [4]. The annual incidence of ITP in Northern Europe is estimated to be 2.7 cases per 100,000 and tends to increase with age [5]. In the age group between 30 and 60 years, a preponderance of women is found [4, 5].

Historically, the pathogenesis of ITP has been attributed solely to platelet autoantibody production and subsequent platelet destruction [6]. Recent findings support involvement of impaired platelet production as an additional cause for thrombocytopenia. Suppression of megakaryopoiesis by autoantibodies and dysfunction in the regulation of thrombopoietin (TPO) synthesis give rise to impaired thrombopoiesis [7]. The clinical course of ITP shows high variability in duration and severity, and response to most conventional therapeutic strategies remains largely unpredictable. Treatment is clearly indicated in patients with platelet counts below 30×10^9/l and presence of active bleeding [4, 8, 9]. Corticosteroids are the standard initial treatment for newly diagnosed patients [1, 4]. Intravenous immunoglobulin (IV IG) is also a recommended first-line treatment strategy with an expected shorter time to response and possible enhancement of response if given together with corticosteroids [1, 4]. Second-line treatment options for adult ITP patients include various immunosuppressants, splenectomy, and the TPO receptor agonists romiplostim and eltrombopag. TPO receptor agonists stimulate platelet production and enable patients to discontinue an often long-term immunosuppressive therapy [1, 4, 10]. Therapeutic decisions for individual ITP patients, particularly those with chronic ITP, often have to be made considering bleeding history, potential risks of different therapies, the patient's age, pre-existing diseases, and lifestyle [3, 4].

To date, no information is available on treatment patterns and costs for ITP patients in Germany. Therefore, we conducted a retrospective, single-centre, observational study to describe therapeutic characteristics of these patients in Germany. A large referral centre was chosen to study the course of the disease and its clinical management, as well as resource consumption and costs in a group of adult patients with ITP.

Patients and Methods

A retrospective, observational, single-centre study of ITP was conducted in the Department of Haematology/Oncology at the University Hospital of Munich, Germany. Inclusion criteria for eligible patients were a minimum age of 18 years, first diagnosis of ITP between 1 January 2000 and 31 December 2007, and either inpatient or outpatient treatment in the hospital during this time period. Diagnosis of ITP had to be established by a platelet count below 100×10^9/l and exclusion of other reasons for secondary ITP (e.g., the presence of chronic lymphocytic leukaemia, myelodysplastic syndrome or any other active malignancy, as well as thrombocytopenia associated with drug intake). Study approval by the local ethics committee was obtained. 2 databases available at the hospital site were screened to identify eligible patients, one reporting diagnosis-related groups (DRGs) and one containing discharge letters of all patients treated at the Department of Haematology. Search terms were as follows: ITP, Morbus Werlhof, immune thrombocytopenia, and thrombocytopenia. Exclusion of patients with a diagnosis of thrombocytopenia other than ITP and subsequent data collection was based on chart review. The first visit of a patient to the hospital as an in- or outpatient after 1 January 2000 was defined as the start of the observation period for the individual ITP patient enrolled in the study. The end of the individual observation period of each ITP patient was either the date of her or his last visit to the hospital as an in- or outpatient or the end of the study on 31 July 2008. Information about patient characteristics, platelet counts, complications, treatment, and resource utilization during inpatient hospital stays and outpatient visits was abstracted for each patient by 1 investigator (A.B.) using a standardized study form. Pre-existing diseases not related to thrombocytopenia were also recorded. Data were entered in a Microsoft Access database. A bleeding event was defined as presentation at the hospital or to an office-based physician with bleeding and could include bleeds at several sites. All infections reported in patient records during the observation period and all wound infections having occurred after splenectomy were included.

Cost Analysis

Direct medical costs were evaluated from the hospital provider's (HP) perspective. Unit costs for diagnostics, medication, hospitalization, and hospital outpatient care were provided by the controlling department of the university hospital for the year 2008. Because of the chronic, yet episodic and relapsing nature of ITP, costs were calculated as average costs per patient after evaluation of total ITP-related costs for each patient accumulated during his or her individual observation period. Costs were stratified according to the revised definitions of Rodeghiero et al. [3] as costs for 'newly diagnosed ITP' defined by a new diagnosis of ITP less than 3 months ago, 'persistent ITP' with disease duration from first diagnosis of ITP of ≥ 3 to < 12 months, and 'chronic ITP' with disease duration of ≥ 12 months [3].

Statistical Analysis

Data were analyzed with SAS software version 9.1 (SAS Institute Inc., Cary, NC, USA). Descriptive statistics were calculated by reporting frequency distributions of study parameters as well as means, standard deviations (SD), and medians.

Results

Database screening provided 194 patients of whom 144 patients were not eligible for the study because of other reasons for thrombocytopenia and 50 patients with ITP were included for evaluation. The median age of eligible patients was 55.5 years at the first ITP-related visit to the hospital (interquartile range 34–71 years) (table 1), whereby female patients were on average younger than male patients (29 female patients, median age 43.0 years, interquartile range 34–66 years, not normally distributed versus 21 male patients, median age 61 years, interquartile range 45–71 years, normally distributed). In 45 patients (90%), the start of the observation

period with the first visit to the hospital was also the date of the first ITP diagnosis. The remaining 5 patients had a first diagnosis of ITP after 1 January 2000, but had been diagnosed elsewhere 1, 7, 21, 31, and 35 months, respectively, before their first visit to this hospital and therefore did not have a complete dataset for resource consumption and costs for the whole disease duration. At the time of the first visit to the hospital, 42 patients (84%) suffered from additional, not thrombocytopenia-related pre-existing diseases, mainly cardiovascular, endocrine, and genitourinary (38, 36, and 32%, respectively) (table 1). A total of 33 patients (66%) presented on their first visit to the hospital with platelet counts $\leq 10 \times 10^9$/l, 12 patients (24%) with platelet counts > 10 to $\leq 30 \times 10^9$/l, and 5 patients (10%) with platelet counts > 30 to $\leq 100 \times 10^9$/l. At the end of the observation period, 32 patients (64%) had platelet counts $> 100 \times 10^9$/l, 15 patients (30%) had platelet counts of > 30 to $\leq 100 \times 10^9$/l, and 3 patients had platelet counts of only > 10 to $\leq 30 \times 10^9$/l (table 1). The average length of the observation period per patient was 15 ± 18 months (mean ± SD) (median 5 months, minimum 0.2, maximum 72).

Table 1. Patient characteristics and complications

Age, median (range), years	
Total	55.5 (18–92)
Female	43.0 (18–84)
Male	61.0 (18–92)
Total patients, n (%)	50 (100)
	n (%)
Sex	
Female	29 (58)
Male	21 (42)
Platelet count	
Start[a]	
$\leq 10 \times 10^9$/l	33 (66)
> 10 to $\leq 30 \times 10^9$/l	12 (24)
> 30 to $\leq 100 \times 10^9$/l	5 (10)
$> 100 \times 10^9$/l	–
End[b]	
$\leq 10 \times 10^9$/l	–
> 10 to $\leq 30 \times 10^9$/l	3 (6)
> 30 to $\leq 100 \times 10^9$/l	15 (30)
$> 100 \times 10^9$/l	32 (64)
Pre-existing diseases	
Total patients	42 (84)
Cardiovascular	19 (38)
Endocrine	18 (36)
Genitourinary	16 (32)
Immunologic	13 (26)
Neuropsychiatric	13 (26)
Gastrointestinal	13 (26)
Complications during the course of ITP	
Bleeding events (n)	
Total patients (122)	43 (86)
Purpura/petechiae (53)	35 (70)
Epistaxis (19)	11 (22)
Bruising (13)	11 (22)
Gastrointestinal (9)	8 (16)
Oral bleeding (8)	6 (12)
Haematuria (8)	5 (10)
Menorrhagia (4)	4 (8)
Intracranial (3)	3 (6)
Surgery associated (4)	3 (6)
Muscular (1)	1 (2)
Infections (n)	
Total patients (20)	12 (24)
Respiratory (10)	5 (10)
Wound infection (4)	3 (6)
Dermatologic (1)	1 (2)
Cardiovascular (1)	1 (2)
Unknown (4)	2 (4)

[a]Lowest platelet count measured at the start of the observation period. Of the 5 patients with platelet counts > 30 to ≤ 100, 1 had already received steroids, 3 stayed without treatment, and 1 had a platelet count of 33×10^9/l.
[b]Last platelet count obtained at the end of the observation period.
ITP = Immune thrombocytopenia.

Complications

In 43 patients (86%) with bleeding (table 1), a total of 85 bleeding events were observed. Since each bleeding event could include several sites of bleeding at a particular point in time, the 85 bleeding events consisted of 122 bleedings classified in table 1 according to location. Purpura/petechiae prevailed with 53 cases, followed by 19 cases of epistaxis. 3 patients experienced intracranial haemorrhage. Of the 85 bleeding events, 20 (23.5%) required transfusion or other therapeutic and/or diagnostic intervention, e.g. craniotomy or emergency gastroscopy. 12 patients (24%) experienced infectious complications during the observation period (table 1). A total of 20 infections were observed with an average duration of 8.7 ± 6.4 days (mean ± SD), 16 under immunosuppressive therapy and 4 wound infections after splenectomy. 3 infections required hospitalization. 1 82-year-old patient with multiple (not ITP-related) pre-existing diseases, who was treated with steroids and IV IG, died early in the course of disease from sepsis as could be confirmed by post mortem examination.

Resource Consumption

Table 2 contains data on resource consumption during the observation period. A total of 45 patients were hospitalized, with a mean of 2 admissions per person and a total of 92 ITP-related inpatient admissions. A first diagnosis of ITP was made during 37 of these inpatient admissions (40%). For 19 admissions to the hospital (21%), the ITP-related reasons were diverse, including 4 relapses, 2 rehabilitations, 2 adverse events, 1 plastic surgery of the skullcap after intracranial haemorrhage, complications after splenectomy, and infections. Overall, 955 outpatient visits were documented, 752 were to the hospital outpatient ward, and 203 were visits to office-based physicians. The most common reasons for ITP-related outpatient visits were check-ups during therapy (50%) or routine monitoring of blood count before or after therapy (33%). 26 patients (52%) were tested for platelet antibodies, and 50% of the tests (17 of 34) were positive (table 2).

Duration of ITP

A total of 19 patients (38%) had a duration of ITP after diagnosis for less than 3 months and therefore had newly diagnosed ITP by the revised definitions of Rodeghiero et al.

Table 2. Resource consumption during the observation period

Inpatient admissions in 45 patients, n (%)	92 (100)
Admissions per patient[a], n	2 ± 1.7
Length of stay[a], days	12 ± 9
Reason for ITP-related admission, n (%)	
Initial diagnosis of ITP	37 (40)
Splenectomy	9 (10)
Consultation	6 (7)
Intravenous drug administration	9 (10)
Emergency visit due to bleeding	12 (13)
Other reasons	19 (21)
Outpatient visits in 43 patients[b], n (%)	955 (100)
Visits per patient[a], n	22.2 ± 24.5
Reason for ITP-related outpatient visit, n (%)	
Check-up during therapy	476 (50)
Monitoring blood count (no therapy)	311 (33)
Consultation	39 (4)
Intravenous drug administration	19 (2)
Emergency visit due to bleeding	15 (2)
Other reasons	95 (10)
Diagnostic procedures (tests per patient[a]), n (%)	
Platelet count (34.5 ± 33.3)	50 (100)
Antibody testing (1.3 ± 0.8)	26 (52)
Bone marrow biopsies (2.8 ± 1.3)	36 (72)
X-ray (2.1 ± 2.2)	28 (56)
Ultrasound (2.2 ± 1.9)	41 (82)
Computer tomography (2.8 ± 2.4)	20 (40)
Magnetic resonance tomography (2.2 ± 0.8)	6 (12)
Bone density scan (1 ± 0)	4 (8)

[a]Mean ± standard deviation.

[b]Including hospital outpatient visits and visits to office-based physicians.

Table 3. Duration of immune thrombocytopenia (ITP) after first diagnosis and treatment

	Patients, n (%)	Active treatment at end of observation period yes/no, n
Duration of ITP, months		
< 3	19 (38)	17/2
≥ 3 to < 12	12 (24)	5/7
≥ 12	19 (38)	4/15
Treatment		
None	4 (8)	
Corticosteroids	46 (92)	
IV IG	25 (50)	
Splenectomy	12 (24)	
Rituximab	5 (10)	
Cyclophosphamide	2 (4)	
Vinca-loaded platelets[a]	2 (4)	
Azathioprine	2 (4)	
ITP related transfusions (units/patient, mean ± SD)		
Total	17 (34)	
Packed red cells (3.8 ± 3.9)	9 (18)	
Platelets (3.8 ± 4.8)	13 (26)	
Fresh frozen plasma (9)	1 (2)	

[a]Platelets loaded with the vinca alkaloid vincristine [11].

IV IG = Intravenous immunoglobulin; SD = standard deviation.

[3] (table 3). 12 patients (24%) had an observation time of ≥ 3 to < 12 months from the first diagnosis of ITP. 7 of them (14%), who recovered between 3 and 12 months, were termed persistent ITP and compared to acute and chronic ITP. The other 19 patients (38%) had chronic ITP with the disease lasting longer than 12 months [2]. 4 of these patients were still on active treatment at the end of the observation period (table 3).

Treatment

A total of 4 patients received no therapy but regular controls only, 1 of these patients having ITP during pregnancy (table 3). Steroid therapy was suggested to this patient before delivery, but she refused treatment.

All 46 patients (92%) with drug treatment of ITP received corticosteroids as a standard initial treatment. 25 patients (50%) received IV IG in addition, and 7 patients (14%) obtained further drug therapies including 2 patients treated with platelets loaded with the vinca alkaloid vincristine (vinca-loaded platelets [11]) (table 3). Most patients were treated starting with 1–1.5 mg/kg/day prednisone only, either with fast or slow tapering off of the dose. 5 patients (10%) obtained several cycles of high-dose dexamethasone (40 mg/day for 4 days). Corticosteroid therapy was given in 22 patients (44%) with a maximum continuous duration of 17 ± 10 days (mean ± SD; median 15, range 4–36), in 14 patients (28%) during 16 episodes for 134 ± 36 days (mean ± SD; median 148, range 65–179) with gradual tapering off of the dose until complete cessation, and in 9 patients (18%) during 11 long-term episodes with a mean duration of 362 ± 289 days (mean ± SD; median 277, range 50–1,049). 1 patient had received corticosteroid therapy before the first visit to this hospital.

A total of 12 patients (24%) underwent splenectomy, and in 1 patient 2 surgeries were performed because of accessory splenic tissue (table 3). The mean time interval between ITP diagnosis and splenectomy was 18.7 ± 20.5 months (mean ± SD; median 10.8, range 1–64; data not shown), whereby 6 patients underwent splenectomy early in the course of disease between > 1 month and ≤ 1 year, and 6 patients late between > 1 year until up to 5.4 years after diagnosis. 5 patients (42% of all splenectomised patients) received further drug treatments after splenectomy.

A total of 17 patients (34%) received transfusions of packed red cells, platelets, or fresh frozen plasma (table 3). 3 of these patients received platelets in preparation for splenectomy.

Costs

The average total direct medical cost per patient associated with ITP during the individual observation period was €17,091 ± €18,859 (n = 50; mean ± SD) from the HP perspective (table 4), with over 90% of those costs (€15,710 ± €18,068; n = 50) attributable to inpatient care. Average costs for outpatient care comprised €1,381 ± €1,988 (n = 50). The average cost per inpatient admission in our sample (n = 92) was €8,519 from the HP perspective. In total, the mean direct cost per patient (n = 45) for an inpatient stay amounted to €17,455, and the mean cost per patient (n = 39) for an outpa-

Table 4. Direct medical costs per patient associated with immune thrombocytopenia (ITP) and accumulated during the individual observation period calculated from the hospital provider's perspective

	Costs, €	
	mean ± SD	median (range)
Cost for patients with inpatient admissions (n = 45)		
Hospital care and laboratory	9,658 ± 7,972	6,879 (1,810–32,776)
Splenectomy	757 ± 1,324	0 (0–5,239)
Radiology	259 ± 364	148 (0–1,872)
Bone marrow biopsies	316 ± 468	211 (0–1,933)
Transfusion	618 ± 1,918	0 (0–12,275)
Drug therapy	5,847 ± 10,713	295 (0–65,308)
Total	17,455 ± 18,231	11,143 (1,858–97,893)
Cost for patients with hospital outpatient visits (n = 39)		
Outpatient care and laboratory	1,543 ± 1,821	1,040 (80–8,160)
Radiology	84 ± 172	0 (0–806)
Bone marrow biopsies	144 ± 406	0 (0–1,722)
Total	1,771 ± 2,095	1,120 (80–8,296)
Cost per patient including inpatient admissions and hospital outpatient visits (n = 50)		
Total	17,091 ± 18,859	10,650 (1,188–105,701)

SD = Standard deviation.

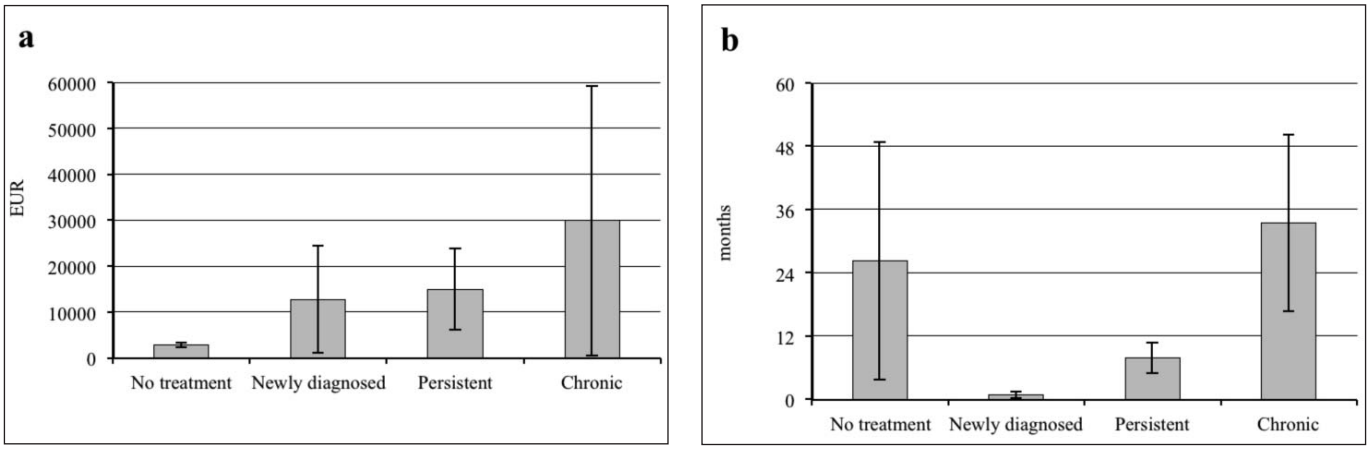

Fig. 1. Costs (**a**) and duration (**b**) of immune thrombocytopenia (ITP). Mean direct medical costs from the perspective of the hospital provider are given. Bars represent standard deviation. Patients were classified according to treatment and duration: 4 patients with ITP and no treatment; 17 patients with newly diagnosed ITP, 6 patients with persistent ITP, and 13 patients with chronic ITP, all receiving treatment. Newly diagnosed ITP is defined by a new diagnosis of ITP less than 3 months ago, persistent ITP by disease duration of ≥ 3 to < 12 months, and chronic ITP by a duration of ≥ 12 months [3]. Only patients with a complete data set, i.e. first diagnosis of ITP in this hospital, and complete cost data could be included. For persistent ITP, cessation of treatment and normalisation of platelet counts after < 12 months following first diagnosis was an additional requirement.

tient visit to €1,771 (table 4). The highest mean costs arose from hospital care including laboratory tests with €9,658 and drug therapy with €5,847 for inpatient admissions, and from hospital outpatient care and laboratory tests with €1,543 for outpatient visits (table 4).

Average costs for the 12 splenectomised patients were €39,490 ± €22,020 (mean ± SD; median €32,649, range €17,235–105,235) compared to average costs of €10,018 ± €9,850 for non-splenectomised patients (mean ± SD; median €7,769, range €1,188–56,904).

Stratification of the total direct medical costs from the HP perspective according to duration and treatment of ITP is shown in figure 1. Only patients with a complete data set, i.e. first diagnosis of ITP in this hospital, could be included. Average costs for the 4 patients without ITP-related treatment amounted to €2,877 ± €537 (mean ± SD; median €2,927, range €2,190–3,465). For the 17 patients with newly diagnosed ITP, average costs were €12,749 ± €11,663 (mean ± SD; median €8,446, range €2,243–45,605), and average follow-up was 0.88 months ± 0.65 months (mean ± SD; median 0.62 months, range 0.20–2.26 months). For the 6 patients with persistent ITP, average costs amounted to €14,899 ± €8,832 (mean ± SD; median €13,537, range €1,188–26,418), and average follow-up was 7.91 months ± 2.97 months (mean ± SD; median 7.85 months, range 4.33–11.25 months). For the 13 patients with chronic ITP, average costs were €29,868 ± €29,397 (mean ± SD; median €17,235, range €2,480–105,701), and average follow-up was 33.47 months ± 16.79 months (mean ± SD; median 35.44 months, range 13.54–72.30 months).

Discussion

Bleeding events and sepsis are the 2 major complications in ITP leading to an increased mortality rate [12, 13]. Our small group of 50 ITP patients comprised 3 patients with intracranial haemorrhage and 1 patient who died of sepsis. Our findings underscore the need to choose therapy to avoid fatal haemorrhage [1, 4, 9]. In addition, the risk of severe infection has to be considered especially in elderly patients with multiple pre-existing diseases. 2 major treatment options are associated with an increased risk of infection, immunosuppressive drug treatment and splenectomy. Standard initial treatment for newly diagnosed ITP is still corticosteroids [1, 4]. In a recent database study on the burden of illness of adult chronic ITP in the US, 96.5% of the patients who received pharmacologic therapy during the first 1–1.5 years of follow-up were treated with oral corticosteroids [14].

A relatively low rate of 24% for splenectomy (12 patients) was observed. 1 patient underwent 2 surgical procedures due to the presence of accessory splenic tissue as found in up to 12% of non-responding patients [9]. Splenectomy rates reported in other studies vary considerably (e.g., 12% [15] or 24% [16] or 58% [13]). Available study data on splenectomy show a consistent response rate of over 60%, and it is therefore an established treatment option with the goal of long-term remission [3, 17–19]. However, for the single ITP patient, outcome of splenectomy cannot be predicted [17]. Therefore, several authors propose a delay of several years before proceeding to splenectomy [16, 20, 21]. We have no information on whether additional reasons like refusal of the patient to undergo surgery or pre-existing diseases precluded splenectomy as a treatment option in some of the patients in our study. In the mean time, new treatment options have emerged with the TPO receptor agonists romiplostim and eltrombopag. TPO receptor agonists are highly effective and indicated for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy [1, 4, 10].

A considerable amount of ITP-related healthcare resources was used by the patients in our study, with the main cost drivers being inpatient hospital stays. Patients and their observation periods were heterogeneous, resulting in a broad variation of the total costs per patient (€1,188–105,701). Therefore, patients with treatment were classified. Newly diagnosed ITP patients used on average €12,749 ± €11,663 and these costs more than doubled for chronic ITP patients with an amount of €29,868 ± €29,397. The calculated average yearly costs for a chronic ITP patient in our study amount to €10,667, which is in the order of the mean cost per patient and year^{-1} of €7,293 evaluated for 57 patients with chronic ITP in a recent retrospective French study [22]. Average costs per ITP-related hospitalisation (n = 92) amounted to €8,519 from the HP perspective, which is considerably higher than the average costs per hospitalisation in German university hospitals with €5,238 [23].

In a large database study on hospitalisation costs for ITP patients in the US for the time period of 2003–2006, costs amounted to $16,476 (€13,347, 18/6/2010) compared to average costs from all hospitalisations in the US population during the same period with $10,039 (€8,132, 18/6/2010) [12]. The mean length of hospital stay in our small sample from a large referral centre was 12 days, which is almost twice as much as the average length of stay of ITP patients in the US database study with 6.4 days [12]. A considerable proportion of the patients in our study presented with severe ITP, namely clinically relevant bleeding [3]. Choosing a university hospital could therefore be a limitation of the study due to pre-selection of more severe ITP cases. Although the different healthcare systems of the US and Germany as well as the different study designs argue against a direct comparison, both studies show that hospitalisation for ITP is economically and clinically relevant. Overall consumption of healthcare resources might still have been underestimated in our study for the following reasons: Documentation of patients' office-based visits was not comprehensive. There was no defined minimum observation time after the first visit to the hospital because it was a retrospective study. More than half of the patients were still on therapy at the end of the study, and in 5 patients the first visit to the hospital was considerably later than the date of the first diagnosis of ITP.

The baseline demographics of our sample appear to be consistent with the ITP patient populations in other published studies [13, 15, 16]. However, a single-centre study does not allow extrapolation for the general situation regarding costs and resource consumption of ITP patients in Germany. There are additional limitations of our study partly caused by the heterogeneity of this rare disease and by the study design. The study was conducted retrospectively, and tests for HIV, hepatitis C or *H. pylori*, and serologies ruling out other autoimmune diseases were not part of routine clinical testing in all patients. The design was single-centre over a long time period in the past yielding only a small and heterogenous group of patients with a large proportion of newly diagnosed ITP patients. And finally, a standardized observation period and detailed data from office-based physicians were not available.

In conclusion, we have described for the first time current healthcare provision in routine clinical practice including treatment, resource consumption, and costs for a group of ITP patients in Germany. Different treatment options for this rare disease with their accompanying risks, episodes of bleeding and infection, and increasing age of the patients generate high costs. Further investigations are necessary to obtain a more complete picture of the total burden of ITP including a broader spectrum of hospitals and private practices, the patients' view of the disease affecting quality of life, patients' preferences, and last but not least new and effective treatment

options. Initial investigations have shown that the TPO receptor agonist romiplostim can enable patients to reduce or discontinue other ITP medications [24], and may therefore be a cost-effective treatment option for chronic ITP patients [25–27].

Acknowledgement

M. Bauer and A. Baumann contributed equally to this study. This study was sponsored by AMGEN EUROPE, Zug, Switzerland. The sponsor was not involved in the writing of the manuscript but was allowed to comment on the draft versions.

Disclosure Statement

M. Bauer and A. Baumann have no conflicts of interest. K. Berger, B. Ackermann, R. Shlaen, and D. Schopohl received research funding from Amgen. H. Ostermann recived honoraries for lectures/advisory boards and research funding from Amgen.

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