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Original article

Comparative net cost impact of the utilization of romiplostim and intravenous immunoglobulin for the treatment of patients with immune thrombocytopenia in Québec, Canada

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Abstract

Objectives:
Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by platelet destruction, sub-optimal platelet production, and mild-to-severe bleeding. Nplate® (romiplostim), a thrombopoietin receptor agonist, and intravenous immunoglobulin (IVIg), an expensive and occasionally scarce blood product, are used in the treatment of ITP. The objective of this study was to compare the total cost of treating patients with romiplostim vs IVIg in Québec, Canada.

Methods:
A net cost impact model was developed to calculate the annual cost of romiplostim compared with IVIg based on actual practice observations in all patients ($n = 95$) treated for chronic ITP with IVIg from April 2010 to March 2011 in two participating hospitals. The model included costs of: drug acquisition, drug preparation and administration, patient monitoring, and indirect costs. Healthcare practitioners were consulted regarding romiplostim and IVIg treatment algorithms and the resources involved in patient monitoring.

Results:
The average annual drug acquisition costs of romiplostim and IVIg were $48,024 and $98,868, respectively. Lower costs for drug preparation and administration ($309 vs $1245) and less time lost from work ($256 vs $2086) were attributed to romiplostim. The cost of follow-up monitoring was the same for both romiplostim and IVIg ($121). The total average annual per patient costs for romiplostim vs IVIg were, respectively, $48,710 and $102,320. The use of romiplostim was projected to save, on average, almost $54,000 per patient per year.

Limitations:
The study was conducted in two hospitals in Québec. Romiplostim may show different cost savings in other hospitals and other provincial and national jurisdictions.

Conclusions:
Scarce blood products must be used wisely. Romiplostim can allow for improved healthcare resource allocation by reserving IVIg for use in other areas of greater need while also providing cost savings for the overall provincial healthcare budget.

Introduction

Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by increased platelet destruction and sub-optimal platelet production, which results in low platelet counts and mild-to-severe bleeding[1]. Bleeding events may range from petechiae and purpura to severe intracranial and gastrointestinal haemorrhage[1,2]. The prevalence of diagnosed cases of chronic ITP in the overall population is reported to be 20.3 per 100,000[3] or 60,000 adults in the US[4]. An extrapolation to Québec would suggest that there would be ~1500 adults in Québec with chronic ITP. Approximately 0.4% of adult chronic ITP patients less than 40 years of age suffer from a fatal bleeding event each year; the incidence of fatal bleeds rises to 13% per year for patients greater than 60 years of age[5].

Therapeutic management of ITP includes the use of corticosteroids, immunosuppressive agents, and intravenous immunoglobulin (IVIg). Intravenous immunoglobulin is an expensive and, occasionally, scarce blood product. Surgical management includes splenectomy. Most recently, thrombopoietin (TPO) receptor agonists such as Nplate® (romiplostim) and Revolade® (eltrombopag) have been used to treat ITP[6].

The efficacy of romiplostim in the treatment of chronic ITP has been demonstrated in two pivotal parallel placebo-controlled studies of patients having a mean of three platelet counts $\leq 30 \times 10^9$/L[7]. In the pivotal trials, patients received subcutaneous (SC) doses of romiplostim or placebo every week for 24 weeks. Doses of medication were adjusted to maintain platelet counts between 50×10^9/L and 200×10^9/L. A statistically significantly greater proportion of splenectomized patients receiving romiplostim vs placebo achieved a durable response defined as a platelet count $\geq 50 \times 10^9$/L during 6 or more of the last 8 weeks of treatment (38.1% vs 0%; 95% CI = 23.4–52.8, $p = 0.0013$). A similar result was found with non-splenectomized patients (61% vs 5%; 95% CI = 38.7–73.7, $p < 0.0001$). An overall platelet response rate, defined as either durable or transient platelet response, was attained in 79% and 88% of romiplostim-treated splenectomized and non-splenectomized patients, respectively, compared with 0% and 14% in the corresponding placebo-treated patients.

A large, open-label, 52-week study of romiplostim vs standard of care in the treatment of non-splenectomized patients has also been conducted. Patients treated with romiplostim received weekly SC injections[8]. Patients in the romiplostim group had fewer treatment failures (11% vs 30%, $p < 0.001$) and underwent splenectomy less frequently (9% vs 36%, $p < 0.001$) compared with those receiving the standard of care. In addition, platelet response was achieved 2.3-times faster with romiplostim, and the romiplostim-treated patients had lower rates of bleeding events, fewer blood transfusions, and greater improvements in the quality-of-life than the standard of care group.

An international consensus statement on the diagnosis and management of chronic ITP suggests that corticosteroids should be the standard initial treatment for newly diagnosed ITP[6]. Other first-line treatment options include IVIg or anti-D. TPO receptor agonists (including romiplostim) are recommended as the only treatments for refractory ITP that have been shown to be effective in randomized controlled trials. Other second-line options include splenectomy. The guidelines suggest that TPO receptor agonists have the potential to minimize morbidity and mortality because they are associated with low rates of toxicity and good tolerability. The authors further noted that long-term administration of romiplostim for up to 4 years has been shown to be well tolerated without loss of efficacy, and that most patients treated with romiplostim were able to decrease or discontinue their corticosteroid therapy[9]. This finding was noted in the guidelines to be particularly important for patients that have been on long-term immunosuppressive treatment[6]. Other studies have also demonstrated that immunoglobulin use can decline over time with romiplostim treatment, where 1–6% of patients treated with romiplostim over a 24-week period required rescue immunoglobulin compared with 19–37% of patients treated with placebo ($p < 0.05$)[10]. Romiplostim recipients were over 5-times less likely to receive immunoglobulin.

There are two TPO receptor agonists available in Canada; romiplostim and eltrombopag. Unfortunately, there are no head-to-head trials comparing the efficacy and safety of these agents in patients with ITP. Zeng *et al.*[11] conducted a systematic review and found that the TPO receptor agonists romiplostim and eltrombopag significantly reduced the number of overall bleeding events (compared with placebo (RR = 0.78, 95% CI = 0.68–0.89)), but not with a standard of care arm that included treatment with glucocorticoid, anti-D immune globulin, intravenous immune globulin, rituximab, or azathioprine (RR = 0.97, 95% CI = 0.75–1.26). The author further criticized the TPO receptor agonists trials for inadequately assessing clinically relevant bleeding events and survival. Due to ethical considerations, clinical trials in ITP must allow for medications that 'rescue' patients from severe thrombocytopenia, which are also expected to reduce the risk of bleeding. Because ITP is a rare disease and severe bleeding events and death occur infrequently with treatment, it is not feasible to conduct clinical trials of sufficient size to measure these events[12]. Since the relationship between bleeding and platelet counts has been well established, regulatory agencies have accepted durable platelet response as the primary end-point for ITP clinical trials, and bleeding data were collected as adverse events.

A public drug programme expert review of romiplostim was conducted in Québec[13]. The review acknowledged the therapeutic value of romiplostim in increasing platelet levels and the further benefits of a substantial reduction in the use of IVIg and other rescue medication. However, because the reviewers did not recognize the use of IVIg as a maintenance therapy for chronic ITP, romiplostim was thought to be too costly and is not publicly reimbursed in the province of Québec as a result. The aim of this study was to collect information on the use of romiplostim and IVIg and compare the total costs of treating patients with romiplostim and IVIg in Québec in the real-world setting.

Methods

A net cost impact model was developed to provide a detailed analysis of the cost implications of romiplostim utilization compared with that of IVIg in a 'real world' analysis of patients in Québec. The net impact analysis is a required element of drug reviews in Québec to show the societal impact of providing access[14]. As such, the analysis was conducted from the societal perspective and outlines both the direct and indirect cost consequences on the population with listing of romiplostim. The categories of costs included in the model were related to: drug treatment, preparation and administration of medications, monitoring, and indirect costs (including patients' time away from usual activities or work). Incorporation of the impact of romiplostim and IVIg on treatment outcomes or on resources required to manage complications arising from treatment was not conducted as it was considered outside the scope of the net cost analysis and is typically included in a pharmacoeconomic evaluation of new health technologies. The analysis was undertaken in 2011 and used 2011 costs.

Two Québec hospitals (Hôpital Maisonneuve-Rosemont in Montréal and Hôpital L'Enfant-Jésus in Québec City) participated in the collection of healthcare resources. The resources consumed in the preparation and administration of the romiplostim and IVIg were obtained through interviews with the personnel responsible for the activities. Physicians and nurses at the two study sites were interviewed to define treatment algorithms for the use of romiplostim and IVIg and to collect and quantify all healthcare resource utilization required for the injection of romiplostim or infusion of IVIg. The estimated professional time spent for laboratory technicians and assistant technicians was obtained through expert consultation. Nursing time required for IVIg administration and monitoring was prospectively recorded while following nurses as they performed their regular duties. To standardize data collection, a digital stopwatch was used to measure time spent on different tasks related to IVIg administration and monitoring. All IVIg administration information was gathered by eight nurses in the two centres.

The initial dose of IVIg assumed in the analysis followed the recommendation for the management of adults with ITP from an International Consensus Report on Management of Primary Immune Thrombocytopenia[6]. This assumption was validated at the two hospitals in Québec and was aligned with the experts' recommendations. The initial dose was assumed to be 1 g/kg per day delivered intravenously (IV) over 2.5–5 h for 2 consecutive days. Because the maintenance dose and dosing frequency of IVIg used in practice may vary due to patient variability, data were collected from the blood bank information system of the participating hospitals for a full year from April 1, 2010 to March 31, 2011 on all patients with chronic ITP having an order for IVIg. To distinguish rescue from maintenance therapy, the analysis only included patients who received more than two doses on non-consecutive days where the doses were given at fairly regular intervals (i.e., a patient who received one treatment followed by a second treatment several months later was considered to be receiving rescue therapy).

The analysis was conducted over a 1-year time horizon. Although ITP is a chronic condition and individual patients may require higher doses of IVIg over time, data were collected in a mixed cohort of patients that included patients new to treatment and patients that had been treated with maintenance therapy longer term. As such, it was assumed that the observed average dose of IVIg in the mixed group would not vary much from one year to another and would reflect the expected average in future years. Other assumptions that were used to calculate the total dose and cost of IVIg are shown in Table 1.

Without reimbursement of romiplostim in Québec, insufficient patient data were available for a determination of the actual dose of romiplostim that would be required to treat patients. Therefore, the romiplostim product monograph[15] and experts' recommendations were used to guide assumptions about the average dose of romiplostim that would be used in clinical practice. Although, in the pivotal study of romiplostim[7], time to response (i.e., a platelet count $\leq 30 \times 10^9$/L to achieve $\geq 50 \times 10^9$/L) was achieved by 25% of both splenectomized and non-splenectomized patients after 1 week and by 50% within 2–3 weeks, expert recommendations suggested that patients at the two Québec sites typically required treatment for 3–4 weeks to achieve response. To be conservative, the analysis assumed that patients would respond after 4 weeks at the initial dose of 1 μg/kg subcutaneous (SC) once weekly adjusted in weekly increments of 1μg/kg to achieve and maintain a platelet count $\geq 50 \times 10^9$/L as necessary to reduce the risk for bleeding. Thereafter, the dose of romiplostim was assumed to be the median dose according to the pivotal studies: 3 μg/kg in splenectomized patients and

Table 1. Resources assumed in calculating the costs of drug acquisition, preparation, and administration of romiplostim and IVIg, and patient follow-up monitoring.

	Romiplostim	IVIg
Drug acquisition resources		
Usual dose	Initial dose: 1 μg/kg SC once weekly adjusted by increments of 1 μg/kg to achieve and maintain a platelet count $\geq 50 \times 10^9$/L	Initial dose: 1 g/kg IV per patient per day for 2 days[a]
	Median dose: 3 μg/kg/week	Maintenance dose 0.62 g/kg IV every 2.6 weeks[b]
Dose per 70 kg person	210 μg weekly	140 g for first 2 days then 43.3 g per infusion provided every 2.6 weeks[b]
Wholesaler mark-up	$39.00[c]	Not applicable
Dispensing fees	13 scripts per year	Not applicable
Resources consumed in the preparation and administration of romiplostim and IVIg		
Clinical nursing time	6.93 h to complete 52 injections per year[d] Each injection requires a total of 8 min (5 min for reconstitution + 3 min for SC injection)	17.98 h to complete 21.6 infusions of IVIg[e] Each infusion requires a total of 29.94 min (includes review patient files, IV set-up and disconnection, pump set-up, and for four vital sign measurements)
Laboratory technician time	Not applicable	3.6 h for 21.6 infusions[e] Each infusion requires a total of 10 min to register IVIg product in patient files, review prescription, and label product
Assistant technician time	Not applicable	5.4 h for 21.6 infusions[e] Each infusion requires a total of 15 min for script requisition, drug distribution to infusion clinic and patient appointment follow-up
Medical supplies for drug administration	52 of each: • Sterile water for dilution (10 mL) • Syringes 1 ml 25G × 5/8	21.6 [e] of each: • Primary IV lines • 250 ml dextrose 5% • Tubing with 15 μg filter • Gelco BDInsyte 22Ga (0.9 × 25 mm) • BD Lever lock cannulas
Follow-up monitoring resources		
Auxiliary nursing time	88 min 8 min to draw blood each time[f]	88 min 8 min to draw blood each time[f]
Laboratory tests	CBC, platelets, peripheral blood smear	CBC, platelets, peripheral blood smear
Medical supplies for blood tests	11 of each[f]: • Venous collection tubes • Haematology tubes • Syringes hypo 10–12 ml	11 of each[f]: • Venous collection tubes • Haematology tubes • Syringes hypo 10–12 ml

[a]Based on international consensus[6].
[b]Based on data collected from the participating hospitals in Québec.
[c]Based on a maximum mark-up of $39.00 per vial for products over $600.00 per unit in 2012.
[d]Romiplostim injections were provided in the hospital outpatient setting. Although some patients may self-inject romiplostim, self-administration is not an approved dosing method in Canada.
[e]Two infusions were required to initiate treatment and 19.6 infusions were required for maintenance (calculated as 52 weeks − 1 initial week = 51 weeks divided by average 2.6 week infusion frequency as reported at the participating hospitals).
[f]At baseline and weekly for weeks 1–4 then every 8 weeks thereafter.

Table 2. Lost productivity associated with treatment of ITP with romiplostim or IVIg.

	Romiplostim	IVIg
Patient time away from work	11.27 h total for 52 visits • 8 min injection time • 5 min waiting time	91.8 h total for 21.6 infusions • 15 min waiting time • 30 min to set up IV line for infusion • 210 min for IVIg administration

Table 3. Unit costs.

Resource	Unit cost ($CAD)	Data source
Romiplostim cost per 250 μg vial	$882.50	Amgen Canada
IVIg cost/g	$100.00	Canadian Blood Services
Dispensing fee per prescription (romiplostim only)	$8.17	Régie de l'assurance maladie du Québec (RAMQ) formulary[a]
Wholesaler mark-up per vial(romiplostim only)	$39.00	RAMQ formulary[a]
Clinical nurse hourly wage	$35.15	Comité patronal de négociation du secteur de la santé et des services sociaux, April 2012 (CPNSSS)
Laboratory technician hourly wage	$29.63	CPNSSS
Assistant technician hourly wage	$21.53	CPNSSS
Sterile water (10 mL)	$0.02	Buying group in Québec[b]
Primary IV lines	$10.99	Buying group in Québec[b]
Dextrose 5% (250 mL)	$1.10	Buying group in Québec[b]
Gelco BDInsyte 22 Ga	$1.24	Buying group in Québec[b]
BD Lever lock cannulas	$0.46	Buying group in Québec[b]
Tubing with 15 μg filter	$4.25	Buying group in Québec[b]
CBC, platelets, blood smear	$6.00	Ministère de la santé et des services sociaux du Québec (2011/12)
Venous blood collection tube	$0.13	Buying group in Québec[b]
Haematology collection tube	$0.11	Buying group in Québec[b]
Syringes hypo (10–12 ml)	$0.10	Buying group in Québec[b]
Average hourly Québec wage for employees ≥25 years of age	$22.72	Statistics Canada (2010/11)

[a]2010 Pharmacists' fees, 2012 wholesaler mark-up.
[b]Costs obtained as of November 2011.

2 μg/kg in non-splenectomized patients. The higher dose of 3 μg/kg was chosen as the maintenance dose[7].

Monitoring of ITP patients treated with romiplostim or IVIg in clinical practice was also determined by consultation with experts. The healthcare resource use involved: phlebotomist or nurse time to draw blood for blood tests; laboratory charges for complete blood count, platelets, and peripheral blood smear tests; and medical supplies for blood collection. Patients had blood monitoring tests 11 times per year on average (i.e., at baseline and weekly for weeks 1–4 then every 8 weeks thereafter). Although some blood tests may be conducted outside of the hospital, it was assumed that the tests were performed in the hospital and that the resources required would be the same, irrespective of the location in which they would be conducted.

Table 1 outlines all of the data and assumptions that were made in determining the healthcare resources required to deliver treatment and monitor patients managed with each of the ITP treatments.

Assumptions regarding patients' time off work or usual activities were made based on the typical duration of the infusion/injection appointments at the hospital/clinic. The estimated time was validated with the clinical experts. Travel time to appointments from home or work was determined to be too variable and difficult to estimate, so it was not included in the total time. The lost productivity resulting from treatment with romiplostim or IVIg is shown in Table 2.

Unit costs were assigned to all direct healthcare resources including the comparator drugs, medical supplies for the administration of the comparator drugs, and for obtaining blood samples for patient safety follow-up, laboratory blood work test costs, and healthcare professionals' time. The most recent updates for publicly available provincial government publications were consulted. Indirect resources, in the form of lost productivity, were also valued according to an average hourly wage for employees in Québec. Unit costs were obtained from a variety of sources. Each of the unit costs ($CAD) and their data source are shown in Table 3.

Sensitivity analyses were conducted by varying assumptions on romiplostim and IVIg dosing requirements.

The dose of romiplostim was varied according to the available size of vials, whereby the base case used the 250 μg vial weekly and the sensitivity analysis used the 500 μg vial weekly. The IVIg dose was varied around the observed mean dose of 0.62 g/kg. Although the lowest dose observed at the study centres was 0.4 g/kg, clinical practice guidelines[6] indicate doses as low as 0.3 g/kg can be used. Thus, the IVIg dose was varied from 0.3 to 0.8 g/kg (as observed in the study centres) in the sensitivity analysis. The IVIg infusion time was varied from 2.5–5 h (base case 3.5 h), thereby increasing or decreasing, as applicable, the nursing time and patient time off work, while the laboratory technician and other technicians' time was held constant. Finally, the IVIg maintenance dosing frequency was varied according to the ranges observed in the data collection period from a low of 12.4 doses per year up to a high of 42.5 doses per year (base case = 19.6 doses). It should be noted that a lower dose of romiplostim was not examined in a sensitivity analysis because romiplostim vials are manufactured for single use only and it was assumed that there would be no sharing of vials.

Statistical analysis was performed to calculate the mean and standard deviation of IVIg doses prescribed for patients at the two Québec hospitals.

Table 4. Comparative total costs ($CAD) of managing ITP patients with romiplostim vs IVIg.

Cost category	Romiplostim	IVIg
Drug acquisition	$48,024	$98,868
Medication preparation and administration	$309	$1245
Patient monitoring	$121	$121
Lost productivity	$256	$2086
Total	$48,710	$102,320

Results

In total, 95 ITP patients were treated with IVIg. Of all IVIg patients, 48% (46 of 95) received maintenance therapy. The average maintenance dose for the 46 patients was 43.3 g (range = 28.7–57.9 g) or 0.62 g/kg based on a 70 kg patient weight. The observed frequency of dosing was every 18.5 days (2.6 weeks; range = 8.4–28.6 days). Based on a dosing frequency of every 2.6 weeks, the total number of maintenance infusions each year was calculated to be 19.6 (52 weeks – 1 initial week = 51 weeks; 51 weeks/2.6 weeks = 19.6).

The total costs related to drug acquisition; medication preparation and administration; patient monitoring; and lost productivity were more than double for IVIg relative to romiplostim. The total annual per patient costs of romiplostim and IVIg were $48,710 and $102,320, respectively. The use of romiplostim would save, on average, ~$53,610 per patient per year. Costs related to patient safety monitoring and follow-up were identical for patients treated with romiplostim and IVIg due to similar monitoring requirements. However, the cost of drug administration and the value of lost productivity were much higher for IVIg due to the substantially longer drug administration time with IVIg (3.5 h) compared with romiplostim (8 minutes). The overwhelming cost driver, though, was the drug acquisition expense.

Total costs for each cost category are shown in Table 4. The cost savings that were achieved with romiplostim varied as the assumptions of the analysis changed. The results of the analysis assuming higher doses of romiplostim, lower and higher doses of IVIg, shorter and longer IVIg infusion times, and lower and higher IVIg maintenance dosing frequencies are shown in Table 5. The total annual per patient cost of romiplostim was between $48,710 and $91,071. The total cost of IVIg per patient varied from a low of $58,612 to a high of $201,477. Changing the assumption for the length of the infusion time did not change the cost of IVIg to a noticeable extent. The greatest driver of the cost of both drug

Table 5. Incremental cost with IVIg under various sensitivity scenarios ($CAD).

	Romiplostim	IVIg	Incremental cost of IVIg
Base case:Romiplostim 250 μg/week and IVIg dose 0.62 g/kg with 3.5 h infusion	$48,710	$102,320	$53,610
Higher romiplostim dose (500 μg/week)	$91,071	$102,320	$11,249
Lower IVIg dose (0.3 g/kg)	$48,710	$58,612	$9902
Higher romiplostim dose (500 μg/week) and lower IVIg dose (0.3 g/kg)	$91,071	$58,612	−$32,459*
Higher IVIg dose (0.8 g/kg)	$48,710	$130,936	$82,226
Shorter IVIg infusion time (2.5 h)	$48,710	$101,765	$53,055
Longer IVIg infusion time (5 h)	$48,710	$103,119	$54,409
Lower IVIg maintenance dosing frequency (12.4 doses/year)	$48,710	$71,144	$22,434
Higher IVIg maintenance dosing frequency (42.5 doses/year)	$48,710	$201,477	$152,767

*IVIg was cost-saving in this scenario.

treatments was the dose administered and, in the case of IVIg, also the dosing frequency. The total annual per patient savings with romiplostim varied from $9902 to $152,767. In one scenario—high dose romiplostim vs low dose IVIg—use of IVIg would result in savings of $32,459 per patient.

Discussion

The total annual cost for the management of chronic ITP was calculated to be, on average, $48,710 for romiplostim and $102,320 for IVIg. Compared with IVIg, the use of romiplostim resulted in lower direct costs, reduced healthcare resource utilization, and less indirect costs (measured as lost productivity). The difference in total cost was primarily due to the differences in drug acquisition costs. However, indirect costs incurred by patients, and the preparation and administration costs incurred by the healthcare system, were considerably higher for patients treated with IVIg. Because IVIg is administered through IV infusion, the costs for nursing and other healthcare professionals to administer treatment were much higher than with romiplostim administered via SC injection. Similarly, because patients treated with romiplostim spend less time at the hospital or clinic, away from work or their usual activities while receiving treatment, indirect costs are also reduced with romiplostim. Self-administration of romiplostim is not approved in Canada, and, thus, administration costs for the SC injection of romiplostim in outpatient clinics were included. Costs related to patient monitoring were the same for each treatment.

In sensitivity analyses where the dose, dosing schedule, or infusion duration was changed, the total cost of IVIg varied from a low of $58,612 per patient to $201,477 per patient and the cost of romiplostim was between $48,710 and $91,071. The total annual per patient savings that can be achieved with the use of romiplostim rather than IVIg varied from $9902 to $152,767 per patient per year. In only the scenario comparing high dose romiplostim with low dose IVIg, there was an overall cost savings with IVIg of ~$32,000 per patient. The likelihood of this scenario is thought to be low given that it is highly unlikely that all patients would be treated with the larger 500 μg vial of romiplostim (i.e., sufficient for a dose of ~3.59–7.14 μg/kg in a 70 kg patient) or with the lowest recommended 0.3 g/kg dose of IVIg (i.e., considerably lower than the actual average dose of 0.62 g/kg observed in Québec).

The maintenance dose of IVIg observed in the Québec hospitals was higher than expected based on international consensus guidelines for patients with common variable immunodeficiency disorder[6]. This may have been due, in part, to the fact that the haematology centres specialize in ITP treatment and care for a percentage of patients that may require higher doses of IVIg, including patients with a contraindication to long-term steroid use or patients with refractory ITP (particularly post-splenectomy failure). Historically, the recommended maintenance dose for patients with chronic ITP including those not responding to splenectomy has been 0.8–1.0 g/kg every 21 days[16]. However, because different centres may have different experiences with the optimal dose to achieve efficacy and some dosing guidelines may be older, it was important to determine the actual average dose used in practice in Québec. For confidentiality reasons, individual patient characteristics and demographic information were not collected; therefore, the study does not permit a comparison of demographics of the study cohort with that of a general ITP population. Nevertheless, the patient data included in the dose calculation is representative of actual practice at the sites and is thought to reflect treatment patterns that occur across the province of Québec, where ITP care is centralized in a small number of hospitals.

There are no other known published studies of the cost impact of romiplostim vs IVIg. A study of the long-term safety and efficacy of romiplostim use in clinical practice has been conducted in France[17]. In the study, 72 primary ITP patients were enrolled in a compassionate use programme and followed for 2 years. The study included patients that would not ordinarily be followed in clinical trials due to chronic severe ITP complicated by co-morbidities. The majority of patients had previously been treated with corticosteroids and IVIg. After 2 years of follow-up, a sustained response to romiplostim was achieved in 65% of patients. The mean doses of romiplostim at 1 and 2 years were 4.7 ± 2.1 μg/kg and 5.1 ± 2.8 μg/kg, respectively, which is higher than what was observed in the pivotal trials

IVIg is funded in Québec by the provincial healthcare budget, distributed by Héma-Québec and accessed in the hospital setting. From the societal perspective, as required by the Québec evidence review committee[14], treating ITP patients with romiplostim has been shown to provide a lower cost alternative to IVIg for the overall provincial healthcare budget. As a precious commodity, blood products must be used wisely. As stated by the expert review committee in Québec, IVIg should remain a last resort option to treat ITP[13]. Pivotal studies have demonstrated the ability of romiplostim to maintain adequate platelet counts and reduce bleeding related events, thereby reducing the need for IVIg to treat ITP. If fewer ITP patients were to use IVIg, this expensive and relatively scarce blood product[18] can be reserved for other disorders and healthcare resources can be re-allocated elsewhere within a provincial health budget.

This study was conducted from a societal perspective as recommended by Québec's health technology agency (*L'institut national d'excellence en santé et en services sociaux* – INESSS[14]). The societal perspective allows decision-makers to consider health system and social benefits

alongside clinical benefits, and to examine the full impact of a new drug on a provincial budget. Another strength of this study comes from its 'real world' design. Assumptions about medication doses and dose frequency derived from pivotal studies were validated with input from healthcare professionals involved in the management of ITP patients. For example, the actual dose of IVIg used in Québec clinics (0.4–0.8 g/kg) was found to be higher than the dose expected according to international consensus (0.3–0.4 g/kg)[6]. In addition, interviews with nurses were conducted to obtain actual practice data on the nursing resources required to prepare and administer the treatments.

A limitation of the study stems from the fact that romiplostim was not widely used at the sites due to lack of reimbursement and, as a result, actual data on dosing was not available for comparison with the actual observed doses of IVIg. However, the analysis calculated the cost impact attributed to commercially available vial sizes (i.e., 250 μg and the 500 μg vials). The study results are also limited by the fact that the data were derived from two hospitals in Québec. It is possible that the net costs of romiplostim and IVIg will differ among different hospitals, even within the same province. The results may also not be generalized to other provinces, as professional practices may vary across Canada. To complement the differential cost findings of the present study, future research should examine the relative health benefits and safety risks (including risks associated with IV administration vs SC injection) of the two treatments and the potential impact of a delay in IVIg administration or a missed IVIg dose due to the unavailability of the blood product.

Conclusions

This study demonstrated that romiplostim can allow for improved healthcare resource allocation by reserving IVIg for use for other therapeutic areas of greater need while also providing annual average cost savings between $9900–$153,000 per patient. Romiplostim also potentially avoids the risks associated with IV administration of a blood product.

Transparency

Declaration of funding
The study was funded by Amgen Canada Inc. Approval and preparation of the manuscript for publication was not dependent upon approval of the sponsor.

Declaration of financial/other relationships
JK and VL have participated in Amgen advisory board meetings. MP has completed work for Amgen on a consulting basis. RD is an employee of Amgen Inc. and KG is an employee of Amgen Canada Inc.

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