Cost-Effectiveness of Avatrombopag for the Treatment of Thrombocytopenia in Patients with Chronic Liver Disease

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Background and Aim: Thrombocytopenia is common in people with chronic liver disease, who frequently undergo invasive procedures. To minimize the risk of bleeding, prophylactic platelet transfusions have traditionally been used but carry many risks. The aim of this study was to evaluate the cost-effectiveness of avatrombopag compared with platelet transfusion and lusutrombopag as a treatment for thrombocytopenia in adult patients with chronic liver disease scheduled to undergo a medical procedure.

Methods: A decision-tree model was developed from a US payer perspective to capture acute events observed in phase 3 global randomized controlled clinical trials and, to support exploratory analyses, potential longer-term complications resulting from a major bleed or thromboembolic event. Treatment costs were taken from publicly available data sources. The interventions were evaluated in the overall trial populations and in subpopulations with higher and lower baseline platelet counts. Results were presented as incremental cost per platelet transfusion avoided. One-way and probabilistic sensitivity analyses were conducted.

Results: In the overall population, avatrombopag reduced the need for platelet transfusions and produced cost-savings compared with platelet transfusion (80% fewer prophylactic platelet transfusions, $4250 lower costs) and lusutrombopag (42% fewer prophylactic platelet transfusions, $5819 lower costs). Similar results were seen in both the higher and lower platelet count subpopulations. The one-way and probabilistic sensitivity analyses found that the use of avatrombopag is cost-saving with the incremental cost-effectiveness ratio in quadrant IV (decreased costs, prophylactic platelet transfusions avoided).

Conclusion: The use of avatrombopag is expected to be cost-saving while reducing the need for prophylactic platelet transfusions compared with platelet transfusion and lusutrombopag.

Keywords: liver diseases, platelet transfusion, thrombocytopenia, cost-effectiveness

Introduction
Thrombocytopenia is common in patients with chronic liver disease (CLD) and is characterized by a deficiency of platelets (ie, <150×10^9/L) in the circulatory system. Patients with CLD undergo a variety of interventions that are associated with risk, including treatments for hepatocellular carcinoma and dental extractions in preparation for transplants, as part of their ongoing care. Standard clinical practice for patients with CLD undergoing a procedure has been to correct platelet counts to >50×10^9/L to reduce the risk of bleeding complications from these surgical procedures. The increased risk of bleeding complications is often
managed with preoperative platelet transfusion; however, this treatment often does not adequately address the therapeutic need and is associated with substantial risk of allergic reactions, reduced efficacy over time, costs, and potential adverse effects. Given the limitations with current standard of care, there is a need for a safe and cost-effective alternative treatment for thrombocytopenia in patients with CLD who are preparing for a procedure.

Oral thrombopoietin receptor agonists present an alternative treatment option that may be more effective while reducing risk to patients. Avatrombopag (Doptele, Dova Pharmaceuticals, Durham, NC, USA) is a thrombopoietin receptor agonist approved in the United States (US) for the treatment of thrombocytopenia in adults with CLD who are scheduled to undergo a procedure. Avatrombopag, dosed over 5 days is tailored to the baseline platelet count, with patients receiving 40 mg daily for counts ≥40×10^9/L to <50×10^9/L and 60 mg daily for counts <40×10^9/L. Avatrombopag has been shown to significantly increase the percentage of patients not requiring a platelet transfusion prior to the scheduled procedure and decrease the need for a rescue procedure for bleeding during the 7 days following the scheduled procedure. Additionally, avatrombopag is generally well tolerated in patients with CLD. Lusutrombopag (Mulpleta, Shionogi, Osaka, Japan) is another thrombopoietin receptor agonist approved for this indication. In contrast to avatrombopag, the dose of lusutrombopag (3 mg per day) was fixed, irrespective of baseline platelet count. Randomization in Peck-Radosavljevic et al (2019) was stratified according to baseline platelet counts (<35×10^9/L, ≥35×10^9/L). Lusutrombopag has demonstrated efficacy in treating thrombocytopenia in patients with CLD undergoing invasive procedures.

The objective of this analysis was to evaluate, from a third-party US payer perspective, the potential cost-effectiveness of avatrombopag compared with prophylactic platelet transfusion and lusutrombopag as treatments for adult patients with CLD and severe thrombocytopenia (platelet counts <50×10^9/L) who are scheduled for an invasive procedure.

**Methods**

**Model Overview**

A decision-tree model was used to describe the possible pertinent outcomes for patients with CLD undergoing treatment for severe thrombocytopenia before a scheduled procedure. In addition to avatrombopag, the model included prophylactic platelet transfusion and lusutrombopag as comparator strategies.

The model structure (Figure 1) captured the following events for each treatment strategy: treatment success (ie, sufficiently high platelet count to proceed with the scheduled procedure with no need for a prophylactic platelet transfusion [assumed to be 0% for the platelet transfusion strategy]); prophylactic platelet transfusion in the case of lack of treatment success (assumed to be 100% for platelet transfusion); and periprocedural bleeding event requiring a rescue procedure. Each treatment and model event was associated with a cost of treatment and the expected cost of a thromboembolic event, adjusted by the probability of experiencing the event. If a strategy was successful, the patient underwent the scheduled procedure, resulting in either no complications and no further treatment or a bleeding event that required a rescue procedure. If a prophylactic strategy was unsuccessful, the patient received a platelet transfusion prior to undergoing the scheduled procedure, resulting in either no complications and no further treatment or a bleeding event that required a rescue procedure. If the original prophylactic strategy was unsuccessful, the cost of a platelet transfusion had incorporated costs associated with a possible adverse event to the platelet transfusion, which may have delayed the scheduled procedure and required an additional platelet transfusion. The time horizon for the base-case analysis was the period required to capture the base-case model events. Scenario analysis was conducted to examine the effect of longer-term serious events. The cost-effectiveness analyses were conducted using the most recent estimates of resource use and treatment costs available from published sources. Costs obtained from the literature were inflated to 2018 costs, as applicable.

**Model Population**

The base-case cost-effectiveness analysis considered adult patients with CLD and severe thrombocytopenia (platelet count <50×10^9/L) who were scheduled to undergo a procedure. In addition, the model facilitated analyses in two subpopulations classified in the avatrombopag clinical trials (Table 1): adult patients with a mean baseline platelet count <40×10^9/L (ie, lower platelet count population) and adult patients with a mean baseline platelet count ≥40×10^9/L to <50×10^9/L (ie, higher platelet count population). The subpopulations in the lusutrombopag clinical
trials were defined slightly differently, using a cut-point of $35 \times 10^9/\text{L}$. Additionally, the avatrombopag and lusutrombopag trials had different proportions in the two subpopulations: 42.3% of patients in the avatrombopag trials and 64.7% in the lusutrombopag trials had higher baseline platelet counts.

**Model Inputs**

**Event Probabilities**

The probabilities that each drug treatment successfully raised a patient’s platelet count, thus avoiding the need for a prophylactic platelet transfusion, were based on the phase 3 multinational clinical trials conducted for avatrombopag and the prescribing information for lusutrombopag (Table S-1).\(^8,12,13\) Prophylactic transfusions prior to the procedure were needed by 20.3% of overall avatrombopag patients and 35% of overall lusutrombopag patients. For the platelet transfusion model comparator, it was assumed that 100% of patients received a prophylactic platelet transfusion. Thromboembolic events were experienced by 0.4% of overall avatrombopag patients and 1.2% of overall lusutrombopag patients. Based on the pooled placebo arms of the avatrombopag trials, in which 64.7% of patients received a prophylactic platelet transfusion, the model conservatively assumed that 1.3% of the patients receiving a prophylactic platelet transfusion experienced a thromboembolic event. Bleeding events requiring a rescue procedure were experienced by 1.1% of overall avatrombopag patients and 0% of overall lusutrombopag patients and, based on the avatrombopag placebo arms, were conservatively assumed to be experienced by 4.0% of patients receiving prophylactic platelet transfusion. Probability estimates of model events for subgroups are presented in Table S-1.
Table 1 Population and Subpopulations for Base-Case Analysis

| Parameter                                      | Value                                                                 | Sources and Assumptions                                                                 |
|------------------------------------------------|----------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Population selected for comparison            | Overall population (all patients with a platelet count <5×10^9/L)     |                                                                                         |
| Platelet count cut-point                      |                                                                      |                                                                                         |
| Avatrombopag                                   |                                                                      |                                                                                         |
| Lower platelet count population                | <4×10^9/L                                                             | Doptelet prescribing information (2018)^29                                              |
| Higher platelet count population               | ≥4×10^9/L to <5×10^9/L                                               | Doptelet prescribing information (2018)^29                                              |
| Lusutrombopag                                  |                                                                      |                                                                                         |
| Lower platelet count population                | <35×10^9/L                                                           | Peck-Radosavljevic et al (2019)^10                                                       |
| Higher platelet count population               | ≥35×10^9/L to <5×10^9/L                                              | Peck-Radosavljevic et al (2019)^10                                                       |
| Proportion of population with lower and higher platelet counts |                                                                      |                                                                                         |
| Avatrombopag                                   |                                                                      |                                                                                         |
| Lower platelet count population                | 57.7%                                                                | Doptelet prescribing information (2018)^29                                              |
| Higher platelet count population               | 42.3%                                                                | Doptelet prescribing information (2018)^29                                              |
| Lusutrombopag                                  |                                                                      |                                                                                         |
| Lower platelet count population                | 35.3%                                                                | AASLD 2017^13                                                                           |
| Higher platelet count population               | 64.7%                                                                | AASLD 2017^13                                                                           |

Note: ^9Presented at the AASLD 2017 Annual Meeting.
Abbreviation: AASLD, American Association for the Study of Liver Diseases.

Cost Inputs

Cost of Drug Treatments

All costs are from a US payer perspective. The treatment costs for the dosages for each drug regimen considered in the model were obtained as wholesale acquisition costs from Red Book Online (2019)^14 and are presented in Table 2. Drug costs per scheduled procedure were $3827 for the overall avatrombopag population, $2970 for the higher platelet count avatrombopag population, $4455 for the lower platelet count avatrombopag population, and $8500 for all lusutrombopag populations.

Cost of Platelet Transfusions

The direct cost of platelet transfusion in a patient with CLD was based on Barnett et al (2018),^7 which included the cost of platelet collection, the platelet transfusion event, adverse events from transfusion, and the need for subsequent platelet transfusions in the case of refractoriness with human leukocyte antigen–matched platelets in case of immune refractoriness. The cost of a platelet transfusion as a treatment strategy in this modeled analysis depended on the number of apheresis-equivalent platelet units per platelet transfusion, which varied by population. Based on data from the placebo arm of the avatrombopag trials, the cost of platelet transfusion as a treatment strategy was $9271 for the overall platelet transfusion population, $8564 for the higher platelet count platelet transfusion population, and $9790 for the lower platelet count population.

Table 2 Model Inputs: Treatment Costs per Procedure for Avatrombopag and Lusutrombopag (2019 USD)

| Source                                          | Notes                                                                 | Avatrombopag (40 mg) | Avatrombopag (60 mg) | Lusutrombopag (3 mg) |
|------------------------------------------------|----------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Dose per package/scheduled procedure (mg)       |                                                                    | 200                  | 300                  | 21                   |
| WAC per package/scheduled procedure             |                                                                    | $2970                | $4455                | $8500                |
| Weighted average WAC per package/scheduled procedure for avatrombopag | $3827                                                                | Not applicable       |                      |                      |

Abbreviations: USD, US dollar; WAC, wholesale acquisition cost.
Some patients receiving the drug treatments also received platelet transfusions, the cost of which depended on the number of apheresis-equivalent units of platelets, which varied by drug and population. The cost of a prophylactic platelet transfusion was $7253 for the overall avatrombopag population. The number of apheresis-equivalent platelet units per platelet transfusion for lusutrombopag was unavailable from the published literature; it was assumed to be the same as for avatrombopag, yielding the same cost for platelet transfusion ($7253). The number of apheresis-equivalent platelet units per platelet transfusion for all populations are provided in Table S-2.

Cost of Adverse Events

Thromboembolic Event

In a retrospective case-control study comparing the cost of hospitalization for US patients with a diagnosis of CLD and venous thromboembolism (VTE) compared with patients with CLD without VTE from October 2006 to July 2010, Walsh et al (2013)\textsuperscript{15} reported that patients with CLD and VTE had significantly more costly hospitalizations (median $20,137 vs $8450, \( P = 0.03 \)). We assumed that a patient with CLD who experiences a thromboembolic event has an additional cost of $11,687 based on this information, which we assumed to be in 2008 US dollars (the middle of the study period). This estimate was updated to 2018 US dollars to be $15,344.

Rescue Procedure for Bleeding

Ineffective treatment for thrombocytopenia prior to a procedure may lead to a periprocedural bleeding event that may require a rescue procedure. Our model assumed that the rescue procedure for bleeding is a platelet transfusion. The cost of a platelet transfusion was derived from Barnett et al (2018)\textsuperscript{7} assuming no refractoriness and no delay in procedure following a major adverse event, resulting in an estimate of $4745.

Sensitivity Analysis Inputs

One-way sensitivity analyses were conducted to estimate the effects of parameter uncertainty on the incremental cost per prophylactic platelet transfusion avoided (the incremental cost-effectiveness ratio [ICER] most relevant to understanding the economic value of the treatment). One-way sensitivity analyses compared avatrombopag with prophylactic platelet transfusion or lusutrombopag in the overall population. Probabilistic sensitivity analyses were conducted to compare the ICER of avatrombopag with prophylactic platelet transfusion or lusutrombopag in the overall population. Reported values from the literature or assumptions were used to support the one-way and probabilistic sensitivity analyses (Table S-3).

Long-Term Outcomes Scenario Design and Inputs

Long-term outcomes were considered using a scenario analysis. Longer-term health outcomes were discounted by 3%.\textsuperscript{16} Table S-4 presents the additional model parameters required to perform the scenario analysis incorporating long-term outcomes. To estimate the cost of a surgical repair for bleeding, the 2013 Healthcare Cost and Utilization Project’s National Inpatient Sample, a publicly available database,\textsuperscript{17} was analyzed to estimate the mean cost (adjusted to 2017 US dollars) of a hospitalization for patients with a primary discharge diagnosis of a gastrointestinal bleed (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] Diagnoses Codes: 530.82, 569.3, 578.0, or 578.9) who had an intestinal surgical procedure (International Classification of Diseases, 9th Revision [ICD-9] Procedure Codes: 46.71, 46.73, 46.75, 46.79) during the hospitalization. This 2017 estimate was updated to 2018 US dollars.\textsuperscript{11}

Results

Base-Case Results

The use of avatrombopag in the overall population (Table 3) resulted in an average per-person cost-savings of $4250 (44% reduction) compared with prophylactic platelet transfusion and $5819 (52% reduction) compared with lusutrombopag. Avatrombopag also reduced prophylactic platelet transfusions by 80% compared with a strategy where 100% of patients received a prophylactic platelet transfusion and by 42% compared with lusutrombopag. In the subgroup analyses for higher and lower platelet count groups, the findings from the overall analysis were replicated. In patients with higher platelet counts (Table S-5), avatrombopag reduced costs by 60% and prophylactic transfusions by 92% compared with the prophylactic transfusion strategy. Avatrombopag reduced costs by 64% and prophylactic transfusions by 64% compared with lusutrombopag. In the lower platelet group (Table S-6), avatrombopag reduced costs by 33% and prophylactic transfusions by 71% compared with the prophylactic transfusion strategy. Avatrombopag reduced costs by 48% and prophylactic transfusions by 49% compared with lusutrombopag. In an analysis based strictly on
Table 3 Base-Case Results: Overall Population (Platelet Count <50×10^9/L)

| Outcome                                      | Avatrombopag | Prophylactic Platelet Transfusion | Lusutrombopag |
|----------------------------------------------|--------------|----------------------------------|---------------|
| Economic outcomes (per person)               |              |                                  |               |
| Costs of drug treatment                      | $3827        | $0                               | $8500         |
| Costs of prophylactic platelet transfusion   | $1475        | $9271                            | $2525         |
| Costs of thromboembolic events               | $56          | $200                             | $179          |
| Costs of bleeding events requiring rescue procedure | $54          | $191                             | $0            |
| Total costs                                  | $5412        | $9662                            | $11,231       |
| Health outcomes (per person)                 |              |                                  |               |
| Number of prophylactic platelet transfusions | 0.2034       | 1.0000                           | 0.3519        |
| Number of thromboembolic events              | 0.0037       | 0.0130                           | 0.0117        |
| Number of bleeding events requiring rescue procedure | 0.0113       | 0.0403                           | 0.0000        |
| Incremental outcomes (per person)            |              |                                  |               |
| Incremental costs                            |              |                                  |               |
| Number of prophylactic platelet transfusions avoided |          |                                  |               |
| Cost per prophylactic platelet transfusion avoided |          |                                  |               |

Note: Avatrombopag compared with both prophylactic platelet transfusion and lusutrombopag resulted in lower costs and fewer prophylactic platelet transfusions, yielding a negative cost per prophylactic platelet transfusion avoided, which suggests that avatrombopag is the dominant treatment.

Sensitivity Analysis Results

One-Way Sensitivity Analysis Results

One-way sensitivity analyses comparing avatrombopag with prophylactic platelet transfusion and lusutrombopag in the overall population were performed (Figure 2A and B). The analyses found that the use of avatrombopag remained cost-saving, ie, the ICER moved to quadrant IV (decreased costs, prophylactic platelet transfusions avoided), over a wide range of values for the input variables. The use of avatrombopag remained cost-saving in both the higher and lower platelet count subpopulations. The three variables that had the greatest effect on the cost per prophylactic platelet transfusion avoided for avatrombopag versus prophylactic platelet transfusion were (1) cost of prophylactic platelet transfusion for patients treated with prophylactic platelet transfusion, (2) cost of prophylactic platelet transfusion for patients treated with avatrombopag, and (3) prophylactic platelet transfusion probability of thromboembolic event. The three variables that had the greatest effect on the cost per prophylactic platelet transfusion avoided for avatrombopag versus lusutrombopag were (1) probability of inadequate platelet count for procedure for patients receiving lusutrombopag, (2) probability of inadequate platelet count for procedure for patients receiving avatrombopag, and (3) cost of prophylactic platelet transfusion for patients treated with lusutrombopag.

Probabilistic Sensitivity Analysis Results

A probabilistic sensitivity analysis on the ICER of avatrombopag in comparison with prophylactic platelet transfusion in the overall population was performed (Figure 3A). In total, 99.3% of the 10,000 iterations had results in quadrant IV, and the remaining percentage (0.7%) were in quadrant I (increased costs and decreased number of prophylactic platelet transfusions). A probabilistic sensitivity analysis on the ICER for avatrombopag in comparison with lusutrombopag in the overall population was performed (Figure 3B). In total, 98.9% of the 10,000 iterations had results in quadrant IV, and the remaining percentage (1.1%) was in quadrant III (decreased costs and increased number of prophylactic platelet transfusions).

Long-Term Outcomes Scenario

Avatrombopag maximized expected life-years, while prophylactic platelet transfusion resulted in the lowest number of expected life-years. The incremental average per-person increase in life-years due to avatrombopag compared with
prophylactic platelet transfusion (0.0076 additional undiscounted life-years and 0.0036 additional discounted life-years) (Table 4) was not significant due to the low probability of a major event with long-term costs and negative health outcomes. In the long-term scenario analysis, the use of avatrombopag remained cost-saving across all scenarios, including in both the higher and lower platelet count subpopulations (Tables S-7 and S-8).

Figure 2 One-way sensitivity analyses results. (A) Cost per prophylactic platelet transfusion avoided with avatrombopag in comparison with prophylactic platelet transfusion in the overall patient population. (B) One-way sensitivity analysis results: cost per prophylactic platelet transfusion avoided with avatrombopag in comparison with lusutrombopag in the overall population.

Note: Gray indicates the lower bound and black indicates the upper bound.
Discussion
The main finding in this study is that the use of avatrombopag reduces health care costs compared with prophylactic platelet transfusion and lusutrombopag while decreasing the number of prophylactic platelet transfusions required regardless of treatment strategy. In the base-case, one-way sensitivity, and probabilistic sensitivity analyses, avatrombopag compared favorably to prophylactic platelet transfusion and lusutrombopag in the overall population as well as in both the higher and lower platelet count subpopulations. Avatrombopag continued to be the most cost-effective treatment option in the long-term outcomes scenario for the overall population and subpopulations, as well as in a strictly trial-based analysis comparing avatrombopag with placebo.

In the one-way sensitivity analysis comparing avatrombopag with prophylactic platelet transfusion, two of the three variables with the greatest impact on the results were

Figure 3 Probabilistic sensitivity analyses results. (A) Probabilistic sensitivity analysis results: cost per prophylactic platelet transfusion avoided with avatrombopag in comparison with prophylactic platelet transfusion in the overall population. (B) Probabilistic sensitivity analysis results: cost per prophylactic platelet transfusion avoided with avatrombopag in comparison with lusutrombopag in the overall population.
related to the cost of prophylactic platelet transfusion ($9662). Additionally, the cost of platelet transfusion depends on the risk of adverse events. However, the risks of adverse events are not well understood in this patient population. If adverse event risks are significantly higher in this patient population than those in the overall group of patients who may receive a platelet transfusion, the cost of platelet transfusions may increase, which could change the cost-effectiveness analysis results.

Thrombocytopenia can cause the delay or cancellation of procedures in patients with CLD. In CLD patients, even procedures considered routine in other populations, such as dental extraction, can carry a risk of bleeding due to thrombocytopenia. Although prophylactic platelet transfusion can be recommended to increase platelet count prior to conducting a procedure, platelet transfusions may not be effective in preventing bleeding. Consequently, transfusion continues to impose a substantial economic burden on health care systems. A recent retrospective study of claims data found a mean payment increase of $11,100 (25%) in total costs for patients with CLD and thrombocytopenia who received platelet transfusions during a planned invasive procedure-related hospital admission and matched patients who did not receive transfusion. The increased cost of platelet transfusions was attributed to increased resource utilization and lengths of hospital stay driven by a significant increase in bleeding events and acute respiratory failure. A 2013 AABB survey reported 54 hospitals (10.5% of those surveyed) delayed elective surgeries due to unmet platelet needs, demonstrating that reliance on platelet transfusion can cause the postponement of procedures. Platelet transfusions also can present additional burdens to patients through decreased quality of life and increased time away from work. We found that avatrombopag provides an effective option to reduce both the cost and risk to patients with CLD and thrombocytopenia prior to undergoing a planned procedure.

While lusutrombopag reduced risk to patients compared with prophylactic platelet transfusion, the use of lusutrombopag was associated with a 16% ($1569) increased cost for the overall population. Although the

### Table 4 Base-Case Results for Scenario Analysis Incorporating Long-Term Outcomes: Overall Population (Platelet Count <50×10⁹/L)

| Outcome                                      | Avatrombopag | Prophylactic Platelet Transfusion | Lusutrombopag |
|----------------------------------------------|--------------|----------------------------------|---------------|
| **Economic outcomes (per person)**           |              |                                  |               |
| Costs of treatment                           | $3827        | $0                               | $8500         |
| Costs of prophylactic platelet transfusion   | $1475        | $9271                            | $2552         |
| Costs of thromboembolic events               | $56          | $200                             | $179          |
| Costs of bleeding events requiring surgical repair | $19        | $68                              | $0            |
| Costs of bleeding events requiring other rescue procedure | $52        | $185                             | $0            |
| **Total costs**                              | $5429        | $9724                            | $11,231       |
| **Health outcomes (per person)**             |              |                                  |               |
| Number of prophylactic platelet transfusions | 0.2034       | 1.0000                           | 0.3519        |
| Number of thromboembolic events              | 0.0037       | 0.0130                           | 0.0117        |
| Number of bleeding events requiring surgical repair | 0.0004       | 0.0014                           | 0.0000        |
| Number of bleeding events requiring other rescue procedure | 0.0109       | 0.0389                           | 0.0000        |
| Number of life-years (undiscounted)          | 24.2619      | 24.2543                          | 24.2585       |
| Number of life-years (discounted)            | 18.0606      | 18.0570                          | 18.0590       |
| **Incremental outcomes**                     |              |                                  |               |
| Incremental costs                            | -$4294       | Avatrombopag vs prophylactic platelet transfusion | -$5802 |
| Incremental life-years (undiscounted)        | 0.0076       | 0.0034                           | 0.0016        |
| Incremental life-years (discounted)          | 0.0036       | 0.0036                           | 0.0036        |
| Cost per prophylactic platelet transfusion avoided | -$5391*       | -$39,084*                        |               |

Note: Avatrombopag compared with both prophylactic platelet transfusion and lusutrombopag resulted in lower costs and fewer prophylactic platelet transfusions, yielding a negative cost per prophylactic platelet transfusion avoided, which suggests that avatrombopag is the dominant treatment.
increased expense may be partly explained by the difference in cost of drug, efficacy differences at lower baseline platelet count with lusutrombopag may also be a factor. Lusutrombopag is dosed only as a single strength regardless of platelet count, whereas avatrombopag dosing is tailored based on baseline platelet count.

This analysis has been completed for the US; however, the burden of disease may be greater in other regions, in particular lower-income countries, where the prevalence of HCV is higher.\textsuperscript{26} Non-communicable diseases also impose an increasing burden on developing nations.\textsuperscript{27} Additional research on the cost-effectiveness of treating non-communicable diseases, including thrombocytopenia in patients with CLD, is needed to generate health economic evaluations applicable to lower and middle-income countries.\textsuperscript{28}

This cost-effectiveness analysis has several limitations. It is important to note the lack of head-to-head data comparing avatrombopag with lusutrombopag. The base-case parameters used an unadjusted comparison with lusutrombopag, which may make it difficult to make a robust estimate of comparative effectiveness. Additionally, the base-case analysis assumed that lusutrombopag and avatrombopag required equivalent platelet units per prophylactic platelet transfusion following drug treatment, resulting in the same cost per prophylactic platelet transfusion. Additionally, because of the nature of conducting registration-directed clinical trials, there is a lack of data on less-common, longer-term outcomes. Therefore, the base-case modeled analysis focused on short-term outcomes observed in clinical trials (eg, platelet transfusions to elevate platelet count, rescue procedures for bleeding). The results of the one-way sensitivity analysis suggest that further research into the full cost of platelet transfusion could affect the findings from this analysis. Although Barnett et al (2018)\textsuperscript{7} detailed the cost of a platelet transfusion in the US, there is a lack of information crucial to understanding the full cost of a platelet transfusion, as the authors noted data gaps in the literature. Since not all costs could be accounted for in the cost estimate from that study, the platelet transfusion cost used here may be an underestimate. Finally, the trial-based outcomes need to be validated in a real-world setting. For example, the risk of bleeding may be higher in a real-world than in a trial setting.

**Conclusion**

Patients with CLD and thrombocytopenia often have their platelet counts increased to reduce the risk of bleeding before undergoing a variety of procedures. The introduction of the thrombopoietin receptor agonists, avatrombopag and lusutrombopag, can reduce the use of platelet transfusions and decrease the associated patient burdens and risks. The administration of avatrombopag has shown to be cost-saving compared with prophylactic platelet transfusion and lusutrombopag, while also reducing the risk of thromboembolic events or bleeding events requiring rescue procedures in this patient population.

**Abbreviations**

CLD, Chronic liver disease; ICER, Incremental cost-effectiveness ratio; US, United States; VTE, venous thromboembolism.

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**Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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