CADTH

CADTH DRUG REIMBURSEMENT REVIEW

CADTH Drug Reimbursement Recommendation

(FINAL)

Von Willebrand Factor (Recombinant) (Vonvendi — Takeda Canada Inc.)
Indication: Treatment and control of bleeding episodes in adults (age ≥ 18) diagnosed with von Willebrand disease (VWD) and perioperative management of bleeding in adults (age ≥ 18) diagnosed with VWD.

RECOMMENDATION

The CADTH Canadian Plasma Protein Product Expert Committee (CPEC) recommends that von Willebrand factor (recombinant; rVWF) should be reimbursed for the treatment and control of bleeding episodes or perioperative management of bleeding in adults (aged ≥ 18) diagnosed with VWD only if the following conditions are met.

Initiation criteria

1. Adult patients with severe non-type 3 and type 3 VWD defined as any of the following:
   1.1. Type 1 (VWF:RCo < 20 IU/dL)
   1.2. Type 2A (VWF:RCo < 20 IU/dL), Type 2B (diagnosed by genotype), Type 2N (FVIII:C < 10% and historically documented genetics), or Type 2M
   1.3. Type 3 (VWF:Ag ≤ 3 IU/dL)

Prescribing conditions

1. The patients must be under the care of a hematologist with experience in the diagnosis and management of VWD.

Pricing conditions

1. The public payer cost for rVWF with concomitant rFVIII should not exceed the public payer cost of treatment with the least costly alternative treatment regimen for the management of VWD.

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Recommendation

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Conditions for Reimbursement

Initiation criteria

1. Adult patients with severe non–type 3 and type 3 VWD defined as any of the following:
   1.1. Type 1 (VWF:RCo < 20 IU/dL)
   1.2. Type 2A (VWF:RCo < 20 IU/dL), Type 2B (diagnosed by genotype), Type 2N (FVIII:C < 10% and historically documented genetics), or Type 2M
   1.3. Type 3 (VWF:Ag ≤ 3 IU/dL)

Prescribing conditions

1. The patients must be under the care of a hematologist with experience in the diagnosis and management of VWD.

Pricing conditions

1. The public payer cost for rVWF with concomitant rFVIII should not exceed the public payer cost of treatment with the least costly alternative treatment regimen for the management of VWD.

Reasons for the Recommendation

1. In one open-label, non-comparative phase III study evaluating the efficacy and safety of rVWF for the treatment of bleeding episodes in adult patients diagnosed with severe type 3 and severe non–type 3 VWD (Study 071001), all 40 patients (100%) treated with rVWF, with or without rFVIII, achieved treatment success (defined as a mean efficacy rating score of < 2.5) during the study period (Clopper-Pearson exact 90% confidence interval [CI], 84.7% to 100%). The results of Study 071001 also showed that hemostatic efficacy of the study drug was rated as “excellent” or “good” for all treated bleeding episodes: 100% ([redacted]).

2. In one open-label, non-comparative phase III trial conducted to evaluate the efficacy and safety of rVWF with or without rFVIII in major or minor elective surgeries in adult patients with severe VWD (Study 071101), overall hemostatic efficacy was rated as excellent or good for all 15 treated patients (100%, Clopper-Pearson exact 90% CI, 81.9 to 100) including 10 with major surgery, four with minor surgery and one with oral surgery. Further, the intra-operative hemostatic efficacy was also rated as excellent or good in all 15 patients.

3. rVWF is the only VWF replacement therapy approved by Health Canada that is not derived from human or animal plasma. The risk of transmitting blood-borne infection was not assessed in either Study 071001 or 071101, but rVWF does not contain any exogenous human or animal plasma-derived components. The availability of rVWF represents an alternative treatment that could be used should there ever be a concern about the transmission of blood-borne infections through plasma.

4. The cost-effectiveness of rVWF±rFVIII for the recommended population in the Canadian setting is uncertain. If only blood product acquisition cost was considered, rVWF±rFVIII was found to be $4,514 and $19,240 more costly per patient than antihemophilic factor/VWF complex for an on-demand bleeding episode and for a course of perioperative management, respectively. Although CADTH re-analyses demonstrated that a price reduction of 40% on rVWF is required for rVWF±rFVIII to have similar treatment acquisition cost as antihemophilic factor/VWF complex, the price reduction is sensitive to the price of

plasma protein products (i.e., plasma-derived VWF; rFVIII); and the proportion of patients who require rFVIII dosed concomitantly with rVWF.

Discussion Points

- CPEC identified several limitations of the available evidence from Studies 71001 and 71101. These trials were not randomized, had small sample sizes, and the primary outcome of hemostatic efficacy was based on a subjective and non-validated rating scale. While both CPEC and clinical experts agreed the studies had significant methodological flaws, the data were considered sufficient to support the efficacy of rVWF given the similar mechanism of action to plasma-derived VWF.
- Plasma-derived VWF containing factor VIII (FVIII) and concentrate (FVIII-VWF) are used currently for the control of bleeding episodes or for perioperative management in patients with VWD. Plasma-derived products may have the potential to increase the risk of transmission of blood-borne infections from pathogens that are currently known or will emerge in the future. CPEC acknowledged such risk and noted that the risk of infection of known transfusion-transmitted pathogens is presently considered to be extremely low in Canada based on modern risk mitigation strategies and modelling done at Canadian Blood Services. Patients raised concerns about the risk of viral contamination in plasma-derived factor concentrates and cited this as a reason to prefer treatment with a non–plasma-derived VWF replacement therapy.
- CPEC discussed the potential for shortages of plasma-derived products but resolved that this risk is very low for plasma-derived VWF. CPEC also agreed that there is also a potential for a shortage of a recombinant product, similar to other manufactured therapies. Although threats to the source plasma pool and/or demand exceeding supply for purified plasma products may potentially put the supply of currently available plasma-derived VWF products at risk, and consequently increase the attractiveness of rVWF as a possible alternative, there have been no recent reported shortages of plasma-derived VWF concentrates, and the supply of plasma-derived VWF concentrate has been adequate.
- CPEC acknowledged that rVWF is the only treatment for VWD that does not contain FVIII and it may be suited for patients who do not need additional FVIII, such as those with elevated FVIII or those who require repeated doses of VWF replacement therapy. Although supratherapeutic levels of FVIII have been associated with thrombosis, causality has not been confirmed. In Studies 071001 and 071101, rVWF was administered with or without FVIII; however, it is unclear whether the treatment effect or harms of rVWF alone is different from FVIII/VWF. Clinical experts acknowledged that the majority of cases where rVWF is used would also have concomitant FVIII administered, consistent with the studies 071001 and 071101. CPEC noted the concomitant use of rVWF with FVIII increases the complexity of treatment; however, this was considered acceptable by clinical experts.
- No direct or indirect evidence was available comparing the efficacy or safety of rVWF with plasma-derived FVIII-VWF (the current standard of care). CPEC identified this as a significant evidence gap and was unable to determine the potential clinical benefits of rVWF compared with plasma-derived FVIII-VWF. In the absence of a control group or any comparative data there is no evidence to support a price premium over currently available plasma-derived treatments for the control of bleeding episodes or perioperative management in patients with VWD.
- Clinical experts suggested that there is potential for use of rVWF in pediatric populations, similar to the manner in which plasma-derived VWF is used in clinical practice. However, this is beyond the indication approved by Health Canada and CPEC noted that the evidence provided supports the use of rVWF in adult patients only. Therefore, CPEC is unable to comment on the safety and efficacy in this patient population.

Background

rVWF has a Health Canada indication for the treatment and control of bleeding episodes in adults (age ≥ 18) diagnosed with VWD, and for the perioperative management of bleeding in adults (age ≥ 18) diagnosed with VWD. rVWF is a factor replacement therapy produced and formulated without exogenous human- or animal-derived plasma proteins. It is available as lyophilized powder for intravenous injection: 650 and 1,300 IU VWF ristocetin cofactor (VWF:RCo)/vial. Dosage and frequency of rVWF administration must be personalized according to clinical judgment and based on the patient's weight, type and severity of the bleeding episodes, the bleeding risk of the surgical intervention, and the monitoring of appropriate clinical and laboratory measures.

For the treatment and control of bleeding episodes: The first dose of rVWF should be 40 IU/kg to 80 IU/kg body weight. A single infusion of rVWF is expected to increase endogenous Factor VIII coagulant (FVIII:C) activity by more than 40% within six hours in a majority of patients, depending on their baseline FVIII:C levels. However, if the patient's baseline plasma FVIII:C level is less than 40% or is unknown, a recombinant FVIII (rFVIII) product should be administered with the first infusion of rVWF to achieve a hemostatic plasma FVIII:C level. Subsequent doses of 40 IU/kg to 60 IU/kg of rVWF every 8 to 24 hours are needed to maintain the hemostatic effect, depending on the severity of bleeding.

For perioperative management of bleeding: Prior to initiation of any surgical procedure, baseline VWF:RCo and FVIII:C levels should be assessed. The recommended minimum FVIII:C target levels before initiating the surgery are 30 IU/dL for minor surgery and 60 IU/dL for major surgery. In the case of major bleeding events or major surgical procedures requiring repeated, frequent infusions, monitoring of FVIII levels is recommended to decide if rFVIII is required for subsequent infusions and to avoid an excessive rise of FVIII.

Summary of Evidence

The committee considered the following information prepared by CADTH: a systematic review of two non-controlled, non-randomized clinical trials of rVWF and a critique of the sponsor's pharmacoeconomic evaluation. The committee also considered input from clinical experts with experience in treating patients with VWD and patient group–submitted information about outcomes and issues important to patients.

Summary of Patient Input

One patient group, the Canadian Hemophilia Society (CHS), provided input for this submission. Patient perspectives were obtained from an online survey conducted in January 2020 with individuals affected by VWD. CHS also consulted leading physicians with respect to the treatment of VWD. The following is a summary of key input from the perspective of CHS:

- Respondents to the CHS survey described VWD as a condition that can be very disabling and can have widespread negative effects on many aspects of their lives. VWD can cause frequent nosebleeds, bruises and joint bleeds, and can involve painful swelling of limbs, muscles, ligaments, and joints. Women with VWD can suffer from long and heavy menstrual bleeding and increased postpartum bleeding. Patients noted that joint pain and menstrual issues increase with age. As a result, many patients suffer lost time at work and school and their quality of life is significantly reduced.
- The respondents reported that their current treatments with plasma-derived factor concentrates were effective in stopping and preventing bleeding, but they can be associated with various adverse effects common to this class of therapies.
- Easier accessibility and administration of drugs, longer-lasting benefits, fewer adverse effects, and reduced sick days from work or school are important to patients with VWD. Patients are also willing to try recombinant VWD therapy if it is related to lower risk of viral contamination, which has previously occurred in plasma-derived factor concentrates. In addition, because rVWF is the first therapeutic to contain only VWF without FVIII, it may have the potential to fill an unmet need, where additional FVIII is not needed or in patients in whom it is contraindicated.

Clinical Trials

The systematic review included two phase III, open-label, non-controlled clinical trials of patients with severe VWD (Study 071001 for the treatment and control of bleeding episodes, N = 37; Study 071101 for perioperative management, N = 15).

Treatment and Control of Bleeding Episodes (Study 071001)

Study 071001 was a phase III, parallel-group, open-label, non-controlled, multicenter trial that assessed the efficacy, safety, and pharmacokinetics (PK) of rVWF with or without rFVIII (rVWF ± rFVIII) in the treatment of bleeding episodes in adult patients diagnosed with severe type 3 and severe non–type 3 VWD. Eligible study participants were assigned to one of four treatment groups at the discretion of the investigator:

1. PK50 (PK assessment with 50 IU/kg VWF:RCo rVWF with 38.5 IU/kg rFVIII or 50 IU/kg VWF:RCo rVWF with placebo) and 12-month on-demand treatment for bleeding episodes, n = 9

2. PK50 only (PK assessment with 50 IU/kg VWF:RCo rVWF), n = 9
3. PK80 (PK assessment with 80 IU/kg VWF:RCo rVWF) and 12-month on-demand treatment for bleeding episodes, n = 16
4. assessment of 12-month on-demand treatment for bleeding episodes only, n = 6.

The primary end point of this study was the number of patients with treatment success for treated bleeding episodes at the end of the study. Secondary efficacy end points included the number of study drug–treated bleeding episodes with an efficacy rating of "excellent" or "good," and the number of infusions and number of units of rVWF ± rFVIII per bleeding episode. The PK profile of rVWF was also examined. In this study, the mean age of the patients was 37 years, and most were white ([redacted]). The majority of the study participants (78%) had type 3 VWD and were receiving on-demand treatment exclusively in the 24 months prior to and at study enrolment ([redacted] and [redacted], respectively).

Perioperative Management (Study 071101)

Study 071101 was a phase III, open-label, non-randomized, non-controlled trial that evaluated the efficacy and safety of rVWF ± rFVIII in major or minor elective surgical procedures in adult patients with severe VWD (N = 15: 10 major and four minor surgical procedures and one oral surgery). Eligible study participants who planned for major surgery had an initial PK evaluation on rVWF over a 72-hour period within 42 days before surgery. A priming dose with rVWF 40 IU/kg to 60 IU/kg was given to patients 12 to 24 hours before surgery to allow the endogenous FVIII levels to increase to target levels before the loading dose of rVWF ± rFVIII was administered. Within one hour prior to surgery, an rVWF loading dose was administered, with or without rFVIII (depending on the FVIII:C levels). Intra-operative and post-operative dosing was individualized according to the PK results, intensity and duration of the hemostatic challenge, and the institution's standard of care. Doses were either rVWF alone or rVWF + rFVIII, depending on the respective VWF and FVIII levels. [redacted]. The primary efficacy outcome measure was the percentage of patients in each overall investigator-assessed hemostatic efficacy category (i.e., "excellent," "good," "moderate," and "none") 24 hours after the last perioperative infusion or at completion of the study, whichever occurred earlier. Secondary efficacy end points included intra- and post-operative blood loss and dose of rVWF required for perioperative management in the study population. The PK profile of rVWF was also examined. In this study, the mean age of the patients was 39 years. More than half of the study participants (53%) had type 3 VWD. Ten of 15 patients underwent major surgical procedures.

The major limitations of the two included trials are the non-randomized, non-controlled study design, small number of patients, and a lack of statistical comparison between the study drug and other active treatments. In both studies, patients and the attending physicians were not blinded to the treatment. Therefore, because a subjective rating scale was used to measure the treatment effect, the results of the assessment could be biased.

Outcomes

Outcomes were defined a priori in CADTH's systematic review protocol.

Treatment and Control of Bleeding Episodes (Study 071001)

Outcomes of Study 71001 that were discussed by the committee include the proportion of patients with treatment success, proportion of study drug–treated bleeding episodes with an "excellent" or "good" efficacy rating, total dose of the study drug per bleeding episode, number of infusions required for treatment of a bleeding episode, and health-related quality of life (HRQoL).

The primary outcome in Study 071001 was the proportion of patients with treatment success. Treatment success was defined as a mean efficacy rating score of less than 2.5, taking into account all bleeding episodes, and was measured using a physician-completed hemostatic efficacy rating scale. The mean efficacy score was based on a four-point rating scale defined using the prospectively estimated number of infusions needed to treat the bleeding episodes as assessed by the investigator versus the actual number of infusions administered: 1 = excellent, 2 = good, 3 = moderate, and 4 = none. Note that this rating scale is unvalidated, and a minimal clinically important difference has not been established in the study population.

HRQoL was measured using [redacted].

- [redacted].
- [redacted].

Perioperative Management (Study 071101)

Outcomes of Study 71101 that were discussed by the committee included overall hemostatic efficacy and intra-operative hemostatic efficacy, actual versus predicted intra-operative blood loss at surgery completion, and HRQoL.

In Study 071101, hemostatic efficacy was examined using a physician-completed rating scale: “excellent,” “good,” “moderate,” or “none.” No literature was identified that tested the hemostatic efficacy rating scale for reliability, validity, or responsiveness in patients with VWD. No minimal important difference was identified in the literature for this rating scale. It was used as guidance to assess the overall hemostatic efficacy of the study drug.

Results of hemostatic efficacy were presented as:

- Overall hemostatic efficacy 24 hours after last perioperative study drug infusion or at completion of the day 14 visit, whichever occurred earlier, as assessed by a physician. The proportion of patients rated “excellent” or “good” was reported. This was the primary end point in Study 071101. For the overall primary efficacy assessment rating, the following were considered: severity of bleedings observed during surgery, need for additional hemostatic medications, blood loss during surgery, and post-operative bleedings.
- Actual versus predicted intra-operative blood loss (assessed by the operating surgeon) at completion of surgery. This was the secondary efficacy end point in Study 071101.

End points related to HRQoL included the [redacted] and [redacted], as previously described.

Efficacy

Several efficacy outcomes were descriptively reported without performing formal statistical testing, including the dose of infused study drug required for treatment of bleeding episodes and the number of infusions required per bleeding episode in Study 071001, the actual intra-operative blood loss and dose of study drug in Study 071101, and HRQoL and any subgroup analyses in both trials.

Treatment and Control of Bleeding Episodes (Study 071001)

Hemostatic Efficacy

All patients achieved treatment success (primary efficacy end point) when they were treated with rVWF ± rFVIII during the study period. Treatment was successful in 100% (18 of 18) of patients with on-demand treatment for bleeding episodes (Clopper-Pearson exact [redacted] confidence interval [CI], [redacted]). In addition, hemostatic efficacy of the study drug was rated as “excellent” or “good” (secondary efficacy outcome) for [redacted] of treated bleeding episodes (Clopper-Pearson exact [redacted]). These results were based on a subjective, physician-completed rating scale; however, the accuracy of this scale is unclear.

Total Dose of rVWF ± rFVIII per Bleeding Episode

The mean total dose of rVWF ± rFVIII was 57.4 IU/kg (standard deviation [SD] = 30.3) per bleeding episode. [redacted].

Number of Infusions Required for Treatment of a Bleeding Episode

In 192 bleeding episodes, the mean number of infusions was 1.2 (SD = 0.6) infusions for treatment of a bleeding episode, and the median number of infusions was 1.0 (range = 1 to 6). For 81.8% (157/192) of the bleeding episodes, one infusion of rVWF + rFVIII or rVWF alone was required for bleeding control. Of these, 94.8% of the bleeding episodes were controlled with one infusion of rVWF + rFVIII.

HRQoL

In this study, HRQoL was included as [redacted]. Therefore, the potential benefit of rVWF on HRQoL is unknown.

Perioperative Management (Study 071101)

Hemostatic Efficacy

Overall hemostatic efficacy was rated as "excellent" or "good" for all 15 treated patients (100%, Clopper-Pearson exact 90% CI, 81.9 to 100). The intra-operative hemostatic efficacy was also rated as "excellent" or "good" in all 15 patients. As in Study 071001, the primary efficacy outcome of this study was based on a subjective, unvalidated, physician-completed rating scale; therefore, the accuracy of this scale is unclear.

Intra-operative Blood Loss

During surgery, the actual blood loss assessed by the operating surgeon was less than the predicted blood loss in the study population (actual blood loss = 94.3 mL vs. predicted blood loss = 106.1 mL). The clinical experts consulted by CADTH for this review did not consider this difference clinically important, given the challenges of accurately measuring intra-operative blood loss and the small sample size of this study.

HRQoL

HRQoL was included as an exploratory outcome. [redacted]; therefore, no inferences can be made because no hypotheses were tested.

Harms (Safety)

Treatment and Control of Bleeding Episodes (Study 071001)

[redacted]. None of these SAEs occurred in more than one patient. One patient discontinued treatment because of an AE of chest discomfort and increased heart rate. For the AEs of special interest, one patient reported a hypersensitivity reaction and one patient reported an infusion-related reaction of tachycardia.

Perioperative Management (Study 071101)

A total of 12 AEs were reported by six patients ([redacted]) during or after infusion with the study drug, including acne, dry skin, iron deficiency anemia, peripheral swelling, nasopharyngitis, joint swelling, dizziness, headache, pelvic pain, and deep vein thrombosis. These AEs were mild to moderate in severity. Two patients reported SAEs (one reported deep vein thrombosis and one reported diverticulitis). No patient withdrew from the study because of AEs and no deaths were reported during the study. For AEs of special interest, one patient had thrombotic events and another patient developed anti-VWF binding antibodies.

Indirect Treatment Comparisons

No indirect evidence was submitted by the sponsor for this review. CADTH conducted a literature search to identify potentially relevant indirect treatment comparisons in patients with VWD. No relevant indirect comparisons were identified in the literature search.

Cost and Cost-Effectiveness

The sponsor's submitted price for rVWF is $1,002.89 per 650 IU vial and $2,005.77 per 1,300 IU vial. The recommended dosage regimen is personalized according to clinical judgment based on the patient's weight, disease type, severity of the bleeding episodes or type of surgical intervention, and clinical and laboratory measures. The average daily treatment costs for on-demand treatment ranges from $5,014 to $17,049 for minor bleeding episodes and $6,017 to $22,063 for major bleeding episodes. For perioperative management, costs range from $2,006 to $3,009 per day for minor surgery and $5,014 per day for major surgery.

The sponsor submitted a cost-utility analysis comparing rVWF ± rFVIII with FVIII-VWF complex (Humate-P), stratified based on the following clinical scenarios in adult patients diagnosed with VWD: (1) on-demand treatment of bleeding episodes and (2) peri-operative management of bleeding. The analysis was conducted from the perspective of the Canadian publicly funded health care system with the time horizon corresponding to the time to manage hemostasis and subsequent consequences for an episode of care (i.e., 8 days for on-demand bleeding episode and 16 days for perioperative episode). A decision tree was employed to capture an episode of care for both the on-demand bleeding and the perioperative management scenarios. Patients enter the model at the start of a bleeding episode or in a perioperative setting. Following initial treatment, patients may or may not achieve hemostasis. In those who achieve hemostasis, bleeding is resolved. Patients who do not achieve hemostasis are assumed to experience uncontrolled bleeding that requires subsequent treatment to achieve hemostasis. Mortality was not considered in the model. Efficacy, safety, and resource use inputs into the model were from different sources, including prospective single-arm trials for rVWF ± rFVIII (Studies 071001 and 071101) and multiple observational studies for FVIII-VWF complex. In the sponsor's base case, rVWF ± rFVIII was less costly and more effective than FVIII-VWF complex (i.e., rVWF ± rFVIII dominant); whereas, for the perioperative management subgroup, the incremental cost-effectiveness ratio for rVWF ± rFVIII was $30,997 per quality-adjusted life-year gained compared to FVIII-VWF complex.

CADTH identified several key limitations with the submitted analysis:

- There was no head-to-head comparative study to inform relative efficacy and safety or differences in resource use between rVWF ± rFVIII and FVIII-VWF complex. Estimates from different sources were selected, which favoured rVWF ± rFVIII. Clinical experts consulted by CADTH suggested that they would not expect a difference between products, which raised concerns in predicted differences in clinical effects and expected quality-adjusted life-years.
- FVIII-VWF (Wilate) was not included as a comparator in the analysis.
- The prices of FVIII-VWF complex and rFVIII were based on US prices and are unlikely to reflect the prices in Canada.

Without comparative clinical evidence to support a difference in efficacy, safety, or resource use between rVWF ± rFVIII and FVIII-VWF complex, CADTH assumed these model inputs were identical for the two products; therefore, the analysis captured differences in the acquisition costs. In the CADTH base case, rVWF ± rFVIII was $4,514 and $19,240 more expensive than FVIII-VWF complex for the on-demand bleeding and perioperative management subgroups, respectively. A price reduction of 40% was required for rVWF to have similar treatment acquisition cost as FVIII-VWF complex, although this is sensitive to the price of plasma protein products (i.e., FVIII-VWF complex and rFVIII) and the proportion of patients on rVWF who require concomitant dosing with rFVIII.

September 16, 2020 Meeting (Initial)

CPEC Members

Dr. James Silvius (Chair), Dr. Ahmed Bayoumi, Dr. Sally Bean, Dr. Bruce Carleton, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Mr. Allen Lefebvre, Ms. Heather Neville, Dr. Rakesh Patel, Dr. Danyaal Raza, Dr. Emily Reynen, Dr. Yvonne Shevchuk, Dr. Andrew Shih, Dr. Irene Sadek, and Dr. Adil Virani.

Regrets

One expert committee member did not attend.

Conflicts of Interest

None

February 17, 2021 Meeting (Reconsideration)

CPEC Members

Dr. James Silvius (Chair), Dr. Ahmed Bayoumi, Dr. Sally Bean, Dr. Bruce Carleton, Dr. Alun Edwards, Mr. Bob Gagne, Dr. Ran Goldman, Dr. Allan Grill, Mr. Allen Lefebvre, Dr. Kerry Mansell, Ms. Heather Neville, Dr. Danyaal Raza, Dr. Emily Reynen, Dr. Irene Sadek, Dr. Yvonne Shevchuk, Dr. Andrew Shih, and Dr. Adil Virani.

Regrets

None

Conflicts of Interest

None