From:	Bouma, Susan HLTH:EX
To:	Chong, Elaine HLTH:EX; Fazlagic, Tijana HLTH:EX; Pang, Walton HLTH:EX; Lun, Eric HLTH:EX; Weston, Megan D HLTH:EX
Cc:	Naumann, Terryn HLTH:EX; Weston, Megan D HLTH:EX
Subject:	RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects
Date:	Tuesday, March 6, 2018 10:42:11 AM

Hi Elaine!

Terryn, you are fabulous! Agree with all three.

s.13

Sue
-----Original Message-----
From: Chong, Elaine HLTH:EX
Sent: Monday, March 5, 2018 5:28 PM
To: Fazlagic, Tijana HLTH:EX; Bouma, Susan HLTH:EX; Pang, Walton HLTH:EX; Lun, Eric HLTH:EX; Weston, Megan D HLTH:EX
Cc: Naumann, Terryn HLTH:EX
Subject: FW: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Thanks Terryn for her thoughts - others?

EC

-----Original Message-----
From: Naumann, Terryn HLTH:EX
Sent: Monday, March 5, 2018 3:58 PM
To: Chong, Elaine HLTH:EX
Subject: RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Hi Elaine,

s.13

s.13

Terryn

-----Original Message-----
From: Chong, Elaine HLTH:EX
Sent: Friday, March 2, 2018 10:59 AM
To: Fazlagic, Tijana HLTH:EX; Bouma, Susan HLTH:EX; Pang, Walton HLTH:EX; Naumann, Terryn HLTH:EX; Lun, Eric HLTH:EX; Weston, Megan D HLTH:EX
Subject: FW: Therapeutic Initiative Bi Weekly Meetings: PEG projects
Importance: High

All,

s.13

EC

-----Original Message-----
From: Colin Dormuth [mailto:colin.dormuth@ti.ubc.ca]
Sent: Friday, February 23, 2018 4:03 PM
To: Moneo, Mitch HLTH:EX; 'Bob Nakagawa'
Cc: 'Jim Wright'; El Agab, Charlotte S HLTH:EX; ken.bassett@ti.ubc.ca; Lun, Eric HLTH:EX; Fazlagic, Tijana HLTH:EX; Chong, Elaine HLTH:EX
Subject: Therapeutic Initiative Bi Weekly Meetings: PEG projects

All,

s.13

Have a good weekend.

Colin Dormuth, Sc.D.
Associate Professor
Dept. of Anesthesiology, Pharmacology & Therapeutics (APT) UBC Victoria Office Suite 210, 1110 Government Street Victoria, BC V8W 1Y2 UBC Vancouver Office Room 309, 2176 Health Sciences Mall Vancouver, BC V6T 1Z3
Phone: 250-388-9912
Fax: 250-595-5954

DIABETES CANADA

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Call us: 1-800-BANTING (226-8464)
Visit us: www.diabetes.ca
Charitable number: 11883 0744 RR0001

Dr. Jan Hux
President, Diabetes Canada

January 30, 2018

Therapeutics Initiative
2176 Health Sciences Mall
Vancouver, BC
V6T 1Z3

Re: Therapeutics Initiative's assessment of the EMPA-REG OUTCOME trial

To whom it may concern,

Diabetes Canada appreciates the opportunity to comment on the Therapeutics Initiative's assessment of the EMPA-REG OUTCOME trial. We are concerned with several points made in Therapeutics Letter 107 and with the overall tone and message of the review. It gives the impression of a bias against medication use in people with diabetes. This is a position we patently disagree with. We believe that people living with diabetes deserve every available opportunity to achieve their full health potential. This includes having access both to medications and to nonpharmacologic interventions that could improve their outcomes and reduce their risk of disease-related complications. It is important for Therapeutics Initiative reviewers to declare their perspectives against medications and specific populations up-front when writing editorials about clinical trials and medical therapy. There are significant policy implications to a publicly funded institution taking a position that appears biased against people living with a progressive, chronic condition with no known cure.

1. In interpreting the EMPA-REG OUTCOME trial results, the authors posit that "the more aggressive use of other glucose-lowering medications in the placebo group increases mortality and serious adverse events". As the authors likely know, the Food and Drug Administration (FDA), through its 2008 guidance document[i], mandated that all the cardiovascular outcome trials (CVOTs) with antihyperglycemic agents be carried out with a design of glycemic equipoise (both the drug and placebo arms should continue to be treated during the trial to standard of care and HbA1c targets according to local guidelines in every country). All CVOTs, since this regulation was applied, have had an increased utilization of glucose lowering agents in the placebo and comparator arms of the trials and resulted in minimal HbA1c difference between the two arms (ranging from 0.2%-0.3%). This is relevant because the HbA1c effects are minimized between the groups and unlikely to be the reason for differences in serious adverse events.

2. Empagliflozin was noted to cause harm to study participants, in the form of genital infections for 1 in 29 men and 1 in 14 women over a three year period, and that this adversely affected their quality of life. Indeed, increased risk of genitourinary infections is a known side effect of empagliflozin. It is an effect that many people living with diabetes would be willing to chance and/or to bear for an opportunity at longer life. Decreased risk of cardiovascular mortality – i.e. survival – is the most important outcome for the majority of people with diabetes. However, we strongly support patients being informed of the potential benefits and harms of therapy and being part of the decision-making for their own treatment.

jan.hux@diabetes.ca
Executive Assistant: Antonella Polera antonella.polera@diabetes.ca, Direct: 416-408-7024

DIABETES CANADA

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Call us: 1-800-BANTING (226-8464)
Visit us: www.diabetes.ca
Charitable number: 11883 0744 RR0001

3. The FDA's rejection of the claim that empagliflozin reduces the risk of nephropathy was also noted in the Therapeutics Letter as another "reason for scepticism". We agree that this evidence should direct regulatory approval and clinical recommendations. In a 2016 update to Diabetes Canada's 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada, empagliflozin was recommended as a treatment for suboptimal glycemic control in people with type 2 diabetes and clinical cardiovascular disease. Though the potential microvascular benefits of the drug are recognized, the guidelines suggest the addition of empagliflozin specifically for its cardioprotective effects, as follows: "In adults with type 2 diabetes with clinical cardiovascular disease in whom glycemic targets are not met, an antihyperglycemic agent with demonstrated cardiovascular outcome benefit should be added to reduce the risk of major cardiovascular events (Grade 1, Level 1A for empagliflozin)."

   The lack of demonstrated clinical benefit to reduce the risk of nephropathy does not negate the demonstrated cardiovascular outcome benefits.

4. The conclusion states that "the EMPA-REG OUCTOME Trial tested the addition of empagliflozin to a 'standard of care' for T2DM whose impact on clinically important outcomes is currently unknown". Recommendations for current standards of care are based on trials that have measured HbA1c. Glycemic control measured by HbA1c is a surrogate outcome used in clinical trials that has been a standard metric for decades. In the absence of outcome data, HbA1c is useful to guide decision making. Therapeutics Initiative reviewers have previously questioned the validity of HbA1c as a surrogate outcome. Now that health outcome data are available, these data are also being discarded. The reviewers seem to be systematically biased against people with diabetes having access to medications that can improve their health outcomes.

Diabetes Canada asserts that education, behavioural interventions and support are essential for optimal diabetes management. Medications can be added to therapy as an important adjunct to the care regimen for many Canadians. Therapy must always be individualized, and should include evidence-based options for people living with this disease. Diabetes Canada highlights that the evidence for the role of empagliflozin in the population with type 2 diabetes and clinical cardiovascular disease is robust and we continue to recommend this medication as a choice for those clinicians and patients who wish to access it. We would welcome a discussion with you about these very important issues and the evidence that supports this position.

Sincerely,

Dr. Jan Hux

[i] U.S. Food and Drug Administration. Guidance for Industry: Diabetes Mellitus – Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes. 2008, Center for Drug Evaluation and Research. Available from https://www.fda.gov/downloads/Drugs/Guidances/ ucm071627.pdf.

jan.hux@diabetes.ca
Executive Assistant: Antonella Polera antonella.polera@diabetes.ca, Direct: 416-408-7024

From:	Lun, Eric HLTH:EX
To:	Chong, Elaine HLTH:EX; XT:Dormuth, Colin 0 HLTH:IN; "Jim Wright"; ken.bassett@ti.ubc.ca
Cc:	Moneo, Mitch HLTH:EX; "Bob Nakagawa"; Pang, Walton HLTH:EX; Fazlagic, Tijana HLTH:EX
Subject:	Re: Therapeutic Initiative Bi Weekly Meetings: PEG projects
Date:	Monday, March 5, 2018 10:28:19 PM
Attachments:	Therapeutics Initiative letter Jan 2018 JH.pdf

s.13

Thanks,

Eric

Eric Lun, PharmD
Executive Director, Drug Intelligence, Optimization, Outcomes, and Strategy
Pharmaceutical Services Division
BC Ministry of Health
Original Message
From: Chong, Elaine HLTH:EX
Sent: Friday, March 2, 2018 11:11
To: XT:Dormuth, Colin 0 HLTH:IN; 'Jim Wright'; ken.bassett@ti.ubc.ca
Cc: Lun, Eric HLTH:EX; Moneo, Mitch HLTH:EX; 'Bob Nakagawa'; Pang, Walton HLTH:EX; Fazlagic, Tijana HLTH:EX
Subject: RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Colin, Jim, and Ken,

s.13

Many thanks,
EC

-----Original Message-----
From: Colin Dormuth [mailto:colin.dormuth@ti.ubc.ca]
Sent: Friday, February 23, 2018 4:03 PM
To: Moneo, Mitch HLTH:EX; 'Bob Nakagawa'
Cc: 'Jim Wright'; El Agab, Charlotte S HLTH:EX; ken.bassett@ti.ubc.ca; Lun, Eric HLTH:EX; Fazlagic, Tijana HLTH:EX; Chong, Elaine HLTH:EX
Subject: Therapeutic Initiative Bi Weekly Meetings: PEG projects

All,

s.13

s.13

Have a good weekend.

Colin Dormuth, Sc.D.
Associate Professor
Dept. of Anesthesiology, Pharmacology & Therapeutics (APT) UBC Victoria Office Suite 210, 1110 Government Street Victoria, BC V8W 1Y2 UBC Vancouver Office Room 309, 2176 Health Sciences Mall Vancouver, BC V6T 1Z3
Phone: 250-388-9912
Fax: 250-595-5954

Page 007

Withheld pursuant to/removed as

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- CANVAS study recently published in June 2017, second SGLT2 inhibitor, canagliflozin, evaluating cardiovascular (CV) safety in type 2 diabetic patients.

Empagliflozin:

- First SGLT2i with published data suggesting no increased risk of major CV adverse events – based on 1 single trial
- Health Canada indication: as an add-on therapy to standard diabetes care to reduce the incidence of CV death in patients with type 2 diabetes mellitus (T2DM) and established CV disease who have inadequate glycemic control.
- CDR Drug recommendations (Oct. 2016):
  - Reimbursed as an adjunct to diet, exercise, and standard care therapy to reduce the incidence of CV death in patients with T2DM and established CV disease who have inadequate glycemic control, if the following criteria are met:
    - Patients have inadequate glycemic control despite an adequate trial of metformin
    - Patients have established CV disease as defined in the EMPA-REG OUTCOME trial
- CDR Discussion Points (Oct. 2016):
  - "CDEC recognizes that there is a further need for evidence development to confirm the results of this trial."
  - "…most patients were on two or more antidiabetic drugs at baseline."
- CADTH Therapeutic Review for Second-Line Therapy (May 2017):
  - For adults with type 2 diabetes and established cardiovascular disease, CDEC recommends that therapy be considered in accordance with CDEC recommendations for individual drugs that have been reviewed specifically for this indication.
  - "Data regarding the comparative long-term efficacy and safety of different classes of second-line antidiabetes drugs on clinically important complications of diabetes, particularly cardiovascular outcomes, are currently sparse and of limited quality."

Some points to keep in mind when considering the following studies:

- Inadequate glycemic control: based on surrogate marker, which does not correlate well with clinical outcomes
- Evidence for T2DM will continue to evolve in the next several years

CVD-REAL 2017

- Retrospective study with data from 6 countries: US, Germany, Sweden, Norway, Denmark, UK, funded by AstraZeneca
- Identified T2DM patients on SGLT2 inhibitors and other glucose lowering agents (oral and insulin)
- Mean age 57 yo, 44% women, 13% established CV disease, 67% on statins, 80% anti-hypertensive meds, 74% ACEi/ARBs, 79% metformin
- Follow up of approximately 200 000 patient years --> less than a year on average per patient

	Follow Up (person-years)	Pts in each group	Mean duration of Follow-Up (days)		HR (95% CI, p-value)
			SGLT2i	Others	
Hospitalization for heart failure	190 164	309 056	239	211	0.61 (0.51-0.73, p<0.001) SGLT2i lower incidence
All cause death	153 990	107 811	271	251	0.49 (0.41-0.57, p<0.001) SGLT2i lower incidence
Composite: hospitalization for heart failure & death	143 342	107 811	253	233	0.54 (0.48-0.60, p<0.001) SGLT2i lower incidence

- Observational study with extremely short follow-up period, results should only be considered as associations.
- There were many people that were excluded from analysis with no clear reason.
- Results suggest an association between SGLT2 inhibitors and low risk of hospitalization and all cause death.
- No discussion of any adverse events for SGLT2 inhibitors compared with other glucose lowering agents.
- Would be concerned for diabetic ketoacidosis and other harms. Recent editorial has indicated SGLT2 inhibitors are associated with two times more likely to cause DKA compared with DPP4 inhibitors. (http://www.nejm.org/doi/full/10.1056/NEJMc1701990)

Prepared by: Shirley Yeung, BSc (Pharm), July 2017

CANVAS 2017 – sponsored by Janssen Research

Objective: assess CV safety & efficacy of canagliflozin in 30 countries, 667 centers (R, DB PC)

T2DM, mean duration 13.5 yrs Mean age 63.3, 64.2% ♂ 65.6% CVD 50% insulin; 75% metformin; 50% sulfonylurea Mean HbA1c 8.2% Median Follow-up: 2.4 yrs **1° outcome**: composite of death from CV causes, non-fatal MI, non-fatal stroke	CANVAS N=4330	100 mg canagliflozin daily 300 mg canagliflozin daily	Canagliflozin N = 5795	**26.9** events per 1000 patient years	HR 0.86 95% CI 0.75 to 0.97 p<0.001 non inferiority (margin at 1.3) p=0.02 for superiority* ~$660/yr ~$660 000 to ↓ 4 events	**10.1%** 585/5795
		Placebo (standard of care)				
	CANVAS-R N=5812	100 mg canagliflozin daily x 12 weeks, ↑ 300 mg canagliflozin daily	Placebo N = 4347	**31.5** Events per 1000 patient years		**9.8%** 426/4347
		Placebo (standard of care)				

Safety Concerns (/1000 pt-yrs)	Canagliflozin	Placebo	HR (95% CI, p)
Amputation of toes, feet, legs	6.3	3.4	1.97 (1.41 to 2.75, <0.001)
All fractures	15.4	11.9	1.26 (1.04 to 1.52, 0.02)
♂ genitalia infection	34.9	10.8	P<0.001
♀ mycotic genital infection	68.8	17.5	P<0.001

New FDA Warning: ↑ leg & foot amputations

30% dropped out from the study
Designed to assess safety
Event rate lower in placebo
Short duration of study

EMPA-REG 2015 – sponsored by Boehringer Ingelheim

Objective: examine the effects of empaglifozin on CV morbidity & mortality in T2DM at high risk of CV events in 42 countries, 590 sites (R, DB, PC)

T2DM, 57% > 10 yrs duration Mean age 63, 70% ♂ 99% CVD, 46% history of MI 50% dual glucose-lowering therapy Mean HbA1c 8.1% Median Follow-up: 3.1 yrs **1° outcome**: composite of death from CV causes, non-fatal MI, non-fatal stroke	10 mg empagliflozin daily	Empagliflozin N = 4687	**37.4** events per 1000 patient years	**10.5%** 490/4687	HR 0.86 95% CI 0.74 to 0.99 P<0.001 non inferiority (margin at 1.3) P=0.04 for superiority* ~$540/yr ~$540 000 to ↓ 6 events
	25 mg empaglifozin daily	Placebo N = 2333	**43.9** events per 1000 patient years	**12.1%** 282/2333	
	Placebo (standard of care)				

Safety Concerns (events)	Empagliflozin	Placebo	P value
Genital infection	301 (6.4%)	42 (1.8%)	P< 0.001
♂ genital infection	166 (5.0%)	25 (1.5%)	P<0.001
♂ genital infection	135 (10.0%)	17 (2.6%)	P<0.001
acute kidney injury	45 (1.0%)	37 (1.6%)	P<0.05

25.4% discontinued the drug early

Designed to assess safety
Methodological flaws
Short duration of study

*For superiority, the FDA statutory criterion of "substantial evidence" requires a persuasive P-value of <0.001 based on a single trial

Prepared by: Shirley Yeung, BSc (Pharm), July 2017

Comments/Concerns:

s.13

Page 011 to/à Page 025

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From:	Chong, Elaine HLTH:EX
To:	Fazlagic, Tijana HLTH:EX; Bouma, Susan HLTH:EX; Pang, Walton HLTH:EX; Naumann, Terryn HLTH:EX; Lun, Eric HLTH:EX; Weston, Megan D HLTH:EX
Subject:	FW: Therapeutic Initiative Bi Weekly Meetings: PEG projects
Date:	Friday, March 2, 2018 10:58:00 AM
Attachments:	List of PEG projects 23FEB2018.docx RE Victoza.msg
Importance:	High

All,

s.13

EC

-----Original Message-----
From: Colin Dormuth [mailto:colin.dormuth@ti.ubc.ca]
Sent: Friday, February 23, 2018 4:03 PM
To: Moneo, Mitch HLTH:EX; 'Bob Nakagawa'
Cc: 'Jim Wright'; El Agab, Charlotte S HLTH:EX; ken.bassett@ti.ubc.ca; Lun, Eric HLTH:EX; Fazlagic, Tijana HLTH:EX; Chong, Elaine HLTH:EX
Subject: Therapeutic Initiative Bi Weekly Meetings: PEG projects

All,

s.13

Have a good weekend.

Colin Dormuth, Sc.D.
Associate Professor
Dept. of Anesthesiology, Pharmacology & Therapeutics (APT) UBC Victoria Office Suite 210, 1110 Government Street Victoria, BC V8W 1Y2 UBC Vancouver Office Room 309, 2176 Health Sciences Mall Vancouver, BC V6T 1Z3
Phone: 250-388-9912
Fax: 250-595-5954

Page 027 to/à Page 029

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Page 030 to/à Page 065

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SUPPLEMENTAL MATERIAL

Page 067 to/à Page 145

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From:	Chong, Elaine HLTH:EX
To:	XT:Dormuth, Colin 0 HLTH:IN; "Jim Wright"; ken.bassett@ti.ubc.ca
Cc:	Lun, Eric HLTH:EX; Moneo, Mitch HLTH:EX; "Bob Nakagawa"; Pang, Walton HLTH:EX; Fazlagic, Tijana HLTH:EX
Subject:	RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects
Date:	Friday, March 2, 2018 11:10:00 AM
Attachments:	Empagliflozin_Liraglutide_Study_Proposal_20180227_EC.DOCX EMPA-REG_empagliflozin_CANVAS_canagliflozin_CriticalAppraisal.pdf LEADER - Liraglutide NEJM.PDF LEADER_liraglutide_CriticalAppraisal.pdf CVD-REAL 2017.pdf

---

Colin, Jim, and Ken,

s.13

Many thanks,
EC

-----Original Message-----
From: Colin Dormuth [mailto:colin.dormuth@ti.ubc.ca]
Sent: Friday, February 23, 2018 4:03 PM
To: Moneo, Mitch HLTH:EX; 'Bob Nakagawa'
Cc: 'Jim Wright'; El Agab, Charlotte S HLTH:EX; ken.bassett@ti.ubc.ca; Lun, Eric HLTH:EX; Fazlagic, Tijana HLTH:EX; Chong, Elaine HLTH:EX
Subject: Therapeutic Initiative Bi Weekly Meetings: PEG projects

All,

s.13

Have a good weekend.

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Associate Professor
Dept. of Anesthesiology, Pharmacology & Therapeutics (APT) UBC Victoria Office Suite 210, 1110 Government Street Victoria, BC V8W 1Y2 UBC Vancouver Office Room 309, 2176 Health Sciences Mall Vancouver, BC V6T 1Z3
Phone: 250-388-9912
Fax: 250-595-5954

From:	Joan King
To:	Lun, Eric HLTH:EX
Cc:	Maglanque, Joyce HLTH:EX; Sheila Kern
Subject:	Diabetes Canada"s response to TI letter #107
Date:	Thursday, February 22, 2018 2:51:27 PM
Attachments:	Therapeutics Initiative letter Jan 2018 JH.pdf

Good day, Mr. Lun and Joyce. I hope this note finds you both well.

I have attached for your information our President's recent submission to the Therapeutics Initiative in response to its Letter #107. Unfortunately it has not yet been posted, but I expect it will be soon.

Also, the following statements released by Diabetes Canada may be of interest to you:

- DC's response to budget 2018 https://www.diabetes.ca/newsroom/search-news/bc-budget-2018
- DC announces HQO recommendation to publicly fund CGMs https://www.diabetes.ca/newsroom/search-news/health-quality-on-cgm

Mr. Lun, I have not yet had an opportunity to meet you and wonder if you have 30 minutes available on March 7 or 8 to meet with me and my colleague, Sheila Kern, Regional Director, BC and Yukon?

Thank you both and truly appreciate your consideration.

Best wishes, Joan

Joan King
Government Relations, Western Canada
Diabetes Canada
T: 780-423-5722 ext 1211
diabetes.ca | 1-800-banting | Leading the fight to end diabetes

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Dr. Jan Hux
President, Diabetes Canada

January 30, 2018

Therapeutics Initiative
2176 Health Sciences Mall
Vancouver, BC
V6T 1Z3

Re: Therapeutics Initiative's assessment of the EMPA-REG OUTCOME trial

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1. In interpreting the EMPA-REG OUTCOME trial results, the authors posit that "the more aggressive use of other glucose-lowering medications in the placebo group increases mortality and serious adverse events". As the authors likely know, the Food and Drug Administration (FDA), through its 2008 guidance document[i], mandated that all the cardiovascular outcome trials (CVOTs) with antihyperglycemic agents be carried out with a design of glycemic equipoise (both the drug and placebo arms should continue to be treated during the trial to standard of care and HbA1c targets according to local guidelines in every country). All CVOTs, since this regulation was applied, have had an increased utilization of glucose lowering agents in the placebo and comparator arms of the trials and resulted in minimal HbA1c difference between the two arms (ranging from 0.2%-0.3%). This is relevant because the HbA1c effects are minimized between the groups and unlikely to be the reason for differences in serious adverse events.

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jan.hux@diabetes.ca
Executive Assistant: Antonella Polera antonella.polera@diabetes.ca, Direct: 416-408-7024

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Visit us: www.diabetes.ca
Charitable number: 11883 0744 RR0001

3. The FDA's rejection of the claim that empagliflozin reduces the risk of nephropathy was also noted in the Therapeutics Letter as another "reason for scepticism". We agree that this evidence should direct regulatory approval and clinical recommendations. In a 2016 update to Diabetes Canada's 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada, empagliflozin was recommended as a treatment for suboptimal glycemic control in people with type 2 diabetes and clinical cardiovascular disease. Though the potential microvascular benefits of the drug are recognized, the guidelines suggest the addition of empagliflozin specifically for its cardioprotective effects, as follows: "In adults with type 2 diabetes with clinical cardiovascular disease in whom glycemic targets are not met, an antihyperglycemic agent with demonstrated cardiovascular outcome benefit should be added to reduce the risk of major cardiovascular events (Grade 1, Level 1A for empagliflozin)."

   The lack of demonstrated clinical benefit to reduce the risk of nephropathy does not negate the demonstrated cardiovascular outcome benefits.

4. The conclusion states that "the EMPA-REG OUCTOME Trial tested the addition of empagliflozin to a 'standard of care' for T2DM whose impact on clinically important outcomes is currently unknown". Recommendations for current standards of care are based on trials that have measured HbA1c. Glycemic control measured by HbA1c is a surrogate outcome used in clinical trials that has been a standard metric for decades. In the absence of outcome data, HbA1c is useful to guide decision making. Therapeutics Initiative reviewers have previously questioned the validity of HbA1c as a surrogate outcome. Now that health outcome data are available, these data are also being discarded. The reviewers seem to be systematically biased against people with diabetes having access to medications that can improve their health outcomes.

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Sincerely,

Dr. Jan Hux

[i] U.S. Food and Drug Administration. Guidance for Industry: Diabetes Mellitus – Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes. 2008, Center for Drug Evaluation and Research. Available from https://www.fda.gov/downloads/Drugs/Guidances/ ucm071627.pdf.

jan.hux@diabetes.ca
Executive Assistant: Antonella Polera antonella.polera@diabetes.ca, Direct: 416-408-7024

Maglanque, Joyce HLTH:EX

From: Lun, Eric HLTH:EX
Sent: Thursday, March 8, 2018 11:28 PM
To: Chong, Elaine HLTH:EX; XT:Dormuth, Colin 0 HLTH:IN
Cc: Dizon, Kristine D HLTH:EX; Maglanque, Joyce HLTH:EX
Subject: RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Follow Up Flag: Follow up
Flag Status: Completed

Joyce/Kristine - high priority meeting so if there is a conflict in our calendars, please let us know so we can find the time/space for this meeting.
Thanks,
Eric

-----Original Message-----
From: Chong, Elaine HLTH:EX
Sent: Thursday, March 8, 2018 11:49 AM
To: XT:Dormuth, Colin 0 HLTH:IN
Cc: Dizon, Kristine D HLTH:EX; Lun, Eric HLTH:EX
Subject: RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Colin,

Yes, absolutely. Copying Kristine to assist with our calendars. Please advise when you are available.

EC

-----Original Message-----
From: Colin Dormuth [mailto:colin.dormuth@ti.ubc.ca]
Sent: Thursday, March 8, 2018 10:59 AM
To: Chong, Elaine HLTH:EX
Cc: Lun, Eric HLTH:EX
Subject: RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Hi Eric and Elaine,
Can we talk tomorrow or Monday about choosing some initial PEG projects?
Colin

-----Original Message-----
From: Chong, Elaine HLTH:EX <Elaine.Chong@gov.bc.ca>
Sent: March 6, 2018 7:32 AM
To: XT:Dormuth, Colin 0 HLTH:IN <colin.dormuth@ti.ubc.ca>
Cc: Lun, Eric HLTH:EX <Eric.Lun@gov.bc.ca>; Jim Wright <jim.wright@ti.ubc.ca>; ken.bassett@ti.ubc.ca; Moneo, Mitch HLTH:EX <Mitch.Moneo@gov.bc.ca>; Bob Nakagawa <Bob.Nakagawa@bcpharmacists.org>; Pang, Walton HLTH:EX <Walton.Pang@gov.bc.ca>; Fazlagic, Tijana HLTH:EX <Tijana.Fazlagic@gov.bc.ca>
Subject: Re: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Colin - thanks and yes, happy to discuss further on tomorrow's agenda.

EC

> On Mar 6, 2018, at 7:02 AM, Colin Dormuth <colin.dormuth@ti.ubc.ca> wrote:
>
> Elaine, all,
> I am in Vancouver teaching. I think we should have this matter as an agenda item for our meeting tomorrow.
> Colin
>
>
> Sent from my iPhone
>
>> On Mar 5, 2018, at 10:31 PM, Chong, Elaine HLTH:EX <Elaine.Chong@gov.bc.ca> wrote:
>>
>> Thanks Eric.
>>
>> Colin - I'm still keen to meet with you tomorrow if you are available. I'm in an all day meeting but will step out to take a call with you if you can advise when you might be free.
>>
>> EC
>>
>>> On Mar 5, 2018, at 10:28 PM, Lun, Eric HLTH:EX <Eric.Lun@gov.bc.ca> wrote:
>>>
s.13

>>>
>>> Thanks,
>>>
>>> Eric
>>>
>>> Eric Lun, PharmD
>>> Executive Director, Drug Intelligence, Optimization, Outcomes, and
>>> Strategy Pharmaceutical Services Division BC Ministry of Health
>>> Original Message
>>> From: Chong, Elaine HLTH:EX
>>> Sent: Friday, March 2, 2018 11:11
>>> To: XT:Dormuth, Colin 0 HLTH:IN; 'Jim Wright'; ken.bassett@ti.ubc.ca
>>> Cc: Lun, Eric HLTH:EX; Moneo, Mitch HLTH:EX; 'Bob Nakagawa'; Pang,
>>> Walton HLTH:EX; Fazlagic, Tijana HLTH:EX
>>> Subject: RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects
>>>
>>> Colin, Jim, and Ken,
>>>
s.13

>>>

>>>
>>> Many thanks,
>>> EC
>>>
>>> -----Original Message-----
>>> From: Colin Dormuth [mailto:colin.dormuth@ti.ubc.ca]
>>> Sent: Friday, February 23, 2018 4:03 PM
>>> To: Moneo, Mitch HLTH:EX; 'Bob Nakagawa'
>>> Cc: 'Jim Wright'; El Agab, Charlotte S HLTH:EX;
>>> ken.bassett@ti.ubc.ca; Lun, Eric HLTH:EX; Fazlagic, Tijana HLTH:EX;
>>> Chong, Elaine HLTH:EX
>>> Subject: Therapeutic Initiative Bi Weekly Meetings: PEG projects
>>>
>>> All,
>>>
>> s.13
>>
>>
>>>
>>> Have a good weekend.
>>>
>>> Colin Dormuth, Sc.D.
>>> Associate Professor
>>> Dept. of Anesthesiology, Pharmacology & Therapeutics (APT) UBC
>>> Victoria Office Suite 210, 1110 Government Street Victoria, BC V8W
>>> 1Y2 UBC Vancouver Office Room 309, 2176 Health Sciences Mall
>>> Vancouver, BC V6T 1Z3
>>> Phone: 250-388-9912
>>> Fax: 250-595-5954
>>>
>>> <Therapeutics Initiative letter Jan 2018 JH.pdf>
>> <winmail.dat>

Maglanque, Joyce HLTH:EX

From: Naumann, Terryn HLTH:EX
Sent: Thursday, March 22, 2018 10:29 AM
To: Maglanque, Joyce HLTH:EX
Subject: FW: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Another email (within PSD only), where I commented on PEG projects idea that involved diabetes drugs.
There are 2 sections in the chai (highlighted in yellow) where I mention diabetes topics.

Terryn

-----Original Message-----
From: Naumann, Terryn HLTH:EX
Sent: Wednesday, March 7, 2018 10:16 AM
To: Weston, Megan D HLTH:EX; Bouma, Susan HLTH:EX
Cc: Chong, Elaine HLTH:EX; Fazlagic, Tijana HLTH:EX; Pang, Walton HLTH:EX; Lun, Eric HLTH:EX
Subject: RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects

s.13

Terryn

-----Original Message-----
From: Weston, Megan D HLTH:EX
Sent: Tuesday, March 6, 2018 11:11 AM
To: Bouma, Susan HLTH:EX
Cc: Chong, Elaine HLTH:EX; Fazlagic, Tijana HLTH:EX; Pang, Walton HLTH:EX; Lun, Eric HLTH:EX; Naumann, Terryn HLTH:EX
Subject: Re: Therapeutic Initiative Bi Weekly Meetings: PEG projects

I second (third?) Terryn's suggestions

Megan

Please excuse the clumsy typing: Sent from my iPhone

On Mar 6, 2018, at 10:42 AM, Bouma, Susan HLTH:EX <Susan.Bouma@gov.bc.ca> wrote:

Hi Elaine!

Terryn, you are fabulous! Agree with all three.

s.13

s.13

Sue
-----Original Message-----
From: Chong, Elaine HLTH:EX
Sent: Monday, March 5, 2018 5:28 PM
To: Fazlagic, Tijana HLTH:EX; Bouma, Susan HLTH:EX; Pang, Walton HLTH:EX; Lun, Eric HLTH:EX; Weston, Megan D HLTH:EX
Cc: Naumann, Terryn HLTH:EX
Subject: FW: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Thanks Terryn for her thoughts - others?

EC

-----Original Message-----
From: Naumann, Terryn HLTH:EX
Sent: Monday, March 5, 2018 3:58 PM
To: Chong, Elaine HLTH:EX
Subject: RE: Therapeutic Initiative Bi Weekly Meetings: PEG projects

Hi Elaine,

s.13

Terryn

-----Original Message-----

From: Chong, Elaine HLTH:EX
Sent: Friday, March 2, 2018 10:59 AM
To: Fazlagic, Tijana HLTH:EX; Bouma, Susan HLTH:EX; Pang, Walton HLTH:EX; Naumann, Terryn HLTH:EX; Lun, Eric HLTH:EX; Weston, Megan D HLTH:EX
Subject: FW: Therapeutic Initiative Bi Weekly Meetings: PEG projects
Importance: High

All,

s.13

EC

-----Original Message-----
From: Colin Dormuth [mailto:colin.dormuth@ti.ubc.ca]
Sent: Friday, February 23, 2018 4:03 PM
To: Moneo, Mitch HLTH:EX; 'Bob Nakagawa'
Cc: 'Jim Wright'; El Agab, Charlotte S HLTH:EX; ken.bassett@ti.ubc.ca; Lun, Eric HLTH:EX; Fazlagic, Tijana HLTH:EX; Chong, Elaine HLTH:EX
Subject: Therapeutic Initiative Bi Weekly Meetings: PEG projects

All,

s.13

Have a good weekend.

Colin Dormuth, Sc.D.
Associate Professor
Dept. of Anesthesiology, Pharmacology & Therapeutics (APT) UBC Victoria Office Suite 210, 1110 Government Street Victoria, BC V8W 1Y2 UBC Vancouver Office Room 309, 2176 Health Sciences Mall Vancouver, BC V6T 1Z3
Phone: 250-388-9912
Fax: 250-595-5954

Maglanque, Joyce HLTH:EX

From: Naumann, Terryn HLTH:EX
Sent: Thursday, March 22, 2018 10:25 AM
To: Maglanque, Joyce HLTH:EX
Subject: FW: DRAFT: Therapeutics Letter #107: Does empaglifozin reduce cardiovascular mortality in Type 2 Diabetes? The EMPA-REG OUTCOME Trial
Attachments: TL107DRFT.docx; ATT00001.htm; TL107DRFT.pdf; ATT00002.htm

Importance: High

This is the email I received from the TI about diabetes drugs during the FOI time period.
I did not send a response.

Terryn

From: Ciprian Jauca [mailto:jauca@ti.ubc.ca]
Sent: Tuesday, October 24, 2017 11:17 PM
To: Therapeutics Initiative
Subject: DRAFT: Therapeutics Letter #107: Does empaglifozin reduce cardiovascular mortality in Type 2 Diabetes? The EMPA-REG OUTCOME Trial
Importance: High

Dear reviewer,

Please find attached a confidential draft of Therapeutics Letter #107, for your review. A final, revised version of this will be published next month as the July-August 2017 issue (#107) under the proposed title "*Does empaglifozin reduce cardiovascular mortality in Type 2 Diabetes? The EMPA-REG OUTCOME Trial*" (subject to change, feel free to suggest alternate title if a better one comes to mind) and will be distributed free of charge at the end of this month to some 15,000 physicians and pharmacists in BC, as well as made available free of charge on our web site www.ti.ubc.ca

We appreciate your expertise in this area of therapeutics, therefore we would appreciate if you could review this draft and send us your comments, feedback and/or suggestions **by Wednesday, November 1st**. I am sending this draft to you as an attachment in both MS Word and Adobe PDF formats. Please contact me immediately if you'd rather have us send it to you in a different format or if you wish to receive it by fax.

The main target audience of the Therapeutics Letter consists of primary care physicians, pharmacists and nurse practitioners, therefore the Letter is written with that audience in mind.

You can send your feedback/comments by email to: jauca@ti.ubc.ca or by fax: 604-822-0701. Thank you for your assistance.

Best regards,
Ciprian Jauca
Program Coordinator, Therapeutics Initiative
University of British Columbia
jauca@ti.ubc.ca
+1-604-822-0700
www.ti.ubc.ca

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Withheld pursuant to/removed as

s.13