6

Ward, Ronald

From: Ward, Richard
Sent: Monday, July 16, 2012 12:11 PM
To: 'Fernando Tricta (ftricta@apopharma.com)'
Subject: App for Iron Chelation
Attachments: iron_chelation_app.pdf

Fernando,
As discussed previously, please find attached the draft quote from Media Platforms for developing an independent chelation app.
I am seeking 50% sponsorship from Apopharma for this project and suggest $15,000, with return of any unneeded funds at the end of the project.
The project will form part of an educational program for a medical student at UofT in the Determinants Of Community Health 2 (DOCH2) course, with a focus on development of educational material.
Please let me know if this meets with your approval and if you have any comments or questions.
Many thanks, **Richard**

Richard Ward MSc, MRCP (UK), FRCPath (UK)
Staff Hematologist, University Health Network
Red Blood Cell Disorders Program, Toronto General Hospital
Assistant Professor, Dept of Medicine, University of Toronto
8N-887, 200 Elizabeth St,
Toronto, ON. M5G 2C4
Tel: 416 340 5233
Fax: 416 340 3799
Pager: 416 790 8066
richard.ward@uhn.ca

http://www.md.utoronto.ca/program/preclerkship/year2/DOC_211Y.htm

MEDIA PLATFORMS
DIGITAL IMAGINATION

21 Camden Street, Third Floor
Toronto, Ontario M5V 1V2
416.598.8806 | 416.598.0884
www.mediaplatforms.ca

Quote to: Richard Ward
Address: 8N-887 200 Elizabeth Street
Toronto, Ontario
M5G 2C4
Contact Name: Richard Ward
Email: richard.ward@uhn.on.ca
Project: Iron Chelation Mobile Application

Date: Thursday, June 28th, 2012

Item #	Quantity	Description	Price	Amount
DESIGN	1	- wireframes and graphic design for all buttons, pages and functions	$5800.00	$5800.00
WEBDE	1	- development of the Iron Chelation Mobile Application in HTML 5 - information on the condition, drugs to treat the condition etc. (based on 5x content of the supplied Iron Chelation Therapy booklet) - dose calculator for Ferriprox and Exjade from supplied excel sheets for calculations - safety calculations for Desferal from supplied calculations - entering blood results and tracking them over time in a bar graph - entering MRI results for liver and heart adn tracking them over time in a bar graph - feedback on how well their condition is being managed - link to an online survey created in Survey Monkey at intervals of 1, 3 and 6 months after beginning using the application - reminders for doctor's appointments and blood tranfusions	$15,080.00	$15,080.00

All prices are in Canadian dollars. Quotation valid for 30 days. A 50% deposit is required on all projects. Balance of payment is due upon receipt unless otherwise stated.

Subtotal	
HST	
Grand Total	

MEDIA PLATFORMS

DIGITAL IMAGINATION

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Toronto, Ontario M5V 1V2
416.598.8806 | 416.598.0884
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Quote to: Richard Ward
Address: 8N-887 200 Elizabeth Street
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Contact Name: Richard Ward
Email: richard.ward@uhn.on.ca
Project: Iron Chelation Mobile Application

Date: Thursday, June 28th, 2012

Item #	Quantity	Description	Price	Amount
iOS	1	- packaging the application in an iOS wrapper and distributing on the Apple app store	$2320.00	$2320.00
ANDROI	1	- packing the application in an Android wrapper and distributing on the Android app store	$2320.00	$2320.00
BB	1	- packing the application in a Blackberry wrapper and distributing on Blackberry app world		

All prices are in Canadian dollars. Quotation valid for 30 days. A 50% deposit is required on all projects. Balance of payment is due upon receipt unless otherwise stated.

Subtotal	
HST	
Grand Total	

Ward, Ronald

From: Ward, Richard
Sent: Thursday, June 14, 2012 9:37 AM
To: 'Fernando Tricta'
Subject: RE: grant request
Attachments: Apopharma unrestricted grant letter_Apr2012.pdf

Attached is the letter I sent in April.
Thank you, Richard

From: Fernando Tricta [mailto:ftricta@apopharma.com]
Sent: Thursday, June 14, 2012 9:12 AM
To: Ward, Richard
Subject: RE: grant request

Richard,

Other than the request from last year, I do not recall another request. Please re-send it to me as I may have missed it.

Fernando

From: Ward, Richard [mailto:Richard.Ward@uhn.ca]
Sent: June-14-12 8:26 AM
To: Fernando Tricta
Subject: grant request

Fernando,
A while back I sent a formal request for an unrestricted education grant to support the Fellowship program, and other scholarly activities. A new fellow is starting in the Fall and I do need to ensure funding is in place for her.
I would therefore be grateful if you could give me an indication of Apopharma's response to the request. I am happy to resend the details if you do not have them to hand.
Thank you for your consideration, **Richard**

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Toronto General Hospital
200 Elizabeth Street, 8N-887
Toronto, ON M5G 2C4

Tel: 416 340 5233
Fax: 416 340 3799
richard.ward@uhn.ca

University Health Network
Toronto General Hospital | Toronto Western Hospital | Princess Margaret Hospital

By Email: ftricta@apotex.com

Dr F Tricta
Vice President, Medical Affairs
Apopharma Inc
200 Barmac Drive,
Toronto, Ontario M9L 2Z7

10 April 2012

Dear Fernando,

I would like to take this opportunity to thank Apopharma for the support of the Red Blood Cell Disorders Program over the past year. With this significant contribution, RBCD program undertook several initiatives in research projects and established an unique advanced fellowship training program in Adult Hemoglobinopathy. This is exemplified by numbers of presentations at the recent ASH 2011, San Diego. Dr Kuo is now coming towards the end of his Fellowship training. Some of his achievements during the past year are outlined below for your review. We are delighted to have recruited a new Fellow from Quebec to join the team in the Fall of 2012 for 2 years of advanced Hemoglobinopathy training. We consider this particularly significant given our remit to train physicians from across Canada, not just from Toronto. Alongside this, the clinical program continues to grow in size and gain a reputation across North America as a centre of excellence in Adult Hemoglobinopathy care.

I would like to provide an update on the progress made with respect to some of the proposed projects that accompanied the grant request last year (please note, this is not a complete list).

- *Analysis and reporting of our centre's experience with Deferiprone:
  ASH 2011 Poster, manuscript in preparation
- *Analysis of our cardiac data with respect to Deferiprone:
  ASH 2011 Poster, manuscript in preparation
- Initiation of a research study evaluating 2D-ECHO, Perfusion cardiac MRI and cardiac catheterisation in Sickle Cell Disease: Protocol being finalised for MRI study; ongoing retrospective analysis of cardiac catheterisation results in this population
- Collaboration with other US centres on a common protocol for Deferiprone-Deferasirox combination therapy: Protocol being finalised; agreement reached with Philadelphia Children Hospital, Philadelphia; continued data collection of small cohort in Toronto
- Development of a Clinical database for the RBCD Program at TGH: In development stages with plans for linked database at Hospital for Sick Children, Toronto, to provide longitudinal data
- Prospective evaluation of relaxed CBC monitoring frequency for Deferiprone:
  Not pursued due to regulatory concerns
- Pharmaco-vigilance/Safety Monitoring/Reporting (LA-04 Compassionate Use): Ongoing successful provision and monitoring of Deferiprone for patients in the GTA, including patients with Sickle Cell Disease
- *Study Evaluating compliance and barriers to compliance with chelating agents:
  ASH 2011 abstract
- *Manuscript on Pregnancy outcomes in Thalassemia and Sickle Cell Disease:

Richard Ward MSc, MRCP (UK), FRCPath (UK)
Division of Medical Oncology & Hematology, Dept of Medicine, University Health Network
Assistant Professor, Division of Hematology, Dept of Medicine, University of Toronto
CPSO: # 89247 OHIP: # 024759

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University Health Network
Toronto General Hospital | Toronto Western Hospital | Princess Margaret Hospital

ASH 2011 abstract
- Osteopenia/Osteoporosis in Sickle Cell Disease: Manuscript in preparation
- Continuing professional development of RBCD team members: Ongoing, including Social Worker, Nurse Practitioners and Research team

- *Selected Fellow Presentations:
  - Kuo K: "Effectiveness, Time Utilization and Clinical Outcome of Partial Manual Red Cell Exchange in Patients with Sickle Cell Disease", Canadian Blood Services special seminar, January 26, 2012
  - Kuo K: "Be a Blood Detective", American Society of Hematology High School Student Symposium, San Diego, CA, December 8, 2011
  - Kuo K: "Sickle Cell Disease in the Genomic Era", Canadian Haemoglobinopathy Group Videoconference Rounds, September 20, 2011
  - Kuo K: Hemoglobinopathy Workshop Case Studies, 5th Annual National Hematology Residents' Retreat, Toronto, Canada, July 15, 2011
  - Kuo K: "The diagnosis of transfusional iron overload" in Simultaneous Session: Transfusional Iron Overload. Canadian Society for Transfusion Medicine Conference, Toronto, Canada, May 13, 2011
  - Kuo K: "Does Chronic Transfusion Prevent Silent Cerebral Infarcts in Patients with Sickle Cell Disease?" Canadian Blood Services Rounds, Toronto, Canada, March 2011

*Fellow's work

I hope the above provides an impression of what RBDC program have accomplished over the past year in line with educational and research activities. In addition to finalizing ongoing projects, there are a number of new research initiatives we would like to undertake over the next 12 months, some of which were outlined when we met a few weeks ago. I would be happy to discuss these further with you.

I would kindly ask for your consideration of a further unrestricted grant in support of continued research and teaching initiatives for the following year at the level of approximately $170,000. Please, find attached a proposed breakdown of perceived costs for your review and consideration. Should the proposal meet with your approval, it would be appreciated to make the cheque payable to "The Department of Hematology, University Health Network" c/o Dr Malcolm Moore, and to mail it to the address above.

Please, do not hesitate to contact me directly for further information or clarification.

Yours sincerely,

R Ward.

Richard Ward
Staff Hematologist, University Health Network
Red Blood Cell Disorders Program, Toronto General Hospital

Richard Ward MSc, MRCP (UK), FRCPath (UK)
Division of Medical Oncology & Hematology, Dept of Medicine, University Health Network
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University Health Network
Toronto General Hospital | Toronto Western Hospital | Princess Margaret Hospital

08 April 2012

APOPHARMA Inc - RBCD Program Grant Request 2012

Item	Cost	Frequency/year	Year
1. Clinical Fellow Full Time Salary	$90,000.00	1	$90,000.00
3. Clinical Research Assistant/Data Analyst Full time		1	$55,000.00
4. Research Student/Summer/Part Time/Casual		1	$15,000.00
5. Support Staff Preparation for Conference(s) and Attendance	$5,000.00	2	$10,000.00
TOTAL			**$170,000.00**

Richard Ward MSc, MRCP (UK), FRCPath (UK)
Division of Medical Oncology & Hematology, Dept of Medicine, University Health Network
Assistant Professor, Division of Hematology, Dept of Medicine, University of Toronto
CPSO: # 89247 OHIP: # 024759

(5)

Ward, Ronald

From: John Connelly <jconnell@apopharma.com>
Sent: Thursday, June 07, 2012 9:47 AM
To: Ward, Richard
Cc: John Connelly; John Connelly
Subject: RE: R Ward - request for Pre-NDS Mtg info

Richard,

We will have a meeting room at the Radisson Ottawa where we will be staying on the night of 11 June, booked from 8 am to noon. In practice I will not be surprised if the first part of the discussion is over breakfast, with the 'formal' meeting starting about 9 am. We will probably have lunch at the hotel towards the end of the meeting, and leave by cab for the TPD building at Tunney's Pasture to arrive about 12.30/12.45 pm. The pre-NDS meeting is from 1-3 pm, after which I anticipate that we will have a short initial de-briefing discussion and take cabs to the airport. What time is your return flight?

I have an outline of the agenda for the TPD meeting itself, although timeslots are still somewhat fluid. Approximately, the meeting will be: Introductions (TPD, ApoPharma, RW) and aims/principal questions to the agency (10 min); your presentation (15 min); Fernando's data presentation and clarification questions (30 min); discussion with TPD and review of action items/decisions (remainder). We should aim to keep presentation times to the minimum, as the main value of the meeting comes from having TPD's position on our requests, especially priority review, and hearing what concerns they want us to focus on in the NDS itself.

Please let me know if you need any more information.

John

From: Ward, Richard [mailto:Richard.Ward@uhn.ca]
Sent: June-06-12 12:42 PM
To: John Connelly
Subject: RE: R Ward - request for Pre-NDS Mtg info

John
Do you have a schedule for the Tues.
Thanks, Richard

Ward, Ronald

C

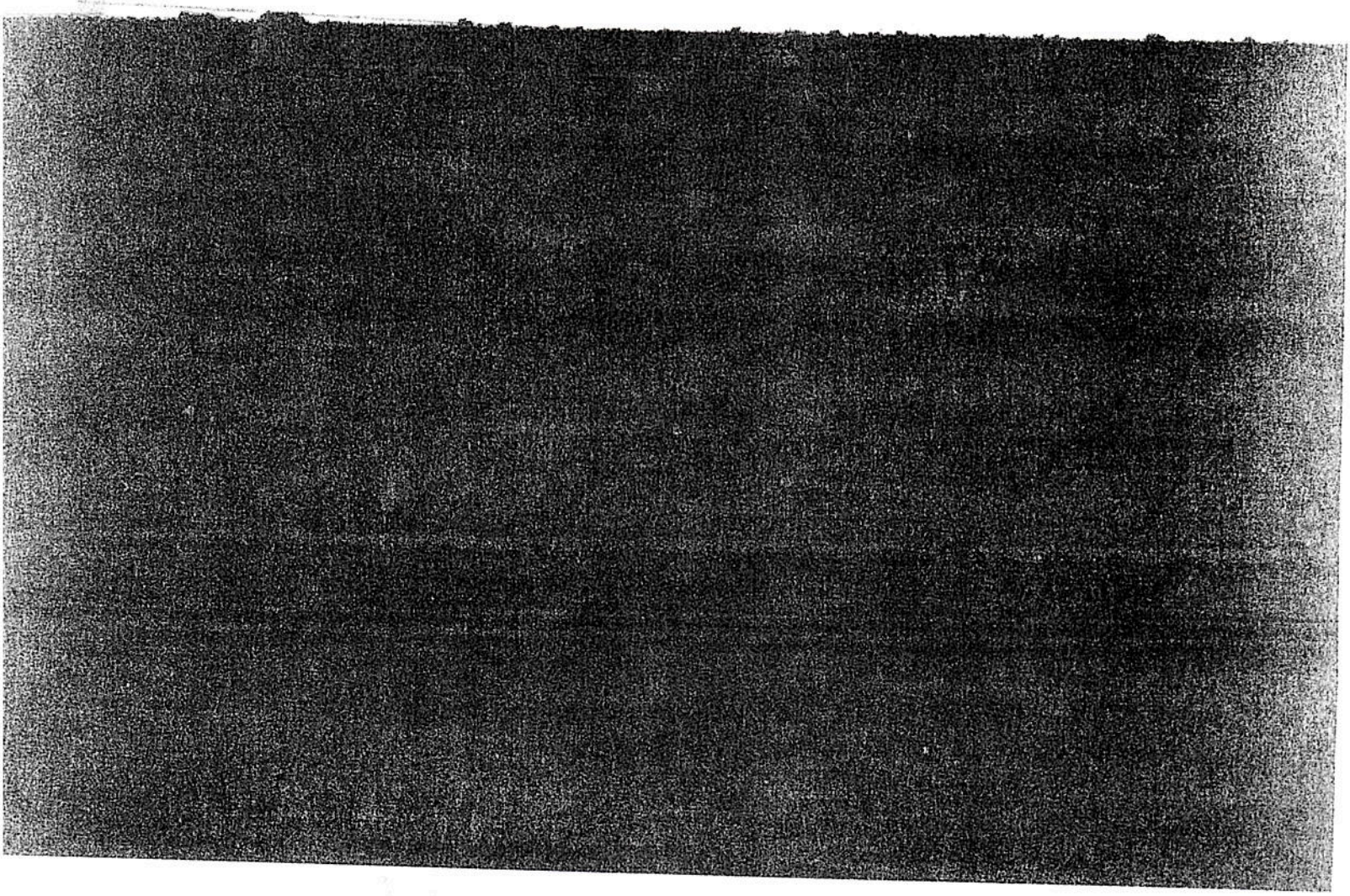
From: Fernando Tricta <ftricta@apopharma.com>
Sent: Wednesday, June 06, 2012 9:41 PM
To: Ward, Richard
Subject: FW: Pre-submission meeting for Ferriprox, Control #155181
Attachments: Ferriprox Pre-NDS Prep Meeting (155181) - Advanced Feedback highlighted.doc

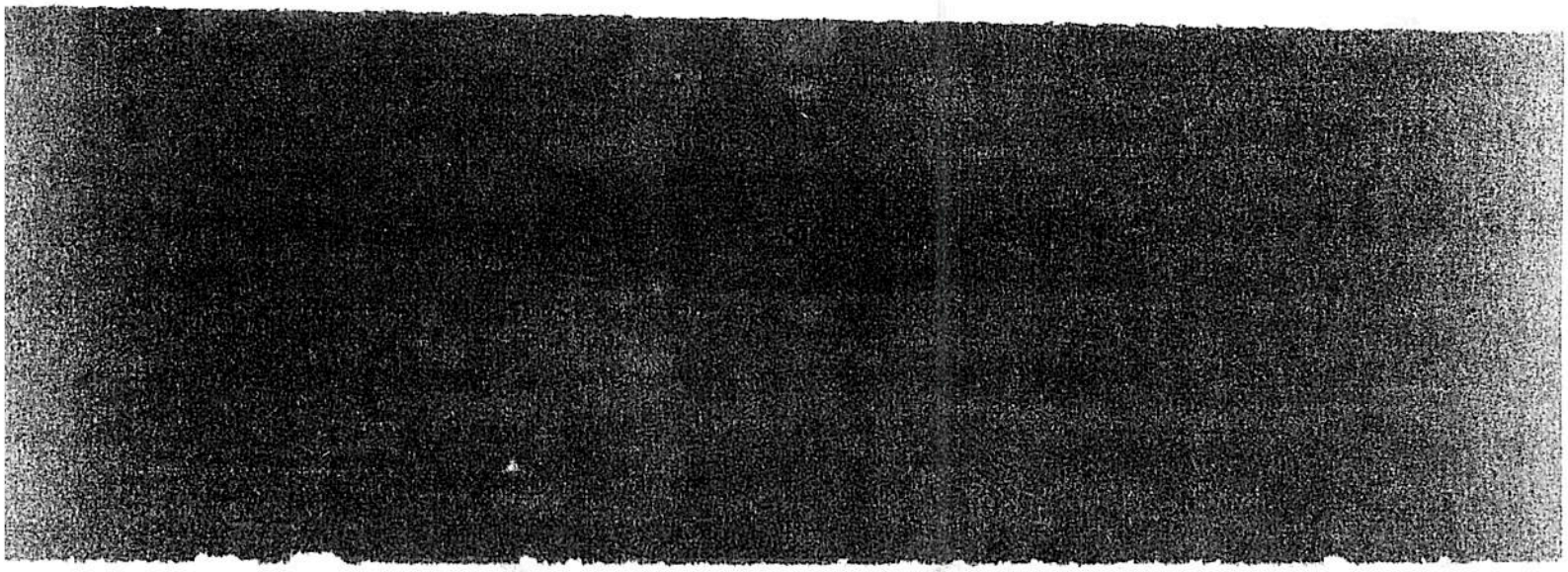
Richard,

We have received this afternoon the list of people from Health Canada who will attend the meeting on Tuesday.

Health Canada also send us a list of 14 questions (see attachment) that we should address at the meeting and I would like you to address the 2 questions highlighted in yellow. Would that be OK with you?

Fernando



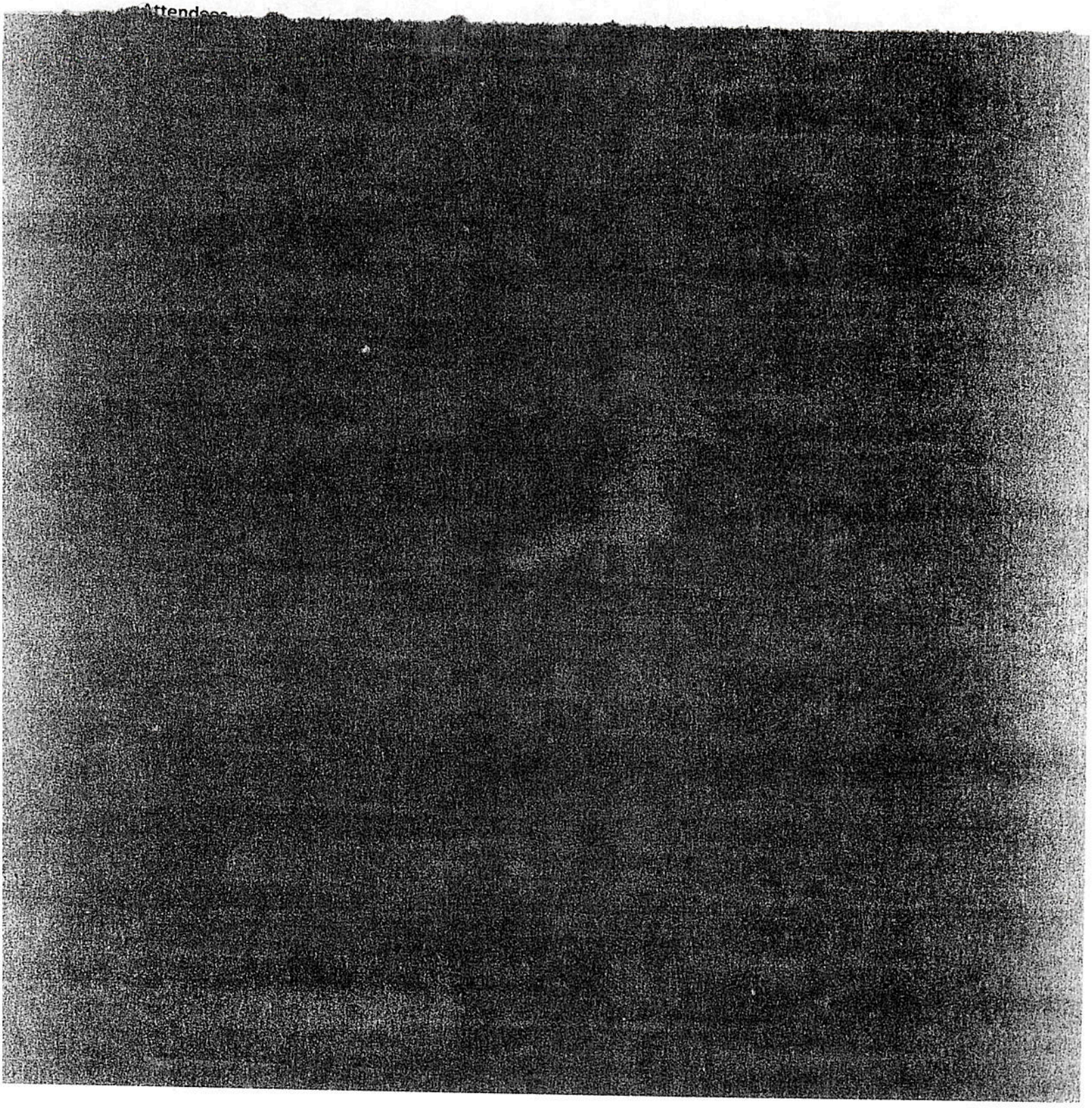


/GC/CA]

Prep Meeting for Ferriprox Pre-NDS – 155181

June 5, 2012
(Meeting to be held Jun 12, 2012)

Attendees



(7)

Ward, Ronald

From: John Connelly <jconnell@apopharma.com>
Sent: Tuesday, May 08, 2012 10:48 AM
To: Ward, Richard
Cc: John Connelly; John Connelly
Subject: RE: R Ward - request for Pre-NDS Mtg info

Richard,

Karen is looking at hotel options now based on availability of meeting rooms. I'll let you know as soon as I can.

John

From: Ward, Richard [mailto:Richard.Ward@uhn.ca]
Sent: May-08-12 10:42 AM
To: John Connelly
Subject: Re: R Ward - request for Pre-NDS Mtg info

Thanks for the clarification.
Which hotel will the group be using?
Richard

From: John Connelly [mailto:jconnell@apopharma.com]
Sent: Tuesday, May 08, 2012 09:55 AM
To: Ward, Richard
Cc: Karen Sison <ksison@apopharma.com>; Fernando Tricta <ftricta@apopharma.com>; John Connelly <jconnell@apopharma.com>; John Connelly <jconnell@apopharma.com>
Subject: R Ward - request for Pre-NDS Mtg info

Dear Richard,

Thank you for your reply. The meeting with TPD is scheduled for 1-3 pm on 12 June; it may overrun slightly, but as regulatory agencies tend to have many meetings booked it is very likely that we will finish close to the stated time. The invitation to you is from ApoPharma, although it arises from a direct request from TPD, made at our last meeting with their staff, to hear from a specialist familiar with the thalassemia population in Canada, current use of iron chelation therapy, and the desirability of an additional chelator as an option for transfusionally iron-overloaded patients. We will get together in the morning before the TPD meeting, but will also aim to discuss this invitation with you as soon as possible. Fernando will be in touch with you to explain further and to arrange a mutually convenient time to meet.

Best wishes,

John

From: Ward, Richard [mailto:Richard.Ward@uhn.ca]
Sent: Monday, May 07, 2012 10:08 PM
To: Karen Sison
Subject: RE: Flight Arrangements - ApoPharma meeting with Health Canada 12 June

Hello Karen
Thank you for getting in touch and for your kind offer.

I think it would be appropriate for me to make my own travel arrangements.
Can you clarify if I am being invited by Apopharma or by Health Canada, and if any briefing will take place as I have yet to receive details from either party. Do you know what time the hearing will finish on the Tuesday, to give me an idea of flights to book? As I have clinic on the Monday afternoon, I likely won't arrive in Ottawa until late in the evening.
Many thanks, **Richard**

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(9)

University Health Network

Toronto General Hospital Toronto Western Hospital Princess Margaret Hospital

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Toronto, Ont M5G 2C4
Tel: (416)340-4069
Fax: (416)340-3799
Erik.yeo@uhn.on.ca

August 23, 2011

FAO: Caleb Briggs, Pharm.D.
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Avenue
WO31-2428
Silver Spring, MD 20993-0002

By Email: ODAC@fda.hhs.gov

Re: New drug application 021825, Ferriprox (Deferiprone); Proposed indication (use) for this product is for the treatment of patients with transfusional iron overload, when current chelation therapy is inadequate; September 14, 2011

Introduction

At the request of Cooley's Anemia Foundation, we are writing in support of the new drug application (#021825) for the oral chelator Ferriprox, which is to be discussed at the September 14 ODAC meeting. As the medical director (EY) and primary physician (RW) of the Red Blood Cell Disorders Program (RBCDP) at Toronto General Hospital, University Health Network, we represent the largest adult Hemoglobinopathy program in Canada. For the past 2 years, we have gained considerable experience in the safe and effective prescribing of Ferriprox to our patients. Also included in this package are personal testimonies from a few of our patients who have been treated with this drug, outlining their personal stories and perspective.

We cannot state how strongly we support this initiative and our positive clinical experience with Ferriprox when followed within accepted guidelines. Our experience is similar to that reported in the literature in European, Mediterranean and Asian countries (eg England, Italy, Cyprus and Greece, Thailand) where the drug is used in a similar medical population.

As the largest comprehensive Hemoglobinopathy program in Canada, we are aware that smaller centres across the country look to us for a lead in clinical care expertise. We are

aware, that since our change in chelation practice in summer 2009, a number of other patients across Canada, who would greatly benefit from Ferriprox, have now been prescribed it, based on the positive experience we have had, and our ability to offer expert advice to other physicians.

Background to RBCDP

The RBCDP is situated at the Toronto General Hospital and works closely with the pediatric program at the Hospital for Sick Children, Toronto. Together, we care for >80% of Canada's Hemoglobinopathy patients, providing comprehensive and lifelong care. At the present time we have 500 adult patients Sickle Cell Disease and Thalassemia Syndromes. The healthcare team comprises: 4 Hematologists, 2 Nurse Practitioners, 1 Social Worker and clerical support. We also run a Hemoglobinopathy fellowship training program supported in part by an award from the American Society of Hematology. Specialty Hemoglobinopathy clinics are run 5 days per week in dedicated space within the Toronto General Hospital, and care provided involves managing all aspects of iron chelation management. Although the program has been in existence for more than 20 years, the current clinic director and team have been in place since January 2009. Prior to this time the majority of patients where prescribed iron chelation with subcutaneous or intravenous Desferal and with Exjade, although 3 patients had chosen to independently source Ferriprox from overseas. Other patients had received Ferriprox at various times as participants in clinical studies under the responsibility of another Hematologist. In 2009, we moved to regularize Ferriprox for these three patients by obtaining Health Canada SAP approval. At the same time we initiated approval to address the addition of chelation with Ferriprox to our pharmacopeia for all of our chelated patients (see indications below).

RBCDP Indications for Ferriprox

Exjade is the first line iron chelation medication in the RBCDP. The RBCDP uses the following criteria as indications for commencing a patient on Ferriprox:

1. Severe cardiac iron overload whilst chelating with Exjade, Desferal or combination of Exjade and Desferal
2. Severe cardiac iron overload with a cardiac MRI T2* <10msec; Left Ventricular Ejection Fraction <50%; or >10% fall in EF
3. Severe hepatic iron overload unresponsive to Desferal, Exjade or combination of Exjade and Desferal
4. Intolerance, significant adverse event, or refusal to use Exjade or Desferal

Cardiac events are the leading cause of death in patients with β Thalassemia Major. Ferriprox has been reported in many studies to reduce cardiac siderosis, cardiac events, and deaths in this patient population. The decision to commence Ferriprox for a cardiac indication is taken in conjunction with a specialist heart failure cardiologist who is directly allied to the Program.

Amongst our cohort of 160 patients (both thalassemics and sickle cell) on any chelator, 23 patients were prescribed Ferriprox because of severe cardiac iron overload, 4 for

severe hepatic iron unresponsive to all other chelators, 10 who were intolerant of or had significant adverse events with other chelators, and 3 for other reasons.

RBCDP Experience

In the last 2 years we have prescribed Ferriprox to 40 patients with β Thalassemia Major (39) and Sickle Cell Disease (1) who have complications of transfusion related iron overload, for a total in excess of 30 patient years of Ferriprox therapy. These numbers represent approximately 25% of our chelated population, a proportion in line with that in other major Hemoglobinopathy centres across the World (excluding USA). Half of our patients received standard dose Ferriprox at 75mg/kg/day, the remainder (predominantly those with severe cardiac siderosis) at the higher dose of 100mg/kg/d. 18 patients were prescribed Ferriprox in combination with Desferal or Exjade, and 22 as monotherapy. Of patients still receiving Ferriprox, the longest duration of continuous exposure has been 25 months in a patient with severe cardiac iron overload. Six of 40 patients are no longer taking Ferriprox, three because they have had resolution of their cardiac siderosis and normalisation of cardiac MRI T2* values, 1 moved out of province, 1 had mild but persistent gastrointestinal upset, and 1 was non-compliant with taking the drug. Of note, 5 patients commenced on Ferriprox in the past year have been transitioned from the HSC pediatric program, highlighting the ongoing need for effective alternative iron chelators.

With respect to adverse events, we recognise that total duration of exposure is such that rare adverse effects would not be expected to have been detected to date in our patient cohort. 75-80% of patients are adherent to the prescribed dose more than 90% of the time. Neutropenia (ANC < 1.5), has been observed in 4 patients on 11 occasions, but with no episodes of agranulocytosis (ANC <0.5). All have recovered with close attention or drug at altered dosage. Patients have complied with requests for a CBC every 5-10 days. Consideration could be given to relaxing monitoring to every month after 6-12 months of therapy as this is beyond the period of highest risk for agranulocytosis. Four patients had an asymptomatic transient increase in alanine transaminase (> 5x upper limit of normal), which settled either spontaneously or with transient interruption of Ferriprox. Two of these patients were referred to a Hepatologist who did not definitively implicate Ferriprox in the etiology of the hepatitis's. None of the patients required a liver biopsy as part of further investigation. Four patients had arthralgias, which resolved with dose reduction or interruption. All of our patients on chelation have MRI Ferriscans every 3-6 months. We have no data to support an effect on liver fibrosis as liver biopsy and histological examination is no longer performed as part of routine clinical care, and liver MRI assessment is unable to comment on tissue architecture. However, none of our patients have had clinical or biochemical evidence of cirrhosis or worsening liver function whilst taking Ferriprox.

A recent analysis of serial cardiac MRI T2* and EF measurements in 22 patients from this cohort has demonstrated a mean change in T2* of +2.6 ms/year and also improvement in EF +1.5%/year after an average of 425 days of therapy. These are statistically significant results. To date, the improvements in cardiac T2* in the total patient group ranges from -0.9ms to +25.6ms. There have been no episodes of cardiac failure requiring admission to hospital/CCU. It is important to note these improvements

have been achieved, in the main, without the need for insertion of an intravenous line for continuous IV Desferal (and its attendant risks and toxicities), which is the only other proven effective method for removing cardiac iron.

Canadian Access to Ferriprox

Since 1996, Ferriprox has been available via a compassionate use program (CUP) from Apopharma Inc (a division of Apotex) in conjunction with Section A approval from Health Canada's Special Access Programme. This provides access to non-marketed drugs for practitioners treating patients with serious or life-threatening conditions when conventional therapies have failed, are unsuitable, or unavailable. As part of this process, we gain informed consent from patients informing them as to the status of the drug in Canada, and its published efficacy and safety/toxicity data. A stipulation of approval to supply the drug by Apopharma is the careful logging of regular Complete Blood Counts and other measures to ensure safe use of the drug and drug accountability. Advice is followed to monitor for neutropenia on a weekly basis (every 5-10 days) for the duration of therapy, with reporting of these results to Apopharma as part of pharmacovigilance. The drug is delivered to a single pharmacy (at Toronto General Hospital) and thereafter collected in person by patients or shipped to their home address.

Monitoring of Ferriprox

It is recognised that the time required in preparing, and maintaining the documentation for the CUP (Apopharma) and SAP (Health Canada) is incredibly burdensome and time consuming. We have heard anecdotal reports that this has been a barrier to some US based physicians attempting to access the drug.

We have allocated this role to a single administrative individual under the supervision of a physician (RW). In addition to pre-approval applications to Health Canada and Apopharma, there are ongoing weekly CBC results to monitor and quarterly reporting of these and any adverse events to Apopharma. As well, every 6 months, a renewal request is required from Health Canada. The administrative role includes checking CBC results, reminding patients to attend their community blood lab for blood draws, liaising with patients as to when their supply of medication will need renewing, and liaising with Apopharma for timely delivery of drug to the hospital pharmacy. A shadow chart is kept by the administrator to facilitate all this data collection.

An internal review of the Ferriprox access process, described above, was undertaken by our Institution in 2011. UHN's medical and legal auditors were satisfied that the process and documentation undertaken to obtain and monitor patients receiving Ferriprox was of the standard expected by the institution, and comparable to that required as part of Good Clinical Practice in the setting of research studies.

In Winter 2010/11, an external review of the RBCDP took place. Amongst its findings was that use of Ferriprox was "in line with standard practice in the UK".

Concluding Comments

We believe that the RBCDP currently has the largest active population of patients receiving chelation with Ferriprox in North America. Our experience is much in line with that seen in other centres across the World (excluding USA). We have had no reason to abandon the use of Ferriprox and continue to use where indicated. As our understanding of the basic science of iron homeostasis improves, along with our ability to closely monitor its effect on vital organs, it is essential that patients and their physicians have access to the full range of iron chelation options, in order to tailor chelation to the individual's personal circumstances and needs.

Disclosure Statement

None of the physicians in the RBCDP have received personal funding of any sort from, nor hold stocks or ownership in Apopharma/Apotex. The RBCD Program and the Division of Hematology have received unrestricted educational grants from Apotex (Ferriprox) and Novartis (Exjade, Desferal). The physicians do not consider there to be any relevant personal conflicts of interest.

Respectfully
Dr. Erik Yeo

Erik Yeo, MD FRCP(C)
Head of Benign Hematology
Department of Medicine
University Health Network
University of Toronto

(10)

Ward, Ronald

From: Dian Shaw <dshaw@apotex.com>
Sent: Tuesday, August 23, 2011 4:18 PM
To: Ward, Richard
Cc: Fernando Tricta; Jenny Wong
Subject: Patients exposed in the compassionate use program in Canada data up to 23AUG2011.xls
Attachments: Patients exposed in the compassionate use program in Canada data up to 23AUG2011.pdf; Patients exposed in the compassionate use program in Canada data up to 23AUG2011.xls

Dear Dr. Ward:

As requested. Please find in the attached, number of patients enrolled and exposed per year in Canada since the beginning of the program and a second table with the number of patients enrolled and exposed in Toronto (TGH and HSC).

Please let me know if you have any questions.

Regards

Dian

Patients exposed in Canada - compassionate use program data up to 23AUG2011

Year exposed in the compassionate program	No. patients	%
1996	4	6.35
1997	4	6.35
2004	3	4.76
2005	2	3.17
2006	2	3.17
2007	2	3.17
2009	18	28.57
2010	21	33.33
2011	7	11.11
Total	63	

Patients exposed in Canada that started under WARD, SHER, ODAME and QUIRT - compassionate u

Year exposed in the compassionate program	No. patients	%
1996	3	7.32
1997	1	2.44
2009	17	41.46
2010	16	39.02
2011	4	9.76
Total	41	

se program data up to 23AUG2011