How to get your paper published in a high-impact English language Journal

Dr. Gordon S. Doig
Associate Professor in Intensive Care
Northern Clinical School Intensive Care Research Unit,
University of Sydney, Sydney, Australia
www.EvidenceBased.net
gdoig@med.usyd.edu.au

A pdf version of this talk can be downloaded from the Talks section of our outreach education web site (www.EvidenceBased.net).

I will also show this QR code at the end of the talk

Editorial responsibilities

- Past section Editor at ICM

Editorial responsibilities

- Past section Editor at ICM

Editorial responsibilities

- Past section Editor at ICM

- Past Editorial Board Member for CCM

Editorial Board

Critical Care Medicine

EDITORIAL BOARD MEMBERS

Edward Abraham, MD, FCCM
Professor and Dean
Wake Forest School of Medicine
Winston-Salem, North Carolina

Hasan B. Alam, MD, FACS
Professor of Surgery
Harvard Medical School
Program Director, Surgical Critical Care Fellowship Program
Massachusetts General Hospital
Boston, Massachusetts

Theodore A. Alston, MD, PhD
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

John H. Arnold, MD
Professor of Anaesthesia (Pediatrics)
Harvard Medical School
Senior Associate, Anesthesia and Critical Care
Medical Director, Respiratory Care/ECMO
Boston Children's Hospital
Boston, Massachusetts

Philip S. Barie, MD, MBA, MCCM
Professor of Surgery and Public Health
Weil Cornell Medical College
New York, New York

Anish Bhardwaj, MD, MBA, CPE, FAHA, FCCM, FAAN, FANA

Charles Cairns, MD
Dean, College of Medicine
Professor, Department of Emergency Medicine
Assistant Vice President, Clinical Research
University of Arizona Health Sciences
Tucson, Arizona

Cherylee W. Chang, MD, FCCM
Associate Clinical Professor
Department of Medicine and Surgery
The Queen's Medical Center, University of Hawaii, John Burns School of Medicine
Honolulu, Hawaii

Davide Chiumello, MD
Dipartimento di Anestesia, Rianimazione Emergenza Urgenza
Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico
Milan, Italy

David A. Cook, PhD, FANZCA, FCICM
Professor of Anaethesia and Critical Care
Intensive Care Unit
Princess Alexandra Hospital
Brisbane, Australia

Craig M. Coopersmith, MD, FCCM
Professor of Surgery
Emory Center for Critical Care
Emory University School of Medicine
Atlanta, Georgia

Douglas B. Coursin, MD
Professor, Anesthesiology and Medicine
University of Wisconsin School of Medicine and Public Health
Madison, Wisconsin

Elliott Crouser, MD
Associate Professor of Medicine

John W. Devlin, PharmD, FCCP, FCCM
Professor, Department of Pharmacy Practice
Bouve College
Northeastern University
Special and Scientific Staff
Division of Pulmonary, Critical Care and Sleep Medicine
Critical Care Pharmacist
Tufts Medical Center
Boston, Massachusetts

Gordon S. Doig, PhD
Head, Northern Clinical School Intensive Care Research Unit
University of Sydney
Royal North Shore Hospital
Sydney, Australia

Todd Dorman, MD
Senior Associate Dean for Education Coordination
Associate Dean for CME
Professor and Vice Chair for Critical Care
Department of Anesthesiology and Critical Care Medicine
Joint Appointments in Internal Medicine, Surgery, and the School of Nursing
Johns Hopkins University School of Medicine
Baltimore, Maryland

David J. Dries, MSE, MD, MCCM
Assistant Medical Director for Surgical Care
Health Partners Medical Group, Regions Hospital
Professor of Surgery and Anesthesiology
University of Minnesota
Saint Paul, Minnesota

Philip A. Efron, MD, FACS, FCCM
Associate Professor, Departments of Surgery

Editorial responsibilities

- Past section Editor at ICM

- Past Editorial Board Member for CCM

Editorial Board

Critical Care Medicine

EDITORIAL BOARD MEMBERS

Edward Abraham, MD, FCCM
Professor and Dean
Wake Forest School of Medicine
Winston-Salem, North Carolina

Hasan B. Alam, MD, FACS
Professor of Surgery
Harvard Medical School
Program Director, Surgical Critical Care Fellowship Program
Massachusetts General Hospital
Boston, Massachusetts

Theodore A. Alston, MD, PhD
Department of Anesthesia, Critical Care, and Pain Medicine
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

John H. Arnold, MD
Professor of Anaesthesia (Pediatrics)
Harvard Medical School
Senior Associate, Anesthesia and Critical Care
Medical Director, Respiratory Care/ECMO
Boston Children's Hospital
Boston, Massachusetts

Philip S. Barie, MD, MBA, MCCM
Professor of Surgery and Public Health
Weil Cornell Medical College
New York, New York

Anish Bhardwaj, MD, MBA, CPE, FAHA, FCCM, FAAN, FANA

Charles Cairns, MD
Dean, College of Medicine
Professor, Department of Emergency Medicine
Assistant Vice President, Clinical Research
University of Arizona Health Sciences
Tucson, Arizona

Cherylee W. Chang, MD, FCCM
Associate Clinical Professor
Department of Medicine and Surgery
The Queen's Medical Center, University of Hawaii, John Burns School of Medicine
Honolulu, Hawaii

Davide Chiumello, MD
Dipartimento di Anestesia, Rianimazione Emergenza Urgenza
Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico
Milan, Italy

David A. Cook, PhD, FANZCA, FCICM
Professor of Anaethesia and Critical Care
Intensive Care Unit
Princess Alexandra Hospital
Brisbane, Australia

Craig M. Coopersmith, MD, FCCM
Professor of Surgery
Emory Center for Critical Care
Emory University School of Medicine
Atlanta, Georgia

Douglas B. Coursin, MD
Professor, Anesthesiology and Medicine
University of Wisconsin School of Medicine and Public Health
Madison, Wisconsin

Elliott Crouser, MD
Associate Professor of Medicine

John W. Devlin, PharmD, FCCP, FCCM
Professor, Department of Pharmacy Practice
Bouve College
Northeastern University
Special and Scientific Staff
Division of Pulmonary, Critical Care and Sleep Medicine
Critical Care Pharmacist
Tufts Medical Center
Boston, Massachusetts

Gordon S. Doig, PhD
Head, Northern Clinical School Intensive Care Research Unit
University of Sydney
Royal North Shore Hospital
Sydney, Australia

Todd Dorman, MD
Senior Associate Dean for Education Coordination
Associate Dean for CME
Professor and Vice Chair for Critical Care
Department of Anesthesiology and Critical Care Medicine
Joint Appointments in Internal Medicine, Surgery, and the School of Nursing
Johns Hopkins University School of Medicine
Baltimore, Maryland

David J. Dries, MSE, MD, MCCM
Assistant Medical Director for Surgical Care
Health Partners Medical Group, Regions Hospital
Professor of Surgery and Anesthesiology
University of Minnesota
Saint Paul, Minnesota

Philip A. Efron, MD, FACS, FCCM
Associate Professor, Departments of Surgery

Reviewer

American Journal of Clinical Nutrition
Intensive Care Medicine Experimental
Lipids in Health and Disease
Advances in Medical Education and Practice
Journal of Pain and Symptom Management
Saudi Medical Journal
Patient Preference and Adherence
Journal of Clinical Epidemiology
American Journal of Respiratory and Critical Care Medicine
New England Journal of Medicine
Acta Anaesthesiologica Scandinavica
Canadian Medical Association Journal
Journal of Parenteral and Enteral Nutrition
Critical Care and Resuscitation
Injury
Clinical Nutrition
Respirology
British Medical Journal
Journal of the American Medical Association
British Journal of Nutrition
Asia Pacific Journal of Clinical Nutrition
Hemodialysis International,
Anesthesia & Analgesia
Journal of Critical Care
Critical Care
Anaesthesia and Intensive Care
Intensive Care Medicine
Critical Care Medicine
Chest

Reviewer

American Journal of Clinical Nutrition
Intensive Care Medicine Experimental
Lipids in Health and Disease
Advances in Medical Education and Practice
Journal of Pain and Symptom Management
Saudi Medical Journal
Patient Preference and Adherence
Journal of Clinical Epidemiology
American Journal of Respiratory and Critical Care Medicine
New England Journal of Medicine
Acta Anaesthesiologica Scandinavica
Canadian Medical Association Journal
Journal of Parenteral and Enteral Nutrition
Critical Care and Resuscitation
Injury
Clinical Nutrition
Respirology
British Medical Journal
Journal of the American Medical Association
British Journal of Nutrition
Asia Pacific Journal of Clinical Nutrition
Hemodialysis International,
Anesthesia & Analgesia
Journal of Critical Care
Critical Care
Anaesthesia and Intensive Care
Intensive Care Medicine
Critical Care Medicine
Chest

Intensive Care Research Unit University of Sydney Northern Clinical School Nil nisi verum ex testimonium

THE OFFICIAL JOURNAL OF ESICM

INTENSIVE CARE MEDICINE

THE OFFICIAL JOURNAL OF
INTENSIVE CARE MEDICINE

1,038 original research papers (observational study, RCT) were received in 2015

THE OFFICIAL JOURNAL OF
INTENSIVE CARE MEDICINE

1,038 original research papers (observational study, RCT) were received in 2015

- 63% (654/1,038) rejected by Editor

ICM INTENSIVE CARE MEDICINE
THE OFFICIAL JOURNAL OF ESICM

1,038 original research papers (observational study, RCT) were received in 2015

- 63% (654/1,038) rejected by Editor

348 of 1,038 papers sent by Editor to external reviewers

- 86% (301/348) rejected after negative comments from reviewers

ICM INTENSIVE CARE MEDICINE
THE OFFICIAL JOURNAL OF ESICM

1,038 original research papers (observational study, RCT) were received in 2015

- 63% (654/1,038) rejected by Editor

348 of 1,038 papers sent by Editor to external reviewers

- 86% (301/348) rejected after negative comments from reviewers

83 submissions accepted

- 8% (83/1,038) of total submissions!!!

Summary of this talk

- Perspective of an Editor, Reviewer and Researcher.
- Avoiding rejection by the Editor
- Avoiding rejection by Reviewers
- Responding to Reviewers Comments
- General Insights
- Summary

Summary of this talk

- Perspective of an Editor, Reviewer and Researcher.
- Avoiding rejection by the Editor
- Avoiding rejection by Reviewers
- Responding to Reviewers Comments
- General Insights
- Summary

Summary of this talk

- Perspective of an Editor, Reviewer and Researcher.
- Avoiding rejection by the Editor
- Avoiding rejection by Reviewers
- Responding to Reviewers Comments
- General Insights
- Summary

Summary of this talk

- Perspective of an Editor, Reviewer and Researcher.
- Avoiding rejection by the Editor
- Avoiding rejection by Reviewers
- Responding to Reviewers Comments
- General Insights
- Summary

Summary of this talk

- Perspective of an Editor, Reviewer and Researcher.
- Avoiding rejection by the Editor
- Avoiding rejection by Reviewers
- Responding to Reviewers Comments
- General Insights
- Summary

Summary of this talk

- Perspective of an Editor, Reviewer and Researcher.
- Avoiding rejection by the Editor
- Avoiding rejection by Reviewers
- Responding to Reviewers Comments
- General Insights
- Summary

Summary of this talk

- Perspective of an Editor, Reviewer and Researcher.
- Avoiding rejection by the Editor
- Avoiding rejection by Reviewers
- Responding to Reviewers Comments
- General Insights
- Summary

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Undertake journal selection *before* you start your research project.

- Identify a small number of candidate journals and retrieve 2 or 3 published papers from each.
- Use these papers as a guide for journal selection *and* study design.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Undertake journal selection *before* you start your research project.

- Identify a small number of candidate journals and retrieve 2 or 3 published papers from each.
- Use these papers as a guide for journal selection *and* study design.

If you cannot find a project like your intended study published in your target journal, choose another journal.

- Ex. ICM does not publish animal laboratory work or single centre retrospective observational data.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Identify a small number of candidate journals and retrieve 2 or 3 published papers from each.

- Read these papers thoroughly:
  - They have successfully made it through the review process!
  - They can teach us journal preferences, good study design and good presentation styles.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Identify a small number of candidate journals and retrieve 2 or 3 published papers from each.

- Read these papers thoroughly:
  - They have successfully made it through the review process!
  - They can teach us journal preferences, good study design and good presentation styles.

Ensure your study collects and presents information in a similar way to other papers published in your target journals.

- Severity of illness for ICU patients is traditionally captured with APACHE score in the US but SAPS score in Europe.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Journal Editors are very busy.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Journal Editors are very busy.

- Carry a clinical load, have their own research programs, usually *not* paid as Editors.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Journal Editors are very busy.

- Carry a clinical load, have their own research programs, usually *not* paid as Editors.
- The *easiest* decision for an Editor to make is 'Reject without Review'.
  - Immediately removes work from their inbox.
  - Reduces future work, as they will never see the paper again!

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Journal Editors are very busy.

- Carry a clinical load, have their own research programs, usually *not* paid as Editors.
- The *easiest* decision for an Editor to make is 'Reject without Review'.
  - Immediately removes work from their inbox.
  - Reduces future work, as they will never see the paper again!

There is only one section of your paper you can guarantee an Editor will read:

- But we usually write it last, when we are tired, yet it might be the most important section.

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Journal Editors are very busy.

- Carry a clinical load, have their own research programs, usually *not* paid as Editors.
- The *easiest* decision for an Editor to make is 'Reject without Review'.
  - Immediately removes work from their inbox.
  - Reduces future work, as they will never see the paper again!

There is only one section of your paper you can guarantee an Editor will read:

- But we usually write it last, when we are tired, yet it might be the most important section.

If your Abstract is poorly written, you make it easy for the Editor to 'Reject without Review'!

Lancet, Respiratory Medicine

Lancet, Respiratory Medicine

Eltrombopag for children with chronic immune thrombocytopenia (PETIT2): a randomised, multicentre, placebo-controlled trial

John D Grainger, Franco Locatelli, Thirachit Chotsampancharoen, Elena Donyush, Bunchoo Pongtanakul, Patcharee Komvilaisak, Darintr Sosothikul, Guillermo Drelichman, Nongnuch Sirachainan, Susanne Holzhauer, Vladimir Lebedev, Richard Lemons, Dagmar Pospisilova, Ugo Ramenghi, James B Bussel, Kalpana K Bakshi, Malini Iyengar, Geoffrey W Chan, Karen D Chagin, Dickens Theodore, Lisa M Marcello, Christine K Bailey

Summary

Background The thrombopoietin receptor agonist eltrombopag has been shown to be safe, tolerable, and effective for adults with chronic immune thrombocytopenia. We aimed to investigate the safety and efficacy of eltrombopag for children with chronic immune thrombocytopenia.

Methods PETIT2 was a two part, randomised, multicentre, placebo-controlled study done at 38 centres in 12 countries (Argentina, Czech Republic, Germany, Hong Kong, Israel, Italy, Russia, Spain, Taiwan, Thailand, UK, and USA). Paediatric patients aged 1–17 years who had chronic immune thrombocytopenia and platelet counts less than 30×10^9 per L were randomly assigned (2:1) to receive eltrombopag or placebo. We stratified patients by age into three cohorts (patients aged 12–17 years, 6–11 years, and 1–5 years) before randomly entering them into a 13 week, double-blind period. Randomisation was done by the GlaxoSmithKline Registration and Medication Ordering System and both patients and study personnel were masked to treatment assignments. Patients who were allocated eltrombopag received tablets (except for those aged 1–5 years who received an oral suspension formulation) once per day for 13 weeks. Starting doses for patients aged 6–17 were based on bodyweight, and ethnic origin and ranged between 50 mg/day and 25 mg/day (starting dose for patients aged 1–5 years was 1·2 mg/kg/day or 0·8 mg/kg/day for east Asian patients). Patients who completed the double-blind period entered a 24 week open-label treatment period in which all patients received eltrombopag at either the starting dose (if they were formerly on placebo) or their established dose. The primary outcome was the proportion of patients achieving platelet counts of at least 50×10^9 per L in the absence of rescue therapy for 6 or more weeks from weeks 5 to 12 of the double-blind period. The intention-to-treat population included in the efficacy assessment consisted of all patients who were randomly assigned to one of the treatment groups, and the safety population included all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT01520909.

Findings Beginning in March 15, 2012, 92 patients were enrolled, and the trial was completed on Jan 2, 2014. 63 patients were assigned to receive eltrombopag and 29 were assigned to receive placebo. In the double-blind period, three patients discontinued treatment because of adverse events: two patients in the eltrombopag group withdrew because of increased liver aminotransferases and one in the placebo group withdrew because of abdominal haemorrhage. 25 (40%) patients who received eltrombopag compared with one (3%) patient who received placebo achieved the primary outcome of platelet counts of at least 50×10^9 per L for 6 of the last 8 weeks of the double-blind period (odds ratio 18·0, 95% CI, 2·3–140·9; p=0·0004). Responses were similar in all cohorts (eltrombopag *vs* placebo: 39% *vs* 10% for patients aged 12–17 years, 42% *vs* 0% for patients aged 6–11 years, and 36% *vs* 0% for patients aged 1–5 years). Proportionately fewer patients who received eltrombopag (23 [37%] of 63 patients) had WHO grades 1–4 bleeding at the end of the double-blind period than did those who received placebo (16 [55%] of 29 patients); grades 2–4 bleeding were similar (three [5%] patients who received eltrombopag *vs* two [7%] patients who received placebo). During the 24-week open-label treatment period, 70 [80%] of 87 patients achieved platelet counts of 50×10^9 per L or more at least once. Adverse events that occurred more frequently with eltrombopag than with placebo included nasopharyngitis (11 [17%] patients), rhinitis (10 [16%] patients), upper respiratory tract infection (7 [11%] patients), and cough (7 [11%] patients). Serious adverse events occurred in five (8%) patients who received eltrombopag and four (14%) who received placebo. Safety was consistent between the open-label and double-blind periods. No deaths, malignancies, or thromboses occurred during the trial.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

Published Online July 29, 2015 http://dx.doi.org/10.1016/S0140-6736(15)61107-2

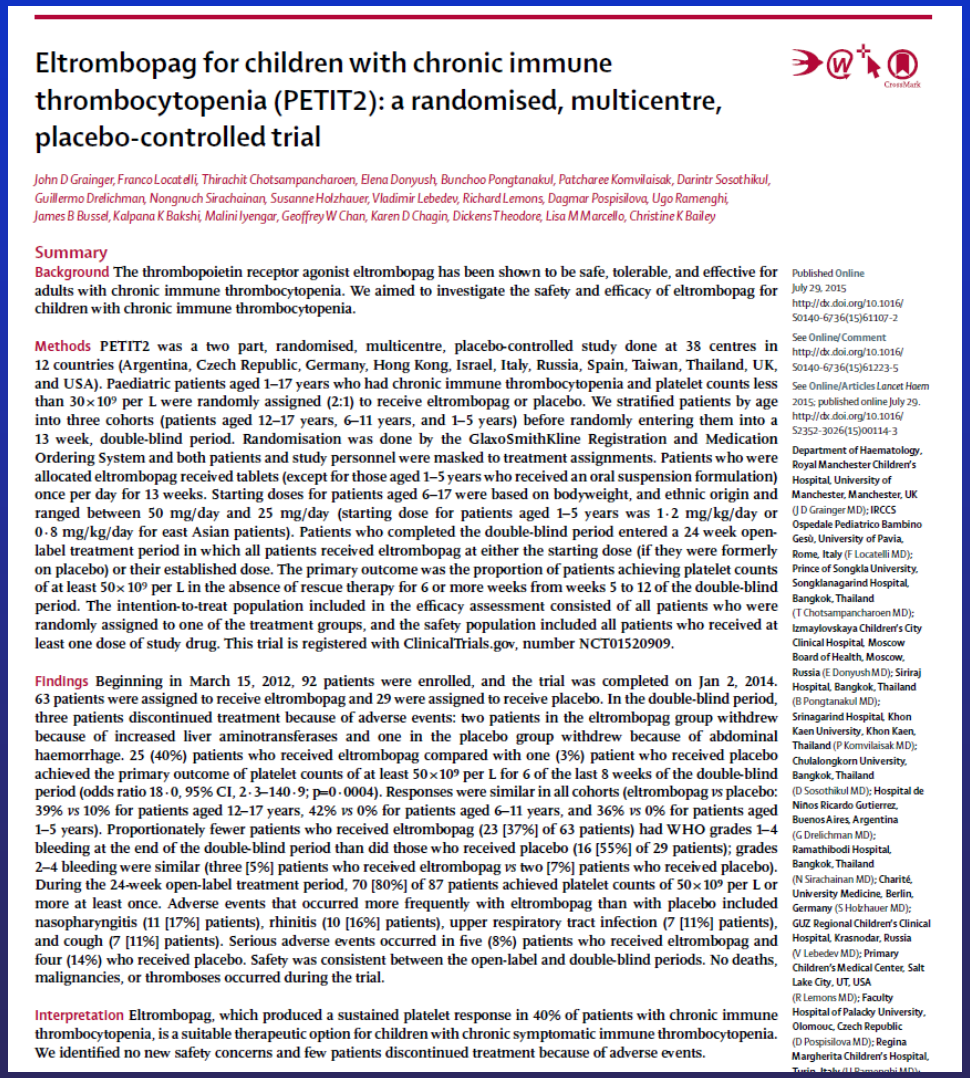
See Online/Comment http://dx.doi.org/10.1016/S0140-6736(15)61223-5

See Online/Articles *Lancet Haem* 2015; published online July 29. http://dx.doi.org/10.1016/S2352-3026(15)00114-3

Department of Haematology, Royal Manchester Children's Hospital, University of Manchester, Manchester, UK (J D Grainger MD); IRCCS Ospedale Pediatrico Bambino Gesù, University of Pavia, Rome, Italy (F Locatelli MD); Prince of Songkla University, Songklanagarind Hospital, Bangkok, Thailand (T Chotsampancharoen MD); Izmaylovskaya Children's City Clinical Hospital, Moscow Board of Health, Moscow, Russia (E Donyush MD); Siriraj Hospital, Bangkok, Thailand (B Pongtanakul MD); Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand (P Komvilaisak MD); Chulalongkorn University, Bangkok, Thailand (D Sosothikul MD); Hospital de Niños Ricardo Gutierrez, Buenos Aires, Argentina (G Drelichman MD); Ramathibodi Hospital, Bangkok, Thailand (N Sirachainan MD); Charité, University Medicine, Berlin, Germany (S Holzhauer MD); GUZ Regional Children's Clinical Hospital, Krasnodar, Russia (V Lebedev MD); Primary Children's Medical Center, Salt Lake City, UT, USA (R Lemons MD); Faculty Hospital of Palacky University, Olomouc, Czech Republic (D Pospisilova MD); Regina Margherita Children's Hospital, Turin, Italy (U Ramenghi MD);

Lancet, Respiratory Medicine

Journal Style Sheet



Eltrombopag for children with chronic immune thrombocytopenia (PETIT2): a randomised, multicentre, placebo-controlled trial

John D Grainger, Franco Locatelli, Thirachit Chotsampancharoen, Elena Donyush, Bunchoo Pongtanakul, Patcharee Komvilaisak, Darintr Sosothikul, Guillermo Drelichman, Nongnuch Sirachainan, Susanne Holzhauer, Vladimir Lebedev, Richard Lemons, Dagmar Pospisilova, Ugo Ramenghi, James B Bussel, Kalpana K Bakshi, Malini Iyengar, Geoffrey W Chan, Karen D Chagin, Dickens Theodore, Lisa M Marcello, Christine K Bailey

Summary

Background The thrombopoietin receptor agonist eltrombopag has been shown to be safe, tolerable, and effective for adults with chronic immune thrombocytopenia. We aimed to investigate the safety and efficacy of eltrombopag for children with chronic immune thrombocytopenia.

Methods PETIT2 was a two part, randomised, multicentre, placebo-controlled study done at 38 centres in 12 countries (Argentina, Czech Republic, Germany, Hong Kong, Israel, Italy, Russia, Spain, Taiwan, Thailand, UK, and USA). Paediatric patients aged 1–17 years who had chronic immune thrombocytopenia and platelet counts less than 30×10^9 per L were randomly assigned (2:1) to receive eltrombopag or placebo. We stratified patients by age into three cohorts (patients aged 12–17 years, 6–11 years, and 1–5 years) before randomly entering them into a 13 week, double-blind period. Randomisation was done by the GlaxoSmithKline Registration and Medication Ordering System and both patients and study personnel were masked to treatment assignments. Patients who were allocated eltrombopag received tablets (except for those aged 1–5 years who received an oral suspension formulation) once per day for 13 weeks. Starting doses for patients aged 6–17 were based on bodyweight, and ethnic origin and ranged between 50 mg/day and 25 mg/day (starting dose for patients aged 1–5 years was 1·2 mg/kg/day or 0·8 mg/kg/day for east Asian patients). Patients who completed the double-blind period entered a 24 week open-label treatment period in which all patients received eltrombopag at either the starting dose (if they were formerly on placebo) or their established dose. The primary outcome was the proportion of patients achieving platelet counts of at least 50×10^9 per L in the absence of rescue therapy for 6 or more weeks from weeks 5 to 12 of the double-blind period. The intention-to-treat population included in the efficacy assessment consisted of all patients who were randomly assigned to one of the treatment groups, and the safety population included all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT01520909.

Findings Beginning in March 15, 2012, 92 patients were enrolled, and the trial was completed on Jan 2, 2014. 63 patients were assigned to receive eltrombopag and 29 were assigned to receive placebo. In the double-blind period, three patients discontinued treatment because of adverse events: two patients in the eltrombopag group withdrew because of increased liver aminotransferases and one in the placebo group withdrew because of abdominal haemorrhage. 25 (40%) patients who received eltrombopag compared with one (3%) patient who received placebo achieved the primary outcome of platelet counts of at least 50×10^9 per L for 6 of the last 8 weeks of the double-blind period (odds ratio 18·0, 95% CI, 2·3–140·9; p=0·0004). Responses were similar in all cohorts (eltrombopag *vs* placebo: 39% *vs* 10% for patients aged 12–17 years, 42% *vs* 0% for patients aged 6–11 years, and 36% *vs* 0% for patients aged 1–5 years). Proportionately fewer patients who received eltrombopag (23 [37%] of 63 patients) had WHO grades 1–4 bleeding at the end of the double-blind period than did those who received placebo (16 [55%] of 29 patients); grades 2–4 bleeding were similar (three [5%] patients who received eltrombopag *vs* two [7%] patients who received placebo). During the 24-week open-label treatment period, 70 [80%] of 87 patients achieved platelet counts of 50×10^9 per L or more at least once. Adverse events that occurred more frequently with eltrombopag than with placebo included nasopharyngitis (11 [17%] patients), rhinitis (10 [16%] patients), upper respiratory tract infection (7 [11%] patients), and cough (7 [11%] patients). Serious adverse events occurred in five (8%) patients who received eltrombopag and four (14%) who received placebo. Safety was consistent between the open-label and double-blind periods. No deaths, malignancies, or thromboses occurred during the trial.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

Published Online July 29, 2015 http://dx.doi.org/10.1016/S0140-6736(15)61107-2

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(15)61223-5

See Online/Articles *Lancet Haem* 2015; published online July 29. http://dx.doi.org/10.1016/S2352-3026(15)00114-3

Department of Haematology, Royal Manchester Children's Hospital, University of Manchester, Manchester, UK (J D Grainger MD); IRCCS Ospedale Pediatrico Bambino Gesù, University of Pavia, Rome, Italy (F Locatelli MD); Prince of Songkla University, Songklanagarind Hospital, Bangkok, Thailand (T Chotsampancharoen MD); Izmaylovskaya Children's City Clinical Hospital, Moscow Board of Health, Moscow, Russia (E Donyush MD); Siriraj Hospital, Bangkok, Thailand (B Pongtanakul MD); Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand (P Komvilaisak MD); Chulalongkorn University, Bangkok, Thailand (D Sosothikul MD); Hospital de Niños Ricardo Gutierrez, Buenos Aires, Argentina (G Drelichman MD); Ramathibodi Hospital, Bangkok, Thailand (N Sirachainan MD); Charité, University Medicine, Berlin, Germany (S Holzhauer MD); GUZ Regional Children's Clinical Hospital, Krasnodar, Russia (V Lebedev MD); Primary Children's Medical Center, Salt Lake City, UT, USA (R Lemons MD); Faculty Hospital of Palacky University, Olomouc, Czech Republic (D Pospisilova MD); Regina Margherita Children's Hospital, Turin, Italy (U Ramenghi MD);

Lancet, Respiratory Medicine

Journal Style Sheet

Background:

~~Introduction~~

Findings:

~~Results:~~

Interpretation:

~~Conclusions:~~

Eltrombopag for children with chronic immune thrombocytopenia (PETIT2): a randomised, multicentre, placebo-controlled trial

John D Grainger, Franco Locatelli, Thirachit Chotsampancharoen, Elena Donyush, Bunchoo Pongtanakul, Patcharee Komvilaisak, Darintr Sosothikul, Guillermo Drelichman, Nongnuch Sirachainan, Susanne Holzhauer, Vladimir Lebedev, Richard Lemons, Dagmar Pospisilova, Ugo Ramenghi, James B Bussel, Kalpana K Bakshi, Malini Iyengar, Geoffrey W Chan, Karen D Chagin, Dickens Theodore, Lisa M Marcello, Christine K Bailey

Summary

Background The thrombopoietin receptor agonist eltrombopag has been shown to be safe, tolerable, and effective for adults with chronic immune thrombocytopenia. We aimed to investigate the safety and efficacy of eltrombopag for children with chronic immune thrombocytopenia.

Methods PETIT2 was a two part, randomised, multicentre, placebo-controlled study done at 38 centres in 12 countries (Argentina, Czech Republic, Germany, Hong Kong, Israel, Italy, Russia, Spain, Taiwan, Thailand, UK, and USA). Paediatric patients aged 1–17 years who had chronic immune thrombocytopenia and platelet counts less than 30×10^9 per L were randomly assigned (2:1) to receive eltrombopag or placebo. We stratified patients by age into three cohorts (patients aged 12–17 years, 6–11 years, and 1–5 years) before randomly entering them into a 13 week, double-blind period. Randomisation was done by the GlaxoSmithKline Registration and Medication Ordering System and both patients and study personnel were masked to treatment assignments. Patients who were allocated eltrombopag received tablets (except for those aged 1–5 years who received an oral suspension formulation) once per day for 13 weeks. Starting doses for patients aged 6–17 were based on bodyweight, and ethnic origin and ranged between 50 mg/day and 25 mg/day (starting dose for patients aged 1–5 years was 1·2 mg/kg/day or 0·8 mg/kg/day for east Asian patients). Patients who completed the double-blind period entered a 24 week open-label treatment period in which all patients received eltrombopag at either the starting dose (if they were formerly on placebo) or their established dose. The primary outcome was the proportion of patients achieving platelet counts of at least 50×10^9 per L in the absence of rescue therapy for 6 or more weeks from weeks 5 to 12 of the double-blind period. The intention-to-treat population included in the efficacy assessment consisted of all patients who were randomly assigned to one of the treatment groups, and the safety population included all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT01520909.

Findings Beginning in March 15, 2012, 92 patients were enrolled, and the trial was completed on Jan 2, 2014. 63 patients were assigned to receive eltrombopag and 29 were assigned to receive placebo. In the double-blind period, three patients discontinued treatment because of adverse events: two patients in the eltrombopag group withdrew because of increased liver aminotransferases and one in the placebo group withdrew because of abdominal haemorrhage. 25 (40%) patients who received eltrombopag compared with one (3%) patient who received placebo achieved the primary outcome of platelet counts of at least 50×10^9 per L for 6 of the last 8 weeks of the double-blind period (odds ratio 18·0, 95% CI, 2·3–140·9; p=0·0004). Responses were similar in all cohorts (eltrombopag *vs* placebo: 39% *vs* 10% for patients aged 12–17 years, 42% *vs* 0% for patients aged 6–11 years, and 36% *vs* 0% for patients aged 1–5 years). Proportionately fewer patients who received eltrombopag (23 [37%] of 63 patients) had WHO grades 1–4 bleeding at the end of the double-blind period than did those who received placebo (16 [55%] of 29 patients); grades 2–4 bleeding were similar (three [5%] patients who received eltrombopag *vs* two [7%] patients who received placebo). During the 24-week open-label treatment period, 70 [80%] of 87 patients achieved platelet counts of 50×10^9 per L or more at least once. Adverse events that occurred more frequently with eltrombopag than with placebo included nasopharyngitis (11 [17%] patients), rhinitis (10 [16%] patients), upper respiratory tract infection (7 [11%] patients), and cough (7 [11%] patients). Serious adverse events occurred in five (8%) patients who received eltrombopag and four (14%) who received placebo. Safety was consistent between the open-label and double-blind periods. No deaths, malignancies, or thromboses occurred during the trial.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

Published Online July 29, 2015 http://dx.doi.org/10.1016/S0140-6736(15)61107-2

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(15)61223-5

See Online/Articles *Lancet Haem* 2015; published online July 29. http://dx.doi.org/10.1016/S2352-3026(15)00114-3

Department of Haematology, Royal Manchester Children's Hospital, University of Manchester, Manchester, UK (J D Grainger MD); IRCCS Ospedale Pediatrico Bambino Gesù, University of Pavia, Rome, Italy (F Locatelli MD); Prince of Songkla University, Songklanagarind Hospital, Bangkok, Thailand (T Chotsampancharoen MD); Izmaylovskaya Children's City Clinical Hospital, Moscow Board of Health, Moscow, Russia (E Donyush MD); Siriraj Hospital, Bangkok, Thailand (B Pongtanakul MD); Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand (P Komvilaisak MD); Chulalongkorn University, Bangkok, Thailand (D Sosothikul MD); Hospital de Niños Ricardo Gutierrez, Buenos Aires, Argentina (G Drelichman MD); Ramathibodi Hospital, Bangkok, Thailand (N Sirachainan MD); Charité, University Medicine, Berlin, Germany (S Holzhauer MD); GUZ Regional Children's Clinical Hospital, Krasnodar, Russia (V Lebedev MD); Primary Children's Medical Center, Salt Lake City, UT, USA (R Lemons MD); Faculty Hospital of Palacky University, Olomouc, Czech Republic (D Pospisilova MD); Regina Margherita Children's Hospital, Turin, Italy (U Ramenghi MD)

Lancet, Respiratory Medicine

Journal Style Sheet

Background:

~~Introduction~~

Findings:

~~Results:~~

Interpretation:

~~Conclusions:~~

Eltrombopag for children with chronic immune thrombocytopenia (PETIT2): a randomised, multicentre, placebo-controlled trial

John D Grainger, Franco Locatelli, Thirachit Chotsampancharoen, Elena Donyush, Bunchoo Pongtanakul, Patcharee Komvilaisak, Darintr Sosothikul, Guillermo Drelichman, Nongnuch Sirachainan, Susanne Holzhauer, Vladimir Lebedev, Richard Lemons, Dagmar Pospisilova, Ugo Ramenghi, James B Bussel, Kalpana K Bakshi, Malini Iyengar, Geoffrey W Chan, Karen D Chagin, Dickens Theodore, Lisa M Marcello, Christine K Bailey

Summary

Background The thrombopoietin receptor agonist eltrombopag has been shown to be safe, tolerable, and effective for adults with chronic immune thrombocytopenia. We aimed to investigate the safety and efficacy of eltrombopag for children with chronic immune thrombocytopenia.

Methods PETIT2 was a two part, randomised, multicentre, placebo-controlled study done at 38 centres in 12 countries (Argentina, Czech Republic, Germany, Hong Kong, Israel, Italy, Russia, Spain, Taiwan, Thailand, UK, and USA). Paediatric patients aged 1–17 years who had chronic immune thrombocytopenia and platelet counts less than 30×10^9 per L were randomly assigned (2:1) to receive eltrombopag or placebo. We stratified patients by age into three cohorts (patients aged 12–17 years, 6–11 years, and 1–5 years) before randomly entering them into a 13 week, double-blind period. Randomisation was done by the GlaxoSmithKline Registration and Medication Ordering System and both patients and study personnel were masked to treatment assignments. Patients who were allocated eltrombopag received tablets (except for those aged 1–5 years who received an oral suspension formulation) once per day for 13 weeks. Starting doses for patients aged 6–17 were based on bodyweight, and ethnic origin and ranged between 50 mg/day and 25 mg/day (starting dose for patients aged 1–5 years was 1·2 mg/kg/day or 0·8 mg/kg/day for east Asian patients). Patients who completed the double-blind period entered a 24 week open-label treatment period in which all patients received eltrombopag at either the starting dose (if they were formerly on placebo) or their established dose. The primary outcome was the proportion of patients achieving platelet counts of at least 50×10^9 per L in the absence of rescue therapy for 6 or more weeks from weeks 5 to 12 of the double-blind period. The intention-to-treat population included in the efficacy assessment consisted of all patients who were randomly assigned to one of the treatment groups, and the safety population included all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT01520909.

Findings Beginning in March 15, 2012, 92 patients were enrolled, and the trial was completed on Jan 2, 2014. 63 patients were assigned to receive eltrombopag and 29 were assigned to receive placebo. In the double-blind period, three patients discontinued treatment because of adverse events: two patients in the eltrombopag group withdrew because of increased liver aminotransferases and one in the placebo group withdrew because of abdominal haemorrhage. 25 (40%) patients who received eltrombopag compared with one (3%) patient who received placebo achieved the primary outcome of platelet counts of at least 50×10^9 per L for 6 of the last 8 weeks of the double-blind period (odds ratio 18·0, 95% CI, 2·3–140·9; p=0·0004). Responses were similar in all cohorts (eltrombopag *vs* placebo: 39% *vs* 10% for patients aged 12–17 years, 42% *vs* 0% for patients aged 6–11 years, and 36% *vs* 0% for patients aged 1–5 years). Proportionately fewer patients who received eltrombopag (23 [37%] of 63 patients) had WHO grades 1–4 bleeding at the end of the double-blind period than did those who received placebo (16 [55%] of 29 patients); grades 2–4 bleeding were similar (three [5%] patients who received eltrombopag *vs* two [7%] patients who received placebo). During the 24-week open-label treatment period, 70 [80%] of 87 patients achieved platelet counts of 50×10^9 per L or more at least once. Adverse events that occurred more frequently with eltrombopag than with placebo included nasopharyngitis (11 [17%] patients), rhinitis (10 [16%] patients), upper respiratory tract infection (7 [11%] patients), and cough (7 [11%] patients). Serious adverse events occurred in five (8%) patients who received eltrombopag and four (14%) who received placebo. Safety was consistent between the open-label and double-blind periods. No deaths, malignancies, or thromboses occurred during the trial.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

Published Online July 29, 2015 http://dx.doi.org/10.1016/S0140-6736(15)61107-2

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(15)61223-5

See Online/Articles *Lancet Haem* 2015; published online July 29. http://dx.doi.org/10.1016/S2352-3026(15)00114-3

Department of Haematology, Royal Manchester Children's Hospital, University of Manchester, Manchester, UK (J D Grainger MD); IRCCS Ospedale Pediatrico Bambino Gesù, University of Pavia, Rome, Italy (F Locatelli MD); Prince of Songkla University, Songklanagarind Hospital, Bangkok, Thailand (T Chotsampancharoen MD); Izmaylovskaya Children's City Clinical Hospital, Moscow Board of Health, Moscow, Russia (E Donyush MD); Siriraj Hospital, Bangkok, Thailand (B Pongtanakul MD); Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand (P Komvilaisak MD); Chulalongkorn University, Bangkok, Thailand (D Sosothikul MD); Hospital de Niños Ricardo Gutierrez, Buenos Aires, Argentina (G Drelichman MD); Ramathibodi Hospital, Bangkok, Thailand (N Sirachainan MD); Charité, University Medicine, Berlin, Germany (S Holzhauer MD); GUZ Regional Children's Clinical Hospital, Krasnodar, Russia (V Lebedev MD); Primary Children's Medical Center, Salt Lake City, UT, USA (R Lemons MD); Faculty Hospital of Palacky University, Olomouc, Czech Republic (D Pospisilova MD); Regina Margherita Children's Hospital, Turin, Italy (U Ramenghi MD)

Lancet, Respiratory Medicine

Eltrombopag for children with chronic immune thrombocytopenia (PETIT2): a randomised, multicentre, placebo-controlled trial

John D Grainger, Franco Locatelli, Thirachit Chotsampancharoen, Elena Donyush, Bunchoo Pongtanakul, Patcharee Komvilaisak, Darintr Sosothikul, Guillermo Drelichman, Nongnuch Sirachainan, Susanne Holzhauer, Vladimir Lebedev, Richard Lemons, Dagmar Pospisilova, Ugo Ramenghi, James B Bussel, Kalpana K Bakshi, Malini Iyengar, Geoffrey W Chan, Karen D Chagin, Dickens Theodore, Lisa M Marcello, Christine K Bailey

Summary

Background The thrombopoietin receptor agonist eltrombopag has been shown to be safe, tolerable, and effective for adults with chronic immune thrombocytopenia. We aimed to investigate the safety and efficacy of eltrombopag for children with chronic immune thrombocytopenia.

Methods PETIT2 was a two part, randomised, multicentre, placebo-controlled study done at 38 centres in 12 countries (Argentina, Czech Republic, Germany, Hong Kong, Israel, Italy, Russia, Spain, Taiwan, Thailand, UK, and USA). Paediatric patients aged 1–17 years who had chronic immune thrombocytopenia and platelet counts less than 30×10^9 per L were randomly assigned (2:1) to receive eltrombopag or placebo. We stratified patients by age into three cohorts (patients aged 12–17 years, 6–11 years, and 1–5 years) before randomly entering them into a 13 week, double-blind period. Randomisation was done by the GlaxoSmithKline Registration and Medication Ordering System and both patients and study personnel were masked to treatment assignments. Patients who were allocated eltrombopag received tablets (except for those aged 1–5 years who received an oral suspension formulation) once per day for 13 weeks. Starting doses for patients aged 6–17 were based on bodyweight, and ethnic origin and ranged between 50 mg/day and 25 mg/day (starting dose for patients aged 1–5 years was 1·2 mg/kg/day or 0·8 mg/kg/day for east Asian patients). Patients who completed the double-blind period entered a 24 week open-label treatment period in which all patients received eltrombopag at either the starting dose (if they were formerly on placebo) or their established dose. The primary outcome was the proportion of patients achieving platelet counts of at least 50×10^9 per L in the absence of rescue therapy for 6 or more weeks from weeks 5 to 12 of the double-blind period. The intention-to-treat population included in the efficacy assessment consisted of all patients who were randomly assigned to one of the treatment groups, and the safety population included all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT01520909.

Published Online July 29, 2015 http://dx.doi.org/10.1016/S0140-6736(15)61107-2

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(15)61223-5

See Online/Articles Lancet Haem 2015; published online July 29. http://dx.doi.org/10.1016/S2352-3026(15)00114-3

Department of Haematology, Royal Manchester Children's Hospital, University of Manchester, Manchester, UK (J D Grainger MD); IRCCS Ospedale Pediatrico Bambino Gesù, University of Pavia, Rome, Italy (F Locatelli MD); Prince of Songkla University, Songklanagarind Hospital, Bangkok, Thailand (T Chotsampancharoen MD); Izmaylovskaya Children's City Clinical Hospital, Moscow Board of Health, Moscow, (N Sirachainan MD); Charité, University Medicine, Berlin, Germany (S Holzhauer MD); GUZ Regional Children's Clinical Hospital, Krasnodar, Russia (V Lebedev MD); Primary Children's Medical Center, Salt Lake City, UT, USA (R Lemons MD); Faculty Hospital of Palacky University, Olomouc, Czech Republic (D Pospisilova MD); Regina Margherita Children's Hospital,

During the 24-week open-label treatment period, 70 [80%] of 87 patients achieved platelet counts of 50×10^9 per L or more at least once. Adverse events that occurred more frequently with eltrombopag than with placebo included nasopharyngitis (11 [17%] patients), rhinitis (10 [16%] patients), upper respiratory tract infection (7 [11%] patients), and cough (7 [11%] patients). Serious adverse events occurred in five (8%) patients who received eltrombopag and four (14%) who received placebo. Safety was consistent between the open-label and double-blind periods. No deaths, malignancies, or thromboses occurred during the trial.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

Lancet, Respiratory Medicine

Eltrombopag for children with chronic immune thrombocytopenia (PETIT2): a randomised, multicentre, placebo-controlled trial

John D Grainger, Franco Locatelli, Thirachit Chotsampancharoen, Elena Donyush, Bunchoo Pongtanakul, Patcharee Komvilaisak, Darintr Sosothikul, Guillermo Drelichman, Nongnuch Sirachainan, Susanne Holzhauer, Vladimir Lebedev, Richard Lemons, Dagmar Pospisilova, Ugo Ramenghi, James B Bussel, Kalpana K Bakshi, Malini Iyengar, Geoffrey W Chan, Karen D Chagin, Dickens Theodore, Lisa M Marcello, Christine K Bailey

Summary

Background The thrombopoietin receptor agonist eltrombopag has been shown to be safe, tolerable, and effective for adults with chronic immune thrombocytopenia. We aimed to investigate the safety and efficacy of eltrombopag for children with chronic immune thrombocytopenia.

Methods PETIT2 was a two part, randomised, multicentre, placebo-controlled study done at 38 centres in 12 countries (Argentina, Czech Republic, Germany, Hong Kong, Israel, Italy, Russia, Spain, Taiwan, Thailand, UK, and USA). Paediatric patients aged 1–17 years who had chronic immune thrombocytopenia and platelet counts less than 30×10^9 per L were randomly assigned (2:1) to receive eltrombopag or placebo. We stratified patients by age into three cohorts (patients aged 12–17 years, 6–11 years, and 1–5 years) before randomly entering them into a 13 week, double-blind period. Randomisation was done by the GlaxoSmithKline Registration and Medication Ordering System and both patients and study personnel were masked to treatment assignments. Patients who were allocated eltrombopag received tablets (except for those aged 1–5 years who received an oral suspension formulation) once per day for 13 weeks. Starting doses for patients aged 6–17 were based on bodyweight, and ethnic origin and ranged between 50 mg/day and 25 mg/day (starting dose for patients aged 1–5 years was 1·2 mg/kg/day or 0·8 mg/kg/day for east Asian patients). Patients who completed the double-blind period entered a 24 week open-label treatment period in which all patients received eltrombopag at either the starting dose (if they were formerly on placebo) or their established dose. The primary outcome was the proportion of patients achieving platelet counts of at least 50×10^9 per L in the absence of rescue therapy for 6 or more weeks from weeks 5 to 12 of the double-blind period. The intention-to-treat population included in the efficacy assessment consisted of all patients who were randomly assigned to one of the treatment groups, and the safety population included all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT01520909.

Published Online July 29, 2015 http://dx.doi.org/10.1016/S0140-6736(15)61107-2

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(15)61223-5

See Online/Articles Lancet Haem 2015; published online July 29. http://dx.doi.org/10.1016/S2352-3026(15)00114-3

Department of Haematology, Royal Manchester Children's Hospital, University of Manchester, Manchester, UK (J D Grainger MD); IRCCS Ospedale Pediatrico Bambino Gesù, University of Pavia, Rome, Italy (F Locatelli MD); Prince of Songkla University, Songklanagarind Hospital, Bangkok, Thailand (T Chotsampancharoen MD); Izmaylovskaya Children's City Clinical Hospital, Moscow Board of Health, Moscow, (N Sirachainan MD); Charité, University Medicine, Berlin, Germany (S Holzhauer MD); GUZ Regional Children's Clinical Hospital, Krasnodar, Russia (V Lebedev MD); Primary Children's Medical Center, Salt Lake City, UT, USA (R Lemons MD); Faculty Hospital of Palacky University, Olomouc, Czech Republic (D Pospisilova MD); Regina Margherita Children's Hospital,

During the 24-week open-label treatment period, 70 [80%] of 87 patients achieved platelet counts of 50×10^9 per L or more at least once. Adverse events that occurred more frequently with eltrombopag than with placebo included nasopharyngitis (11 [17%] patients), rhinitis (10 [16%] patients), upper respiratory tract infection (7 [11%] patients), and cough (7 [11%] patients). Serious adverse events occurred in five (8%) patients who received eltrombopag and four (14%) who received placebo. Safety was consistent between the open-label and double-blind periods. No deaths, malignancies, or thromboses occurred during the trial.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

Lancet, Respiratory Medicine

Eltrombopag for children with chronic immune

Conclusions In patients with acute lung injury and the acute respiratory distress syndrome, mechanical ventilation with a lower tidal volume than is traditionally used results in decreased mortality and increases the number of days without ventilator use. (N Engl J Med 2000;342:1301-8.)

least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT01520909.

Izmaylovskaya Children's City Clinical Hospital, Moscow Board of Health, Moscow,

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

During the 24-week open-label treatment period, 70 [80%] of 87 patients achieved platelet counts of 50×10^9 per L or more at least once. Adverse events that occurred more frequently with eltrombopag than with placebo included nasopharyngitis (11 [17%] patients), rhinitis (10 [16%] patients), upper respiratory tract infection (7 [11%] patients), and cough (7 [11%] patients). Serious adverse events occurred in five (8%) patients who received eltrombopag and four (14%) who received placebo. Safety was consistent between the open-label and double-blind periods. No deaths, malignancies, or thromboses occurred during the trial.

Interpretation Eltrombopag, which produced a sustained platelet response in 40% of patients with chronic immune thrombocytopenia, is a suitable therapeutic option for children with chronic symptomatic immune thrombocytopenia. We identified no new safety concerns and few patients discontinued treatment because of adverse events.

(N Sirachainan MD); Charité, University Medicine, Berlin, Germany (S Holzhauer MD); GUZ Regional Children's Clinical Hospital, Krasnodar, Russia (V Lebedev MD); Primary Children's Medical Center, Salt Lake City, UT, USA (R Lemons MD); Faculty Hospital of Palacky University, Olomouc, Czech Republic (D Pospisilova MD); Regina Margherita Children's Hospital,

Lancet, Respiratory Medicine

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

*Gordon S Doig, Fiona Simpson, Philippa T Heighes, Rinaldo Bellomo, Douglas Chesher, Ian D Caterson, Michael C Reade, Peter W J Harrigan, for the Refeeding Syndrome Trial Investigators Group**

Summary

Background Equipoise exists regarding the benefits of restricting caloric intake during electrolyte replacement for refeeding syndrome, with half of intensive care specialists choosing to continue normal caloric intake. We aimed to assess whether energy restriction affects the duration of critical illness, and other measures of morbidity, compared with standard care.

Methods We did a randomised, multicentre, single-blind clinical trial in 13 hospital intensive care units (ICUs) in Australia (11 sites) and New Zealand (two sites). Adult critically ill patients who developed refeeding syndrome within 72 h of commencing nutritional support in the ICU were enrolled and allocated to receive continued standard nutritional support or protocolised caloric restriction. 1:1 computer-based randomisation was done in blocks of variable size, stratified by enrolment serum phosphate concentration (>0·32 mmol/L *vs* ≤0·32 mmol/L) and body-mass index (BMI; >18 kg/m² *vs* ≤18 kg/m²). The primary outcome was the number of days alive after ICU discharge, with 60 day follow-up, in a modified intention-to-treat population of all randomly allocated patients except those mistakenly enrolled. Days alive after ICU discharge was a composite outcome based on ICU length of stay, overall survival time, and mortality. The Refeeding Syndrome Trial was registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR number 12609001043224).

Findings Between Dec 3, 2010, and Aug 13, 2014, we enrolled 339 adult critically ill patients: 170 were randomly allocated to continued standard nutritional support and 169 to protocolised caloric restriction. During the 60 day follow-up, the mean number of days alive after ICU discharge in 165 assessable patients in the standard care group was 39·9 (95% CI 36·4–43·7) compared with 44·8 (95% CI 40·9–49·1) in 166 assessable patients in the caloric restriction group (difference 4·9 days, 95% CI −2·3 to 13·6, p=0·19). Nevertheless, protocolised caloric restriction improved key individual components of the primary outcome: more patients were alive at day 60 (128 [78%] of 163 *vs* 149 [91%] of 164, p=0·002) and overall survival time was increased (48·9 [SD 1·46] days *vs* 53·65 [0·97] days, log-rank p=0·002).

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

Lancet Respir Med 2015; 3: 943–52

Published Online November 17, 2015 http://dx.doi.org/10.1016/S2213-2600(15)00418-X

See Comment page 904

*see appendix for the full list of investigators

Northern Clinical School Intensive Care Research Unit (G S Doig PhD, F Simpson PhD, P T Heighes MNE), **and The Boden Institute of Obesity, Nutrition Exercise, and Eating Disorders** (Prof I D Caterson FRACP), **University of Sydney, Sydney, NSW, Australia; School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia** (Prof R Bellomo MD); **New South Wales Health, Pathology, Sydney, NSW, Australia** (D Chesher PhD); **Burns, Trauma and Critical Care Research Centre, University of Queensland, Brisbane, QLD, Australia** (Prof M C Reade DPhil); **and John Hunter Hospital, New Lambton Heights, NSW,**

Lancet, Respiratory Medicine

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

Gordon S Doig, Fiona Simpson, Philippa T Heighes, Rinaldo Bellomo, Douglas Chesher, Ian D Caterson, Michael C Reade, Peter W J Harrigan, for the Refeeding Syndrome Trial Investigators Group*

Summary

Background Equipoise exists regarding the benefits of restricting caloric intake during electrolyte replacement for refeeding syndrome, with half of intensive care specialists choosing to continue normal caloric intake. We aimed to assess whether energy restriction affects the duration of critical illness, and other measures of morbidity, compared with standard care.

Methods We did a randomised, multicentre, single-blind clinical trial in 13 hospital intensive care units (ICUs) in Australia (11 sites) and New Zealand (two sites). Adult critically ill patients who developed refeeding syndrome within 72 h of commencing nutritional support in the ICU were enrolled and allocated to receive continued standard nutritional support or protocolised caloric restriction. 1:1 computer-based randomisation was done in blocks of variable size, stratified by enrolment serum phosphate concentration (>0·32 mmol/L *vs* ≤0·32 mmol/L) and body-mass index (BMI; >18 kg/m² *vs* ≤18 kg/m²). The primary outcome was the number of days alive after ICU discharge, with 60 day follow-up, in a modified intention-to-treat population of all randomly allocated patients except those mistakenly enrolled. Days alive after ICU discharge was a composite outcome based on ICU length of stay, overall survival time, and mortality. The Refeeding Syndrome Trial was registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR number 12609001043224).

Findings Between Dec 3, 2010, and Aug 13, 2014, we enrolled 339 adult critically ill patients: 170 were randomly allocated to continued standard nutritional support and 169 to protocolised caloric restriction. During the 60 day follow-up, the mean number of days alive after ICU discharge in 165 assessable patients in the standard care group was 39·9 (95% CI 36·4–43·7) compared with 44·8 (95% CI 40·9–49·1) in 166 assessable patients in the caloric restriction group (difference 4·9 days, 95% CI −2·3 to 13·6, p=0·19). Nevertheless, protocolised caloric restriction improved key individual components of the primary outcome: more patients were alive at day 60 (128 [78%] of 163 *vs* 149 [91%] of 164, p=0·002) and overall survival time was increased (48·9 [SD 1·46] days *vs* 53·65 [0·97] days, log-rank p=0·002).

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

Lancet Respir Med 2015; 3: 943–52

Published Online November 17, 2015 http://dx.doi.org/10.1016/S2213-2600(15)00418-X

See Comment page 904

*see appendix for the full list of investigators

Northern Clinical School Intensive Care Research Unit (G S Doig PhD, F Simpson PhD, P T Heighes MNE), **and The Boden Institute of Obesity, Nutrition Exercise, and Eating Disorders** (Prof I D Caterson FRACP), **University of Sydney, Sydney, NSW, Australia; School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia** (Prof R Bellomo MD); **New South Wales Health, Pathology, Sydney, NSW, Australia** (D Chesher PhD); **Burns, Trauma and Critical Care Research Centre, University of Queensland, Brisbane, QLD, Australia** (Prof M C Reade DPhil); **and John Hunter Hospital, New Lambton Heights, NSW,**

Lancet, Respiratory Medicine

Journal Style Sheet

Background:

~~Introduction~~

Findings:

~~Results:~~

Interpretation:

~~Conclusions:~~

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

Gordon S Doig, Fiona Simpson, Philippa T Heighes, Rinaldo Bellomo, Douglas Chesher, Ian D Caterson, Michael C Reade, Peter W J Harrigan, for the Refeeding Syndrome Trial Investigators Group*

Summary

Background Equipoise exists regarding the benefits of restricting caloric intake during electrolyte replacement for refeeding syndrome, with half of intensive care specialists choosing to continue normal caloric intake. We aimed to assess whether energy restriction affects the duration of critical illness, and other measures of morbidity, compared with standard care.

Methods We did a randomised, multicentre, single-blind clinical trial in 13 hospital intensive care units (ICUs) in Australia (11 sites) and New Zealand (two sites). Adult critically ill patients who developed refeeding syndrome within 72 h of commencing nutritional support in the ICU were enrolled and allocated to receive continued standard nutritional support or protocolised caloric restriction. 1:1 computer-based randomisation was done in blocks of variable size, stratified by enrolment serum phosphate concentration (>0·32 mmol/L *vs* ≤0·32 mmol/L) and body-mass index (BMI; >18 kg/m² *vs* ≤18 kg/m²). The primary outcome was the number of days alive after ICU discharge, with 60 day follow-up, in a modified intention-to-treat population of all randomly allocated patients except those mistakenly enrolled. Days alive after ICU discharge was a composite outcome based on ICU length of stay, overall survival time, and mortality. The Refeeding Syndrome Trial was registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR number 12609001043224).

Findings Between Dec 3, 2010, and Aug 13, 2014, we enrolled 339 adult critically ill patients: 170 were randomly allocated to continued standard nutritional support and 169 to protocolised caloric restriction. During the 60 day follow-up, the mean number of days alive after ICU discharge in 165 assessable patients in the standard care group was 39·9 (95% CI 36·4–43·7) compared with 44·8 (95% CI 40·9–49·1) in 166 assessable patients in the caloric restriction group (difference 4·9 days, 95% CI −2·3 to 13·6, p=0·19). Nevertheless, protocolised caloric restriction improved key individual components of the primary outcome: more patients were alive at day 60 (128 [78%] of 163 *vs* 149 [91%] of 164, p=0·002) and overall survival time was increased (48·9 [SD 1·46] days *vs* 53·65 [0·97] days, log-rank p=0·002).

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

Lancet Respir Med 2015; 3: 943–52

Published Online November 17, 2015 http://dx.doi.org/10.1016/S2213-2600(15)00418-X

See Comment page 904

*see appendix for the full list of investigators

Northern Clinical School Intensive Care Research Unit (G S Doig PhD, F Simpson PhD, P T Heighes MNE), **and The Boden Institute of Obesity, Nutrition Exercise, and Eating Disorders** (Prof I D Caterson FRACP), **University of Sydney, Sydney, NSW, Australia; School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia** (Prof R Bellomo MD); **New South Wales Health, Pathology, Sydney, NSW, Australia** (D Chesher PhD); **Burns, Trauma and Critical Care Research Centre, University of Queensland, Brisbane, QLD, Australia** (Prof M C Reade DPhil); **and John Hunter Hospital, New Lambton Heights, NSW,**

Lancet, Respiratory Medicine

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

Gordon S Doig, Fiona Simpson, Philippa T Heighes, Rinaldo Bellomo, Douglas Chesher, Ian D Caterson, Michael C Reade, Peter W J Harrigan, for the Refeeding Syndrome Trial Investigators Group*

Summary

Background Equipoise exists regarding the benefits of restricting caloric intake during electrolyte replacement for refeeding syndrome, with half of intensive care specialists choosing to continue normal caloric intake. We aimed to assess whether energy restriction affects the duration of critical illness, and other measures of morbidity, compared with standard care.

Methods We did a randomised, multicentre, single-blind clinical trial in 13 hospital intensive care units (ICUs) in Australia (11 sites) and New Zealand (two sites). Adult critically ill patients who developed refeeding syndrome within 72 h of commencing nutritional support in the ICU were enrolled and allocated to receive continued standard nutritional support or protocolised caloric restriction. 1:1 computer-based randomisation was done in blocks of variable size, stratified by enrolment serum phosphate concentration (>0·32 mmol/L *vs* ≤0·32 mmol/L) and body-mass index (BMI; >18 kg/m² *vs* ≤18 kg/m²). The primary outcome was the number of days alive after ICU discharge, with 60 day follow-up, in a modified intention-to-treat population of all randomly allocated patients except those mistakenly enrolled. Days alive after ICU discharge was a composite outcome based on ICU length of stay, overall survival time, and mortality. The Refeeding Syndrome Trial was registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR number 12609001043224).

Findings Between Dec 3, 2010, and Aug 13, 2014, we enrolled 339 adult critically ill patients: 170 were randomly allocated to continued standard nutritional support and 169 to protocolised caloric restriction. During the 60 day follow-up, the mean number of days alive after ICU discharge in 165 assessable patients in the standard care group was 39·9 (95% CI 36·4–43·7) compared with 44·8 (95% CI 40·9–49·1) in 166 assessable patients in the caloric restriction group (difference 4·9 days, 95% CI −2·3 to 13·6, p=0·19). Nevertheless, protocolised caloric restriction improved key individual components of the primary outcome: more patients were alive at day 60 (128 [78%] of 163 *vs* 149 [91%] of 164, p=0·002) and overall survival time was increased (48·9 [SD 1·46] days *vs* 53·65 [0·97] days, log-rank p=0·002).

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

Lancet Respir Med 2015; 3: 943–52

Published Online November 17, 2015 http://dx.doi.org/10.1016/S2213-2600(15)00418-X

See Comment page 904

*see appendix for the full list of investigators

Northern Clinical School Intensive Care Research Unit (G S Doig PhD, F Simpson PhD, P T Heighes MNE), **and The Boden Institute of Obesity, Nutrition Exercise, and Eating Disorders** (Prof I D Caterson FRACP), **University of Sydney, Sydney, NSW, Australia; School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia** (Prof R Bellomo MD); **New South Wales Health, Pathology, Sydney, NSW, Australia** (D Chesher PhD); **Burns, Trauma and Critical Care Research Centre, University of Queensland, Brisbane, QLD, Australia** (Prof M C Reade DPhil); **and John Hunter Hospital, New Lambton Heights, NSW,**

Lancet, Respiratory Medicine

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

Gordon S Doig, Fiona Simpson, Philippa T Heighes, Rinaldo Bellomo, Douglas Chesher, Ian D Caterson, Michael C Reade, Peter W J Harrigan, for the Refeeding Syndrome Trial Investigators Group*

Summary

Background Equipoise exists regarding the benefits of restricting caloric intake during electrolyte replacement for refeeding syndrome, with half of intensive care specialists choosing to continue normal caloric intake. We aimed to assess whether energy restriction affects the duration of critical illness, and other measures of morbidity, compared with standard care.

Methods We did a randomised, multicentre, single-blind clinical trial in 13 hospital intensive care units (ICUs) in Australia (11 sites) and New Zealand (two sites). Adult critically ill patients who developed refeeding syndrome within 72 h of commencing nutritional support in the ICU were enrolled and allocated to receive continued standard nutritional support or protocolised caloric restriction. 1:1 computer-based randomisation was done in blocks of variable size, stratified by enrolment serum phosphate concentration (>0·32 mmol/L *vs* ≤0·32 mmol/L) and body-mass index (BMI; >18 kg/m² *vs* ≤18 kg/m²). The primary outcome was the number of days alive after ICU discharge,

Findings Between Dec 3, 2010, and Aug 13, 2014, we enrolled 339 adult critically ill patients: 170 were randomly allocated to continued standard nutritional support and 169 to protocolised caloric restriction. During the 60 day follow-up, the mean number of days alive after ICU discharge in 165 assessable patients in the standard care group was 39·9 (95% CI 36·4–43·7) compared with 44·8 (95% CI 40·9–49·1) in 166 assessable patients in the caloric restriction group (difference 4·9 days, 95% CI −2·3 to 13·6, p=0·19). Nevertheless, protocolised caloric restriction improved key individual components of the primary outcome: more patients were alive at day 60 (128 [78%] of 163 *vs* 149 [91%] of 164, p=0·002) and overall survival time was increased (48·9 [SD 1·46] days *vs* 53·65 [0·97] days, log-rank p=0·002).

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

Lancet Respir Med 2015; 3: 943–52

Published Online November 17, 2015 http://dx.doi.org/10.1016/S2213-2600(15)00418-X

See Comment page 904

*see appendix for the full list of investigators

Northern Clinical School Intensive Care Research Unit (G S Doig PhD, F Simpson PhD, P T Heighes MNE), **and The Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia** (Prof R Bellomo MD); **New South Wales Health, Pathology, Sydney, NSW, Australia** (D Chesher PhD); **Burns, Trauma and Critical Care Research Centre, University of Queensland, Brisbane, QLD, Australia** (Prof M C Reade DPhil); **and John Hunter Hospital, New Lambton Heights, NSW,**

Lancet, Respiratory Medicine

Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial

Gordon S Doig, Fiona Simpson, Philippa T Heighes, Rinaldo Bellomo, Douglas Chesher, Ian D Caterson, Michael C Reade, Peter W J Harrigan, for the Refeeding Syndrome Trial Investigators Group*

Summary

Background Equipoise exists regarding the benefits of restricting caloric intake during electrolyte replacement for refeeding syndrome, with half of intensive care specialists choosing to continue normal caloric intake. We aimed to assess whether energy restriction affects the duration of critical illness, and other measures of morbidity, compared with standard care.

Methods We did a randomised, multicentre, single-blind clinical trial in 13 hospital intensive care units (ICUs) in Australia (11 sites) and New Zealand (two sites). Adult critically ill patients who developed refeeding syndrome within 72 h of commencing nutritional support in the ICU were enrolled and allocated to receive continued standard nutritional support or protocolised caloric restriction. 1:1 computer-based randomisation was done in blocks of variable size, stratified by enrolment serum phosphate concentration (>0·32 mmol/L *vs* ≤0·32 mmol/L) and body-mass index (BMI; >18 kg/m² *vs* ≤18 kg/m²). The primary outcome was the number of days alive after ICU discharge,

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

Findings Between Dec 3, 2010, and Aug 13, 2014, we enrolled 339 adult critically ill patients: 170 were randomly allocated to continued standard nutritional support and 169 to protocolised caloric restriction. During the 60 day follow-up, the mean number of days alive after ICU discharge in 165 assessable patients in the standard care group was 39·9 (95% CI 36·4–43·7) compared with 44·8 (95% CI 40·9–49·1) in 166 assessable patients in the caloric restriction group (difference 4·9 days, 95% CI −2·3 to 13·6, p=0·19). Nevertheless, protocolised caloric restriction improved key individual components of the primary outcome: more patients were alive at day 60 (128 [78%] of 163 *vs* 149 [91%] of 164, p=0·002) and overall survival time was increased (48·9 [SD 1·46] days *vs* 53·65 [0·97] days, log-rank p=0·002).

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

Lancet Respir Med 2015; 3: 943–52
Published Online November 17, 2015
http://dx.doi.org/10.1016/S2213-2600(15)00418-X

See Comment page 904

*see appendix for the full list of investigators

Northern Clinical School Intensive Care Research Unit (G S Doig PhD, F Simpson PhD, P T Heighes MNE), **and The Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia** (Prof R Bellomo MD); **New South Wales Health, Pathology, Sydney, NSW, Australia** (D Chesher PhD); **Burns, Trauma and Critical Care Research Centre, University of Queensland, Brisbane, QLD, Australia** (Prof M C Reade DPhil); **and John Hunter Hospital, New Lambton Heights, NSW,**

1) Avoiding rejection by Editor

63% (654/1,038) rejected by Editor

- Never sent to external reviewers
- Editor determines content not appropriate for journal, content not interesting to journal, very bad study, very poorly written.

Journal Editors are very busy.

- Carry a clinical load, have their own research programs, usually *not* paid as Editors.
- The *easiest* decision for a Editor to make is 'Reject without Review'.
  - Immediately removes work from their inbox.
  - Reduces future work, as they will never see the paper again!

There is only one section of your paper you can guarantee an Editor will read:

- But we usually write it last, when we are tired, yet it might be the most important section.

If your Abstract is poorly written, you make it easy for the Editor to 'Reject without Review'!

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

Reviewers are very busy.

- Carry a clinical load and have their own research programs.

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

Reviewers are very busy.

- Carry a clinical load and have their own research programs.
- Reviewers cannot 'Reject without Review'. They must read your whole paper but:

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

Reviewers are very busy.

- Carry a clinical load and have their own research programs.
- Reviewers cannot 'Reject without Review'. They must read your whole paper but:
  - If your paper is poorly written and difficult to understand, they will stop reading and recommend 'Reject'!
  - If your paper is difficult to understand, Reviewers do not usually provide objective reasons for Rejection. They just send a Confidential Comment to the Editor recommending Reject.

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

Reviewers are very busy.

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

Reviewers are very busy.

- Make your papers *easy* to understand.

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

Reviewers are very busy.

- Make your papers *easy* to understand.
- Identify a small number of candidate journals and retrieve 2 or 3 published papers from each.
  - Use these papers as a guide for journal selection and study design.
  - Use these papers as a guide for English language use.

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

Reviewers are very busy.

- Make your papers *easy* to understand.
- Identify a small number of candidate journals and retrieve 2 or 3 published papers from each.
  - Use these papers as a guide for journal selection and study design.
  - Use these papers as a guide for English language use.
- Every journal has its own unique conventions.

Interpretation Protocolised caloric restriction is a suitable therapeutic option for critically ill adults who develop refeeding syndrome. We did not identify any safety concerns associated with the use of protocolised caloric restriction.

2) Avoiding rejection by Reviewers

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

Reviewers are very busy.

- Make your papers *easy* to understand.
- Identify a small number of candidate journals and retrieve 2 or 3 published papers from each.
  - Use these papers as a guide for journal selection and study design.
  - Use these papers as a guide for English language use.
- Every journal has its own unique conventions.
- Conversational English is different to Scientific English.
  - Have two translators: One who is good at conversational English and one who is a content area expert.

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

If the Editor returns your paper and asks for Minor or Major Revisions based on Reviewers comments, you are almost published!

- 85% of submissions do not make it to this stage!

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

If the Editor returns your paper and asks for Minor or Major Revisions based on Reviewers comments, you are almost published!

- 85% of submissions do not make it to this stage!

Do not argue with your Reviewers!

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

If the Editor returns your paper and asks for Minor or Major Revisions based on Reviewers comments, you are almost published!

- 85% of submissions do not make it to this stage!

Do not argue with your Reviewers!

- The Editor is often one of your Reviewers!!! So, if you choose to argue, you may be arguing with the Editor.

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

If the Editor returns your paper and asks for Minor or Major Revisions based on Reviewers comments, you are almost published!

- 85% of submissions do not make it to this stage!

Do not argue with your Reviewers!

- The Editor is often one of your Reviewers!!! So, if you choose to argue, you may be arguing with the Editor.
  - You will always lose an argument with the Editor!

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

If the Editor returns your paper and asks for Minor or Major Revisions based on Reviewers comments, you are almost published!

- 85% of submissions do not make it to this stage!

Do not argue with your Reviewers! But you can Negotiate! Gently!

- The Editor is often one of your Reviewers!!! So, if you choose to argue, you may be arguing with the Editor.
  - You will always lose an argument with the Editor!

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

If the Editor returns your paper and asks for Minor or Major Revisions based on Reviewers comments, you are almost published!

- 85% of submissions do not make it to this stage!

Do not argue with your Reviewers! But you can Negotiate! Gently!

- The Editor is often one of your Reviewers!!! So, if you choose to argue, you may be arguing with the Editor.
    - You will always lose an argument with the Editor!

If a Reviewer wants 57 changes, and you disagree with all 57 requests:

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

If the Editor returns your paper and asks for Minor or Major Revisions based on Reviewers comments, you are almost published!

- 85% of submissions do not make it to this stage!

Do not argue with your Reviewers! But you can Negotiate! Gently!

- The Editor is often one of your Reviewers!!! So, if you choose to argue, you may be arguing with the Editor.
    - You will always lose an argument with the Editor!

If a Reviewer wants 57 changes, and you disagree with all 57 requests:

- Make all 57 changes anyway or...

3) Responding to Reviewers Comments

86% (301/348) rejected after negative comments from reviewers

- Reviewers determine bad study, poorly explained or poorly written.
- *Sometimes* reviewers recommend Reject after Authors fail to make recommended corrections!

If the Editor returns your paper and asks for Minor or Major Revisions based on Reviewers comments, you are almost published!

- 85% of submissions do not make it to this stage!

Do not argue with your Reviewers! But you can Negotiate! Gently!

- The Editor is often one of your Reviewers!!! So, if you choose to argue, you may be arguing with the Editor.
  - You will always lose an argument with the Editor!

If a Reviewer wants 57 changes, and you disagree with all 57 requests:

- Make all 57 changes anyway or...
- Make 55 changes.... and point out politely why you can't make the last 2 changes.

4) General Insights

4) General Insights

99% of the Editors and Reviewers who read *your* paper have never been to an ICU in *your* country.

4) General Insights

99% of the Editors and Reviewers who read *your* paper have never been to an ICU in *your* country.

- They do not understand the care you provide is just as good, or better, than the care they provide!

4) General Insights

99% of the Editors and Reviewers who read *your* paper have never been to an ICU in *your* country.

- They do not understand the care you provide is just as good, or better, than the care they provide!

Describe your patients and your ICU in terms they understand.

4) General Insights

99% of the Editors and Reviewers who read *your* paper have never been to an ICU in your country.

- They do not understand the care you provide is just as good, or better, than the care they provide!

Describe your patients and your ICU in terms they understand.

- Admission APACHE for US journals / SAPS for European journals.

4) General Insights

99% of the Editors and Reviewers who read *your* paper have never been to an ICU in your country.

- They do not understand the care you provide is just as good, or better, than the care they provide!

Describe your patients and your ICU in terms they understand.

- Admission APACHE for US journals / SAPS for European journals.

Describe routine care using statements to demonstrate you are familiar with best practice:

4) General Insights

99% of the Editors and Reviewers who read *your* paper have never been to an ICU in your country.

- They do not understand the care you provide is just as good, or better, than the care they provide!

Describe your patients and your ICU in terms they understand.

- Admission APACHE for US journals / SAPS for European journals.

Describe routine care using statements to demonstrate you are familiar with best practice:

- “Nutrition support was provided in line with” SCCM guidelines (for US journals) / ESPEN guidelines (for European journals).

4) General Insights

99% of the Editors and Reviewers who read *your* paper have never been to an ICU in your country.

- They do not understand the care you provide is just as good, or better, than the care they provide!

Describe your patients and your ICU in terms they understand.

- Admission APACHE for US journals / SAPS for European journals.

Describe routine care using statements to demonstrate you are familiar with best practice:

- "Nutrition support was provided in line with" SCCM guidelines (for US journals) / ESPEN guidelines (for European journals).
- "Patients with ARDs were ventilated using low tidal volumes (ref to US study) and proned (ref to French study) when required."

4) General Insights

99% of the Editors and Reviewers who read *your* paper have never been to an ICU in your country.

- They do not understand the care you provide is just as good, or better, than the care they provide!

Describe your patients and your ICU in terms they understand.

- Admission APACHE for US journals / SAPS for European journals.

Describe routine care using statements to demonstrate you are familiar with best practice:

- "Nutrition support was provided in line with" SCCM guidelines (for US journals) / ESPEN guidelines (for European journals).
- "Patients with ARDs were ventilated using low tidal volumes (ref to US study) and proned (ref to French study) when required."

If you use your *country name* in the title, the Editor or Reviewer may conclude your results apply only to your country and perhaps your paper is not interesting to their Journal!

Summary

Summary

63% (654/1,038) of papers are rejected by the Editor,

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.
  - Select your target Journal before you start your Research.
  - Make sure your target Journal has published research projects similar to yours in the past.

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.
  - Select your target Journal before you start your Research.
  - Make sure your target Journal has published research projects similar to yours in the past.
- Remember, the Editor is busy. Make your Abstract easy to understand!

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.
  - Select your target Journal before you start your Research.
  - Make sure your target Journal has published research projects similar to yours in the past.
- Remember, the Editor is busy. Make your Abstract easy to understand!

86% (301/348) of papers sent to Reviewers are rejected

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.
  - Select your target Journal before you start your Research.
  - Make sure your target Journal has published research projects similar to yours in the past.
- Remember, the Editor is busy. Make your Abstract easy to understand!

86% (301/348) of papers sent to Reviewers are rejected

- Usually because Reviewers disagree with what you have done or the way you present or interpret your data.

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.
  - Select your target Journal before you start your Research.
  - Make sure your target Journal has published research projects similar to yours in the past.
- Remember, the Editor is busy. Make your Abstract easy to understand!

86% (301/348) of papers sent to Reviewers are rejected

- Usually because Reviewers disagree with what you have done or the way you present or interpret your data.
  - Use successful publications to guide your data collection (APACHE/SAPS), study design, and use of English.

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.
  - Select your target Journal before you start your Research.
  - Make sure your target Journal has published research projects similar to yours in the past.
- Remember, the Editor is busy. Make your Abstract easy to understand!

86% (301/348) of papers sent to Reviewers are rejected

- Usually because Reviewers disagree with what you have done or the way you present or interpret your data.
  - Use successful publications to guide your data collection (APACHE/SAPS), study design, and use of English.
- *Always* change your manuscript in response to Reviewer's comments

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.
  - Select your target Journal before you start your Research.
  - Make sure your target Journal has published research projects similar to yours in the past.
- Remember, the Editor is busy. Make your Abstract easy to understand!

86% (301/348) of papers sent to Reviewers are rejected

- Usually because Reviewers disagree with what you have done or the way you present or interpret your data.
  - Use successful publications to guide your data collection (APACHE/SAPS), study design, and use of English.
- *Always* change your manuscript in response to Reviewer's comments

Finally, remember that only 8% (83/1,038) of submissions get Accepted.

Summary

63% (654/1,038) of papers are rejected by the Editor,

- Usually because the Editor determines your content is not appropriate for the Journal.
  - Select your target Journal before you start your Research.
  - Make sure your target Journal has published research projects similar to yours in the past.
- Remember, the Editor is busy. Make your Abstract easy to understand!

86% (301/348) of papers sent to Reviewers are rejected

- Usually because Reviewers disagree with what you have done or the way you present or interpret your data.
  - Use successful publications to guide your data collection (APACHE/SAPS), study design, and use of English.
- *Always* change your manuscript in response to Reviewer's comments

Finally, remember that only 8% (83/1,038) of submissions get Accepted.

- Don't give up. *Your research is important to your patients!*

Questions??

A pdf version of this talk can be downloaded from the Talks section of our outreach education web site (www.EvidenceBased.net).