

# A HaemSTAR-led, UK-wide ‘flash-mob’ audit of intravenous immunoglobulin use in immune thrombocytopenia

**Authors:** Phillip Nicolson,<sup>A</sup> Rita Perry,<sup>B</sup> Amelia Fisher,<sup>C</sup> Gemma Scott,<sup>D</sup> Laura Magill,<sup>B</sup> Dominique Chan-Lam,<sup>E</sup> Alice Thorpe,<sup>E</sup> Mac Macheta,<sup>F</sup> Luke Carter-Brzezinski,<sup>F</sup> Sam Ackroyd,<sup>G</sup> Alvin Katumba,<sup>G</sup> Charlotte Bradbury,<sup>H</sup> Sheila Jen,<sup>H</sup> Marquita Camillieri,<sup>H</sup> Martin Besser,<sup>I</sup> Tom Bull,<sup>I</sup> Katherine Leighton,<sup>J</sup> Yezenash Ayalew,<sup>J</sup> John Willan,<sup>K</sup> Edmund Watson,<sup>K</sup> Pamela Oshinyemi,<sup>K</sup> Yogesh Upadhye,<sup>L</sup> Keir Pickard,<sup>L</sup> Imogen Swart-Rimmer,<sup>M</sup> Chloe Knott,<sup>M</sup> Sally Chown,<sup>M</sup> Francesca Crolla,<sup>M</sup> Daire Quinn,<sup>N</sup> Lindsay McLeod-Kennedy,<sup>N</sup> Hajer Oun,<sup>N</sup> Christopher McDermott,<sup>N</sup> Mairi Walker,<sup>N</sup> Ryan Mullally,<sup>O</sup> Naoimh Herlihy,<sup>O</sup> Gulnaz Shah,<sup>O</sup> Andrew Doyle,<sup>O</sup> Susan Robinson,<sup>O</sup> Zara Sayar,<sup>P</sup> Rebecca Pryor,<sup>Q</sup> Chris Peet,<sup>Q</sup> Amir Shenouda,<sup>Q</sup> Indrani Venkatadasari,<sup>Q</sup> Jorge Cartier,<sup>R</sup> Melek Akay,<sup>R</sup> Dimitris Tsitsikas,<sup>R</sup> Suthesh Sivapalaratnam,<sup>R</sup> Nichola Cooper,<sup>S</sup> Claire Lentaigne,<sup>S</sup> Chris Bailey,<sup>S</sup> Dan Mei Xu,<sup>S</sup> Sine Janum,<sup>S</sup> Arunodaya Mohan,<sup>S</sup> Katja Kimberger,<sup>C</sup> Maipelo Kgologolo,<sup>S</sup> Belen Sevillano,<sup>T</sup> Sophie Hanina,<sup>T</sup> Akila Danga,<sup>T</sup> Chira Mustafa,<sup>T</sup> Charlotte Wilding,<sup>T</sup> Roochi Trikha,<sup>T</sup> Han Wang,<sup>T</sup> Cristina Crossette-Thambiah,<sup>T</sup> Andrew Hastings,<sup>T</sup> Sree Sreedhara,<sup>T</sup> David Wright,<sup>U</sup> Laura Batey,<sup>U</sup> Abigail Atkin,<sup>U</sup> Sarah Davis,<sup>V</sup> Sarah Jaafar,<sup>V</sup> Ayesha Ejaz,<sup>V</sup> Tina Biss,<sup>W</sup> Jennifer Swieton,<sup>W</sup> Mohd Sharin Mohd Noh,<sup>W</sup> Holly Gibson,<sup>X</sup> Tanya Freeman,<sup>X</sup> Upekha Badaguma,<sup>X</sup> Olivia Kreze,<sup>X</sup> Suriya Kirkpatrick,<sup>Y</sup> Surenthini Suntharalingam,<sup>Y</sup> Miroslab Kmonicek,<sup>Y</sup> Michael Joffe,<sup>Z</sup> Dan Halperin,<sup>Z</sup> Michael Desborough,<sup>AA</sup> Alexandros Rampotas,<sup>AA</sup> Elissa Dhillon,<sup>AA</sup> Paul Greaves,<sup>AB</sup> Edward Blacker,<sup>AB</sup> Laura Aiken,<sup>AB</sup> Jesca Boot,<sup>AB</sup> Nithya Prasannan,<sup>AB</sup> Jonathan Kerr,<sup>AC</sup> Abi Martin,<sup>AC</sup> Sarah Wexler,<sup>AD</sup> Claire Burney,<sup>AD</sup> Michelle Melly,<sup>AD</sup> Regina Nolan,<sup>AD</sup> Rupert Hipkins,<sup>AE</sup> Israa Kaddam,<sup>AE</sup> Shereef Elmoamly,<sup>AE</sup> Jennifer Darlow,<sup>AF</sup> Dianne Plews,<sup>AG</sup> Caroline Shrubsole,<sup>AG</sup> Eleana Loizou,<sup>AH</sup> Louise Garth,<sup>AH</sup> Hina Peter,<sup>AI</sup> Julia Wolf,<sup>AI</sup> Shivali Walia,<sup>AI</sup> Vickie MacDonald,<sup>AJ</sup> Abbas Zaidi,<sup>AJ</sup> Robert Dunk,<sup>AJ</sup> Haroon Miah,<sup>AJ</sup> Atiqah Miah,<sup>AJ</sup> David Tucker,<sup>AK</sup> Thomas Skinner,<sup>AK</sup> Seda Cakmak,<sup>AK</sup> Ipek Cakmak,<sup>AK</sup> Hayder Hussein,<sup>A</sup> Richard Buka,<sup>A</sup> Lydia Wilson,<sup>A</sup> Georgina Talbot,<sup>A</sup> Hafiz Qureshi,<sup>AL</sup> Sarah Wharin,<sup>AL</sup> Anna Dillon,<sup>AL</sup> Benjamin Bailiff,<sup>AM</sup> Graham McIlroy,<sup>AM</sup> Duncan Murray,<sup>AM</sup> Frances Seymour,<sup>AM</sup> Jane Graham,<sup>AN</sup> Samuel Harrison,<sup>AN</sup> Beena Salhan,<sup>AN</sup> David Sharpe,<sup>AN</sup> Wayne Thomas,<sup>AO</sup> Rory McCulloch,<sup>AO</sup> Nicola Crosbie,<sup>AO</sup> Gillian Lowe<sup>A</sup> and Quentin Hill<sup>C</sup>

**Authors:** <sup>A</sup>University Hospitals Birmingham NHS Foundation Trust; <sup>B</sup>University of Birmingham; <sup>C</sup>Leeds Teaching Hospitals NHS Trust; <sup>D</sup>University Hospital of Wales; <sup>E</sup>Barnsley District General Hospital; <sup>F</sup>Blackpool Victoria Hospital; <sup>G</sup>Bradford Teaching Hospitals NHS Foundation Trust; <sup>H</sup>Bristol Royal Infirmary; <sup>I</sup>Cambridge University Hospitals NHS Foundation Trust; <sup>J</sup>Forth Valley Hospital; <sup>K</sup>Frimley Health NHS Foundation Trust; <sup>L</sup>Gateshead Health NHS Foundation Trust; <sup>M</sup>Gloucestershire Hospitals NHS Foundation Trust; <sup>N</sup>Greater Glasgow and Clyde NHS Trust; <sup>O</sup>Guy's and St Thomas' NHS Foundation Trust; <sup>P</sup>Kings College Hospital NHS Foundation Trust; <sup>Q</sup>Heartlands Hospital, Birmingham; <sup>R</sup>Homerton University Hospital Trust; <sup>S</sup>Imperial College Healthcare Trust; <sup>T</sup>London North West University Healthcare NHS Trust; <sup>U</sup>Mid Yorkshire Hospitals NHS Trust; <sup>V</sup>Milton Keynes University Hospital NHS Foundation Trust; <sup>W</sup>Newcastle upon Tyne Hospitals NHS Foundation Trust; <sup>X</sup>Newham University Hospital; <sup>Y</sup>North Bristol NHS Trust; <sup>Z</sup>Northampton General Hospital; <sup>AA</sup>Oxford University Hospitals NHS Foundation Trust; <sup>AB</sup>Queen's Hospital, Romford; <sup>AC</sup>Royal Devon and Exeter

Hospital; <sup>AD</sup>Royal United Hospitals Bath NHS Foundation Trust; <sup>AE</sup>Russells Hall Hospital, Dudley; <sup>AF</sup>Salford Royal Hospital; <sup>AG</sup>South Tees Hospitals NHS Foundation Trust; <sup>AH</sup>St Helens and Knowsley Teaching Hospitals NHS Trust; <sup>AI</sup>Great Western Hospital, Swindon; <sup>AJ</sup>The Royal London Hospital; <sup>AK</sup>Torbay and South Devon NHS Foundation Trust; <sup>AL</sup>University Hospitals of Leicester NHS Trust; <sup>AM</sup>University Hospitals Coventry and Warwickshire NHS Trust; <sup>AN</sup>University Hospitals of North Midlands NHS Trust; <sup>AO</sup>University Hospitals Plymouth NHS Trust

## Introduction

Intravenous immunoglobulin (IVIg) is a common therapy for patients with immune thrombocytopenia (ITP). The initial response rate for IVIg is 80%<sup>1</sup> and is typically rapid, with some patients responding in 24 hours, although usually in 2–4 days.<sup>2</sup> When IVIg is used alone, the response is relatively short, averaging around 2–4 weeks. Potential side effects include headache, renal failure,

thrombosis and transfusion-transmitted infection. The cost of IVIg is significant, averaging £400 for 10 g.<sup>3</sup> Historic dosing regimens for IVIg are either 1 g/kg/day for 1–2 days or 0.4 g/kg/day for 5 days.<sup>4</sup> There are data to suggest an increased likelihood of response with 1 g/kg/day for 1–2 days than with 0.4 g/kg/day for 5 days.<sup>5</sup> Recent guidance from NHS England recommends 1 g/kg for 1 day, with a second dose of 1 g/kg at 7 days only if there is failure to achieve a haemostatically adequate platelet count.<sup>6</sup> Using the optimal dosing regimen is important for maximum efficacy, the avoidance of side effects and prudent healthcare.

HaemSTAR (Haematology Specialty Trainee Audit and Research) is a UK-wide network of clinical haematology registrars that is supported by the National Institute of Health Research (NIHR) Haematology Clinical Research Network (CRN). We have members in each NIHR local CRN who coordinate local research activity and involvement of other participants as is needed. Our overarching aim is to promote clinical research in non-malignant haematology. One way that we intend to do this is by enabling effective transition of worthy local audits to a national scale.

## Methods

This project aimed to audit the IVIg prescribing practices for treatment of ITP in the UK. Data from a 5-year period between 2013 and 2018 were eligible for inclusion. The primary outcome measure was the proportion of IVIg treatments that were dosed according to the 2011 American Society of Hematology guidelines.<sup>4</sup> We also collected data on concomitant treatments and platelet count responses. We aimed to use this project to develop a generalisable methodology for future mass participation audits in non-malignant haematology.

With competitively won support of a data manager from the West Midlands Local CRN, we set up a data collection tool on a secure server running the Research Electronic Data Capture (REDCap) web application.<sup>7</sup> With the help of our network, in late 2018, 134 collaborators across 39 hospital sites inputted data from the IVIg treatment episodes of 978 adult patients with ITP, over the course of just 80 days. This was all at no extra financial cost to the NHS.

## Results and discussion

Nine hundred and fifty-six treatment episodes of IVIg were recorded with enough data for inclusion in the assessment of the primary outcome measure. Of these, 671 (70.2%) used

the recommended dose of 1 g/kg/day, and 324 of these 671 (48.2%) were either given on a single day, or had a second dose after an adequate interval to allow for a response assessment. Three hundred and forty-seven (51.7%) treatments involved the use of additional doses given in a manner not endorsed by the guidelines; 324 had IVIg over two consecutive days, three were dosed over 5 days and 20 received a different dosing regimen. The platelet response following treatment with 1 g/kg on a single day was non-inferior to when IVIg was given over two consecutive days.

Not only do these data suggest that we may be spending more money than we should and exposing our patients to unnecessary risk by using significantly more IVIg than is recommended to treat ITP, but they also show that it is possible to collect valuable health data rapidly utilising minimal resources, by coordinating audit activity across the country with research networks such as HaemSTAR. We intend to repeat this national audit model annually with other important questions in haematology. ■

## References

- 1 Godeau B, Chevret S, Varet B *et al*. Intravenous immunoglobulin or high-dose methylprednisolone, with or without oral prednisone, for adults with untreated severe autoimmune thrombocytopenic purpura: a randomised, multicentre trial. *Lancet* 2002;359:23–9.
- 2 Provan D, Stasi R, Newland AC *et al*. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood* 2010;115:168–86.
- 3 British National Formulary Joint Formulary Committee. *MedicinesComplete*. London: The Royal Pharmaceutical Society, 2019. www.medicinescomplete.com
- 4 Neunert C, Lim W, Crowther M *et al*. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood* 2011;117:4190–207.
- 5 Bussel J. Intravenous immune serum globulin in immune thrombocytopenia: clinical results and biochemical evaluation. *Vox Sang* 1985;49(Suppl 1):44–50.
- 6 NHS England. *Specialised Services Circular SSC1529*. NHS, 2015:1–16.
- 7 Harris PA, Taylor R, Thielke R *et al*. Research electronic data capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.