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# EVALUATION OF THE EFFICACY OF INTERMITTENT VANCOMYCIN INFUSION DOSING IN A PAEDIATRIC POPULATION

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**Aims** Anecdotal evidence has suggested that patients prescribed intermittent intravenous vancomycin infusion do not achieve plasma vancomycin concentrations within the therapeutic range in a timely manner when dosed according to Trust guidelines. The aims of this study were: to evaluate adherence to Trust dosing and therapeutic drug monitoring guidelines<sup>1</sup> for intermittent intravenous vancomycin infusion, and, to determine whether adherence to these guidelines achieves and maintains therapeutic vancomycin plasma concentrations in paediatric patients.

**Method** A retrospective audit of vancomycin dosing and therapeutic drug monitoring was carried out over a 12-month period. Patients aged between 1 month and 18 years at the start of treatment who were prescribed an inpatient course of intermittent intravenous vancomycin consisting of at least three doses were identified from electronic prescribing records. Electronic medical notes and prescribing records were used to retrieve demographic data, vancomycin prescription data, serum creatinine levels and data relating to vancomycin therapeutic drug monitoring. Vancomycin plasma concentrations between 10–15 mg/L were considered therapeutic unless an alternative range was stated in the patient's medical notes. Data analysis was conducted on SigmaPlot, Version 14.5. Ethical approval was not required.

**Results** Fifty treatment courses and an associated 171 plasma vancomycin concentrations were identified and included for analysis. Treatment duration ranged from 2.9 to 50 days (mean 8.9 days). The initial prescribed dose and dosing interval were fully adherent to the guidelines for 41/50 (82%) treatment courses. The initial vancomycin plasma concentration was measured at the recommended time for 20/50 (40%) courses. The action taken in response to a plasma concentration was in accordance with the guideline recommendation in 129/171 (75%) cases. One treatment course was completed without measurement of a vancomycin plasma concentration. Plasma concentrations within the therapeutic range were achieved for 22/49 (45%) treatment courses for which concentrations were monitored. The mean time taken to reach the therapeutic range was 2.3 days (standard deviation 1.9 days) from when treatment was commenced. Collectively, 21.5% of time from all treatment courses was spent with plasma concentrations within the therapeutic range.

**Conclusion** The study showed good adherence to guidelines for the prescribing of the initial vancomycin dose and dosing frequency. Despite suboptimal timing of the measurement of initial vancomycin plasma concentrations, the actions taken (such as dose alteration) in response to plasma concentrations were in accordance with the guideline in three-quarters of cases. However, less than half of all treatment courses achieved therapeutic plasma concentrations, and for those that did, a mean of 2.3 days from when treatment was commenced was required to reach therapeutic range. This suggests that Trust vancomycin dosing recommendations may be insufficient to achieve plasma concentrations within the therapeutic range in a timely manner for most patients. An increase to

the recommended initial dosing of intermittent intravenous vancomycin infusion should be considered.

## REFERENCE

1. Paediatric Formulary Vancomycin Monograph, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust (2022).

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# DOES KAFTRIO® REDUCE IV ANTIBIOTIC BURDEN IN CYSTIC FIBROSIS? A RETROSPECTIVE OBSERVATIONAL EVALUATION

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**Aim** Respiratory failure remains the most common cause of death in Cystic Fibrosis (CF) with chronic/complex infection a significant contributory factor. Infection frequency and associated treatment burden increase the risk drug-resistant organisms; however, stewardship strategies are challenging to translate to CF care.

The CFTR modulator Kaftrio® (elexacaftor/tezacaftor/ivacaftor) launched in the UK in August 2020. Initial phase 3 clinical trials<sup>1 2</sup> and a subsequent open-label extension study<sup>3</sup> demonstrated promising data on health-related quality of life, including reduced pulmonary exacerbation (PEX) rates (63%), hospitalisation (71%) and PEX requiring IV antibiotics (78%). This evaluation aimed to provide a 'real-world' review of the impact of Kaftrio® on IV antibiotic burden (admission rates, 'bed-days', bed-day cost, total IV antibiotic use and 'AWaRE' antibiotic use) in CF patients aged 12–16 years at a single tertiary centre.

**Method** A single-centre retrospective observational evaluation was conducted. All 12–16 year olds on Kaftrio® were identified using the local CF database. For each patient: month/year Kaftrio® commenced and prior CFTR modulator therapy were determined. Clinical trial patients were excluded. Digital clinical information systems were used to identify 'chest-related' admissions for IV antibiotics in the 24 months prior to starting Kaftrio® and the treatment period post, up to June 2022. For each admission, drugs, doses administered and 'IV antibiotic bed-days' were determined. 'Bed-day' costs were calculated and use of 'Restricted' or 'Watch' antibiotics (WHO AWaRE/local Policy) were identified. IV antibiotic burden pre- and post Kaftrio® was evaluated.

**Results** 44 admissions in 33 patients were identified prior to Kaftrio®, compared with 13 admissions post-Kaftrio®, demonstrating a 65–70% overall reduction in admissions (PEX: rate 66/100patient/year vs 23/100patient/year). Pre-Kaftrio® 639 'bed days'/24 months were directly attributed to delivery of IV antibiotics—a total estimated cost of £383,400 (estimate £600/day/medical bed). From October 2020–June 2022, the number of IV antibiotic 'bed days' fell to 183. A total reduction of 71%, with an estimated cost saving of £273,600. In the 24 months prior to Kaftrio® a total 2849 doses of IV antibiotics were administered vs 657 doses in the same patient cohort in the period post-Kaftrio® to June 2022, an absolute reduction of 2192 doses (77%). Of the 2849 IV antibiotics pre-Kaftrio® doses, 84% were restricted/watch antibiotics (R=706; W= 1681). Usage dropped by 37.5% and 89% respectively post-Kaftrio®.

**Conclusion** Results suggest Kaftrio® reduces overall IV antibiotic burden in CF patients, providing real-world data