Once daily dosing of Tigecycline to facilitate Outpatient Parenteral Antibiotic Therapy (OPAT)

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Background

Tigecycline is increasingly being used to treat complicated skin and soft tissue infections [cSSTI], intra-abdominal infections [cIAI] and off-label bone and joint infections [BJI], typically where resistant organisms or polymicrobial infections are identified. The licensed dose for tigecycline is 100mg stat loading dose by intravenous administration, followed by 50mg every 12 hours. However, the long half-life (36 hours) and prolonged post-antibiotic effect of tigecycline suggest that once daily administration with appropriate dosed tigecycline should provide adequate antimicrobial activity *in vivo*. To investigate the impact of this dosing strategy, a retrospective observational study was undertaken in a single London Teaching hospital of all patients who had received once-daily intravenous tigecycline via an established OPAT service

Method

All adult patients that received once daily tigecycline (>3 days) between Jan-2016 and Jun-2018 were reviewed. Electronic patient records were used to identify patients treated and collect treatment related outcomes. Treatment outcomes were defined by the OPAT multidisciplinary team at the end of each individual treatment course and grouped as a) Complete cure (completed course of tigecycline in line with recognised international guidelines and/or resolution of infection), b) Treatment failure (premature cessation of tigecycline due to adverse effects or non-response of infection to antibiotic) and c) Failure due to disease progression (disease progressed which required alternative aggressive treatment although there was response to infection)

Results

A total of 18 cases among 17 unique patients were identified. Female patients were more common (56%), average age was 62 years (range 44-85 years) and a high prevalence of patients with a documented previous antibiotic allergy (42%) were included. Average treatment duration was 36 days with a total of 648 bed-days saved by the OPAT service.

Overall treatment 'complete cure' was 83% in this cohort. Complications of treatment include nausea and vomiting (22% of cases; none requiring treatment withdrawal). A delayed rash (five weeks into therapy) developed in one patient but this was not re-challenged and persisted with subsequent beta-lactam therapy and may not relate to the tigecycline therapy. Transient increases in amylase were evident in two patients, but neither patient required withdrawal of treatment as amylase did not exceed the two-fold lab increase (>180iu/L) or develop any signs of drug-related pancreatitis

Pt. no.	Age/ gender	Co-morbidities	Antibiotic allergy	Diagnosis	Microbiology results	Concurrent antibiotics/ antifungal	Duration of IV tigecycline OPAT (Total duration) (days)	Amylase (during treatment) (U/L)	Adverse effects	Clinical outcome
1	71/M	Diabetes, Hypertension	Nil	Bone and Joint-Osteomyelitis	ESBL Morganella morganii in tissue	Nil	28 (31)	N/A	Nil	**Cure** Completed course and de-escalated to oral antibiotics for further 6 weeks.
2	66/M	Diabetes, Heart diseases, Asthma/copd	Penicillin V	Intra-abdominal-Post operation small bowel perforation	ESBL E.coli and VRE colonised; no active infection with microbes confirmed	Fluconazole	6 (15)	N/A	Nil	**Cure** Successful treatment.
3	80/F	Diabetes	Ertapenem	Bone and Joint-Chronic left hip osteomyelitis	Citrobacter koseri from aspiration	Nil	12 (27)	26	Nil	**Cure** Completed course and de-escalated to oral antibiotics for further suppressive treatment.
4	85/F	Diabetes, Heart diseases	Nil	Intra-abdominal-Gastric ulcer perforation	VRE, ESBL Klebsiella	Nil	26 (29)	80; 121	Rash (19.7.18)	**Failure** (Treatment) Discontinued due to rash.
5	82/F	Bronchiectasis, Pulmonary fibrosis, Malignant melanoma	Clarithromycin	Intra-abdominal-Mesorectal abscess	No positive culture	Caspofungin	26 (n/a)	52	Nausea and diarrhoea; Aprepitant given as prophylaxis.	**Unclassified** Passed away at the end of treatment, no evidence of infection (CRP 6).
6	61/F	Diabetes	Nil	Bone and Joint-Osteomyelitis	Klebsiella, Proteus, Pseudomonas colonisation - ESBL/CRO - including Proteus/ Kleb with TIG R	Nil	111 (203)	9; 12	Mild vomitting initially.	**Failure** (disease progression)- Suppressive treatment; patient clinically stable but referred from amputation as MDR-infection.
7	72/M	Mucinous adenocarcinoma	Nil	Intra-abdominal-Illiopsoas abscess	MSSA, E.faecalis, ESBL E.coli	Fluconazole	71 (97)	10	Nil	**Cure** Suppressive treatment; patient passed away following admission in June 2017.
8	46/M	Nil	Ceftriaxone, Meropenem, Flucoxacillin, Teicoplanin	Bone and Joint-Septic arthritis	No positive culture	Nil	18 (25)	N/A	Nausea and loose stools; Antiemetics supplied.	**Cure** Successful treatment.
9a	56/M	NASH cirrhosis (awaiting transplant), Diabetes	Vancomycin	Intra-abdominal-Spontaneous bacterial peritonitis	E.Faecium, S.Haemolyticus	Nil	5 (8)	47	Nil	**Cure** Successful treatment.
9b				Intra-abdominal-Spontaneous bacterial peritonitis	E.Faecium, S.Haemolyticus	Nil	2 (7)	N/A	Nil	**Cure** Successful treatment.
10	58/M	Chronic pancreatitis, Cirrhosis, Left inguinal hernia repair	Nil	Unclassified-Obliterated gall bladder sepsis	ESBL E.coli from wound	Voriconazole	21 (n/a)	134; 121	Nil	**Cure** Successful treatment.
11	50/F	Metastatic breast carcinoma	Penicillins	Bone and Joint-Right femur chronic osteomyelitis	E.Coli, Morganella (AMPC), Proteus	Ciprofloxacin	117 (127)	6	Nil	**Cure** Suppressive treatment; under Nail removed.
12	44/F	Nil	Nil	Gynaecological-Infection in uterus due to copper coil insertion	ESBL E.coli	Nil	7 (15)	N/A	Nil	**Cure** Successful treatment.
13	60/F	Neuroendocrine head of pancreas tumour (T4N1M1)	Nil	Hepatobiliary-Infection and bacteraemia secondary to stent replacement	ESBL Citrobacter and VRE from blood culture (stent)	Nil	42 (45)	36; 32	Nil	**Cure** Successful treatment.
14	44/F	Nil	Nil	Gynaecological-Uterine-collection post rupture; abscess	NDM E.coli	Nil	105 (n/a)	61; 57	Nausea; Cyclizine given.	**Cure** Successful treatment.
15	73/M	Diabetes, heart diseases, COPD	Azithromycin Streptomycin	Urological-Prostate abcess	Achromobacter xylosoxidans, S.Haemolyticus from abscess aspirate	Nil	15 (35)	55	Nil	**Failure** (Treatment)- Failure of antibiotic to treat abscess; admission for TURP.
16	59/F	Diabetes, Pancreatic adenocarcinoma	Nil	Hepatobiliary-Biliary obstruction secondary to cancer; bacteraemia	ESBL E.coli	Voriconazole	7 (14)	N/A	Nil	**Cure** Successful treatment.
17	51/M	Diabetes, peripheral neuropathy	Nil	Bone and Joint-Left foot osteomyelitis	MSSA , VRE , Serratia, Enterobacter	Nil	33 (41)	64	Nil	**Cure** Successful treatment.

Indication for OPAT	Successful Outcome (%)
Bone & joint infections / diabetic foot	**5/6 (83%)**
Intra-abdominal infections	**5/6 (83%)**
Gynaecolological / urological infections	**2/3 (67%)**
Hepatobiliary infections	**3/3 (100%)**
Total	**15/18 (83%)**

Microbiology results	
Enterobacteriaceae	**13 (72%)**
• ESBL / AmpC resistance	**10 (77%)**
• NDM resistance	**1 (8%)**
Enterococcus	**6 (33%)**
• VRE resistance	**4 (67%)**
Staphylococcus	**4 (22%)**
Polymicrobial	**10 (56%)**

Conclusions

In this study, tigecycline administered once daily facilitated out-patient treatment with a high rates of treatment success (83%). The main adverse events related to the once daily administration was nausea/vomiting (22%), comparable to what was reported in the product's datasheet (21%), and was managed by antiemetic or alteration of infusion speeds. No pancreatic related complications were identified.

With extensive antimicrobial coverage, including MRSA, VRE and ESBL/CRO coverage, tigecycline provides clinicians with a valuable option for treatment of chronic infections where oral options are unavailable or first-line therapy is precluded by allergy or drug-resistance

References

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