O564
1-hour Oral Session
Tackling MDR & XDR tuberculosis

A retrospective review of the tolerability and utility of linezolid in a large North West London cohort of multi and extensively drug resistant tuberculosis

Aula Abbara*[1], Alison Lievesley[1], Jason Biswas[1], Simon Collin[2], Tumena Corrah[1], Alastair Mcgregor[1], Laurence John[1], Robert Davidson[1]

[1]*Northwick Park Hospital, London, United Kingdom*

[2]*University of Bristol, Bristol, United Kingdom*

Background: *In vitro* and pharmacologic data on the oxazolidinone antibiotic linezolid suggest effectiveness in drug resistant tuberculosis (DR-TB) however the few clinical studies available show high rates of significant adverse effects and therapy discontinuation. In this study, we review the tolerability and efficacy of linezolid in our DR-TB patient cohort in North West London.

Material/methods: Patients treated for DR-TB at our TB centre were identified from the London TB register (LTBR;) comprehensive data were obtained from clinical case and electronic records. Drug susceptibility testing for anti-TB drugs was performed at the National Mycobacterial Reference Laboratory for all isolates. Dose, duration, adverse effects and reason for stopping linezolid were noted. At this site, standard of care is for linezolid 600mg *b.i.d* for the induction phase then *q.d.*

Results: Of 43 DR-TB cases, 41 had multidrug-resistant (MDR) and 2 had extensively-drug resistant (XDR) TB. Median age was 30 years (IQR: 24-44.5) and 23/43 (53%) were male; 24 (56%) were South Asian, 8 (18.6%) were Eastern European and 5 (12%) African. 7 (16%) had a social risk factor (5 alcohol excess, 2 homeless) and 1 had HIV co-infection. 28 (65%) had pulmonary TB (PTB.)

28/43 (65%) received a linezolid containing regimen. Median duration of linezolid was 98 days (IQR: 33-276.) 12 commenced linezolid at 600mg *b.i.d*. Adverse events occurred in 18/28 (64%.) 10 (36%) had peripheral neuropathy, 3 (11%) optic neuritis, 3 (11%) neutropenia, 1 (4%) anaemia and 1 (4%) thrombocytopenia. In 13 (46%), adverse events led to cessation of linezolid.

In the linezolid treated group, the mean number of drugs the isolate was resistant to was 4.4 compared to 3.4 in the non-linezolid treated group. Of those with PTB, culture conversion occurred at a median of 33 days (IQR: 21.5-39) in the linezolid treated group compared to 58 days (IQR:30-63.5) in the non-linezolid treated group. Treatment outcomes are summarized in table 1.

Table 1:

	Linezolid Containing Regimen n=28	**Non-Linezolid Containing Regimen n=15**
Completed treatment	13 (47%)	8 (54%)
Currently on treatment	2 (7%)	2 (13%)
Transferred to another centre	6 (21%)	2 (13%)
Died	2 (7%)	0

Lost to follow up	5 (18%)	3 (20%)

Conclusions: Commencing a twice daily regimen of linezolid was associated with a higher prevalence of adverse events; recent studies suggest that lower doses of linezolid may be efficacious with a more favourable adverse event profile.

It is hard to ascertain whether the shortened median duration to culture conversion in the linezolid treated group is due to linezolid treatment alone as other factors may confound. No difference in completion rate was noted.

Risk of adverse events and treatment discontinuation support the view that linezolid can be considered if there are no safer, alternative therapeutics agents.