

P0166 **Correlation of gliotoxin and bis(methylthio)gliotoxin production with *Aspergillus* spp viability during voriconazole treatment**

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Background:

Gliotoxin (GT) and bis(methylthio)gliotoxin (bmGT) are secondary metabolites produced by *Aspergillus* spp. Both molecules had been purposed as diagnostic biomarkers of invasive aspergilosis. Moreover, bmGT shows a potential utility as prognostic marker: its serum presence correlates with clinical severity whereas its clearance could correlate with antifungal effectiveness. The aim of this study was to assess the effect of voriconazole within *Aspergillus* spp viability and its ability to produce GT and bmGT.

Materials/methods:

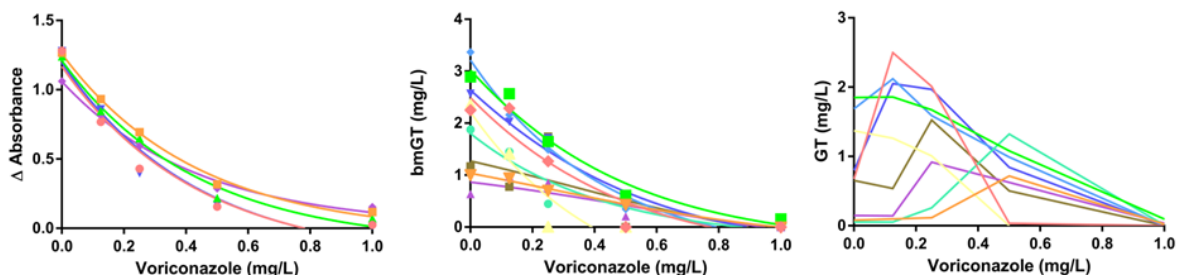
We performed an *in vitro* study within *A. fumigatus* isolates. Isolates were incubated in RPMI 1640 liquid medium (Lonza) with voriconazole (Sigma Aldrich) at different final concentrations: 0, 0.125, 0.25, 0.5 and 1 mg/L. Cultures were analyzed for cell proliferation and GT/bmGT production. Fungal proliferation was assessed by tetrazolium (XTT) reduction assay. GT and bmGT detection and quantification was performed by High Performance Thin Layer Chromatography.

Statistical analysis and Graphs had been performed with Prism 6 (GraphPad Software, Inc).

Results:

There was a correlation between voriconazole and fungal proliferation (nonlinear regression: R^2 : 0,95 - 0,99); at higher voriconazole concentrations, less viable cells were. We found out the same correlation with bmGT production (nonlinear regression: R^2 : 0,52 - 0,99): it was lower at higher voriconazole concentrations. Nevertheless, there was no correlation between GT production and voriconazole, which showed an erratic production. In fact, at low voriconazole levels GT tended to increase whereas it decreased at high voriconazole levels. These results are shown in Figure 1.

Figure 1: Correlation between voriconazole and fungal proliferation (left), bmGT production (centre) and GT production (right) within *Aspergillus fumigatus* isolates



Conclusions:

There is a relation between voriconazole, bmGT and cell proliferation: at higher voriconazole levels, less bmGT is produced because there is less viable fungi. There is no such a relation in the case of GT. Moreover, at voriconazole concentrations able to kill the fungi, neither GT nor bmGT is produced, thus suggesting that *in vivo*, serum clearance of toxins could correlate with fungal eradication. It seems that bmGT could be a better treatment response biomarker than GT as it correlates with fungal death; nevertheless, clinical studies are required and are being performed in order to assess these results.