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MEETING ABSTRACTS

SYNTHESIS OF PURINE DERIVATIVES WITH ANTIMYCOBACTERIAL ACTIVITY

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Tuberculosis (TB) is one of the top 10 causes of death worldwide from a single infectious agent. The World Health Organization (WHO) estimated 10 million new cases and 1.5 million deaths from TB in 2020 (1). Some strains of mycobacteria causing TB show numerous resistances to first-line drugs (isoniazid /INH/ and rifampicin) and to second-line drugs (fluoroquinolones, amikacin, bedaquilin, etc.). The development of new anti-TB drugs with new mechanism of action is necessary to improve TB therapy and to fight against resistant TB as well.

We screened our in-house library of small molecules for their therapeutic potential and identified compound K1297 with good anti-TB activity with minimum inhibitory concentration MIC_{99} = 4 μM against $H_{37}R_v$ strain (for comparison, MIC_{99} (INH) = 0.5 μM). The main structural motif of this molecule is purine scaffold, which was modified and functionalized to elucidate the structure-activity relationships (SAR) and to identify derivatives with low toxicity and higher efficiency than the initial hit K1297. The effect of individual structural fragments on *in vitro* antimycobacterial activity, toxicity and selectivity of action have been evaluated. Finally, derivatives with optimized activity/toxicity ratio have been found and their pharmacokinetic profile and *in vivo* efficacy will be evaluated.

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Keywords: tuberculosis; purine

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