For Safer, Faster Tuberculosis Treatment Quabodepistat Combo Shows Promise

Study investigates the safety and bactericidal efficacy of quabodepistat in combination with delamanid and bedaquiline for treating pulmonary tuberculosis.

Study

Study participants were randomly divided into four quabodepistat treatment groups: quabodepistat (30 mg) + delamanid (300 mg), quabodepistat (30 mg) + bedaquiline (400 mg), and quabodepistat (30 mg) + delamanid (300 mg) + bedaquiline (400 mg) for two weeks, as well as the control standard combination therapy of rifampicin, isoniazid, ethambutol, and pyrazinamide for twenty days.

Each participant received one oral dose daily. The safety and tolerability of each treatment during and after the 14-day period was assessed.

A pilot study was also conducted to evaluate the pharmacokinetics and bactericidal activity of quabodepistat when combined with delamanid and bedaquiline on days one and 14 of the trial.

The efficacy of the quabodepistat treatment for tuberculosis was determined based on the reduction of sputum colony-forming units (CFUs) on agar media from baseline to day 14. Sputum lipoarabinomannan concentrations were determined through a lipoarabinomannan enzyme-linked immunosorbent assay (ELISA) and mycobacterial growth indicator tube (MGIT) time-to-detection method.

Lipoarabinomannan was selected as a biomarker because it is an important cell wall component of M. tuberculosis. Therefore, a decrease in sputum lipoarabinomannan concentrations reflected a decline in viral load.

Results

Among the 98 participants initially screened for participating in the second stage of the EBA study, 44 received at least one of the medications for two weeks for safety analysis. Most study participants were male, whereas 63% of the cohort constituted Black or African participants.

Approximately 73% of the patients experienced at least one treatment-emergent adverse event. Furthermore, most study participants developed side effects of mild or moderate severity, such as headache, abdominal pain, pruritus, and nausea. About 5% of participants belonging to the quabodepistat + bedaquiline group developed serious adverse events; however, these effects were not attributed to the studied drug.

Hyperkalemia of moderate severity occurred in the bedaquiline cohort, which was due to a pre-existing medical condition at baseline. Overall, 7% of all study participants developed adverse events of greater severity. No change in physical examinations, vital signs, laboratory parameters, or electrocardiograms (ECGs) was observed that indicated any clinical significance.

Maximum quabodepistat concentrations were observed three hours after administration of quabodepistat in all combinations. The mean elimination half-life was shorter in quabodepistat combined with bedaquiline than without bedaquiline.

Although CFU counts of sputum samples were similar in all participants across study groups at baseline, changes were observed after the study period. The maximum change in CFU count from baseline was observed in the quabodepistat + delamanid + bedaquiline treatment and for the control.

Conclusion

The current study indicated a robust bacteriological effect and safety of quabodepistat when administered in combination with delamanid and bedaquiline to treat tuberculosis in adults. Nevertheless, these findings must be validated by large-scale and long-term trials in the future.

Source:

https://www.news-medical.net/news/20241201/Quabodepistat-combo-shows-promise-for-safer-faster-tuberculosis-treatment.aspx