

ABSTRACT

Poster Presentation 921

Pulmonary Safety of Inhaled Technosphere® Insulin Therapy in Adults with Diabetes Using High- Resolution Computerized Tomography of the Chest

Alicia Rossiter, Nikhil Amin, Russell Harris, Anders H. Boss, Peter C. Richardson

MannKind Corporation, Valencia, CA, United States

Background and aims: Technosphere® Insulin (TI) is a rapid-acting inhaled insulin with pharmacokinetics well suited for control of postprandial plasma glucose. Because TI is intended to be administered via the pulmonary route, the TI clinical program was designed to assess possible radiological changes associated with the chronic use of TI therapy.

Materials and methods: Adult subjects with diabetes were evaluated with high-resolution computerized tomography (HRCT) of the chest during the clinical trials. In controlled clinical trials, MKC-TI-005 (N = 217; 174 TI group, 43 Technosphere® Inhalation Powder [T Powder] group) and PDC-INS-0008 (N = 121; 60 TI group, 61 T Powder group) subjects were randomized to receive TI or T Powder without insulin. Chest HRCTs were obtained at baseline and at the end of the 12-week treatment period. After completion of these two trials, 206 subjects continued in the uncontrolled open-label extension trial (MKC-TI-010) and underwent annual chest HRCTs (or magnetic resonance imaging [MRI] in Germany) for up to 4 years. In addition, subsets of subjects with type 1 or type 2 diabetes participating in trial MKC-TI-030 (n = 127; 55 TI group, 72 usual care [UC] group) were also randomized to an annual chest HRCT during the 24-month treatment period. All HRCT images were reviewed centrally following a prespecified adjudication protocol by an independent, blinded, board-certified radiologist. All images for any subject with HRCT findings other than normal underwent secondary joint review by an independent board-certified radiologist (different from the primary reviewer) and an independent board-certified pulmonologist, who were blinded to the treatment group.

Results: A total of 667 subjects had a baseline and at least one post-baseline chest HRCT or MRI examination. Of these, 494 subjects were treated with TI, 101 were exposed to T Powder, and 72 were in the UC group with no exposure to TI or T Powder. Chest HRCTs for 94% of the TI group, 92% of the T Powder group, and 96% of the UC group showed normal findings or the findings were not clinically significant. Radiological findings considered abnormal and clinically significant consisted of atelectasis, septal thickening, peri-bronchial thickening, bronchial dilatation or mild bronchiectasis, one or more new or non-enlarging nodules, and ground glass densities; these findings were seen with comparable frequency in all three treatment groups.

Conclusions: Overall, HRCT and MRI findings suggest that there were no clinically significant radiological changes from baseline in all three groups. Observed radiological findings were not suggestive of a safety signal with the long-term use of TI therapy.