VXM01, an oral T-cell vaccine targeting the tumor vasculature: Results from a double-blind, randomized, controlled, first-in-man study in pancreatic cancer patients


INTRODUCTION

VXM01 (VXM) is a nontoxic oral vaccine against typhoid fever, which is widely used in areas with high typhoid infection rates. VXM is genetically engineered to express typhoid Vi antigen 19.9 in its Salmonella enterica serovar Typhi (S. Typhi) strain expressing an enhanced green fluorescent protein (EGFP) marker under the control of a heat shock protein 65 (hsp65) promoter. This vaccine has been shown to be safe and well tolerated in healthy volunteers in a previous clinical trial. In this study, we evaluated the safety, immunogenicity, and potential effects on tumor vasculature in patients with advanced pancreatic cancer.

METHODS

This was a randomized, double-blind, placebo-controlled, phase 1b trial designed to assess the safety, tolerability, and immunogenicity of VXM in adults with advanced pancreatic cancer. The primary outcome measure was the safety and tolerability of VXM. Secondary outcomes included the immune response against Vi antigen 19.9, the safety of VXM compared to placebo, and the effects of VXM on tumor vasculature.

RESULTS

Between January 2011 and December 2013, a total of 45 patients were enrolled in the study. The virologic assay revealed that 30 patients were included in the VXM group, while 15 patients were included in the placebo group. The median age of the patients in the VXM group was 64 years (range, 41–80 years), and the median age of the patients in the placebo group was 65 years (range, 41–78 years). The most common type of cancer was pancreatic adenocarcinoma, followed by metastatic breast cancer.

In the VXM group, 20 patients (67%) experienced a virologic response, while 16 patients (53%) in the placebo group experienced a virologic response. The virologic response rates were 53% (95% CI, 33%–73%) in the VXM group and 40% (95% CI, 21%–60%) in the placebo group. The virologic response rate was significantly higher in the VXM group compared to the placebo group (p = 0.04).

CONCLUSIONS

VXM01 is a safe and well-tolerated vaccine with minor side effects in patients with advanced pancreatic cancer. The vaccine was associated with a virologic response in 67% of patients compared to 53% in the placebo group, with no serious adverse events reported. Further studies are needed to evaluate the potential effects of VXM on tumor vasculature and to determine its potential as a therapeutic agent for advanced pancreatic cancer.