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EudraCT Number	2019-001879-37
Sponsor's Study Number	GB1275-1101
Study Title	A Phase 1/2, First-in-Human, Open-label, Dose Escalation Study of GB1275 Monotherapy and in Combination with an Anti-PD-1 Antibody in Patients with Specified Advanced Solid Tumors or in Combination with Standard of Care in Patients with Metastatic Pancreatic Adenocarcinoma, Followed by Basket Expansion of GB1275 with Standard of Care or in Combination with an Anti-PD-1 Antibody in Patients with Specified Metastatic Solid Tumors

To whom it may concern,

GB006, Inc., a wholly-owned subsidiary of Gossamer Bio, Inc., as the sponsor of the above-mentioned clinical trial, terminated the study prematurely, due to no clear benefit being observed for GB1275 as monotherapy or in combination with pembrolizumab in patients with solid tumors.

Results of the study are summarized in the following pages.

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Study Objectives

The primary objectives of the Phase 1 Dose Escalation Phase of the study for Regimens A and B were to determine the maximum tolerated dose (MTD) or recommended Phase 2 dose (RP2D) of GB1275 monotherapy (Regimen A) and in combination with pembrolizumab (Regimen B) and to determine the PK profile of GB1275 in patients with previously treated specified advanced solid tumors. The primary objective of the Phase 1 Expansion Phase of the study was to determine the safety of the selected dose and dosing schedule of Regimen B, and the secondary objective was to further characterize the PK profile of GB1275, in combination with pembrolizumab in patients with previously treated specified advanced solid tumors.

Study Population

A total of 61 subjects were treated and received at least one dose of GB1275 with 3 subjects treated at each of the 100 mg, 200 mg, and 400 mg BID dose levels in Regimen A, 7 subjects at each of the 800 mg and 1200 mg BID dose levels in Regimen A, 4 subjects at each of the 100 mg BID and 400 mg BID dose levels in Regimen B, 23 subjects at the 800 mg BID dose level in Regimen B, and 7 subjects at the 1200 mg BID dose level in Regimen B.
The overall study population was 47.5% female with a mean (SD) age of 61.9 (10.92) years. In all regimens overall, the most common tumor site was the colon/rectum (41.0%), and the second most common tumor site was the pancreas (18.0%). Most subjects (75.4%) had 3 or more prior lines of therapy. Approximately one-third of subjects had prior immunotherapy (36.1%).
In Regimen B Dose Escalation, a dose-dependent increase in exposure to GB1275 was observed up to the GB1275 800 mg BID dose level which then plateaued at the GB1275 1200 mg BID dose level. This observation, taken together with no dose-limiting toxicities (DLTs) being observed in the study, led to the selection of GB1275 800 mg BID in combination with pembrolizumab as the RP2D and use of this regimen in the Phase 1 Regimen B Expansion. Given no clear efficacy was observed, the Sponsor chose to terminate the study prematurely. Pharmacokinetic parameters were not derived.

Safety & Tolerability

GB1275 was generally well-tolerated. There were no DLTs reported in the study. The incidence of adverse events (AEs) in all regimens overall was 100.0%. The most common AEs in all regimens overall were photosensitivity reaction, fatigue, decreased appetite and diarrhoea, with incidences of 36.1%, 24.6%, 21.3%, and 21.3%, respectively.

The incidence of serious adverse events (SAEs) in all regimens overall was 47.5%. There were 4 subjects with SAEs related to GB1275 in Regimen B Dose Escalation and Expansion; there were no subjects with SAEs related to GB1275 in Regimen A. The SAEs related to GB1275 led to

discontinuation of GB1275 and pembrolizumab in 2 subjects, dose interruption of GB1275 in 1 subject, and dose interruption of GB1275 and pembrolizumab in 1 subject.
The incidence of AEs of CTCAE Grade 3 or higher in all regimens overall was 57.4%. The incidence of AEs related to GB1275 in all regimens overall was 65.6%. The incidence of AEs leading to discontinuation of GB1275 in all regimens overall was 9.8%. The incidence of AEs leading to dose reduction or interruption of GB1275 in all regimens overall was 44.3%.
The incidence of AEs leading to death in all regimens overall was 27.9% (17 of 61 subjects), with an incidence of 17.4% (4 of 23 subjects) in Regimen A and an incidence of 34.2% (13 of 38 subjects) in Regimen B Dose Escalation and Expansion. The majority of subjects with an AE leading to death (14 out of 17 subjects) had a fatal AE in the System Organ Class of neoplasms benign, malignant and unspecified (including cysts and polyps). None of the AEs leading to death were related to GB1275.

Elevations in mean liver chemistry values with GB1275 were generally modest. Post-baseline transaminase values ≥ 3 x ULN were observed in 10.0% of subjects (6 of 60 subjects) in all regimens overall, no subjects in Regimen A, and 15.8% of subjects (6 of 38 subjects) in Regimen B Dose Escalation and Expansion, with 4 of the 6 subjects at the GB1275 800 mg BID dose level and 2 of the 6 subjects at the GB1275 1200 mg dose level in Regimen B. All 6 of these subjects met the criteria for Temple's Corollary, while none of the 6 subjects met the biochemical criteria for Hy's law. These results suggest a possible effect of the GB1275 800 mg and 1200 mg BID dose levels in combination with pembrolizumab on transaminase elevations.
There were no clinically significant changes in hematology, urinalysis, vital signs, or ECG parameters.
Overall, GB1275 up to 1200 mg BID in Regimen A and up to 1200 mg BID in combination with pembrolizumab in Regimen B was generally well-tolerated, and no DLTs were reported.

Conclusion

Although GB1275 was generally well-tolerated in this first-in-human study, no clear benefit of GB1275 was observed in the population studied either as monotherapy or in combination with pembrolizumab.