A Phase 1 Cohort Expansion Trial of OBI-833 in Non-Small Cell Lung Cancer Patients

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Introduction

- Globo H, a glycan initially isolated from the MCF-7 breast cancer cell line, is overexpressed in a variety of epithelial cell tumors such as colon, ovarian, gastric, pancreatic, lung, prostate, and breast cancers, and has limited expression in normal tissue.
- Experimental data suggest that Globo H promotes immunosuppression, tumor survival signaling, and angiogenesis.
- Globo H expression in tumor cells and its function as a potential immune checkpoint make it a target for immunotherapy.
- OBI-833, a novel cancer active immunotherapy, comprises of a synthetic Globo H conjugated with a recombinant CRM 197.

Background

- Lung cancer is the leading cause of cancer-related deaths worldwide (Jemal et al, 2009) and non-small cell lung cancer (NSCLC) accounts for 80-85% of all lung cancers (Sher et al, 2008; Wang et al, 2011).
- Mutations in the epidermal growth factor receptor (EGFR) gene are commonly observed in NSCLC, particularly in tumors of adenocarcinoma histology. *EGFR* mutation frequency was 47.9% in Asian patients, as compared with 19.2% in Western patients.
- Globo H is highly expressed in epithelial cancers such as lung cancer, breast cancer, prostate cancer (Zhang et al, 1997b) and pancreatic, gastric and esophageal cancer (AACR; 2020. Abstract nr 2946)
- OBI-833 is a novel cancer vaccine targeting Globo H. Results of the dose-escalation trial showed a favorable safety profile and supported the cohort expansion trial in NSCLC patients at a dose of 30 μg.
- Patients with Globo H-positive metastatic NSCLC who had achieved stable disease (SD) or partial response (PR) after at least one regimen of anticancer therapy were enrolled. For patients who were on the targeted therapy, OBI-833 was added to their ongoing therapies. Humoral immune responses and relevant tumor biomarkers were monitored.

Disposition

	Number of Patients Cohort Expansion
Screened	24
Enrolled Population	14
Safety Population	14
	Number of Study Discontinuation
Disease Progression	11
SUSAR*	1
Withdrawal of Consent	0

*Grade 4 acute pancreatitis, possibly related

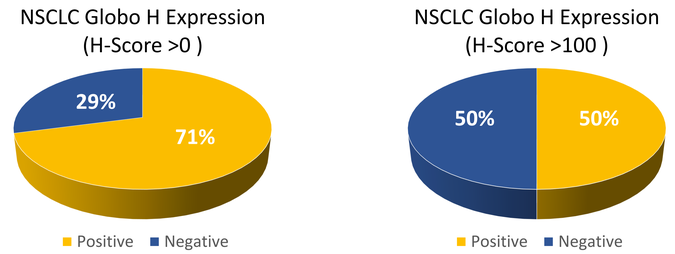
Adverse Events

- As of June 2020, a total of 126 AEs were reported, of which 79 were considered as treatment related AEs. Most of them were injection site reactions. Among the 3 reported SAEs, one was treatment-related, which was Grade 4 acute pancreatitis, and two were non-treatment related.
- Injection site reactions were less than Grade 2, occurred on the day of injection, recovered within 2-3 days without medical treatment, and usually recurred after each subsequent injection.

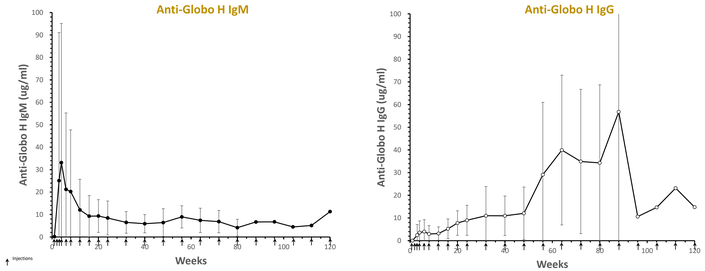
Summary of Serious Adverse Events

Subject ID	SAE (Preferred Term)	Severity	Relationship
034-005	Ascites	Grade 3	Not-related
034-008	Pneumonia	Grade 5	Not-related
034-006	Acute pancreatitis	Grade 4	Possibly-related

Globo H Expression in 24 Screened Subjects

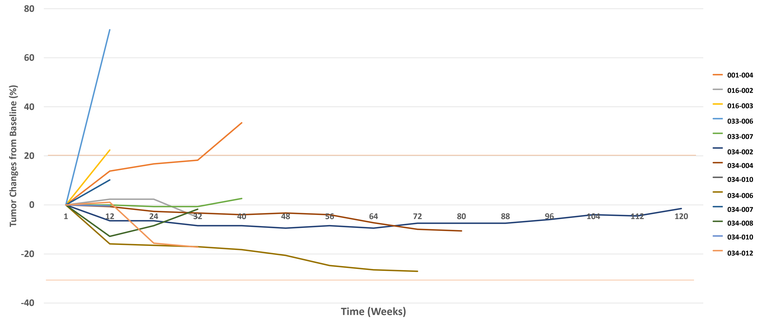


Antibody Responses

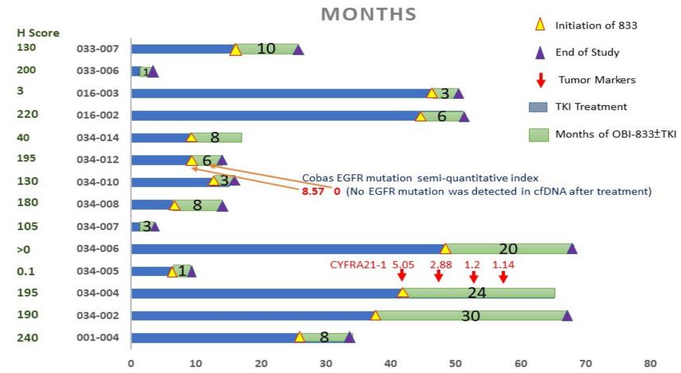


93% and 64% of patients showed positive blood anti-Globo H IgM and IgG results, respectively. The positivity was defined as the anti-Globo H IgM or IgG concentration ≥ 3 μg/mL at least once during the study period.

Tumor Responses



Swimmer Plot of Time to Progression



Median PFS was 31 weeks (range, 3–108). Six of the 11 EGFR TKI-treated patients had SD for over six months. One patient has been treated for more than two years and his treatment is still ongoing. Of note, one patient's tumor size had reduced by 27% after 16 months of OBI-833 treatment.

Conclusions

- OBI-833 can elicit a beneficial immune response in NSCLC patients and rendered durable stable disease status for some TKI-treated patients.
- Further development of OBI-833 in *EGFR*-mutated NSCLC patients to assess the potential benefits of combination therapy of OBI-833 with TKIs is ongoing.