Session Info: Mini Oral Abstract Session, [MO08] NSCLC - Early Stage
Day/Date: Monday, October 28, 2013
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MO08.04 | Phase 2 study of the GI-4000 KRAS vaccine following curative therapy in patients with stage I-III lung adenocarcinoma harboring a KRAS G12C, G12D, G12V or G12R mutation

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Background:
Most patients with early-stage lung cancer will die of recurrent disease despite multimodality therapy with curative intent. KRAS is the most commonly mutated oncogene in lung adenocarcinomas, and patients with resected disease are a unique population amenable to a personalized clinical trial approach. GI4000 is a vaccine created from whole, heat killed recombinant Saccharomyces cerevisiae yeast, overexpressing KRAS Q61L plus Q61(R or H) and either a G12C, G12D, G12V, or G12R mutation. This study aimed to assess the feasibility and immunogenicity of the GI4000 vaccine in patients with KRAS-mutant lung cancers and to compare the outcomes of patients to matched controls.

Methods:
Patients with Stage I-III KRAS-mutant lung cancers who completed curative therapy were enrolled. Each patient was routinely administered the genotype-matched vaccine from the GI4000 series subcutaneously starting 1-4 months after standard treatment completion: weekly x 3, monthly x 6 and every 3 months for a total of 3 years (19 doses). KRAS-antigen T-cell response was assessed by interferon-γ ELISpot assay in peripheral blood mononuclear cells. The study was powered to detect an immune response rate of ≥25% (N=24 patients). A comparison group matched for age, sex, KRAS genotype and stage was used to compare recurrence and survival using the Kaplan-Meier method with a hazard ratio for survival adjusted for age, sex and stage.

Results:
In 28 months, 33 patients were screened and 24 patients enrolled. The study met its primary endpoint with 63% of evaluable patients (50% of all patients) developing an antigen-specific immune response. 19 patients had evaluable baseline samples, 9/13 with a negative response at baseline developed a treatment emergent response and 3/6 with a pre-existing baseline response had an increased response over baseline that met pre-specified immunologic criteria. There were no treatment-related Grade 3/4 or severe AEs. The median number of vaccinations received was 15 (range 1-19). 1 patient withdrew consent due to local injection site reaction and 2 died of recurrent disease during study. The baseline characteristics and clinical outcomes of the trial patients and a group of matched controls is presented in the Table below.

GI4000 vs. Matched controls	GI4000 N=24 N(%)	Matched controls N=64 N(%)
Stage		
I	12 (50)	42 (66)
II	5 (21)	2 (3)
III	7 (29)	20 (31)

Age at diagnosis (median)	63	66
Sex Male Female	 7 (29) 17 (71)	 21 (33) 43 (67)
Recurrence free survival per year 1 2 3	 86% 68% 60%	 85% 71% 69%
Overall survival per year 1 2 3	 100% 100% 92%	 93% 88% 83%
Hazard ratio for survival (p-value)	0.58 (0.29)	

Conclusion:
The GI4000 vaccine is safe, feasible and immunogenic after completion of curative-intent therapy in patients with KRAS-mutant lung cancers. Recurrence rates are equivalent but overall survival trends favorably when compared to matched controls. Exploratory analysis of survival in the immune responders versus matched controls is underway. A randomized study with prospective biomarker analyses is warranted.