RESULTS OF THE PHASE 2B PART OF TIME STUDY EVALUATING TG4010 IMMUNOTHERAPY IN STAGE IV NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS RECEIVING FIRST-LINE CHEMOTHERAPY

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Study Design

- Phase 2b part
  - Primary Objective: Prospective validation of the predictive value of the biomarker (2012-007556) (Bayesian design with respect to PFS (primary endpoint)).
  - In patients with normal TrPAL before treatment (baseline); <95% probability that HR=1
  - Secondary Objectives: ORR, Duration of Response, OS, Safety, Subgroup analyses
  - PFS and OS were assessed using RUCISTU 1.1

Study Treatments:
- TG4010 or placebo: SC injections weekly for 6 weeks and every 3 weeks thereafter or until progression
- Chemotherapy (if 1 to 2 Cycles):
  - Non-selected tumors: pembrolizumab or pemetrexed/cisplatin
  - Squamous tumors: gemcitabine/pemetrexed or cisplatin/ramucirumab
- Bevacizumab allowed
- Maintenance Therapy: Pembrolizumab or pemetrexed/cisplatin or pembrolizumab/cisplatin

CONCLUSIONS
- TG4010 in combination with chemotherapy has demonstrated clinical efficacy:
  - Improved response rate and longer duration of response, including delayed and durable responses
  - Significant improvement in PFS
  - Improvement in overall survival
- TG4010 efficacy is greater in patients with low level of TrPAL
- TG4010 shows efficacy in patients having <5% of tumor cells expressing PD-L1 (70% of patients)
- Excellent safety profile of TG4010 when added to first-line chemotherapy
- Results warrant pursuing further development in NSCLC
- Phase 3 trials exploring TG4010 in combination with immune checkpoint inhibitors

SAFETY

- Frequency of adverse events (AEs) in patients receiving TG4010 (p=0.001 vs Placebo)
- 3.7% of patients treated with TG4010 versus 4.5% of patients treated with placebo

REFERENCES

- patients and their families
- investigators and their staff
- AdCom members
- Indulge Genetics (Wells Fargo) Services providers

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Background: TG4010 is an immunotherapy agent that is reported to attenuate and modified mRNA (mRNA) coding for MUC1 and MUC2. A previous study showed that the baseline level of TrPAL expression in NSCLC patients (Combes et al 2012) might be a predictive biomarker for TG4010 efficacy in NSCLC Methods: TUE was a double-blind, placebo-controlled phase 2B part of a 3 part, line chemotherapy combined with TG4010 in a study design with an additional part assessing the predictive value of the baseline level of TrPAL. Eligibility criteria included patients with stage IV squamous NSCLC who were previously treated or untreated with chemotherapy. Patients received TG4010 10 0 or placebo once SC every 3 weeks for 6 weeks. Then, every 3 weeks progression, gemcitabine/cisplatin or pembrolizumab. Chemotherapy and primary endpoint was progression-free survival (PFS). Results: 222 patients were randomized 1:1 in two groups with normal TrPAL, the study met its primary endpoint in a Bayesian probability higher than 95% that HR = 1. TG4010 was significantly improved in the TUE arm in OS with a log rank time HR = 0.82 (95% CI: 0.68-0.99) p = 0.006). TG4010 was significantly improved in patients with non-squamous tumors (16 hr HR = 0.89 (95% CI: 0.71-1.11) p = 0.33). Overall survival showed an improvement in OS in line with primary data for both patients, the effect of the efficacy of TG4010 analysis by HR was on the tumor cells support the activity of TG4010 in patients with low normal TrPAL: expression of L1 in patients with low (<5%) PD-L1 expression on tumor cells. The frequency and severity of adverse events were similar in two treatment arms. Conclusions: These results provide additional data supporting the efficiency of TG4010, particularly in patients with non-squamous tumors and/or a low level of TrPAL, overall.