TG4010 immunotherapy plus chemotherapy as first-line treatment of advanced NSCLC: Phase 2b Results of the TIME trial


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Abstract #115420 Poster #463

Study Design

Background: TG4010 is an immunotherapy using an attenuated and modified poxvirus (MVA) coding for MUC1 and interleukin-2 to induce a cellular immune response against MUC1 expressing tumors. Previous Phase 2 trials have demonstrated the efficacy and safety of TG4010 in combination with chemotherapy. In addition, level of Triple Positive Activated Lymphocytes (TrPAL, CD16+, CD69+, CD25+) was identified as a potential biomarker predictive of efficacy. TIME is a double blind, placebo-controlled phase 2b study.

TG4010 (1.0 x 10^9 PFU) or Placebo: SC injection weekly for 6 weeks and then once every 3 weeks until progression

1st Line Therapy: Cisplatin + gemcitabine (for squamous), or Cisplatin + pemetrexed (for non-squamous) Up to 6 cycles Best supportive care at investigator’s discretion Maintenance therapy (pemetrexed or erlotinib) if eligible at investigator’s discretion

Study endpoints

- Primary endpoint: PFS (Bayesian probability)
- Secondary endpoints: Overall response rate (ORR), Duration of response, Overall survival (OS), Safety
- Pre-planned analyses using cut-off value for TrPAL (based on screened patients) defining 2 patients populations: Low or High TrPAL

Pre-planned analyses in non-squamous patients

PRE-PLANNED ANALYSES

- Based on previous study results, definition of 2 populations with TrPAL cut-off according to observed values in patients (low and high TrPAL)
- Analysis also performed according to histology (stratification factor)

DURATION OF RESPONSE

- In patients with non squamous tumors and low TrPAL, the Overall Response Rate was 39.3% in the TG4010 arm versus 30.3% in the placebo arm.
- Delayed responses (218 weeks) were observed more often in the TG4010 arm.
- Duration of response was more than 2-times longer in the TG4010 arm with 45.8% (11/24) of patients still responder at 1 year versus 15% (3/20) in the placebo arm

RESULTS

- OS in patients with Low TrPAL (n=147)
- OS in patients with High TrPAL (n=75)

SAFETY

- Most frequent AEs (%) in either arm
- Safety Population**

CONCLUSION

- TG4010 has demonstrated efficacy in combination with first-line chemotherapy. The greatest improvement is seen in patients who have both a low level of TrPAL at baseline and a non squamous tumor.
- Delayed and durable responses were observed.
- TG4010 shows efficacy in patients with low PD-L1 expression (either in tumor cells or tumor infiltrate immune cells).
- Further development is planned in combination with chemotherapy and checkpoint inhibitors.

ACKNOWLEDGMENTS

- Patients and their families
- Investigators and their staff
- A. Adam (Hospital G. Rouxey, Villejuif, France)
- Services providers

SITC Annual Meeting 2015 – November 4-8, 2015 – National Harbor, MD