

NLG-0301: An Open-label, Randomized Phase 2b Active Control Study of Second-line Tergenpumatucl-L Immunotherapy versus Docetaxel in Patients with Progressive or Relapsed Non-small Cell Lung Cancer (NSCLC)

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INTRODUCTION

Tergenpumatucl-L immunotherapy (HyperAcute™ Lung) consists of allogeneic (non-patient source) lung cancer cells that have been genetically modified to express the carbohydrate $\alpha(1,3)\text{Gal}$, to which humans have an inherent pre-existing immunity.

αGal is primarily responsible for the hyperacute rejection of foreign tissue that comprises a potent immune defense mechanism in humans. Tergenpumatucl-L leverages this mechanism of hyperacute rejection to educate the immune system towards components of the patients' own tumor cells.

In a Phase 2 study of tergenpumatucl-L, patients showed:

- Evidence of immune activation after therapy (11/18 patients with elevated IFN gamma via ELISPOT)
- Median survival of 21.9 months
- 16 of 28 patients went on to salvage therapy after progression and 9 of these 16 had objective responses (5PR, 4SD) to the post immunotherapy chemotherapy

This phase 2b study is designed to further evaluate the potential chemo-sensitization effect of tergenpumatucl-L.

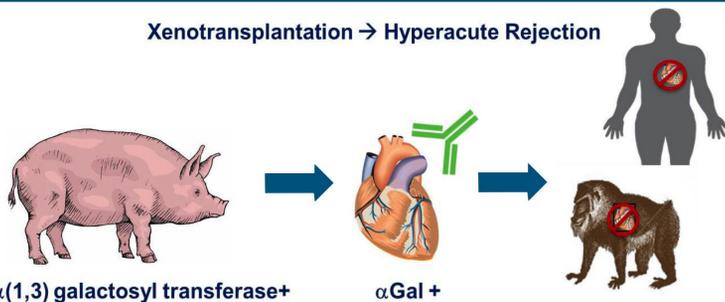
HYPERACUTE REJECTION

Figure 1



Anti- αGal antibodies in primates are responsible for hyperacute rejection of xenotransplants

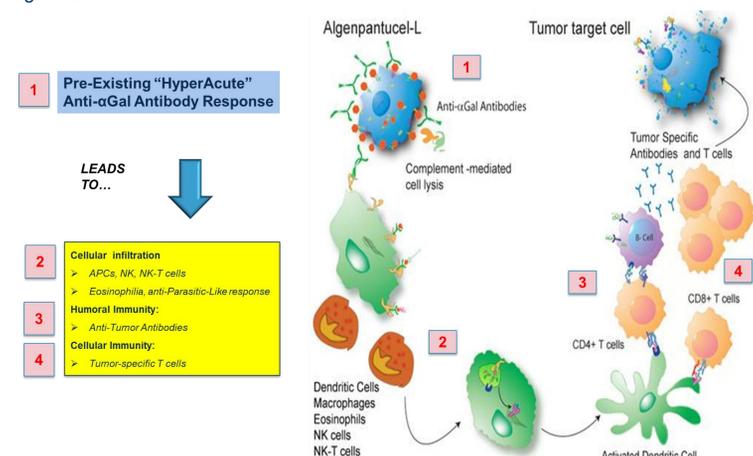
Xenotransplantation → Hyperacute Rejection



- The $\alpha(1,3)\text{galactosyltransferase}$ (αGT) gene is expressed by lower mammals, but not in humans or other Old World primates [1,2]
- Humans naturally acquire anti- αGal antibodies to levels that can reach 1% of total circulating antibodies [1,2]
- Anti- αGal antibodies responsible for HyperAcute rejection of xenotransplants (Fig. 1) [2]
- Animal models demonstrate efficacy in treating tumors when αGal expressing cells are utilized [3,4,5]

MECHANISM OF ACTION

Figure 2

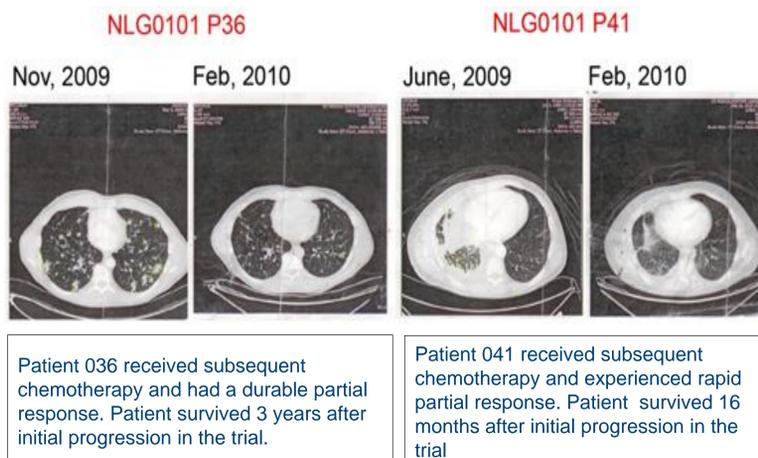


Mechanism of action for tergenpumatucl-L immunotherapy which consists of stably transduced human lung cancer cell lines expressing the murine αGT gene

CHEMO-SENSITIZATION

- In the phase 2 study, all patients received 300 million cells per injection every 2 weeks for eight scheduled doses
- Figure 3 shows examples of a potential chemo-sensitization effect

Figure 3



Patient 036 received subsequent chemotherapy and had a durable partial response. Patient survived 3 years after initial progression in the trial.

Patient 041 received subsequent chemotherapy and experienced rapid partial response. Patient survived 16 months after initial progression in the trial.

STUDY OVERVIEW

This Phase 2b study is an open label, multi center randomized trial of single agent tergenpumatucl-L versus docetaxel in patients with progressed or relapsed NSCLC that have been previously treated.

Eligibility

- Pathologically confirmed NSCLC (adenocarcinoma, bronchoalveolar carcinoma, large cell anaplastic carcinoma and squamous cell carcinoma)
- Stage IIIB/IV, recurrent or treatment refractory disease.
- Prior therapy may include surgery, radiation, and/or ≤ 2 prior chemotherapy regimens excluding docetaxel. EGFR inhibitors or monoclonal antibodies are included as chemotherapy.
- Patients must have a granulocyte count of $\geq 1000/\mu\text{L}$, platelets $\geq 100,000/\mu\text{L}$, hemoglobin $\geq 10.0 \text{ gm/dL}$, albumin $\geq 3.0 \text{ gm/dL}$ and acceptable hepatic and renal function.

Study Design

- 240 patients randomized 2:1:1 to the following groups:
- Arm 1: Docetaxel - 75mg/m² q3 weeks x 4 doses
- Arm 2a: Tergenpumatucl-L - 300 million cells intradermally weekly for 11 weeks and then q2 months for 5 additional doses
- Arm 2b: Tergenpumatucl-L - 300 million cells q2 weeks for 6 doses and then monthly for 10 months

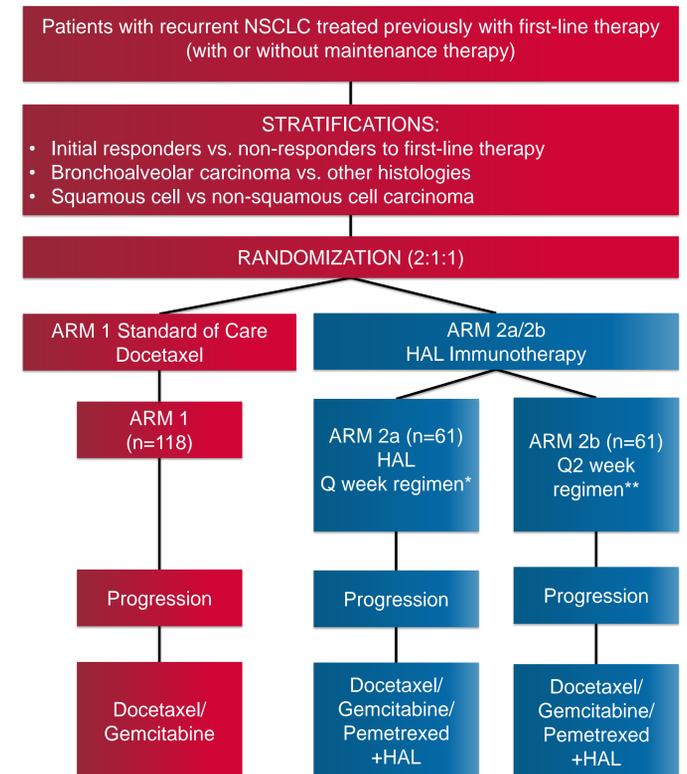
Continuation

- With first progression, subjects stay on study and receive:
- Arm 1: gemcitabine 1250 mg/m²/week for 2 weeks with 1 week rest or pemetrexed 500 mg/m² every 3 weeks until disease progression or significant toxicity
- Arm 2a/2b: docetaxel 75 mg/m² I.V. given every 3 weeks or gemcitabine 1250 mg/m²/week for 2 weeks with 1 week rest or pemetrexed 500 mg/m² every 3 weeks until disease progression or significant toxicity and continue with HAL administration given every 2 weeks (not to exceed 16 total immunizations)

Study Objectives

- Overall survival
- Overall objective tumor response rate with study drug
- Immunologic correlates

STUDY SCHEMA



*Receive HAL once a week initially and every 2 weeks during salvage regimens for a maximum of 16 doses

** Receive HAL q 2 weeks initially and during salvage regimens for a maximum of 16 doses

SUMMARY

- Evidence of chemo-sensitization by Tergenpumatucl-L was shown in a prior phase 2 study
 - 11.3 month median survival compared to current standard of care of ~8mo
 - Well tolerated, no drug related grade 4 events reported
 - 31% response rate in patients receiving subsequent chemotherapy after progressing on tergenpumatucl-L
 - An additional 25% of patients achieved SD
- This phase 2b study further explores the potential chemo-sensitization effect of tergenpumatucl-L in progressed or relapsed NSCLC patients by comparing 2 different dosing regimens of tergenpumatucl-L to single agent docetaxel

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CLINICAL TRIALS IDENTIFIER

Clinicaltrials.gov identifier NCT01774578

