

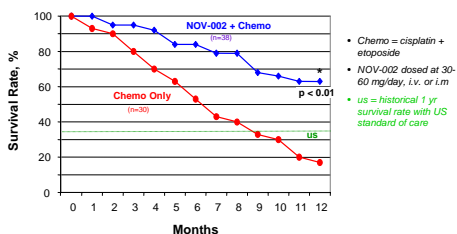
A Randomized Phase 1/2, Open-Label, Controlled Study of NOV-002 in Non-Small Cell Lung Cancer

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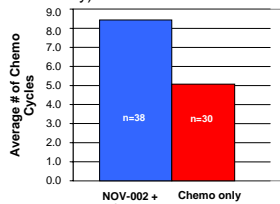
Introduction

- NOV-002, a chemoprotectant and immunomodulator, is a proprietary and stabilized formulation of oxidized glutathione, a key element of the ubiquitous, redox-controlling glutathione pathway.
- Oxidized glutathione is known to modulate intracellular signal transduction pathways in immune cells (e.g. NFkB activity), and pre-clinical studies have shown that NOV-002 modulates the production of cytokines and hematopoietic factors *in vitro* and *in vivo*.
- The overall objective of this U.S.-based clinical study was to confirm the safety and efficacy of NOV-002 seen in a randomized, multi-site NSCLC trial conducted in the Russian Federation where it is approved and marketed as Glutoxim® (by an unrelated entity) for use in combination with cytotoxic chemotherapy.

The Russian study showed a one-year survival rate of 63% with combination therapy compared to 17% with chemotherapy alone.

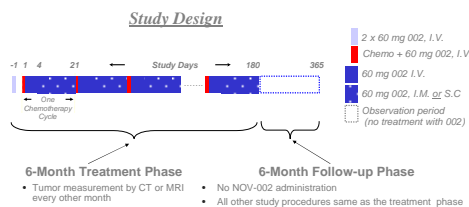


- In addition, patients receiving combination therapy were able to tolerate more cycles of chemotherapy compared to the chemotherapy alone group (8.3 vs. 5.0).
- This improved toleration was reflected in multiple indices of chemotherapy-related toxicity (hematologic, liver and kidney).



Methodology

The primary objectives of the study were to evaluate the safety of NOV-002 injection, tumor response, one year survival and hematopoietic recovery.



Patients

- Forty-four, chemotherapy-naive
- Stage IIIB/IV NSCLC

Randomization

Group A (n=13): NOV-002, administered intravenously (IV) and intramuscularly (IM), in combination with cytotoxic chemotherapy (carboplatin + paclitaxel)

Group B (n=16): NOV-002, administered IV and subcutaneously (SC), in combination with cytotoxic chemotherapy

Group C (n=15): Cytotoxic chemotherapy alone was administered to this control group

Dosing

- For each nominal 21-day chemotherapy cycle, patients received 60 mg of NOV-002 intravenously (as a push) daily for the first 4 days, followed by 60 mg of NOV-002 IM (Group A) or SC (Group B) daily for the next 17 days (weekdays only).
- The initial dose of chemotherapy was 225 mg/m² of paclitaxel, as a 3-hour infusion, followed by carboplatin at an AUC of 6
- Initiation of repeat chemotherapy cycles required an absence of hematologic and other toxicities in excess of pre-defined values.

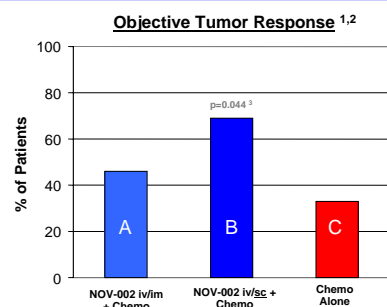
Treatment Duration

Groups A & B: NOV-002 for 6 months or until dose limiting toxicity

Groups A, B & C: Chemotherapy capped at 8 cycles or until disease progression, severe toxicity or maximum benefit

Efficacy Results

NOV-002 + chemotherapy resulted in a greater objective tumor response than chemotherapy alone.

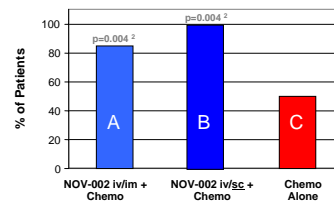


¹ Intent to treat population
² Best overall response = ≥ 50% reduction in tumor size
³ Compared to Chemo Alone; logistic regression stratified on disease stage

In addition, while not reaching statistical significance, investigator determined tumor response results also favored Groups A and B.

Patients treated with NOV-002 received more cycles of chemotherapy.

% of Patients Receiving At Least Four Cycles of Chemotherapy^{1,2}



Group	Average Total # of Cycles:
NOV-002 iv/im + Chemo (A)	5.3
NOV-002 iv/sc + Chemo (B)	6.6
Chemo Alone (C)	4.4

¹ Safety population
² Exploratory overall analysis of variance test

Due to enrollment of fewer than expected patients, statistical analyses of survival and hematopoietic recovery were not feasible.

Safety Results

NOV-002 was well tolerated in this patient population, adding to NOV-002's already extensive safety database.

- No deaths in the study were attributed to NOV-002
- Forty-one patients reported 923 adverse events (AEs)
 - AEs were typical of those seen in advanced NSCLC patients treated with carboplatin and paclitaxel
 - AEs that had either a possible or unknown association with NOV-002 administration were distributed across multiple system organ classes and treatment groups and resolved despite continuing treatment with study medications.
 - Six patients discontinued from the study because of AEs; these AEs were considered by the investigators to be unrelated to NOV-002 administration.
- Twenty-six patients reported 78 SAEs
 - One NOV-002 treated patient was hospitalized for three SAEs, including Grade III diarrhea and hypotension, and Grade IV neutropenia, which were considered to be possibly associated with the combination of intravenous and intramuscular NOV-002 and chemotherapy by the investigators.
 - Other SAEs were not attributed to NOV-002

Conclusions

- There are anti-tumor benefits associated with NOV-002 administered in combination with chemotherapy when compared with chemo alone in the treatment of late stage NSCLC
- This is supported by improved tumor response rates and increased exposure to chemotherapy in NOV-002 treated patients
- NOV-002 is well tolerated and did not add to chemotherapy-related toxicity
- Larger clinical studies are warranted to provide a complete efficacy profile for NOV-002 in patients with late-stage NSCLC and to further extend its safety profile.