SYNOPTIC CLINICAL STUDY REPORT FOR NLG2101

A PHASE 2 DOUBLE-BLINDED, RANDOMIZED, PLACEBO-CONTROLLED STUDY OF INDOXIMOD IN COMBINATION WITH A TAXANE CHEMOTHERAPY IN METASTATIC BREAST CANCER

Protocol Number:	NLG2101
Test Drug:	Indoximod (1-methyl-D-tryptophan)
IND Number	078189
Study Phase:	2
Study Dates:	26 Aug 2013 (date of first informed consent) – 17 Aug 2017 (date of last survival follow-up contact)
Principal Investigators:	Dr. Soliman (lead investigator)– H. Lee Moffitt Cancer Center, Tampa, FL; Dr. Karwal – University of Iowa, Iowa City, IA; Dr. Daily – University of Florida, Gainesville, FL; Dr. Montero – Cleveland Clinic, Cleveland, OH;, OH; Dr. Poklepovic – Virginia Commonwealth University, Richmond, VA; Dr. Dillon – University of Virginia, Charlottesville, VA; Dr. Truica – Penn State Hershey Cancer Institute, Hershey, PA; Dr. Melin – Wake Forest Baptist Health, Winston – Salem, NC; Dr. Oldham – Lynchburg Hematology Oncology Clinica, Lynchburg, VA; Dr. Patel – Vince Lombardi Cancer Clinic, Green Bay, WI; Dr. Gilman – Lankenau Medical Center, Wynnewood, PA; Bryn Mawr Hospital, Bryn Mawr, PA; Paoli Hospital, Paoli, PA; Dr. Boppidi – Augusta University, Augusta, GA; Dr. Panella - University of Tennessee Medical Center, Knoxville, TN; Dr. Bruetman – Indiana University Health Goshen Center for Cancer Care, Goshen, IN; Dr. Treisman – Wheaton Fransciscan Healthcare Reiman Cancer Center, Franklin, WI; Dr. Samuel – Cleveland Clinic Florida, Weston, FL; Dr.

	Volterra, Eastchester Center for Cancer Care, Bronx, NY; Dr. Ibrahim – University of Texas MD Anderson Cancer Center, Houston, TX; Dr. Nikolinakos– University Cancer and Blood Center, Athens, GA; Dr. Danciu – University of Illinois Cancer Center, Chicago, IL; Dr. MacLaughlin – Peninsula Cancer Institute, Newport News, VA; Dr. Karaszewska – Komed, Poland; Dr. Lesniewski-Kmak – Gdynia, Pomorskie, Poland; Dr. Pikiel – Gdansk, Poland; Dr. Tomczak – Poznan, Poland; Dr. Nowecki – Warswaza, Poland; Dr. Cedrych – Krakow, Poland; Dr. Suszko-Kazarnowicz – Olsztyn, Poland; Dr. Slomian – Poland; Dr. Slowinska – Olsztyn, Poland; Dr. Deliiewski – Gorzow Wielkopolski, Poland.
Sponsor Signatory:	Eugene P. Kennedy, MD, FACS Chief Medical Officer Phone: (515) 296-5555 Fax: (515) 296-3520
Sponsor:	NewLink Genetics Corporation 2503 South Loop Drive, Suite 5100 Ames, Iowa 50010
Document Date:	17 Jul 2019 (FINAL)

This study was conducted in compliance with Good Clinical Practices, including the archiving of essential documents.

SYNOPTIC CLINICAL STUDY REPORT APPROVAL

Sponsor: NewLink Genetics Corporation; 2503 South Loop Drive, Suite 5100; Ames, Iowa 50010

Clinical Protocol Number: NLG2101

Drug Name: Indoximod (1-methyl-D-tryptophan)

Protocol Title: A Phase 2 double-blinded, randomized, placebo-controlled study of indoximod in combination with a taxane chemotherapy in metastatic breast cancer

Approved by:

09 December 2019

Eugene P. Kennedy, MD, FACS
Chief Medical Officer

Date

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NewLink Genetics Corporation	Indoximod	1-methyl-D-tryptophan

Protocol Number: NLG2101

Title of Study: A Phase 2 double-blinded, randomized, placebo-controlled study of indoximod in combination with a taxane chemotherapy in metastatic breast cancer

Investigators and Study Centers: The study was conducted by 34 investigators in 43 centers across 2 countries (United States [US] and Poland). The following investigators (affiliation[s]) were involved in the study:

- Dr. Hatem Soliman (lead investigator)– H. Lee Moffitt Cancer Center, Tampa, FL
- Dr. Mark Karwal – University of Iowa, Iowa City, IA
- Dr. Karen Daily – University of Florida, Gainesville, FL
- Dr. Alberto Montero – Cleveland Clinic, Cleveland, OH
- Dr. Andrew Poklepovic – Virginia Commonwealth University, Richmond, VA
- Dr. Patrick Dillon – University of Virginia, Charlottesville, VA
- Dr. Cristina Truica – Penn State Hershey Cancer Institute, Hershey, PA
- Dr. Susan Melin – Wake Forest Baptist Health, Winston – Salem, NC
- Dr. Dwight Oldham – Lynchburg Hematology Oncology Clinic, Lynchburg, VA
- Dr. Dhimant Patel – Vince Lombardi Cancer Clinic, Green Bay, WI
- Dr. Paul Gilman – Lankenau Medical Center, Wynnewood, PA; Bryn Mawr Hospital, Bryn Mawr, PA; Paoli Hospital, Paoli, PA
- Dr. Hima Boppidi – Augusta University, Augusta, GA
- Dr. Timothy Panella - University of Tennessee Medical Center, Knoxville, TN
- Dr. Daniel Bruetman – Indiana University Health Goshen Center for Cancer Care, Goshen, IN
- Dr. Jonathan Treisman – Wheaton Fransciscan Healthcare Reiman Cancer Center, Franklin, WI
- Dr. Thomas Samuel – Cleveland Clinic Florida, Weston, FL
- Dr. Fabio Volterra, Eastchester Center for Cancer Care, Bronx, NY
- Dr. Nuhad Ibrahim – University of Texas MD Anderson Cancer Center, Houston, TX
- Dr. Petros Nikolinakos – University Cancer and Blood Center, Athens, GA
- Dr. Oana Danciu – University of Illinois Cancer Center, Chicago, IL
- Dr. William MacLaughlin – Peninsula Cancer Institute, Newport News, VA
- Dr. Boguslawa Karaszewska – Komed, Poland
- Dr. Krysztof Lesniewski-Kmak – Gdynia, Pomorskie, Poland
- Dr. Joanna Pikiel – Gdansk, Poland
- Dr. Piotr Tomczak – Poznan, Poland
- Dr. Zbignieuw Nowecki – Warswaza, Poland

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- Dr. Ida Cedrych – Krakow, Poland
- Dr. Suszko-Kazarnowicz – Olsztyn, Poland
- Dr. Grzegorz Slomian – Poland
- Dr. Anna Slowinska – Olsztyn, Poland
- Dr. Bartlomiej Deliiewski – Gorzow Wielkopolski, Poland

Publication (reference): None at time of writing this report

Study Period (years):	**Phase of Development:**
26 Aug 2013 (date of first informed consent) – 17 Aug 2017 (date of last survival follow-up contact)	2

Objectives

Primary Objective:

- To assess the progression-free survival (PFS) after treatment with docetaxel or paclitaxel in combination with indoximod compared to docetaxel or paclitaxel alone in metastatic breast cancer.

Secondary Objective:

- To assess the median overall survival after treatment with docetaxel or paclitaxel in combination with indoximod compared to docetaxel or paclitaxel alone in metastatic breast cancer and to conduct correlative scientific studies of subject samples to determine the mechanism of any observed pathologic variables and clinical benefits. As well as assess the objective response rate, as measured by Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1, of docetaxel or paclitaxel in combination with indoximod compared to docetaxel or paclitaxel alone in addition to safety**.**

Methodology:

This was a double-blind, placebo-controlled study in patients with metastatic breast cancer designed to assess the PFS after treatment with docetaxel or paclitaxel in combination with indoximod compared to docetaxel or paclitaxel given alone:

- Arm 1A: docetaxel 75 mg/m² intravenous (IV) given every 3 weeks on Day 8 along with placebo oral (PO) given twice daily (BID) on Days 1-14.
- Arm 1B: docetaxel 75 mg/m² IV given every 3 weeks on Day 8 along with indoximod PO given BID on Days 1-14.
- Arm 2A: paclitaxel 80 mg/m² IV given weekly x 3 followed by a week of rest (28-day cycle) along with placebo PO given BID on Days 1-21.
- Arm 2B: paclitaxel 80 mg/m² IV given weekly x 3 followed by a week of rest (28-day cycle) along with indoximod PO given BID on Days 1-21.

All arms of study were open for enrollment at United States (US) sites. Only Arms 1A and 1B were open for enrollment outside the US.

At enrollment into the study, the treating physician had to determine whether a subject was to be enrolled on the docetaxel or the paclitaxel arm of the study. This had to be done prior to randomization and changes after randomization were not permitted.

Treatment was administered on an outpatient basis. Reported adverse events (AEs) and potential risks as well as appropriate dose modifications are described below.

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No investigational or commercial agents or therapies other than those described below could be administered with the intent to treat the patient's malignancy (Table 1).

Table 1 Treatment Regimen Description

Agent	Premedication/ Precautions	Dose	Route	Schedule	Cycle Length
Indoximod or placebo	On an empty stomach with water	1200 mg (six 200-mg capsules)	Twice daily; oral	Days 1-14 with docetaxel or Days 1-21 with paclitaxel	21 days with docetaxel, 28 days with paclitaxel
Docetaxel	Premedicate with dexamethasone 8 mg (oral) twice daily for 3 days starting 1 day prior to docetaxel	75 mg/m²	Intravenous over 1 hour	Day 8	21 days
Paclitaxel	Standard institutional premedication orders utilizing dexamethasone and anti-histamines should be used	80 mg/m²	Intravenous over 1 hour	Weekly x3 of 4-week cycle	28 days

Indoximod or Placebo Administration

The six 200-mg capsules (1200 mg) had to be taken on an empty stomach with water by mouth at least one hour before breakfast and one hour prior to dinner. The medication had to be taken on Days 1-14 of each 21-day cycle (2 weeks on, 1 week off) when given with docetaxel or on Days 1-21 of each 28-day cycle (3 weeks on, 1 week off) when given with paclitaxel. No specific premedication was required. Patients had to be advised to wear ultraviolet (UV) protective eyewear when exposed to direct sunlight outdoors while on indoximod.

Subjects were asked to document daily indoximod/placebo on a medication diary during treatment, which was collected by the institution as source documentation.

Docetaxel administration

Docetaxel is a cytotoxic anticancer drug and, as with other potentially toxic compounds, caution had to be exercised when handling and preparing docetaxel solutions. The use of gloves was recommended. If docetaxel injection concentrate came into contact with the skin, it needed to be immediately and thoroughly washed with soap and water. If docetaxel injection concentrate came into contact with mucosa, they needed to be immediately and thoroughly washed with water.

Contact of the docetaxel concentrate with plasticized polyvinylchloride (PVC) equipment or devices used to prepare solutions for infusion was not recommended. In order to minimize patient exposure to the plasticizer DEHP (di-2-ethylhexyl phthalate), which could be leached from PVC infusion bags or sets, the final docetaxel dilution for infusion had to be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets.

Preparation and Administration: The docetaxel had to be prepared for administration per the packaging insert instructions. Docetaxel had to be administered IV as a 1-hour infusion under ambient room temperature and lighting conditions. All subjects had to be premedicated with oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg BID) for 3 days starting 1 day prior to docetaxel to reduce the severity of fluid retention and hypersensitivity reactions. Subjects had to be observed closely for hypersensitivity reactions, especially during the first and second infusions. Severe hypersensitivity reactions characterized by generalized rash/erythema, hypotension and/or bronchospasm, or very rarely fatal anaphylaxis, have been reported in patients premedicated with 3 days of corticosteroids. Severe hypersensitivity reactions required immediate discontinuation of the

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docetaxel infusion and aggressive therapy. Subjects with a history of severe hypersensitivity reactions could not be rechallenged with docetaxel.

Hypersensitivity reactions could occur within a few minutes following initiation of a docetaxel infusion. If minor reactions such as flushing or localized skin reactions occurred, interruption of therapy was not required. All patients had to be premedicated with an oral corticosteroid prior to the initiation of the infusion of docetaxel. H1 (diphenhydramine, chlorimpramine) and H2 histamine (ranitidine) receptor blockers and/or slowing the infusion rate could be used to minimize mild infusion reactions as needed.

In vitro studies have shown that the metabolism of docetaxel could be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 type 3A4 (CYP3A4), such as cyclosporine, terfenadine, ketoconazole, erythromycin, and troleandomycin. Caution had to be exercised with these drugs when treating patients receiving docetaxel as there was a potential for a significant interaction. *In vivo* investigations showed that caution had to be exercised when administering ketoconazole to patients as concomitant therapy since there was a potential for a significant interaction. Docetaxel had to be administered with caution in patients concomitantly receiving protease inhibitors which are inhibitors and substrates of CYP3A4.

Paclitaxel administration

Paclitaxel is a cytotoxic anticancer drug and, as with other potentially toxic compounds, caution had to be exercised when handling and preparing paclitaxel solutions. The use of gloves was recommended. If paclitaxel injection concentrate came into contact with the skin, it needed to be immediately and thoroughly washed with soap and water. If paclitaxel injection concentrate came into contact with mucosa, they needed to be immediately and thoroughly washed with water.

Preparation and Administration: The paclitaxel had to be prepared for administration per the packaging insert instructions. Paclitaxel was administered as a 1-hour IV infusion using non-PVC tubing and connectors. A 22-micron filter had to be placed on the distal end of the infusion line. Nothing else was to be infused through the line where paclitaxel was being administered.

Subjects received prophylactic anti-allergy standard institutional premedications utilizing dexamethasone and anti-histamines.

Reported AEs and Potential Risks

In addition to routine reporting, several AEs with possible relationship to indoximod (such as abdominal pain, nausea, etc) required expedited reporting. A complete list is provided in the protocol.

A list of AEs with possible relationship to docetaxel and paclitaxel is provided in the package inserts.

Appropriate Dose Modifications

Docetaxel: Subjects could not be given docetaxel with an absolute neutrophil count (ANC) <1500 cells/mm^3. Subjects who were dosed at 75 mg/m^2 and who experienced either febrile neutropenia or neutrophils <500 cells/mm^3 for more than 1 week during docetaxel therapy had to have the dosage adjusted from 75 mg/m^2 to 60 mg/m^2. The use of peg-filgrastim (Neulasta/Neupogen) was permitted if the patient experienced febrile neutropenia or an ANC <500 cells/mm^3 for >7 days. Prophylactic use of Neulasta/Neupogen was allowed if the treating physician deemed it necessary for patient safety. If the subject continued to experience these reactions at 60 mg/m^2 despite adequate supportive care, the treatment had to be discontinued. Subjects who developed >grade 3 peripheral neuropathy had to have docetaxel treatment discontinued entirely.

In case of aspartate aminotransferase (AST)/alanine aminotransferase (ALT) >2.5 to <5 x the upper limit of normal (ULN) and alkaline phosphatase (ALP) <2.5 x ULN, or AST/ALT >1.5 to <5 x ULN and ALP >2.5 to <5 x ULN, docetaxel at 75 mg/m^2 had to be reduced to 60 mg/m^2. If this occurred at 60 mg/m^2 treatment had to be stopped. In case of AST/ALT >5 x ULN and/or ALP >5 x ULN docetaxel had to be stopped.

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Dosing of both drugs had to be withheld for any other grade 3 or 4 non-hematologic or hematologic toxicity not described above until it resolved to a grade 0-1. Dosing delays of up to 21 days for resolution of AEs were permitted.

Paclitaxel: Paclitaxel could not be administered to subjects with a baseline ANC <1500 cells/mm^3. In order to monitor the occurrence of myelotoxicity, it was recommended that weekly peripheral blood cell counts were performed on all patients receiving paclitaxel. An overview of paclitaxel dose modifications is given in Table 2.

Table 2 Paclitaxel Dose Modifications

Event	Dose Modification
ANC ≤800 mm³ or platelets ≤50000/mm³	Hold treatment until ANC >800 mm³ and platelets >50,000/mm³, then resume with weekly paclitaxel dosage reduced by 10 mg/m².
Grade 2 motor or sensory neuropathies	Reduce weekly paclitaxel dosage by 10 mg/m² without interrupting planned treatment.
Other non-hematologic AEs grade 2 or grade 3	Hold treatment until AEs resolve to grade ≤1, then resume with weekly paclitaxel dosage reduced by 10 mg/m².
Treatment delay >3 weeks	Decrease weekly paclitaxel dosage by 10 mg/m² or consider discontinuing treatment.

Subjects who cannot tolerate paclitaxel at 60 mg/m² were to discontinue treatment.

The use of peg-filgrastim (Neulasta/Neupogen) was permitted if the subject experienced febrile neutropenia or an ANC <500 cells/mm³ for >7 days. Prophylactic use of Neulasta/Neupogen was allowed if the treating physician deemed it necessary for subject safety. If the subject continued to experience these reactions at a reduced dose despite adequate supportive care, the treatment had to be discontinued.

Although the occurrence of peripheral neuropathy was frequent, the development of severe symptomatology was unusual. Subjects who developed >grade 3 peripheral neuropathy had to have paclitaxel treatment discontinued entirely.

Indoximod: In general, indoximod was very well tolerated in both Phase 1 studies and seldom required any dose reductions. If a dose reduction was deemed necessary due to intolerance from taking the required number of pills or a grade 3-4 nausea, one dose reduction to 800 mg BID (PO) was permitted. If this was not tolerated then discontinuation of the study treatment was required.

Number of Subjects (planned and analyzed):

- Planned: up to 154 subjects (77 subjects per treatment arm 1:1 randomization – indoximod/placebo).
- Enrolled: 169 subjects (88 on indoximod and 81 on placebo).
- Treated: 164 subjects (85 on indoximod and 79 on placebo).

The study was prematurely discontinued in June 2017 after it became clear that there was no supporting evidence that receiving indoximod immunotherapy benefits patients over the existing standard of care chemotherapy. All subjects that were still in this study at this point, were immediately discontinued (n=47; 23 in the indoximod arm and 24 in the placebo arm).

Diagnosis and Criteria for Inclusion:

Inclusion Criteria:

In order to be considered eligible, all of the following criteria must have been met:

1. Subjects had to have histologically or cytologically confirmed estrogen receptor (ER)/ progesterone receptor (PR) +/–; human epithelial growth factor receptor 2 (HER2) –, metastatic breast cancer.
2. Subjects had to have metastatic disease that was evaluable on imaging studies. Subjects could have measurable disease, defined as at least one lesion that could be accurately measured in at least one dimension

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(longest diameter to be recorded for non-nodal lesions and short axis for nodal lesions) as >20 mm with conventional techniques or as >10 mm with spiral computed tomography (CT) scan, magnetic resonance imaging (MRI), or calipers by clinical examination. Subjects could also have non-measurable disease only as defined by RECIST 1.1, particularly subjects with bone only metastatic disease. These subjects were also eligible if their disease could be documented / evaluated by bone scans, positron emission tomography (PET), or MRI.

3. Any number of prior endocrine therapies in the metastatic setting were allowed. The subject could not have received any prior chemotherapy agents in the metastatic setting. Prior treatment with adjuvant docetaxel or paclitaxel was allowed if disease relapse occurred greater than 6 months from the completion of adjuvant therapy.
4. Age >18 years. Because no dosing or AE data were currently available on the use of docetaxel or paclitaxel in combination with indoximod in subjects <18 years of age, children were excluded from this study.
5. Eastern Cooperative Oncology Group (ECOG) performance status $\leq$1.
6. Life expectancy of >4 months.
7. Subjects had to have normal organ and marrow function as defined below:
   - Leukocytes $\geq$3000/µL.
   - ANC $\geq$1500/µL.
   - Platelets $\geq$100,000/µL.
   - Total bilirubin within normal institutional limits.
   - AST/ALT $\leq$2.5 X institutional ULN.
   - Creatinine within normal institutional limits or creatinine clearance $\geq$60 mL/min/1.73 m^2 for subjects with creatinine levels above institutional normal.
8. Subjects with known brain metastases were only eligible after their tumors had been treated with definitive resection and/or radiotherapy and they were neurologically stable for at least 1 month off steroids.
9. The effects of indoximod on the developing human fetus are unknown. For this reason and because indoximod may affect maternal immune tolerance of the fetus, sexually active women of child-bearing potential had to agree to use adequate forms of contraception prior to study entry and for the duration of study participation. Use of contraception or abstinence had to continue for a minimum of 1 month after completion of the study. If a woman became pregnant or it was suspect she was pregnant while participating in this study, she had to discontinue the study drug and inform her treating physician immediately. Also men had to be discouraged from fathering children while on treatment.
10. Ability to understand and the willingness to sign a written informed consent document.

Exclusion Criteria:

Subjects presenting with any of the following could not participate in the study:

1. Subjects who had had chemotherapy for the treatment of metastatic breast cancer were not eligible. Subjects who had had radiotherapy within 3 weeks prior to entering the study or those who had not recovered from AEs due to agents administered >3 weeks earlier were not eligible.
2. Subjects who were currently receiving any other investigational agents.
3. Subjects with known active, untreated brain metastases had to be excluded from this clinical study because of their poor prognosis and because they often develop progressive neurologic dysfunction that could confound the evaluation of neurologic and other AEs. Those with previously treated inactive brain metastases

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with no evidence of active disease documented on brain MRI ≥4 weeks after radiation and off all steroids could be eligible.

4. History of allergic reactions attributed to compounds of similar chemical or biologic composition to docetaxel or tryptophan containing substances. This included L-tryptophan or 5-hydroxy-tryptophan supplements. Also subjects with a history of severe hypersensitivity reactions to docetaxel or to other drugs formulated with polysorbate 80 were excluded.
5. Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
6. Pregnant women were excluded from this study because indoximod is an immunoregulatory agent with the potential for abortifacient effects due to fetal rejection by the maternal immune system. Because there was an unknown but potential risk for AEs in nursing infants secondary to treatment of the mother with indoximod, breastfeeding had to be discontinued if the mother was treated with indoximod. Also, docetaxel and paclitaxel were category D cytotoxic agents and were not administered to pregnant females.
7. Known human immunodeficiency virus (HIV)-positive subjects and those with other acquired/inherited immunodeficiencies were ineligible due to the possibility of affecting the response to indoximod and the higher risk of active opportunistic infections.
8. Subjects with more than one active malignancy at the time of enrollment.
9. Subjects who had received any prior experimental active immunotherapy consisting of targeted monoclonal antibodies (ipilimumab) or pharmaceutical compounds were excluded.
10. Subjects with any active autoimmune disease (i.e., psoriasis, extensive atopic dermatitis, asthma, inflammatory bowel disease, multiple sclerosis, uveitis, vasculitis), chronic inflammatory condition, or any condition requiring concurrent use of any systemic immunosuppressants or steroids for any reason were excluded from the study. Any subject with an allo-transplant of any kind was excluded as well. This included those with a xenograft heart valve to avoid the potential risk of any immune reaction causing valvular degeneration. Mild-intermittent asthma requiring only occasional beta-agonist inhaler use or mild localized eczema were not excluded.

Subject Disposition: The study was prematurely discontinued in June 2017 after it became clear that there was no supporting evidence that receiving indoximod immunotherapy benefits patients over the existing standard of care chemotherapy. All subjects that were still in this study at this point, were immediately discontinued (n=47; 23 in the indoximod arm and 24 in the placebo arm).

A total of 169 subjects were enrolled (88 in the indoximod arm and 81 in the placebo arm). Of these subjects, 164 (85 and 79 subjects, respectively) were treated.

None of the subjects completed treatment. The most common reasons for treatment discontinuation were disease progression (56 subjects [65.9%] in the indoximod arm and 43 subjects [54.4%] in the placebo arm), withdrawal of consent (8 subjects [9.4%] and 13 subjects [16.5%], respectively), and the occurrence of AEs (6 subjects [7.1%] and 11 subjects [13.9%], respectively).

None of the subjects completed the study. The most common reasons for study discontinuation were death (35 subjects [41.2%] and 29 subjects [36.7%], respectively), sponsor decision (24 subjects [28.2%] and 24 subjects [30.4%], respectively), disease progression (12 subjects [14.1%] and 11 subjects [13.9%], respectively).

Key Demographics: The mean (standard deviation [SD]) age of the population was 56.3 (10.53) years. Most subjects were female (161 subjects [98.2%]) and White (137 subjects [83.5%]). Subject's baseline ECOG status

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was mostly 0 (84 subjects [51.5%]) or 1 (76 subjects [46.6%]) and most subjects had more than 1 disease site (131 subjects [79.9%]). The taxane chosen for most subjects was docetaxel (121 subjects [73.8%]).

Most subject's hormone receptor status was positive (118 subjects [72.0%]). In the subgroup of subjects with a negative hormone receptor status, the mean (SD) age was 56.1 (10.95) years. Subjects in this subgroup also mostly had a baseline ECOG status of 0 (21 subjects [46.7%]) or 1 (23 subjects [51.1%]) and more than 1 disease site (35 subjects [76.1%]).

Demographics were generally well balanced between the treatment arms.

Test Product, Dose and Mode of Administration, Batch Number:

Subjects received either docetaxel or paclitaxel in combination with indoximod or docetaxel or paclitaxel given with placebo.

Indoximod and placebo was supplied by NewLink Genetics as 200-mg capsules. Lot numbers for the indoximod capsules were: 11JM-265, 064I0614, 036I0315, 081I0815, 129I1215, and 039I0216. Lot numbers for the placebo capsules were: 11JM-255, 080I0814, and 080I0815.

Docetaxel and paclitaxel were commercially obtained.

Duration of Treatment: In the absence of treatment delays due to AE(s), treatment could continue until one of the following criteria applied:

- Disease progression.
- Intercurrent illness that prevented further administration of treatment.
- Unacceptable AE(s).
- Subject decided to withdraw from the study.
- General or specific changes in the subject's condition rendered him/her unacceptable for further treatment in the judgment of the investigator.

Subjects who were taken off docetaxel or paclitaxel due to toxicity could remain on study drug alone at the discretion of the investigator. They could remain on study drug until evidence of progression. This could only be done after a thorough discussion between the subject and the investigator as half of these subjects would be on placebo alone in this situation. Such discussion had to be documented in the subject's medical record. It was expected that only subjects who had, in the opinion of the investigator, demonstrated a better than expected response to study treatment (objective response or prolonged disease stabilization) could be considered for study drug alone.

Subjects were followed for up to five years, until they were lost to follow up, or death, whichever occurred first. Subjects removed from study for unacceptable AE(s) were followed for resolution or stabilization of the AE as well. Follow-up off study was performed using telephone contact, correspondence with treating physicians, and death records as necessary to update vital status at least every 6 months.

Endpoints for Evaluation:

- PFS: Disease progression was assessed every 6 weeks by tumor measurements (radiologic evaluation).
- Median overall survival and objective response rate.
- Safety/toxicity: Safety was assessed by the evaluation of AEs, clinical laboratory measurements, vital signs measurements, and physical examinations.

Statistical Methods:

Sample Size/Accrual Rate:

A planned accrual of up to 154 subjects (77 per study arm [indoximod versus [vs] placebo]) were planned to enter this two treatment parallel-design study. Accounting for a dropout rate of up to 10% (evenly distributed between the two arms), 154 subjects enrolled with analysis planned to occur after 95 events were observed would provide at least 80% power with a one-sided type I error rate of 0.10 to detect a hazard ratio (HR) of 0.64. The assumed accrual period was 18 months, the follow up period was 6 months, and the median PFS for the control group was 5 months. The accrual pattern across time periods was assumed to be uniform (all periods equal). This sample size was calculated based on a one-sided log rank test.

Stratification Factors:

Stratification between arms included physician choice of taxane (docetaxel or paclitaxel), hormone receptor status (+ vs. -), and number of disease sites (1, >1).

Analysis of Efficacy and Safety Endpoints:

All data were summarized using descriptive statistics. If needed, the point estimates and 95% confidence intervals (CIs) were calculated.

Primary endpoint: PFS, defined as the time from study entry to documentation of radiologic progressive disease or death, whichever was earlier, between the two treatment arms. PFS was summarized using the method of Kaplan-Meier. CIs for the median and survival rates at different time points were constructed when appropriate. The stratified logrank test was used to evaluate the treatment efficacy while accounting for the three stratification factors.

Additional supportive analyses could be performed using Cox proportional hazard models to adjust for stratification variables as well as covariates. An exploratory analysis was performed to compare PFS between taxane strata.

Safety/toxicity: Toxicity data were described for both treatment arms using Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03 terminology with frequency and grade of AEs.

Overall survival: Overall survival between the two treatment arms were analyzed in a similar manner to the primary endpoint of PFS.

Objective response rate: Objective response rate (complete and partial response [CR and PR]) as defined by RECIST 1.1 was analyzed using a Fisher exact test between the two treatment arms. Objective response rate estimates and 95% Wilson CIs were presented.

Retrospective exploratory analysis of clinical/pathologic variables: Regression techniques were employed to study the relationships of these biomarkers with the study treatment after adjusting for important prognostic predictors and/or possible confounders such as age (≤50 or > 50) and hormone receptor status (e.g., estrogen receptor or progesterone receptor = + or -). Transformations such as log and square root were considered to ensure there was no serious departure from the usual regression distributional assumptions, when appropriate. For instance, mixed effects models could be utilized to evaluate these biomarkers and their change patterns over time as related to the study treatment. Consideration was also given to dichotomize these measurements when appropriate.

Data Safety Monitoring Committee:

The Independent Data Safety Monitoring Committee (DSMC) was responsible for periodic review of the safety data from NewLink Genetics Corporation study NLG2101. The DSMC reviewed the study protocol and other appropriate study documents, proposed appropriate safety summaries and analyses, and periodically reviewed data on safety and outcome. The DSMC convened quarterly. The DSMC had full access to all data needed for the safety assessments. For the assessment of safety during the closed sessions, the DSMC received safety data displayed by treatment arm as well as pooled safety data for subjects across all groups. All data from prior to randomization through the most recently completed cycle was provided for each subject. A data cut-off date was established that allows a reasonable amount of time to process the data required for the DSMC meeting, for

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example, all data that was available at least 2 weeks in advance of the meeting. Such data were accurate to the extent possible.

The DSMC was tasked with reviewing the data from a safety standpoint and could make recommendations regarding stopping the study from a safety perspective at any time. A detailed description of analysis methods was prepared by the Sponsor designated study biostatistician in the study's statistical analysis plan (SAP).

Summary of Results:

Efficacy:

PFS:

Overall, the median (95% CI) PFS was lower in the indoximod group (6.0 [4.5, 8.1]) compared with the placebo group (8.4 [5.6, 9.8]). The hazard ratio (95% CI) was 1.144 (0.813, 1.609). When comparing different strata, the median (95% CI) PFS was 7.9 (5.7, 9.5) when indoximod was combined with docetaxel and 3.6 (1.9, 5.5) when indoximod was combined with paclitaxel.

Table 3 Progression-free survival (Safety Analysis Set)

Variable Statistic	**Indoximod N=85**	**Placebo N=79**	**Overall N=164**
Number of subjects with events, n (%)			
Disease progression	66 (80.5)	53 (69.7)	119 (75.3)
Death	6 (7.3)	12 (15.8)	18 (11.4)
Number of subjects censored[a]	10 (12.2)	11 (14.5)	21 (13.3)
Summary of statistics of PFS[b]			
Q1 (95% CI)	2.5 (1.9, 3.8)	4.7 (2.5, 5.5)	3.5 (2.3, 4.6)
Median (95% CI)	6.0 (4.5, 8.1)	8.4 (5.6, 9.8)	7.3 (5.6, 8.7)
Q3 (95% CI)	11.0 (8.8, 16.1)	11.6 (10.0, 15.3)	11.5 (10.0, 12.9)
Follow-up time[c]			
n	82	76	158
Mean (SD)	7.5 (6.61)	8.1 (5.49)	7.8 (6.08)
Median	5.8	7.3	6.0
Q1, Q3	2.5, 10.2	3.9, 11.1	2.8, 11.0
Min, Max	0.1, 31.3	1.1, 26.5	0.1, 31.3
Hazard ratio (95% CI), Indoximod versus placebo[d]			1.44 (0.813, 1.609)

CI=confidence interval; N=number of subjects per treatment group; PFS=progression-free survival; Q1=quartile 1; Q3=quartile 3; SD=standard deviation

Note: There were 6 subjects without definitive lack of progression documented and therefore they were excluded from this summary.

[a] Subjects who have not experienced disease progression or death at the time of analysis will be censored at the last time that lack of definitive progression was objectively documented.

[b] Progression Free Survival (PFS) represents the number of months from first dose to disease progression or death, whichever occurs first. Kaplan-Meier estimates were used.

[c] Follow up time is the number of months from first dose to progressive disease, death or last time lack of definitive progression was documented.

[d] Based on Cox Proportional Hazards Model.

Overall Survival:

The median (95% CI) overall survival was not different in the indoximod group (21.6 [16.0, 39.1]) compared with the placebo group (21.2 [19.1, 32.1]).

Objective Response Rate:

Overall, the proportion of subjects with complete response was 3.5% in the indoximod group and 2.5% in the placebo group. The proportion of subjects with partial response was 36.5% and 34.2%, respectively. The

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proportion of subjects with a complete or partial response was not statistically different in the indoximod versus the placebo group (p=0.7414).

Table 4 Objective Response Rate (Safety Analysis Set)

Variable Statistic	**Indoximod N=85**	**Placebo N=79**	**Overall N=164**
	n (%)		
RECIST best response			
Complete response	3 (3.5)	2 (2.5)	5 (3.0)
Partial response	31 (36.5)	27 (34.2)	58 (35.4)
Stable disease	31 (36.5)	35 (44.3)	66 (40.2)
Progressive disease	13 (15.3)	9 (11.4)	22 (13.4)
Not evaluable	0	0	0
Complete or partial response	34 (40.0)	29 (36.7)	63 (38.4)
p-value[a]	0.7414		
95% CI[b]	33.1, 54.6	29.3, 51.2	34.2, 49.7

CI=confidence interval; N=number of subjects per treatment group; RECIST= Response Evaluation Criteria In Solid Tumors
[a] P-value based on Fishers Exact Test.
[b] 95%CI is based on Wilsons Method.

Safety:

Extent of Exposure

In the indoximod group, subjects received a mean (SD) cumulative dose of 1713233 (1327420 mg). The mean (SD) number of actual pills taken was 1428 (1106) in the indoximod group and 1660 (1315) in the placebo group. Mean compliance ranged from 85-100% in both groups. A total of 19 subjects 22.4%) in the indoximod group and 17 subjects (21.5%) in the placebo group modified their dose during the study.

Adverse Events (General Overview):

The majority of subjects in both treatment arms had ≥1 treatment-emergent adverse event (TEAE) (85 subjects [100.0%] in the indoximod group and 78 subjects [98.7%] in the placebo group). Related TEAEs occurred in 58 subjects (68.2%) and 63 subjects (79.7%), respectively. TEAEs of ≥grade 3 in severity occurred in 51 subjects (60.0%) and 48 subjects (60.8%), respectively.

Four subjects (4.7%) in the indoximod arm and 2 subjects (2.5%) in the placebo arm died due to unrelated TEAEs during the study. Also, 29 subjects (34.1%) and 28 subjects (35.4%) had ≥1 serious TEAE (which included the deaths cited above). A total of 11 subjects (12.9%) and 10 subjects (12.7%), respectively, permanently discontinued the study due to ≥1 TEAE.

Adverse Events (Most Common Events):

The most common TEAEs (preferred terms [PTs] in order of overall incidence; PTs observed in ≥10% of subjects overall) were alopecia (44.7% in the indoximod group and 64.6% in the placebo group, respectively), fatigue (61.2% and 45.6%, respectively), nausea (47.1% and 48.1%, respectively), diarrhea (35.3% and 39.2%, respectively), constipation (28.2% and 34.2%, respectively), edema peripheral (30.6% and 29.1%, respectively), vomiting (23.5% and 35.4%, respectively), anemia (32.9% and 19.0% , respectively), headache (22.4% and 30.4%, respectively), neuropathy peripheral (22.4% and 24.1%, respectively), decreased appetite (20.0% and 24.1%, respectively), bone pain (22.4% and 17.7%, respectively), arthralgia (20.0% and 20.3%, respectively), dizziness (12.9% and 24.1%, respectively), dysgeusia (14.1% and 21.5%, respectively), neutropenia (16.5% and 19.0%, respectively), abdominal pain (15.3% and 19.0%, respectively), dyspnea (18.8% and 15.2%, respectively), lymphocyte count decreased (21.2% and 12.7%, respectively), hyperglycemia (23.5% and 8.9%, respectively), cough (20.0% and 12.7%, respectively), peripheral sensory neuropathy (11.8% and 17.7%, respectively), insomnia (15.3% and 13.9%, respectively), asthenia (10.6% and 17.7%, respectively), lacrimation increased (11.8% and 13.9%, respectively), back pain (9.4% and 16.5%, respectively), stomatitis (12.9% and

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12.7%, respectively), pain in extremity (15.3% and 10.1%, respectively), AST increased (12.9% and 11.4%, respectively), myalgia (8.2% and 15.2%, respectively), vision blurred (9.4% and 12.7%, respectively), white blood cell (WBC) count decreased (9.4% and 12.7%, respectively), urinary tract infection (5.9% and 15.2%, respectively), pruritus (11.8% and 8.9%, respectively), rash (8.2% and 12.7%, respectively), and rash maculo-papular (11.8% and 8.9%, respectively) (Table 5). Of these, events reported with a higher incidence (≥5% difference in incidence) in the indoximod group were anemia, fatigue, lymphocyte count decreased, hyperglycemia, pain in extremity, and cough. Events reported with a higher incidence in the placebo group were constipation, asthenia, urinary tract infection, back pain, myalgia, dizziness, headache, peripheral sensory neuropathy, vomiting, dysgeusia, and alopecia.

Table 5 Most Common (≥5% in Any Treatment Arm) Treatment-emergent Adverse Events (Safety Analysis Set)

System Organ Class Preferred Term	Indoximod N=85	Placebo N=79	Overall N=164
	n (%)		
Blood and lymphatic system disorders	43 (50.6)	32 (40.5)	75 (45.7)
Anaemia	28 (32.9)	15 (19.0)	43 (26.2)
Febrile neutropenia	2 (2.4)	4 (5.1)	6 (3.7)
Neutropenia	14 (16.5)	15 (19.0)	29 (17.7)
Cardiac disorders	12 (14.1)	9 (11.4)	21 (12.8)
Sinus tachycardia	4 (4.7)	5 (6.3)	9 (5.5)
Ear and labyrinth disorders	3 (3.5)	10 (12.7)	13 (7.9)
Eye disorders	20 (23.5)	27 (34.2)	47 (28.7)
Dry eye	0	4 (5.1)	4 (2.4)
Lacrimation increased	10 (11.8)	11 (13.9)	21 (12.8)
Vision blurred	8 (9.4)	10 (12.7)	18 (11.0)
Visual impairment	1 (1.2)	4 (5.1)	5 (3.0)
Gastrointestinal disorders	63 (74.1)	64 (81.0)	127 (77.4)
Abdominal distension	2 (2.4)	5 (6.3)	7 (4.3)
Abdominal pain	13 (15.3)	15 (19.0)	28 (17.1)
Abdominal pain upper	3 (3.5)	6 (7.6)	9 (5.5)
Constipation	24 (28.2)	27 (34.2)	51 (31.1)
Diarrhea	30 (35.3)	31 (39.2)	61 (37.2)
Dry mouth	6 (7.1)	5 (6.3)	11 (6.7)
Gastroesophageal reflux disease	4 (4.7)	4 (5.1)	8 (4.9)
Nausea	40 (47.1)	38 (48.1)	78 (47.6)
Oral pain	3 (3.5)	6 (7.6)	9 (5.5)
Stomatitis	11 (12.9)	10 (12.7)	21 (12.8)
Vomiting	20 (23.5)	28 (35.4)	48 (29.3)
General disorders and administration site conditions	68 (80.0)	60 (75.9)	128 (78.0)
Asthenia	9 (10.6)	14 (17.7)	23 (14.0)
Fatigue	52 (61.2)	36 (45.6)	88 (53.7)
Mucosal inflammation	5 (5.9)	3 (3.8)	8 (4.9)
Non-cardiac chest pain	4 (4.7)	5 (6.3)	9 (5.5)
Oedema peripheral	26 (30.6)	23 (29.1)	49 (29.9)
Pain	0	4 (5.1)	4 (2.4)
Pyrexia	6 (7.1)	7 (8.9)	13 (7.9)
Hepatobiliary disorders	4 (4.7)	7 (8.9)	11 (6.7)
Infections and infestations	32 (37.6)	38 (48.1)	70 (42.7)
Nasopharyngitis	2 (2.4)	4 (5.1)	6 (3.7)
Pneumonia	3 (3.5)	4 (5.1)	7 (4.3)
Upper respiratory tract infections	9 (10.6)	7 (8.9)	16 (9.8)
Urinary tract infection	5 (5.9)	12 (15.2)	17 (10.4)
Injury, poisoning, and procedural complications	7 (8.2)	14 (7.7)	21 (12.8)
Fall	1 (1.2)	4 (5.1)	5 (3.0)

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Table 5 Most Common (≥5% in Any Treatment Arm) Treatment-emergent Adverse Events (Safety Analysis Set), continued

System Organ Class Preferred Term	Indoximod N=85	Placebo N=79	Overall N=164
	n (%)		
Investigations	37 (37.6)	33 (41.8)	65 (39.6)
ALT increased	6 (7.1)	7 (8.9)	13 (7.9)
AST increased	11 (12.9)	9 (11.4)	20 (12.2)
Blood bilirubin increased	1 (1.2)	4 (5.1)	5 (3.0)
Blood ALP increased	6 (7.1)	3 (3.8)	9 (5.5)
Blood creatinine increased	8 (9.4)	3 (3.8)	11 (6.7)
Lymphocyte count decreased	18 (21.2)	10 (12.7)	28 (17.1)
Neutrophil count decreased	6 (7.1)	6 (7.6)	12 (7.3)
Weight decreased	2 (2.4)	6 (7.6)	8 (4.9)
WBC count decreased	8 (9.4)	10 (12.7)	18 (11.0)
Metabolism and nutrition disorders	51 (60.0)	40 (50.6)	91 (55.5)
Decreased appetite	17 (20.0)	19 (24.1)	36 (22.0)
Dehydration	4 (4.7)	6 (7.6)	10 (6.1)
Hypercalcemia	5 (5.9)	4 (5.1)	9 (5.5)
Hyperglycemia	20 (23.5)	7 (8.9)	27 (16.5)
Hyperkalemia	5 (5.9)	4 (5.1)	9 (5.5)
Hypoalbuminemia	6 (7.1)	5 (6.3)	11 (6.7)
Hypocalcemia	8 (9.4)	6 (7.6)	14 (8.5)
Hypokalemia	5 (5.9)	8 (10.1)	13 (7.9)
Hyponatremia	5 (5.9)	3 (3.8)	8 (4.9)
Hypophosphatemia	6 (7.1)	6 (7.6)	12 (7.3)
Musculoskeletal and connective tissue disorders	56 (65.9)	45 (57.0)	101 (61.6)
Arthralgia	17 (20.0)	16 (20.3)	33 (20.1)
Back pain	8 (9.4)	13 (16.5)	21 (12.8)
Bone pain	19 (22.4)	14 (17.7)	33 (20.1)
Muscular weakness	8 (9.4)	7 (8.9)	15 (9.1)
Musculoskeletal chest pain	5 (5.9)	7 (8.9)	12 (7.3)
Musculoskeletal pain	5 (5.9)	4 (5.1)	9 (5.5)
Myalgia	7 (8.2)	12 (15.2)	19 (11.6)
Pain in extremity	13 (15.3)	8 (10.1)	21 (12.8)
Nervous system disorders	55 (64.7)	56 (70.9)	111 (67.7)
Dizziness	11 (12.9)	19 (24.1)	30 (18.3)
Dysgeusia	12 (14.1)	17 (21.5)	29 (17.7)
Headache	19 (22.4)	24 (30.4)	43 (26.2)
Neuropathy peripheral	19 (22.4)	19 (24.1)	38 (23.2)
Paraesthesia	3 (3.5)	6 (7.6)	9 (5.5)
Peripheral sensory neuropathy	10 (11.8)	14 (17.7)	24 (14.6)
Psychiatric disorders	25 (29.4)	17 (21.5)	42 (25.6)
Anxiety	7 (8.2)	5 (6.3)	12 (7.3)
Insomnia	13 (15.3)	11 (13.9)	24 (14.6)
Renal and urinary disorders	4 (4.7)	7 (8.9)	11 (6.7)
Reproductive system and breast disorders	5 (5.9)	3 (3.8)	8 (4.9)
Respiratory, thoracic, and mediastinal disorders	43 (50.6)	36 (45.6)	79 (48.2)
Cough	17 (20.0)	10 (12.7)	27 (16.5)
Dyspnea	16 (18.8)	12 (15.2)	28 (17.1)
Epistaxis	2 (2.4)	5 (6.3)	7 (4.3)
Nasal congestion	9 (10.6)	1 (1.3)	10 (6.1)
Oropharyngeal pain	4 (4.7)	10 (12.7)	14 (8.5)
Pleural effusion	5 (5.9)	2 (2.5)	7 (4.3)
Productive cough	6 (7.1)	0	6 (3.7)
Skin and subcutaneous tissue disorders	56 (65.9)	61 (77.2)	117 (71.3)
Alopecia	38 (44.7)	51 (64.6)	89 (54.3)

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Table 5 Most Common (≥5% in Any Treatment Arm) Treatment-emergent Adverse Events (Safety Analysis Set), continued

System Organ Class Preferred Term	Indoximod N=85	Placebo N=79	Overall N=164
	n (%)		
Dry skin	2 (2.4)	10 (12.7)	12 (7.3)
Hyperhidrosis	2 (2.4)	4 (5.1)	6 (3.7)
Nail discolouration	5 (5.9)	10 (12.7)	15 (9.1)
Onychomadesis	2 (2.4)	5 (6.3)	7 (4.3)
Pruritus	10 (11.8)	7 (8.9)	17 (10.4)
Rash	7 (8.2)	10 (12.7)	17 (10.4)
Rash maculo-papular	10 (11.8)	7 (8.9)	17 (10.4)
Vascular disorders	12 (14.1)	19 (24.1)	31 (18.9)
Flushing	4 (4.7)	4 (5.1)	8 (4.9)
Hot flush	2 (2.4)	4 (5.1)	6 (3.7)
Hypotension	3 (3.5)	5 (6.3)	8 (4.9)
Lymphoedema	2 (2.4)	4 (5.1)	6 (3.7)

ALT=alanine aminotransferase; ALP=alkaline phosphatase; AST=aspartate aminotransferase; MedDRA=Medical Dictionary for Regulatory Activities; N=number of subjects per treatment group; n=number of subjects with event
Adverse Events were coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given system organ class, that subject was counted once for that system organ class. If a subject experienced more than one event within a given preferred term, that subject was counted only once for that preferred term.

Adverse Events (Related Events):

Related TEAEs occurred in 58 subjects (68.2%) in the indoximod group and 63 subjects (79.7%) in the placebo group. The most common related TEAEs (PTs in order of overall incidence; PTs observed in ≥10% of subjects overall) were fatigue (29.4% in the indoximod group and 34.2% in the placebo group, respectively), nausea (16.5% and 26.6%, respectively), diarrhea (9.4% and 20.3%, respectively), decreased appetite (11.8% and 13.9%, respectively), headache (10.6% and 13.9%, respectively), and lymphocyte count decreased (14.1% and 8.9%, respectively).

Adverse Events (Most Common >Grade 3 Events)

TEAEs of ≥grade 3 in severity occurred in 51 subjects (60.0%) in the indoximod group and 48 subjects (60.8%) in the placebo group. The only grade 3 events observed in >10% of subjects overall was neutropenia (9.4% in the indoximod group and 17.7% in the placebo group).

Adverse Events (Most Common Serious Events):

A total of 29 subjects (34.1%) in the indoximod group and 28 subjects (35.4%) in the placebo group had ≥1 serious TEAE. The most common serious TEAEs (PTs in order of overall incidence; PTs observed in ≥1% of subjects overall) were dyspnea (4.7% in the indoximod group and 0% in the placebo group), respiratory failure (2.4% and 1.3%, respectively), febrile neutropenia (1.2% and 2.5%, respectively), asthenia (0% and 3.8%, respectively), pneumonia (2.4% and 1.3%, respectively), anemia, large intestine perforation, non-cardiac chest pain, and headache (2.4% and 0%, respectively, each), hepatitis, urinary tract infection, dehydration, pleural effusion, and pulmonary embolism (1.2% and 1.3%, respectively, each).

Adverse Events (Events Leading to Death):
Four subjects (4.7%) in the indoximod arm and 2 subjects (2.5%) in the placebo arm died during the study:

- Subject 2101038 (indoximod group) was a 35-year-old female with a positive hormone receptor status (ER+/PR-) who died due to multi-organ failure. This subject entered the study with infiltrating ductal carcinoma (T1, N1, M1).

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- Subject 2101082 (indoximod group) was a 39-year-old female with a negative hormone receptor status who died due to respiratory failure. This subject entered the study with infiltrating ductal carcinoma (T2, N1, M0).
- Subject 2101099 (indoximod group) was a 58-year-old female with a positive hormone receptor (ER+/PR+) status who died due to cardiopulmonary failure. This subject entered the study with an unspecified cancer (T2, N0, M0).
- Subject 2101137 (indoximod group) was a 59-year-old female with a positive hormone receptor (ER+/PR+) status who suddenly died (PT: sudden death). This subject entered the study with infiltrating ductal carcinoma (T2, N1, M0).
- Subject 2101032 (placebo group) was a 50-year-old female with a negative hormone receptor status who died due to sepsis. This subject entered the study with infiltrating ductal carcinoma (T2, N1, M1).
- Subject 2101047 (placebo group) was a 69-year-old female with a positive hormone receptor status (ER+/PR+) who died due to respiratory failure. This subject entered the study with infiltrating ductal carcinoma (T4, N3, M1).

Individual subject narratives are provided in Section 2.3.5.

Clinical Laboratory:
Shifts in clinical laboratory values over time were reviewed. Overall, no unexpected changes occurred given the disease status of the population and the known safety profile of the 3 cancer treatments provided.

Vital Signs:
Overall, no unexpected changes occurred given the disease status of the population and the known safety profile of the 3 cancer treatments provided.

Conclusions:

Efficacy:

- The median (95% CI) PFS was lower in the indoximod group (6.0 [4.5, 8.1]) compared with the placebo group (8.4 [5.6, 9.8]).
- The median (95% CI) overall survival was not different in the indoximod group (21.6 [16.0, 39.1]) compared with the placebo group (21.2 [19.1, 32.1]).
- The proportion of subjects with a complete or partial response was not statistically different in the indoximod versus the placebo group (p=0.7414).

Safety:

- The majority of subjects in both treatment arms had ≥1 TEAE (85 subjects [100.0%] in the indoximod group and 78 subjects [98.7%] in the placebo group).
- Related TEAEs occurred in 58 subjects (68.2%) and 63 subjects (79.7%), respectively. TEAEs of ≥grade 3 in severity occurred in 51 subjects (60.0%) and 48 subjects (60.8%), respectively.
- Four subjects (4.7%) in the indoximod arm and 2 subjects (2.5%) in the placebo arm died due to unrelated TEAEs during the study. Further, 29 subjects (34.1%) and 28 subjects (35.4%) had ≥1 serious TEAE (which included the deaths cited above). A total of 11 subjects (12.9%) and 10 subjects (12.7%), respectively, permanently discontinued the study due to ≥1 TEAE.
- No unexpected changes in laboratory or vital signs parameters occurred given the disease status of the population and the known safety profile of the 3 cancer treatments provided.

Date of the Report: 17 Jul 2019

2 TABLES, FIGURES, AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT

2.1 Demographic Data

2.1.1 Analysis Populations and Subject Disposition

Table Number	Table Title
Table 14.1.1	Subject disposition (Safety Analysis Set)

Table 14.1.1
Subject Disposition (Safety Analysis Set)

Analysis group, n (%)	NLG-2101	Placebo	Overall
Number of Subjects Screened	88	81	169
Number of Subjects Enrolled [1]	88 (100.0)	81 (100.0)	169 (100.0)
Number of Subjects Treated [2]	85 (96.6)	79 (97.5)	164 (97.0)
Number of Subjects Dosed with Indoximod [3]	85 (100.0)	0	85 (51.8)
Number of Subjects Who Discontinued Treatment	85 (100.0)	79 (100.0)	164 (100.0)
Intercurrent illness that prevents further administration of treatment	0	1 (1.3)	1 (0.6)
Adverse Event	6 (7.1)	11 (13.9)	17 (10.4)
Withdrawal of consent	8 (9.4)	13 (16.5)	21 (12.8)
Investigator decision	6 (7.1)	5 (6.3)	11 (6.7)
Sponsor decision	3 (3.5)	2 (2.5)	5 (3.0)
Disease Progression	56 (65.9)	43 (54.4)	99 (60.4)
Non-compliance	1 (1.2)	2 (2.5)	3 (1.8)
Death	3 (3.5)	0	3 (1.8)
Other	2 (2.4)	2 (2.5)	4 (2.4)

Table 14.1.1
Subject Disposition (Safety Analysis Set)

Analysis group, n (%)	NLG-2101	Placebo	Overall
Number of Subjects Who Discontinued Study	85 (100.0)	79 (100.0)	164 (100.0)
Disease Progression	12 (14.1)	11 (13.9)	23 (14.0)
Adverse Event	1 (1.2)	2 (2.5)	3 (1.8)
Unable to comply with protocol	1 (1.2)	0	1 (0.6)
Lost to follow- up	3 (3.5)	4 (5.1)	7 (4.3)
Withdrawal of consent	8 (9.4)	7 (8.9)	15 (9.1)
Investigator decision	1 (1.2)	0	1 (0.6)
Sponsor decision	24 (28.2)	24 (30.4)	48 (29.3)
Death	35 (41.2)	29 (36.7)	64 (39.0)
Other	0	2 (2.5)	2 (1.2)

2.1.2 Demographics

Table Number	Table Title
Table 14.1.2	Demographic and baseline characteristics (Safety Analysis Set)
Table 14.1.2.1	Demographic and baseline characteristics: negative hormone receptors (Safety Analysis Set)
Table 14.1.3	Disease history (Safety Analysis Set)

Table 14.1.2
Demographic and Baseline Characteristics (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Age (years)				
	n	85	79	164
	Mean (SD)	56.5 (10.13)	56.0 (11.00)	56.3 (10.53)
	Median	58.0	57.0	58.0
	Q1, Q3	52.0, 63.0	48.0, 64.0	50.5, 64.0
	Min, Max	29, 76	29, 85	29, 85
Gender				
Male	n (%)	1(1.2)	2(2.5)	3(1.8)
Female	n (%)	84(98.8)	77(97.5)	161(98.2)
Race				
White	n (%)	71(83.5)	66(83.5)	137(83.5)
Black or African American	n (%)	12(14.1)	10(12.7)	22(13.4)
Asian	n (%)	1(1.2)	0	1(0.6)
Other	n (%)	1(1.2)	3(3.8)	4(2.4)
Ethnicity				
Hispanic or Latino	n (%)	3(3.5)	3(3.8)	6(3.7)
Not Hispanic or Latino	n (%)	80(94.1)	75(94.9)	155(94.5)
Not Reported	n (%)	2(2.4)	1(1.3)	3(1.8)

Table 14.1.2
Demographic and Baseline Characteristics (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Country				
Poland	n (%)	25(29.4)	25(31.6)	50(30.5)
United States	n (%)	60(70.6)	54(68.4)	114(69.5)
Baseline Height (cm)				
	n	80	71	151
	Mean (SD)	162.8 (7.556)	162.7 (7.275)	162.8 (7.401)
	Median	164.5	162.0	163.0
	Q1, Q3	159.5, 167.6	157.4, 168.5	157.5, 168.0
	Min, Max	137.2, 181.0	149.0, 178.0	137.2, 181.0
Baseline Weight (kg)				
	n	82	74	156
	Mean (SD)	76.71 (17.401)	77.01 (18.887)	76.85 (18.063)
	Median	74.10	73.85	74.00
	Q1, Q3	63.80, 88.00	63.00, 88.70	63.10, 88.35
	Min, Max	46.8, 129.4	46.0, 134.0	46.0, 134.0

Table 14.1.2
Demographic and Baseline Characteristics (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Baseline ECOG Status				
0	n (%)	41(48.8)	43(54.4)	84(51.5)
1	n (%)	41(48.8)	35(44.3)	76(46.6)
2	n (%)	2(2.4)	1(1.3)	3(1.8)
Missing	n (%)	1	0	1
Hormone Receptor Status				
Negative	n (%)	23(27.1)	23(29.1)	46(28.0)
Positive	n (%)	62(72.9)	56(70.9)	118(72.0)
Number of Disease Sites				
1	n (%)	20(23.5)	13(16.5)	33(20.1)
>1	n (%)	65(76.5)	66(83.5)	131(79.9)
Choice of Taxane				
Docetaxel	n (%)	62(72.9)	59(74.7)	121(73.8)
Paclitaxel	n (%)	23(27.1)	20(25.3)	43(26.2)

Table 14.1.2.1
Demographic and Baseline Characteristics: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Age (years)				
	n	23	23	46
	Mean (SD)	57.2 (10.83)	55.0 (11.20)	56.1 (10.95)
	Median	59.0	54.0	58.5
	Q1, Q3	52.0, 64.0	47.0, 64.0	50.0, 64.0
	Min, Max	31, 73	29, 74	29, 74
Gender				
Female	n (%)	23(100.0)	23(100.0)	46(100.0)
Race				
White	n (%)	14(60.9)	21(91.3)	35(76.1)
Black or African American	n (%)	9(39.1)	2(8.7)	11(23.9)
Ethnicity				
Not Hispanic or Latino	n (%)	23(100.0)	22(95.7)	45(97.8)
Not Reported	n (%)	0	1(4.3)	1(2.2)

Table 14.1.2.1
Demographic and Baseline Characteristics: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Country				
Poland	n (%)	2(8.7)	5(21.7)	7(15.2)
United States	n (%)	21(91.3)	18(78.3)	39(84.8)
Baseline Height (cm)				
	n	21	22	43
	Mean (SD)	164.7 (6.999)	162.4 (7.239)	163.5 (7.137)
	Median	165.0	162.3	165.0
	Q1, Q3	162.0, 167.6	156.0, 168.5	157.5, 168.0
	Min, Max	148.5, 181.0	149.0, 175.2	148.5, 181.0
Baseline Weight (kg)				
	n	23	23	46
	Mean (SD)	84.15 (19.917)	76.78 (22.238)	80.47 (21.204)
	Median	78.50	75.00	76.65
	Q1, Q3	71.50, 96.50	57.90, 88.70	64.00, 90.90
	Min, Max	53.5, 129.4	47.5, 127.7	47.5, 129.4

Table 14.1.2.1
Demographic and Baseline Characteristics: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Baseline ECOG Status				
0	n (%)	11(50.0)	10(43.5)	21(46.7)
1	n (%)	10(45.5)	13(56.5)	23(51.1)
2	n (%)	1(4.5)	0	1(2.2)
Missing	n (%)	1	0	1
Hormone Receptor Status				
Negative	n (%)	23(100.0)	23(100.0)	46(100.0)
Number of Disease Sites				
1	n (%)	5(21.7)	6(26.1)	11(23.9)
>1	n (%)	18(78.3)	17(73.9)	35(76.1)
Choice of Taxane				
Docetaxel	n (%)	14(60.9)	16(69.6)	30(65.2)
Paclitaxel	n (%)	9(39.1)	7(30.4)	16(34.8)

Table 14.1.3
Disease History (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Initial Histology				
Infiltrating ductal carcinoma	n (%)	50 (58.8)	56 (70.9)	106 (64.6)
Infiltrating lobular carcinoma	n (%)	6 (7.1)	7 (8.9)	13 (7.9)
Inflamatory carcinoma	n (%)	2 (2.4)	1 (1.3)	3 (1.8)
Medullary carcinoma	n (%)	1 (1.2)	0	1 (0.6)
Other	n (%)	26 (30.6)	15 (19.0)	41 (25.0)
Initial T Classification				
TX	n (%)	2 (2.4)	2 (2.5)	4 (2.4)
T0	n (%)	0	1 (1.3)	1 (0.6)
Tis	n (%)	1 (1.2)	1 (1.3)	2 (1.2)
T1	n (%)	17 (20.0)	26 (32.9)	43 (26.2)
T2	n (%)	45 (52.9)	20 (25.3)	65 (39.6)
T3	n (%)	8 (9.4)	11 (13.9)	19 (11.6)
T4	n (%)	10 (11.8)	17 (21.5)	27 (16.5)
Initial N Classification				
NX	n (%)	8 (9.4)	8 (10.1)	16 (9.8)
N0	n (%)	22 (25.9)	25 (31.6)	47 (28.7)
N1	n (%)	32 (37.6)	29 (36.7)	61 (37.2)
N2	n (%)	10 (11.8)	8 (10.1)	18 (11.0)
N3	n (%)	11 (12.9)	8 (10.1)	19 (11.6)
Initial M Classification				
MX	n (%)	23 (27.1)	14 (17.7)	37 (22.6)
M0	n (%)	42 (49.4)	45 (57.0)	87 (53.0)
M1	n (%)	19 (22.4)	19 (24.1)	38 (23.2)

Table 14.1.3
Disease History (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
HHER2 Status				
Positive	n (%)	1 (1.2)	2 (2.5)	3 (1.8)
Negative	n (%)	84 (98.8)	77 (97.5)	161 (98.2)
Hormone Receptor Status				
ER + / PR +	n (%)	45 (52.9)	45 (57.0)	90 (54.9)
ER + / PR -	n (%)	18 (21.2)	12 (15.2)	30 (18.3)
ER - / PR +	n (%)	1 (1.2)	1 (1.3)	2 (1.2)
ER - / PR -	n (%)	21 (24.7)	21 (26.6)	42 (25.6)
Method of confirmation				
Histological	n (%)	79 (92.9)	65 (82.3)	144 (87.8)
Cytological	n (%)	6 (7.1)	14 (17.7)	20 (12.2)

2.1.3 Exposure and Compliance

Table Number	Table Title
Table 14.3.5.1A	Study drug exposure (Safety Analysis Set)
Table 14.3.5.1B	Study drug exposure: negative hormone receptors (Safety Analysis Set)

Table 14.3.5.1A
Study Drug Exposure (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Cumulative Dose (mg)	n	85	0	85
	Mean (SD)	1713233 (1327420)		1713233 (1327420)
	Median	1353600		1353600
	Min, Max	0.0, 5566800		0.0, 5566800
Cycles Received				
Received 1 Cycle	n (%)	4(4.7)	6(7.6)	10(6.1)
Received 2 Cycles	n (%)	16(18.8)	10(12.7)	26(15.9)
Received 3 Cycles	n (%)	6(7.1)	4(5.1)	10(6.1)
Received 4 Cycles	n (%)	9(10.6)	7(8.9)	16(9.8)
Received 5 Cycles	n (%)	2(2.4)	3(3.8)	5(3.0)
Received 6 Cycles	n (%)	7(8.2)	7(8.9)	14(8.5)
Received 7 Cycles	n (%)	1(1.2)	2(2.5)	3(1.8)
Received 8 Cycles	n (%)	4(4.7)	3(3.8)	7(4.3)
Received 9 Cycles	n (%)	7(8.2)	4(5.1)	11(6.7)
Received 10 Cycles	n (%)	3(3.5)	3(3.8)	6(3.7)
Received 11 Cycles	n (%)	1(1.2)	1(1.3)	2(1.2)
Received 12 Cycles	n (%)	1(1.2)	6(7.6)	7(4.3)
Received 13 Cycles	n (%)	5(5.9)	4(5.1)	9(5.5)
Received 14 Cycles	n (%)	6(7.1)	2(2.5)	8(4.9)
Received 15 Cycles	n (%)	0	4(5.1)	4(2.4)
Received 16 Cycles	n (%)	1(1.2)	3(3.8)	4(2.4)
Received 17 Cycles	n (%)	2(2.4)	0	2(1.2)
Received 18 Cycles	n (%)	1(1.2)	0	1(0.6)
Received 19 Cycles	n (%)	2(2.4)	1(1.3)	3(1.8)
Received 20 Cycles	n (%)	2(2.4)	1(1.3)	3(1.8)
Received 21 Cycles	n (%)	0	1(1.3)	1(0.6)
Received 22 Cycles	n (%)	1(1.2)	1(1.3)	2(1.2)
Received 23 Cycles	n (%)	0	1(1.3)	1(0.6)
Received 24 Cycles	n (%)	0	1(1.3)	1(0.6)
Received 25 Cycles	n (%)	2(2.4)	0	2(1.2)
Received 27 Cycles	n (%)	0	2(2.5)	2(1.2)
Received 28 Cycles	n (%)	1(1.2)	0	1(0.6)
Received 29 Cycles	n (%)	0	1(1.3)	1(0.6)
Received 31 Cycles	n (%)	0	1(1.3)	1(0.6)
Actual Doses Taken [1]	n	85	79	164
	Mean (SD)	1428 (1106)	1660 (1315)	1540 (1213)

Table 14.3.5.1A
Study Drug Exposure (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
	Median	1128	1344	1191
	Min, Max	0, 4639	18, 5196	0, 5196
Percent Compliance - Cycle 1	n	88	79	167
	Mean (SD)	93.76 (10.240)	92.21 (15.432)	93.03 (12.941)
	Median	96.00	96.00	96.00
	Min, Max	52.9, 100	6.0, 100	6.0, 100
Percent Compliance - Cycle 2	n	80	72	152
	Mean (SD)	93.29 (13.648)	94.75 (9.077)	93.98 (11.693)
	Median	96.00	96.00	96.00
	Min, Max	30.6, 100	48.3, 100	30.6, 100
Percent Compliance - Cycle 3	n	64	62	126
	Mean (SD)	95.82 (6.551)	92.00 (15.368)	93.94 (11.856)
	Median	96.00	96.00	96.00
	Min, Max	59.8, 100	17.7, 100	17.7, 100

Table 14.3.5.1A
Study Drug Exposure (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Percent Compliance - Cycle 4	n	61	58	119
	Mean (SD)	90.67 (19.844)	93.13 (12.074)	91.87 (16.498)
	Median	96.00	96.00	96.00
	Min, Max	0.0, 100	28.6, 100	0.0, 100
Percent Compliance - Cycle 5	n	50	52	102
	Mean (SD)	93.12 (15.463)	95.14 (7.425)	94.15 (12.036)
	Median	96.00	96.00	96.00
	Min, Max	0.0, 100	68.6, 100	0.0, 100
Percent Compliance - Cycle 6	n	46	50	96
	Mean (SD)	94.22 (10.503)	94.00 (9.229)	94.10 (9.808)
	Median	96.00	96.00	96.00
	Min, Max	46.7, 100	61.7, 100	46.7, 100
Percent Compliance - Cycle 7	n	40	42	82
	Mean (SD)	95.99 (4.436)	90.32 (20.598)	93.08 (15.243)
	Median	96.00	96.00	96.00
	Min, Max	74.1, 100	0.0, 100	0.0, 100
Percent Compliance - Cycle 8	n	39	40	79
	Mean (SD)	95.59 (7.860)	95.76 (7.189)	95.68 (7.480)
	Median	96.00	96.00	96.00
	Min, Max	50.0, 100	61.7, 100	50.0, 100

Table 14.3.5.1A
Study Drug Exposure (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Percent Compliance - Cycle 9	n	36	37	73
	Mean (SD)	94.84 (7.450)	88.58 (21.422)	91.67 (16.321)
	Median	96.00	96.00	96.00
	Min, Max	58.3, 100	0.0, 100	0.0, 100
Percent Compliance - Cycle 10	n	29	33	62
	Mean (SD)	92.71 (18.336)	90.18 (21.702)	91.36 (20.075)
	Median	96.00	96.00	96.00
	Min, Max	0.0, 100	0.0, 100	0.0, 100
Percent Compliance - Cycle 11	n	25	30	55
	Mean (SD)	96.46 (3.261)	94.47 (13.629)	95.37 (10.270)
	Median	96.00	96.00	96.00
	Min, Max	85.4, 100	27.7, 100	27.7, 100
Percent Compliance - Cycle 12	n	25	29	54
	Mean (SD)	93.04 (19.475)	96.40 (4.830)	94.84 (13.672)
	Median	96.00	96.00	96.00
	Min, Max	0.0, 100	77.7, 100	0.0, 100
Percent Compliance - Cycle 13	n	23	24	47
	Mean (SD)	88.34 (19.729)	92.82 (20.129)	90.63 (19.846)
	Median	96.00	96.00	96.00
	Min, Max	25.1, 100	0.0, 100	0.0, 100

Table 14.3.5.1A
Study Drug Exposure (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Percent Compliance - Cycle 14	n	19	18	37
	Mean (SD)	88.36 (23.768)	94.68 (10.474)	91.44 (18.560)
	Median	96.00	96.00	96.00
	Min, Max	0.0, 100	54.9, 100	0.0, 100
Percent Compliance - Cycle 15	n	12	17	29
	Mean (SD)	94.50 (10.059)	93.18 (12.794)	93.73 (11.564)
	Median	96.00	96.00	96.00
	Min, Max	64.0, 100	50.0, 100	50.0, 100
Percent Compliance - Cycle 16	n	12	13	25
	Mean (SD)	94.22 (9.760)	90.48 (25.561)	92.28 (19.338)
	Median	96.00	96.00	96.00
	Min, Max	64.6, 100	5.7, 100	5.7, 100
Percent Compliance - Cycle 17	n	11	9	20
	Mean (SD)	85.33 (28.831)	96.73 (1.908)	90.46 (21.746)
	Median	96.00	96.00	96.00
	Min, Max	4.0, 100	94.6, 100	4.0, 100
Percent Compliance - Cycle 18	n	9	10	19
	Mean (SD)	90.89 (17.732)	97.10 (2.025)	94.16 (12.327)
	Median	96.00	96.00	96.00
	Min, Max	44.6, 100	95.0, 100	44.6, 100

Table 14.3.5.1A
Study Drug Exposure (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Percent Compliance - Cycle 19	n	8	10	18
	Mean (SD)	91.20 (15.304)	97.06 (2.074)	94.46 (10.377)
	Median	96.00	96.00	96.00
	Min, Max	54.9, 100	94.6, 100	54.9, 100
Percent Compliance - Cycle 20	n	6	10	16
	Mean (SD)	89.22 (22.580)	87.69 (30.866)	88.26 (27.242)
	Median	98.00	96.00	96.00
	Min, Max	43.3, 100	0.0, 100	0.0, 100
Percent Compliance - Cycle 21	n	4	8	12
	Mean (SD)	97.10 (1.943)	97.50 (2.070)	97.37 (1.948)
	Median	96.20	96.00	96.00
	Min, Max	96.0, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 22	n	4	7	11
	Mean (SD)	98.00 (2.309)	97.14 (1.952)	97.45 (2.018)
	Median	98.00	96.00	96.00
	Min, Max	96.0, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 23	n	3	6	9
	Mean (SD)	97.33 (2.309)	97.33 (2.066)	97.33 (2.000)
	Median	96.00	96.00	96.00
	Min, Max	96.0, 100	96.0, 100	96.0, 100

Table 14.3.5.1A
Study Drug Exposure (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Percent Compliance - Cycle 24	n	3	5	8
	Mean (SD)	97.33 (2.309)	97.60 (2.191)	97.50 (2.070)
	Median	96.00	96.00	96.00
	Min, Max	96.0, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 25	n	3	4	7
	Mean (SD)	97.33 (2.309)	97.00 (2.000)	97.14 (1.952)
	Median	96.00	96.00	96.00
	Min, Max	96.0, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 26	n	1	4	5
	Mean (SD)	100.0	97.00 (2.000)	97.60 (2.191)
	Median	100.0	96.00	96.00
	Min, Max	100, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 27	n	1	4	5
	Mean (SD)	100.0	85.00 (24.739)	88.00 (22.450)
	Median	100.0	96.00	96.00
	Min, Max	100, 100	48.0, 100	48.0, 100
Percent Compliance - Cycle 28	n	1	3	4
	Mean (SD)	100.0	97.33 (2.309)	98.00 (2.309)
	Median	100.0	96.00	98.00
	Min, Max	100, 100	96.0, 100	96.0, 100

Table 14.3.5.1A
Study Drug Exposure (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Percent Compliance - Cycle 29	n	0	2	2
	Mean (SD)		96.00 (0.000)	96.00 (0.000)
	Median		96.00	96.00
	Min, Max		96.0, 96.0	96.0, 96.0
Percent Compliance - Cycle 30	n	0	1	1
	Mean (SD)		96.00	96.00
	Median		96.00	96.00
	Min, Max		96.0, 96.0	96.0, 96.0
Percent Compliance - Cycle 31	n	0	1	1
	Mean (SD)		96.00	96.00
	Median		96.00	96.00
	Min, Max		96.0, 96.0	96.0, 96.0
Number of subjects who modified their dose	n (%)	19(22.4)	17(21.5)	36(22.0)
Reason for dose modification				
Adverse Event	n (%)	8(9.4)	9(11.4)	17(10.4)
Other	n (%)	14(16.5)	10(12.7)	24(14.6)

Table 14.3.5.1B
Study Drug Exposure: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Cumulative Dose (mg)	n	23	0	23
	Mean (SD)	1426017 (1269995)		1426017 (1269995)
	Median	885600		885600
	Min, Max	28800.0, 4089600		28800.0, 4089600
Cycles Received				
Received 1 Cycle	n (%)	3(13.0)	1(4.3)	4(8.7)
Received 2 Cycles	n (%)	5(21.7)	4(17.4)	9(19.6)
Received 3 Cycles	n (%)	2(8.7)	2(8.7)	4(8.7)
Received 4 Cycles	n (%)	3(13.0)	2(8.7)	5(10.9)
Received 6 Cycles	n (%)	2(8.7)	1(4.3)	3(6.5)
Received 7 Cycles	n (%)	0	1(4.3)	1(2.2)
Received 8 Cycles	n (%)	0	1(4.3)	1(2.2)
Received 9 Cycles	n (%)	3(13.0)	1(4.3)	4(8.7)
Received 10 Cycles	n (%)	1(4.3)	2(8.7)	3(6.5)
Received 11 Cycles	n (%)	0	1(4.3)	1(2.2)
Received 12 Cycles	n (%)	1(4.3)	1(4.3)	2(4.3)
Received 13 Cycles	n (%)	0	1(4.3)	1(2.2)
Received 14 Cycles	n (%)	1(4.3)	0	1(2.2)
Received 15 Cycles	n (%)	0	2(8.7)	2(4.3)
Received 16 Cycles	n (%)	1(4.3)	1(4.3)	2(4.3)
Received 20 Cycles	n (%)	1(4.3)	0	1(2.2)
Received 24 Cycles	n (%)	0	1(4.3)	1(2.2)
Received 27 Cycles	n (%)	0	1(4.3)	1(2.2)
Actual Doses Taken [1]	n	23	23	46
	Mean (SD)	1188 (1058)	1620 (1290)	1404 (1187)
	Median	738	1092	1002
	Min, Max	24, 3408	87, 4422	24, 4422
Percent Compliance - Cycle 1	n	23	23	46
	Mean (SD)	93.29 (11.391)	89.45 (19.644)	91.37 (15.995)
	Median	98.80	96.90	97.25
	Min, Max	56.7, 100	21.4, 100	21.4, 100
Percent Compliance - Cycle 2	n	20	22	42
	Mean (SD)	91.96 (15.459)	95.31 (9.885)	93.72 (12.794)
	Median	98.20	99.40	98.80

Table 14.3.5.1B
Study Drug Exposure: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
	Min, Max	39.3, 100	56.7, 100	39.3, 100
Percent Compliance - Cycle 3	n	15	17	32
	Mean (SD)	96.91 (4.895)	88.92 (24.212)	92.66 (18.160)
	Median	98.80	97.30	98.20
	Min, Max	81.3, 100	17.7, 100	17.7, 100

Table 14.3.5.1B
Study Drug Exposure: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Percent Compliance - Cycle 4	n	13	15	28
	Mean (SD)	95.84 (7.143)	95.37 (8.962)	95.59 (8.024)
	Median	97.60	97.10	97.35
	Min, Max	72.9, 100	64.3, 100	64.3, 100
Percent Compliance - Cycle 5	n	10	14	24
	Mean (SD)	96.17 (5.586)	96.76 (7.069)	96.51 (6.367)
	Median	98.20	100.0	99.40
	Min, Max	82.1, 100	73.2, 100	73.2, 100
Percent Compliance - Cycle 6	n	9	14	23
	Mean (SD)	97.33 (2.961)	96.92 (7.042)	97.08 (5.704)
	Median	97.60	100.0	100.0
	Min, Max	91.8, 100	73.2, 100	73.2, 100
Percent Compliance - Cycle 7	n	8	12	20
	Mean (SD)	98.03 (2.259)	94.54 (14.130)	95.94 (10.979)
	Median	98.80	99.40	99.40
	Min, Max	94.6, 100	50.0, 100	50.0, 100
Percent Compliance - Cycle 8	n	8	12	20
	Mean (SD)	98.03 (2.259)	98.68 (1.782)	98.42 (1.956)
	Median	98.80	100.0	100.0
	Min, Max	94.6, 100	96.0, 100	94.6, 100

Table 14.3.5.1B
Study Drug Exposure: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Percent Compliance - Cycle 9	n	8	10	18
	Mean (SD)	93.61 (14.430)	94.13 (14.343)	93.90 (13.954)
	Median	100.0	99.40	100.0
	Min, Max	58.3, 100	53.6, 100	53.6, 100
Percent Compliance - Cycle 10	n	6	9	15
	Mean (SD)	82.37 (40.407)	96.56 (5.979)	90.88 (25.599)
	Median	99.80	98.80	99.60
	Min, Max	0.0, 100	81.3, 100	0.0, 100
Percent Compliance - Cycle 11	n	4	8	12
	Mean (SD)	96.35 (7.300)	89.81 (25.158)	91.99 (20.680)
	Median	100.0	99.40	100.0
	Min, Max	85.4, 100	27.7, 100	27.7, 100
Percent Compliance - Cycle 12	n	4	7	11
	Mean (SD)	98.05 (2.563)	98.17 (1.958)	98.13 (2.067)
	Median	98.80	98.80	98.80
	Min, Max	94.6, 100	96.0, 100	94.6, 100
Percent Compliance - Cycle 13	n	3	6	9
	Mean (SD)	98.20 (3.118)	98.57 (2.002)	98.44 (2.229)
	Median	100.0	99.70	100.0
	Min, Max	94.6, 100	96.0, 100	94.6, 100

Table 14.3.5.1B
Study Drug Exposure: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Percent Compliance - Cycle 14	n	3	5	8
	Mean (SD)	98.20 (3.118)	99.20 (1.789)	98.83 (2.208)
	Median	100.0	100.0	100.0
	Min, Max	94.6, 100	96.0, 100	94.6, 100
Percent Compliance - Cycle 15	n	2	4	6
	Mean (SD)	100.0 (0.000)	86.50 (24.406)	91.00 (20.149)
	Median	100.0	98.00	100.0
	Min, Max	100, 100	50.0, 100	50.0, 100
Percent Compliance - Cycle 16	n	2	3	5
	Mean (SD)	100.0 (0.000)	98.67 (2.309)	99.20 (1.789)
	Median	100.0	100.0	100.0
	Min, Max	100, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 17	n	1	2	3
	Mean (SD)	100.0	98.00 (2.828)	98.67 (2.309)
	Median	100.0	98.00	100.0
	Min, Max	100, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 18	n	1	2	3
	Mean (SD)	100.0	98.00 (2.828)	98.67 (2.309)
	Median	100.0	98.00	100.0
	Min, Max	100, 100	96.0, 100	96.0, 100

Table 14.3.5.1B
Study Drug Exposure: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Percent Compliance - Cycle 19	n	1	2	3
	Mean (SD)	100.0	98.00 (2.828)	98.67 (2.309)
	Median	100.0	98.00	100.0
	Min, Max	100, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 20	n	1	2	3
	Mean (SD)	100.0	98.00 (2.828)	98.67 (2.309)
	Median	100.0	98.00	100.0
	Min, Max	100, 100	96.0, 100	96.0, 100
Percent Compliance - Cycle 21	n	0	2	2
	Mean (SD)		98.00 (2.828)	98.00 (2.828)
	Median		98.00	98.00
	Min, Max		96.0, 100	96.0, 100
Percent Compliance - Cycle 22	n	0	2	2
	Mean (SD)		98.00 (2.828)	98.00 (2.828)
	Median		98.00	98.00
	Min, Max		96.0, 100	96.0, 100
Percent Compliance - Cycle 23	n	0	2	2
	Mean (SD)		98.00 (2.828)	98.00 (2.828)
	Median		98.00	98.00
	Min, Max		96.0, 100	96.0, 100

Table 14.3.5.1B
Study Drug Exposure: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Percent Compliance - Cycle 24	n	0	2	2
	Mean (SD)		98.00 (2.828)	98.00 (2.828)
	Median		98.00	98.00
	Min, Max		96.0, 100	96.0, 100
Percent Compliance - Cycle 25	n	0	1	1
	Mean (SD)		96.00	96.00
	Median		96.00	96.00
	Min, Max		96.0, 96.0	96.0, 96.0
Percent Compliance - Cycle 26	n	0	1	1
	Mean (SD)		96.00	96.00
	Median		96.00	96.00
	Min, Max		96.0, 96.0	96.0, 96.0
Percent Compliance - Cycle 27	n	0	1	1
	Mean (SD)		48.00	48.00
	Median		48.00	48.00
	Min, Max		48.0, 48.0	48.0, 48.0

Table 14.3.5.1B
Study Drug Exposure: Negative Hormone Receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Number of subjects who modified their dose	n (%)	6(26.1)	5(21.7)	11(23.9)
Reason for dose modification				
Adverse Event	n (%)	3(13.0)	2(8.7)	5(10.9)
Other	n (%)	5(21.7)	4(17.4)	9(19.6)

2.2 Efficacy Data

Table Number	Table Title
Table 14.2.1.1A	Progression-free survival (PFS) (Safety Analysis Set)
Table 14.2.1.1B	Progression-free survival (PFS): negative hormone receptor (Safety Analysis Set)
Table 14.2.1.2A	Comparison of progression-free survival (PFS) rate between two taxane strata (Safety Analysis Set)
Table 14.2.1.2B	Comparison of progression-free survival (PFS) rate between two taxane strata: negative hormone receptors (Safety Analysis Set)
Table 14.2.2A	Kaplan-Meier estimate of overall survival (OS) (Safety Analysis Set)
Table 14.2.2B	Kaplan-Meier estimate of overall survival (OS): negative hormone receptors (Safety Analysis Set)
Table 14.2.3A	Objective response rate (Safety Analysis Set)
Table 14.2.3B	Objective response rate: negative hormone receptors (Safety Analysis Set)

Table 14.2.1.1A
Progression Free Survival (PFS) (Safety Analysis Set)

Variable Statistic	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Number (%) of Subjects with Events				
Disease Progression	n (%)	66 (80.5%)	53 (69.7%)	119 (75.3%)
Death	n (%)	6 (7.3%)	12 (15.8%)	18 (11.4%)
Number (%) of Subjects Censored [1]	n (%)	10 (12.2%)	11 (14.5%)	21 (13.3%)
Summary Statistics of PFS [2]	Q1 (95% CI)	2.5 (1.9, 3.8)	4.7 (2.5, 5.5)	3.5 (2.3, 4.6)
	Median (95% CI)	6.0 (4.5, 8.1)	8.4 (5.6, 9.8)	7.3 (5.6, 8.7)
	Q3 (95% CI)	11.0 (8.8, 16.1)	11.6 (10.0, 15.3)	11.5 (10.0, 12.9)
Follow Up Time [3]	n	82	76	158
	Mean (SD)	7.5 (6.61)	8.1 (5.49)	7.8 (6.08)
	Median	5.8	7.3	6.0
	Q1, Q3	2.5, 10.2	3.9, 11.1	2.8, 11.0
	Min, Max	0.1, 31.3	1.1, 26.5	0.1, 31.3
Hazard Ratio, NLG-2101 versus Placebo [4]	HR (95% CI)	1.144 (0.813, 1.609)		

Note: There were 6 subjects without definitive lack of progression documented and therefore they were excluded from this summary.
[1] Subjects who have not experienced disease progression or death at the time of analysis will be censored at the last time that lack of definitive progression was objectively documented.
[2] Progression Free Survival (PFS) represents the number of months from first dose to disease progression or death, whichever occurs first. Kaplan-Meier estimates were used.
[3] Follow up time is the number of months from first dose to progressive disease, death or last time lack of definitive progression was documented.
[4] Based on Cox Proportional Hazards Model.

Table 14.2.1.1B
Progression-Free Survival (PFS): Negative Hormone Receptors (Safety Analysis Set)

Variable Statistic	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Number (%) of Subjects with Events				
Disease Progression	n (%)	20 (87.0%)	18 (78.3%)	38 (82.6%)
Death	n (%)	1 (4.3%)	1 (4.3%)	2 (4.3%)
Number (%) of Subjects Censored [1]	n (%)	2 (8.7%)	4 (17.4%)	6 (13.0%)
Summary Statistics of PFS [2]	Q1 (95% CI)	1.9 (0.1, 2.5)	2.5 (1.1, 5.1)	2.2 (1.4, 2.7)
	Median (95% CI)	2.8 (2.2, 5.8)	7.1 (2.5, 9.6)	5.1 (2.5, 7.1)
	Q3 (95% CI)	8.1 (3.6, 13.0)	9.8 (7.3, NA)	8.8 (6.9, 13.0)
Follow Up Time [3]	n	23	23	46
	Mean (SD)	5.1 (4.19)	6.7 (4.77)	5.9 (4.51)
	Median	2.8	5.5	5.1
	Q1, Q3	1.9, 8.1	2.5, 9.8	2.2, 8.8
	Min, Max	0.1, 13.5	1.1, 18.0	0.1, 18.0
Hazard Ratio, NLG-2101 versus Placebo [4]	HR (95% CI)	1.385 (0.738, 2.600)		

Note: There were 6 subjects without definitive lack of progression documented and therefore they were excluded from this summary.
[1] Subjects who have not experienced disease progression or death at the time of analysis will be censored at the last time that lack of definitive progression was objectively documented.
[2] Progression Free Survival (PFS) represents the number of months from first dose to disease progression or death, whichever occurs first. Kaplan-Meier estimates were used.
[3] Follow up time is the number of months from first dose to progressive disease, death or last time lack of definitive progression was documented.
[4] Based on Cox Proportional Hazards Model.

Table 14.2.1.2A
Comparison of Progression Free Survival (PFS) Rate between Two Taxane Strata (Safety Analysis Set)

Variable -tic	Statis -tic	------- NLG-2101 ------- Docetaxel (N=62)	Paclitxel (N=23)	------- Placebo ------- Docetaxel (N=59)	Paclitxel (N=20)	------- Overall ------- Docetaxel (N=121)	Paclitxel (N=43)
Number (%) of Subjects with Events							
Disease Progression	n (%)	45(75.0%)	21(95.5%)	39(68.4%)	14(73.7%)	84(71.8%)	35(85.4%)
Death	n (%)	6(10.0%)	0	9(15.8%)	3(15.8%)	15(12.8%)	3(7.3%)
Number (%) of Subjects Censored [1]	n (%)	9(15.0%)	1(4.5%)	9(15.8%)	2(10.5%)	18(15.4%)	3(7.3%)
Summary Statistics of PFS [2]	Q1 (95% CI)	2.9(1.5,5.7)	1.9(1.5,2.7)	4.7(2.5,5.5)	3.5(1.4,7.3)	4.0(2.5,5.1)	2.3(1.8,3.6)
	Median (95% CI)	7.9(5.7,9.5)	3.6(1.9,5.5)	8.4(5.5,10.0)	8.7(3.5,10.9)	8.1(5.7,9.2)	5.5(2.7,8.7)
	Q3 (95% CI)	12.3(9.5,20.0)	5.8(3.6,13.0)	12.4(10.0,15.4)	11.0(8.7,16.8)	12.4(10.3,15.4)	9.9(7.3,11.6)

Note: There were 6 subjects without definitive lack of progression documented and therefore they were excluded from this summary.
[1] Subjects who have not experienced disease progression or death at the time of analysis will be censored at the last time that lack of definitive progression was objectively documented.
[2] Progression Free Survival (PFS) represents the number of months from first dose to disease progression or death, whichever occurs first. Kaplan-Meier estimates were used.
[3] Follow up time is the number of months from first dose to progressive disease, death or last time lack of definitive progression was documented.

Table 14.2.1.2A
Comparison of Progression Free Survival (PFS) Rate between Two Taxane Strata (Safety Analysis Set)

Variable -tic	Statis -tic	NLG-2101 Docetaxel (N=62)	NLG-2101 Paclitxel (N=23)	Placebo Docetaxel (N=59)	Placebo Paclitxel (N=20)	Overall Docetaxel (N=121)	Overall Paclitxel (N=43)
Follow Up Time [3]	n	60	22	57	19	117	41
	Mean (SD)	8.4(7.08)	5.0(4.27)	8.2(5.87)	7.7(4.25)	8.3(6.49)	6.2(4.43)
	Median	7.0	3.4	6.0	8.7	6.9	5.5
	Q1, Q3	2.9,11.4	1.9,5.8	4.0,11.6	3.5,10.9	3.7,11.5	2.3,9.6
	Min, Max	0.1,31.3	1.5,17.9	1.1,26.5	1.4,16.8	0.1,31.3	1.4,17.9

Note: There were 6 subjects without definitive lack of progression documented and therefore they were excluded from this summary.
[1] Subjects who have not experienced disease progression or death at the time of analysis will be censored at the last time that lack of definitive progression was objectively documented.
[2] Progression Free Survival (PFS) represents the number of months from first dose to disease progression or death, whichever occurs first. Kaplan-Meier estimates were used.
[3] Follow up time is the number of months from first dose to progressive disease, death or last time lack of definitive progression was documented.

Table 14.2.1.2B
Comparison of Progression Free Survival (PFS) Rate between two Taxane Strata: Negative Hormone Receptors (Safety Analysis Set)

Variable -tic	Statis -tic	------- NLG-2101 ------- Docetaxel (N=14)	Paclitxel (N=9)	------- Placebo ------- Docetaxel (N=16)	Paclitxel (N=7)	------- Overall ------- Docetaxel (N=30)	Paclitxel (N=16)
Number (%) of Subjects with Events							
Disease Progression	n (%)	11(78.6%)	9(100%)	12(75.0%)	6(85.7%)	23(76.7%)	15(93.8%)
Death	n (%)	1(7.1%)	0	1(6.3%)	0	2(6.7%)	0
Number (%) of Subjects Censored [1]	n (%)	2(14.3%)	0	3(18.8%)	1(14.3%)	5(16.7%)	1(6.3%)
Summary Statistics of PFS [2]	Q1 (95% CI)	1.4(0.1,2.5)	2.5(1.9,3.6)	2.5(1.1,5.1)	1.8(1.4,8.7)	1.6(1.1,2.5)	2.4(1.4,5.8)
	Median (95% CI)	2.7(1.2,6.9)	3.6(1.9,11.0)	5.1(2.5,9.8)	8.7(1.4,9.9)	5.1(2.5,6.9)	6.6(2.3,9.6)
	Q3 (95% CI)	6.9(2.5,NA)	8.8(2.7,13.0)	9.8(5.1,NA)	9.9(7.3,NA)	8.1(5.5,NA)	9.8(5.8,13.0)

Note: There were 6 subjects without definitive lack of progression documented and therefore they were excluded from this summary.
[1] Subjects who have not experienced disease progression or death at the time of analysis will be censored at the last time that lack of definitive progression was objectively documented.
[2] Progression Free Survival (PFS) represents the number of months from first dose to disease progression or death, whichever occurs first. Kaplan-Meier estimates were used.
[3] Follow up time is the number of months from first dose to progressive disease, death or last time lack of definitive progression was documented.

Table 14.2.1.2B
Comparison of Progression Free Survival (PFS) Rate between two Taxane Strata: Negative Hormone Receptors (Safety Analysis Set)

Variable -tic	Statis -tic	------- NLG-2101 ------- Docetaxel (N=14)	Paclitxel (N=9)	------- Placebo ------- Docetaxel (N=16)	Paclitxel (N=7)	------- Overall ------- Docetaxel (N=30)	Paclitxel (N=16)
Follow Up Time [3]	n	14	9	16	7	30	16
	Mean (SD)	4.6(4.29)	5.7(4.19)	6.5(5.19)	7.1(3.94)	5.6(4.80)	6.3(4.01)
	Median	2.7	3.6	5.1	8.7	4.9	6.6
	Q1, Q3	1.4,6.9	2.5,8.8	2.5,9.3	1.8,9.9	1.6,8.1	2.4,9.8
	Min, Max	0.1,13.5	1.9,13.0	1.1,18.0	1.4,11.1	0.1,18.0	1.4,13.0

Note: There were 6 subjects without definitive lack of progression documented and therefore they were excluded from this summary.
[1] Subjects who have not experienced disease progression or death at the time of analysis will be censored at the last time that lack of definitive progression was objectively documented.
[2] Progression Free Survival (PFS) represents the number of months from first dose to disease progression or death, whichever occurs first. Kaplan-Meier estimates were used.
[3] Follow up time is the number of months from first dose to progressive disease, death or last time lack of definitive progression was documented.

Table 14.2.2A
Kaplan-Meier Estimate of Overall Survival (OS) (Safety Analysis Set)

Variable Statistic	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Number (%) of Subjects with Events Death	n (%)	43 (50.6%)	37 (46.8%)	80 (48.8%)
Number (%) of Subjects Censored [1]	n (%)	42 (49.4%)	42 (53.2%)	84 (51.2%)
Summary Statistics of OS [2]	Q1 (95% CI)	9.9 (6.8, 12.9)	10.9 (6.0, 16.3)	10.2 (7.5, 12.4)
	Median (95% CI)	21.6 (16.0, 39.1)	21.2 (19.1, 32.1)	21.4 (19.4, 31.2)
	Q3 (95% CI)	39.1 (31.2, NA)	NA (23.70, NA)	39.1 (31.2, NA)
Follow Up Time [3]	n	85	79	164
	Mean (SD)	16.5 (9.30)	15.3 (8.53)	16.0 (8.93)
	Median	18.6	16.6	17.4
	Q1, Q3	9.2, 21.9	7.5, 21.2	8.8, 21.6
	Min, Max	0.1, 39.4	0.3, 35.0	0.1, 39.4

[1] Subjects who are still alive at the time of analysis will be censored at the last day they were known to be alive.
[2] Overall (OS) represents the number of months from first dose to the date of death. Kaplan-Meier estimates are presented.
[3] Follow up time is the number of months from first dose to death or last time that subject was known to be alive was documented.

Table 14.2.2B
Kaplan-Meier Estimate of Overall Survival (OS): Negative Hormone Receptors (Safety Analysis Set)

Variable Statistic	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Number (%) of Subjects with Events Death	n (%)	16 (69.6%)	11 (47.8%)	27 (58.7%)
Number (%) of Subjects Censored [1]	n (%)	7 (30.4%)	12 (52.2%)	19 (41.3%)
Summary Statistics of OS [2]	Q1 (95% CI)	6.8 (0.1, 10.0)	10.2 (3.4, 19.5)	8.0 (3.6, 10.4)
	Median (95% CI)	10.6 (8.0, 21.6)	21.2 (10.2, NA)	15.4 (10.2, 21.6)
	Q3 (95% CI)	NA (12.60, NA)	NA (21.20, NA)	NA (21.20, NA)
Follow Up Time [3]	n	23	23	46
	Mean (SD)	13.6 (9.74)	14.0 (8.20)	13.8 (8.90)
	Median	10.6	12.1	11.8
	Q1, Q3	6.8, 20.5	7.4, 20.3	7.4, 20.5
	Min, Max	0.1, 35.7	3.4, 32.7	0.1, 35.7

[1] Subjects who are still alive at the time of analysis will be censored at the last day they were known to be alive.
[2] Overall (OS) represents the number of months from first dose to the date of death. Kaplan-Meier estimates are presented.
[3] Follow up time is the number of months from first dose to death or last time that subject was known to be alive was documented.

Table 14.2.3A
Objective Response Rate (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
RECIST Best Response				
Complete Response	n (%)	3 (3.5)	2 (2.5)	5 (3.0)
Partial response	n (%)	31 (36.5)	27 (34.2)	58 (35.4)
Stable disease	n (%)	31 (36.5)	35 (44.3)	66 (40.2)
Progressive disease	n (%)	13 (15.3)	9 (11.4)	22 (13.4)
Not Evaluable	n (%)	0	0	0
Complete or Partial Response	n (%)	34 (40.0)	29 (36.7)	63 (38.4)
P-value [1]		0.7414		
95% CI [2]		33.1, 54.6	29.3, 51.2	34.2, 49.7

[1] P-value based on Fishers Exact Test.
[2] 95%CI is based on Wilsons Method.

Table 14.2.3B
Objective Response Rate: Negative Hormone receptors (Safety Analysis Set)

Parameter	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
RECIST Best Response				
Complete Response	n (%)	1 (4.3)	1 (4.3)	2 (4.3)
Partial response	n (%)	5 (21.7)	8 (34.8)	13 (28.3)
Stable disease	n (%)	9 (39.1)	8 (34.8)	17 (37.0)
Progressive disease	n (%)	5 (21.7)	5 (21.7)	10 (21.7)
Not Evaluable	n (%)	0	0	0
Complete or Partial Response	n (%)	6 (26.1)	9 (39.1)	15 (32.6)
P-value [1]		0.5311		
95% CI [2]		14.5, 51.9	23.3, 61.3	23.0, 50.8

[1] P-value based on Fishers Exact Test.
[2] 95%CI is based on Wilsons Method.

2.3 Safety Data

2.3.1 Display of Adverse Events

Table Number	Table Title
Table 14.3.1.1A	Summary of treatment-emergent adverse events (Safety Analysis Set)
Table 14.3.1.1B	Summary of treatment-emergent adverse events: negative hormone receptors (Safety Analysis Set)
Table 14.3.1.2A	Treatment-emergent adverse events by system organ class and preferred term (Safety Analysis Set)
Table 14.3.1.2B	Treatment-emergent adverse events by system organ class and preferred term: negative hormone receptors (Safety Analysis Set)
Table 14.3.1.3A	Related treatment-emergent adverse events by system organ class and preferred term (Safety Analysis Set)
Table 14.3.1.4A	Serious treatment-emergent adverse events by system organ class and preferred term (Safety Analysis Set)
Table 14.3.1.4B	Serious treatment-emergent adverse events by system organ class and preferred term: negative hormone receptors (Safety Analysis Set)
Table 14.3.1.5A	Treatment-emergent adverse events with CTCAE severity >= grade 3 by system organ class and preferred term (Safety Analysis Set)
Table 14.3.1.5B	Treatment-emergent adverse events with CTCAE severity >= grade 3 by system organ class and preferred term: negative hormone receptors (Safety Analysis Set)
Table 14.3.2.1	Listing of adverse events leading to subject deaths (Safety Analysis Set)
Table 14.3.2.2	Listing of subjects with serious adverse events (Safety Analysis Set)
Table 14.3.2.3	Listing of subjects with adverse events leading to study discontinuation (Safety Analysis Set)

Table 14.3.1.1A
Summary of Treatment-Emergent Adverse Events (Safety Analysis Set)

Category	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
At Least 1 TEAE	n (%)	85 (100)	78 (98.7)	163 (99.4)
At Least 1 Related TEAE	n (%)	58 (68.2)	63 (79.7)	121 (73.8)
At Least 1 Grade >=3 TEAE	n (%)	51 (60.0)	48 (60.8)	99 (60.4)
At Least 1 SAE	n (%)	29 (34.1)	28 (35.4)	57 (34.8)
At Least 1 TEAE Leading to Study Discontinuation	n (%)	11 (12.9)	10 (12.7)	21 (12.8)
At Least 1 TEAE Leading to Death	n (%)	4 (4.7)	2 (2.5)	6 (3.7)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.1B
Summary of Treatment-Emergent Adverse Events: Negative Hormone Receptors (Safety Analysis Set)

Category	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
At Least 1 TEAE	n (%)	23 (100)	22 (95.7)	45 (97.8)
At Least 1 Related TEAE	n (%)	17 (73.9)	20 (87.0)	37 (80.4)
At Least 1 Grade >=3 TEAE	n (%)	15 (65.2)	13 (56.5)	28 (60.9)
At Least 1 SAE	n (%)	10 (43.5)	7 (30.4)	17 (37.0)
At Least 1 TEAE Leading to Study Discontinuation	n (%)	2 (8.7)	1 (4.3)	3 (6.5)
At Least 1 TEAE Leading to Death	n (%)	1 (4.3)	1 (4.3)	2 (4.3)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
At Least 1 TEAE	n (%)	85(100.0)	78(98.7)	163(99.4)
Blood and lymphatic system disorders	n (%)	43(50.6)	32(40.5)	75(45.7)
Anaemia	n (%)	28(32.9)	15(19.0)	43(26.2)
Febrile neutropenia	n (%)	2(2.4)	4(5.1)	6(3.7)
Granulocytopenia	n (%)	0	1(1.3)	1(0.6)
Iron deficiency anaemia	n (%)	1(1.2)	0	1(0.6)
Leukocytosis	n (%)	1(1.2)	2(2.5)	3(1.8)
Leukopenia	n (%)	2(2.4)	1(1.3)	3(1.8)
Lymphopenia	n (%)	0	1(1.3)	1(0.6)
Neutropenia	n (%)	14(16.5)	15(19.0)	29(17.7)
Pancytopenia	n (%)	0	1(1.3)	1(0.6)
Thrombocytopenia	n (%)	3(3.5)	3(3.8)	6(3.7)
Thrombocytosis	n (%)	0	1(1.3)	1(0.6)
Cardiac disorders	n (%)	12(14.1)	9(11.4)	21(12.8)
Angina pectoris	n (%)	2(2.4)	2(2.5)	4(2.4)
Arrhythmia	n (%)	2(2.4)	0	2(1.2)
Atrial fibrillation	n (%)	0	1(1.3)	1(0.6)
Coronary artery disease	n (%)	0	1(1.3)	1(0.6)
Coronary artery insufficiency	n (%)	0	1(1.3)	1(0.6)
Palpitations	n (%)	2(2.4)	0	2(1.2)
Pericardial effusion	n (%)	1(1.2)	0	1(0.6)
Sinus tachycardia	n (%)	4(4.7)	5(6.3)	9(5.5)
Tachycardia	n (%)	3(3.5)	0	3(1.8)
Ear and labyrinth disorders	n (%)	3(3.5)	10(12.7)	13(7.9)
Cerumen impaction	n (%)	1(1.2)	0	1(0.6)
Ear discomfort	n (%)	0	1(1.3)	1(0.6)
Ear pain	n (%)	2(2.4)	1(1.3)	3(1.8)
Hearing impaired	n (%)	1(1.2)	0	1(0.6)
Hypoacusis	n (%)	0	1(1.3)	1(0.6)
Tinnitus	n (%)	0	3(3.8)	3(1.8)
Vertigo	n (%)	1(1.2)	3(3.8)	4(2.4)
Vertigo labyrinthine	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Vestibular disorder	n (%)	0	1(1.3)	1(0.6)
Endocrine disorders	n (%)	0	1(1.3)	1(0.6)
Adrenal insufficiency	n (%)	0	1(1.3)	1(0.6)
Eye disorders	n (%)	20(23.5)	27(34.2)	47(28.7)
Altered visual depth perception	n (%)	0	1(1.3)	1(0.6)
Chalazion	n (%)	0	1(1.3)	1(0.6)
Conjunctival haemorrhage	n (%)	0	1(1.3)	1(0.6)
Conjunctivitis	n (%)	3(3.5)	0	3(1.8)
Dry eye	n (%)	0	4(5.1)	4(2.4)
Eye irritation	n (%)	1(1.2)	0	1(0.6)
Eye pain	n (%)	1(1.2)	1(1.3)	2(1.2)
Eyelid oedema	n (%)	1(1.2)	0	1(0.6)
Lacrimation increased	n (%)	10(11.8)	11(13.9)	21(12.8)
Ocular hyperaemia	n (%)	1(1.2)	1(1.3)	2(1.2)
Periorbital oedema	n (%)	1(1.2)	1(1.3)	2(1.2)
Photophobia	n (%)	2(2.4)	4(5.1)	6(3.7)
Photopsia	n (%)	1(1.2)	0	1(0.6)
Vision blurred	n (%)	8(9.4)	10(12.7)	18(11.0)
Visual impairment	n (%)	1(1.2)	4(5.1)	5(3.0)
Gastrointestinal disorders	n (%)	63(74.1)	64(81.0)	127(77.4)
Abdominal distension	n (%)	2(2.4)	5(6.3)	7(4.3)
Abdominal pain	n (%)	13(15.3)	15(19.0)	28(17.1)
Abdominal pain upper	n (%)	3(3.5)	6(7.6)	9(5.5)
Aphthous stomatitis	n (%)	1(1.2)	1(1.3)	2(1.2)
Ascites	n (%)	1(1.2)	3(3.8)	4(2.4)
Colitis	n (%)	1(1.2)	0	1(0.6)
Constipation	n (%)	24(28.2)	27(34.2)	51(31.1)
Dental caries	n (%)	0	1(1.3)	1(0.6)
Diarrhoea	n (%)	30(35.3)	31(39.2)	61(37.2)
Dry mouth	n (%)	6(7.1)	5(6.3)	11(6.7)
Dyspepsia	n (%)	4(4.7)	3(3.8)	7(4.3)
Dysphagia	n (%)	2(2.4)	2(2.5)	4(2.4)
Enterocolitis	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Eructation	n (%)	1(1.2)	0	1(0.6)
Faecal incontinence	n (%)	1(1.2)	0	1(0.6)
Flatulence	n (%)	0	1(1.3)	1(0.6)
Gastric dilatation	n (%)	1(1.2)	0	1(0.6)
Gastric stenosis	n (%)	0	1(1.3)	1(0.6)
Gastric varices haemorrhage	n (%)	0	1(1.3)	1(0.6)
Gastrointestinal haemorrhage	n (%)	1(1.2)	0	1(0.6)
Gastrooesophageal reflux disease	n (%)	4(4.7)	4(5.1)	8(4.9)
Gingival bleeding	n (%)	0	1(1.3)	1(0.6)
Gingival erythema	n (%)	0	1(1.3)	1(0.6)
Gingival pain	n (%)	0	1(1.3)	1(0.6)
Glossitis	n (%)	0	1(1.3)	1(0.6)
Glossodynia	n (%)	1(1.2)	1(1.3)	2(1.2)
Haemorrhoidal haemorrhage	n (%)	1(1.2)	0	1(0.6)
Haemorrhoids	n (%)	1(1.2)	2(2.5)	3(1.8)
Hypoaesthesia oral	n (%)	0	1(1.3)	1(0.6)
Ileus	n (%)	1(1.2)	0	1(0.6)
Large intestine perforation	n (%)	2(2.4)	0	2(1.2)
Lip dry	n (%)	1(1.2)	0	1(0.6)
Lip swelling	n (%)	1(1.2)	0	1(0.6)
Mouth ulceration	n (%)	1(1.2)	0	1(0.6)
Mucous stools	n (%)	0	2(2.5)	2(1.2)
Nausea	n (%)	40(47.1)	38(48.1)	78(47.6)
Obstruction gastric	n (%)	0	1(1.3)	1(0.6)
Oesophageal pain	n (%)	0	1(1.3)	1(0.6)
Oesophagitis	n (%)	1(1.2)	1(1.3)	2(1.2)
Oral discomfort	n (%)	1(1.2)	0	1(0.6)
Oral pain	n (%)	3(3.5)	6(7.6)	9(5.5)
Paraesthesia oral	n (%)	1(1.2)	0	1(0.6)
Reflux gastritis	n (%)	0	1(1.3)	1(0.6)
Salivary hypersecretion	n (%)	0	1(1.3)	1(0.6)
Stomatitis	n (%)	11(12.9)	10(12.7)	21(12.8)
Swollen tongue	n (%)	1(1.2)	0	1(0.6)
Tongue coated	n (%)	1(1.2)	0	1(0.6)
Vomiting	n (%)	20(23.5)	28(35.4)	48(29.3)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
General disorders and administration site conditions	n (%)	68(80.0)	60(75.9)	128(78.0)
Asthenia	n (%)	9(10.6)	14(17.7)	23(14.0)
Axillary pain	n (%)	1(1.2)	3(3.8)	4(2.4)
Catheter site oedema	n (%)	0	1(1.3)	1(0.6)
Catheter site pain	n (%)	2(2.4)	2(2.5)	4(2.4)
Chest discomfort	n (%)	1(1.2)	1(1.3)	2(1.2)
Chest pain	n (%)	0	2(2.5)	2(1.2)
Chills	n (%)	2(2.4)	2(2.5)	4(2.4)
Device dislocation	n (%)	1(1.2)	0	1(0.6)
Early satiety	n (%)	1(1.2)	0	1(0.6)
Effusion	n (%)	0	1(1.3)	1(0.6)
Face oedema	n (%)	2(2.4)	3(3.8)	5(3.0)
Facial pain	n (%)	1(1.2)	0	1(0.6)
Fatigue	n (%)	52(61.2)	36(45.6)	88(53.7)
Gait disturbance	n (%)	2(2.4)	3(3.8)	5(3.0)
Generalised oedema	n (%)	1(1.2)	0	1(0.6)
Influenza like illness	n (%)	2(2.4)	3(3.8)	5(3.0)
Injection site pain	n (%)	0	1(1.3)	1(0.6)
Localised oedema	n (%)	3(3.5)	2(2.5)	5(3.0)
Malaise	n (%)	0	2(2.5)	2(1.2)
Mucosal dryness	n (%)	1(1.2)	0	1(0.6)
Mucosal inflammation	n (%)	5(5.9)	3(3.8)	8(4.9)
Multi-organ failure	n (%)	1(1.2)	0	1(0.6)
Non-cardiac chest pain	n (%)	4(4.7)	5(6.3)	9(5.5)
Oedema	n (%)	3(3.5)	2(2.5)	5(3.0)
Oedema peripheral	n (%)	26(30.6)	23(29.1)	49(29.9)
Pain	n (%)	0	4(5.1)	4(2.4)
Pyrexia	n (%)	6(7.1)	7(8.9)	13(7.9)
Spinal pain	n (%)	1(1.2)	3(3.8)	4(2.4)
Sudden death	n (%)	1(1.2)	0	1(0.6)
Thrombosis in device	n (%)	0	1(1.3)	1(0.6)
Hepatobiliary disorders	n (%)	4(4.7)	7(8.9)	11(6.7)
Bile duct stenosis	n (%)	0	1(1.3)	1(0.6)
Cholecystitis	n (%)	1(1.2)	0	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Hepatic failure	n (%)	1(1.2)	1(1.3)	2(1.2)
Hepatic pain	n (%)	0	1(1.3)	1(0.6)
Hepatitis	n (%)	1(1.2)	1(1.3)	2(1.2)
Hyperbilirubinaemia	n (%)	0	2(2.5)	2(1.2)
Hypertransaminasaemia	n (%)	1(1.2)	0	1(0.6)
Jaundice	n (%)	1(1.2)	1(1.3)	2(1.2)
Immune system disorders	n (%)	2(2.4)	1(1.3)	3(1.8)
Allergic sinusitis	n (%)	0	1(1.3)	1(0.6)
Hypersensitivity	n (%)	1(1.2)	0	1(0.6)
Seasonal allergy	n (%)	1(1.2)	0	1(0.6)
Infections and infestations	n (%)	32(37.6)	38(48.1)	70(42.7)
Atypical pneumonia	n (%)	1(1.2)	0	1(0.6)
Bacterial infection	n (%)	0	1(1.3)	1(0.6)
Bronchitis	n (%)	0	1(1.3)	1(0.6)
Candidiasis	n (%)	2(2.4)	2(2.5)	4(2.4)
Cellulitis	n (%)	0	1(1.3)	1(0.6)
Clostridium difficile infection	n (%)	0	1(1.3)	1(0.6)
Cystitis	n (%)	1(1.2)	0	1(0.6)
Diverticulitis	n (%)	1(1.2)	1(1.3)	2(1.2)
Ear infection	n (%)	1(1.2)	0	1(0.6)
Eye infection	n (%)	0	3(3.8)	3(1.8)
Fungal infection	n (%)	1(1.2)	0	1(0.6)
Fungal skin infection	n (%)	0	1(1.3)	1(0.6)
Furuncle	n (%)	1(1.2)	0	1(0.6)
Herpes zoster	n (%)	0	1(1.3)	1(0.6)
Infection	n (%)	1(1.2)	0	1(0.6)
Influenza	n (%)	0	1(1.3)	1(0.6)
Laryngitis	n (%)	0	1(1.3)	1(0.6)
Lung infection	n (%)	0	1(1.3)	1(0.6)
Mucosal infection	n (%)	1(1.2)	0	1(0.6)
Nail infection	n (%)	0	2(2.5)	2(1.2)
Nasopharyngitis	n (%)	2(2.4)	4(5.1)	6(3.7)
Onychomycosis	n (%)	1(1.2)	1(1.3)	2(1.2)
Oral candidiasis	n (%)	3(3.5)	1(1.3)	4(2.4)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Oral herpes	n (%)	1(1.2)	1(1.3)	2(1.2)
Oral infection	n (%)	2(2.4)	0	2(1.2)
Paronychia	n (%)	1(1.2)	2(2.5)	3(1.8)
Periodontitis	n (%)	1(1.2)	0	1(0.6)
Pharyngitis	n (%)	0	2(2.5)	2(1.2)
Pneumonia	n (%)	3(3.5)	4(5.1)	7(4.3)
Respiratory tract infection	n (%)	1(1.2)	1(1.3)	2(1.2)
Rhinitis	n (%)	3(3.5)	0	3(1.8)
Sepsis	n (%)	1(1.2)	1(1.3)	2(1.2)
Sinusitis	n (%)	3(3.5)	2(2.5)	5(3.0)
Skin infection	n (%)	1(1.2)	2(2.5)	3(1.8)
Tinea infection	n (%)	0	1(1.3)	1(0.6)
Upper respiratory tract infection	n (%)	9(10.6)	7(8.9)	16(9.8)
Urinary tract infection	n (%)	5(5.9)	12(15.2)	17(10.4)
Vaginal infection	n (%)	2(2.4)	0	2(1.2)
Vaginitis bacterial	n (%)	0	1(1.3)	1(0.6)
Viral infection	n (%)	1(1.2)	1(1.3)	2(1.2)
Viral upper respiratory tract infection	n (%)	0	1(1.3)	1(0.6)
Vulvovaginal mycotic infection	n (%)	1(1.2)	1(1.3)	2(1.2)
Wound infection	n (%)	1(1.2)	0	1(0.6)
Injury, poisoning and procedural complications	n (%)	7(8.2)	14(17.7)	21(12.8)
Ankle fracture	n (%)	0	1(1.3)	1(0.6)
Contrast media reaction	n (%)	0	1(1.3)	1(0.6)
Contusion	n (%)	0	2(2.5)	2(1.2)
Fall	n (%)	1(1.2)	4(5.1)	5(3.0)
Femur fracture	n (%)	1(1.2)	1(1.3)	2(1.2)
Graft complication	n (%)	1(1.2)	0	1(0.6)
Ilium fracture	n (%)	0	1(1.3)	1(0.6)
Infusion related reaction	n (%)	3(3.5)	2(2.5)	5(3.0)
Nail injury	n (%)	0	2(2.5)	2(1.2)
Post procedural discharge	n (%)	0	1(1.3)	1(0.6)
Post procedural haemorrhage	n (%)	0	1(1.3)	1(0.6)
Scar	n (%)	0	1(1.3)	1(0.6)
Wound complication	n (%)	2(2.4)	0	2(1.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Investigations	n (%)	32(37.6)	33(41.8)	65(39.6)
Alanine aminotransferase increased	n (%)	6(7.1)	7(8.9)	13(7.9)
Anion gap decreased	n (%)	1(1.2)	0	1(0.6)
Aspartate aminotransferase increased	n (%)	11(12.9)	9(11.4)	20(12.2)
Blood albumin decreased	n (%)	3(3.5)	0	3(1.8)
Blood alkaline phosphatase increased	n (%)	6(7.1)	3(3.8)	9(5.5)
Blood bilirubin increased	n (%)	1(1.2)	4(5.1)	5(3.0)
Blood calcium decreased	n (%)	1(1.2)	0	1(0.6)
Blood calcium increased	n (%)	1(1.2)	0	1(0.6)
Blood creatine increased	n (%)	1(1.2)	0	1(0.6)
Blood creatinine increased	n (%)	8(9.4)	3(3.8)	11(6.7)
Blood folate decreased	n (%)	1(1.2)	0	1(0.6)
Blood glucose increased	n (%)	1(1.2)	0	1(0.6)
Blood lactate dehydrogenase increased	n (%)	1(1.2)	1(1.3)	2(1.2)
Blood potassium decreased	n (%)	1(1.2)	1(1.3)	2(1.2)
Blood pressure decreased	n (%)	0	3(3.8)	3(1.8)
Blood sodium decreased	n (%)	0	1(1.3)	1(0.6)
C-reactive protein increased	n (%)	0	1(1.3)	1(0.6)
General physical condition normal	n (%)	1(1.2)	0	1(0.6)
Haemoglobin decreased	n (%)	3(3.5)	1(1.3)	4(2.4)
Heart rate increased	n (%)	1(1.2)	0	1(0.6)
Hepatic enzyme increased	n (%)	1(1.2)	1(1.3)	2(1.2)
International normalised ratio increased	n (%)	0	1(1.3)	1(0.6)
Lipase increased	n (%)	0	1(1.3)	1(0.6)
Lymphocyte count decreased	n (%)	18(21.2)	10(12.7)	28(17.1)
Mean cell volume abnormal	n (%)	0	1(1.3)	1(0.6)
Neutrophil count decreased	n (%)	6(7.1)	6(7.6)	12(7.3)
Platelet count decreased	n (%)	4(4.7)	1(1.3)	5(3.0)
Platelet count increased	n (%)	1(1.2)	0	1(0.6)
Protein total decreased	n (%)	1(1.2)	0	1(0.6)
Vitamin B12 decreased	n (%)	1(1.2)	0	1(0.6)
Vitamin D decreased	n (%)	2(2.4)	1(1.3)	3(1.8)
Weight decreased	n (%)	2(2.4)	6(7.6)	8(4.9)
Weight increased	n (%)	3(3.5)	3(3.8)	6(3.7)
White blood cell count decreased	n (%)	8(9.4)	10(12.7)	18(11.0)
White blood cell count increased	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Metabolism and nutrition disorders	n (%)	51(60.0)	40(50.6)	91(55.5)
Cachexia	n (%)	1(1.2)	0	1(0.6)
Decreased appetite	n (%)	17(20.0)	19(24.1)	36(22.0)
Dehydration	n (%)	4(4.7)	6(7.6)	10(6.1)
Hypercalcaemia	n (%)	5(5.9)	4(5.1)	9(5.5)
Hyperglycaemia	n (%)	20(23.5)	7(8.9)	27(16.5)
Hyperkalaemia	n (%)	5(5.9)	4(5.1)	9(5.5)
Hypernatraemia	n (%)	4(4.7)	0	4(2.4)
Hyperphosphataemia	n (%)	1(1.2)	0	1(0.6)
Hyperuricaemia	n (%)	0	1(1.3)	1(0.6)
Hypoalbuminaemia	n (%)	6(7.1)	5(6.3)	11(6.7)
Hypocalcaemia	n (%)	8(9.4)	6(7.6)	14(8.5)
Hypochloraemia	n (%)	0	1(1.3)	1(0.6)
Hypoglycaemia	n (%)	0	1(1.3)	1(0.6)
Hypokalaemia	n (%)	5(5.9)	8(10.1)	13(7.9)
Hypomagnesaemia	n (%)	2(2.4)	2(2.5)	4(2.4)
Hyponatraemia	n (%)	5(5.9)	3(3.8)	8(4.9)
Hypophosphataemia	n (%)	6(7.1)	6(7.6)	12(7.3)
Increased appetite	n (%)	1(1.2)	0	1(0.6)
Malnutrition	n (%)	0	1(1.3)	1(0.6)
Vitamin D deficiency	n (%)	1(1.2)	1(1.3)	2(1.2)
Musculoskeletal and connective tissue disorders	n (%)	56(65.9)	45(57.0)	101(61.6)
Arthralgia	n (%)	17(20.0)	16(20.3)	33(20.1)
Back pain	n (%)	8(9.4)	13(16.5)	21(12.8)
Bone pain	n (%)	19(22.4)	14(17.7)	33(20.1)
Flank pain	n (%)	0	1(1.3)	1(0.6)
Groin pain	n (%)	0	1(1.3)	1(0.6)
Joint range of motion decreased	n (%)	1(1.2)	0	1(0.6)
Joint stiffness	n (%)	1(1.2)	0	1(0.6)
Joint swelling	n (%)	2(2.4)	3(3.8)	5(3.0)
Muscle spasms	n (%)	3(3.5)	3(3.8)	6(3.7)
Muscle tightness	n (%)	0	1(1.3)	1(0.6)
Muscular weakness	n (%)	8(9.4)	7(8.9)	15(9.1)
Musculoskeletal chest pain	n (%)	5(5.9)	7(8.9)	12(7.3)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Musculoskeletal pain	n (%)	5(5.9)	4(5.1)	9(5.5)
Musculoskeletal stiffness	n (%)	0	1(1.3)	1(0.6)
Myalgia	n (%)	7(8.2)	12(15.2)	19(11.6)
Neck pain	n (%)	2(2.4)	0	2(1.2)
Osteonecrosis of jaw	n (%)	0	1(1.3)	1(0.6)
Pain in extremity	n (%)	13(15.3)	8(10.1)	21(12.8)
Pain in jaw	n (%)	1(1.2)	1(1.3)	2(1.2)
Pathological fracture	n (%)	0	1(1.3)	1(0.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	n (%)	0	3(3.8)	3(1.8)
Metastases to meninges	n (%)	0	1(1.3)	1(0.6)
Skin papilloma	n (%)	0	1(1.3)	1(0.6)
Tumour haemorrhage	n (%)	0	1(1.3)	1(0.6)
Nervous system disorders	n (%)	55(64.7)	56(70.9)	111(67.7)
Burning sensation	n (%)	1(1.2)	1(1.3)	2(1.2)
Convulsion	n (%)	0	1(1.3)	1(0.6)
Disturbance in attention	n (%)	2(2.4)	1(1.3)	3(1.8)
Dizziness	n (%)	11(12.9)	19(24.1)	30(18.3)
Dysgeusia	n (%)	12(14.1)	17(21.5)	29(17.7)
Epilepsy	n (%)	0	1(1.3)	1(0.6)
Headache	n (%)	19(22.4)	24(30.4)	43(26.2)
Hyperaesthesia	n (%)	0	1(1.3)	1(0.6)
Hypersomnia	n (%)	0	2(2.5)	2(1.2)
Hypoaesthesia	n (%)	2(2.4)	2(2.5)	4(2.4)
Memory impairment	n (%)	0	1(1.3)	1(0.6)
Migraine	n (%)	1(1.2)	0	1(0.6)
Neuralgia	n (%)	1(1.2)	0	1(0.6)
Neuropathy peripheral	n (%)	19(22.4)	19(24.1)	38(23.2)
Paraesthesia	n (%)	3(3.5)	6(7.6)	9(5.5)
Parkinson's disease	n (%)	1(1.2)	0	1(0.6)
Parosmia	n (%)	1(1.2)	0	1(0.6)
Peripheral motor neuropathy	n (%)	1(1.2)	0	1(0.6)
Peripheral sensorimotor neuropathy	n (%)	4(4.7)	1(1.3)	5(3.0)
Peripheral sensory neuropathy	n (%)	10(11.8)	14(17.7)	24(14.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Polyneuropathy	n (%)	3(3.5)	2(2.5)	5(3.0)
Reflexes abnormal	n (%)	1(1.2)	0	1(0.6)
Restless legs syndrome	n (%)	0	1(1.3)	1(0.6)
Sinus headache	n (%)	1(1.2)	0	1(0.6)
Somnolence	n (%)	1(1.2)	2(2.5)	3(1.8)
Syncope	n (%)	2(2.4)	2(2.5)	4(2.4)
Tremor	n (%)	3(3.5)	0	3(1.8)
Trigeminal neuralgia	n (%)	1(1.2)	0	1(0.6)
Psychiatric disorders	n (%)	25(29.4)	17(21.5)	42(25.6)
Affective disorder	n (%)	0	1(1.3)	1(0.6)
Anxiety	n (%)	7(8.2)	5(6.3)	12(7.3)
Confusional state	n (%)	1(1.2)	2(2.5)	3(1.8)
Depression	n (%)	2(2.4)	2(2.5)	4(2.4)
Disorientation	n (%)	1(1.2)	0	1(0.6)
Insomnia	n (%)	13(15.3)	11(13.9)	24(14.6)
Mental status changes	n (%)	1(1.2)	0	1(0.6)
Mood altered	n (%)	2(2.4)	1(1.3)	3(1.8)
Panic attack	n (%)	0	1(1.3)	1(0.6)
Restlessness	n (%)	1(1.2)	1(1.3)	2(1.2)
Renal and urinary disorders	n (%)	4(4.7)	7(8.9)	11(6.7)
Dysuria	n (%)	1(1.2)	2(2.5)	3(1.8)
Haematuria	n (%)	0	1(1.3)	1(0.6)
Hydronephrosis	n (%)	0	1(1.3)	1(0.6)
Micturition urgency	n (%)	1(1.2)	0	1(0.6)
Pollakiuria	n (%)	0	1(1.3)	1(0.6)
Renal failure acute	n (%)	1(1.2)	0	1(0.6)
Urinary incontinence	n (%)	1(1.2)	1(1.3)	2(1.2)
Urinary tract inflammation	n (%)	0	1(1.3)	1(0.6)
Reproductive system and breast disorders	n (%)	5(5.9)	3(3.8)	8(4.9)
Breast pain	n (%)	1(1.2)	1(1.3)	2(1.2)
Ovarian vein thrombosis	n (%)	0	1(1.3)	1(0.6)
Premature menopause	n (%)	1(1.2)	0	1(0.6)
Vaginal discharge	n (%)	0	1(1.3)	1(0.6)

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Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Vulvovaginal dryness	n (%)	1(1.2)	0	1(0.6)
Vulvovaginal pruritus	n (%)	2(2.4)	0	2(1.2)
Respiratory, thoracic and mediastinal disorders	n (%)	43(50.6)	36(45.6)	79(48.2)
Allergic sinusitis	n (%)	0	1(1.3)	1(0.6)
Atelectasis	n (%)	1(1.2)	0	1(0.6)
Cough	n (%)	17(20.0)	10(12.7)	27(16.5)
Dysphonia	n (%)	2(2.4)	1(1.3)	3(1.8)
Dyspnoea	n (%)	16(18.8)	12(15.2)	28(17.1)
Dyspnoea exertional	n (%)	4(4.7)	3(3.8)	7(4.3)
Epistaxis	n (%)	2(2.4)	5(6.3)	7(4.3)
Hypoxia	n (%)	2(2.4)	1(1.3)	3(1.8)
Laryngeal inflammation	n (%)	1(1.2)	0	1(0.6)
Nasal congestion	n (%)	9(10.6)	1(1.3)	10(6.1)
Nasal dryness	n (%)	0	1(1.3)	1(0.6)
Nasal obstruction	n (%)	1(1.2)	0	1(0.6)
Nasal ulcer	n (%)	1(1.2)	1(1.3)	2(1.2)
Oropharyngeal pain	n (%)	4(4.7)	10(12.7)	14(8.5)
Pharyngeal inflammation	n (%)	1(1.2)	0	1(0.6)
Pleural effusion	n (%)	5(5.9)	2(2.5)	7(4.3)
Pleuritic pain	n (%)	1(1.2)	0	1(0.6)
Productive cough	n (%)	6(7.1)	0	6(3.7)
Pulmonary embolism	n (%)	2(2.4)	1(1.3)	3(1.8)
Pulmonary haemorrhage	n (%)	1(1.2)	0	1(0.6)
Respiratory failure	n (%)	2(2.4)	1(1.3)	3(1.8)
Respiratory tract inflammation	n (%)	0	1(1.3)	1(0.6)
Rhinitis allergic	n (%)	0	2(2.5)	2(1.2)
Rhinorrhoea	n (%)	1(1.2)	1(1.3)	2(1.2)
Sinus congestion	n (%)	1(1.2)	1(1.3)	2(1.2)
Upper respiratory tract congestion	n (%)	1(1.2)	0	1(0.6)
Upper-airway cough syndrome	n (%)	2(2.4)	2(2.5)	4(2.4)
Wheezing	n (%)	2(2.4)	3(3.8)	5(3.0)
Skin and subcutaneous tissue disorders	n (%)	56(65.9)	61(77.2)	117(71.3)
Alopecia	n (%)	38(44.7)	51(64.6)	89(54.3)
Blister	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Dermatitis	n (%)	1(1.2)	0	1(0.6)
Dermatitis acneiform	n (%)	2(2.4)	3(3.8)	5(3.0)
Dry skin	n (%)	2(2.4)	10(12.7)	12(7.3)
Eczema	n (%)	1(1.2)	0	1(0.6)
Erythema	n (%)	3(3.5)	0	3(1.8)
Erythema multiforme	n (%)	0	1(1.3)	1(0.6)
Exfoliative rash	n (%)	0	1(1.3)	1(0.6)
Hyperhidrosis	n (%)	2(2.4)	4(5.1)	6(3.7)
Madarosis	n (%)	1(1.2)	0	1(0.6)
Nail bed disorder	n (%)	1(1.2)	0	1(0.6)
Nail bed tenderness	n (%)	1(1.2)	0	1(0.6)
Nail discolouration	n (%)	5(5.9)	10(12.7)	15(9.1)
Nail disorder	n (%)	4(4.7)	2(2.5)	6(3.7)
Nail growth abnormal	n (%)	1(1.2)	1(1.3)	2(1.2)
Nail ridging	n (%)	4(4.7)	3(3.8)	7(4.3)
Night sweats	n (%)	2(2.4)	2(2.5)	4(2.4)
Onychalgia	n (%)	0	1(1.3)	1(0.6)
Onychoclasis	n (%)	2(2.4)	1(1.3)	3(1.8)
Onycholysis	n (%)	2(2.4)	0	2(1.2)
Onychomadesis	n (%)	2(2.4)	5(6.3)	7(4.3)
Pain of skin	n (%)	1(1.2)	1(1.3)	2(1.2)
Palmar erythema	n (%)	0	1(1.3)	1(0.6)
Palmar-plantar erythrodysaesthesia syndrome	n (%)	3(3.5)	4(5.1)	7(4.3)
Pruritus	n (%)	10(11.8)	7(8.9)	17(10.4)
Pruritus generalised	n (%)	1(1.2)	0	1(0.6)
Rash	n (%)	7(8.2)	10(12.7)	17(10.4)
Rash erythematous	n (%)	1(1.2)	0	1(0.6)
Rash follicular	n (%)	1(1.2)	0	1(0.6)
Rash maculo-papular	n (%)	10(11.8)	7(8.9)	17(10.4)
Rash pruritic	n (%)	0	1(1.3)	1(0.6)
Rosacea	n (%)	1(1.2)	0	1(0.6)
Scar pain	n (%)	2(2.4)	0	2(1.2)
Skin discolouration	n (%)	1(1.2)	0	1(0.6)
Skin disorder	n (%)	1(1.2)	2(2.5)	3(1.8)
Skin exfoliation	n (%)	3(3.5)	0	3(1.8)
Skin lesion	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2A
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Skin ulcer	n (%)	0	1(1.3)	1(0.6)
Swelling face	n (%)	3(3.5)	0	3(1.8)
Urticaria	n (%)	0	2(2.5)	2(1.2)
Surgical and medical procedures	n (%)	0	1(1.3)	1(0.6)
Colporrhaphy	n (%)	0	1(1.3)	1(0.6)
Vascular disorders	n (%)	12(14.1)	19(24.1)	31(18.9)
Deep vein thrombosis	n (%)	1(1.2)	0	1(0.6)
Embolism	n (%)	0	1(1.3)	1(0.6)
Flushing	n (%)	4(4.7)	4(5.1)	8(4.9)
Hot flush	n (%)	2(2.4)	4(5.1)	6(3.7)
Hypertension	n (%)	3(3.5)	2(2.5)	5(3.0)
Hypotension	n (%)	3(3.5)	5(6.3)	8(4.9)
Lymphoedema	n (%)	2(2.4)	4(5.1)	6(3.7)
Varicose vein	n (%)	0	1(1.3)	1(0.6)
Vena cava thrombosis	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2B
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
At Least 1 TEAE	n (%)	23(100.0)	22(95.7)	45(97.8)
Blood and lymphatic system disorders	n (%)	13(56.5)	9(39.1)	22(47.8)
Anaemia	n (%)	11(47.8)	4(17.4)	15(32.6)
Febrile neutropenia	n (%)	2(8.7)	0	2(4.3)
Granulocytopenia	n (%)	0	1(4.3)	1(2.2)
Leukocytosis	n (%)	1(4.3)	2(8.7)	3(6.5)
Lymphopenia	n (%)	0	1(4.3)	1(2.2)
Neutropenia	n (%)	2(8.7)	2(8.7)	4(8.7)
Thrombocytopenia	n (%)	1(4.3)	0	1(2.2)
Thrombocytosis	n (%)	0	1(4.3)	1(2.2)
Cardiac disorders	n (%)	3(13.0)	2(8.7)	5(10.9)
Angina pectoris	n (%)	1(4.3)	0	1(2.2)
Sinus tachycardia	n (%)	2(8.7)	2(8.7)	4(8.7)
Ear and labyrinth disorders	n (%)	1(4.3)	4(17.4)	5(10.9)
Ear pain	n (%)	1(4.3)	0	1(2.2)
Tinnitus	n (%)	0	2(8.7)	2(4.3)
Vertigo	n (%)	0	2(8.7)	2(4.3)
Vestibular disorder	n (%)	0	1(4.3)	1(2.2)
Eye disorders	n (%)	6(26.1)	9(39.1)	15(32.6)
Altered visual depth perception	n (%)	0	1(4.3)	1(2.2)
Conjunctivitis	n (%)	2(8.7)	0	2(4.3)
Dry eye	n (%)	0	1(4.3)	1(2.2)
Eye pain	n (%)	1(4.3)	1(4.3)	2(4.3)
Lacrimation increased	n (%)	2(8.7)	5(21.7)	7(15.2)
Ocular hyperaemia	n (%)	0	1(4.3)	1(2.2)
Photophobia	n (%)	0	1(4.3)	1(2.2)
Vision blurred	n (%)	2(8.7)	4(17.4)	6(13.0)
Visual impairment	n (%)	0	1(4.3)	1(2.2)
Gastrointestinal disorders	n (%)	16(69.6)	19(82.6)	35(76.1)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2B
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Abdominal distension	n (%)	0	1(4.3)	1(2.2)
Abdominal pain	n (%)	4(17.4)	6(26.1)	10(21.7)
Abdominal pain upper	n (%)	1(4.3)	3(13.0)	4(8.7)
Colitis	n (%)	1(4.3)	0	1(2.2)
Constipation	n (%)	7(30.4)	7(30.4)	14(30.4)
Diarrhoea	n (%)	9(39.1)	9(39.1)	18(39.1)
Dry mouth	n (%)	2(8.7)	0	2(4.3)
Dysphagia	n (%)	1(4.3)	1(4.3)	2(4.3)
Flatulence	n (%)	0	1(4.3)	1(2.2)
Gastrointestinal haemorrhage	n (%)	1(4.3)	0	1(2.2)
Glossodynia	n (%)	0	1(4.3)	1(2.2)
Haemorrhoids	n (%)	0	1(4.3)	1(2.2)
Lip dry	n (%)	1(4.3)	0	1(2.2)
Mucous stools	n (%)	0	1(4.3)	1(2.2)
Nausea	n (%)	10(43.5)	15(65.2)	25(54.3)
Oral pain	n (%)	2(8.7)	2(8.7)	4(8.7)
Reflux gastritis	n (%)	0	1(4.3)	1(2.2)
Stomatitis	n (%)	1(4.3)	2(8.7)	3(6.5)
Vomiting	n (%)	7(30.4)	7(30.4)	14(30.4)
General disorders and administration site conditions	n (%)	19(82.6)	15(65.2)	34(73.9)
Asthenia	n (%)	3(13.0)	2(8.7)	5(10.9)
Axillary pain	n (%)	1(4.3)	2(8.7)	3(6.5)
Chest discomfort	n (%)	0	1(4.3)	1(2.2)
Chest pain	n (%)	0	1(4.3)	1(2.2)
Chills	n (%)	0	2(8.7)	2(4.3)
Device dislocation	n (%)	1(4.3)	0	1(2.2)
Effusion	n (%)	0	1(4.3)	1(2.2)
Face oedema	n (%)	0	2(8.7)	2(4.3)
Fatigue	n (%)	16(69.6)	11(47.8)	27(58.7)
Gait disturbance	n (%)	1(4.3)	1(4.3)	2(4.3)
Injection site pain	n (%)	0	1(4.3)	1(2.2)
Localised oedema	n (%)	0	1(4.3)	1(2.2)
Mucosal inflammation	n (%)	2(8.7)	1(4.3)	3(6.5)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2B
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Non-cardiac chest pain	n (%)	2(8.7)	3(13.0)	5(10.9)
Oedema	n (%)	2(8.7)	0	2(4.3)
Oedema peripheral	n (%)	7(30.4)	5(21.7)	12(26.1)
Pyrexia	n (%)	3(13.0)	2(8.7)	5(10.9)
Thrombosis in device	n (%)	0	1(4.3)	1(2.2)
Hepatobiliary disorders	n (%)	1(4.3)	2(8.7)	3(6.5)
Bile duct stenosis	n (%)	0	1(4.3)	1(2.2)
Hepatic failure	n (%)	1(4.3)	0	1(2.2)
Hepatic pain	n (%)	0	1(4.3)	1(2.2)
Hepatitis	n (%)	1(4.3)	0	1(2.2)
Infections and infestations	n (%)	10(43.5)	11(47.8)	21(45.7)
Atypical pneumonia	n (%)	1(4.3)	0	1(2.2)
Bronchitis	n (%)	0	1(4.3)	1(2.2)
Candidiasis	n (%)	0	1(4.3)	1(2.2)
Diverticulitis	n (%)	0	1(4.3)	1(2.2)
Eye infection	n (%)	0	2(8.7)	2(4.3)
Infection	n (%)	1(4.3)	0	1(2.2)
Laryngitis	n (%)	0	1(4.3)	1(2.2)
Nail infection	n (%)	0	1(4.3)	1(2.2)
Nasopharyngitis	n (%)	0	1(4.3)	1(2.2)
Onychomycosis	n (%)	1(4.3)	0	1(2.2)
Oral candidiasis	n (%)	2(8.7)	0	2(4.3)
Oral herpes	n (%)	1(4.3)	0	1(2.2)
Oral infection	n (%)	1(4.3)	0	1(2.2)
Paronychia	n (%)	0	1(4.3)	1(2.2)
Pharyngitis	n (%)	0	1(4.3)	1(2.2)
Pneumonia	n (%)	3(13.0)	2(8.7)	5(10.9)
Rhinitis	n (%)	1(4.3)	0	1(2.2)
Sepsis	n (%)	0	1(4.3)	1(2.2)
Sinusitis	n (%)	1(4.3)	1(4.3)	2(4.3)
Skin infection	n (%)	0	1(4.3)	1(2.2)
Upper respiratory tract infection	n (%)	2(8.7)	3(13.0)	5(10.9)
Urinary tract infection	n (%)	1(4.3)	5(21.7)	6(13.0)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2B
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Vulvovaginal mycotic infection	n (%)	1(4.3)	0	1(2.2)
Injury, poisoning and procedural complications	n (%)	2(8.7)	5(21.7)	7(15.2)
Ankle fracture	n (%)	0	1(4.3)	1(2.2)
Contusion	n (%)	0	1(4.3)	1(2.2)
Fall	n (%)	0	2(8.7)	2(4.3)
Infusion related reaction	n (%)	1(4.3)	0	1(2.2)
Nail injury	n (%)	0	2(8.7)	2(4.3)
Post procedural discharge	n (%)	0	1(4.3)	1(2.2)
Wound complication	n (%)	1(4.3)	0	1(2.2)
Investigations	n (%)	7(30.4)	12(52.2)	19(41.3)
Alanine aminotransferase increased	n (%)	1(4.3)	2(8.7)	3(6.5)
Aspartate aminotransferase increased	n (%)	1(4.3)	3(13.0)	4(8.7)
Blood alkaline phosphatase increased	n (%)	2(8.7)	1(4.3)	3(6.5)
Blood bilirubin increased	n (%)	0	2(8.7)	2(4.3)
Blood pressure decreased	n (%)	0	2(8.7)	2(4.3)
Haemoglobin decreased	n (%)	1(4.3)	0	1(2.2)
Lymphocyte count decreased	n (%)	6(26.1)	5(21.7)	11(23.9)
Neutrophil count decreased	n (%)	2(8.7)	2(8.7)	4(8.7)
Platelet count decreased	n (%)	0	1(4.3)	1(2.2)
Weight decreased	n (%)	0	3(13.0)	3(6.5)
Weight increased	n (%)	0	1(4.3)	1(2.2)
White blood cell count decreased	n (%)	4(17.4)	4(17.4)	8(17.4)
Metabolism and nutrition disorders	n (%)	13(56.5)	15(65.2)	28(60.9)
Decreased appetite	n (%)	4(17.4)	7(30.4)	11(23.9)
Dehydration	n (%)	1(4.3)	0	1(2.2)
Hypercalcaemia	n (%)	0	2(8.7)	2(4.3)
Hyperglycaemia	n (%)	3(13.0)	2(8.7)	5(10.9)
Hyperkalaemia	n (%)	1(4.3)	1(4.3)	2(4.3)
Hypernatraemia	n (%)	3(13.0)	0	3(6.5)
Hyperphosphataemia	n (%)	1(4.3)	0	1(2.2)
Hypoalbuminaemia	n (%)	4(17.4)	2(8.7)	6(13.0)
Hypocalcaemia	n (%)	3(13.0)	3(13.0)	6(13.0)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2B
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Hypokalaemia	n (%)	3(13.0)	1(4.3)	4(8.7)
Hypomagnesaemia	n (%)	1(4.3)	0	1(2.2)
Hyponatraemia	n (%)	2(8.7)	1(4.3)	3(6.5)
Hypophosphataemia	n (%)	4(17.4)	3(13.0)	7(15.2)
Increased appetite	n (%)	1(4.3)	0	1(2.2)
Musculoskeletal and connective tissue disorders	n (%)	16(69.6)	10(43.5)	26(56.5)
Arthralgia	n (%)	2(8.7)	4(17.4)	6(13.0)
Back pain	n (%)	3(13.0)	4(17.4)	7(15.2)
Bone pain	n (%)	1(4.3)	1(4.3)	2(4.3)
Joint stiffness	n (%)	1(4.3)	0	1(2.2)
Joint swelling	n (%)	1(4.3)	1(4.3)	2(4.3)
Muscle spasms	n (%)	2(8.7)	1(4.3)	3(6.5)
Muscular weakness	n (%)	2(8.7)	1(4.3)	3(6.5)
Musculoskeletal chest pain	n (%)	3(13.0)	2(8.7)	5(10.9)
Musculoskeletal pain	n (%)	1(4.3)	0	1(2.2)
Musculoskeletal stiffness	n (%)	0	1(4.3)	1(2.2)
Myalgia	n (%)	1(4.3)	3(13.0)	4(8.7)
Neck pain	n (%)	1(4.3)	0	1(2.2)
Pain in extremity	n (%)	1(4.3)	1(4.3)	2(4.3)
Nervous system disorders	n (%)	14(60.9)	19(82.6)	33(71.7)
Convulsion	n (%)	0	1(4.3)	1(2.2)
Dizziness	n (%)	3(13.0)	7(30.4)	10(21.7)
Dysgeusia	n (%)	1(4.3)	3(13.0)	4(8.7)
Headache	n (%)	7(30.4)	9(39.1)	16(34.8)
Hyperaesthesia	n (%)	0	1(4.3)	1(2.2)
Hypoaesthesia	n (%)	0	1(4.3)	1(2.2)
Neuropathy peripheral	n (%)	6(26.1)	8(34.8)	14(30.4)
Peripheral sensorimotor neuropathy	n (%)	0	1(4.3)	1(2.2)
Peripheral sensory neuropathy	n (%)	4(17.4)	4(17.4)	8(17.4)
Syncope	n (%)	1(4.3)	2(8.7)	3(6.5)
Tremor	n (%)	1(4.3)	0	1(2.2)
Psychiatric disorders	n (%)	5(21.7)	4(17.4)	9(19.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2B
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Anxiety	n (%)	0	1(4.3)	1(2.2)
Confusional state	n (%)	0	1(4.3)	1(2.2)
Insomnia	n (%)	4(17.4)	3(13.0)	7(15.2)
Mental status changes	n (%)	1(4.3)	0	1(2.2)
Restlessness	n (%)	1(4.3)	0	1(2.2)
Renal and urinary disorders	n (%)	3(13.0)	4(17.4)	7(15.2)
Dysuria	n (%)	1(4.3)	1(4.3)	2(4.3)
Hydronephrosis	n (%)	0	1(4.3)	1(2.2)
Micturition urgency	n (%)	1(4.3)	0	1(2.2)
Renal failure acute	n (%)	1(4.3)	0	1(2.2)
Urinary incontinence	n (%)	0	1(4.3)	1(2.2)
Urinary tract inflammation	n (%)	0	1(4.3)	1(2.2)
Reproductive system and breast disorders	n (%)	2(8.7)	1(4.3)	3(6.5)
Breast pain	n (%)	1(4.3)	0	1(2.2)
Vaginal discharge	n (%)	0	1(4.3)	1(2.2)
Vulvovaginal dryness	n (%)	1(4.3)	0	1(2.2)
Respiratory, thoracic and mediastinal disorders	n (%)	15(65.2)	12(52.2)	27(58.7)
Atelectasis	n (%)	1(4.3)	0	1(2.2)
Cough	n (%)	6(26.1)	5(21.7)	11(23.9)
Dyspnoea	n (%)	8(34.8)	2(8.7)	10(21.7)
Dyspnoea exertional	n (%)	2(8.7)	1(4.3)	3(6.5)
Epistaxis	n (%)	1(4.3)	1(4.3)	2(4.3)
Hypoxia	n (%)	2(8.7)	1(4.3)	3(6.5)
Nasal congestion	n (%)	3(13.0)	0	3(6.5)
Oropharyngeal pain	n (%)	1(4.3)	5(21.7)	6(13.0)
Pleural effusion	n (%)	3(13.0)	1(4.3)	4(8.7)
Productive cough	n (%)	2(8.7)	0	2(4.3)
Pulmonary embolism	n (%)	2(8.7)	1(4.3)	3(6.5)
Pulmonary haemorrhage	n (%)	1(4.3)	0	1(2.2)
Respiratory failure	n (%)	1(4.3)	0	1(2.2)
Respiratory tract inflammation	n (%)	0	1(4.3)	1(2.2)
Rhinorrhoea	n (%)	0	1(4.3)	1(2.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.2B
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Upper respiratory tract congestion	n (%)	1(4.3)	0	1(2.2)
Wheezing	n (%)	1(4.3)	1(4.3)	2(4.3)
Skin and subcutaneous tissue disorders	n (%)	13(56.5)	20(87.0)	33(71.7)
Alopecia	n (%)	6(26.1)	17(73.9)	23(50.0)
Dermatitis acneiform	n (%)	0	2(8.7)	2(4.3)
Dry skin	n (%)	0	3(13.0)	3(6.5)
Eczema	n (%)	1(4.3)	0	1(2.2)
Hyperhidrosis	n (%)	0	2(8.7)	2(4.3)
Nail bed disorder	n (%)	1(4.3)	0	1(2.2)
Nail discolouration	n (%)	0	2(8.7)	2(4.3)
Nail ridging	n (%)	1(4.3)	1(4.3)	2(4.3)
Onychoclasis	n (%)	0	1(4.3)	1(2.2)
Onychomadesis	n (%)	0	1(4.3)	1(2.2)
Palmar-plantar erythrodysaesthesia syndrome	n (%)	0	1(4.3)	1(2.2)
Pruritus	n (%)	2(8.7)	2(8.7)	4(8.7)
Rash	n (%)	2(8.7)	2(8.7)	4(8.7)
Rash maculo-papular	n (%)	4(17.4)	3(13.0)	7(15.2)
Rash pruritic	n (%)	0	1(4.3)	1(2.2)
Skin disorder	n (%)	1(4.3)	0	1(2.2)
Skin exfoliation	n (%)	1(4.3)	0	1(2.2)
Urticaria	n (%)	0	1(4.3)	1(2.2)
Vascular disorders	n (%)	1(4.3)	6(26.1)	7(15.2)
Flushing	n (%)	1(4.3)	2(8.7)	3(6.5)
Hot flush	n (%)	0	2(8.7)	2(4.3)
Lymphoedema	n (%)	0	2(8.7)	2(4.3)
Varicose vein	n (%)	0	1(4.3)	1(2.2)
Vena cava thrombosis	n (%)	0	1(4.3)	1(2.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.3A
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
At Least 1 Treatment Related TEAE	n (%)	58(68.2)	63(79.7)	121(73.8)
Blood and lymphatic system disorders	n (%)	13(15.3)	9(11.4)	22(13.4)
Anaemia	n (%)	10(11.8)	4(5.1)	14(8.5)
Febrile neutropenia	n (%)	0	2(2.5)	2(1.2)
Leukopenia	n (%)	1(1.2)	0	1(0.6)
Neutropenia	n (%)	3(3.5)	3(3.8)	6(3.7)
Pancytopenia	n (%)	0	1(1.3)	1(0.6)
Thrombocytopenia	n (%)	0	2(2.5)	2(1.2)
Thrombocytosis	n (%)	0	1(1.3)	1(0.6)
Cardiac disorders	n (%)	1(1.2)	0	1(0.6)
Arrhythmia	n (%)	1(1.2)	0	1(0.6)
Ear and labyrinth disorders	n (%)	1(1.2)	1(1.3)	2(1.2)
Hypoacusis	n (%)	0	1(1.3)	1(0.6)
Vertigo	n (%)	1(1.2)	0	1(0.6)
Endocrine disorders	n (%)	0	1(1.3)	1(0.6)
Adrenal insufficiency	n (%)	0	1(1.3)	1(0.6)
Eye disorders	n (%)	9(10.6)	10(12.7)	19(11.6)
Dry eye	n (%)	0	3(3.8)	3(1.8)
Eye irritation	n (%)	1(1.2)	0	1(0.6)
Eyelid oedema	n (%)	1(1.2)	0	1(0.6)
Lacrimation increased	n (%)	3(3.5)	5(6.3)	8(4.9)
Photophobia	n (%)	2(2.4)	4(5.1)	6(3.7)
Photopsia	n (%)	1(1.2)	0	1(0.6)
Vision blurred	n (%)	6(7.1)	5(6.3)	11(6.7)
Gastrointestinal disorders	n (%)	32(37.6)	39(49.4)	71(43.3)
Abdominal distension	n (%)	1(1.2)	4(5.1)	5(3.0)
Abdominal pain	n (%)	3(3.5)	5(6.3)	8(4.9)
Abdominal pain upper	n (%)	1(1.2)	2(2.5)	3(1.8)
Colitis	n (%)	1(1.2)	0	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.3A
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Constipation	n (%)	9(10.6)	6(7.6)	15(9.1)
Diarrhoea	n (%)	8(9.4)	16(20.3)	24(14.6)
Dry mouth	n (%)	3(3.5)	3(3.8)	6(3.7)
Dyspepsia	n (%)	2(2.4)	2(2.5)	4(2.4)
Dysphagia	n (%)	0	1(1.3)	1(0.6)
Faecal incontinence	n (%)	1(1.2)	0	1(0.6)
Gastric dilatation	n (%)	1(1.2)	0	1(0.6)
Gastrooesophageal reflux disease	n (%)	2(2.4)	1(1.3)	3(1.8)
Lip dry	n (%)	1(1.2)	0	1(0.6)
Mucous stools	n (%)	0	1(1.3)	1(0.6)
Nausea	n (%)	14(16.5)	21(26.6)	35(21.3)
Oral pain	n (%)	1(1.2)	2(2.5)	3(1.8)
Paraesthesia oral	n (%)	1(1.2)	0	1(0.6)
Reflux gastritis	n (%)	0	1(1.3)	1(0.6)
Stomatitis	n (%)	4(4.7)	2(2.5)	6(3.7)
Vomiting	n (%)	7(8.2)	9(11.4)	16(9.8)
General disorders and administration site conditions	n (%)	30(35.3)	36(45.6)	66(40.2)
Asthenia	n (%)	3(3.5)	7(8.9)	10(6.1)
Chills	n (%)	0	1(1.3)	1(0.6)
Early satiety	n (%)	1(1.2)	0	1(0.6)
Effusion	n (%)	0	1(1.3)	1(0.6)
Face oedema	n (%)	0	1(1.3)	1(0.6)
Fatigue	n (%)	25(29.4)	27(34.2)	52(31.7)
Gait disturbance	n (%)	0	1(1.3)	1(0.6)
Influenza like illness	n (%)	1(1.2)	2(2.5)	3(1.8)
Malaise	n (%)	0	1(1.3)	1(0.6)
Mucosal dryness	n (%)	1(1.2)	0	1(0.6)
Mucosal inflammation	n (%)	1(1.2)	2(2.5)	3(1.8)
Oedema	n (%)	2(2.4)	1(1.3)	3(1.8)
Oedema peripheral	n (%)	2(2.4)	7(8.9)	9(5.5)
Pain	n (%)	0	1(1.3)	1(0.6)
Pyrexia	n (%)	1(1.2)	1(1.3)	2(1.2)
Hepatobiliary disorders	n (%)	0	2(2.5)	2(1.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.3A
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Hepatitis	n (%)	0	1(1.3)	1(0.6)
Jaundice	n (%)	0	1(1.3)	1(0.6)
Infections and infestations	n (%)	5(5.9)	3(3.8)	8(4.9)
Infection	n (%)	1(1.2)	0	1(0.6)
Mucosal infection	n (%)	1(1.2)	0	1(0.6)
Nail infection	n (%)	0	1(1.3)	1(0.6)
Onychomycosis	n (%)	0	1(1.3)	1(0.6)
Oral candidiasis	n (%)	1(1.2)	0	1(0.6)
Pneumonia	n (%)	0	1(1.3)	1(0.6)
Upper respiratory tract infection	n (%)	2(2.4)	0	2(1.2)
Vulvovaginal mycotic infection	n (%)	1(1.2)	0	1(0.6)
Wound infection	n (%)	1(1.2)	0	1(0.6)
Injury, poisoning and procedural complications	n (%)	1(1.2)	0	1(0.6)
Wound complication	n (%)	1(1.2)	0	1(0.6)
Investigations	n (%)	16(18.8)	14(17.7)	30(18.3)
Alanine aminotransferase increased	n (%)	1(1.2)	2(2.5)	3(1.8)
Aspartate aminotransferase increased	n (%)	3(3.5)	2(2.5)	5(3.0)
Blood albumin decreased	n (%)	2(2.4)	0	2(1.2)
Blood alkaline phosphatase increased	n (%)	0	1(1.3)	1(0.6)
Blood bilirubin increased	n (%)	0	1(1.3)	1(0.6)
Blood calcium decreased	n (%)	1(1.2)	0	1(0.6)
Blood creatinine increased	n (%)	1(1.2)	0	1(0.6)
Blood pressure decreased	n (%)	0	1(1.3)	1(0.6)
Blood sodium decreased	n (%)	0	1(1.3)	1(0.6)
Haemoglobin decreased	n (%)	1(1.2)	1(1.3)	2(1.2)
Lipase increased	n (%)	0	1(1.3)	1(0.6)
Lymphocyte count decreased	n (%)	12(14.1)	7(8.9)	19(11.6)
Neutrophil count decreased	n (%)	4(4.7)	3(3.8)	7(4.3)
Platelet count decreased	n (%)	1(1.2)	0	1(0.6)
Weight decreased	n (%)	1(1.2)	2(2.5)	3(1.8)
White blood cell count decreased	n (%)	5(5.9)	6(7.6)	11(6.7)
White blood cell count increased	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.3A
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Metabolism and nutrition disorders	n (%)	20(23.5)	20(25.3)	40(24.4)
Decreased appetite	n (%)	10(11.8)	11(13.9)	21(12.8)
Dehydration	n (%)	0	1(1.3)	1(0.6)
Hyperglycaemia	n (%)	5(5.9)	2(2.5)	7(4.3)
Hyperkalaemia	n (%)	0	1(1.3)	1(0.6)
Hypernatraemia	n (%)	2(2.4)	0	2(1.2)
Hyperuricaemia	n (%)	0	1(1.3)	1(0.6)
Hypoalbuminaemia	n (%)	1(1.2)	0	1(0.6)
Hypocalcaemia	n (%)	2(2.4)	2(2.5)	4(2.4)
Hypoglycaemia	n (%)	0	1(1.3)	1(0.6)
Hypokalaemia	n (%)	1(1.2)	3(3.8)	4(2.4)
Hypomagnesaemia	n (%)	1(1.2)	1(1.3)	2(1.2)
Hyponatraemia	n (%)	0	2(2.5)	2(1.2)
Hypophosphataemia	n (%)	1(1.2)	2(2.5)	3(1.8)
Malnutrition	n (%)	0	1(1.3)	1(0.6)
Musculoskeletal and connective tissue disorders	n (%)	10(11.8)	13(16.5)	23(14.0)
Arthralgia	n (%)	4(4.7)	2(2.5)	6(3.7)
Back pain	n (%)	0	4(5.1)	4(2.4)
Bone pain	n (%)	0	1(1.3)	1(0.6)
Flank pain	n (%)	0	1(1.3)	1(0.6)
Groin pain	n (%)	0	1(1.3)	1(0.6)
Muscle spasms	n (%)	1(1.2)	0	1(0.6)
Muscle tightness	n (%)	0	1(1.3)	1(0.6)
Muscular weakness	n (%)	1(1.2)	2(2.5)	3(1.8)
Musculoskeletal pain	n (%)	1(1.2)	2(2.5)	3(1.8)
Myalgia	n (%)	2(2.4)	3(3.8)	5(3.0)
Pain in extremity	n (%)	3(3.5)	3(3.8)	6(3.7)
Nervous system disorders	n (%)	15(17.6)	25(31.6)	40(24.4)
Burning sensation	n (%)	1(1.2)	1(1.3)	2(1.2)
Disturbance in attention	n (%)	2(2.4)	0	2(1.2)
Dizziness	n (%)	2(2.4)	5(6.3)	7(4.3)
Dysgeusia	n (%)	4(4.7)	8(10.1)	12(7.3)
Headache	n (%)	9(10.6)	11(13.9)	20(12.2)
Hypersomnia	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.3A
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Neuropathy peripheral	n (%)	3(3.5)	2(2.5)	5(3.0)
Paraesthesia	n (%)	1(1.2)	0	1(0.6)
Parkinson's disease	n (%)	1(1.2)	0	1(0.6)
Parosmia	n (%)	1(1.2)	0	1(0.6)
Peripheral sensory neuropathy	n (%)	1(1.2)	1(1.3)	2(1.2)
Somnolence	n (%)	0	1(1.3)	1(0.6)
Tremor	n (%)	1(1.2)	0	1(0.6)
Psychiatric disorders	n (%)	3(3.5)	5(6.3)	8(4.9)
Anxiety	n (%)	1(1.2)	0	1(0.6)
Confusional state	n (%)	0	2(2.5)	2(1.2)
Insomnia	n (%)	2(2.4)	1(1.3)	3(1.8)
Mood altered	n (%)	0	1(1.3)	1(0.6)
Restlessness	n (%)	0	1(1.3)	1(0.6)
Reproductive system and breast disorders	n (%)	1(1.2)	0	1(0.6)
Vulvovaginal pruritus	n (%)	1(1.2)	0	1(0.6)
Respiratory, thoracic and mediastinal disorders	n (%)	9(10.6)	8(10.1)	17(10.4)
Cough	n (%)	2(2.4)	2(2.5)	4(2.4)
Dyspnoea	n (%)	4(4.7)	2(2.5)	6(3.7)
Laryngeal inflammation	n (%)	1(1.2)	0	1(0.6)
Nasal ulcer	n (%)	0	1(1.3)	1(0.6)
Oropharyngeal pain	n (%)	1(1.2)	2(2.5)	3(1.8)
Pleural effusion	n (%)	1(1.2)	0	1(0.6)
Productive cough	n (%)	1(1.2)	0	1(0.6)
Rhinorrhoea	n (%)	1(1.2)	0	1(0.6)
Upper-airway cough syndrome	n (%)	1(1.2)	0	1(0.6)
Wheezing	n (%)	0	1(1.3)	1(0.6)
Skin and subcutaneous tissue disorders	n (%)	15(17.6)	26(32.9)	41(25.0)
Alopecia	n (%)	6(7.1)	10(12.7)	16(9.8)
Dermatitis acneiform	n (%)	0	1(1.3)	1(0.6)
Dry skin	n (%)	1(1.2)	2(2.5)	3(1.8)
Erythema multiforme	n (%)	0	1(1.3)	1(0.6)
Hyperhidrosis	n (%)	0	2(2.5)	2(1.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.3A
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Nail discolouration	n (%)	0	1(1.3)	1(0.6)
Night sweats	n (%)	0	1(1.3)	1(0.6)
Onychoclasis	n (%)	1(1.2)	1(1.3)	2(1.2)
Onychomadesis	n (%)	0	1(1.3)	1(0.6)
Pain of skin	n (%)	1(1.2)	0	1(0.6)
Palmar erythema	n (%)	0	1(1.3)	1(0.6)
Palmar-plantar erythrodysaesthesia syndrome	n (%)	1(1.2)	2(2.5)	3(1.8)
Pruritus	n (%)	3(3.5)	2(2.5)	5(3.0)
Rash	n (%)	4(4.7)	6(7.6)	10(6.1)
Rash maculo-papular	n (%)	4(4.7)	5(6.3)	9(5.5)
Skin disorder	n (%)	0	1(1.3)	1(0.6)
Skin lesion	n (%)	0	1(1.3)	1(0.6)
Vascular disorders	n (%)	2(2.4)	4(5.1)	6(3.7)
Flushing	n (%)	2(2.4)	0	2(1.2)
Hot flush	n (%)	0	3(3.8)	3(1.8)
Hypotension	n (%)	0	1(1.3)	1(0.6)
Lymphoedema	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.4A
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
At Least 1 Serious TEAE	n (%)	29(34.1)	28(35.4)	57(34.8)
Blood and lymphatic system disorders	n (%)	3(3.5)	3(3.8)	6(3.7)
Anaemia	n (%)	2(2.4)	0	2(1.2)
Febrile neutropenia	n (%)	1(1.2)	2(2.5)	3(1.8)
Neutropenia	n (%)	0	1(1.3)	1(0.6)
Cardiac disorders	n (%)	1(1.2)	2(2.5)	3(1.8)
Coronary artery disease	n (%)	0	1(1.3)	1(0.6)
Coronary artery insufficiency	n (%)	0	1(1.3)	1(0.6)
Tachycardia	n (%)	1(1.2)	0	1(0.6)
Ear and labyrinth disorders	n (%)	0	1(1.3)	1(0.6)
Vertigo labyrinthine	n (%)	0	1(1.3)	1(0.6)
Endocrine disorders	n (%)	0	1(1.3)	1(0.6)
Adrenal insufficiency	n (%)	0	1(1.3)	1(0.6)
Gastrointestinal disorders	n (%)	5(5.9)	3(3.8)	8(4.9)
Abdominal pain	n (%)	1(1.2)	0	1(0.6)
Diarrhoea	n (%)	0	1(1.3)	1(0.6)
Enterocolitis	n (%)	0	1(1.3)	1(0.6)
Gastrointestinal haemorrhage	n (%)	1(1.2)	0	1(0.6)
Large intestine perforation	n (%)	2(2.4)	0	2(1.2)
Nausea	n (%)	0	1(1.3)	1(0.6)
Vomiting	n (%)	1(1.2)	0	1(0.6)
General disorders and administration site conditions	n (%)	5(5.9)	4(5.1)	9(5.5)
Asthenia	n (%)	0	3(3.8)	3(1.8)
Gait disturbance	n (%)	1(1.2)	0	1(0.6)
Multi-organ failure	n (%)	1(1.2)	0	1(0.6)
Non-cardiac chest pain	n (%)	2(2.4)	0	2(1.2)
Pain	n (%)	0	1(1.3)	1(0.6)
Sudden death	n (%)	1(1.2)	0	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.4A
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Hepatobiliary disorders	n (%)	3(3.5)	4(5.1)	7(4.3)
Bile duct stenosis	n (%)	0	1(1.3)	1(0.6)
Cholecystitis	n (%)	1(1.2)	0	1(0.6)
Hepatic failure	n (%)	0	1(1.3)	1(0.6)
Hepatitis	n (%)	1(1.2)	1(1.3)	2(1.2)
Hyperbilirubinaemia	n (%)	0	1(1.3)	1(0.6)
Jaundice	n (%)	1(1.2)	0	1(0.6)
Infections and infestations	n (%)	4(4.7)	5(6.3)	9(5.5)
Cellulitis	n (%)	0	1(1.3)	1(0.6)
Clostridium difficile infection	n (%)	0	1(1.3)	1(0.6)
Pneumonia	n (%)	2(2.4)	1(1.3)	3(1.8)
Sepsis	n (%)	0	1(1.3)	1(0.6)
Skin infection	n (%)	1(1.2)	0	1(0.6)
Urinary tract infection	n (%)	1(1.2)	1(1.3)	2(1.2)
Injury, poisoning and procedural complications	n (%)	1(1.2)	1(1.3)	2(1.2)
Ankle fracture	n (%)	0	1(1.3)	1(0.6)
Femur fracture	n (%)	1(1.2)	0	1(0.6)
Investigations	n (%)	0	1(1.3)	1(0.6)
Blood bilirubin increased	n (%)	0	1(1.3)	1(0.6)
Metabolism and nutrition disorders	n (%)	2(2.4)	2(2.5)	4(2.4)
Dehydration	n (%)	1(1.2)	1(1.3)	2(1.2)
Hypercalcaemia	n (%)	1(1.2)	0	1(0.6)
Hypoglycaemia	n (%)	0	1(1.3)	1(0.6)
Musculoskeletal and connective tissue disorders	n (%)	2(2.4)	2(2.5)	4(2.4)
Back pain	n (%)	0	1(1.3)	1(0.6)
Bone pain	n (%)	0	1(1.3)	1(0.6)
Muscular weakness	n (%)	1(1.2)	0	1(0.6)
Pain in extremity	n (%)	1(1.2)	0	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.4A
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	n (%)	0	1(1.3)	1(0.6)
Metastases to meninges	n (%)	0	1(1.3)	1(0.6)
Nervous system disorders	n (%)	3(3.5)	1(1.3)	4(2.4)
Headache	n (%)	2(2.4)	0	2(1.2)
Parkinson's disease	n (%)	1(1.2)	0	1(0.6)
Peripheral sensory neuropathy	n (%)	0	1(1.3)	1(0.6)
Psychiatric disorders	n (%)	1(1.2)	0	1(0.6)
Mental status changes	n (%)	1(1.2)	0	1(0.6)
Reproductive system and breast disorders	n (%)	1(1.2)	0	1(0.6)
Breast pain	n (%)	1(1.2)	0	1(0.6)
Respiratory, thoracic and mediastinal disorders	n (%)	8(9.4)	2(2.5)	10(6.1)
Dyspnoea	n (%)	4(4.7)	0	4(2.4)
Pleural effusion	n (%)	1(1.2)	1(1.3)	2(1.2)
Pulmonary embolism	n (%)	1(1.2)	1(1.3)	2(1.2)
Respiratory failure	n (%)	2(2.4)	1(1.3)	3(1.8)
Skin and subcutaneous tissue disorders	n (%)	0	2(2.5)	2(1.2)
Palmar-plantar erythrodysaesthesia syndrome	n (%)	0	1(1.3)	1(0.6)
Rash maculo-papular	n (%)	0	1(1.3)	1(0.6)
Vascular disorders	n (%)	1(1.2)	1(1.3)	2(1.2)
Deep vein thrombosis	n (%)	1(1.2)	0	1(0.6)
Hypotension	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.4B
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
At Least 1 Serious TEAE	n (%)	10(43.5)	7(30.4)	17(37.0)
Blood and lymphatic system disorders	n (%)	1(4.3)	0	1(2.2)
Febrile neutropenia	n (%)	1(4.3)	0	1(2.2)
Gastrointestinal disorders	n (%)	1(4.3)	0	1(2.2)
Gastrointestinal haemorrhage	n (%)	1(4.3)	0	1(2.2)
General disorders and administration site conditions	n (%)	2(8.7)	1(4.3)	3(6.5)
Asthenia	n (%)	0	1(4.3)	1(2.2)
Gait disturbance	n (%)	1(4.3)	0	1(2.2)
Non-cardiac chest pain	n (%)	1(4.3)	0	1(2.2)
Hepatobiliary disorders	n (%)	1(4.3)	1(4.3)	2(4.3)
Bile duct stenosis	n (%)	0	1(4.3)	1(2.2)
Hepatitis	n (%)	1(4.3)	0	1(2.2)
Infections and infestations	n (%)	2(8.7)	3(13.0)	5(10.9)
Pneumonia	n (%)	2(8.7)	1(4.3)	3(6.5)
Sepsis	n (%)	0	1(4.3)	1(2.2)
Urinary tract infection	n (%)	0	1(4.3)	1(2.2)
Injury, poisoning and procedural complications	n (%)	0	1(4.3)	1(2.2)
Ankle fracture	n (%)	0	1(4.3)	1(2.2)
Metabolism and nutrition disorders	n (%)	1(4.3)	0	1(2.2)
Dehydration	n (%)	1(4.3)	0	1(2.2)
Musculoskeletal and connective tissue disorders	n (%)	1(4.3)	1(4.3)	2(4.3)
Back pain	n (%)	0	1(4.3)	1(2.2)
Muscular weakness	n (%)	1(4.3)	0	1(2.2)
Nervous system disorders	n (%)	1(4.3)	0	1(2.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.4B
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Headache	n (%)	1(4.3)	0	1(2.2)
Psychiatric disorders	n (%)	1(4.3)	0	1(2.2)
Mental status changes	n (%)	1(4.3)	0	1(2.2)
Reproductive system and breast disorders	n (%)	1(4.3)	0	1(2.2)
Breast pain	n (%)	1(4.3)	0	1(2.2)
Respiratory, thoracic and mediastinal disorders	n (%)	5(21.7)	1(4.3)	6(13.0)
Dyspnoea	n (%)	2(8.7)	0	2(4.3)
Pleural effusion	n (%)	1(4.3)	0	1(2.2)
Pulmonary embolism	n (%)	1(4.3)	1(4.3)	2(4.3)
Respiratory failure	n (%)	1(4.3)	0	1(2.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.5A
Treatment-Emergent Adverse Events with CTCAE Severity >= Grade 3 by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
At Least 1 TEAE with CTCAE Severity >= Grade 3	n (%)	51(60.0)	48(60.8)	99(60.4)
Blood and lymphatic system disorders	n (%)	19(22.4)	20(25.3)	39(23.8)
Anaemia	n (%)	7(8.2)	3(3.8)	10(6.1)
Febrile neutropenia	n (%)	2(2.4)	4(5.1)	6(3.7)
Granulocytopenia	n (%)	0	1(1.3)	1(0.6)
Leukocytosis	n (%)	1(1.2)	0	1(0.6)
Leukopenia	n (%)	1(1.2)	1(1.3)	2(1.2)
Neutropenia	n (%)	8(9.4)	14(17.7)	22(13.4)
Thrombocytopenia	n (%)	1(1.2)	1(1.3)	2(1.2)
Cardiac disorders	n (%)	0	1(1.3)	1(0.6)
Coronary artery insufficiency	n (%)	0	1(1.3)	1(0.6)
Gastrointestinal disorders	n (%)	8(9.4)	13(16.5)	21(12.8)
Abdominal pain	n (%)	4(4.7)	1(1.3)	5(3.0)
Ascites	n (%)	0	1(1.3)	1(0.6)
Constipation	n (%)	0	1(1.3)	1(0.6)
Diarrhoea	n (%)	1(1.2)	6(7.6)	7(4.3)
Enterocolitis	n (%)	0	1(1.3)	1(0.6)
Gastrointestinal haemorrhage	n (%)	1(1.2)	0	1(0.6)
Large intestine perforation	n (%)	2(2.4)	0	2(1.2)
Nausea	n (%)	2(2.4)	2(2.5)	4(2.4)
Oesophagitis	n (%)	0	1(1.3)	1(0.6)
Stomatitis	n (%)	0	1(1.3)	1(0.6)
Vomiting	n (%)	3(3.5)	1(1.3)	4(2.4)
General disorders and administration site conditions	n (%)	13(15.3)	9(11.4)	22(13.4)
Asthenia	n (%)	2(2.4)	4(5.1)	6(3.7)
Axillary pain	n (%)	1(1.2)	0	1(0.6)
Fatigue	n (%)	6(7.1)	4(5.1)	10(6.1)
Gait disturbance	n (%)	1(1.2)	0	1(0.6)
Mucosal inflammation	n (%)	1(1.2)	0	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.5A
Treatment-Emergent Adverse Events with CTCAE Severity >= Grade 3 by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Multi-organ failure	n (%)	1(1.2)	0	1(0.6)
Non-cardiac chest pain	n (%)	2(2.4)	0	2(1.2)
Oedema peripheral	n (%)	1(1.2)	1(1.3)	2(1.2)
Pain	n (%)	0	1(1.3)	1(0.6)
Sudden death	n (%)	1(1.2)	0	1(0.6)
Hepatobiliary disorders	n (%)	3(3.5)	5(6.3)	8(4.9)
Bile duct stenosis	n (%)	0	1(1.3)	1(0.6)
Cholecystitis	n (%)	1(1.2)	0	1(0.6)
Hepatic failure	n (%)	1(1.2)	1(1.3)	2(1.2)
Hepatic pain	n (%)	0	1(1.3)	1(0.6)
Hepatitis	n (%)	1(1.2)	1(1.3)	2(1.2)
Hyperbilirubinaemia	n (%)	0	1(1.3)	1(0.6)
Jaundice	n (%)	1(1.2)	0	1(0.6)
Infections and infestations	n (%)	5(5.9)	8(10.1)	13(7.9)
Cellulitis	n (%)	0	1(1.3)	1(0.6)
Clostridium difficile infection	n (%)	0	1(1.3)	1(0.6)
Pneumonia	n (%)	3(3.5)	3(3.8)	6(3.7)
Sepsis	n (%)	1(1.2)	1(1.3)	2(1.2)
Skin infection	n (%)	1(1.2)	0	1(0.6)
Urinary tract infection	n (%)	1(1.2)	2(2.5)	3(1.8)
Injury, poisoning and procedural complications	n (%)	1(1.2)	1(1.3)	2(1.2)
Ankle fracture	n (%)	0	1(1.3)	1(0.6)
Fall	n (%)	1(1.2)	0	1(0.6)
Femur fracture	n (%)	1(1.2)	0	1(0.6)
Investigations	n (%)	8(9.4)	11(13.9)	19(11.6)
Alanine aminotransferase increased	n (%)	0	1(1.3)	1(0.6)
Aspartate aminotransferase increased	n (%)	1(1.2)	1(1.3)	2(1.2)
Blood alkaline phosphatase increased	n (%)	1(1.2)	1(1.3)	2(1.2)
Blood bilirubin increased	n (%)	1(1.2)	1(1.3)	2(1.2)
Hepatic enzyme increased	n (%)	1(1.2)	0	1(0.6)
Lymphocyte count decreased	n (%)	3(3.5)	3(3.8)	6(3.7)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.
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Table 14.3.1.5A
Treatment-Emergent Adverse Events with CTCAE Severity >= Grade 3 by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Neutrophil count decreased	n (%)	3(3.5)	4(5.1)	7(4.3)
White blood cell count decreased	n (%)	1(1.2)	5(6.3)	6(3.7)
White blood cell count increased	n (%)	0	1(1.3)	1(0.6)
Metabolism and nutrition disorders	n (%)	9(10.6)	7(8.9)	16(9.8)
Cachexia	n (%)	1(1.2)	0	1(0.6)
Decreased appetite	n (%)	1(1.2)	0	1(0.6)
Dehydration	n (%)	1(1.2)	2(2.5)	3(1.8)
Hypercalcaemia	n (%)	2(2.4)	0	2(1.2)
Hyperglycaemia	n (%)	3(3.5)	0	3(1.8)
Hyperkalaemia	n (%)	1(1.2)	0	1(0.6)
Hypocalcaemia	n (%)	1(1.2)	0	1(0.6)
Hypoglycaemia	n (%)	0	1(1.3)	1(0.6)
Hypokalaemia	n (%)	2(2.4)	0	2(1.2)
Hyponatraemia	n (%)	1(1.2)	1(1.3)	2(1.2)
Hypophosphataemia	n (%)	2(2.4)	2(2.5)	4(2.4)
Malnutrition	n (%)	0	1(1.3)	1(0.6)
Musculoskeletal and connective tissue disorders	n (%)	6(7.1)	6(7.6)	12(7.3)
Back pain	n (%)	2(2.4)	2(2.5)	4(2.4)
Bone pain	n (%)	2(2.4)	3(3.8)	5(3.0)
Muscular weakness	n (%)	1(1.2)	0	1(0.6)
Musculoskeletal chest pain	n (%)	1(1.2)	0	1(0.6)
Myalgia	n (%)	0	1(1.3)	1(0.6)
Pain in extremity	n (%)	1(1.2)	0	1(0.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	n (%)	0	1(1.3)	1(0.6)
Metastases to meninges	n (%)	0	1(1.3)	1(0.6)
Nervous system disorders	n (%)	4(4.7)	4(5.1)	8(4.9)
Headache	n (%)	1(1.2)	2(2.5)	3(1.8)
Parkinson's disease	n (%)	1(1.2)	0	1(0.6)
Peripheral sensory neuropathy	n (%)	0	1(1.3)	1(0.6)
Polyneuropathy	n (%)	0	1(1.3)	1(0.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.5A
Treatment-Emergent Adverse Events with CTCAE Severity >= Grade 3 by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=85)	Placebo (N=79)	Overall (N=164)
Syncope	n (%)	2(2.4)	0	2(1.2)
Psychiatric disorders	n (%)	1(1.2)	0	1(0.6)
Mental status changes	n (%)	1(1.2)	0	1(0.6)
Reproductive system and breast disorders	n (%)	2(2.4)	0	2(1.2)
Breast pain	n (%)	1(1.2)	0	1(0.6)
Premature menopause	n (%)	1(1.2)	0	1(0.6)
Respiratory, thoracic and mediastinal disorders	n (%)	11(12.9)	4(5.1)	15(9.1)
Atelectasis	n (%)	1(1.2)	0	1(0.6)
Dyspnoea	n (%)	6(7.1)	2(2.5)	8(4.9)
Hypoxia	n (%)	1(1.2)	0	1(0.6)
Pleural effusion	n (%)	2(2.4)	1(1.3)	3(1.8)
Pleuritic pain	n (%)	1(1.2)	0	1(0.6)
Pulmonary embolism	n (%)	2(2.4)	1(1.3)	3(1.8)
Respiratory failure	n (%)	2(2.4)	1(1.3)	3(1.8)
Skin and subcutaneous tissue disorders	n (%)	3(3.5)	3(3.8)	6(3.7)
Alopecia	n (%)	1(1.2)	0	1(0.6)
Nail growth abnormal	n (%)	0	1(1.3)	1(0.6)
Onycholysis	n (%)	1(1.2)	0	1(0.6)
Palmar-plantar erythrodysaesthesia syndrome	n (%)	0	2(2.5)	2(1.2)
Rash maculo-papular	n (%)	1(1.2)	0	1(0.6)
Vascular disorders	n (%)	4(4.7)	1(1.3)	5(3.0)
Deep vein thrombosis	n (%)	1(1.2)	0	1(0.6)
Hypertension	n (%)	2(2.4)	0	2(1.2)
Hypotension	n (%)	1(1.2)	1(1.3)	2(1.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.5B
Treatment-Emergent Adverse Events with CTCAE Severity >= Grade 3 by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
At Least 1 TEAE with CTCAE Severity >= Grade 3	n (%)	15(65.2)	13(56.5)	28(60.9)
Blood and lymphatic system disorders	n (%)	7(30.4)	2(8.7)	9(19.6)
Anaemia	n (%)	4(17.4)	0	4(8.7)
Febrile neutropenia	n (%)	2(8.7)	0	2(4.3)
Granulocytopenia	n (%)	0	1(4.3)	1(2.2)
Leukocytosis	n (%)	1(4.3)	0	1(2.2)
Neutropenia	n (%)	0	1(4.3)	1(2.2)
Thrombocytopenia	n (%)	1(4.3)	0	1(2.2)
Gastrointestinal disorders	n (%)	2(8.7)	4(17.4)	6(13.0)
Abdominal pain	n (%)	2(8.7)	1(4.3)	3(6.5)
Diarrhoea	n (%)	0	2(8.7)	2(4.3)
Gastrointestinal haemorrhage	n (%)	1(4.3)	0	1(2.2)
Nausea	n (%)	0	1(4.3)	1(2.2)
General disorders and administration site conditions	n (%)	5(21.7)	3(13.0)	8(17.4)
Asthenia	n (%)	1(4.3)	1(4.3)	2(4.3)
Axillary pain	n (%)	1(4.3)	0	1(2.2)
Fatigue	n (%)	1(4.3)	1(4.3)	2(4.3)
Gait disturbance	n (%)	1(4.3)	0	1(2.2)
Mucosal inflammation	n (%)	1(4.3)	0	1(2.2)
Non-cardiac chest pain	n (%)	1(4.3)	0	1(2.2)
Oedema peripheral	n (%)	1(4.3)	1(4.3)	2(4.3)
Hepatobiliary disorders	n (%)	1(4.3)	2(8.7)	3(6.5)
Bile duct stenosis	n (%)	0	1(4.3)	1(2.2)
Hepatic failure	n (%)	1(4.3)	0	1(2.2)
Hepatic pain	n (%)	0	1(4.3)	1(2.2)
Hepatitis	n (%)	1(4.3)	0	1(2.2)
Infections and infestations	n (%)	3(13.0)	4(17.4)	7(15.2)
Pneumonia	n (%)	3(13.0)	1(4.3)	4(8.7)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.5B
Treatment-Emergent Adverse Events with CTCAE Severity >= Grade 3 by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Sepsis	n (%)	0	1(4.3)	1(2.2)
Urinary tract infection	n (%)	0	2(8.7)	2(4.3)
Injury, poisoning and procedural complications	n (%)	0	1(4.3)	1(2.2)
Ankle fracture	n (%)	0	1(4.3)	1(2.2)
Investigations	n (%)	2(8.7)	3(13.0)	5(10.9)
Blood alkaline phosphatase increased	n (%)	0	1(4.3)	1(2.2)
Lymphocyte count decreased	n (%)	2(8.7)	2(8.7)	4(8.7)
Neutrophil count decreased	n (%)	1(4.3)	1(4.3)	2(4.3)
White blood cell count decreased	n (%)	1(4.3)	2(8.7)	3(6.5)
Metabolism and nutrition disorders	n (%)	3(13.0)	2(8.7)	5(10.9)
Dehydration	n (%)	1(4.3)	0	1(2.2)
Hyperglycaemia	n (%)	2(8.7)	0	2(4.3)
Hypocalcaemia	n (%)	1(4.3)	0	1(2.2)
Hypokalaemia	n (%)	1(4.3)	0	1(2.2)
Hypophosphataemia	n (%)	0	2(8.7)	2(4.3)
Musculoskeletal and connective tissue disorders	n (%)	3(13.0)	1(4.3)	4(8.7)
Back pain	n (%)	2(8.7)	1(4.3)	3(6.5)
Muscular weakness	n (%)	1(4.3)	0	1(2.2)
Musculoskeletal chest pain	n (%)	1(4.3)	0	1(2.2)
Nervous system disorders	n (%)	2(8.7)	0	2(4.3)
Headache	n (%)	1(4.3)	0	1(2.2)
Syncope	n (%)	1(4.3)	0	1(2.2)
Psychiatric disorders	n (%)	1(4.3)	0	1(2.2)
Mental status changes	n (%)	1(4.3)	0	1(2.2)
Reproductive system and breast disorders	n (%)	1(4.3)	0	1(2.2)
Breast pain	n (%)	1(4.3)	0	1(2.2)
Respiratory, thoracic and mediastinal disorders	n (%)	7(30.4)	2(8.7)	9(19.6)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.1.5B
Treatment-Emergent Adverse Events with CTCAE Severity >= Grade 3 by System Organ Class and Preferred Term: Negative Hormone Receptors (Safety Analysis Set)

System Organ Class (SOC) Preferred Term (PT)	Statistic	NLG-2101 (N=23)	Placebo (N=23)	Overall (N=46)
Atelectasis	n (%)	1(4.3)	0	1(2.2)
Dyspnoea	n (%)	4(17.4)	1(4.3)	5(10.9)
Hypoxia	n (%)	1(4.3)	0	1(2.2)
Pleural effusion	n (%)	2(8.7)	0	2(4.3)
Pulmonary embolism	n (%)	2(8.7)	1(4.3)	3(6.5)
Respiratory failure	n (%)	1(4.3)	0	1(2.2)
Skin and subcutaneous tissue disorders	n (%)	1(4.3)	0	1(2.2)
Alopecia	n (%)	1(4.3)	0	1(2.2)

Adverse Events are coded using MedDRA version 16.0.
Note: If a subject experienced more than one event within a given SOC, that subject is counted once for that SOC.
If a subject experienced more than one event within a given PT, that subject is counted only once for that PT.

Table 14.3.2.1
Listing of Adverse Events Leading to Subject Deaths (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101038	35/F/WH	V:multi-organ failure P:Multi-organ failure S:General disorders and administration site conditions	2015-04-30 (130)	2015-05-08 (138)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN
2101082	39/F/BL	V:Respiratory Failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-06-01 (4)	2015-06-01 (4)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN
2101099	58/F/WH	V:cardio-pulmonary failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-08-24 (54)	2015-08-24 (54)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DOSE NOT CHANGED
2101137	59/F/WH	V:Sudden death P:Sudden death S:General disorders and administration site conditions	2016-02-23 (148)	2016-02-23 (148)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN

[1] Abbreviations: Sex Code: M = Male, F = Female. Race Code: BL = Black or African American, AI = American Indian or Alaska Native, AS = Asian, NH = Native Hawaiian, WH = White, OT = Other.
Source: Listing 16.2.7.1
Program: tl2101ae.sas Output Generation: 05/07/2018 12:10

Table 14.3.2.1
Listing of Adverse Events Leading to Subject Deaths (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101032	50/F/WH	V:sepsis P:Sepsis S:Infections and infestations	2015-03-16 (97)	2015-04-04 (116)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN
2101047	69/F/BL	V:respiratory failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-03-15 (41)	2015-03-18 (44)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN

[1] Abbreviations: Sex Code: M = Male, F = Female. Race Code: BL = Black or African American, AI = American Indian or Alaska Native, AS = Asian, NH = Native Hawaiian, WH = White, OT = Other.
Source: Listing 16.2.7.1
Program: tl2101ae.sas Output Generation: 05/07/2018 12:10

Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101001	64/F/WH	V:Respiratory, thoracic, and mediastinal disorders-other, post obstructive pneumonia P:Pneumonia S:Infections and infestations	2013-10-01 (22)	2013-10-03 (24)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101003	63/F/WH	V:colonic perforation P:Large intestine perforation S:Gastrointestinal disorders	2014-04-12 (178)	2014-05-15 (211)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101004	54/F/WH	V:NON CARDIAC CHEST PAIN P:Non-cardiac chest pain S:General disorders and administration site conditions	2014-01-08 (69)	2014-01-12 (73)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101021	72/F/WH	V:Dyspnea P:Dyspnoea S:Respiratory, thoracic and mediastinal disorders	2015-03-03 (155)	2015-03-12 (164)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101022	66/F/WH	V:Non-cardiac chest Pain P:Non-cardiac chest pain S:General disorders and administration site conditions	2014-10-17 (11)	2014-10-27 (21)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
	66/F/WH	V:Pleural Effusion P:Pleural effusion S:Respiratory, thoracic and mediastinal disorders	2014-10-10 (4)	2014-10-11 (5)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101026	56/F/WH	V:skin infection P:Skin infection S:Infections and infestations	2015-01-16 (82)	2015-01-19 (85)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED

[1] Abbreviations: Sex Code: M = Male, F = Female. Race Code: BL = Black or African American, AI = American Indian or Alaska Native, AS = Asian, NH = Native Hawaiian, WH = White, OT = Other.
Source: Listing 16.2.7.1
Program: tl2101ae.sas Output Generation: 05/07/2018 12:10

Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101038	35/F/WH	V:multi-organ failure P:Multi-organ failure S:General disorders and administration site conditions	2015-04-30 (130)	2015-05-08 (138)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN
2101041	31/F/WH	V:breast pain P:Breast pain S:Reproductive system and breast disorders	2015-01-12 (7)	2015-01-13 (8)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED
2101042	67/F/WH	V:fracture R femur P:Femur fracture S:Injury, poisoning and procedural complications	2015-02-18 (36)	2015-02-19 (37)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101051	61/F/WH	V:febrile neutropenia P:Febrile neutropenia S:Blood and lymphatic system disorders	2015-03-19 (36)	2015-03-26 (43)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED
2101061	64/F/WH	V:DEHYDRATION P:Dehydration S:Metabolism and nutrition disorders	2015-05-18 (75)	2015-05-19 (76)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
	64/F/WH	V:DYSPNEA P:Dyspnoea S:Respiratory, thoracic and mediastinal disorders	2016-05-03 (426)	2016-05-05 (428)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN

[1] Abbreviations: Sex Code: M = Male, F = Female. Race Code: BL = Black or African American, AI = American Indian or Alaska Native, AS = Asian, NH = Native Hawaiian, WH = White, OT = Other.
Source: Listing 16.2.7.1
Program: tl2101ae.sas Output Generation: 05/07/2018 12:10

Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
	64/F/WH	V:PNEUMONIA P:Pneumonia S:Infections and infestations	2015-04-30 (57)	2015-05-03 (60)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101062	65/F/WH	V:Cholecystitis P:Cholecystitis S:Hepatobiliary disorders	2015-07-26 (138)	2015-08-13 (156)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101069	51/F/WH	V:Dyspnea P:Dyspnoea S:Respiratory, thoracic and mediastinal disorders	2015-05-02 (18)	2015-05-08 (24)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED
	51/F/WH	V:headache P:Headache S:Nervous system disorders	2015-07-06 (83)	2015-07-10 (87)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101072	49/F/WH	V:Anemia P:Anaemia S:Blood and lymphatic system disorders	2015-05-04 (7)	2015-05-05 (8)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101077	72/F/WH	V:Gait disturbance P:Gait disturbance S:General disorders and administration site conditions	2016-03-06 (293)	2016-03-08 (295)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED
2101082	39/F/BL	V:Respiratory Failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-06-01 (4)	2015-06-01 (4)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN

[1] Abbreviations: Sex Code: M = Male, F = Female. Race Code: BL = Black or African American, AI = American Indian or Alaska Native, AS = Asian, NH = Native Hawaiian, WH = White, OT = Other.
Source: Listing 16.2.7.1
Program: tl2101ae.sas Output Generation: 05/07/2018 12:10

Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101090	58/F/WH	V:headache P:Headache S:Nervous system disorders	2016-07-04 (389)	2016-07-22 (407)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101096	66/F/BL	V:Generalized Muscle Weakness P:Muscular weakness S:Musculoskeletal and connective tissue disorders	2016-04-04 (267)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DOSE NOT CHANGED
	66/F/BL	V:Mental Status Change P:Mental status changes S:Psychiatric disorders	2016-04-22 (285)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DOSE NOT CHANGED
	66/F/BL	V:Pulmonary Embolism P:Pulmonary embolism S:Respiratory, thoracic and mediastinal disorders	2015-09-08 (58)	2015-09-13 (63)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:
2101099	58/F/WH	V:Abdominal pain P:Abdominal pain S:Gastrointestinal disorders	2015-08-23 (53)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DOSE NOT CHANGED
	58/F/WH	V:cardio-pulmonary failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-08-24 (54)	2015-08-24 (54)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DOSE NOT CHANGED
2101109	57/F/WH	V:Dyspnea P:Dyspnoea S:Respiratory, thoracic and mediastinal disorders	2016-01-20 (176)	2016-02-09 (196)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED

[1] Abbreviations: Sex Code: M = Male, F = Female. Race Code: BL = Black or African American, AI = American Indian or Alaska Native, AS = Asian, NH = Native Hawaiian, WH = White, OT = Other.
Source: Listing 16.2.7.1
Program: tl2101ae.sas Output Generation: 05/07/2018 12:10

Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101110	57/F/WH	V:jaundice P:Jaundice S:Hepatobiliary disorders	2016-02-08 (190)	2016-02-13 (195)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101124	60/F/WH	V:Parkinson's Disease P:Parkinson's disease S:Nervous system disorders	2015-11-24 (78)	2016-02-15 (161)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Probable A:DRUG WITHDRAWN
2101128	52/F/WH	V:Gastrointestinal hemorrhage P:Gastrointestinal haemorrhage S:Gastrointestinal disorders	2015-12-02 (78)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DOSE NOT CHANGED
	52/F/WH	V:Hepatitis P:Hepatitis S:Hepatobiliary disorders	2015-11-18 (64)	ONGOING	Life Threatening (Grade 4)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101137	59/F/WH	V:Sudden death P:Sudden death S:General disorders and administration site conditions	2016-02-23 (148)	2016-02-23 (148)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN
2101138	62/F/WH	V:Colonic perforation P:Large intestine perforation S:Gastrointestinal disorders	2015-11-16 (47)	2015-12-11 (72)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
	62/F/WH	V:Urinary Tract Infection P:Urinary tract infection S:Infections and infestations	2015-10-25 (25)	2015-10-28 (28)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED

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Source: Listing 16.2.7.1
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Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101140	51/F/WH	V:anemia P:Anaemia S:Blood and lymphatic system disorders	2015-11-09 (8)	2015-11-10 (9)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
	51/F/WH	V:tachycardia P:Tachycardia S:Cardiac disorders	2016-05-24 (205)	2016-05-26 (207)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101156	48/F/WH	V:deep vein thrombosis P:Deep vein thrombosis S:Vascular disorders	2016-02-17 (69)	2016-03-10 (91)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED
	48/F/WH	V:vomiting P:Vomiting S:Gastrointestinal disorders	2016-02-23 (75)	2016-02-27 (79)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101163	57/F/WH	V:Hypercalcemia P:Hypercalcaemia S:Metabolism and nutrition disorders	2016-01-30 (6)	2016-03-16 (52)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101166	54/F/WH	V:left upper limb pain P:Pain in extremity S:Musculoskeletal and connective tissue disorders	2016-05-24 (118)	2016-06-17 (142)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED

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Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101002	45/F/OT	V:Adrenal Insufficiency P:Adrenal insufficiency S:Endocrine disorders	2013-12-07 (73)	2014-06-04 (252)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
	45/F/OT	V:BONE PAIN P:Bone pain S:Musculoskeletal and connective tissue disorders	2013-10-03 (8)	2013-10-08 (13)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101005	51/F/WH	V:Febrile Neutropenia P:Febrile neutropenia S:Blood and lymphatic system disorders	2014-01-01 (38)	2014-01-08 (45)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
2101028	41/F/WH	V:Dehydration P:Dehydration S:Metabolism and nutrition disorders	2014-12-22 (35)	2014-12-23 (36)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
2101029	66/F/WH	V:Hepatobiliary disorders-other (Hepatitis) P:Hepatitis S:Hepatobiliary disorders	2015-01-26 (75)	2015-01-29 (78)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
2101032	50/F/WH	V:sepsis P:Sepsis S:Infections and infestations	2015-03-16 (97)	2015-04-04 (116)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN
2101045	34/F/OT	V:Rash, Maculo-papular P:Rash maculo-papular S:Skin and subcutaneous tissue disorders	2015-05-24 (119)	2015-05-26 (121)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED

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Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101047	69/F/BL	V:pleural effusion P:Pleural effusion S:Respiratory, thoracic and mediastinal disorders	2015-03-03 (29)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DRUG WITHDRAWN
	69/F/BL	V:respiratory failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-03-15 (41)	2015-03-18 (44)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN
2101048	48/F/WH	V:Blood bilirubin increased P:Blood bilirubin increased S:Investigations	2015-07-25 (171)	ONGOING	Life Threatening (Grade 4)	O:NOT RECOVERED/NOT RESOLVED R:Unlikely A:DOSE NOT CHANGED
	48/F/WH	V:Palmar-plantar syndrome P:Palmar-plantar erythrodysaesthesia syndrome S:Skin and subcutaneous tissue disorders	2015-07-25 (171)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Possible A:DRUG WITHDRAWN
	48/F/WH	V:enterocolitis P:Enterocolitis S:Gastrointestinal disorders	2015-07-15 (161)	2015-07-18 (164)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101049	33/F/WH	V:Hepatic Failure P:Hepatic failure S:Hepatobiliary disorders	2015-06-12 (123)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101054	57/F/WH	V:biliary duct stenosis P:Bile duct stenosis S:Hepatobiliary disorders	2016-05-11 (449)	2016-05-15 (453)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN

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Source: Listing 16.2.7.1
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Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101071	66/F/WH	V:Diarrhea P:Diarrhoea S:Gastrointestinal disorders	2015-05-29 (32)	2015-06-03 (37)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
2101075	59/F/WH	V:vertigo (labyrinth disorder) P:Vertigo labyrinthine S:Ear and labyrinth disorders	2016-11-04 (541)	2016-11-08 (545)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101078	85/F/WH	V:coronary insufficiency artery P:Coronary artery insufficiency S:Cardiac disorders	2015-09-26 (130)	2015-10-02 (136)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101079	56/F/WH	V:cellulitis (soft tissue infection) P:Cellulitis S:Infections and infestations	2015-07-06 (41)	2015-07-20 (55)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
	56/F/WH	V:hypoglycemia P:Hypoglycaemia S:Metabolism and nutrition disorders	2015-06-12 (17)	2015-06-12 (17)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Possible A:DOSE NOT CHANGED
	56/F/WH	V:peripheral sensory neuropathy P:Peripheral sensory neuropathy S:Nervous system disorders	2015-07-06 (41)	2015-07-20 (55)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101081	65/F/WH	V:generalized weakness P:Asthenia S:General disorders and administration site conditions	2016-03-21 (299)	2016-03-23 (301)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED

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Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101084	57/F/WH	V:Neutropenia P:Neutropenia S:Blood and lymphatic system disorders	2015-10-06 (120)	2015-10-12 (126)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101085	57/F/WH	V:Hypotension P:Hypotension S:Vascular disorders	2015-08-10 (69)	2015-08-12 (71)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101088	54/F/WH	V:urinary tract infection P:Urinary tract infection S:Infections and infestations	2015-10-10 (128)	2015-10-20 (138)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101098	49/F/WH	V:febrile neutropenia P:Febrile neutropenia S:Blood and lymphatic system disorders	2015-07-14 (15)	2015-07-16 (17)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101101	63/F/WH	V:Right Lung Pneumonia P:Pneumonia S:Infections and infestations	2015-09-10 (66)	2015-09-16 (72)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED
2101105	65/F/WH	V:INTRACTABLE PAIN P:Pain S:General disorders and administration site conditions	2016-04-04 (265)	2016-04-06 (267)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101112	54/F/WH	V:hyperbilirubinemia P:Hyperbilirubinaemia S:Hepatobiliary disorders	2015-08-17 (8)	2015-09-21 (43)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN

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Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101118	74/F/WH	V:Ankle Fracture P:Ankle fracture S:Injury, poisoning and procedural complications	2015-11-24 (85)	2016-02-15 (168)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED
2101121	68/F/WH	V:back pain P:Back pain S:Musculoskeletal and connective tissue disorders	2015-09-02 (2)	2015-09-07 (7)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
	68/F/WH	V:thromboembolic event--acute pulmonary embolism P:Pulmonary embolism S:Respiratory, thoracic and mediastinal disorders	2015-11-17 (78)	2015-11-20 (81)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101123	77/F/WH	V:Asthenia P:Asthenia S:General disorders and administration site conditions	2015-09-18 (12)	2015-09-25 (19)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Highly Probable/Definite A:DOSE NOT CHANGED
	77/F/WH	V:Clostridium difficile infection P:Clostridium difficile infection S:Infections and infestations	2016-02-05 (152)	2016-02-17 (164)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
	77/F/WH	V:Nausea P:Nausea S:Gastrointestinal disorders	2015-10-17 (41)	2015-10-22 (46)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED

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Table 14.3.2.2
Listing of Subjects with Serious Adverse Events (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101126	60/F/BL	V:leptomeningeal carcinomatosis P:Metastases to meninges S:Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2015-12-18 (95)	2015-12-23 (100)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101136	60/F/WH	V:asthenia P:Asthenia S:General disorders and administration site conditions	2016-05-28 (249)	ONGOING	Life Threatening (Grade 4)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101148	59/F/WH	V:coronary artery diseases P:Coronary artery disease S:Cardiac disorders	2016-04-23 (158)	2016-04-28 (163)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unlikely A:DOSE NOT CHANGED

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Table 14.3.2.3
Listing of Subjects with Adverse Events Leading to Study Discontinuation (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101003	63/F/WH	V:colonic perforation P:Large intestine perforation S:Gastrointestinal disorders	2014-04-12 (178)	2014-05-15 (211)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101004	54/F/WH	V:NON CARDIAC CHEST PAIN P:Non-cardiac chest pain S:General disorders and administration site conditions	2014-01-08 (69)	2014-01-12 (73)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101016	61/F/BL	V:NEUROPATHY,WORSENING OF FEET P:Neuropathy peripheral S:Nervous system disorders	2015-01-07 (211)	ONGOING	Moderate (Grade 2)	O:NOT RECOVERED/NOT RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101021	72/F/WH	V:Dyspnea P:Dyspnoea S:Respiratory, thoracic and mediastinal disorders	2015-03-03 (155)	2015-03-12 (164)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101082	39/F/BL	V:Respiratory Failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-06-01 (4)	2015-06-01 (4)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN
	39/F/BL	V:Worsening Dyspnea P:Dyspnoea S:Respiratory, thoracic and mediastinal disorders	2015-05-31 (3)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DRUG WITHDRAWN
	39/F/BL	V:Worsening Hypoxia P:Hypoxia S:Respiratory, thoracic and mediastinal disorders	2015-05-31 (3)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DRUG WITHDRAWN

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Table 14.3.2.3
Listing of Subjects with Adverse Events Leading to Study Discontinuation (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101093	60/F/WH	V:Neutropenia P:Neutropenia S:Blood and lymphatic system disorders	2016-03-15 (272)	2016-06-23 (372)	Life Threatening (Grade 4)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101099	58/F/WH	V:cardio-pulmonary failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-08-24 (54)	2015-08-24 (54)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DOSE NOT CHANGED
2101110	57/F/WH	V:Fatigue P:Fatigue S:General disorders and administration site conditions	2016-02-08 (190)	2016-02-13 (195)	Mild (Grade 1)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
	57/F/WH	V:increase of liver enzymes P:Hepatic enzyme increased S:Investigations	2016-02-08 (190)	ONGOING	Severe (Grade 3)	O:NOT RECOVERED/NOT RESOLVED R:Unrelated A:DOSE NOT CHANGED
	57/F/WH	V:jaundice P:Jaundice S:Hepatobiliary disorders	2016-02-08 (190)	2016-02-13 (195)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101124	60/F/WH	V:Parkinson's Disease P:Parkinson's disease S:Nervous system disorders	2015-11-24 (78)	2016-02-15 (161)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Probable A:DRUG WITHDRAWN
2101137	59/F/WH	V:Sudden death P:Sudden death S:General disorders and administration site conditions	2016-02-23 (148)	2016-02-23 (148)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN

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Table 14.3.2.3
Listing of Subjects with Adverse Events Leading to Study Discontinuation (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101150	49/F/WH	V:Fatigue P:Fatigue S:General disorders and administration site conditions	2016-02-04 (73)	2016-04-06 (135)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Possible A:DOSE NOT CHANGED
	49/F/WH	V:Neuropathy-peripheral P:Neuropathy peripheral S:Nervous system disorders	2016-02-04 (73)	2016-04-06 (135)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
	49/F/WH	V:Parasthesia P:Paraesthesia S:Nervous system disorders	2016-02-17 (86)	2016-04-06 (135)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Highly Probable/Definite A:DOSE REDUCED

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Table 14.3.2.3
Listing of Subjects with Adverse Events Leading to Study Discontinuation (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101002	45/F/OT	V:Adrenal Insufficiency P:Adrenal insufficiency S:Endocrine disorders	2013-12-07 (73)	2014-06-04 (252)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
2101028	41/F/WH	V:Edema face P:Face oedema S:General disorders and administration site conditions	2015-02-25 (100)	2015-03-26 (129)	Mild (Grade 1)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
	41/F/WH	V:Edema limbs (ankles) P:Oedema peripheral S:General disorders and administration site conditions	2015-02-12 (87)	2015-02-25 (100)	Mild (Grade 1)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
	41/F/WH	V:Edema limbs (ankles) P:Oedema peripheral S:General disorders and administration site conditions	2015-02-25 (100)	2015-03-26 (129)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101029	66/F/WH	V:ALT INCREASED WORSENING P:Alanine aminotransferase increased S:Investigations	2015-01-23 (72)	2015-03-05 (113)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
	66/F/WH	V:AST INCREASED, WORSENING P:Aspartate aminotransferase increased S:Investigations	2015-01-23 (72)	2015-03-05 (113)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101047	69/F/BL	V:respiratory failure P:Respiratory failure S:Respiratory, thoracic and mediastinal disorders	2015-03-15 (41)	2015-03-18 (44)	Fatal (Grade 5)	O:FATAL R:Unrelated A:DRUG WITHDRAWN

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Table 14.3.2.3
Listing of Subjects with Adverse Events Leading to Study Discontinuation (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101054	57/F/WH	V:biliary duct stenosis P:Bile duct stenosis S:Hepatobiliary disorders	2016-05-11 (449)	2016-05-15 (453)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN
2101068	69/F/WH	V:Diarrhea P:Diarrhoea S:Gastrointestinal disorders	2015-05-26 (42)	2015-05-29 (45)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Probable A:DRUG WITHDRAWN
	69/F/WH	V:Fatigue P:Fatigue S:General disorders and administration site conditions	2015-05-26 (42)	ONGOING	Moderate (Grade 2)	O:NOT RECOVERED/NOT RESOLVED R:Probable A:DRUG WITHDRAWN
	69/F/WH	V:Mucositis P:Mucosal inflammation S:General disorders and administration site conditions	2015-05-24 (40)	2015-05-29 (45)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
	69/F/WH	V:Vomiting P:Vomiting S:Gastrointestinal disorders	2015-05-26 (42)	2015-06-05 (52)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
2101079	56/F/WH	V:palmar-plantar erythrodysesthesia syndrome P:Palmar-plantar erythrodysaesthesia syndrome S:Skin and subcutaneous tissue disorders	2015-06-27 (32)	2015-07-20 (55)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Possible A:DRUG WITHDRAWN
	56/F/WH	V:peripheral sensory neuropathy P:Peripheral sensory neuropathy S:Nervous system disorders	2015-07-06 (41)	2015-07-20 (55)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unlikely A:DRUG WITHDRAWN

[1] Abbreviations: Sex Code: M = Male, F = Female. Race Code: BL = Black or African American, AI = American Indian or Alaska Native, AS = Asian, NH = Native Hawaiian, WH = White, OT = Other.
Source: Listing 16.2.7.1
Program: tl2101ae.sas Output Generation: 05/07/2018 12:10

Table 14.3.2.3
Listing of Subjects with Adverse Events Leading to Study Discontinuation (Safety Analysis Set)

Treatment Group: NLG2101

Subject	Age/Sex/ Race [1]	A:AE Verbatim P:Preferred Term S:System Organ Class	Start Date(Day)	Stop Date(Day)	CTCAE Grade	O:Outcome R:Relation A:Action Taken
2101112	54/F/WH	V:hyperbilirubinemia P:Hyperbilirubinaemia S:Hepatobiliary disorders	2015-08-17 (8)	2015-09-21 (43)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN
2101123	77/F/WH	V:Appetite loss P:Decreased appetite S:Metabolism and nutrition disorders	2015-09-22 (16)	2015-09-25 (19)	Moderate (Grade 2)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
	77/F/WH	V:Neutropenia P:Neutropenia S:Blood and lymphatic system disorders	2015-09-21 (15)	2015-09-23 (17)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DOSE NOT CHANGED
2101126	60/F/BL	V:leptomeningeal carcinomatosis P:Metastases to meninges S:Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2015-12-18 (95)	2015-12-23 (100)	Severe (Grade 3)	O:RECOVERED/RESOLVED R:Unrelated A:DRUG WITHDRAWN

[1] Abbreviations: Sex Code: M = Male, F = Female. Race Code: BL = Black or African American, AI = American Indian or Alaska Native, AS = Asian, NH = Native Hawaiian, WH = White, OT = Other.
Source: Listing 16.2.7.1
Program: tl2101ae.sas Output Generation: 05/07/2018 12:10

2.3.2 Display of Laboratory Data

Table Number	Table Title
Table 14.3.5.3A	Laboratory shifts from baseline based on the normal range: hematology (Safety Analysis Set)
Table 14.3.5.3B	Laboratory shifts from baseline based on the normal range: chemistry (Safety Analysis Set)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Basophils (10^9/L)	Low	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.2)
		Normal	3 (3.5)	52 (61.2)	5 (5.9)	1 (1.2)	61 (71.8)
		High	0 (0.0)	0 (0.0)	2 (2.4)	0 (0.0)	2 (2.4)
		Missing	0 (0.0)	8 (9.4)	0 (0.0)	13 (15.3)	21 (24.7)
		Total	3 (3.5)	60 (70.6)	8 (9.4)	14 (16.5)	85 (100.0)
PLACEBO	Basophils (10^9/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	2 (2.5)	51 (64.6)	7 (8.9)	2 (2.5)	62 (78.5)
		High	0 (0.0)	1 (1.3)	2 (2.5)	0 (0.0)	3 (3.8)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	11 (13.9)	14 (17.7)
		Total	2 (2.5)	55 (69.6)	9 (11.4)	13 (16.5)	79 (100.0)
NLG2101	Basophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	9 (10.6)	1 (1.2)	3 (3.5)	13 (15.3)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	1 (1.2)	0 (0.0)	71 (83.5)	72 (84.7)
		Total	0 (0.0)	10 (11.8)	1 (1.2)	74 (87.1)	85 (100.0)
PLACEBO	Basophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	6 (7.6)	0 (0.0)	1 (1.3)	7 (8.9)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	3 (3.8)	1 (1.3)	68 (86.1)	72 (91.1)
		Total	0 (0.0)	9 (11.4)	1 (1.3)	69 (87.3)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Eosinophils (10^9/L)	Low	1 (1.2)	0 (0.0)	1 (1.2)	0 (0.0)	2 (2.4)
		Normal	20 (23.5)	34 (40.0)	6 (7.1)	1 (1.2)	61 (71.8)
		High	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)
		Missing	0 (0.0)	8 (9.4)	0 (0.0)	13 (15.3)	21 (24.7)
		Total	22 (25.9)	42 (49.4)	7 (8.2)	14 (16.5)	85 (100.0)
PLACEBO	Eosinophils (10^9/L)	Low	3 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.8)
		Normal	13 (16.5)	39 (49.4)	6 (7.6)	2 (2.5)	60 (75.9)
		High	1 (1.3)	0 (0.0)	1 (1.3)	0 (0.0)	2 (2.5)
		Missing	1 (1.3)	2 (2.5)	0 (0.0)	11 (13.9)	14 (17.7)
		Total	18 (22.8)	41 (51.9)	7 (8.9)	13 (16.5)	79 (100.0)
NLG2101	Eosinophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	7 (8.2)	2 (2.4)	4 (4.7)	13 (15.3)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	1 (1.2)	0 (0.0)	71 (83.5)	72 (84.7)
		Total	0 (0.0)	8 (9.4)	2 (2.4)	75 (88.2)	85 (100.0)
PLACEBO	Eosinophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)	1 (1.3)
		Normal	0 (0.0)	5 (6.3)	1 (1.3)	0 (0.0)	6 (7.6)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	1 (1.3)	3 (3.8)	0 (0.0)	68 (86.1)	72 (91.1)
		Total	1 (1.3)	8 (10.1)	1 (1.3)	69 (87.3)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Hemoglobin (g/L)	Low	33 (38.8)	0 (0.0)	1 (1.2)	0 (0.0)	34 (40.0)
		Normal	33 (38.8)	12 (14.1)	4 (4.7)	1 (1.2)	50 (58.8)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)
		Total	66 (77.6)	12 (14.1)	5 (5.9)	2 (2.4)	85 (100.0)
PLACEBO	Hemoglobin (g/L)	Low	18 (22.8)	0 (0.0)	0 (0.0)	2 (2.5)	20 (25.3)
		Normal	35 (44.3)	23 (29.1)	0 (0.0)	1 (1.3)	59 (74.7)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	53 (67.1)	23 (29.1)	0 (0.0)	3 (3.8)	79 (100.0)
NLG2101	Lymphocytes (10^9/L)	Low	16 (18.8)	0 (0.0)	0 (0.0)	1 (1.2)	17 (20.0)
		Normal	37 (43.5)	14 (16.5)	1 (1.2)	0 (0.0)	52 (61.2)
		High	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	2 (2.4)
		Missing	7 (8.2)	3 (3.5)	0 (0.0)	4 (4.7)	14 (16.5)
		Total	60 (70.6)	18 (21.2)	2 (2.4)	5 (5.9)	85 (100.0)
PLACEBO	Lymphocytes (10^9/L)	Low	17 (21.5)	0 (0.0)	0 (0.0)	0 (0.0)	17 (21.5)
		Normal	28 (35.4)	20 (25.3)	1 (1.3)	1 (1.3)	50 (63.3)
		High	0 (0.0)	0 (0.0)	1 (1.3)	1 (1.3)	2 (2.5)
		Missing	6 (7.6)	2 (2.5)	0 (0.0)	2 (2.5)	10 (12.7)
		Total	51 (64.6)	22 (27.8)	2 (2.5)	4 (5.1)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Lymphocytes/Leukocytes (%)	Low	2 (2.4)	0 (0.0)	0 (0.0)	1 (1.2)	3 (3.5)
		Normal	3 (3.5)	4 (4.7)	0 (0.0)	1 (1.2)	8 (9.4)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	4 (4.7)	2 (2.4)	0 (0.0)	68 (80.0)	74 (87.1)
		Total	9 (10.6)	6 (7.1)	0 (0.0)	70 (82.4)	85 (100.0)
PLACEBO	Lymphocytes/Leukocytes (%)	Low	3 (3.8)	0 (0.0)	1 (1.3)	1 (1.3)	5 (6.3)
		Normal	2 (2.5)	3 (3.8)	1 (1.3)	0 (0.0)	6 (7.6)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	3 (3.8)	0 (0.0)	1 (1.3)	64 (81.0)	68 (86.1)
		Total	8 (10.1)	3 (3.8)	3 (3.8)	65 (82.3)	79 (100.0)
NLG2101	Monocytes (10^9/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	17 (20.0)	21 (24.7)	20 (23.5)	1 (1.2)	59 (69.4)
		High	0 (0.0)	0 (0.0)	10 (11.8)	0 (0.0)	10 (11.8)
		Missing	1 (1.2)	8 (9.4)	2 (2.4)	5 (5.9)	16 (18.8)
		Total	18 (21.2)	29 (34.1)	32 (37.6)	6 (7.1)	85 (100.0)
PLACEBO	Monocytes (10^9/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	15 (19.0)	26 (32.9)	20 (25.3)	1 (1.3)	62 (78.5)
		High	0 (0.0)	1 (1.3)	5 (6.3)	1 (1.3)	7 (8.9)
		Missing	1 (1.3)	6 (7.6)	1 (1.3)	2 (2.5)	10 (12.7)
		Total	16 (20.3)	33 (41.8)	26 (32.9)	4 (5.1)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Monocytes/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	6 (7.1)	1 (1.2)	3 (3.5)	10 (11.8)
		High	0 (0.0)	0 (0.0)	2 (2.4)	0 (0.0)	2 (2.4)
		Missing	0 (0.0)	7 (8.2)	0 (0.0)	66 (77.6)	73 (85.9)
		Total	0 (0.0)	13 (15.3)	3 (3.5)	69 (81.2)	85 (100.0)
PLACEBO	Monocytes/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	6 (7.6)	1 (1.3)	1 (1.3)	8 (10.1)
		High	0 (0.0)	1 (1.3)	1 (1.3)	0 (0.0)	2 (2.5)
		Missing	0 (0.0)	4 (5.1)	1 (1.3)	64 (81.0)	69 (87.3)
		Total	0 (0.0)	11 (13.9)	3 (3.8)	65 (82.3)	79 (100.0)
NLG2101	Neutrophils (10^9/L)	Low	1 (1.2)	0 (0.0)	2 (2.4)	0 (0.0)	3 (3.5)
		Normal	9 (10.6)	15 (17.6)	36 (42.4)	1 (1.2)	61 (71.8)
		High	0 (0.0)	0 (0.0)	6 (7.1)	0 (0.0)	6 (7.1)
		Missing	1 (1.2)	4 (4.7)	6 (7.1)	4 (4.7)	15 (17.6)
		Total	11 (12.9)	19 (22.4)	50 (58.8)	5 (5.9)	85 (100.0)
PLACEBO	Neutrophils (10^9/L)	Low	0 (0.0)	0 (0.0)	4 (5.1)	0 (0.0)	4 (5.1)
		Normal	5 (6.3)	11 (13.9)	43 (54.4)	1 (1.3)	60 (75.9)
		High	0 (0.0)	2 (2.5)	2 (2.5)	1 (1.3)	5 (6.3)
		Missing	3 (3.8)	0 (0.0)	4 (5.1)	3 (3.8)	10 (12.7)
		Total	8 (10.1)	13 (16.5)	53 (67.1)	5 (6.3)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Neutrophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	2 (2.4)	6 (7.1)	2 (2.4)	10 (11.8)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	2 (2.4)	2 (2.4)	71 (83.5)	75 (88.2)
		Total	0 (0.0)	4 (4.7)	8 (9.4)	73 (85.9)	85 (100.0)
PLACEBO	Neutrophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	2 (2.5)	5 (6.3)	0 (0.0)	7 (8.9)
		High	0 (0.0)	0 (0.0)	2 (2.5)	1 (1.3)	3 (3.8)
		Missing	0 (0.0)	1 (1.3)	4 (5.1)	64 (81.0)	69 (87.3)
		Total	0 (0.0)	3 (3.8)	11 (13.9)	65 (82.3)	79 (100.0)
NLG2101	Platelets (10^9/L)	Low	2 (2.4)	1 (1.2)	0 (0.0)	1 (1.2)	4 (4.7)
		Normal	8 (9.4)	42 (49.4)	14 (16.5)	0 (0.0)	64 (75.3)
		High	0 (0.0)	0 (0.0)	13 (15.3)	0 (0.0)	13 (15.3)
		Missing	0 (0.0)	3 (3.5)	0 (0.0)	1 (1.2)	4 (4.7)
		Total	10 (11.8)	46 (54.1)	27 (31.8)	2 (2.4)	85 (100.0)
PLACEBO	Platelets (10^9/L)	Low	2 (2.5)	2 (2.5)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	7 (8.9)	41 (51.9)	18 (22.8)	2 (2.5)	68 (86.1)
		High	0 (0.0)	1 (1.3)	5 (6.3)	1 (1.3)	7 (8.9)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	9 (11.4)	44 (55.7)	23 (29.1)	3 (3.8)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Leukocytes (10^9/L)	Low	3 (3.5)	0 (0.0)	2 (2.4)	0 (0.0)	5 (5.9)
		Normal	16 (18.8)	13 (15.3)	40 (47.1)	1 (1.2)	70 (82.4)
		High	0 (0.0)	0 (0.0)	6 (7.1)	0 (0.0)	6 (7.1)
		Missing	2 (2.4)	1 (1.2)	0 (0.0)	1 (1.2)	4 (4.7)
		Total	21 (24.7)	14 (16.5)	48 (56.5)	2 (2.4)	85 (100.0)
PLACEBO	Leukocytes (10^9/L)	Low	2 (2.5)	1 (1.3)	1 (1.3)	0 (0.0)	4 (5.1)
		Normal	14 (17.7)	14 (17.7)	41 (51.9)	2 (2.5)	71 (89.9)
		High	0 (0.0)	0 (0.0)	3 (3.8)	1 (1.3)	4 (5.1)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	16 (20.3)	15 (19.0)	45 (57.0)	3 (3.8)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Basophils (10^9/L)	Low	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Normal	0 (0.0)	59 (69.4)	1 (1.2)	1 (1.2)	61 (71.8)
		High	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	2 (2.4)
		Missing	0 (0.0)	8 (9.4)	0 (0.0)	13 (15.3)	21 (24.7)
		Total	0 (0.0)	69 (81.2)	2 (2.4)	14 (16.5)	85 (100.0)
PLACEBO	Basophils (10^9/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	1 (1.3)	55 (69.6)	4 (5.1)	2 (2.5)	62 (78.5)
		High	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	11 (13.9)	14 (17.7)
		Total	1 (1.3)	61 (77.2)	4 (5.1)	13 (16.5)	79 (100.0)
NLG2101	Basophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	10 (11.8)	0 (0.0)	3 (3.5)	13 (15.3)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	1 (1.2)	0 (0.0)	71 (83.5)	72 (84.7)
		Total	0 (0.0)	11 (12.9)	0 (0.0)	74 (87.1)	85 (100.0)
PLACEBO	Basophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	6 (7.6)	0 (0.0)	1 (1.3)	7 (8.9)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	4 (5.1)	0 (0.0)	68 (86.1)	72 (91.1)
		Total	0 (0.0)	10 (12.7)	0 (0.0)	69 (87.3)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Eosinophils (10^9/L)	Low	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	2 (2.4)
		Normal	3 (3.5)	56 (65.9)	1 (1.2)	1 (1.2)	61 (71.8)
		High	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Missing	0 (0.0)	8 (9.4)	0 (0.0)	13 (15.3)	21 (24.7)
		Total	3 (3.5)	66 (77.6)	2 (2.4)	14 (16.5)	85 (100.0)
PLACEBO	Eosinophils (10^9/L)	Low	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Normal	8 (10.1)	49 (62.0)	1 (1.3)	2 (2.5)	60 (75.9)
		High	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	2 (2.5)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	11 (13.9)	14 (17.7)
		Total	8 (10.1)	57 (72.2)	1 (1.3)	13 (16.5)	79 (100.0)
NLG2101	Eosinophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	9 (10.6)	0 (0.0)	4 (4.7)	13 (15.3)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	1 (1.2)	0 (0.0)	71 (83.5)	72 (84.7)
		Total	0 (0.0)	10 (11.8)	0 (0.0)	75 (88.2)	85 (100.0)
PLACEBO	Eosinophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)	1 (1.3)
		Normal	0 (0.0)	6 (7.6)	0 (0.0)	0 (0.0)	6 (7.6)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	1 (1.3)	3 (3.8)	0 (0.0)	68 (86.1)	72 (91.1)
		Total	1 (1.3)	9 (11.4)	0 (0.0)	69 (87.3)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Hemoglobin (g/L)	Low	30 (35.3)	4 (4.7)	0 (0.0)	0 (0.0)	34 (40.0)
		Normal	17 (20.0)	30 (35.3)	2 (2.4)	1 (1.2)	50 (58.8)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)
		Total	47 (55.3)	34 (40.0)	2 (2.4)	2 (2.4)	85 (100.0)
PLACEBO	Hemoglobin (g/L)	Low	17 (21.5)	1 (1.3)	0 (0.0)	2 (2.5)	20 (25.3)
		Normal	19 (24.1)	39 (49.4)	0 (0.0)	1 (1.3)	59 (74.7)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	36 (45.6)	40 (50.6)	0 (0.0)	3 (3.8)	79 (100.0)
NLG2101	Lymphocytes (10^9/L)	Low	13 (15.3)	3 (3.5)	0 (0.0)	1 (1.2)	17 (20.0)
		Normal	13 (15.3)	39 (45.9)	0 (0.0)	0 (0.0)	52 (61.2)
		High	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)	2 (2.4)
		Missing	5 (5.9)	5 (5.9)	0 (0.0)	4 (4.7)	14 (16.5)
		Total	32 (37.6)	48 (56.5)	0 (0.0)	5 (5.9)	85 (100.0)
PLACEBO	Lymphocytes (10^9/L)	Low	15 (19.0)	2 (2.5)	0 (0.0)	0 (0.0)	17 (21.5)
		Normal	14 (17.7)	34 (43.0)	1 (1.3)	1 (1.3)	50 (63.3)
		High	0 (0.0)	1 (1.3)	0 (0.0)	1 (1.3)	2 (2.5)
		Missing	3 (3.8)	5 (6.3)	0 (0.0)	2 (2.5)	10 (12.7)
		Total	32 (40.5)	42 (53.2)	1 (1.3)	4 (5.1)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Lymphocytes/Leukocytes (%)	Low	1 (1.2)	1 (1.2)	0 (0.0)	1 (1.2)	3 (3.5)
		Normal	2 (2.4)	5 (5.9)	0 (0.0)	1 (1.2)	8 (9.4)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	3 (3.5)	3 (3.5)	0 (0.0)	68 (80.0)	74 (87.1)
		Total	6 (7.1)	9 (10.6)	0 (0.0)	70 (82.4)	85 (100.0)
PLACEBO	Lymphocytes/Leukocytes (%)	Low	3 (3.8)	0 (0.0)	1 (1.3)	1 (1.3)	5 (6.3)
		Normal	2 (2.5)	4 (5.1)	0 (0.0)	0 (0.0)	6 (7.6)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	2 (2.5)	1 (1.3)	1 (1.3)	64 (81.0)	68 (86.1)
		Total	7 (8.9)	5 (6.3)	2 (2.5)	65 (82.3)	79 (100.0)
NLG2101	Monocytes (10^9/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	4 (4.7)	50 (58.8)	4 (4.7)	1 (1.2)	59 (69.4)
		High	0 (0.0)	4 (4.7)	6 (7.1)	0 (0.0)	10 (11.8)
		Missing	0 (0.0)	9 (10.6)	2 (2.4)	5 (5.9)	16 (18.8)
		Total	4 (4.7)	63 (74.1)	12 (14.1)	6 (7.1)	85 (100.0)
PLACEBO	Monocytes (10^9/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	5 (6.3)	49 (62.0)	7 (8.9)	1 (1.3)	62 (78.5)
		High	0 (0.0)	5 (6.3)	1 (1.3)	1 (1.3)	7 (8.9)
		Missing	0 (0.0)	8 (10.1)	0 (0.0)	2 (2.5)	10 (12.7)
		Total	5 (6.3)	62 (78.5)	8 (10.1)	4 (5.1)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Monocytes/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	7 (8.2)	0 (0.0)	3 (3.5)	10 (11.8)
		High	0 (0.0)	0 (0.0)	2 (2.4)	0 (0.0)	2 (2.4)
		Missing	0 (0.0)	7 (8.2)	0 (0.0)	66 (77.6)	73 (85.9)
		Total	0 (0.0)	14 (16.5)	2 (2.4)	69 (81.2)	85 (100.0)
PLACEBO	Monocytes/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	6 (7.6)	1 (1.3)	1 (1.3)	8 (10.1)
		High	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	2 (2.5)
		Missing	0 (0.0)	4 (5.1)	1 (1.3)	64 (81.0)	69 (87.3)
		Total	0 (0.0)	12 (15.2)	2 (2.5)	65 (82.3)	79 (100.0)
NLG2101	Neutrophils (10^9/L)	Low	2 (2.4)	1 (1.2)	0 (0.0)	0 (0.0)	3 (3.5)
		Normal	4 (4.7)	47 (55.3)	9 (10.6)	1 (1.2)	61 (71.8)
		High	0 (0.0)	3 (3.5)	3 (3.5)	0 (0.0)	6 (7.1)
		Missing	0 (0.0)	7 (8.2)	4 (4.7)	4 (4.7)	15 (17.6)
		Total	6 (7.1)	58 (68.2)	16 (18.8)	5 (5.9)	85 (100.0)
PLACEBO	Neutrophils (10^9/L)	Low	3 (3.8)	0 (0.0)	1 (1.3)	0 (0.0)	4 (5.1)
		Normal	5 (6.3)	39 (49.4)	15 (19.0)	1 (1.3)	60 (75.9)
		High	0 (0.0)	3 (3.8)	1 (1.3)	1 (1.3)	5 (6.3)
		Missing	1 (1.3)	4 (5.1)	2 (2.5)	3 (3.8)	10 (12.7)
		Total	9 (11.4)	46 (58.2)	19 (24.1)	5 (6.3)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

			Last Post-Baseline Assessment				
Treatment Group	Parameter	Baseline	Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Neutrophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	1 (1.2)	5 (5.9)	2 (2.4)	2 (2.4)	10 (11.8)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	2 (2.4)	2 (2.4)	71 (83.5)	75 (88.2)
		Total	1 (1.2)	7 (8.2)	4 (4.7)	73 (85.9)	85 (100.0)
PLACEBO	Neutrophils/Leukocytes (%)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	5 (6.3)	2 (2.5)	0 (0.0)	7 (8.9)
		High	1 (1.3)	0 (0.0)	1 (1.3)	1 (1.3)	3 (3.8)
		Missing	0 (0.0)	1 (1.3)	4 (5.1)	64 (81.0)	69 (87.3)
		Total	1 (1.3)	6 (7.6)	7 (8.9)	65 (82.3)	79 (100.0)
NLG2101	Platelets (10^9/L)	Low	1 (1.2)	2 (2.4)	0 (0.0)	1 (1.2)	4 (4.7)
		Normal	6 (7.1)	55 (64.7)	3 (3.5)	0 (0.0)	64 (75.3)
		High	0 (0.0)	8 (9.4)	5 (5.9)	0 (0.0)	13 (15.3)
		Missing	0 (0.0)	3 (3.5)	0 (0.0)	1 (1.2)	4 (4.7)
		Total	7 (8.2)	68 (80.0)	8 (9.4)	2 (2.4)	85 (100.0)
PLACEBO	Platelets (10^9/L)	Low	0 (0.0)	4 (5.1)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	4 (5.1)	58 (73.4)	4 (5.1)	2 (2.5)	68 (86.1)
		High	0 (0.0)	2 (2.5)	4 (5.1)	1 (1.3)	7 (8.9)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	4 (5.1)	64 (81.0)	8 (10.1)	3 (3.8)	79 (100.0)

Table 14.3.5.3A
Laboratory Shifts From Baseline Based on the Normal Range: Hematology (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Leukocytes (10^9/L)	Low	4 (4.7)	1 (1.2)	0 (0.0)	0 (0.0)	5 (5.9)
		Normal	9 (10.6)	52 (61.2)	8 (9.4)	1 (1.2)	70 (82.4)
		High	0 (0.0)	2 (2.4)	4 (4.7)	0 (0.0)	6 (7.1)
		Missing	2 (2.4)	1 (1.2)	0 (0.0)	1 (1.2)	4 (4.7)
		Total	15 (17.6)	56 (65.9)	12 (14.1)	2 (2.4)	85 (100.0)
PLACEBO	Leukocytes (10^9/L)	Low	2 (2.5)	2 (2.5)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	8 (10.1)	49 (62.0)	12 (15.2)	2 (2.5)	71 (89.9)
		High	1 (1.3)	1 (1.3)	1 (1.3)	1 (1.3)	4 (5.1)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	11 (13.9)	52 (65.8)	13 (16.5)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Albumin (g/L)	Low	11 (12.9)	1 (1.2)	0 (0.0)	1 (1.2)	13 (15.3)
		Normal	18 (21.2)	47 (55.3)	2 (2.4)	2 (2.4)	69 (81.2)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	2 (2.4)	1 (1.2)	0 (0.0)	3 (3.5)
		Total	29 (34.1)	50 (58.8)	3 (3.5)	3 (3.5)	85 (100.0)
PLACEBO	Albumin (g/L)	Low	4 (5.1)	2 (2.5)	0 (0.0)	0 (0.0)	6 (7.6)
		Normal	19 (24.1)	46 (58.2)	2 (2.5)	3 (3.8)	70 (88.6)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	2 (2.5)	1 (1.3)	0 (0.0)	3 (3.8)
		Total	23 (29.1)	50 (63.3)	3 (3.8)	3 (3.8)	79 (100.0)
NLG2101	Alkaline Phosphatase (U/L)	Low	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Normal	0 (0.0)	46 (54.1)	12 (14.1)	0 (0.0)	58 (68.2)
		High	0 (0.0)	1 (1.2)	19 (22.4)	1 (1.2)	21 (24.7)
		Missing	0 (0.0)	3 (3.5)	1 (1.2)	1 (1.2)	5 (5.9)
		Total	0 (0.0)	51 (60.0)	32 (37.6)	2 (2.4)	85 (100.0)
PLACEBO	Alkaline Phosphatase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	3 (3.8)	40 (50.6)	9 (11.4)	2 (2.5)	54 (68.4)
		High	0 (0.0)	1 (1.3)	21 (26.6)	1 (1.3)	23 (29.1)
		Missing	0 (0.0)	1 (1.3)	1 (1.3)	0 (0.0)	2 (2.5)
		Total	3 (3.8)	42 (53.2)	31 (39.2)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Alanine Aminotransferase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	1 (1.2)	58 (68.2)	10 (11.8)	1 (1.2)	70 (82.4)
		High	0 (0.0)	4 (4.7)	7 (8.2)	1 (1.2)	12 (14.1)
		Missing	0 (0.0)	2 (2.4)	1 (1.2)	0 (0.0)	3 (3.5)
		Total	1 (1.2)	64 (75.3)	18 (21.2)	2 (2.4)	85 (100.0)
PLACEBO	Alanine Aminotransferase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	2 (2.5)	47 (59.5)	9 (11.4)	2 (2.5)	60 (75.9)
		High	0 (0.0)	2 (2.5)	14 (17.7)	1 (1.3)	17 (21.5)
		Missing	0 (0.0)	1 (1.3)	1 (1.3)	0 (0.0)	2 (2.5)
		Total	2 (2.5)	50 (63.3)	24 (30.4)	3 (3.8)	79 (100.0)
NLG2101	Aspartate Aminotransferase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	48 (56.5)	15 (17.6)	1 (1.2)	64 (75.3)
		High	0 (0.0)	4 (4.7)	13 (15.3)	1 (1.2)	18 (21.2)
		Missing	0 (0.0)	1 (1.2)	2 (2.4)	0 (0.0)	3 (3.5)
		Total	0 (0.0)	53 (62.4)	30 (35.3)	2 (2.4)	85 (100.0)
PLACEBO	Aspartate Aminotransferase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	35 (44.3)	15 (19.0)	2 (2.5)	52 (65.8)
		High	1 (1.3)	1 (1.3)	22 (27.8)	1 (1.3)	25 (31.6)
		Missing	0 (0.0)	1 (1.3)	1 (1.3)	0 (0.0)	2 (2.5)
		Total	1 (1.3)	37 (46.8)	38 (48.1)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Bicarbonate (mmol/L)	Low	7 (8.2)	2 (2.4)	0 (0.0)	0 (0.0)	9 (10.6)
		Normal	20 (23.5)	31 (36.5)	5 (5.9)	2 (2.4)	58 (68.2)
		High	0 (0.0)	4 (4.7)	3 (3.5)	1 (1.2)	8 (9.4)
		Missing	5 (5.9)	0 (0.0)	1 (1.2)	4 (4.7)	10 (11.8)
		Total	32 (37.6)	37 (43.5)	9 (10.6)	7 (8.2)	85 (100.0)
PLACEBO	Bicarbonate (mmol/L)	Low	2 (2.5)	1 (1.3)	2 (2.5)	0 (0.0)	5 (6.3)
		Normal	19 (24.1)	31 (39.2)	4 (5.1)	3 (3.8)	57 (72.2)
		High	0 (0.0)	0 (0.0)	4 (5.1)	0 (0.0)	4 (5.1)
		Missing	2 (2.5)	1 (1.3)	0 (0.0)	10 (12.7)	13 (16.5)
		Total	23 (29.1)	33 (41.8)	10 (12.7)	13 (16.5)	79 (100.0)
NLG2101	Calcium (mmol/L)	Low	4 (4.7)	0 (0.0)	0 (0.0)	0 (0.0)	4 (4.7)
		Normal	22 (25.9)	36 (42.4)	10 (11.8)	2 (2.4)	70 (82.4)
		High	0 (0.0)	2 (2.4)	8 (9.4)	0 (0.0)	10 (11.8)
		Missing	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.2)
		Total	26 (30.6)	38 (44.7)	19 (22.4)	2 (2.4)	85 (100.0)
PLACEBO	Calcium (mmol/L)	Low	3 (3.8)	1 (1.3)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	14 (17.7)	42 (53.2)	9 (11.4)	3 (3.8)	68 (86.1)
		High	0 (0.0)	3 (3.8)	3 (3.8)	0 (0.0)	6 (7.6)
		Missing	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
		Total	17 (21.5)	47 (59.5)	12 (15.2)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Chloride (mmol/L)	Low	2 (2.4)	1 (1.2)	0 (0.0)	0 (0.0)	3 (3.5)
		Normal	18 (21.2)	53 (62.4)	4 (4.7)	2 (2.4)	77 (90.6)
		High	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Missing	1 (1.2)	2 (2.4)	1 (1.2)	0 (0.0)	4 (4.7)
		Total	21 (24.7)	57 (67.1)	5 (5.9)	2 (2.4)	85 (100.0)
PLACEBO	Chloride (mmol/L)	Low	3 (3.8)	1 (1.3)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	15 (19.0)	41 (51.9)	11 (13.9)	2 (2.5)	69 (87.3)
		High	0 (0.0)	0 (0.0)	2 (2.5)	1 (1.3)	3 (3.8)
		Missing	0 (0.0)	1 (1.3)	1 (1.3)	1 (1.3)	3 (3.8)
		Total	18 (22.8)	43 (54.4)	14 (17.7)	4 (5.1)	79 (100.0)
NLG2101	Creatinine (umol/L)	Low	9 (10.6)	2 (2.4)	0 (0.0)	0 (0.0)	11 (12.9)
		Normal	12 (14.1)	47 (55.3)	8 (9.4)	2 (2.4)	69 (81.2)
		High	0 (0.0)	0 (0.0)	5 (5.9)	0 (0.0)	5 (5.9)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	21 (24.7)	49 (57.6)	13 (15.3)	2 (2.4)	85 (100.0)
PLACEBO	Creatinine (umol/L)	Low	6 (7.6)	0 (0.0)	0 (0.0)	1 (1.3)	7 (8.9)
		Normal	21 (26.6)	40 (50.6)	4 (5.1)	2 (2.5)	67 (84.8)
		High	0 (0.0)	3 (3.8)	1 (1.3)	0 (0.0)	4 (5.1)
		Missing	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
		Total	27 (34.2)	44 (55.7)	5 (6.3)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Glucose (mmol/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	6 (7.1)	34 (40.0)	0 (0.0)	40 (47.1)
		High	0 (0.0)	2 (2.4)	41 (48.2)	2 (2.4)	45 (52.9)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	0 (0.0)	8 (9.4)	75 (88.2)	2 (2.4)	85 (100.0)
PLACEBO	Glucose (mmol/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	1 (1.3)	4 (5.1)	33 (41.8)	2 (2.5)	40 (50.6)
		High	0 (0.0)	2 (2.5)	35 (44.3)	1 (1.3)	38 (48.1)
		Missing	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
		Total	1 (1.3)	7 (8.9)	68 (86.1)	3 (3.8)	79 (100.0)
NLG2101	Potassium (mmol/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)
		Normal	11 (12.9)	54 (63.5)	14 (16.5)	1 (1.2)	80 (94.1)
		High	0 (0.0)	3 (3.5)	0 (0.0)	0 (0.0)	3 (3.5)
		Missing	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.2)
		Total	11 (12.9)	57 (67.1)	15 (17.6)	2 (2.4)	85 (100.0)
PLACEBO	Potassium (mmol/L)	Low	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
		Normal	10 (12.7)	46 (58.2)	11 (13.9)	3 (3.8)	70 (88.6)
		High	1 (1.3)	3 (3.8)	1 (1.3)	0 (0.0)	5 (6.3)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Total	12 (15.2)	52 (65.8)	12 (15.2)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Lactate Dehydrogenase (U/L)	Low	1 (1.2)	1 (1.2)	1 (1.2)	1 (1.2)	4 (4.7)
		Normal	2 (2.4)	15 (17.6)	30 (35.3)	0 (0.0)	47 (55.3)
		High	1 (1.2)	1 (1.2)	26 (30.6)	2 (2.4)	30 (35.3)
		Missing	0 (0.0)	2 (2.4)	2 (2.4)	0 (0.0)	4 (4.7)
		Total	4 (4.7)	19 (22.4)	59 (69.4)	3 (3.5)	85 (100.0)
PLACEBO	Lactate Dehydrogenase (U/L)	Low	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
		Normal	0 (0.0)	14 (17.7)	21 (26.6)	0 (0.0)	35 (44.3)
		High	0 (0.0)	0 (0.0)	33 (41.8)	3 (3.8)	36 (45.6)
		Missing	0 (0.0)	2 (2.5)	5 (6.3)	0 (0.0)	7 (8.9)
		Total	1 (1.3)	16 (20.3)	59 (74.7)	3 (3.8)	79 (100.0)
NLG2101	Phosphate (mmol/L)	Low	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)	2 (2.4)
		Normal	19 (22.4)	34 (40.0)	18 (21.2)	2 (2.4)	73 (85.9)
		High	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.2)
		Missing	1 (1.2)	2 (2.4)	5 (5.9)	1 (1.2)	9 (10.6)
		Total	21 (24.7)	37 (43.5)	24 (28.2)	3 (3.5)	85 (100.0)
PLACEBO	Phosphate (mmol/L)	Low	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)
		Normal	15 (19.0)	35 (44.3)	10 (12.7)	3 (3.8)	63 (79.7)
		High	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Missing	6 (7.6)	3 (3.8)	2 (2.5)	0 (0.0)	11 (13.9)
		Total	23 (29.1)	41 (51.9)	12 (15.2)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Protein (g/L)	Low	5 (5.9)	0 (0.0)	0 (0.0)	0 (0.0)	5 (5.9)
		Normal	35 (41.2)	39 (45.9)	0 (0.0)	2 (2.4)	76 (89.4)
		High	0 (0.0)	2 (2.4)	0 (0.0)	0 (0.0)	2 (2.4)
		Missing	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)	2 (2.4)
		Total	41 (48.2)	42 (49.4)	0 (0.0)	2 (2.4)	85 (100.0)
PLACEBO	Protein (g/L)	Low	3 (3.8)	3 (3.8)	0 (0.0)	0 (0.0)	6 (7.6)
		Normal	26 (32.9)	35 (44.3)	5 (6.3)	3 (3.8)	69 (87.3)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	2 (2.5)	1 (1.3)	1 (1.3)	4 (5.1)
		Total	29 (36.7)	40 (50.6)	6 (7.6)	4 (5.1)	79 (100.0)
NLG2101	Sodium (mmol/L)	Low	2 (2.4)	2 (2.4)	0 (0.0)	0 (0.0)	4 (4.7)
		Normal	13 (15.3)	58 (68.2)	5 (5.9)	2 (2.4)	78 (91.8)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	2 (2.4)	1 (1.2)	0 (0.0)	3 (3.5)
		Total	15 (17.6)	62 (72.9)	6 (7.1)	2 (2.4)	85 (100.0)
PLACEBO	Sodium (mmol/L)	Low	3 (3.8)	1 (1.3)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	12 (15.2)	54 (68.4)	3 (3.8)	3 (3.8)	72 (91.1)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	1 (1.3)	2 (2.5)	0 (0.0)	0 (0.0)	3 (3.8)
		Total	16 (20.3)	57 (72.2)	3 (3.8)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Worst Post-Baseline Result: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Bilirubin (umol/L)	Low	1 (1.2)	2 (2.4)	0 (0.0)	0 (0.0)	3 (3.5)
		Normal	9 (10.6)	66 (77.6)	5 (5.9)	2 (2.4)	82 (96.5)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	10 (11.8)	68 (80.0)	5 (5.9)	2 (2.4)	85 (100.0)
PLACEBO	Bilirubin (umol/L)	Low	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)
		Normal	7 (8.9)	59 (74.7)	7 (8.9)	3 (3.8)	76 (96.2)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
		Total	9 (11.4)	60 (75.9)	7 (8.9)	3 (3.8)	79 (100.0)
NLG2101	Urea Nitrogen (mmol/L)	Low	0 (0.0)	2 (2.4)	0 (0.0)	0 (0.0)	2 (2.4)
		Normal	8 (9.4)	52 (61.2)	16 (18.8)	2 (2.4)	78 (91.8)
		High	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	2 (2.4)
		Missing	0 (0.0)	0 (0.0)	2 (2.4)	1 (1.2)	3 (3.5)
		Total	8 (9.4)	55 (64.7)	19 (22.4)	3 (3.5)	85 (100.0)
PLACEBO	Urea Nitrogen (mmol/L)	Low	2 (2.5)	0 (0.0)	1 (1.3)	0 (0.0)	3 (3.8)
		Normal	11 (13.9)	42 (53.2)	9 (11.4)	3 (3.8)	65 (82.3)
		High	1 (1.3)	1 (1.3)	6 (7.6)	0 (0.0)	8 (10.1)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Total	14 (17.7)	46 (58.2)	16 (20.3)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Albumin (g/L)	Low	11 (12.9)	1 (1.2)	0 (0.0)	1 (1.2)	13 (15.3)
		Normal	10 (11.8)	57 (67.1)	0 (0.0)	2 (2.4)	69 (81.2)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	3 (3.5)	0 (0.0)	0 (0.0)	3 (3.5)
		Total	21 (24.7)	61 (71.8)	0 (0.0)	3 (3.5)	85 (100.0)
PLACEBO	Albumin (g/L)	Low	4 (5.1)	2 (2.5)	0 (0.0)	0 (0.0)	6 (7.6)
		Normal	8 (10.1)	59 (74.7)	0 (0.0)	3 (3.8)	70 (88.6)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Total	12 (15.2)	64 (81.0)	0 (0.0)	3 (3.8)	79 (100.0)
NLG2101	Alkaline Phosphatase (U/L)	Low	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Normal	0 (0.0)	49 (57.6)	9 (10.6)	0 (0.0)	58 (68.2)
		High	0 (0.0)	7 (8.2)	13 (15.3)	1 (1.2)	21 (24.7)
		Missing	0 (0.0)	4 (4.7)	0 (0.0)	1 (1.2)	5 (5.9)
		Total	0 (0.0)	61 (71.8)	22 (25.9)	2 (2.4)	85 (100.0)
PLACEBO	Alkaline Phosphatase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	1 (1.3)	46 (58.2)	5 (6.3)	2 (2.5)	54 (68.4)
		High	0 (0.0)	10 (12.7)	12 (15.2)	1 (1.3)	23 (29.1)
		Missing	0 (0.0)	1 (1.3)	1 (1.3)	0 (0.0)	2 (2.5)
		Total	1 (1.3)	57 (72.2)	18 (22.8)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Alanine Aminotransferase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	2 (2.4)	64 (75.3)	3 (3.5)	1 (1.2)	70 (82.4)
		High	0 (0.0)	5 (5.9)	6 (7.1)	1 (1.2)	12 (14.1)
		Missing	0 (0.0)	3 (3.5)	0 (0.0)	0 (0.0)	3 (3.5)
		Total	2 (2.4)	72 (84.7)	9 (10.6)	2 (2.4)	85 (100.0)
PLACEBO	Alanine Aminotransferase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	1 (1.3)	52 (65.8)	5 (6.3)	2 (2.5)	60 (75.9)
		High	0 (0.0)	7 (8.9)	9 (11.4)	1 (1.3)	17 (21.5)
		Missing	0 (0.0)	1 (1.3)	1 (1.3)	0 (0.0)	2 (2.5)
		Total	1 (1.3)	60 (75.9)	15 (19.0)	3 (3.8)	79 (100.0)
NLG2101	Aspartate Aminotransferase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	54 (63.5)	9 (10.6)	1 (1.2)	64 (75.3)
		High	0 (0.0)	10 (11.8)	7 (8.2)	1 (1.2)	18 (21.2)
		Missing	0 (0.0)	3 (3.5)	0 (0.0)	0 (0.0)	3 (3.5)
		Total	0 (0.0)	67 (78.8)	16 (18.8)	2 (2.4)	85 (100.0)
PLACEBO	Aspartate Aminotransferase (U/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	44 (55.7)	6 (7.6)	2 (2.5)	52 (65.8)
		High	0 (0.0)	7 (8.9)	17 (21.5)	1 (1.3)	25 (31.6)
		Missing	0 (0.0)	1 (1.3)	1 (1.3)	0 (0.0)	2 (2.5)
		Total	0 (0.0)	52 (65.8)	24 (30.4)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Bicarbonate (mmol/L)	Low	3 (3.5)	6 (7.1)	0 (0.0)	0 (0.0)	9 (10.6)
		Normal	5 (5.9)	48 (56.5)	3 (3.5)	2 (2.4)	58 (68.2)
		High	0 (0.0)	6 (7.1)	1 (1.2)	1 (1.2)	8 (9.4)
		Missing	1 (1.2)	4 (4.7)	1 (1.2)	4 (4.7)	10 (11.8)
		Total	9 (10.6)	64 (75.3)	5 (5.9)	7 (8.2)	85 (100.0)
PLACEBO	Bicarbonate (mmol/L)	Low	2 (2.5)	3 (3.8)	0 (0.0)	0 (0.0)	5 (6.3)
		Normal	5 (6.3)	48 (60.8)	1 (1.3)	3 (3.8)	57 (72.2)
		High	0 (0.0)	1 (1.3)	3 (3.8)	0 (0.0)	4 (5.1)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	10 (12.7)	13 (16.5)
		Total	7 (8.9)	55 (69.6)	4 (5.1)	13 (16.5)	79 (100.0)
NLG2101	Calcium (mmol/L)	Low	3 (3.5)	1 (1.2)	0 (0.0)	0 (0.0)	4 (4.7)
		Normal	12 (14.1)	54 (63.5)	2 (2.4)	2 (2.4)	70 (82.4)
		High	0 (0.0)	8 (9.4)	2 (2.4)	0 (0.0)	10 (11.8)
		Missing	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Total	15 (17.6)	64 (75.3)	4 (4.7)	2 (2.4)	85 (100.0)
PLACEBO	Calcium (mmol/L)	Low	0 (0.0)	4 (5.1)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	6 (7.6)	59 (74.7)	0 (0.0)	3 (3.8)	68 (86.1)
		High	0 (0.0)	5 (6.3)	1 (1.3)	0 (0.0)	6 (7.6)
		Missing	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
		Total	6 (7.6)	69 (87.3)	1 (1.3)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Chloride (mmol/L)	Low	0 (0.0)	3 (3.5)	0 (0.0)	0 (0.0)	3 (3.5)
		Normal	5 (5.9)	69 (81.2)	1 (1.2)	2 (2.4)	77 (90.6)
		High	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Missing	0 (0.0)	4 (4.7)	0 (0.0)	0 (0.0)	4 (4.7)
		Total	5 (5.9)	77 (90.6)	1 (1.2)	2 (2.4)	85 (100.0)
PLACEBO	Chloride (mmol/L)	Low	2 (2.5)	2 (2.5)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	5 (6.3)	61 (77.2)	1 (1.3)	2 (2.5)	69 (87.3)
		High	1 (1.3)	1 (1.3)	0 (0.0)	1 (1.3)	3 (3.8)
		Missing	0 (0.0)	1 (1.3)	1 (1.3)	1 (1.3)	3 (3.8)
		Total	8 (10.1)	65 (82.3)	2 (2.5)	4 (5.1)	79 (100.0)
NLG2101	Creatinine (umol/L)	Low	6 (7.1)	5 (5.9)	0 (0.0)	0 (0.0)	11 (12.9)
		Normal	6 (7.1)	59 (69.4)	2 (2.4)	2 (2.4)	69 (81.2)
		High	0 (0.0)	2 (2.4)	3 (3.5)	0 (0.0)	5 (5.9)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	12 (14.1)	66 (77.6)	5 (5.9)	2 (2.4)	85 (100.0)
PLACEBO	Creatinine (umol/L)	Low	5 (6.3)	1 (1.3)	0 (0.0)	1 (1.3)	7 (8.9)
		Normal	11 (13.9)	53 (67.1)	1 (1.3)	2 (2.5)	67 (84.8)
		High	0 (0.0)	3 (3.8)	1 (1.3)	0 (0.0)	4 (5.1)
		Missing	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
		Total	16 (20.3)	58 (73.4)	2 (2.5)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Glucose (mmol/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	21 (24.7)	19 (22.4)	0 (0.0)	40 (47.1)
		High	0 (0.0)	18 (21.2)	25 (29.4)	2 (2.4)	45 (52.9)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	0 (0.0)	39 (45.9)	44 (51.8)	2 (2.4)	85 (100.0)
PLACEBO	Glucose (mmol/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Normal	0 (0.0)	19 (24.1)	19 (24.1)	2 (2.5)	40 (50.6)
		High	0 (0.0)	11 (13.9)	26 (32.9)	1 (1.3)	38 (48.1)
		Missing	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
		Total	0 (0.0)	31 (39.2)	45 (57.0)	3 (3.8)	79 (100.0)
NLG2101	Potassium (mmol/L)	Low	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)
		Normal	4 (4.7)	72 (84.7)	3 (3.5)	1 (1.2)	80 (94.1)
		High	0 (0.0)	3 (3.5)	0 (0.0)	0 (0.0)	3 (3.5)
		Missing	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Total	4 (4.7)	76 (89.4)	3 (3.5)	2 (2.4)	85 (100.0)
PLACEBO	Potassium (mmol/L)	Low	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
		Normal	4 (5.1)	61 (77.2)	2 (2.5)	3 (3.8)	70 (88.6)
		High	0 (0.0)	5 (6.3)	0 (0.0)	0 (0.0)	5 (6.3)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Total	5 (6.3)	69 (87.3)	2 (2.5)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Lactate Dehydrogenase (U/L)	Low	0 (0.0)	3 (3.5)	0 (0.0)	1 (1.2)	4 (4.7)
		Normal	0 (0.0)	38 (44.7)	9 (10.6)	0 (0.0)	47 (55.3)
		High	0 (0.0)	4 (4.7)	24 (28.2)	2 (2.4)	30 (35.3)
		Missing	0 (0.0)	2 (2.4)	2 (2.4)	0 (0.0)	4 (4.7)
		Total	0 (0.0)	47 (55.3)	35 (41.2)	3 (3.5)	85 (100.0)
PLACEBO	Lactate Dehydrogenase (U/L)	Low	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
		Normal	0 (0.0)	29 (36.7)	6 (7.6)	0 (0.0)	35 (44.3)
		High	0 (0.0)	3 (3.8)	30 (38.0)	3 (3.8)	36 (45.6)
		Missing	0 (0.0)	4 (5.1)	3 (3.8)	0 (0.0)	7 (8.9)
		Total	1 (1.3)	36 (45.6)	39 (49.4)	3 (3.8)	79 (100.0)
NLG2101	Phosphate (mmol/L)	Low	0 (0.0)	2 (2.4)	0 (0.0)	0 (0.0)	2 (2.4)
		Normal	9 (10.6)	59 (69.4)	3 (3.5)	2 (2.4)	73 (85.9)
		High	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	1 (1.2)
		Missing	0 (0.0)	5 (5.9)	3 (3.5)	1 (1.2)	9 (10.6)
		Total	9 (10.6)	67 (78.8)	6 (7.1)	3 (3.5)	85 (100.0)
PLACEBO	Phosphate (mmol/L)	Low	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	2 (2.5)
		Normal	4 (5.1)	51 (64.6)	5 (6.3)	3 (3.8)	63 (79.7)
		High	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Missing	3 (3.8)	8 (10.1)	0 (0.0)	0 (0.0)	11 (13.9)
		Total	7 (8.9)	64 (81.0)	5 (6.3)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Protein (g/L)	Low	4 (4.7)	1 (1.2)	0 (0.0)	0 (0.0)	5 (5.9)
		Normal	21 (24.7)	53 (62.4)	0 (0.0)	2 (2.4)	76 (89.4)
		High	0 (0.0)	2 (2.4)	0 (0.0)	0 (0.0)	2 (2.4)
		Missing	0 (0.0)	2 (2.4)	0 (0.0)	0 (0.0)	2 (2.4)
		Total	25 (29.4)	58 (68.2)	0 (0.0)	2 (2.4)	85 (100.0)
PLACEBO	Protein (g/L)	Low	2 (2.5)	4 (5.1)	0 (0.0)	0 (0.0)	6 (7.6)
		Normal	10 (12.7)	56 (70.9)	0 (0.0)	3 (3.8)	69 (87.3)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	1 (1.3)	4 (5.1)
		Total	12 (15.2)	63 (79.7)	0 (0.0)	4 (5.1)	79 (100.0)
NLG2101	Sodium (mmol/L)	Low	0 (0.0)	4 (4.7)	0 (0.0)	0 (0.0)	4 (4.7)
		Normal	2 (2.4)	74 (87.1)	0 (0.0)	2 (2.4)	78 (91.8)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	3 (3.5)	0 (0.0)	0 (0.0)	3 (3.5)
		Total	2 (2.4)	81 (95.3)	0 (0.0)	2 (2.4)	85 (100.0)
PLACEBO	Sodium (mmol/L)	Low	2 (2.5)	2 (2.5)	0 (0.0)	0 (0.0)	4 (5.1)
		Normal	4 (5.1)	64 (81.0)	1 (1.3)	3 (3.8)	72 (91.1)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	1 (1.3)	2 (2.5)	0 (0.0)	0 (0.0)	3 (3.8)
		Total	7 (8.9)	68 (86.1)	1 (1.3)	3 (3.8)	79 (100.0)

Table 14.3.5.3B
Laboratory Shifts From Baseline Based on the Normal Range: Chemistry (Safety Analysis Set)

Treatment Group	Parameter	Baseline	Last Post-Baseline Assessment: Low n (%)	Normal n (%)	High n (%)	Missing n (%)	Total n (%)
NLG2101	Bilirubin (umol/L)	Low	1 (1.2)	2 (2.4)	0 (0.0)	0 (0.0)	3 (3.5)
		Normal	1 (1.2)	76 (89.4)	3 (3.5)	2 (2.4)	82 (96.5)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Total	2 (2.4)	78 (91.8)	3 (3.5)	2 (2.4)	85 (100.0)
PLACEBO	Bilirubin (umol/L)	Low	1 (1.3)	1 (1.3)	0 (0.0)	0 (0.0)	2 (2.5)
		Normal	0 (0.0)	68 (86.1)	5 (6.3)	3 (3.8)	76 (96.2)
		High	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
		Missing	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
		Total	1 (1.3)	70 (88.6)	5 (6.3)	3 (3.8)	79 (100.0)
NLG2101	Urea Nitrogen (mmol/L)	Low	0 (0.0)	2 (2.4)	0 (0.0)	0 (0.0)	2 (2.4)
		Normal	4 (4.7)	69 (81.2)	3 (3.5)	2 (2.4)	78 (91.8)
		High	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	2 (2.4)
		Missing	0 (0.0)	2 (2.4)	0 (0.0)	1 (1.2)	3 (3.5)
		Total	4 (4.7)	74 (87.1)	4 (4.7)	3 (3.5)	85 (100.0)
PLACEBO	Urea Nitrogen (mmol/L)	Low	2 (2.5)	1 (1.3)	0 (0.0)	0 (0.0)	3 (3.8)
		Normal	6 (7.6)	54 (68.4)	2 (2.5)	3 (3.8)	65 (82.3)
		High	0 (0.0)	6 (7.6)	2 (2.5)	0 (0.0)	8 (10.1)
		Missing	0 (0.0)	3 (3.8)	0 (0.0)	0 (0.0)	3 (3.8)
		Total	8 (10.1)	64 (81.0)	4 (5.1)	3 (3.8)	79 (100.0)

2.3.3 Display of Vital signs Data

Table Number	Table Title
Table 14.3.5.4	Summary of vital signs and changes from baseline by visit (Safety Analysis Set)

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Screening	n	83	83	79	79
		Mean (SD)	84.9 (14.66)	-0.4 (5.77)	84.8 (12.45)	0.0 (7.24)
		Median	84.0	0.0	84.0	0.0
		Min, Max	56, 120	-24, 24	60, 118	-33, 27
	Cycle 1 Day 1	n	23	23	20	20
		Mean (SD)	86.7 (13.39)	0.0 (0.00)	84.9 (14.98)	0.0 (0.00)
		Median	86.0	0.0	82.5	0.0
		Min, Max	63, 110	0, 0	65, 112	0, 0
	Cycle 1 Day 8	n	59	57	56	56
		Mean (SD)	87.6 (15.62)	3.4 (12.49)	87.4 (17.55)	2.7 (12.97)
		Median	84.0	3.0	84.5	1.5
		Min, Max	63, 117	-29, 29	60, 143	-35, 36
	Cycle 2 Day 1	n	23	23	19	19
		Mean (SD)	87.6 (16.37)	0.8 (12.27)	88.9 (14.38)	3.5 (10.72)
		Median	84.0	-3.0	87.0	4.0
		Min, Max	70, 125	-16, 25	67, 120	-11, 23

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Cycle 2 Day 8	n	56	54	55	55
		Mean (SD)	88.4 (13.25)	4.4 (15.75)	86.5 (15.71)	1.1 (12.99)
		Median	86.5	7.0	84.0	-2.0
		Min, Max	67, 118	-45, 35	59, 126	-20, 31
	Cycle 3 Day 1	n	14	14	14	14
		Mean (SD)	82.9 (13.32)	-0.9 (10.58)	86.3 (12.86)	1.9 (18.71)
		Median	85.5	-1.5	80.5	1.5
		Min, Max	57, 100	-19, 28	71, 108	-31, 37
	Cycle 3 Day 8	n	50	48	47	47
		Mean (SD)	88.8 (13.73)	4.8 (15.80)	87.4 (14.16)	2.4 (13.33)
		Median	90.0	6.0	82.0	-1.0
		Min, Max	57, 113	-52, 36	59, 121	-23, 39
	Cycle 4 Day 1	n	12	12	13	13
		Mean (SD)	81.7 (13.66)	-4.8 (9.49)	83.1 (14.92)	-3.8 (16.08)
		Median	83.0	-4.0	78.0	0.0
		Min, Max	54, 102	-24, 8	65, 114	-38, 22

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Cycle 4 Day 8	n	46	45	45	45
		Mean (SD)	91.6 (16.16)	7.7 (19.56)	87.8 (13.61)	2.9 (16.13)
		Median	91.0	7.0	89.0	3.0
		Min, Max	61, 125	-46, 54	66, 121	-42, 27
	Cycle 5 Day 1	n	7	7	11	11
		Mean (SD)	86.4 (14.13)	-0.7 (10.08)	77.5 (11.60)	-10 (18.20)
		Median	85.0	-1.0	72.0	0.0
		Min, Max	70, 113	-14, 11	66, 102	-46, 13
	Cycle 5 Day 8	n	42	41	42	42
		Mean (SD)	92.7 (14.28)	8.9 (17.02)	87.2 (13.83)	2.1 (14.63)
		Median	95.5	10.0	84.0	1.5
		Min, Max	63, 124	-31, 52	70, 118	-18, 41
	Cycle 6 Day 1	n	6	6	10	10
		Mean (SD)	87.3 (15.62)	0.0 (12.49)	83.4 (12.89)	-2.8 (19.45)
		Median	87.5	2.0	79.0	4.5
		Min, Max	66, 111	-20, 15	70, 110	-42, 22

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Cycle 6 Day 8	n	40	40	40	40
		Mean (SD)	92.5 (13.77)	9.6 (17.30)	88.1 (14.92)	2.6 (13.28)
		Median	91.0	10.5	86.5	2.5
		Min, Max	66, 121	-24, 49	68, 130	-24, 55
	Cycle 7 Day 1	n	4	4	7	7
		Mean (SD)	80.3 (10.47)	-6.5 (13.53)	80.7 (15.69)	2.1 (12.75)
		Median	84.0	-3.0	76.0	2.0
		Min, Max	65, 88	-25, 5	65, 111	-16, 19
	Cycle 7 Day 8	n	33	33	31	31
		Mean (SD)	93.8 (16.79)	11.5 (18.76)	85.0 (12.84)	-0.1 (14.99)
		Median	94.0	9.0	82.0	-1.0
		Min, Max	68, 140	-24, 64	70, 118	-30, 42
	Cycle 8 Day 1	n	4	4	9	9
		Mean (SD)	84.3 (9.46)	-2.5 (14.89)	88.3 (13.10)	3.2 (16.78)
		Median	87.0	2.0	89.0	1.0
		Min, Max	71, 92	-23, 9	66, 106	-33, 24

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Cycle 8 Day 8	n	33	33	28	28
		Mean (SD)	90.8 (13.18)	8.5 (15.92)	85.9 (13.71)	1.8 (12.26)
		Median	89.0	8.0	82.0	2.0
		Min, Max	71, 121	-35, 47	67, 120	-27, 22
	Cycle 9 Day 1	n	3	3	7	7
		Mean (SD)	77.0 (6.93)	-6.7 (17.01)	77.3 (8.88)	-5.1 (16.94)
		Median	81.0	0.0	74.0	-5.0
		Min, Max	69, 81	-26, 6	66, 89	-33, 21
	Cycle 9 Day 8	n	30	30	26	26
		Mean (SD)	86.9 (12.64)	3.8 (18.60)	83.6 (12.34)	-0.1 (11.38)
		Median	86.5	6.0	81.5	0.0
		Min, Max	65, 115	-31, 53	62, 125	-22, 22
	Cycle 10 Day 1	n	2	2	7	7
		Mean (SD)	80.5 (7.78)	-4.5 (23.33)	77.1 (10.95)	-5.3 (16.35)
		Median	80.5	-4.5	79.0	-11
		Min, Max	75, 86	-21, 12	57, 88	-24, 18

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Cycle 10 Day 8	n	26	26	26	26
		Mean (SD)	89.3 (12.89)	8.6 (18.42)	84.3 (14.94)	1.1 (14.75)
		Median	87.5	9.5	81.0	-0.5
		Min, Max	69, 119	-30, 42	63, 132	-43, 29
	Cycle 11 Day 1	n	2	2	5	5
		Mean (SD)	74.5 (20.51)	-11 (10.61)	75.6 (8.85)	-2.2 (26.92)
		Median	74.5	-11	78.0	7.0
		Min, Max	60, 89	-18, -3	62, 83	-50, 15
	Cycle 11 Day 8	n	23	23	25	25
		Mean (SD)	85.3 (15.18)	5.0 (17.62)	81.8 (14.06)	-1.7 (14.50)
		Median	80.0	7.0	80.0	0.0
		Min, Max	63, 115	-29, 43	54, 113	-31, 38
	Cycle 12 Day 1	n	2	2	4	4
		Mean (SD)	74.5 (23.33)	-11 (7.78)	86.8 (3.30)	6.5 (19.12)
		Median	74.5	-11	87.0	15.0
		Min, Max	58, 91	-16, -5	83, 90	-22, 18

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Cycle 12 Day 8	n	22	22	25	25
		Mean (SD)	89.9 (13.82)	10.6 (15.67)	82.5 (15.95)	-1.1 (13.47)
		Median	89.5	10.5	80.0	-1.0
		Min, Max	65, 123	-20, 40	62, 132	-29, 29
	Cycle 13 Day 1	n	1	1	3	3
		Mean (SD)	89.0 (NA)	-18 (NA)	92.7 (9.29)	11.0 (30.45)
		Median	89.0	-18	90.0	17.0
		Min, Max	89, 89	-18, -18	85, 103	-22, 38
	Cycle 13 Day 8	n	17	17	22	22
		Mean (SD)	87.1 (15.78)	7.3 (19.41)	84.4 (15.68)	0.7 (15.75)
		Median	85.0	10.0	84.5	2.0
		Min, Max	65, 112	-31, 46	45, 115	-31, 32
	Cycle 14 Day 1	n	1	1	2	2
		Mean (SD)	79.0 (NA)	-28 (NA)	96.5 (4.95)	8.0 (38.18)
		Median	79.0	-28	96.5	8.0
		Min, Max	79, 79	-28, -28	93, 100	-19, 35

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Cycle 14 Day 8	n	14	14	18	18
		Mean (SD)	84.1 (15.90)	4.1 (19.94)	84.7 (17.13)	1.8 (12.51)
		Median	80.0	5.0	85.5	0.5
		Min, Max	61, 114	-27, 34	59, 125	-19, 22
	Off-Study Evaluation	n	69	68	62	62
		Mean (SD)	86.9 (12.82)	1.7 (13.44)	88.7 (14.15)	3.2 (15.29)
		Median	85.0	0.5	86.5	4.0
		Min, Max	61, 121	-28, 31	64, 127	-30, 35
	Additional Visit 1	n	20	20	2	2
		Mean (SD)	92.6 (11.46)	28.1 (13.28)	75.5 (4.95)	-25 (7.78)
		Median	94.0	27.0	75.5	-25
		Min, Max	70, 110	2, 48	72, 79	-30, -19
	Additional Visit 2	n	78	78	137	137
		Mean (SD)	88.8 (13.30)	2.2 (12.03)	79.9 (12.02)	-0.1 (15.86)
		Median	88.0	0.5	80.0	1.0
		Min, Max	65, 125	-23, 32	48, 131	-46, 35

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Heart Rate (beats/min)	Unscheduled	n	24	24	26	26
		Mean (SD)	90.5 (9.62)	9.1 (12.63)	83.3 (14.95)	2.6 (14.53)
		Median	89.0	10.0	80.0	2.0
		Min, Max	64, 118	-11, 37	51, 118	-36, 31
Respiratory Rate (breaths/min)	Screening	n	77	77	69	69
		Mean (SD)	17.3 (1.50)	-0.1 (1.23)	17.2 (2.00)	0.0 (1.17)
		Median	18.0	0.0	17.0	0.0
		Min, Max	12, 20	-4, 4	12, 24	-4, 4
	Cycle 1 Day 1	n	20	20	20	20
		Mean (SD)	17.7 (2.54)	0.0 (0.00)	17.9 (1.79)	0.0 (0.00)
		Median	18.0	0.0	18.0	0.0
		Min, Max	12, 22	0, 0	16, 22	0, 0
	Cycle 1 Day 8	n	56	54	50	48
		Mean (SD)	17.4 (1.64)	0.0 (1.69)	17.1 (1.51)	0.2 (2.04)
		Median	17.0	0.0	17.0	0.0
		Min, Max	15, 22	-4, 4	14, 20	-6, 5
	Cycle 2 Day 1	n	21	19	19	19
		Mean (SD)	17.3 (1.23)	-0.6 (2.04)	17.9 (2.05)	0.2 (1.77)
		Median	18.0	0.0	18.0	0.0
		Min, Max	15, 20	-4, 4	16, 24	-4, 4

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Respiratory Rate (breaths/min)	Cycle 2 Day 8	n	53	51	49	46
		Mean (SD)	17.3 (1.60)	-0.1 (1.87)	17.1 (1.80)	0.2 (1.85)
		Median	17.0	0.0	16.0	0.0
		Min, Max	15, 20	-4, 4	13, 22	-6, 6
	Cycle 3 Day 1	n	13	12	14	14
		Mean (SD)	17.1 (2.10)	-0.8 (2.17)	17.9 (2.23)	0.2 (1.58)
		Median	16.0	0.0	18.0	0.0
		Min, Max	14, 20	-4, 4	16, 24	-2, 4
	Cycle 3 Day 8	n	46	44	43	39
		Mean (SD)	17.0 (1.45)	-0.5 (1.70)	17.0 (1.45)	0.1 (1.46)
		Median	16.0	0.0	17.0	0.0
		Min, Max	14, 20	-4, 4	14, 20	-4, 4
	Cycle 4 Day 1	n	12	11	13	13
		Mean (SD)	17.3 (1.78)	-0.5 (3.11)	17.1 (2.10)	-0.6 (1.71)
		Median	16.0	0.0	18.0	0.0
		Min, Max	16, 20	-6, 4	12, 20	-4, 2

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Respiratory Rate (breaths/min)	Cycle 4 Day 8	n	45	42	43	38
		Mean (SD)	16.8 (1.32)	-0.6 (1.77)	16.9 (1.36)	0.1 (1.47)
		Median	16.0	0.0	17.0	0.0
		Min, Max	12, 20	-4, 4	12, 20	-4, 2
	Cycle 5 Day 1	n	7	6	11	11
		Mean (SD)	16.9 (1.07)	-1.7 (3.44)	16.7 (1.35)	-0.5 (0.93)
		Median	16.0	-2.0	16.0	0.0
		Min, Max	16, 18	-6, 4	16, 20	-2, 0
	Cycle 5 Day 8	n	42	39	40	35
		Mean (SD)	17.0 (1.40)	-0.3 (1.83)	17.2 (1.58)	0.1 (1.54)
		Median	17.0	0.0	16.0	0.0
		Min, Max	13, 22	-4, 6	14, 20	-4, 3
	Cycle 6 Day 1	n	6	5	10	10
		Mean (SD)	17.7 (1.51)	-0.4 (2.97)	17.2 (1.69)	-0.2 (1.48)
		Median	18.0	0.0	18.0	0.0
		Min, Max	16, 20	-4, 4	14, 20	-2, 2

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Respiratory Rate (breaths/min)	Cycle 6 Day 8	n	40	38	39	33
		Mean (SD)	16.9 (1.17)	-0.4 (1.90)	17.3 (1.34)	0.4 (1.48)
		Median	16.0	0.0	18.0	0.0
		Min, Max	16, 20	-4, 4	14, 20	-4, 2
	Cycle 7 Day 1	n	4	3	9	9
		Mean (SD)	17.5 (1.00)	-0.7 (2.31)	17.3 (1.00)	0.2 (1.56)
		Median	18.0	-2.0	18.0	0.0
		Min, Max	16, 18	-2, 2	16, 18	-2, 2
	Cycle 7 Day 8	n	33	32	31	25
		Mean (SD)	17.2 (1.79)	-0.0 (2.39)	16.8 (1.28)	-0.3 (1.28)
		Median	17.0	0.0	17.0	0.0
		Min, Max	14, 24	-6, 8	14, 20	-4, 2
	Cycle 8 Day 1	n	3	3	9	9
		Mean (SD)	16.7 (1.15)	-2.0 (2.00)	17.6 (1.33)	0.4 (1.33)
		Median	16.0	-2.0	18.0	0.0
		Min, Max	16, 18	-4, 0	16, 20	-2, 2

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Respiratory Rate (breaths/min)	Cycle 8 Day 8	n	32	31	28	22
		Mean (SD)	17.1 (1.45)	-0.0 (1.89)	16.8 (1.87)	0.1 (1.72)
		Median	17.0	0.0	16.0	0.0
		Min, Max	13, 20	-4, 4	12, 20	-4, 4
	Cycle 9 Day 1	n	3	2	6	6
		Mean (SD)	19.7 (3.79)	-0.5 (3.54)	17.3 (1.03)	0.0 (1.26)
		Median	18.0	-0.5	18.0	0.0
		Min, Max	17, 24	-3, 2	16, 18	-2, 2
	Cycle 9 Day 8	n	29	28	26	20
		Mean (SD)	16.8 (1.27)	-0.4 (1.77)	17.1 (1.94)	0.1 (1.74)
		Median	16.0	0.0	16.5	0.0
		Min, Max	14, 19	-4, 3	14, 20	-4, 4
	Cycle 10 Day 1	n	2	2	7	7
		Mean (SD)	19.0 (1.41)	1.0 (4.24)	17.1 (2.79)	-0.3 (2.69)
		Median	19.0	1.0	18.0	0.0
		Min, Max	18, 20	-2, 4	12, 20	-4, 4

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Respiratory Rate (breaths/min)	Cycle 10 Day 8	n	26	24	26	20
		Mean (SD)	16.7 (1.00)	-0.4 (1.53)	16.7 (1.65)	-0.1 (1.61)
		Median	17.0	0.0	16.0	0.0
		Min, Max	14, 18	-4, 2	14, 20	-2, 4
	Cycle 11 Day 1	n	2	2	5	5
		Mean (SD)	18.5 (3.54)	0.5 (0.71)	18.0 (0.00)	0.4 (0.89)
		Median	18.5	0.5	18.0	0.0
		Min, Max	16, 21	0, 1	18, 18	0, 2
	Cycle 11 Day 8	n	23	21	25	19
		Mean (SD)	16.8 (1.24)	-0.3 (1.28)	17.0 (1.81)	0.3 (1.60)
		Median	17.0	0.0	17.0	0.0
		Min, Max	14, 20	-3, 1	13, 20	-2, 4
	Cycle 12 Day 1	n	2	2	4	4
		Mean (SD)	19.0 (1.41)	1.0 (1.41)	17.0 (1.15)	-0.5 (1.91)
		Median	19.0	1.0	17.0	-1.0
		Min, Max	18, 20	0, 2	16, 18	-2, 2

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Respiratory Rate (breaths/min)	Cycle 12 Day 8	n	22	20	24	18
		Mean (SD)	16.4 (0.96)	-0.8 (1.64)	17.3 (1.70)	0.3 (1.50)
		Median	16.0	0.0	18.0	0.0
		Min, Max	14, 18	-4, 2	14, 20	-2, 3
	Cycle 13 Day 1	n	1	1	3	3
		Mean (SD)	18.0 (NA)	-2.0 (NA)	18.7 (1.15)	1.3 (1.15)
		Median	18.0	-2.0	18.0	2.0
		Min, Max	18, 18	-2, -2	18, 20	0, 2
	Cycle 13 Day 8	n	17	15	22	17
		Mean (SD)	16.6 (1.41)	-0.7 (1.87)	18.0 (1.59)	0.9 (1.83)
		Median	16.0	0.0	18.0	0.0
		Min, Max	14, 19	-4, 2	15, 20	-2, 4
	Cycle 14 Day 1	n	1	1	2	2
		Mean (SD)	18.0 (NA)	-2.0 (NA)	20.0 (0.00)	2.0 (0.00)
		Median	18.0	-2.0	20.0	2.0
		Min, Max	18, 18	-2, -2	20, 20	2, 2

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Respiratory Rate (breaths/min)	Cycle 14 Day 8	n	14	13	17	12
		Mean (SD)	16.9 (1.23)	-0.5 (1.85)	17.2 (1.59)	0.1 (1.88)
		Median	16.0	0.0	18.0	0.0
		Min, Max	16, 20	-4, 3	15, 20	-2, 4
	Off-Study Evaluation	n	65	61	53	49
		Mean (SD)	17.5 (1.77)	0.1 (1.98)	17.3 (3.72)	0.3 (3.94)
		Median	18.0	0.0	16.0	0.0
		Min, Max	13, 22	-4, 4	12, 40	-6, 23
	Additional Visit 1	n	20	20	2	2
		Mean (SD)	15.8 (0.62)	-0.9 (1.37)	18.0 (2.83)	0.0 (2.83)
		Median	16.0	-2.0	18.0	0.0
		Min, Max	14, 16	-2, 1	16, 20	-2, 2
	Additional Visit 2	n	78	78	132	110
		Mean (SD)	17.5 (1.70)	-0.3 (1.92)	17.4 (1.39)	0.0 (1.76)
		Median	18.0	0.0	18.0	0.0
		Min, Max	13, 22	-5, 3	14, 20	-4, 4

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Respiratory Rate (breaths/min)	Unscheduled	n	21	21	26	25
		Mean (SD)	16.8 (1.73)	-0.8 (1.97)	17.1 (1.44)	-0.2 (1.09)
		Median	16.0	0.0	16.5	0.0
		Min, Max	13, 20	-4, 4	16, 21	-2, 2
Temperature (C)	Screening	n	79	79	70	70
		Mean (SD)	36.58 (0.366)	0.02 (0.193)	36.65 (0.337)	0.06 (0.262)
		Median	36.60	0.00	36.70	0.00
		Min, Max	35.7, 37.3	-1.0, 0.7	35.7, 37.3	-0.6, 1.0
	Cycle 1 Day 1	n	23	23	20	20
		Mean (SD)	36.71 (0.365)	0.00 (0.000)	36.58 (0.365)	0.00 (0.000)
		Median	36.70	0.00	36.50	0.00
		Min, Max	36.0, 37.5	0.0, 0.0	35.9, 37.1	0.0, 0.0
	Cycle 1 Day 8	n	58	54	53	47
		Mean (SD)	36.49 (0.356)	-0.02 (0.423)	36.55 (0.324)	-0.03 (0.326)
		Median	36.50	-0.05	36.60	-0.10
		Min, Max	35.8, 37.6	-1.0, 1.2	35.7, 37.7	-0.6, 1.0
	Cycle 2 Day 1	n	23	23	19	19

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
		Mean (SD)	36.77 (0.443)	0.06 (0.459)	36.78 (0.348)	0.23 (0.361)
		Median	36.60	0.10	36.80	0.20
		Min, Max	35.9, 37.9	-0.7, 1.3	35.8, 37.5	-0.4, 1.1

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Temperature (C)	Cycle 2 Day 8	n	55	51	55	47
		Mean (SD)	36.51 (0.382)	0.00 (0.393)	36.59 (0.316)	-0.01 (0.411)
		Median	36.50	0.00	36.60	0.00
		Min, Max	35.5, 37.5	-0.9, 1.3	35.6, 37.3	-1.2, 1.0
	Cycle 3 Day 1	n	14	14	15	15
		Mean (SD)	36.86 (0.273)	0.14 (0.305)	36.41 (0.323)	-0.12 (0.463)
		Median	36.80	0.05	36.40	0.00
		Min, Max	36.6, 37.6	-0.2, 0.9	35.7, 36.9	-0.9, 0.5
	Cycle 3 Day 8	n	49	45	47	41
		Mean (SD)	36.44 (0.384)	-0.02 (0.400)	36.60 (0.334)	-0.00 (0.346)
		Median	36.50	0.00	36.60	0.00
		Min, Max	35.2, 37.2	-1.2, 0.8	35.7, 37.1	-0.7, 0.8
	Cycle 4 Day 1	n	12	12	12	12
		Mean (SD)	36.61 (0.306)	-0.13 (0.341)	36.65 (0.345)	0.16 (0.466)
		Median	36.70	-0.10	36.60	0.10
		Min, Max	35.9, 36.9	-0.9, 0.5	35.9, 37.3	-0.6, 1.0

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Temperature (C)	Cycle 4 Day 8	n	46	42	45	39
		Mean (SD)	36.51 (0.645)	0.07 (0.696)	36.46 (0.331)	-0.16 (0.439)
		Median	36.50	0.00	36.50	-0.20
		Min, Max	34.6, 39.9	-1.9, 3.5	35.6, 37.0	-0.8, 0.9
	Cycle 5 Day 1	n	7	7	11	11
		Mean (SD)	36.63 (0.206)	-0.07 (0.390)	36.52 (0.473)	-0.01 (0.515)
		Median	36.60	-0.20	36.70	-0.10
		Min, Max	36.4, 36.9	-0.7, 0.4	35.9, 37.3	-0.9, 0.9
	Cycle 5 Day 8	n	42	39	42	36
		Mean (SD)	36.40 (0.362)	-0.04 (0.444)	36.50 (0.329)	-0.12 (0.388)
		Median	36.50	0.00	36.60	-0.10
		Min, Max	35.1, 37.0	-1.3, 0.8	35.7, 37.3	-0.8, 1.1
	Cycle 6 Day 1	n	6	6	9	9
		Mean (SD)	36.47 (0.463)	-0.22 (0.402)	36.58 (0.254)	0.03 (0.381)
		Median	36.55	-0.30	36.70	0.10
		Min, Max	35.6, 36.9	-0.7, 0.5	36.2, 36.9	-0.7, 0.6

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Temperature (C)	Cycle 6 Day 8	n	40	38	40	34
		Mean (SD)	36.36 (0.277)	-0.06 (0.304)	36.49 (0.353)	-0.09 (0.373)
		Median	36.40	-0.10	36.55	-0.15
		Min, Max	35.7, 36.9	-0.6, 0.5	35.7, 37.3	-0.6, 0.9
	Cycle 7 Day 1	n	4	4	9	9
		Mean (SD)	36.53 (0.556)	-0.13 (0.472)	36.70 (0.287)	0.22 (0.399)
		Median	36.50	0.05	36.70	0.10
		Min, Max	35.9, 37.2	-0.8, 0.2	36.2, 37.1	-0.4, 0.8
	Cycle 7 Day 8	n	33	32	31	26
		Mean (SD)	36.44 (0.337)	0.04 (0.416)	36.49 (0.424)	-0.10 (0.459)
		Median	36.40	0.00	36.60	-0.05
		Min, Max	35.7, 37.3	-0.6, 1.1	35.7, 37.5	-1.0, 1.1
	Cycle 8 Day 1	n	4	4	9	9
		Mean (SD)	36.20 (1.010)	-0.45 (0.806)	36.64 (0.219)	0.17 (0.391)
		Median	36.60	-0.50	36.70	0.00
		Min, Max	34.7, 36.9	-1.3, 0.5	36.2, 36.9	-0.4, 0.7

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Temperature (C)	Cycle 8 Day 8	n	33	31	28	23
		Mean (SD)	36.44 (0.355)	0.05 (0.370)	36.60 (0.320)	0.00 (0.455)
		Median	36.50	0.00	36.60	0.00
		Min, Max	35.6, 37.2	-0.7, 0.6	36.1, 37.6	-0.7, 1.2
	Cycle 9 Day 1	n	3	3	7	7
		Mean (SD)	36.33 (0.569)	-0.03 (0.379)	36.46 (0.378)	0.11 (0.313)
		Median	36.50	-0.20	36.40	0.20
		Min, Max	35.7, 36.8	-0.3, 0.4	35.8, 36.9	-0.3, 0.5
	Cycle 9 Day 8	n	30	28	26	21
		Mean (SD)	36.42 (0.319)	0.04 (0.342)	36.51 (0.384)	-0.15 (0.407)
		Median	36.50	0.00	36.60	-0.10
		Min, Max	35.7, 37.0	-0.6, 0.8	35.7, 37.3	-1.0, 0.9
	Cycle 10 Day 1	n	2	2	7	7
		Mean (SD)	36.20 (0.566)	0.15 (0.495)	36.64 (0.369)	0.30 (0.356)
		Median	36.20	0.15	36.60	0.40
		Min, Max	35.8, 36.6	-0.2, 0.5	36.1, 37.1	-0.3, 0.6

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Temperature (C)	Cycle 10 Day 8	n	26	24	26	21
		Mean (SD)	36.51 (0.286)	0.19 (0.326)	36.58 (0.424)	0.02 (0.438)
		Median	36.50	0.10	36.60	0.00
		Min, Max	36.0, 37.2	-0.2, 1.0	35.6, 37.7	-0.8, 1.1
	Cycle 11 Day 1	n	2	2	5	5
		Mean (SD)	36.25 (0.495)	0.20 (0.424)	36.50 (0.274)	0.18 (0.277)
		Median	36.25	0.20	36.50	0.10
		Min, Max	35.9, 36.6	-0.1, 0.5	36.1, 36.8	-0.1, 0.6
	Cycle 11 Day 8	n	23	21	25	20
		Mean (SD)	36.36 (0.644)	0.03 (0.653)	36.46 (0.296)	-0.16 (0.477)
		Median	36.40	0.10	36.60	-0.10
		Min, Max	33.7, 37.2	-2.4, 1.0	35.7, 36.8	-1.2, 1.0
	Cycle 12 Day 1	n	2	2	4	4
		Mean (SD)	36.20 (0.566)	0.15 (0.495)	36.73 (0.250)	0.43 (0.310)
		Median	36.20	0.15	36.60	0.50
		Min, Max	35.8, 36.6	-0.2, 0.5	36.6, 37.1	0.0, 0.7

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Temperature (C)	Cycle 12 Day 8	n	22	20	25	20
		Mean (SD)	36.54 (0.289)	0.24 (0.314)	36.56 (0.354)	-0.01 (0.518)
		Median	36.60	0.20	36.60	-0.10
		Min, Max	35.9, 37.1	-0.3, 0.9	35.6, 37.2	-1.2, 1.0
	Cycle 13 Day 1	n	1	1	3	3
		Mean (SD)	36.10 (NA)	0.10 (NA)	36.60 (0.265)	0.33 (0.252)
		Median	36.10	0.10	36.70	0.30
		Min, Max	36.1, 36.1	0.1, 0.1	36.3, 36.8	0.1, 0.6
	Cycle 13 Day 8	n	17	15	22	17
		Mean (SD)	36.48 (0.298)	0.15 (0.318)	36.54 (0.669)	-0.01 (0.605)
		Median	36.50	0.10	36.60	-0.10
		Min, Max	35.9, 37.0	-0.5, 0.8	34.6, 38.4	-1.4, 1.6
	Cycle 14 Day 1	n	1	1	2	2
		Mean (SD)	36.50 (NA)	0.50 (NA)	36.55 (0.212)	0.25 (0.636)
		Median	36.50	0.50	36.55	0.25
		Min, Max	36.5, 36.5	0.5, 0.5	36.4, 36.7	-0.2, 0.7

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Temperature (C)	Cycle 14 Day 8	n	14	13	18	13
		Mean (SD)	36.56 (0.250)	0.21 (0.296)	36.58 (0.212)	-0.12 (0.409)
		Median	36.55	0.30	36.65	-0.10
		Min, Max	36.1, 37.1	-0.3, 0.9	36.3, 37.0	-0.7, 0.6
	Off-Study Evaluation	n	67	65	55	53
		Mean (SD)	36.57 (0.382)	-0.01 (0.353)	36.61 (0.357)	0.04 (0.468)
		Median	36.60	0.00	36.60	0.00
		Min, Max	35.1, 37.6	-1.2, 0.7	35.8, 37.8	-0.8, 1.6
	Additional Visit 1	n	20	20	2	2
		Mean (SD)	36.76 (0.254)	0.57 (0.247)	36.45 (0.495)	-0.55 (0.212)
		Median	36.80	0.60	36.45	-0.55
		Min, Max	36.3, 37.2	0.1, 1.0	36.1, 36.8	-0.7, -0.4
	Additional Visit 2	n	78	68	136	110
		Mean (SD)	36.58 (0.341)	0.17 (0.331)	36.58 (0.307)	0.04 (0.365)
		Median	36.60	0.20	36.60	-0.05
		Min, Max	34.6, 37.3	-0.5, 0.9	35.6, 37.3	-0.5, 1.1

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Temperature (C)	Unscheduled	n	24	23	25	24
		Mean (SD)	36.66 (0.365)	0.04 (0.301)	36.57 (0.288)	0.00 (0.280)
		Median	36.80	0.00	36.60	-0.05
		Min, Max	35.8, 37.5	-0.6, 0.8	35.7, 37.2	-0.5, 0.8
Diastolic Blood Pressure (mmHg)	Screening	n	82	82	73	73
		Mean (SD)	76.9 (9.46)	0.2 (5.22)	77.4 (12.01)	1.3 (5.21)
		Median	78.0	0.0	80.0	0.0
		Min, Max	59, 99	-23, 15	50, 105	-16, 19
	Cycle 1 Day 1	n	23	23	20	20
		Mean (SD)	77.0 (10.70)	0.0 (0.00)	71.0 (9.19)	0.0 (0.00)
		Median	74.0	0.0	70.0	0.0
		Min, Max	60, 98	0, 0	59, 100	0, 0
	Cycle 1 Day 8	n	59	56	56	51
		Mean (SD)	77.8 (10.50)	0.9 (9.94)	77.5 (8.36)	-1.2 (10.27)
		Median	77.0	0.0	79.0	0.0
		Min, Max	56, 100	-25, 20	48, 94	-28, 21
	Cycle 2 Day 1	n	23	23	19	19
		Mean (SD)	75.4 (9.93)	-1.5 (10.25)	74.2 (10.33)	3.6 (11.06)
		Median	78.0	0.0	73.0	2.0
		Min, Max	50, 93	-22, 16	59, 92	-13, 26

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Diastolic Blood Pressure (mmHg)	Cycle 2 Day 8	n	56	53	55	50
		Mean (SD)	73.8 (8.47)	-2.9 (9.77)	77.2 (9.55)	-2.2 (10.73)
		Median	74.0	-4.0	78.0	-2.0
		Min, Max	52, 90	-24, 15	56, 104	-30, 29
	Cycle 3 Day 1	n	14	14	15	15
		Mean (SD)	79.0 (11.58)	2.2 (11.12)	72.8 (10.66)	1.1 (7.81)
		Median	82.0	-2.0	72.0	-3.0
		Min, Max	58, 96	-12, 30	61, 97	-10, 12
	Cycle 3 Day 8	n	50	47	47	42
		Mean (SD)	76.0 (9.19)	-0.6 (10.77)	77.8 (9.07)	-1.9 (11.02)
		Median	76.5	0.0	78.0	-0.5
		Min, Max	55, 94	-24, 25	55, 93	-26, 25
	Cycle 4 Day 1	n	12	12	13	13
		Mean (SD)	77.3 (12.43)	0.8 (12.82)	73.1 (9.74)	0.2 (10.58)
		Median	81.0	2.0	71.0	3.0
		Min, Max	46, 93	-22, 21	56, 89	-20, 14

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Diastolic Blood Pressure (mmHg)	Cycle 4 Day 8	n	46	43	45	40
		Mean (SD)	76.4 (7.82)	-0.0 (10.53)	76.3 (10.99)	-3.4 (11.89)
		Median	76.0	0.0	78.0	-2.5
		Min, Max	61, 91	-24, 22	48, 100	-40, 24
	Cycle 5 Day 1	n	7	7	11	11
		Mean (SD)	70.1 (11.23)	-0.6 (12.73)	74.6 (11.89)	0.5 (8.73)
		Median	75.0	5.0	70.0	1.0
		Min, Max	49, 79	-16, 16	63, 96	-11, 18
	Cycle 5 Day 8	n	42	40	42	37
		Mean (SD)	75.4 (10.26)	-1.1 (11.03)	75.3 (9.65)	-4.7 (10.86)
		Median	76.0	-1.5	76.0	-4.0
		Min, Max	49, 98	-27, 23	49, 93	-28, 15
	Cycle 6 Day 1	n	6	6	10	10
		Mean (SD)	74.0 (4.20)	3.7 (8.64)	74.5 (9.31)	0.4 (8.42)
		Median	75.0	7.0	75.0	2.0
		Min, Max	66, 78	-13, 10	60, 87	-13, 17

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Diastolic Blood Pressure (mmHg)	Cycle 6 Day 8	n	39	38	40	35
		Mean (SD)	74.6 (9.45)	-1.8 (10.31)	74.9 (10.75)	-4.2 (9.01)
		Median	75.0	-2.0	76.5	-3.0
		Min, Max	55, 97	-21, 19	43, 98	-28, 11
	Cycle 7 Day 1	n	4	4	9	9
		Mean (SD)	78.5 (11.47)	12.8 (9.78)	73.7 (9.08)	-0.8 (7.51)
		Median	76.0	13.5	76.0	-1.0
		Min, Max	68, 94	2, 22	58, 83	-17, 8
	Cycle 7 Day 8	n	33	33	31	27
		Mean (SD)	72.2 (8.85)	-4.5 (10.47)	76.2 (9.88)	-4.0 (10.79)
		Median	72.0	-4.0	75.0	-3.0
		Min, Max	56, 88	-31, 16	56, 100	-28, 17
	Cycle 8 Day 1	n	4	4	9	9
		Mean (SD)	71.3 (7.68)	5.5 (5.69)	77.7 (11.78)	3.2 (8.07)
		Median	70.5	8.0	80.0	4.0
		Min, Max	63, 81	-3, 9	58, 97	-6, 18

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Diastolic Blood Pressure (mmHg)	Cycle 8 Day 8	n	32	31	28	24
		Mean (SD)	76.7 (9.62)	0.1 (11.07)	75.6 (9.17)	-5.0 (11.88)
		Median	78.0	1.0	76.5	-4.5
		Min, Max	60, 93	-25, 33	57, 97	-30, 17
	Cycle 9 Day 1	n	3	3	7	7
		Mean (SD)	75.7 (10.07)	8.0 (9.85)	73.9 (13.17)	2.4 (9.48)
		Median	77.0	5.0	74.0	4.0
		Min, Max	65, 85	0, 19	60, 92	-16, 15
	Cycle 9 Day 8	n	30	29	26	22
		Mean (SD)	74.9 (10.78)	-2.0 (13.74)	75.6 (11.61)	-3.8 (12.13)
		Median	74.0	0.0	75.5	-2.5
		Min, Max	50, 106	-37, 20	45, 94	-34, 13
	Cycle 10 Day 1	n	2	2	7	7
		Mean (SD)	73.0 (7.07)	7.5 (6.36)	70.7 (7.65)	-0.7 (8.04)
		Median	73.0	7.5	73.0	0.0
		Min, Max	68, 78	3, 12	58, 78	-13, 14

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Diastolic Blood Pressure (mmHg)	Cycle 10 Day 8	n	26	25	26	22
		Mean (SD)	72.1 (9.05)	-4.3 (9.64)	72.8 (11.31)	-7.0 (11.87)
		Median	72.5	-2.0	73.0	-4.5
		Min, Max	58, 90	-26, 11	44, 92	-38, 10
	Cycle 11 Day 1	n	2	2	5	5
		Mean (SD)	69.0 (2.83)	3.5 (2.12)	70.4 (10.36)	-3.2 (8.38)
		Median	69.0	3.5	74.0	-1.0
		Min, Max	67, 71	2, 5	59, 82	-17, 5
	Cycle 11 Day 8	n	23	22	25	21
		Mean (SD)	74.0 (7.22)	-2.8 (8.23)	78.3 (11.16)	-2.1 (8.57)
		Median	75.0	-3.5	79.0	0.0
		Min, Max	60, 89	-16, 13	57, 100	-20, 13
	Cycle 12 Day 1	n	2	2	4	4
		Mean (SD)	73.0 (2.83)	7.5 (3.54)	81.5 (10.97)	4.3 (10.78)
		Median	73.0	7.5	81.0	4.5
		Min, Max	71, 75	5, 10	70, 94	-8, 16

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Diastolic Blood Pressure (mmHg)	Cycle 12 Day 8	n	22	21	25	21
		Mean (SD)	77.5 (9.19)	1.2 (7.30)	75.8 (9.78)	-5.1 (12.28)
		Median	79.5	1.0	78.0	-3.0
		Min, Max	60, 95	-15, 16	57, 92	-30, 17
	Cycle 13 Day 1	n	1	1	3	3
		Mean (SD)	71.0 (NA)	5.0 (NA)	71.7 (10.21)	-5.3 (9.29)
		Median	71.0	5.0	76.0	-1.0
		Min, Max	71, 71	5, 5	60, 79	-16, 1
	Cycle 13 Day 8	n	17	16	22	18
		Mean (SD)	74.3 (7.65)	-3.9 (9.70)	76.5 (10.87)	-4.1 (11.96)
		Median	74.0	-3.5	79.0	-4.5
		Min, Max	60, 84	-27, 10	57, 94	-26, 15
	Cycle 14 Day 1	n	1	1	2	2
		Mean (SD)	55.0 (NA)	-11 (NA)	73.0 (15.56)	-3.5 (14.85)
		Median	55.0	-11	73.0	-3.5
		Min, Max	55, 55	-11, -11	62, 84	-14, 7

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Diastolic Blood Pressure (mmHg)	Cycle 14 Day 8	n	14	14	18	14
		Mean (SD)	75.1 (10.35)	-3.9 (12.34)	74.3 (9.57)	-7.4 (11.34)
		Median	73.5	-4.5	74.5	-6.5
		Min, Max	64, 100	-23, 26	50, 92	-34, 13
	Off-Study Evaluation	n	68	66	61	57
		Mean (SD)	76.0 (9.98)	-0.8 (10.37)	75.4 (9.90)	-2.1 (9.98)
		Median	76.0	-2.0	76.0	-2.0
		Min, Max	46, 100	-30, 22	52, 101	-28, 25
	Additional Visit 1	n	20	20	2	2
		Mean (SD)	75.2 (9.24)	-3.3 (5.96)	80.0 (11.31)	-8.5 (3.54)
		Median	73.5	-3.0	80.0	-8.5
		Min, Max	63, 91	-19, 7	72, 88	-11, -6
	Additional Visit 2	n	78	78	136	118
		Mean (SD)	74.5 (11.14)	-4.9 (13.15)	76.3 (9.34)	-3.2 (9.87)
		Median	77.0	-3.0	75.0	-4.0
		Min, Max	18, 94	-63, 21	48, 104	-28, 21

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Diastolic Blood Pressure (mmHg)	Unscheduled	n	24	24	26	25
		Mean (SD)	71.5 (9.52)	-4.6 (9.75)	72.1 (6.97)	-3.3 (12.01)
		Median	73.5	-5.0	72.0	-5.0
		Min, Max	53, 89	-21, 17	60, 87	-28, 21
Systolic Blood Pressure (mmHg)	Screening	n	82	82	73	73
		Mean (SD)	129 (15.53)	-1.0 (8.98)	131 (17.73)	1.1 (7.96)
		Median	128	0.0	130	0.0
		Min, Max	90, 161	-35, 36	92, 190	-25, 35
	Cycle 1 Day 1	n	23	23	20	20
		Mean (SD)	135 (17.93)	0.0 (0.00)	131 (19.00)	0.0 (0.00)
		Median	137	0.0	132	0.0
		Min, Max	98, 160	0, 0	104, 175	0, 0
	Cycle 1 Day 8	n	59	56	56	51
		Mean (SD)	131 (15.67)	2.0 (14.03)	128 (14.51)	-1.0 (18.60)
		Median	130	2.0	129	0.0
		Min, Max	92, 160	-32, 30	94, 164	-66, 39
	Cycle 2 Day 1	n	23	23	19	19
		Mean (SD)	135 (18.70)	-0.5 (16.40)	134 (18.20)	2.9 (16.76)
		Median	131	1.0	130	1.0
		Min, Max	102, 174	-26, 33	106, 176	-22, 44

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Cycle 2 Day 8	n	56	53	55	50
		Mean (SD)	130 (17.47)	0.8 (16.39)	127 (15.83)	-3.6 (18.19)
		Median	129	0.0	126	1.0
		Min, Max	90, 165	-30, 35	96, 174	-54, 28
	Cycle 3 Day 1	n	14	14	15	15
		Mean (SD)	130 (20.60)	-1.1 (18.49)	133 (16.89)	2.3 (17.85)
		Median	133	-2.0	127	-3.0
		Min, Max	93, 171	-28, 41	104, 166	-27, 30
	Cycle 3 Day 8	n	50	47	47	42
		Mean (SD)	129 (13.62)	-1.3 (15.06)	128 (13.42)	-0.8 (17.38)
		Median	131	-2.0	129	-1.0
		Min, Max	99, 154	-31, 31	90, 155	-46, 32
	Cycle 4 Day 1	n	12	12	13	13
		Mean (SD)	128 (17.35)	-3.5 (23.31)	132 (20.15)	-3.3 (25.12)
		Median	123	0.0	129	0.0
		Min, Max	102, 153	-39, 30	99, 174	-52, 42

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Cycle 4 Day 8	n	46	43	45	40
		Mean (SD)	130 (15.20)	0.6 (16.32)	126 (11.92)	-3.5 (18.01)
		Median	132	2.0	126	-3.5
		Min, Max	104, 160	-28, 45	96, 153	-50, 30
	Cycle 5 Day 1	n	7	7	11	11
		Mean (SD)	129 (14.27)	-2.0 (15.67)	130 (15.06)	-4.3 (21.68)
		Median	133	-4.0	131	-1.0
		Min, Max	106, 143	-19, 19	102, 153	-51, 32
	Cycle 5 Day 8	n	42	40	42	37
		Mean (SD)	133 (16.44)	3.0 (16.91)	126 (14.54)	-2.8 (20.81)
		Median	136	-1.5	125	-1.0
		Min, Max	98, 159	-29, 33	92, 159	-56, 44
	Cycle 6 Day 1	n	6	6	10	10
		Mean (SD)	130 (13.29)	3.3 (15.03)	131 (16.79)	-4.6 (19.31)
		Median	133	5.5	133	-13
		Min, Max	108, 148	-17, 25	107, 156	-24, 36

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Cycle 6 Day 8	n	39	38	40	35
		Mean (SD)	127 (16.60)	-2.7 (19.24)	125 (13.86)	-1.8 (15.70)
		Median	127	-4.0	124	-2.0
		Min, Max	100, 160	-54, 34	99, 165	-34, 29
	Cycle 7 Day 1	n	4	4	9	9
		Mean (SD)	133 (11.70)	19.5 (11.96)	129 (7.29)	-5.2 (23.40)
		Median	132	20.5	130	6.0
		Min, Max	120, 148	4, 33	113, 138	-47, 18
	Cycle 7 Day 8	n	33	33	31	27
		Mean (SD)	124 (16.02)	-5.2 (16.80)	126 (14.77)	-2.3 (17.68)
		Median	121	-3.0	123	-1.0
		Min, Max	91, 158	-46, 23	99, 160	-37, 31
	Cycle 8 Day 1	n	4	4	9	9
		Mean (SD)	113 (4.86)	0.0 (10.42)	139 (21.94)	4.3 (28.35)
		Median	116	3.5	142	1.0
		Min, Max	106, 116	-15, 8	103, 182	-33, 50

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Cycle 8 Day 8	n	32	31	28	24
		Mean (SD)	128 (16.40)	-0.2 (15.41)	127 (12.44)	-2.5 (14.54)
		Median	129	2.0	128	0.0
		Min, Max	100, 165	-27, 31	100, 150	-40, 17
	Cycle 9 Day 1	n	3	3	7	7
		Mean (SD)	124 (23.59)	6.0 (13.53)	137 (15.49)	-0.7 (30.52)
		Median	122	7.0	137	10.0
		Min, Max	102, 149	-8, 19	121, 167	-54, 35
	Cycle 9 Day 8	n	30	29	26	22
		Mean (SD)	129 (20.10)	0.5 (19.86)	123 (12.74)	-6.7 (16.75)
		Median	127	0.0	121	-5.0
		Min, Max	96, 194	-41, 45	94, 142	-46, 19
	Cycle 10 Day 1	n	2	2	7	7
		Mean (SD)	127 (16.26)	6.5 (2.12)	127 (9.20)	-11 (25.83)
		Median	127	6.5	129	0.0
		Min, Max	115, 138	5, 8	112, 140	-63, 10

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Cycle 10 Day 8	n	26	25	26	22
		Mean (SD)	125 (14.62)	-3.6 (12.38)	122 (16.33)	-7.8 (19.24)
		Median	122	-5.0	120	-7.5
		Min, Max	97, 154	-31, 27	90, 161	-64, 21
	Cycle 11 Day 1	n	2	2	5	5
		Mean (SD)	121 (20.51)	0.5 (6.36)	127 (14.97)	-16 (37.35)
		Median	121	0.5	131	-10
		Min, Max	106, 135	-4, 5	105, 145	-70, 23
	Cycle 11 Day 8	n	23	22	25	21
		Mean (SD)	122 (14.90)	-6.8 (10.06)	124 (14.48)	-5.7 (17.07)
		Median	121	-6.0	120	-6.0
		Min, Max	91, 153	-28, 10	103, 151	-51, 31
	Cycle 12 Day 1	n	2	2	4	4
		Mean (SD)	124 (5.66)	4.0 (19.80)	143 (19.05)	-6.3 (39.21)
		Median	124	4.0	134	-11
		Min, Max	120, 128	-10, 18	131, 171	-44, 40

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Cycle 12 Day 8	n	22	21	25	21
		Mean (SD)	127 (19.26)	-1.5 (16.70)	125 (13.01)	-5.0 (19.99)
		Median	123	-3.0	120	-4.0
		Min, Max	100, 186	-31, 43	105, 159	-35, 39
	Cycle 13 Day 1	n	1	1	3	3
		Mean (SD)	123 (NA)	-7.0 (NA)	109 (21.94)	-33 (50.14)
		Median	123	-7.0	122	-9.0
		Min, Max	123, 123	-7, -7	84, 122	-91, 0
	Cycle 13 Day 8	n	17	16	22	18
		Mean (SD)	127 (15.36)	-3.6 (14.94)	125 (17.10)	-3.8 (17.26)
		Median	125	-4.5	123	5.0
		Min, Max	103, 159	-31, 16	93, 162	-27, 21
	Cycle 14 Day 1	n	1	1	2	2
		Mean (SD)	113 (NA)	-17 (NA)	128 (24.04)	-21 (61.52)
		Median	113	-17	128	-21
		Min, Max	113, 113	-17, -17	111, 145	-64, 23

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Cycle 14 Day 8	n	14	14	18	14
		Mean (SD)	123 (14.28)	-7.3 (10.42)	120 (13.67)	-8.4 (20.50)
		Median	129	-6.0	121	-5.0
		Min, Max	95, 146	-29, 10	88, 139	-52, 19
	Off-Study Evaluation	n	68	66	61	57
		Mean (SD)	126 (17.33)	-5.1 (18.53)	126 (13.27)	-6.5 (17.61)
		Median	128	-5.0	123	-4.0
		Min, Max	85, 174	-51, 49	98, 159	-70, 28
	Additional Visit 1	n	20	20	2	2
		Mean (SD)	132 (21.35)	6.3 (11.95)	128 (9.19)	-2.0 (4.24)
		Median	128	8.0	128	-2.0
		Min, Max	95, 167	-15, 29	121, 134	-5, 1
	Additional Visit 2	n	78	78	136	118
		Mean (SD)	120 (13.55)	-9.7 (15.30)	127 (13.48)	-9.4 (19.08)
		Median	117	-9.0	125	-8.5
		Min, Max	90, 156	-55, 33	96, 160	-56, 30

Table 14.3.5.4
Summary of Vital Signs and Changes from Baseline by Visit (Safety Analysis Set)

			NLG-2101 (N=85)		Placebo (N=79)	
Parameter	Analysis Visit	Statistic	Actual Value	Change from Baseline	Actual Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Unscheduled	n	24	24	26	25
		Mean (SD)	123 (12.03)	-8.4 (17.29)	124 (12.63)	-12 (21.78)
		Median	127	-7.5	125	-8.0
		Min, Max	99, 142	-38, 29	103, 151	-73, 10

2.3.4 ECOG data

Table Number	Table Title
Table 14.3.5.6	Shifts from baseline in ECOG performance status (Safety Analysis Set)

Table 14.3.5.6
Shifts from Baseline in ECOG Performance Status (Safety Analysis Set)

Treatment Group	Baseline ECOG	Worst Post-Baseline ECOG Result 0 n (%)	1 n (%)	2 n (%)	3 n (%)	4 n (%)	Missing n (%)	Total n (%)
NLG2101	0	16 (18.8)	23 (27.1)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)	41 (48.2)
	1	1 (1.2)	30 (35.3)	7 (8.2)	1 (1.2)	0 (0.0)	0 (0.0)	39 (45.9)
	2	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.4)	3 (3.5)
	Total	17 (20.0)	55 (64.7)	9 (10.6)	2 (2.4)	0 (0.0)	2 (2.4)	85 (100.0)
PLACEBO	0	15 (19.0)	21 (26.6)	2 (2.5)	2 (2.5)	0 (0.0)	0 (0.0)	40 (50.6)
	1	2 (2.5)	24 (30.4)	6 (7.6)	3 (3.8)	0 (0.0)	0 (0.0)	35 (44.3)
	2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)	0 (0.0)	1 (1.3)
	3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.8)	3 (3.8)
	Total	17 (21.5)	45 (57.0)	8 (10.1)	5 (6.3)	1 (1.3)	3 (3.8)	79 (100.0)

2.3.5 Narratives of Deaths, other Serious and Certain Other Significant Adverse Events

A short narrative for each subject who died during the study as well as each subject with a serious TEAE that was considered of special interest is provided below.

Overview of Subjects for whom a narrative is written:

Subject ID	Death	Other Serious TEAE of interest
2101038	X	
2101082	X	
2101099	X	
2101137	X	
2101032	X	
2101047	X	
2101124		X

Subject ID	2101038
Treatment Group	Indoximod
Reason for Narrative	Death
Preferred term(s)	Multi organ failure

Subject 2101038, a 35-year-old female with a positive hormone receptor status (ER+/PR-) entered the study with infiltrating ductal carcinoma (T1, N1, M1).

At the start of the study, the subject had abdominal pain, bloating skin rash, fatigue, hot flashes, pain in extremities (legs), ALT increased (intermittent), ALP increased, AST increased (intermittent), anemia, fever blisters, back pain (intermittent), joint pain, muscle spasms, anxiety, indigestion, mouth sores, nausea, and vaginal dryness.

On 16 Apr 2015, the subject developed moderate ascites. In addition, that same day, the subject's lymphocyte count was found to be decreased (exact value not available). On 23 Apr 2015, the subject had a moderately increased ALP value (410 U/L; normal range: 35-105 U/L), a moderately increased AST value (117 U/L; normal range: 10-35 U/L), mildly increased bilirubin value (1.30 mg/dL; normal range: 0-1.2 mg/dL), mildly increased creatinine value (1.2 mg/dL; normal range: 0.5-1 mg/dL), severe hyperkalemia (5.0 mmol/L; normal range: 3.4-4.5 mmol/L), moderate hypoalbuminemia (2.7 g/dL; normal range 3.5-5.2 g/dL), and life-threatening hypercalcemia (17.4 mg/dL; normal range: 8.6-10.2 mg/dL). Further, the subject was also reported with severe fatigue and severe hypotension. On 30 Apr 2015, the subject's condition worsened. She now had a severely increased ALP value, severely increased bilirubin value, moderately increased creatinine value, severe hyperkalemia, and severe hyponatremia (exact values not available). The calcium level improved to mildly increased (exact value not available).

On 30 Apr 2015, ie, 8 days after the last dose of study drug, the subject developed multi organ failure. She died on 04 May 2015.

Apart from the decreased lymphocyte count, which was considered highly probable or definitely related to the study drug, all aforementioned TEAEs were considered to be unrelated to indoximod by the investigator.

Subject ID	2101082
Treatment Group	Indoximod
Reason for Narrative	Death
Preferred term(s)	Respiratory failure

Subject 2101082, a 39-year-old female with a negative hormone receptor status, entered the study with infiltrating ductal carcinoma (T2, N1, M0).

At the start of the study, the subject had hyperlipidemia, sinus tachycardia, hypercholesterolemia, hypertension, herpes simplex virus, uterine fibroids, left arm lymphedema, neuropathy, anxiety, migraine headaches, anorexia, fatigue, dyspnea, hypoxia, pleural effusion (malignant), and cough.

On 31 May 2015, severe (worsening) dyspnea was reported. The subject was brought to the emergency room after a 20-min episode of confusion. She was reported to have had worsening dyspnea on exertion for the past 2 weeks. Upon arrival the subject was awake, alert and oriented towards date, place, person, and situation. After examination and while waiting to be discharged, the subject's oxygen saturation dropped to 80% despite oxygen via nasal cannula (2L/min). The subject was taken to x-ray for computed tomography angiography to rule out pulmonary embolus. No embolus was found but the examination showed increasing severity of diffuse peribronchovascular ground glass opacities. The subject subsequently became more hypoxic and tachycardic requiring venturi mask with high flow oxygen. She was admitted to the intensive care unit and was started on intravenous antibiotics and gentle diuresis with intravenous Lasix. The subject’s platelet count was 27 and she subsequently received a unit of platelets. The subject then became severely tachypneic and tachycardic. She became altered and was started on oxygen bagging. The subject died later that day due to respiratory failure/arrest (ie, 2 days after the last dose of study drug).

The TEAE of respiratory arrest was considered to be unrelated to indoximod by the investigator.

Subject ID	2101099
Treatment Group	Indoximod
Reason for Narrative	Death
Preferred term(s)	Cardiopulmonary failure

Subject 2101099, a 58-year-old female with a positive hormone receptor (ER+/PR+) entered the study with an unspecified cancer (T2, N0, M0).

At the start of the study, the subject had abdominal petechiae, insomnia, cough, pain in the thoracic region of the spine, dyspnea, and allergies to dust, pollen, and grass.

On 23 Aug 2015, the subject was admitted to the hospital with abdominal pain. Cachexia and leukopenia were reported as a severe TEAEs. On admission, the subject was suffering, anxious, cachectic, pale, with abdominal distension, and had abdominal tenderness over the whole abdominal cavity, poorly audible peristalsis. A digital rectal exam revealed compact stool mass. The subject’s heart rate was 100 bpm and her blood pressure 120/80 mmHg. Abdominal x-ray revealed fluid levels in the right flank region, no free air was found. Ultrasound imaging did not reveal any pathology. The surgery department was consulted and the subject was started on a morphine drip for pain. Spasmolytic medications were also given. The subject’s pain was reduced and she was quieter and sedated. On 24 Aug 2015, ie, 2 days after the last dose of study drug, the subject was pronounced dead. The cause of death was cardiopulmonary failure.

The TEAE of cardiopulmonary failure was considered to be unrelated to indoximod by the investigator.

Subject ID	2101137
Treatment Group	Indoximod
Reason for Narrative	Death
Preferred term(s)	Sudden death

Subject 2101137, a 59-year-old female with a positive hormone receptor (ER+/PR+) status, entered the study with infiltrating ductal carcinoma (T2, N1, M0).

At the start of the study, the subject had intermittent nausea, cancer-related pain, anxiety, constipation, hypocalcemia, and smoked.

On 22 Feb 2016, the subject was seen in the clinic. She reported to have had a bad week. She reported nausea, vomiting, low appetite, and abdominal pain. She also reported she had been in bed for several days. She took

morphine (30 mg) and oxycodone (5 mg) that same that morning. The subject was educated on the use of her medications, specifically pain medication, nausea medication, and lorazepam. On 23 Feb 2016, ie, 3 days after the last dose of study drug, the subject was found dead at her residence. The autopsy results revealed the death was related to an overdose of methamphetamine and morphine toxicity.

The TEAE of sudden death was considered to be unrelated to indoximod by the investigator.

Subject ID	2101032
Treatment Group	Placebo
Reason for Narrative	Death
Preferred term(s)	Sepsis

Subject 2101032, a 50-year-old female with a negative hormone receptor status, entered the study with infiltrating ductal carcinoma (T2, N1, M1).

At the start of the study, the subject had hypertension, Grave's disease with thyroid nodules, uterine polyp, elevated AST/ALT, autoimmune arthritis, sciatic L4/L5, anxiety, and insomnia.

The subject presented to the emergency with an elevated white blood cell count, tachycardia, and was tachypneic. She also presented with redness and swelling in the left shoulder suggestive of possible port-a-cath involvement. The subject was admitted for sepsis (start date: 16 Mar 2015) work up and treatment. She was determined to have cellulitis of the left upper extremity and broad spectrum antibiotics were started. The subject's condition continued to deteriorate despite cultures being negative and was found to have diffuse metastatic disease causing bilateral pleural effusions that were drained by L-sided thoracentesis on 01 Apr 2015 and R-sided thoracentesis on 02 Apr 2015. The subject was transferred to palliative care and died on 04 Apr 15.

The TEAE of sepsis was considered to be unrelated to the study drug by the investigator and possibly related to the port-a-cath infection.

Subject ID	2101047
Treatment Group	Placebo
Reason for Narrative	Death
Preferred term(s)	Respiratory failure

Subject 2101047, a 69-year-old female with a positive hormone receptor status (ER+/PR+), entered the study with infiltrating ductal carcinoma (T4, N3, M1).

At the start of the study, the subject had fatigue, night sweats, back pain, left shoulder pain, muscle weakness, pain in forearm, pain in right breast, hypertension, dry cough, and dyspnea on exertion.

The subject reported to the emergency department with complaints of worsening dyspnea. Respiratory failure was reported as a TEAE (start date 15 Mar 2015). The subject was tachycardic and her troponin level was increased. A chest X-ray showed increased pulmonary metastases and a small right pleural effusion that was thought to be a lymphatic spread of the subject's primary tumor. She died on 18 Mar 2015.

The TEAE of respiratory failure was considered to be unrelated to the study drug by the investigator.

Subject ID	2101124
Treatment Group	Indoximod
Reason for Narrative	TEAE of interest
Preferred term(s)	Parkinson's Disease

Subject 2101124, a 60year-old female with a positive hormone receptor status (ER+/PR-), entered the study with infiltrating ductal carcinoma (T1, N0, M0).

At the start of the study, the subject had carotid artery disease, hyperlipidemia, sinusitis, diverticulosis, gastroesophageal reflux disease, generalized pain, and a history of colon polyps.

Subject tolerated first two cycles of study treatment well. During the third cycle, the subject initially noted some tremor in hands. By Day 16 of the third cycle, the subject was experiencing significant weakness and flat affect. She was started on steroids without improvement. At the scheduled time of the fourth cycle start, the subject's conditioned had worsened and study treatment was discontinued. An extensive evaluation was performed including magnetic resonance of brain and neurology consultation. The subject's symptoms were consistent with Parkinson's disease (reported as a serious TEAE of severe intensity). It should be noted that the subject had a strong family history of Parkinson's disease.

The investigator was concerned about the rapid onset of Parkinson's symptoms. The relationship between study drug and rapid onset of the subject's symptoms is unclear. Given poor understanding of mechanisms underlying onset of Parkinson's symptoms, any possible impact of study drug is unknown. The investigator has attributed a probable relationship between study drug and rapidity of symptom onset.

Given available evidence, a relationship cannot be ruled out. Therefore, the sponsor agreed with a possible related attribution.

Other narratives are available upon request.

4 APPENDICES

4.1 Study Information

4.1.1 Protocol and Protocol Amendments

Protocol Version	Protocol Date
5.0	10 Sep 2014
4.0	10 Jul 2013
3.0	14 May 2013
2.0	13 Mar 2013
1.1 (Original)	07 Aug 2012

4.2 Subject Data Listings

4.2.1 Discontinued Subjects

Listing Number	Listing Title
Listing 16.2.1.1	Study completion status
Listing 16.2.1.2.1	Treatment completion status
Listing 16.2.2.1	Subject eligibility

4.2.2 Protocol Deviations

Listing Number	Listing Title
Listing 16.2.2.2	Protocol deviations

4.2.3 Subjects Excluded from the Efficacy Analysis

Not applicable

4.2.4 Demographic Data

Listing Number	Listing Title
Listing 16.2.4.1	Demographics
Listing 16.2.4.2	Cancer history
Listing 16.2.4.3	Medical history
Listing 16.2.4.4	Prior cancer-related surgeries
Listing 16.2.4.5	Previous radiation therapy
Listing 16.2.4.6	Previous systemic therapy
Listing 16.2.4.7	Pregnancy test results
Listing 16.2.9.3	Concomitant medications
Listing 16.2.9.4	Concurrent procedures
Listing 16.2.9.2	ECOG performance status

4.2.5 Compliance and/or Drug Concentration Data

Listing Number	Listing Title
Listing 16.2.5.1	Taxane administration
Listing 16.2.5.2	Indoximod administration
Listing 16.2.5.3	Exposure

4.2.6 Individual Efficacy Response Data

Listing Number	Listing Title
Listing 16.2.1.3	Follow-up survival status
Listing 16.2.6.1	Response evaluation criteria in solid tumors (RECIST)
Listing 16.2.6.2	Target lesion assessment
Listing 16.2.6.3	Non-target lesion assessment

4.2.7 Adverse Event Listings (Each Subject)

Listing Number	Listing Title
Listing 16.2.7.1	Adverse events by subject, adverse event term, and onset

4.2.8 Listing of Individual Laboratory Measurements by Subject

Listing Number	Listing Title
Listing 16.2.8.1	Clinical laboratory: hematology
Listing 16.2.8.2	Clinical laboratory: chemistry
Listing 16.2.9.1	Vital signs