

#3437: Phase 3 trial ResQ201A of NAI plus tislelizumab and docetaxel vs. docetaxel monotherapy for advanced or metastatic NSCLC resistant to ICI therapy



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BACKGROUND

- Immune checkpoint inhibitors (ICIs) that target PD-1 or PD-L1 are approved for use as in combination with and monotherapy NSCLC. chemotherapy in advanced Unfortunately, patients most experience progressive disease with limited treatment options, warranting better options following progression on an ICI.
- Findings from Phase 2 studies have demonstrated the potential for the IL-15 receptor superagonist nogapendekin alfa inbakicept (NAI; or N-803) as a novel lymphocyte stimulating agent (LSA) to enhance ICI efficacy, prolonging progression-free survival (PFS) and overall survival (OS) when used in combination with an ICI.^{1,2}
- ResQ201A⁵ is informed by the QUILT-3.055 trial wherein mOS was prolonged with NAI at 14.3 months overall among NSCLC patients. Most patients (80%) exceeded and/or maintained an ALC of 1,200 cells/μL which was associated with prolonged mOS compared to patients who failed to achieve ALC>1,200 cells/μ (mOS 15.8 months vs. 11.5 months, [p=0.0057]) and over half of NSCLC patients (60%) treated with NAI experienced lymphopenia reversal during treatment.⁶
- In ResQ201A, monotherapy docetaxel, standard 2nd-line therapy for NSCLC, is being compared to combination therapy with NAI, anti-PD-1 tislelizumab, and 2 cycles of docetaxel.⁴
- NAI proliferates and activates NK and T cells² and is anticipated to contribute to the efficacy of docetaxel plus tislelizumab therapy in ICI-resistant NSCLC and prolong survival as shown in QUILT-3.055 when administered without chemotherapy.

TRIAL DESIGN

Randomized, Open-label, Phase III Clinical Trial of N-803/NAI Plus Tislelizumab and Docetaxel versus Docetaxel Monotherapy in Participants with Advanced or Metastatic Non-Small Cell Lung Cancer who have Acquired Resistance to Immune Checkpoint Inhibitor Therapy⁵

N = 462

Key Inclusion Criteria:

- Age ≥ 18 years
- Ability to provide informed consent
- Pathologically-confirmed stage IV NSCLC with acquired resistance to an ICI (PD after an initial response or stable disease (SD) (≥ 6 mo. duration) to a single line of anti-PD-(L)1 with or without anti-CTLA-4 or chemotherapy
- ECOG performance status of 0 to 2
- Measurable tumor lesions according to RECIST v1.1

Key Exclusion Criteria:

Systemic autoimmune disease, history of organ transplant, and positive for *ALK* rearrangement.

Stratification:

Histology Squamous or non-squamous NSCLC

Geographical Region North America, Europe, Asia,

Other

Alteration
EGFR, ROS, Other, None

Actionable Genomic

Experimental Arm:

- Induction: 3-week cycles NAI [SC 1.2 mg], tislelizumab [IV 200 mg] plus docetaxel [IV 75 mg/m²]
- Maintenance: Repeated 3-week cycles of NAI [SC 1.2 mg] and tislelizumab [IV 200 mg] without docetaxel
 N=308

Control Arm:

 Repeated 3-week cycles with docetaxel [IV 75 mg/m²]

N=154

Treatment until disease progression, unacceptable toxicity, withdrawal of consent, or if the investigator feels it is no longer in their best interest to continue treatment.

Randomization

ENDPOINTS

Primary:

 OS by Kaplan-Meier with treatment arm comparison based on the stratified logrank test and OS hazard ratio (and 95% CI) summarized based on the stratified Cox proportional hazard model, both stratified by the randomization strata.

Secondary:

- Immune disease control rate
 (iDCR iCR + iPR + iSD [≥ 2
 months]) per iRECIST;
 progression-free survival
 (iPFS), overall response rate
 (iORR) and duration of
 response (iDOR).
- Safety assessed by AEs and SAEs graded using the NCI CTCAE v5.0.

Exploratory:

- Disease-specific survival (DSS), defined as time from randomization to death resulting from NSCLC & PFS, DOR, DCR, ORR per RECIST v1.1
- Assess whole slide images and tumor molecular profiles and correlate with participant outcomes.
- Collect blood for analyses, which may include ctDNA testing.

REFERENCES

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