

PROTOCOL SYNOPSIS

Protocol Number:	NVX-1218.22
Protocol Title:	A Phase III, Randomised, Double-Blind Study of NovaPlex-450
IND Number:	IND-145892
Sponsor:	NexaVance Therapeutics Inc., Cambridge, MA, USA
Phase:	Phase III
Indication:	Advanced Non-Small Cell Lung Cancer (NSCLC)
Protocol Version:	v3.0 (incorporating Amendment v2.1)
Protocol Date:	2024-11-01

Primary Objective

To compare progression-free survival (PFS) of NovaPlex-450 plus best supportive care versus platinum-based doublet chemotherapy in treatment-naive patients with advanced NSCLC (Stage IIIB/IV) without known actionable driver mutations.

Primary Endpoint

Progression-Free Survival (PFS) assessed by blinded independent central review (BICR) per RECIST 1.1.

Key Inclusion Criteria

- Age \geq 18 years
- Histologically confirmed advanced NSCLC (Stage IIIB/IV)
- No prior systemic therapy for advanced/metastatic disease
- ECOG Performance Status 0-1
- Adequate organ function (haematology, hepatic, renal)
- No known EGFR/ALK/ROS1 mutations or rearrangements
- Written informed consent obtained prior to any study procedures

Key Exclusion Criteria

- Prior immunotherapy or checkpoint inhibitor therapy
- Active autoimmune disease requiring systemic treatment within 2 years
- Symptomatic brain metastases (stable, treated metastases permitted)
- Active cardiac conditions: NYHA Class III/IV heart failure, unstable angina
- QTc > 480ms on screening ECG
- Known active hepatitis B or C infection
- Pregnancy or breastfeeding

Study Design

Randomisation 1:1 (NovaPlex-450 vs chemotherapy). Stratification by ECOG PS (0 vs 1), histology (squamous vs non-squamous), and geographic region. Treatment continues until disease progression, unacceptable toxicity, or

withdrawal of consent. Tumour assessments every 6 weeks for first 12 months, then every 12 weeks.

Dosing

NovaPlex-450: 450mg IV over 60 minutes, Day 1 of each 21-day cycle

Comparator: Carboplatin AUC5 + Pemetrexed 500mg/m² IV, Day 1 of each 21-day cycle (non-squamous)

Sample Size

Planned Enrollment: 500 subjects (100 per site, 5 sites)

Current Enrollment: 100 subjects across 5 sites (as of 2025-02-01)

Power: 80% to detect HR=0.70 in PFS (median PFS 12 vs 8 months)