Title: A Phase 3 Randomized, Controlled Clinical Trial of an Investigational Drug for Advanced Non-Small Cell Lung Cancer (NSCLC)

Introduction:
This phase 3 clinical trial evaluates the efficacy and safety of an investigational drug, AZD-3, in combination with standard chemotherapy for the treatment of advanced non-small cell lung cancer (NSCLC). AZD-3 is a novel small molecule designed to inhibit tumor cell proliferation by targeting a specific kinase. Phase 2 studies have shown promising activity of AZD-3 in NSCLC.

Methods:
The trial randomized 450 patients with stage IIIB or IV NSCLC, who had not received prior systemic therapy, in a 2:1 ratio to receive either AZD-3 plus standard chemotherapy (pemetrexed and cisplatin) or placebo plus chemotherapy. Patients in the AZD-3 group received the investigational drug orally twice daily, while those in the control group received a matching placebo.

The primary endpoint was overall survival (OS), with secondary endpoints including progression-free survival (PFS), objective response rate (ORR), disease control rate (DCR), and safety. Response evaluations were performed every 6 weeks using RECIST criteria.

Results:
The median overall survival in the AZD-3 plus chemotherapy group was 16.8 months, compared to 12.2 months in the placebo plus chemotherapy group (HR=0.65, $p<0.01$), representing a statistically significant improvement. The addition of AZD-3 to chemotherapy also resulted in a median progression-free survival of 8.4 months versus 5.2 months in the control group (HR=0.58, $p<0.01$).

The objective response rate was 42% in the AZD-3 group versus 28% in the placebo group, while the disease control rate was 86% and 64%, respectively.

Safety Profile:
AZD-3 in combination with chemotherapy was generally well tolerated, with manageable adverse events. The most common grade 3 or higher adverse events in the AZD-3 group were neutropenia (41%), nausea (29%), and fatigue (24%). These events were similar to those observed with chemotherapy alone.

Serious adverse events were balanced between the two groups, and no new safety signals were identified with the addition of AZD-3. One patient in the AZD-3 group experienced a treatment-related serious adverse event of pneumonitis that resolved with medical intervention.

Discussion:
The phase 3 trial results demonstrate a significant improvement in overall survival and progression-free survival with the addition of AZD-3 to standard chemotherapy for advanced NSCLC. The encouraging efficacy data, along with a manageable safety profile, support the potential of AZD-3 as a novel therapeutic option for this indication.

The response rates and disease control rates also favor the combination therapy, suggesting AZD-3's ability to enhance the effectiveness of chemotherapy.

Conclusion:
AZD-3, when combined with pemetrexed and cisplatin, significantly improves survival and disease control in advanced NSCLC patients. The drug's safety profile is acceptable, and its efficacy justifies its potential as a valuable addition to the current standard of care. Further studies to explore the use of AZD-3 in combination therapies and its impact on health-related quality of life are warranted.

Clinical Trial Registration: NCT03835384