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**Trial in progress: REFINE-Lung is a multicentre phase III study to determine the optimal frequency of pembrolizumab in non-small cell lung cancer utilising a novel multi-arm design**

**Background:** Standard regimens for anti-PD1 agents nivo and pembro may result in overtreatment. These agents have high target affinity, saturate PD1 at low concentrations, occupy PD1 long after discontinuation and have a flat dose-response relationship across a wide range tested. Lower doses or longer administration frequency may retain efficacy. New approaches to optimise treatment regimens are required to enhance cost-effectiveness, pt quality of life and toxicity. However, conventional 2-arm non-inferiority designs are inefficient for this. We present a new multi-arm trial design to tackle the problem, implemented in the UK multicentre phase III REFINE-Lung study that aims to determine the optimal treatment frequency of pembro in NSCLC. Pts progression free after 6 months of standard therapy are randomised to 5 pembro frequency reduced arms (q6w , q9w, q12w, q15w and q18w). By evaluating the frequency-response relationship, the longest frequency that is equivalent to standard of care within a pre-defined margin will be determined.

**Methods:** The REFINE-Lung trial (NCT05085028) is a multicentre, randomised open-label, phase III trial in advanced NSCLC, utilising a novel Multi-Arm Multi-Stage Response Over Continuous Interventions (MAMS-ROCI) design. 1750 pts aged ≥18 and progression free at six months of 1st line pembro and planning to continue, will be enrolled from up to UK 35 hospital groups. Pts will be randomised equally to 5 dose frequency arms, starting with q6w (control) vs. q12w arms for an interim analysis of safety. If q12w PFS is not significantly reduced, remaining q9w, q15w and q18w arms will be opened. Pts who progress may re-escalate to q6w therapy. Primary objective is to determine the optimal dose frequency of pembro, defined as the longest dose interval non-inferior to standard therapy using 2-year survival as the primary outcome. Secondary endpoints include OS, PFS, toxicity, quality of life and cost effectiveness. An exploratory sub-study will explore fundamental aspects of cancer immunotherapy and develop novel biomarkers of response, resistance and toxicity. The trial is currently open at 26 centres.