P255 RATE OF LUNG FUNCTION DECLINE IN PATIENTS WITH CYSTIC FIBROSIS (CF) HAVING A RESIDUAL FUNCTION GENE MUTATION

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Objective Patients with cystic fibrosis (CF) and mutations associated with residual CFTR chloride transport have improved survival rates compared with those homozygous for the *F508del*-CFTR mutation. Since little is known about rate of lung function decline in patients with CF and residual function (RF) mutations, we evaluated differences in rates of percent predicted FEV₁ (ppFEV₁) decline between patients with an RF mutation who were heterozygous for *F508del* and those who were homozygous for *F508del*, and whether rates of ppFEV₁ decline differed across age groups.

Methods Patients in the US CF Foundation Patient Registry from 2006 to 2014 with an RF mutation heterozygous for *F508del* were compared with *F508del*-homozygous patients. Mutations were identified based on clinical or *in vitro* evidence of residual ion transport. Annual rates of ppFEV₁ decline were estimated for patients 6 to 45 years of age with ≥ 3 ppFEV₁ values spanning ≥ 0.5 years in a randomly chosen 2 year period that began at the first ppFEV₁ measurement in the calendar year.

Results A total of 1242 RF and 11,916 *F508del*-homozygous patients were included. At the first visit, the RF cohort was older (mean [SD], 23.0 [12.1] vs 18.0 [9.6] years) and had better nutritional status (mean [SD] BMI z score, 0.36 [1.09] vs -0.29 [1.08]). Mean (SD) ppFEV₁ differed at the first visit between cohorts (80.4 [24.8] vs 73.4 [26.5]; $p < 0.001$). Annual rate of ppFEV₁ decline was estimated at -0.70 (SE, 0.20) in the RF cohort compared with -1.91 (0.05) in the *F508del*-homozygous cohort ($p < 0.001$). After excluding patients with *R117H* ($n = 889$), the rate of decline was -1.05 (0.39) ppFEV₁ per year ($p < 0.001$ vs *F508del*). The rate of decline for RF patients was most rapid in the 18 to 24-year age group, -1.38 (0.39), but was

still significantly less than the -2.52 (0.09) for *F508del*-homozygous young adults ($p = 0.004$).

Conclusion Patients with CF and an RF mutation have lower rates of lung function decline compared with *F508del*-homozygous patients. However, patients with an RF mutation still demonstrate progressive lung disease, particularly during young adulthood.

Please refer to page A259 for declarations of interest in relation to abstract P255.

Lung cancer: from virtual contact to invasive procedures

P256 TARGETED STEM CELLS EXPRESSING TRAIL AS A THERAPY FOR LUNG CANCER TACTICAL: A PHASE I/II TRIAL

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Introduction Lung cancer is the leading cause of cancer death worldwide with over 70% presenting with incurable disease and few effective treatments. We previously demonstrated that mesenchymal stem cells (MSCs) transduced to express TNF-related apoptosis inducing ligand (TRAIL), will home to and induce apoptosis of tumour cells *in vitro* and reduce tumour growth in multiple *in vivo* models. We are now undertaking a clinical trial to assess the therapeutic efficacy of this genetically modified cell therapy.

Aim To evaluate the safety and anti-tumour activity of MSC-TRAIL in combination with chemotherapy in patients with metastatic lung adenocarcinoma.

Manufacturing Methods MSCs were isolated from unrelated umbilical cord donors and characterised as MSCs according to international criteria. Cells from individual donors were thawed and transduced with a lentiviral vector encoding for

Abstract P256 Figure 1A Phase I Schema.