ELCC 2016  
13–16 April 2016, Geneva, Switzerland

Authors:  
Tony Mok, 1 Peter Schmid, 2 Osvaldo Arén Frontera, 3 Oscar Arrieta, 4 Maya Gottfried, 5 Abdul Rahman Jazieh, 6 Rodryg Ramlau, 7 Constanta Timcheva, 8 Claudio Martin, 9 Stuart McIntosh10

Affiliations:  
1The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong; 2Centre for Experimental Cancer Medicine, Barts Cancer Institute - a Cancer Research UK Centre of Excellence, Queen Mary University of London, London, UK; 3CIEC - Centro Internacional de Estudios Clínicos, Santiago, Chile, South America; 4Instituto Nacional de Cancerología (INCan), Mexico City, Mexico; 5Meir Medical Center, Kfar Saba, Israel; 6King Saud University for Health Sciences National Guards health Affairs, Riyadh, Saudi Arabia; 7Poznan University of Medical Sciences, Poland; 8MHAT for Women’s Health, Nadezhda, Sofia, Bulgaria; 9Instituto Alexander Fleming, Buenos Aires, Argentina; 10AstraZeneca, Alderley Park, Macclesfield, UK

Title  
NEPTUNE: a global, Phase 3 study of durvalumab (MEDI4736) plus tremelimumab combination therapy versus standard of care (SoC) platinum-based chemotherapy in the first-line treatment of patients (pts) with advanced or metastatic NSCLC

Background  
Current first-line therapy for advanced NSCLC is associated with poor survival and there remains a significant need for new, more effective treatments in this population. The blockade of immune checkpoints, such as programmed cell death-1 (PD-1) and cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4), is a promising novel approach in cancer treatment. Based on preclinical data, targeting both checkpoints provides for non-redundant pathway blockade and potential synergy. Durvalumab (MEDI4736) is a selective, high affinity human IgG1 mAb that blocks programmed cell death ligand-1 (PD-L1) binding to PD-1 (IC50 0.1 nM) and CD80 (IC50 0.04 nM). Tremelimumab is a selective human IgG2 mAb inhibitor of CTLA-4. In a Phase 1b study (NCT02000947), durvalumab + tremelimumab has shown encouraging clinical activity (objective response rate [ORR] 28% [95% CI 15–45%] across tremelimumab 1 mg/kg cohorts [n=39]) and manageable tolerability in pts with NSCLC regardless of PD-L1 status.

Trial design  
NEPTUNE (NCT02542293) is a randomised, open-label, multicentre, global, Phase 3 study. Approximately 800 immunotherapy- and chemotherapy-naïve pts with advanced or metastatic (Stage IV) EGFR and ALK wild-type NSCLC (with either PD-L1+ or PD-L1– tumours) will be randomised (1:1) to receive durvalumab (20 mg/kg i.v. every 4 weeks for up to 12 months) + tremelimumab (1 mg/kg i.v. every 4 weeks for up to 4 doses); or SoC platinum-based doublet chemotherapy. Stratification factors are PD-L1 status, histology and smoking history. The primary endpoint is overall survival (OS). Secondary endpoints will assess progression-free survival (PFS), ORR, duration of response, and proportion of pts alive and progression free at 12 months using investigator assessments (RECIST v1.1); time from randomisation to second progression; OS, PFS, and ORR in pts with PD-L1+ NSCLC; safety (CTCAE v4.03) and tolerability; pharmacokinetics; and immunogenicity. Exploratory outcomes include potential biomarkers of response to treatment, and the impact of subsequent anticancer therapies on OS. Recruitment is ongoing.