ASTRAZENECA'S COMBINATION OF DURVALUMAB WITH TREMELIMUMAB SHOWS CLINICAL ACTIVITY IN NON-SMALL CELL LUNG CANCER IRRESPECTIVE OF PD-L1 STATUS

Lancet Oncology reports Phase Ib study (study 006) of combined PD-L1 and CTLA-4 checkpoint inhibitors in locally advanced or metastatic NSCLC

Early results support AstraZeneca's combination strategy in immuno-oncology with potential combination efficacy for patients with PD-L1 negative NSCLC

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LONDON--(BUSINESS WIRE)--AstraZeneca and MedImmune, its global biologics research and development arm, today announced publication in The Lancet Oncology of a Phase Ib study (study 006), showing antitumour activity of combination treatment with durvalumab and tremelimumab, in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC), irrespective of PD-L1 status.1

In a cohort of 26 patients treated with durvalumab 10-20 mg/kg plus tremelimumab 1 mg/kg, and followed for ≥24 weeks, the confirmed objective response rate (ORR) was 23% (95% confidence interval 9-44%).1 Comparable ORRs were seen in patients from this cohort with PD-L1 positive and negative tumours (22% and 29% respectively). Durvalumab was administered intravenously every four weeks (q4w) for 13 doses or every 2 weeks (q2w) for 26 doses, and tremelimumab was administered q4w for six doses followed by every 12 weeks (q12w) for three doses.

Data on all 56 patients treated with durvalumab 10-20 mg/kg q2w or q4w plus tremelimumab 1 mg/kg showed a manageable safety profile for an advanced NSCLC population. Thirty per cent of patients had ≥1 related Grade 3/4 adverse events (AE) and 16% discontinued treatment due to a related adverse event.

Dr Scott J. Antonia, Chair of the Department of Thoracic Oncology at Moffitt Cancer Center, Tampa, Florida, USA, said: "Combination therapy with durvalumab and tremelimumab demonstrated antitumour activity in patients with NSCLC regardless of PD-L1 status, including in patients with no evidence of tumour cell membrane PD-L1 staining. The results suggest that this combination has potential as a treatment option for patients with PD-L1 negative tumours whose needs are not addressed by currently available therapies, including immunotherapies."

With the recent introduction of checkpoint inhibitors, the presence of PD-L1 expression in a tumour is considered a significant biomarker for response to PD-L1 blockade.2 Less than half of patients with NSCLC have tumours that are PD-L1 positive,1 leaving a significant unmet medical need in the PD-L1 negative patient population.

Dr Ed Bradley, Senior Vice President, Oncology, MedImmune, said: "The newly published data are an important milestone in our scientific understanding of the patient population likely to achieve the greatest benefit from the combination of durvalumab and tremelimumab. The latest findings reinforce our belief that the combination strategy we are pursuing is key to the future success of immuno-oncology treatment."

Durvalumab is an investigational human monoclonal antibody directed against programmed death ligand-1 (PD-L1), which blocks the interactions between PD-L1 and both PD-1 and B7.1, reversing in some tumours the ability of tumour cells to avoid detection by the immune system.3 Tremelimumab inhibits the activity of cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) to boost the immune response against cancer cells.4 Preclinical data suggested that targeting both PD-L1 and CTLA-4 may have additive or synergistic effects.5

A preliminary analysis of data from Study 006 was presented at the annual meeting of the Society for Immunotherapy in Cancer (SITC), in November 2015. The Lancet Oncology publication provides a more detailed analysis with a longer follow up period and more mature data set of confirmed responses, with a

focus on those which informed the selection of durvalumab 20 mg/kg plus tremelimumab 1 mg/kg, every four weeks, for ongoing Phase III trials.1

Durvalumab and tremelimumab are pipeline products under development and, as such, are not approved by the US Food and Drug Administration, European Medicines Agency or any other regulatory agency for the uses under investigation. Information regarding these investigational products should under no circumstances be regarded as a recommendation for their use or of their safety or efficacy.

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NOTES TO EDITORS

About durvalumab (MEDI4736)

Durvalumab is an investigational human monoclonal antibody directed against programmed death ligand-1 (PD-L1). Signals from PD-L1 help tumours avoid detection by the immune system.2 Durvalumab blocks these signals, countering the tumour's immune-evading tactics.3 Durvalumab is being investigated in an extensive clinical trial programme.

About tremelimumab

Tremelimumab is a fully human anti-CTLA-4 antibody. By blocking the activity of CTLA-4, tremelimumab "releases the brakes" on T cell activation and boosts the immune response against cancer cells.4,6 In animal models, CTLA-4 blockade by anti-CTLA-4 antibodies such as tremelimumab, has been shown to promote antitumour immune responses.4 In 2015, tremelimumab was granted Orphan Drug Designation by the US Food and Drug Administration as a potential treatment for malignant mesothelioma.

About AstraZeneca in Oncology

Oncology is a therapy area in which AstraZeneca has deep-rooted heritage. It will be potentially transformational for the company's future, becoming the sixth growth platform. Our vision is to help patients by redefining the cancer treatment paradigm and one day eliminate cancer as a cause of death. By 2020, we are aiming to bring at least six new cancer medicines to patients.

Our broad pipeline of next-generation medicines is focused on four main disease areas – lung, ovarian, breast and haematological cancers. These are being targeted through four key platforms – immuno-oncology, the genetic drivers of cancer and resistance, DNA damage repair and antibody drug conjugates – with a strong focus on combinations.

About AstraZeneca

AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of cardiovascular, metabolic, respiratory, inflammation, autoimmune, oncology, infection and neuroscience diseases. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit www.astrazeneca.com.

About MedImmune

MedImmune is the global biologics research and development arm of AstraZeneca, a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialization of small molecule and biologic prescription medicines. MedImmune is pioneering innovative research and exploring novel pathways across key therapeutic areas, including respiratory, inflammation and autoimmunity; cardiovascular and metabolic disease; oncology; neuroscience; and infection and vaccines. The MedImmune headquarters is located in Gaithersburg, Maryland, USA, one of AstraZeneca's three global R&D centers, with additional sites in Cambridge, UK and Mountain View, California, USA. For more information, please visit www.medimmune.com.

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