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Meeting Abstract

Final results of double-blind, placebo-controlled phase II study to assess the efficacy of MAGE-A3 immunotherapeutic in stage IB/II non-small cell lung cancer (NSCLC)

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Abstract

Background: After complete resection, about 50% of patients with stages IB-II NSCLC disease die within 5 years. Adjuvant chemotherapy improves overall survival at the expense of substantial toxicity. Activity of MAGE-A3 immunotherapeutic (i.e. recombinant MAGE-A3 protein and a potent GlaxoSmithKline immunological adjuvant) was previously demonstrated in metastatic melanoma. As about 35% of NSCLCs express MAGE-A3 antigen, post-operative MAGE-treatment may be a tumor-specific, well tolerated, and effective adjuvant therapy.

Methods: Patients with completely resected, MAGE-A3 (+), stage pIB or pII were randomly assigned to postoperative MAGE-A3 or placebo (2:1), with 5 administrations at 3-week intervals, followed by 8 administrations every 3 months. Randomization was stratified for stage (IB vs. II), histology (squamous vs. other), and lymph-node (LN) procedure (sampling vs. dissection). Primary endpoint was disease-free interval (DFI); other endpoints were safety, disease-free survival (DFS), and overall survival (OS). This exploratory Phase II study was designed to detect a clinically relevant HR with a 10% one-sided α.

Results: 182 patients (122 stage IB, 60 stage II) from 59 centers in 14 countries were randomized over 2 years: Median age 63 (45-81); 87% male; 65% squamous cell carcinoma; 65% lymph-node dissection. After a median follow-up of 28 months, 67 recurrences and 45 deaths were recorded. Group comparisons of DFI, DFS and OS gave respectively a hazard ratio (HR) of 0.74 (95% CI 0.44-1.20, $P = 0.107$), 0.73 (95% CI 0.45-1.16) and 0.66 (95% CI 0.36-1.20) in favor of the MAGE-A3 group. Overall, treatment was well tolerated, with excellent protocol compliance. Subset analysis also suggests that LN dissection may have an effect on survival.

Conclusions: The final analysis of this randomized Phase II study shows a positive trend for activity of MAGE-A3 treatment in NSCLC with a relative improvement of DFI and DFS of 27%. Further Phase III evaluation is planned. This study also suggests that complete lymph-node dissection may have an effect on survival and should be confirmed prospectively.

GSK is now recruiting for a Phase III trial evaluating MAGE-A3 ASCI as adjuvant therapy in MAGE-A3 positive patients with NSCLC. With a target of about 2,270 patients, the randomized, double-blind, and placebo-controlled MAGRIT trial (MAGE-A3 as Adjuvant Non-Small Cell Lung Cancer Immunotherapy) will enroll patients with stage IB, II or IIIA resectable NSCLC. The ASCI administration will be initiated in two groups of patients: after surgery and standard chemotherapy in one group of patients and after surgery in patients who are not eligible for receiving chemotherapy. The primary endpoint of the trial is disease-free survival.