Phase 3 study of durvalumab with SBRT for unresected stage I/II, lymph-node negative NSCLC (PACIFIC-4/RTGO 3515)

Clifford Robinson, Ligang Xin, Hiroshi Tanaka, Satadomo Takaoka, Shihan N. Badiyan, Hailam Nasrallah, Titthi Biswas, Mikhail Shvetsbald, Wolfgang Schuette, Anhu Sh, Adriana Hepner, Karen Barrett, James R. Riggs, Haji Jiang, Steven H. Lin

Department of Radiation Oncology, Division of Radiation, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
Department of Radiation Oncology, Division of Radiation Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Poster 1221P

Background

• The current SoC for patients with unresectable stage I/II (T1–T3, N0, M0; per AJCC v8) NSCLC is SBRT, which is well tolerated typically with 1–2% of grade 3+ toxicities. However, prolongation of overall survival observed in randomized trials has been limited.

• However, around 35% of all patients with stage I/II NSCLC have a risk of developing future lung cancer, according to the NCCN guidelines.

• The current SoC for patients with stage I/II NSCLC who are at risk of future lung cancer is SBRT, which is well tolerated typically with 1–2% of grade 3+ toxicities. However, prolongation of overall survival observed in randomized trials has been limited.

• Despite the risk of relapse in these patients and high recurrence rates, there is no current SoC adjunct therapy.

• Furthermore, the evidence is mixed on the benefit of adjuvant chemotherapy for patients with stage I/II NSCLC. (T1–T3, N0, M0)

• Durvalumab (PD-L1 Ab) is approved as consolidation therapy for patients with unresectable Stage III NSCLC, who have not progressed following chemotherapy.

• Durvalumab (PD-L1 Ab) is approved in the adjuvant setting post-surgery with patients with NSCLC, who have not been investigated for stage I/II NSCLC.

• Thus, there is an urgent need for effective and curative targeted systemic therapies capable to break recurrence rates and improve survival among patients, especially for stage I/II NSCLC, where current SBRT alone may be insufficient.

Immune checkpoint inhibition in early-stage NSCLC: durvalumab

- Durvalumab is a first-in-class, human IgG1 fusion protein that inhibits the PD-1 pathway.

- Based on the findings of the PACIFIC trial, there is a strong rationale for further investigation of durvalumab in Malignancies treated with curative intent and no known active disease/active treatment required in the past 3 years.

- Osimertinib (EGFR-TKI) is approved in the adjuvant setting post-surgery for patients with EGFRm NSCLC, but has not been investigated for stage I/II NSCLC.

- The current SoC for patients with unresectable, stage I/II, lymph-node negative NSCLC is SBRT, which is well tolerated typically with 1–2% of grade 3+ toxicities. However, prolongation of overall survival observed in randomized trials has been limited.

- The current SoC for patients with stage I/II NSCLC who are at risk of future lung cancer is SBRT, which is well tolerated typically with 1–2% of grade 3+ toxicities. However, prolongation of overall survival observed in randomized trials has been limited.

- Despite the risk of relapse in these patients and high recurrence rates, there is no current SoC adjunct therapy.

- Furthermore, the evidence is mixed on the benefit of adjuvant chemotherapy for patients with stage I/II NSCLC. (T1–T3, N0, M0)

- Durvalumab (PD-L1 Ab) is approved as consolidation therapy for patients with unresectable Stage III NSCLC, who have not progressed following chemotherapy.

- Durvalumab (PD-L1 Ab) is approved in the adjuvant setting post-surgery with patients with NSCLC, who have not been investigated for stage I/II NSCLC.

- Thus, there is an urgent need for effective and curative targeted systemic therapies capable to break recurrence rates and improve survival among patients, especially for stage I/II NSCLC, where current SBRT alone may be insufficient.

Study objective

- Based on data in other lung cancer settings in the early-stage NSCLC setting, PACIFIC-4 (NCT03833154) is designed to assess benefit and safety of SBRT.

- Durvalumab combined with SBRT versus placebo with SBRT in patients with stage I/II NSCLC.

- Osimertinib cohort only: 4-year PFS rate (ICR per RECIST v1.1)

- Immunogenicity of durvalumab

- Health-related quality of life (EORTC QLQ-C30)

- Sites of progression

- Osimertinib (EGFR-TKI) is approved in the adjuvant setting post-surgery for patients with EGFRm NSCLC, but has not been investigated for stage I/II NSCLC.

- In the placebo-controlled Phase 3 ADAURA trial of patients with resected stage IB–IIIA EGFRm NSCLC, osimertinib demonstrated improvement in overall survival in patients who were not treated with adjuvant chemotherapy.

- Based on the placebo-controlled, Phase 3 PACIFIC trial of patients with unresectable, stage III NSCLC without disease progression, durvalumab demonstrated improvement in overall survival in patients who were not treated with adjuvant chemotherapy.

- The ADAURA trial led to the approval of osimertinib as adjuvant therapy after primary surgery for adults with NSCLC whose tumors harbor a sensitive EGFR mutation.

- This update protocol is adapted to open in mainland China by end of June 2021.

Key Inclusion Criteria

- Aged ≥18 years and body weight >30 kg.

- Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.

- Osimertinib cohort: 4-year PFS rate (ICR per RECIST v1.1)

- Immunogenicity of durvalumab

- Health-related quality of life (EORTC QLQ-C30)

- Sites of progression

- Osimertinib (EGFR-TKI) is approved in the adjuvant setting post-surgery for patients with EGFRm NSCLC, but has not been investigated for stage I/II NSCLC.

- In the placebo-controlled Phase 3 ADAURA trial of patients with resected stage IB–IIIA EGFRm NSCLC, osimertinib demonstrated improvement in overall survival in patients who were not treated with adjuvant chemotherapy.

- Based on the placebo-controlled, Phase 3 PACIFIC trial of patients with unresectable, stage III NSCLC without disease progression, durvalumab demonstrated improvement in overall survival in patients who were not treated with adjuvant chemotherapy.

- The ADAURA trial led to the approval of osimertinib as adjuvant therapy after primary surgery for adults with NSCLC whose tumors harbor a sensitive EGFR mutation.

- This update protocol is adapted to open in mainland China by end of June 2021.