**Afatinib**

**Head and neck squamous cell carcinoma**

Patients with recurrent and/or metastatic (R/M) HNSCC who progressed after first-line platinum-based chemotherapy in Asia, Middle East and North Africa: LUX-Head & Neck 3

**Phase III study of afatinib versus methotrexate for second-line recurrent and/or metastatic head and neck squamous cell carcinoma patients after platinum-based chemotherapy in Asia, Middle East and North Africa: LUX-Head & Neck 3**

**Introduction**

**Head and neck squamous cell carcinoma**

- Head and neck squamous cell carcinoma (HNSCC) is the seventh most common cancer worldwide, with an estimated annual incidence of more than 650,000 cases

- Current second-line treatment options include chemotherapeutic agents, such as methotrexate and taxanes, and the EGFR-targeted monoclonal antibody cetuximab, despite the lack of randomized trials demonstrating its superiority in terms of efficacy and tolerability compared with standard care for patients with R/M HNSCC.

- EGFR signaling is associated with increased cell survival, proliferation and invasion through the activation of downstream signaling pathways (the ErbB family).

- The ErbB family includes, among others, EGFR, ErbB2, ErbB3, and ErbB4, and the cross-talk between these receptors is thought to play a crucial role in tumorigenesis.

- Afatinib is a irreversible pan-ErbB inhibitor and shows higher inhibitory activity against EGFR and HER4 (ErbB4) than earlier-generation EGFR inhibitors.

**Patient eligibility**

**Inclusion criteria**

- Age ≥ 18 years

- ECOG PS (0 or 1)

- Histologically confirmed R/M HNSCC of the oral cavity, oropharynx, hypopharynx or larynx

- Prior chemotherapy with one previous platinum-based systemic regimen

- No prior EGFR-targeted antibody therapy

- Eastern Cooperative Oncology Group performance status ≤ 2

- Adequate organ function

- Written or oral informed consent

**Exclusion criteria**

- ≥ 3 prior regimens (≥ 2 platinum compounds)

- Localized disease

- Locoregionally advanced or metastatic HNSCC in the R/M setting

- Prior EGFR-targeted antibody therapy

- Prior EGFR-blocking tyrosine kinase inhibitor

- Other prior EGFR inhibitors

- Prior EGFR monoclonal antibody therapy

- Prior EGFR-targeted chemotherapy

- Prior EGFR-directed antibodies

- Prior radiation therapy

- Other active or prior malignancy

**Endpoints and assessments**

**Primary endpoint**

- PFS (progression-free survival) in the R/M setting (Head & Neck)

**Secondary endpoints**

- OS (overall survival)

- Objective response rate

- Duration of response

- Disease control rate

- Safety

**Biomarker analysis**

- The estimated date for final data collection for the primary endpoint is February 2017

**Afatinib vs methotrexate in the same treatment setting as LUX-Head & Neck 1, in Asia, Middle East, and North Africa**

**Trial objective**

**In a global, Phase III trial (LUX-Head & Neck 1) in patients with second-line R/M HNSCC, afatinib significantly improved progression-free survival over methotrexate (median 2.6 vs 1.7 months; hazard ratio=0.80; p=0.030).**

**Randomized 2:1**

**Stratified**

**Participants with R/M HNSCC progressing on or after first-line platinum-based chemotherapy**

**Treatment will continue until progressive disease (PD) or intolerable adverse events (AEs)**

**Afatinib**

- 40 mg/day orally

**Methotrexate**

- 40 mg/day orally

**CROSSTALK (US 1)**

**Pharmacokinetics of afatinib (pre- and post-dose plasma concentrations)**

**ORAL CAVITY**

- EGFR/ERBB1

- HER2/ERBB2

- HER3/ERBB3

- HER4/ERBB4

**References**


11. Alaa Kandil,12 Ezra Cohen,13 Guo-qiang Hu,14 Yuan Geng,14 Eva Ehrnrooth,15 Ye Guo16


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