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1079P Long-term response to second-line afatinib in patients with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC): Analysis of the LUX-Head & Neck 1 (LHN1) trial

J-P. Machiels[1], G. de Castro Jr[2], L. de Souza Viana[3], R. Galiulin[4], M. Tahara[5], U.R. Nicolau[6], C. Le Tourneau[7], K. Okami[8], V. Vladimirov[9], A. Izmailov[10], K. Hoermann[11], L. Licitra[12], R. Haddad[13], E. Cohen[14], N. Dupuis[15], J. Love[16], E. Zografos[17], E. Ehrnrooth[18], J. Fayette[19]

[1]*Institut Roi Albert II, Service d'Oncologie Médicale, Cliniques Universitaires Saint-Luc and Institut de Recherche Clinique et Expérimentale (Pole MIRO), Université Catholique de Louvain, Brussels, Belgium,* [2]*Department of Clinical Oncology, Instituto do Câncer do Estado, São Paulo, Brazil,* [3]*Department of Medical Oncology, Hospital de Câncer de Barretos, São Paulo, Brazil,* [4]*Chemotherapy Department, Omsk Regional Oncology Center, Omsk, Russian Federation,* [5]*Division of Head and Neck Medical Oncology, National Cancer Center Hospital East, Kashiwa, Japan,* [6]*Departamento de Oncologia, Hospital A.C. Camargo, São Paulo, Brazil,* [7]*Department of Medical Oncology, Institut Curie, Paris, France,* [8]*Department of Otolaryngology, Tokai University, Isehara, Japan,* [9]*Policlinic, Pyatigorsk Oncological Dispensary, Pyatigorsk, Russian Federation,* [10]*Department of Oncology, Bashkirin State Medical University, Ufa, Russian Federation,* [11]*Department of Otolaryngology, Head and Neck Surgery, University Hospital Mannheim, Mannheim, Germany,* [12]*Fondazione IRCCS Istituto Nazionale Tumori, Milan, IT, and University of Milan, Milan, Italy,* [13]*Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School and Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA,* [14]*San Diego Moores Cancer Center, University of California, La Jolla, CA, USA,* [15]*Development, Biodesix Inc., Boulder, CO, USA,* [16]*Oncology Statistics, Boehringer Ingelheim Corporation, Ridgefield, CT, USA,* [17]*Boehringer Ingelheim, Bracknell, UK,* [18]*TA Oncology, Boehringer Ingelheim, Danmark A/S, Copenhagen, Denmark,* [19]*Léon Bérard Center and Hospices Civils de Lyon, University of Lyon, Lyon, France*

Background: In the Phase III LHN1 trial, second-line afatinib (A) significantly improved PFS (primary endpoint) vs methotrexate (MTX) in pts with R/M HNSCC. Tumour biomarker analyses have shown that survival benefit with A vs MTX was more pronounced in pts with p16/ErbB3-negative, EGFR-amplified, PTEN-positive disease. We present post-hoc analyses of A long-term responders (LTRs).

Methods: Pts with incurable R/M HNSCC who had received first-line platinum-based therapy were randomised to A (40mg/day) or MTX (40mg/m^2/week) and treated until progression/intolerable AE. LTRs were defined as pts treated with A $\geq$ 12 mos. Tumour biomarkers were assessed by IHC (p16, ErbB3, PTEN, cMET) and FISH (EGFR amplification); pre-treatment (tx) serum samples were analysed with the VeriStrat® (VS) test and classified as VS-Good/Poor.

Results: 11/322 (3%) pts treated with A were LTRs with a median (range) tx-duration of 16 (12−39) mos. All pts had stopped tx at analysis. Baseline characteristics in LTRs were similar to the overall dataset, except (LTRs/overall): oral cavity primary tumour site (45%/29%); M1 disease (45%/66%); previous therapy with EGFR-antibodies (18%/59%). Median OS was 18.1 mos; median PFS (central independent review) was 14.9 mos. ORR was 45% (CR: 18%; n = 2). The frequency of pts who received $\geq$1 subsequent therapy was similar to the overall dataset (LTRs, 45%; overall, 51%). In LTRs with available biomarker data, 3/3 (100%) pts were p16-negative, 4/4 (100%) pts were ErbB3-negative, 2/4 (50%) pts were PTEN-positive, 3/3 (100%) pts were cMET-positive, 2/3 (67%) pts had EGFR-amplification, and 5/5 (100%) pts were VS-Good. Tolerability-guided dose reductions were more frequent among LTRs (55% vs 32% overall).

Conclusions: In the LHN1 study, some platinum-pre-treated pts with R/M HNSCC derived a long-term survival benefit from A; median OS was ~1.5 yrs and >11 mos longer than in the overall dataset. Limited biomarker data available in these LTRs suggests that p16/ErbB3-negativity and EGFR-amplification might be potential predictive biomarkers for long-term benefit from A; however, results were not conclusive due to small sample size.

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