ESMO 2014 Congress Scientific Meeting Report – Head and Neck Cancer Extract

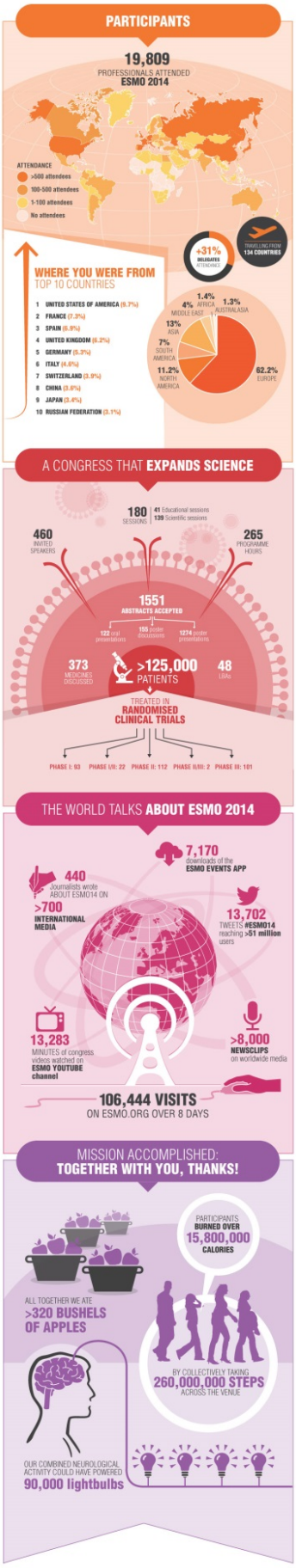
26-30 September 2014

Madrid, Spain

Summary

The European Society for Medical Oncology (ESMO) Congress, held September 26 to 30 in Madrid, Spain, was a record-breaker on nearly all levels. It was resounding success and in a dedicated infographic you can find the congress statistics. A primary emphasis in the scientific programme was placed on precision medicine and how it will change the future treatment landscape in oncology. In addition, a number of scientific presentations were dedicated to cancer immunology and immunotherapy across multiple tumour types. This report is an overview of key scientific presentations made during the congress by leading international investigators. It attempts to represent the diversity and depth of the ESMO 2014 scientific programme, as well as advances in oncology.

Infographic (right): ESMO 2014 record breaking Congress



Contents

Head and Neck Cancer

Afatinib vs. methotrexate in second-line treatment of recurrent and/or metastatic head and neck squamous cell carcinoma: Primary efficacy results of a phase III LUX-Head and Neck 1 trial

Primary efficacy data from the LUX-Head and Neck, phase III trial of second-line treatment with afatinib vs. methotrexate showed improvement in the study's primary endpoint PFS and delayed deterioration of patient-reported outcomes with a manageable safety profile in patients with head and neck squamous cell carcinoma (HNSCC) after failure of platinum-based therapy. The results were presented by Prof. Jean-Pascal Machiels of the Medical Oncology Department, Cliniques Universitaires St. Luc, Brussels, Belgium.

Patients with recurrent/metastatic HNSCC who progress after first-line platinum-based therapy have a dismal prognosis with median OS of approximately 3–6 months.

EGFR is overexpressed in approximately 90% of HNSCC and is associated with poor prognosis. Afatinib, an orally available, irreversible ErbB family blocker, showed promising anti-tumour activity in a phase II trial in patients with recurrent/metastatic HNSCC.

In this phase III trial, patients with recurrent/metastatic HNSCC after progression on/after platinum-based therapy were randomised 2:1 to oral treatment with afatinib (322 patients) or intravenous methorexate (161 patients). They were stratified by ECOG PS (0 vs. 1) and prior use of anti-EGFR antibody therapy in the recurrent/metastatic setting.

The primary endpoint was PFS; secondary endpoints included OS, ORR, patient reported outcomes and safety.

The study used RECIST v1.1 criteria and the primary analysis was based on independent radiology review. It was required 364 independent events to detect HR of 0.70 (increase in median PFS from 2.1 to 3.0 months) at 90% power with one-sided type-I error of α=0.025. For OS analysis it was required 343 deaths to detect HR of 0.73 (increase in median OS from 6.5 to 8.9 months) at 80% power with one-sided type-I error of α=0.025.

The study recruitment in 19 countries around the world started in January 2012 and finished in December 2013 with a median follow-up of 6.7 months. Patient characteristics were well balanced in both groups.

Afatinib improved at a statistically significant level the primary study endpoint of PFS (median 2.6 vs. 1.7 months; p = 0.03). The PFS was more favourable with afatinib in subgroup analysis as well. Howevver, afatinib did not improve OS in comparison with methorexate (median 6.8 vs. 6.0 months).

The DCR was higher with afatinib vs. methotrexate (49.1% vs. 38.5%; p=0.035); the ORR was 10.2% vs. 5.6% (p=0.10).

Tumour shrinkage from baseline was observed in 34.8% afatinib-treated patients compared with 22.4% of methotrexate-treated patients.

Assessed by EORTC questionnaire QLQ-C30 and Head and Neck cancer-specific module (QLQ-H&N35) for pain and swallowing, afatinib showed delay in deterioration of global health status, pain and swallowing (all p ≤ 0.03), and provided improvement in pain.

The most frequent grade 3/4 drug-related adverse events were rash/acne (9.7%) and diarrhoea (9.4%) with afatinib, and leukopaenia (15.6%) and stomatitis (8.1%) with methotrexate.

Prof. Machiels concluded that afatinib significantly improved PFS vs. methotrexate. Tumour shrinkage was greater, RR higher and DCR significantly higher compared to methotrexate. Patient-reported outcomes favoured afatinib over methotrexate. Fewer treatment-related dose reductions, discontinuations and fatal events were recorded with afatinib compared with methotrexate.

Afatinib is the first oral TKI to demonstrate efficacy and improved patient-reported outcomes in a phase III trial in this setting. Investigations with adjuvant afatinib in locally-advanced HNSCC following chemoradiotherapy are ongoing.

At the beginning of the session, the participants were alerted to the fact that the last approved therapy in Head & Neck cancer was cetixumab, 10 years ago, and that there is a desperate need for progress. Cetixumab is the only approved targeted therapy but there are no predictive biomarkers.

LUX-1 trial is the second positive study for recurrent/metastatic Head and Neck cancer since the EXTREME study. Afitinib was shown to be an active agent in this disease and the first oral targeted agent to show benefit, QoL and functional outcome improvements.

Discussing the study results, Dr Tanguy Seiwert of the University of Chicago, Chicago, USA, said that the difference of 0.9 months in PFS is of unclear clinical benefit and uncertain to lead to the drug approval. However, he suggested that there are two potential ways to lead to progress in this setting, one being more passive, waiting for the results of the LUX-2 study results and the second one, active search of predictive biomarkers to identify population with larger effect size.

The subgroup analysis showed that most benefit seemed to be found in the patients who did not receive prior EGFR therapies (suggesting a degree of cross-resistance) and in patients with p16 positive status (HPV negative disease) but this finding should be cautiously interpreted.

The study was sponsored by Boehringer Ingelheim.

Reference

LBA29_PR: Afatinib versus methotrexate (MTX) as second-line treatment for patients with recurrent and/or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC) who progressed after platinum-based therapy: primary efficacy results of LUX-Head & Neck 1, a phase III trial

Randomised phase II study of MEHD7945A vs. cetuximab in at least second-line recurrent/metastatic squamous cell carcinoma of the head and neck progressive on/after platinum-based chemotherapy

Dr Jérôme Fayette of the Léon Bérard Center, University of Lyon, Lyon, France reported that MEHD7945A did not improve outcomes of patients with recurrent/metastatic squamous cell carcinoma of the head and neck when compared with cetuximab.

MEHD7945A, a novel dual-action humanised IgG1 antibody that blocks ligand binding to EGFR and HER3, inhibits signalling from all ligand-dependent HER dimers, and can elicit antibody dependent cell mediated cytotoxicity. MEHD7945A is active in multiple tumour models, including

models resistant to anti-EGFR or anti-HER3 targeting. Preclinical and early clinical data suggest that high expression of neuregulin 1 (NRG1) in tumours may enhance sensitivity to MEHD7945A.

This multicenter, open-label, randomised phase II study evaluated efficacy in recurrent/metastatic squamous cell carcinoma of the head and neck patients progressive on/after platinum-based chemotherapy, and in those whose tumours express high NRG1. Primary endpoint was PFS according to RECIST v1.1, secondary endpoints were ORR, DoR, OS and safety according to CTCAE v4.0.

Patients received MEHD7945 or cetuximab until progression or intolerable toxicity. Upon central confirmation of progression on cetuximab, patients could crossover to MEHD7945A. Mandatory tumour samples were assayed for biomarkers related to mechanism of action and squamous cell carcinoma of the head and neck, including NRG1 expression and HPV status.

In total 121 patients were randomised, 59 in the MEHD7945A arm and 62 in the cetuximab arm. Median age was 62 years, all patients had ECOG PS 0-2. There no differences between the treatment arms; median PFS was 4.1 month in the MEHD7945A arm and 4.0 month in the cetuximab arm; median OS was 7.2 month in the MEHD7945A arm and 8.5 month in the cetuximab arm; ORR was 11.9% in the MEHD7945A arm and 14.5% in the cetuximab arm.

Grade ≥3 adverse events that were more frequent with MEHD7945A (61%) compared to cetuximab (51%) included infections (22.0% vs. 11.5%) and GI disorders (13.6% vs. 6.6%) contributing to higher rates of serious adverse events (40.7% vs. 29.5%); metabolic disorders were less experienced with MEHD7945A (10.2% vs. 14.8%). Any grade skin toxicity was lower with MEHD7945A (45.8% vs. 59.7%).

High NRG1 expression in tumour (primary biomarker hypothesis) did not enhance for MEHD7945 efficacy. Responses to both MEHD7945 and cetuximab associated with higher amphiregulin expression.

Dr Tanguy Seiwert of the University of Chicago, Chicago, USA, who discussed the study results, said that MEHD7945A showed comparable activity to cetuximab. Following the lead of afatinib further development is feasible, however it appears unclear at this point whether MEHD7945A is an improvement upon treatment with cetuximab. Further development in a biomarker defined population may be promising. In this study, outstanding biomarker work was done. HPV-positive tumours have less or no benefit from EGFR targeting agents. HER ligands amphiregulin/heregulin correlate (moderately) with benefit from EGFR/HER agents and can potentially be used for enrichment. Further validation is required, and we still need reliable assays. Prior studies that used p16 should be re-analysed for HPV. The p16 use in the setting of both de-escalation and EGFR targeting is not sufficiently accurate, and accurate HPV testing is necessary.

The study was sponsored by Genentech, Inc.

Reference

986O: Randomized phase II study of MEHD7945A (MEHD) vs cetuximab (Cet) in ≥ 2nd-line recurrent/metastatic squamous cell Carcinoma of the head & neck (RMSCCHN) progressive on/after platinum-based chemotherapy (PtCT)

A phase IB study of pembrolizumab in patients with human papillomavirus (HPV)-positive and -negative head and neck cancer

Dr Laura Chow of the Medical Oncology, University of Washington, Seattle, USA presented updated safety, tolerability, and antitumour activity of pembrolizumab for recurrent/metastatic head and neck cancer. Data from this cohort were previously reported at the ASCO 2014, but the data presented at ESMO 2014 are updated and expanded.

During screening, PD-L1 expression in archival or newly obtained tumour samples was assessed using a prototype IHC assay; PD-L1 expression in stroma or ≥1% of tumour cells was required for study entry.

Pembrolizumab was given every 2 weeks until CR, progression, unacceptable toxicity, physician decision, or consent withdrawal. Adverse events were recorded throughout the study. Response was assessed every 8 weeks. Primary endpoint was ORR per RECIST v1.1.

Out of 104 head and neck cancer patients screened, 81 (78%) were PD-L1-positive of which 61 enrolled, and 60 received ≥1 pembrolizumab dose: 23 HPV-positive, 37 HPV-negative. After a median follow-up of 10.2 months, 15 patients (25%) remain on pembrolizumab.

The ORR (confirmed and unconfirmed) per RECIST v1.1 by investigator review was 20%, and response duration ranged from 8+ to 41+ weeks (median not reached). Nine of 11 responders had a smaller target lesion burden at baseline. The ORR was similar in HPV-positive and HPV-negative patients, whereas PFS and OS were longer in HPV-positive patients. PD-L1 expression was positively correlated with ORR ($p = 0.018$) and PFS ($p = 0.024$). The ORR was 50% in the 12 patients with high PD-L1 expression.

Drug-related adverse events of any grade occurred in 58% of patients (grade ≥3 in 17%). The most common drug-related adverse events were fatigue (18%), pruritus (10%), and nausea (8%). There were no drug-related deaths.

The study researchers concluded that pembrolizumab is safe and tolerable and shows antitumour activity in both HPV-positive and HPV-negative advanced head and neck cancer. These findings support further development of pembrolizumab in advanced head and neck cancer.

The study was supported by Merck Sharp & Dohme Corp.

Reference

LBA31: A phase Ib study of pembrolizumab (Pembro; MK-3475) in patients (Pts) with human papiilloma virus (HPV)-positive and negative head and neck cancer (HNC)

RELATED INFORMATION

Click here to access the Conference abstracts.

Click here to access the meeting webcast page.

Save the date

European Cancer Congress 2015 (ECC 2015), Vienna, Austria, 25-29 September 2015.

Affiliations and Disclosure

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Disclosure

No conflicts of interest to disclose.

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