ESMO 2014 Congress Scientific Meeting Report – Neuroendocrine Cancers Extract

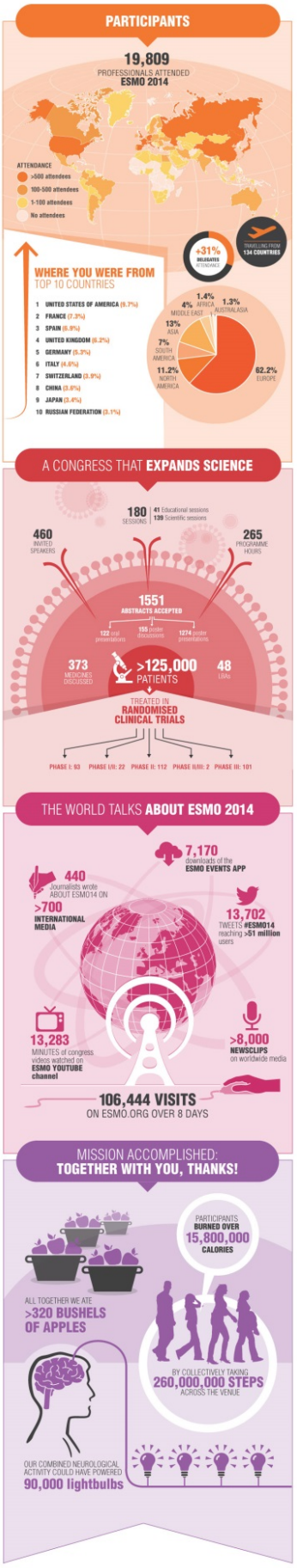
26-30 September 2014

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



Neuroendocrine Cancers

Everolimus for the treatment of advanced pNET: Final OS results of a randomised, double-blind, placebo-controlled, multicenter phase III trial

Prof. James Yao of the University of Texas MD Anderson Cancer Center, Houston, USA reported that everolimus demonstrated a median OS of 44 months, the longest OS reported for progressive advanced pancreatic neuroendocrine tumors (pNET) patients in a phase III study. A clinically important improvement of 6.3 months in median OS vs. placebo was observed in RADIANT-3 study, although the difference did not reach statistical significance. Crossover of majority of patients (85%) may also have confounded OS. The safety of everolimus was consistent with previous experience.

Everolimus significantly improved median PFS vs. placebo in patients with pNET by 6.4 months in RADIANT-3 study (11.0 vs. 4.6 months; HR 0.35, $p < 0.001$). At ESMO 2014, the study researchers presented final OS results and safety findings.

Patients with progressive advanced, low- or intermediate-grade pNET were randomised to everolimus (207 patients) or placebo (203 patients), both with best supportive care. Upon disease progression during double-blind phase, crossover from placebo to open-label everolimus was allowed. At the time of unblinding, all ongoing patients transitioned into the extension phase to receive open-label everolimus. After 256 events, OS analysis was performed in the ITT patient population (410, all randomised patients).

Of 410 patients, 225 switched to open-label everolimus; including 85% of patients initially randomised to placebo (172 of 203). Median open-label everolimus exposure was 67.1 weeks in patients initially randomised to everolimus and 44.0 weeks in patients randomised to placebo.

Median OS was 44.0 months for the everolimus arm and 37.7 months for the placebo arm (HR 0.94, log rank $p = 0.30$; significance boundary 0.0249). The overall survival HR adjusted for for pre-specified baseline covariates including age, gender, region, and prior somatostatin analogue use was 0.90.

With a high crossover rate of 85%, the conventional ITT analysis approach likely underestimated the treatment effect on OS. A rank preserving structural failure time model corrected for the effect of crossover by estimating the multiplicative factor effect of each day of everolimus treatment on OS and subsequently adjusting for effect of everolimus received after crossover in the placebo arm. The rank-preserving structural failure time analysis adjusting for crossover bias showed a survival benefit with everolimus. Estimated OS rates were 82.6% vs. 74.9% at 12 months and 67.7% vs. 55.6% at 24 months.

The safety profile of everolimus observed during open label extension was similar to the known safety profile of everolimus and similar to those observed during double blind phase. The most common adverse event was stomatitis or aphtous ulceration. It occurred among 54% of patients receiving everolimus during double blind phase vs. 13% of patients receiving placebo. This was similar at 47% during the open-label extension phase. The rate of grade 3/4 stomatitis was 4.9% during double blind phase and 2.2% in the open label extension phase. Of note, in a recent meta-analysis of phase III studies with everolimus that included RADIANT3, development of stomatitis

within 8 weeks of treatment start was associated with longer PFS compared those without stomatitis.

Dr Alexandria Phan of the Methodist Cancer Center and Weill Cornell Medical College, Houston, USA, who discussed the study results, said that crossover in randomised clinical trials leads to underestimation of true clinical gain in OS, if the experimental drug has benefit over placebo/control. Even the more complex methods such as rank-preserving structural failure time have important limitations, especially with inaccurate assumptions and increasing crossover percentage. Crossover of 85% of patients from the placebo arm to open-label everolimus likely confounded OS results. However, survival benefit with everolimus is 44 months, at least 6.3 months longer than placebo and at most 23.4 months longer than placebo.

The study was funded by Novartis Pharmaceuticals Corporation.

Reference

1132O: Everolimus (EVE) for the treatment of advanced pancreatic neuroendocrine tumors (pNET): Final overall survival (OS) results of a randomized, double-blind, placebo (PBO)-controlled, multicenter Phase III trial (RADIANT-3)

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

Affiliation

Dr Svetlana Jezdic, ESMO Head Office

Disclosure

No conflicts of interest to disclose.

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