ESMO 2014 Congress Scientific Meeting Report – Haematological Malignancies Extract

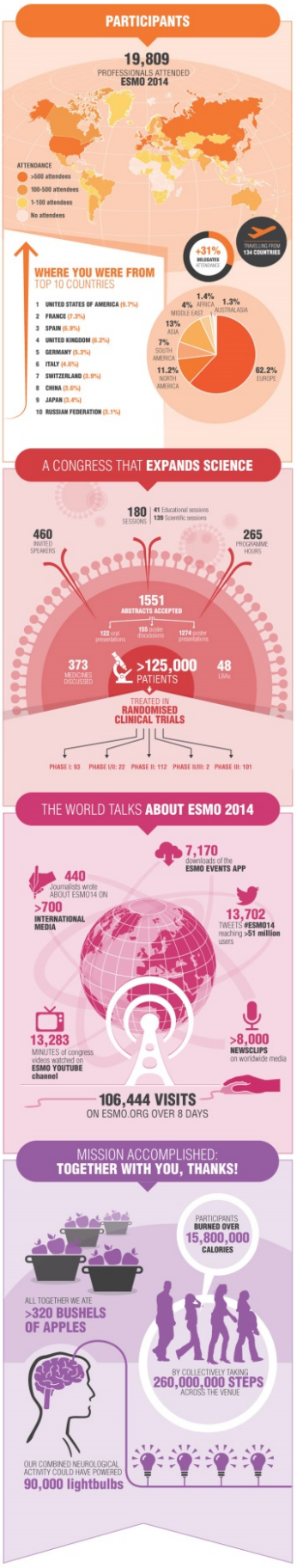
26-30 September 2014

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



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Haematological Malignancies

Brentuximab vedotin in combination with CHP in patients with newly-diagnosed CD30-positive peripheral T-cell lymphomas

Prof. Michelle Fanale of the University of Texas MD Anderson Cancer Center, Houston, USA reported that brentuximab vedotin in combination with CHP chemotherapy delivered durable remissions in newly-diagnosed patients with peripheral T-cell lymphomas, with a 2 year PFS rate of 54%.

Peripheral T-cell lymphomas comprise a subset of aggressive non-Hodgkin lymphomas. Outcomes of frontline treatment are poor, with CR rates of 39%–53% and 5 year OS rates of 12%–49%, depending on subtype.

Brentuximab vedotin has shown clinical activity in a phase I trial of treatment in sequence with CHOP or in combination with CHP in patients with newly-diagnosed peripheral T-cell lymphomas.

This phase I, open-label study conducted in USA and Europe, assessed the safety and efficacy of brentuximab vedotin administered sequentially with standard-dose CHOP or in combination with CHP for the frontline therapy of peripheral T-cell lymphomas. ALK-positive systemic anaplastic large cell lymphoma patients must have had IPI score ≥2. Combination therapy included a cohort to determine the recommended dose of brentuximab vedotin to be evaluated in an expansion cohort. Responders could receive single-agent brentuximab vedotin for up to 10 additional cycles. Updated PFS and OS data from combination therapy were presented.

The median age of patients was 56 years. Diagnoses included systemic anaplastic large cell lymphoma in 19 cases from whom 16 were ALK-negative, peripheral T-cell lymphoma in 2 cases, angioimmunoblastic T-cell lymphoma in 2 cases, adult T-cell leukaemia/lymphoma in 2 cases, and enteropathy-associated T-cell lymphoma in 1 case.

The maximum tolerated dose of brentuximab vedotin in combination with chemotherapy was not exceeded at 1.8 mg/kg i.v., based on 1 DLT (grade 3 rash). Six cycles of combination therapy were completed in 23 of 26 patients.

Treatment-emergent adverse events (≥40%) included peripheral sensory neuropathy, nausea, fatigue, alopecia, diarrhoea, and dyspnoea.

At the end of combination therapy, the ORR was 100% and CR rate was 88%. After a median observation time of 27.1 months, the 2 year PFS rate was 54%. Ten of 19 patients with anaplastic large cell lymphoma and 5 of 7 patients with other entities remain free of disease progression or death. The estimated median PFS was not reached. No patients went on to receive a consolidative stem cell transplant. The 2 year OS rate was 80%. Four patients received subsequent brentuximab vedotin treatment after progression. After progression, 3 patients received stem cell transplants (2 allogeneic, 1 autologous).

ECHELON-2, a phase III study comparing brentuximab vedotin plus CHP to CHOP regimen in the frontline therapy of peripheral T-cell lymphomas is underway.

Dr Enrico Derenzini of the Institute of Hematology and Medical Oncology L.A. Seragnoli, Bologna, Italy, who discussed the study results, said that the question addressed in the presentation was feasibility and activity of a combination strategy including brentuximab vedotin and chemotherapy

in newly diagnosed CD30-positive peripheral T-cell lymphoma, in particular an update focusing on combination arm. The combination of brentuximab vedotin and chemotherapy has manageable toxicity, increased peripheral neuropathy, mainly grade 2, and transient. Efficacy of the combination therapy is impressive with durable remissions seen in poor prognosis non-Hodgkin lymphoma subtype. However, the question is if standard CH(O)P represents the best partner for brentuximab vedotin.

The study was sponsored by Seattle Genetics.

Reference

944O: Brentuximab vedotin in combination with CHP in patients (Pts) with newly-diagnosed CD30+ peripheral T-cell lymphomas (PTCL): 2-year follow-up

Carfilzomib vs. low-dose corticosteroids and optional cyclophosphamide in patients with relapsed and refractory multiple myeloma

Prof. Heinz Ludwig of the Wilhelminenspital, Vienna, Austria reported results from a phase III FOCUS study in heavily pretreated patients with relapsed and refractory multiple myeloma. Median OS for single-agent carfilzomib was similar to the active control arm.

Carfilzomib is a second generation proteasome inhibitor. It irreversibly binds to the constitutive proteasome and the immunoproteasome. It is able to overcome bortezomib resistance and shows less off target activity than bortezomib.

The study aim was to compare carfilzomib with low-dose corticosteroids and optional cyclophosphamide. Patients were randomised 1:1. The primary endpoint was OS with 80% power to detect a HR of 0.7 (median OS assumptions were for the carfilzomib arm 8.6 months and 6 months in the control arm). Secondary endpoints included PFS, ORR and safety.

Between September 2010 and October 2012, 315 patients were randomised, 157 in the carfilzomib arm and 158 in the control group. Baseline characteristics were balanced between the groups. Median age was 65 years. Patients received 5 (median) prior regimens in each group; median time since diagnosis was 6.0 years in the carfilzomib group and 5.4 years in the control group.

Median treatment duration was 16.3 weeks in the carfilzomib group and 10.7 weeks in the control; 92% of patients in the control group received cyclophosphamide. Median relative dose intensity was 99.9% in each group. The study did not meet the primary endpoint for OS (HR 0.975; $p = 0.4172$). Median OS was 10.2 month in the carfilzomib group and 10.0 month in the control group. Median follow-up for OS was 27.8 month in the carfilzomib group and 29.8 month in the control group. Median PFS was 3.7 month in the carfilzomib group and 3.3 month in the control group. The ORR was 19.1% in the carfilzomib group and 11.4% in the control group.

Treatment discontinuation due to an adverse event occurred in 14.6% (carfilzomib group) and 20.3% of patients in the control group; 10.2% in the carfilzomib group and 12.4% of patients in the control group died on study due to an adverse event. Grade ≥3 treatment-emergent adverse events (≥5%) included anaemia (25.5% in the carfilzomib group vs. 30.7% in the control group), thrombocytopaenia (24.2% in the carfilzomib group vs. 22.2% in the control group), neutropaenia (7.6% in the carfilzomib group vs. 12.4% in the control group), acute renal failure (7.6% in the carfilzomib group vs. 3.3% in the control group), pneumonia (6.4% in the carfilzomib group vs.

12.4% in the control group), and renal failure (5.1% in the carfilzomib group vs. 1.3% in the control group).

Prof. Faith Davies of the University of Arkansas for Medical Sciences, USA, who discussed the study results, said that carfilzomib is an effective treatment with a good safety profile. The discussion covered difficulties in developing a drug in the relapsed refractory myeloma seting. It is difficult to design a study that meets regulatory, commercial, patient and scientific needs with an open question what should the control arm be. Regarding use of single agent carfilzomib, Dr Davies said that we never use single agent – always use a combination of a doublet or a triplet.

The study was sponsored by Onyx Therapeutics, Inc.

Reference

LBA28: Carfilzomib (K) vs low-dose corticosteroids and optional cyclophosphamide (Cy) in patients (pts) with relapsed and refractory multiple myeloma (RRMM): Results from a phase 3 study (FOCUS)

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.

Acknowledgment

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