ESMO 2016 Congress

7-11 October, 2016

Copenhagen, Denmark

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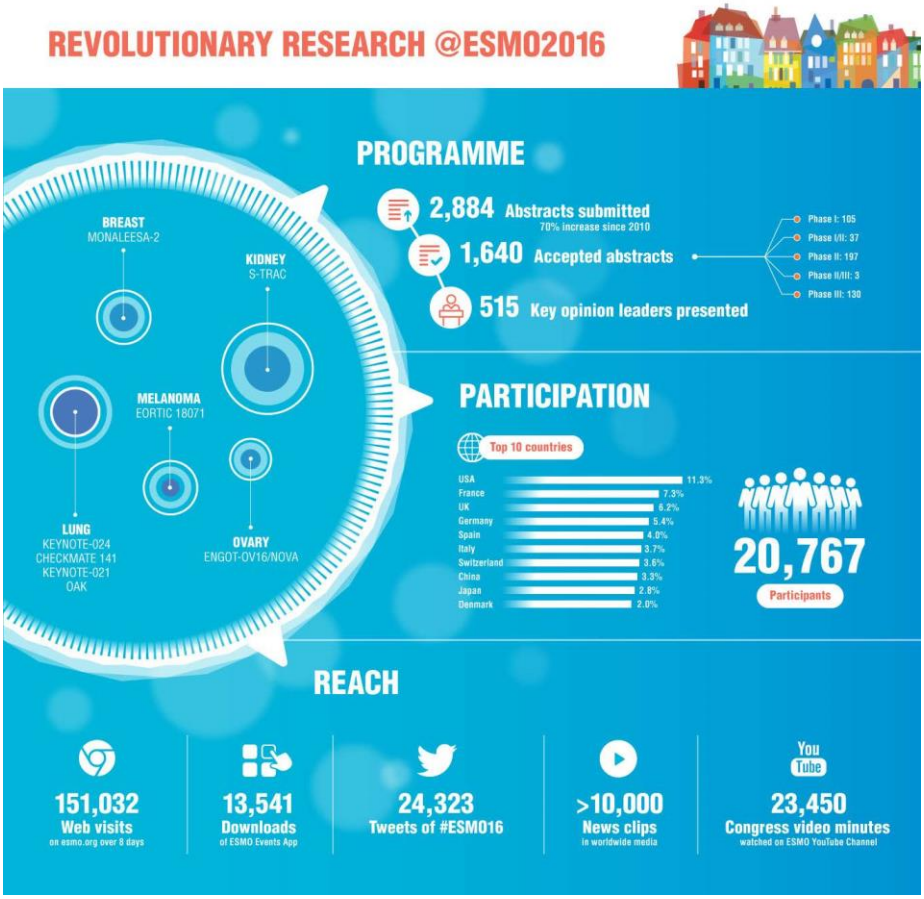
Summary

The European Society for Medical Oncology (ESMO) 2016 Congress, held October 7 to 11 in Copenhagen, Denmark, was a record-breaker on all levels. It was resounding success and in a dedicated infographic you can find the congress programme statistics. A primary emphasis in the scientific programme was placed on two areas: precision medicine and immunology and immunotherapy across multiple tumour types and how these advances change the treatment landscape in oncology. 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 2016 scientific programme, as well as advances in oncology.



ESMO 2016 record breaking Congress

HAEMATOLOGICAL MALIGNANCIES

Phase III results from the CASTOR trial of daratumumab, bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma

Katja Weisel, Universitaetsklinikum Tuebingen der Eberhard-Karls-Universitaet, Abteilung fuer Innere Medizin II, Tuebingen, Germany presented findings from CASTOR, a randomised phase III trial of combined daratumumab, bortezomib, and dexamethasone treatment versus bortezomib and dexamethasone. The CASTOR enrolled 498 patients with relapsed or refractory multiple myeloma who had received a median of 2 prior lines of therapy (range: 1 to 10); 66% of patients had received prior bortezomib, 76% received prior immunomodulatory drugs, and 48% had received prior proteasome inhibitors and immunomodulatory drugs. Patients in the trial were treated with 8 cycles of bortezomib/dexamethasone with or without 16 mg/kg of daratumumab. Bortezomib was administered subcutaneously at 1.3 mg/m2 on days 1, 4, 8, and 11 of each 21-day cycle for a maximum of 8 cycles. Patients received 20 mg of oral dexamethasone on days 1, 2, 4, 5, 8, 9, 11, and 12 of the first 8 bortezomib treatment cycles. Patients in the daratumumab group received an intravenous infusion of daratumumab at 16 mg/kg weekly for the first 3 cycles, on day 1 of cycles 4 to 9, and then every 4 weeks.

The primary endpoint was progression-free survival (PFS) and secondary endpoints include time-to-progression (TTP), objective response rate (ORR), overall survival (OS), and safety.

The 12-month PFS rate was 60.7% in patients receiving the triple combination of daratumumab, bortezomib, and dexamethasone versus 26.9% in patients receiving bortezomib and dexamethasone. After a median follow-up period of 7.4 months, the median PFS was not reached in the daratumumab group versus 7.2 months in the control group, hazard ratio [HR] 0.39; 95% confidence interval [CI] 0.28, 0.53 ($p < 0.0001$). Partial response was attained by 59.2% of daratumumab patients versus 29.1% of control patients ($p < 0.001$) and complete response was achieved by 19.2% versus 9.0% of patients receiving daratumumab versus control, respectively ($p = 0.001$). The ORR was also higher with the addition of daratumumab at 82.9% compared with 63.2% in the control group ($p < 0.001$). After meeting its primary endpoint for PFS, the CASTOR study was halted to allow patients in the control arm to cross over to receive daratumumab.

The most commonly reported grade 3 or 4 adverse events (AEs) in patients treated with daratumumab in combination with bortezomib and dexamethasone compared with those who only received bortezomib and dexamethasone were thrombocytopenia (45.3% versus 32.9%), anaemia (14.4% versus 16.0%), and neutropenia (12.8% versus 4.2%). Daratumumab-associated infusion-related reactions were reported in 45.3% of patients, were mostly grade 1/2, and occurred mainly during the first infusion, which is consistent with the previously reported safety profile of daratumumab monotherapy and background bortezomib/dexamethasone therapy. These findings have been published in *The New England Journal of Medicine*. NCT02136134. Weisel *et al.* Abstract 906O

Practice point and future research opportunities

Daratumumab is the first CD38–targeting monoclonal antibody approved for multiple myeloma; in November 2015, daratumumab was granted an accelerated approval by the FDA as a monotherapy for patients with multiple myeloma who had undergone 3 or more prior therapies based on data from 2 open-label clinical trials. The CASTOR study served as one of the confirmatory trials required for full approval. In this trial, daratumumab significantly improved PFS when added to bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma. These data formed part of the basis of submission of the supplemental Biologics License Application to the US Food and Drug Administration and the submission of the variation to the Marketing Authorisation to the European Medicines Agency for daratumumab. Longer patient follow-up is planned to determine the impact of the daratumumab combination on OS.

Prophylaxis with high-dose methotrexate is highly effective in preventing CNS recurrence in patients with high-risk DLBCL

Theresa Calimeri and colleagues at the IRCCS San Raffaele in Milan, Italy conducted a retrospective analysis that evaluated central nervous system (CNS) prophylaxis in 242 patients with diffuse large B-cell lymphoma (DLBCL) to prevent CNS dissemination. Data from consecutive HIV-negative adults with DLBCL who were treated with first-line R-CHOP or similar chemotherapy with and without radiotherapy were included. The risk of CNS dissemination was based on involvement of specific extranodal organs, including the testis, kidney/adrenal, spine, skull, paranasal sinuses, orbit, and/or breast and/or International Prognostic Index (IPI) of 4-5. Patients diagnosed after 2007 with high CNS recurrence risk received CNS prophylaxis, consisting of 3-4 cycles of methotrexate 3 g/m^2 ± intrathecal chemotherapy (IT). The patients´ median age was 66 (range: 18 to 89) years. The risk of CNS dissemination risk was low in 147 (61%) patients and high in 95 (39%) patients. CNS prophylaxis was indicated for 47 high-risk patients; of these, 36 received high dose methotrexate with or without IT and 11 patients received only IT due to MTHFR polymorphisms, comorbidity or old age.

At follow-up of a median 51 months (range: 12 to171 months), the CNS relapse rate was less than 1%, which represented one patient in the low-risk cohort versus 10 (11%) in the high-risk cohort. CNS relapse was reported in 11 (4.5%) and 8 of these died of CNS progressive disease after a median of 12 months (range: 7 to 37 months). In the high-risk subgroup, the CNS relapse rate was 17% in patients not receiving CNS prophylaxis versus 18% in patients receiving IT alone, and 0% in high risk patients that received CNS prophylaxis consisting of high-dose methotrexate ± IT (p = 0.004). Overall, 38 high-risk patients experienced relapse, and the CNS was the most common involved site in 10 patients. Survival was significantly improved with CNS prophylaxis; the 3-year progression-free survival rate was 81% versus 46% (p = 0.001) and the 3-year overall survival rate was 86% versus 48% (p = 0.00005) in patients receiving and not receiving prophylactic treatment, respectively. Survival rates were independent of IPI score and extranodal sites. NCT0059731. Claimeri *et al.* Abstract 908O

Practice point and future research opportunities

Prophylaxis with high-dose methotrexate was highly effective in preventing CNS disease recurrence in patients with high-risk diffuse large B-cell lymphoma who were at increased risk of CNS recurrence.

RELATED INFORMATION

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ESMO 2017 Congress, Madrid, Spain, 8-12 September 2017.

Affiliations and Disclosure

Affiliation

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Disclosure

No conflicts of interest to disclose.

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