ESMO 2016 Congress

7-11 October, 2016

Copenhagen, Denmark

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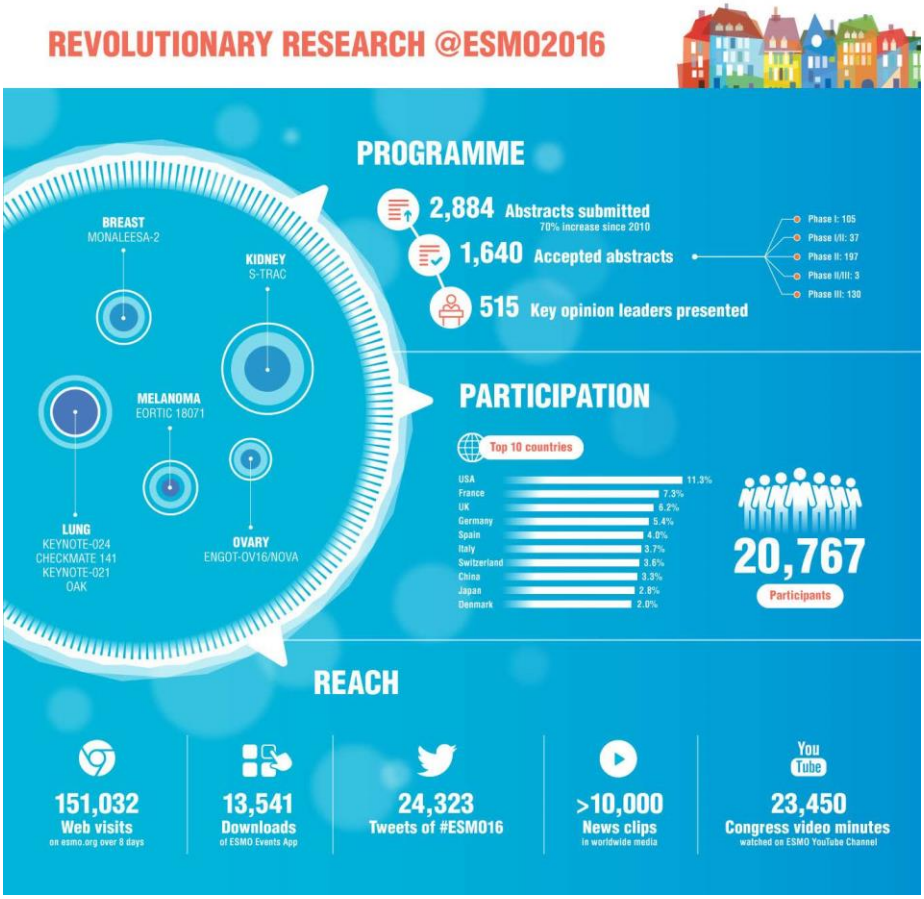
Summary

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

SMALL CELL LUNG CANCER

Alisertib (MLN8237) plus paclitaxel improves PFS over placebo plus paclitaxel as second line therapy for SCLC

Alisertib is an aurora A kinase inhibitor that has already been shown to have antitumor activity in patients with solid tumours, including those with small cell lung cancer (SCLC), explained Taofeek Owonikoko, Department of medical oncology, Emory University, Atlanta, USA. With colleagues, Dr. Owonikoko evaluated the efficacy and safety of alisertib combined with paclitaxel, compared to placebo plus paclitaxel in patients with SCLC who had relapsed within 6 months or did not respond to standard first-line, platinum-based chemotherapy. In the phase II trial, 178 patients were randomised 1:1 to receive alisertib orally at 40 mg, twice-daily on days 1-3, 8-10, and 15-17 and paclitaxel, which was administered intravenously at 60 mg/m^2 on days 1, 8, 15, or to treatment with a matched placebo plus paclitaxel given on the same days but at a dose of 80 mg/m^2. The patients had a mean age of 62 years, and just over half (57%) were men.

The primary endpoint was progression-free survival (PFS), as assessed by stratified log-rank test.

The analysis of PFS using IVRS stratification showed a median PFS of 101 with alisertib/paclitaxel versus 66 days with placebo/paclitaxel, hazard ratio [HR] 0.77; 95% confidence interval [CI] 0.557, 1.067 (p = 0.113). The analysis for PFS using the corrected stratification factors again favoured alisertib/paclitaxel (HR 0.72; p = 0.038). Numerically higher objective response rate (ORR) of 22% versus 18%, disease control rates of 77% versus 67%, and overall survival (OS) of 6.87 versus 5.58 months also were seen with the alisertib/paclitaxel over placebo/paclitaxel, respectively, although statistical significance was not reached. Stable disease was achieved by 55% of patients receiving added alisertib compared to 49% of control patients and progressive disease occurred in 15% versus 26% of patients in the respective treatment arms.

Additional toxicities were observed with the combination treatment. Almost all (99% versus 96%) of patients reported some type of adverse event (AE), of which 75% and 51% were grade 3 or higher, respectively in the alisertib and placebo groups. Common any-grade AEs with the respective treatments were diarrhea (59% versus. 20%), neutropenia (49% versus 8%), anaemia (44% versus. 20%), and fatigue (44% versus 33%). Drug-related serious AEs were reported in 32% versus 7% and treatment discontinuation due to an AE was reported in 15% versus 6% of patients receiving alisertib/paclitaxel versus placebo/paclitaxel, respectively. NCT02038647; EudraCT 2013-003713-18 Owonikoko *et al.* Abstract 1423O

Practice point and future research opportunities

The treatment of SCLC, particularly in the second-line setting, remains challenging, and there are no targeted agents approved for use. When first-line therapies fail, the guideline-recommended option is to put patients back on platinum-based chemotherapy if they were sensitive to this chemotherapy. Alisertib/paclitaxel demonstrated improved PFS over

placebo/paclitaxel and similar favourable trends was observed for OS and the ORR, in this trial. This combination may be a possible option to topotecan for patients who progress on platinum-based chemotherapy that warrants further investigation.

SCLC harbours targetable alterations including MYCL1 fusions that respond to alisertib

Siraj Ali, Clinical Development, Foundation Medicine, Inc., Cambridge, USA, and colleagues used comprehensive genomic profiling (CGP) to assays 689 small-cell lung cancer (SCLC) cases with the aim of detecting targetable genomic alterations to improve treatment options for patients progressing on platin/etoposide. The investigators used hybrid-capture based CGP during the course of clinical care to identify all 4 classes of genomic alterations (GA), base substitutions, short insertions/deletions, copy number alterations, and fusions to suggest possible benefit from targeted therapy. The patients in this series had a median age of 62 years, and 50% were female.

The investigators found the most commonly altered genes were TP53 in 91% of samples, RB in 68%, MLL2 in 13%, LRP1B in 11%, RICTOR in 11% and FGF10 in 9% of cases. MYCL1 amplification was identified in 53 cases, and 6 MYCL1 fusions arising from inter-chromosomal rearrangements were detected, including MYCL1-COL9A2, MYCL1-MSRB2, MYCL1-PABPC4, MYCL1-MACF1, MYCL1-JAZF1, and one MYCl1 with an indeterminate partner. Other rearrangements of cancer relevant genes that were detected included 3 cases of c-MYC rearrangements co-occurring with MYC amplification, three cases of RICTOR rearrangements, and one case each of BRD4-NOTCH3 and EML4-ALK.

One never smoker, 46-year old male was diagnosed with SCLC, which harboured MYCL1-JAZF1 that was detected on CGP. Therefore, he was treated with alisertib and demonstrated an 18-month nearly complete response after failing 3 previous lines of chemotherapy. Ali *et al.* Abstract 1424O

Practice point and future research opportunities

This study identified 6 novel MYCL1 fusions that may be targetable by existing therapies, such as the investigational aurora kinase inhibitor, alisertib, which is hypothesised to target MYCL downstream pathways. In light of the response of the index patient to alisertib, further focused investigation of MYCL1 and other fusions in SCLC is warranted to assess possible oncogenic drivers and targetable genetic alterations.

RELATED INFORMATION

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Save the date

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

Affiliations and Disclosure

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Disclosure

No conflicts of interest to disclose.

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