ESMO 2016 Congress

7-11 October, 2016

Copenhagen, Denmark

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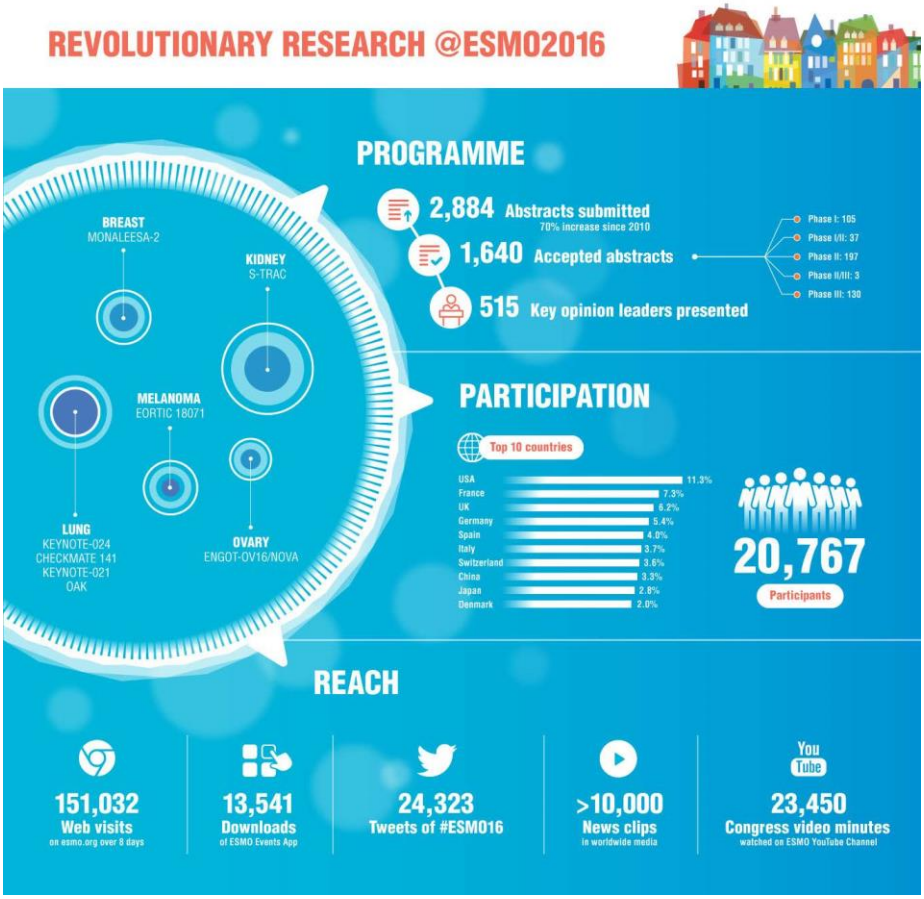
Summary

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

THORACIC MALIGNANCIES - NSCLC, Early Stage

Tumour downsizing possible with neoadjuvant immunotherapy given prior to surgery in early NSCLC

Findings from the first study of neoadjuvant PD-1 blockade in early stage lung cancer were presented by Patrick Forde, Sidney Kimmel Comprehensive Cancer Centre, Johns Hopkins University, Baltimore, US. Dr. Forde and colleagues conducted this study to determine the safety and feasibility of neoadjuvant nivolumab in 18 patients with stages I–IIIA non-small cell lung cancer (NSCLC). Patients received two doses of nivolumab at 4 and 2 weeks prior to surgical resection. Treatment was considered feasible if it did not delay surgery. Pathologic tumour response was the exploratory endpoint. Analyses of the pretreatment biopsy and post-treatment tumour samples, including programmed cell death ligand 1 (PD-L1) staining, multiplex immunohistochemical studies, and T-cell–receptor sequencing were also performed.

An exploratory analysis done in these patients exposed no significant safety concerns and no delays to surgery after neoadjuvant nivolumab. Importantly, 4 (22%) patients achieved radiologic responses, and 13 (72%) patients had stable disease, with just one patient experiencing progressive disease. Of 17 patients undergoing resection, 9 showed at least 50% regression of the tumour. Major pathologic responses after neoadjuvant treatment were reported in 7 (39%) patients, which means they had < 10% residual viable tumour at resection. One patient demonstrated pathologic complete response.

The relationship between response and PD-L1 expression remained unclear; although 3 patients with a robust response were positive for PD-L1 expression (≥ 1%) by immunohistochemical assay, one responder was PD-L1–negative, and one strongly PD-L1–positive patient did not respond to nivolumab. The tumours of responders showed dense infiltration of immune cells, with multiplex immunohistochemistry depicting infiltration of cytotoxic T cells into the tumours. New T-cell clones were detected in the post-treatment tumours that had not been seen in the pretreatment biopsy. Comprehensive genomic profiling had been completed for a small number of tumours that showed patients with major pathologic responses had higher absolute numbers of mutations. Absolute levels of predicted neoantigens were also higher in major responders.

Treatment-related toxicities were consistent with those seen in other studies of nivolumab, and there were no treatment-related deaths. Of 19 patients evaluated for safety, adverse events of any grade were reported by 32%; one (5%) patient had grade 3/4 toxicity leading to treatment discontinuation; however, the patient was still able to undergo surgery, which was uncomplicated.

Based on these results, the study is being expanded: One cohort will receive a third dose of nivolumab, and the other cohort will receive the combination of nivolumab and ipilimumab preoperatively. In addition, comprehensive genomic profiling, immunohistochemical, T-cell–receptor clonality, and tumour-infiltrating lymphocytes functionality studies are ongoing, and larger follow-up clinical studies are planned. NCT02259621. Forde *et al.* Abstract LBA41_PR

Practice point and future research opportunities

The study indicates that neoadjuvant administration of nivolumab is safe and feasible in stages I–IIIA NSCLC, and suggests that anti–PD-1 immunotherapy may have activity in early-stage disease. Nearly 40% of patients with early-stage NSCLC treated with two doses of nivolumab had major pathologic responses associated with immune cell infiltration of tumour, and these tumours could be downstaged prior to surgery. One explanation for this activity is that having tumour in situ means having more antigen present when the anti-PD1 is administered, which may be better than giving it in the adjuvant setting, where only micrometastases may be present with a small amount of antigen. However, there is a potential for bias when comparing a small biopsy, which might not represent the whole tumour, with the resected tumour.

Analysis indicates adjuvant may be more effective than neo-adjuvant chemotherapy with docetaxel plus carboplatin in resectable stage IB to IIIA NSCLC

Yi-Long Wu, Guangdong General Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China, and colleagues located throughout China compared survival in patients receiving adjuvant versus neoadjuvant chemotherapy plus complete resection of stage II-IIIA NSCLC. The study enrolled patients with stage IB-IIIA NSCLC who were randomly assigned to 3 cycles adjuvant docetaxel at 75 mg/m^2, carboplatin at a dose providing AUC5 on day 1 every 3 weeks after resection or 3 cycles of neoadjuvant docetaxel/carboplatin at the same schedule followed by surgery within 6 weeks after chemotherapy. The primary endpoint was disease-free survival (DFS); secondary end points included 3- and 5-year overall survival (OS) and safety. Between March 2006 and May 2011, 214 patients were screened from 13 institutes; the planned sample size was 410 patients, which resulted in early closure of the trial due to slow accrual.

The screening yielded 198 eligible patients who were randomised to the neoadjuvant arm (n=97) or to the adjuvant arm. (n=101). The patients' median age was 58, 80.3% were male and 48.5% of patients had adenocarcinoma.

All patients completed neoadjuvant chemotherapy and 87.4% completed the adjuvant chemotherapy. The objective response rate was 34%, and 12.4% of patients showed disease progression. No statistically significant difference was observed in DFS at 3 and 5 years between treatments. The 3-year DFS rate was 56.0% in the adjuvant arm versus 43.0% in the neoadjuvant arm, hazard ratio [HR] 0.76, 95% confidence interval [CI] 0.51-1.13 (p = 0.172), and the 5-year DFS was 50.0% with adjuvant versus 33.0% with neoadjuvant chemotherapy, HR 0.69; 95% CI 0.48, 1.00 (p = 0.051). The OS results showed an advantage that favoured adjuvant therapy. The 3-year OS was 68.0% versus 64.0%, HR 0.88; 95% CI 0.54,1.43 (p = 0.602), and 5-year OS was 60.0% versus 43.0%, HR 0.66; 95% CI 0.44,1.00 (p = 0.049) in the adjuvant versus neoadjuvant arms, respectively.

No unexpected toxicities were seen; 41.2% of patients experienced grade 3/4 neutropenia. One chemotherapy-related death occurred in the adjuvant arm and one patient died of perioperative pulmonary embolism in the neoadjuvant arm. NCT00321334. Wu *et al.* Abstract 1178O

Practice point and future research opportunities

A previous meta-analysis that indirectly compared adjuvant to neoadjuvant chemotherapy showed no difference in survival. This study adds information that favours adjuvant chemotherapy; a non-statistically significant trend towards improved DFS for adjuvant over neoadjuvant chemotherapy was seen in patients undergoing resection for NSCLC. The trend favouring adjuvant chemotherapy was reflected in the OS results where adjuvant chemotherapy became significantly superior to neo-adjuvant chemotherapy in the 5-year rates. More patients completed the full course of chemotherapy in the adjuvant than in the neoadjuvant group, which could also explain these results.

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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