ESMO 2016 Congress

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Copenhagen, Denmark

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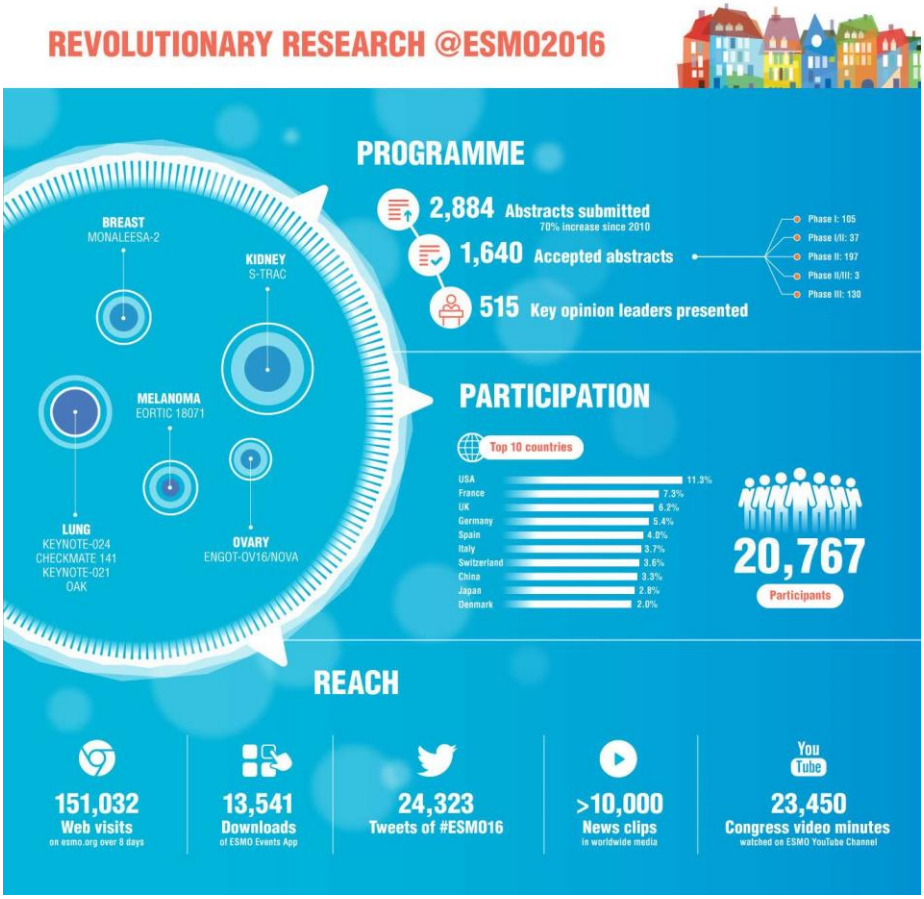
Summary

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

BASIC SCIENCE

EPHA2 as a potential marker of resistance to anti-EGFR agents in metastatic colorectal cancer

Giulia Martini, Department of Oncology, AOU Seconda Università degli Studi di Napoli in Naples, Italy and colleagues studied the possible role of the tyrosine kinase inhibitor, EPHA2, as a potential marker of resistance to anti-EGFR drugs in colorectal cancer (CRC). The effect of the EPHA2 inhibitor ALW-II-41-27 with and without cetuximab on cell survival and drug sensitivity was evaluated by the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide) assay, which measures mitochondrial activity, and by western blot analysis using a panel of CRC cell lines. Cell lines sensitive to anti-EGFR agents included GEO and SW48 cells, and resistant lines included HCT116, SW620, LOVO, SW480, HCT15, and GEO-CR plus SW48-CR, which also demonstrates acquired cetuximab resistance. Flow cytometry was used to analyse apoptosis and for cell cycle analysis, and SW48-CR subcutaneous xenograft models were used for in vivo experiments. EPHA2 expression was assessed by immunohistochemistry (IHC) in metastatic CRC tumours.

Using these methods, the investigators found that EPHA2 was differentially activated among cell lines with high levels of phosphorylation, including HCT116, SW620, LOVO, GEO-CR and SW48-CR cells. The sensitivity of CRC cell lines to ALW-II-41-27, expressed as IC_{50}, differed among the lines studied, and ranged from 0.05 to 2 mM; the most sensitive cell lines were HCT116, SW620, LOVO, SW48-CR, HCT15, and GEO; GEO-CR and SW48 showed the highest resistance to ALW-II-41-27.

To address whether EPHA2 inhibition could overcome primary and acquired resistance to cetuximab, a combination of ALW-II-41-27 plus cetuximab was tested in resistant cell lines. The combination induced synergistic anti-proliferative and apoptotic effects in HCT15 cells with primary, and in GEO-CR and SW48-CR cells, which have acquired resistance to cetuximab. The synergistic activity of the combination was confirmed by a reduction of pEPHA2 levels and a marked inhibition of activated pMAPK and pAKT. Cell cycle analysis showed the combination induced greater G2 phase arrest compared with sole ALW II-41-27. A detailed evaluation of EPHA2 expression by IHC in tumours from patients with mCRC receiving anti-EGFR therapy was presented and the in vivo experiment in SW48-CR subcutaneous xenograft models is ongoing. Martini *et al.* Abstract 1O

Practice point and future research opportunities

Both primary and acquired resistance to anti-EGFR therapy was overcome in vitro by ALW-II-41-27, a selective EPHA2 inhibitor. These results suggest that EPHA2 may be potential therapeutic target, and pEPHA levels may be a putative biomarker in mCRC treatment.

RELATED INFORMATION

Click here to access the Congress abstracts.

Click here to access the meeting webcast page.

Save the date

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

Affiliations and Disclosure

Affiliation

Dr Svetlana Jezdic, ESMO Head Office.

Disclosure

No conflicts of interest to disclose.

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