

# ESMO 2016 Congress

7-11 October, 2016

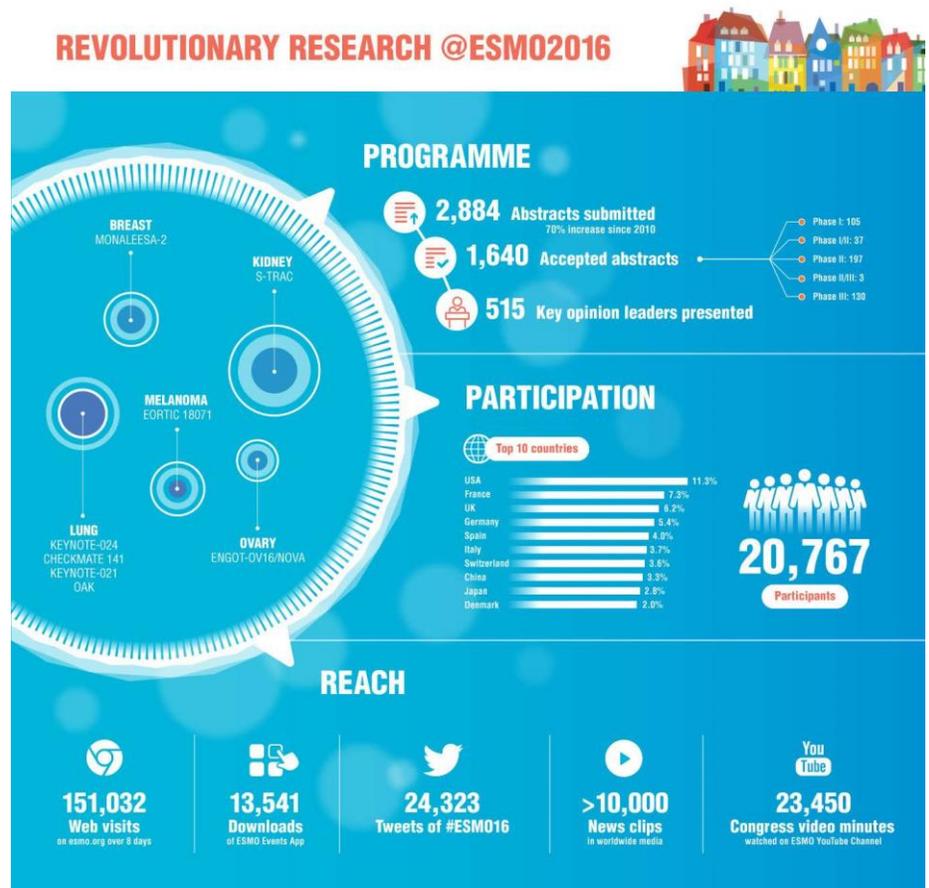
Copenhagen, Denmark

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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*

## DEVELOPMENTAL THERAPEUTICS

### 89Zr-labeled CEA-targeted IL-2 variant immunocytokine in patients with solid tumours demonstrates dose-dependent CEA-mediated tumour accumulation

Findings from a trial of novel CEA-IL2v (cergutuzumab amunaleukin, RG7813), an engineered IL-2 variant antibody directed against carcinoembryonic antigen (CEA) with abolished IL-2 receptor (IL-2R)  $\alpha$  (CD25) binding were reported by Catherina W. Menke-van der Houven van Oordt, Medical Oncology, Vrije University Medical Centre in Amsterdam, Netherlands. She explained that CEA-IL2v was designed to improve the pharmacological and safety profile of IL-2 and direct the local accumulation of IL-2 into CEA-positive tumours. This phase I trial was conducted to demonstrate selective and specific tumour targeting by labelling CEA-IL-2v with <sup>89</sup>Zr to allow evaluation of biodistribution and tumour accumulation at varying doses in tumours having different levels of CEA. A sub-study of the trial enrolled 25 patients with advanced and/or metastatic solid tumours; 16 patients had CEA-positive and 9 patients had CEA-negative tumours. CEA-IL2v was administered intravenously every 2 weeks at total doses of 6 mg, 20 mg and 30 mg. All patients underwent up to 3 <sup>89</sup>Zr-PET assessments during cycle 1, and patients receiving 20 mg showing initial tumour uptake at cycle 1 underwent additional assessments in cycle 4.

At day 5 post injection, accumulation of <sup>89</sup>Zr-CEA-IL-2v was observed that was independent of CEA status in lymphoid tissues, including the spleen (SUV<sub>mean</sub> 10.0±3.1) and non-pathological lymph nodes (SUV<sub>mean</sub> 2.0±1.2) at all doses. The investigators considered this to represent IL-2 receptor-mediated uptake. Intratumoural accumulation of <sup>89</sup>Zr-CEA-IL-2v in cycle 1 was observed in CEA-positive patients, including one of 4 patients receiving the 6 mg dose (SUV<sub>peak</sub> 5.4), 6 of 8 patients dosed at 20 mg (SUV<sub>peak</sub> 5.2±2.7), and all 4 dosed at 30 mg (SUV<sub>peak</sub> 5.8±4.4). By cycle 4, <sup>89</sup>Zr-CEA-IL-2v accumulation in tumour lesions was decreased (SUV<sub>peak</sub> 4.0±1.1). The authors explained this could be due to anti-drug antibodies or an expansion of IL-2R expressing T-cells. In tumours with high accumulation of <sup>89</sup>Zr-CEA-IL-2v at cycle 1, there was a trend towards decreased metabolic activity at early FDG-PET evaluation. NCT02004106 EUDRACT NUMBER: 2013-003041-41. Menke-van der Houven van Oordt *et al.* Abstract 3580

#### Practice point and future research opportunities

The substudy demonstrated that, at all doses, <sup>89</sup>Zr-CEA-IL-2v accumulated in spleen and secondary lymphoid tissues, due to IL-2R mediated uptake, and accumulation was dose-dependent in the tumour. The phase I study investigating CEA-IL2v both as monotherapy and in combination with atezolizumab in patients with solid tumours is ongoing.

### Avitinib (AC0010) a third generation irreversible EGFR inhibitor shows promise in patients with EGFR TKI-resistant NSCLC

Li Zhang, State Key Laboratory of Oncology in South China, Sun Yat-sen University Cancer Center, Guangzhou, China presented first-in-human results from a dose escalation study of

avitinib (AC0010), a third generation irreversible epidermal growth factor receptor (EGFR) inhibitor that has been shown to overcome T790M-induced resistance in preclinical studies. Patients with non-small cell lung cancer (NSCLC) and EGFR positive mutation that developed resistance to the first generation EGFR tyrosine kinase inhibitors (TKIs) were enrolled; both T790M positive and negative patients were eligible. Oral AC0010 capsules were administered in 5 cohorts once daily in 50 mg, 100 mg, 200 mg, 350 mg, and 550 mg tablets, and 3 cohorts received twice daily oral doses of 175 mg, 250 mg, and 300 mg. All patients were required to undergo biopsy for genotyping to confirm T790M status prior to treatment and were assessed for pharmacokinetics (PK), overall response rate (ORR), disease control rate (DCR), and adverse events (AEs).

As of 5 May 2016, the study enrolled 51 patients; 49% were female, the median age was 55 years, and 86% of patients were T790M mutation positive. The maximum tolerated dose had not been reached. PK were dose proportional, and the median plasma half-life was 7.8 (range: 7.6 to 8.0) hours. Twice daily dosing method reduced the fluctuation coefficient of the plasma concentration by 0.40 fold, and improved the area under the curve (AUC) by 1.28 fold, compared to once daily dosing. No food effects were observed.

At data cut-off, 48 patients were evaluated in the once daily cohorts that demonstrated an ORR of 41.7%, and the DCR was 75.0%. All responses were observed at dose levels  $\geq 200$ mg daily. The ORR increased to 57.6% in 33 patients treated daily with avitinib at  $\geq 350$ mg and DCR was 87.9% in this cohort. The 33 evaluated patients in the twice daily dosing regimen showed a better ORR of 66.7% and DCR of 94.4%. The longest duration of response was 11 months and was ongoing at data cut-off.

Adverse events (AEs) were mostly grade 1 and transient. The most commonly reported drug related AEs grade 3 and higher were rash, which occurred in 4% of patients. ALT/AST elevation in 4%, and 2% of patients had pneumonia (2%). No hyperglycaemia or grade 3 QTc prolongation were observed. NCT02274337 Zhang *et al.* Abstract 359O

### Practice point and future research opportunities

These first-in-human results of avitinib (AC0010I), a third generation, irreversible EGFR inhibitor that seems to overcome T790M-induced resistance demonstrated a dose-dependent response in patients with NSCLC. These findings taken together with good safety profile suggest avitinib may have promising anticancer activity for NSCLC patients with T790M mutation who become resistant to first generation TKIs. The ongoing phase I trial is warranted and the results are anticipated.

### Phase I results with novel FGFR inhibitor BAY 1163877 show promise in patients selected by tumour mRNA expression

Markus Joerger, Department of Oncology, Cantonal Hospital, St Gallen, Switzerland reported

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results from the first-in-human dose escalation study of the potent small molecule pan-fibroblast growth factor receptor (FGFR) inhibitor, BAY 1163877. The novel compound was tested in patients with treatment-refractory locally advanced or metastatic solid tumours in a multicentre phase I study that was conducted in 6 countries. Dr. Joerger and colleagues reasoned that since FGFR expression is de-regulated by both genetic and epigenetic mechanisms, levels of FGFR messenger RNA (mRNA) could be measured to identify patients likely to benefit from FGFR-targeted approaches. The trial comprised a dose-escalation study in 23 patients plus followed by an expansion stage that enrolled 57 patients with high tumour FGFR mRNA levels into 3 expansion cohorts that included patients with bladder cancer, head and neck squamous cell carcinoma (HNSCC), squamous non-small cell lung cancer (sqNSCLC), and all comers.

The dose escalation study tested 5 doses ranging from 50 to 800 mg administered twice daily. BAY 1163877 has a half-life of about 12 hours and revealed less than dose-proportional increase in exposure at doses above 200 mg. A maximum tolerated dose was not defined because there were no dose-limiting toxicities. However, on preclinical results, the effect on serum phosphate levels, and clinical analyses, a twice daily dose of 800 mg was taken forward to the expansion phase.

Clinical benefit in 44 evaluable patients was demonstrated with BAY 1163877 in the expansion cohort that included 6 partial responses (PR) in one patient each with HNSCC, sqNSCLC, adenoid cystic carcinoma of the tongue, and 3 patients with bladder cancer. Stable disease (SD) was achieved by 18 patients lasting more than 12 weeks, with 8 showing SD lasting more than 24 weeks. Most patients, including 4 achieving PR, did not have FGFR genetic alterations.

BAY 1163877 was well-tolerated at doses up to 800 mg twice daily, although most patients developed low-grade hyperphosphatemia, which is seen with all FGFR inhibitors. These patients received treatment with a phosphate binder and/or dose reduction of BAY 1163877.

The authors commented that the innovative biomarker approach effectively identified patients with a good chance to benefit from BAY 1163877 and recommended further studies should be conducted, particularly in bladder cancer where approximately 35% of patients are FGFR mRNA positive. Joerger *et al.* Abstract 3600

### Practice point and future research opportunities

Most studies of FGFR inhibitors have looked at FGFR abnormalities in tumours with limited success. This study successfully used measurements of tumour FGFR mRNA expression to select patients for the expansion cohort. FGFR inhibitors may provide a therapeutic opportunity to patients with rare tumours. In this patient population, there were some patients with adenoid cystic carcinoma that demonstrated long-term disease control and a high response rate, particularly in bladder cancer. Taken together with the toxicity profile of BAY 1163877, which is better than other FGFR inhibitors under investigation, further study in larger cohorts and confirmation of these results are warranted. In the context of molecular screening programmes, patients with FGFR mRNA expression may be offered the opportunity for treatment with FGFR inhibitors.

## RELATED INFORMATION

[Click here to access the Congress abstracts.](#)

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Save the date

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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