ESMO 2014 Congress Scientific Meeting Report – Supportive and Palliative Care Extract

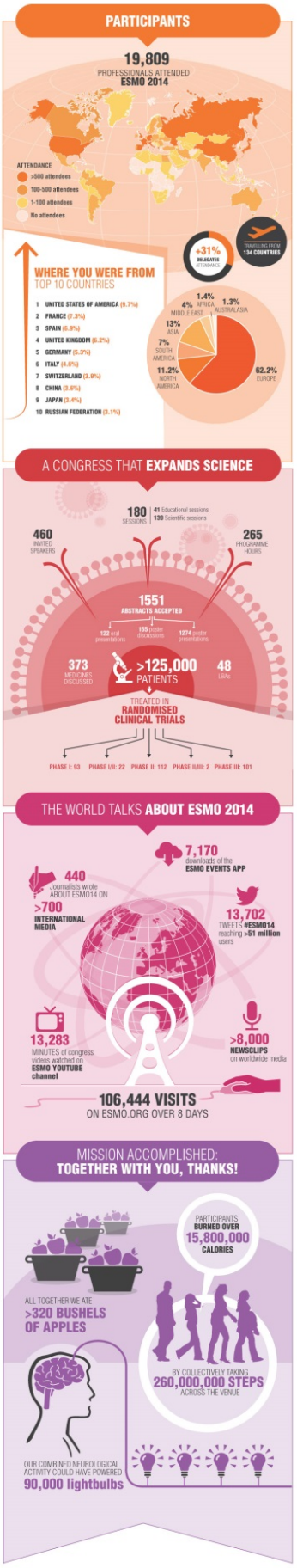
26-30 September 2014

Madrid, Spain

Summary

The European Society for Medical Oncology (ESMO) Congress, held September 26 to 30 in Madrid, Spain, was a record-breaker on nearly all levels. It was resounding success and in a dedicated infographic you can find the congress statistics. A primary emphasis in the scientific programme was placed on precision medicine and how it will change the future treatment landscape in oncology. In addition, a number of scientific presentations were dedicated to cancer immunology and immunotherapy across multiple tumour types. 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 2014 scientific programme, as well as advances in oncology.

Infographic (right): ESMO 2014 record breaking Congress



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Supportive and Palliative Care

Rolapitant plus granisetron/dexamethasone in prevention of chemotherapy-induced nausea and vomiting

A phase III trial of rolapitant plus granisetron/dexamethasone in patients treated with cisplatin-based chemotherapy revealed good tolerance and superiority in preventing chemotherapy-induced nausea and vomiting (CINV) in comparison with granisetron/dexamethasone alone. The results were presented by Dr Martin Chasen from the Elizabeth Bruyere Hospital Division of Palliative Care, Ottawa, Canada.

Rolapitant is a highly selective, competitive, long acting NK-1 receptor antagonist. Its long half-time (approximately 180 hours) suggests that a single dose may be sufficient to prevent CINV during the entire 5-day (0-120 hours) at periods of risk. A dose of 200 mg achieved >90% NK-1 receptor occupancy in the brain and maintained that level for up to 5 days post a single dose. There is a reduced risk of drug interactions as it is not an inducer or inhibitor of CYP3A4.

Rolapitant demonstrated safety and efficacy of a single oral dose in large global randomised, controlled, double blind studies. It was studied in two phase III trials in patients receiving cisplatin-based highly emetogenic chemotherapy and in one phase III study in patients receiving moderately emetogenic anthracycline-based chemotherapy.

Key inclusion criteria for the study were patients ≥18 years of age, of either gender, and of any race, naive to cisplatin-therapy. Cisplatin-based chemotherapy was defined as a dose ≥60 mg/m2. Key exclusion criteria were patients scheduled to receive any other chemotherapeutic agent with an emetogenicity level of ≥4 on Hesketh Scale from day 2 through day 6.

Events of emesis and use of rescue medication were recorded for 5 days.
In this multi-centre, randomised double-blind phase III study, 532 patients were randomised 1:1 to receive oral rolapitant plus granisetron/dexamethasone or placebo plus granisetron/dexamethasone prior to chemotherapy.

The primary endpoint was CR defined as no emesis/no rescue medication in the delayed phase (>24-120 hours post-chemotherapy). Secondary endpoints included safety and tolerability; CR rates during acute (0-24 hours) and overall (0-120 hours) phases post-chemotherapy; incidence of no emesis in the acute, delayed, and overall phases of CINV; incidence of no significant nausea in the overall phase of CINV; and time to first emesis or use of rescue medication. Tertiary endpoints were effect of rolapitant on health-related QoL assessed by the Functional Living Index-Emesis Questionnaire (FLIE); complete protection defined as no emesis, no rescue medication, and maximum nausea VAS <25 mm (scale of 0 to 100 mm) for the Nausea and Vomiting Subject Diary Question 2; and incidence of no significant nausea in acute and delayed phases of CINV.

Demographics were well balanced between rolapitant and control groups with respect to gender, age, tumour type, and CINV risk factors.

The primary objective of this study was achieved with a higher CR rate in the delayed phase compared to placebo (72.7% vs. 58.4%, $p < 0.001$). Statically significant results were also observed in key secondary endpoints of acute phase CR rate (83.7% vs. 73.7%, $p = 0.005$), and overall CR rate (70.1% vs. 56.5%, $p = 0.001$).

Protection from CINV with rolapitant compared to control was observed early and persisted throughout the delayed phase. Treatment effect was initiated in the acute phase at approximately 12 hours following administration of chemotherapy. Time to first emesis or use of rescue medication was longer in rolapitant vs. control group. By days 2–3, the rolapitant curve begins to plateau, indicating these patients are protected for up to 5 days post chemotherapy. In contrast, patients in the control group continued to experience late events of emesis and require rescue medication.

A regional CR analysis was prospectively conducted in North America, Asia/South Africa, Europe, and Central/South America. The CR with rolapitant was observed consistently across geographic regions.

Slightly more patients reported no impact on daily QoL with rolapitant but it was not statistically significant (72.8% vs. 67.8%, p = 0.231).

Treatment emergent adverse events were consistent across both arms (0.8% and 3.8%). Constipation and asthenia were most frequently reported treatment emergent adverse events. The majority of treatment emergent adverse events were considered by investigators to be related to chemotherapy or underlying cancer and not to rolapitant.

The authors concluded that the results of this study demonstrate the clinical benefit achieved over the entire CINV at risk period in the rolapitant group.

A new drug application was submitted to the FDA in early September 2014.

Prof. Jorn Herrstedt of the Odense University Hospital, Odense, Denmark, who discussed the study results, agreed on most of the conclusions from the study authors and added that they may have an impact on future antiemetic guidelines. However, in terms of conclusion that mean QoL (total and vomiting domain scores) improved significantly with rolapitant, he questioned if it is clinically relevant. He also said that rolapitant was well tolerated and overall incidences of treatment emergent adverse events were similar to those in the control group suggesting possibly less risk of drug-drug interactions.

The study was funded by Tesaro, Inc.

Reference

LBA47_PR: Phase 3 (P04832) trial results for rolapitant, a novel NK-1 receptor antagonist, in the prevention of chemotherapy-induced nausea and vomiting (CINV) in patients receiving cisplatin-based chemotherapy

Oral rivaroxaban for the treatment of symptomatic venous thromboembolism in patients with cancer

Prof. Martin Prins of the Maastricht University Medical Center, Maastricht, The Netherlands reported that rivaroxaban has similar efficacy to enoxaparin/vitamin K antagonist in patients with venous thromboembolism and active cancer or a history of cancer, but it was associated with a significant reduction in major bleeding in patients with active cancer.

The aim of the research was to compare the efficacy and safety of oral rivaroxaban with that of enoxaparin/vitamin K antagonist in patients with cancer among 8282 patients with acute venous thromboembolism enrolled in the EINSTEIN programme.

Patients with cancer and venous thromboembolism constitute a medical challenge for physicians because while anticoagulant treatment can prevent recurrent venous thromboembolism it is associated with a high risk of major bleeding.

EINSTEIN deep venous thrombosis and EINSTEIN pulmonary embolism were randomised, event-driven, non-inferiority, open-label phase III studies. Patients were treated for 3, 6 or 12 months with rivaroxaban or enoxaparin/vitamin K antagonist (international normalised ratio 2.0–3.0) and followed for suspected recurrent venous thromboembolism, bleeding and mortality.

Cancer patients were classified as active cancer at baseline (diagnosis or treatment within 6 months before enrolment or recurrent/metastatic cancer) or diagnosed during the study (655 patients) or a history of cancer (469 patients).

Recurrent venous thromboembolism occurred with a similar incidence in the rivaroxaban and enoxaparin/vitamin K antagonist groups in patients with active cancer (HR 0.67) and patients with a history of cancer (HR 0.98). In patients with active cancer, the risk of major bleeding was significantly reduced in the rivaroxaban group (HR 0.42), whereas it was similar between treatments in patients with a history of cancer (HR 0.23). Mortality occurred with a similar incidence between treatments in patients with active cancer (HR 0.93) and patients with a history of cancer (HR 1.12).

Prof. Prins concluded that rivaroxaban is an alternative to standard therapy when a physician decides against long-term low molecular weight heparin. A head-to-head comparison of rivaroxaban with low molecular weight heparin in patients with cancer and venous thromboembolism is warranted.

Following the presentation, the study was published in the Lancet Haematology.

Dr Florian Scotte of the Georges Pompidou European Hospital, Paris, France, who discussed the study results, said that in general physicians tend to under-report patients' subjective toxicities. In this analysis, toxicity rates reported by physicians were always lower than those reported by patients. Under-reporting by physicians was high ranging from 54.2% to 80.2% of cycles when patients reported "any severity" toxicity and ranging from 22.2% to 62.1% examining only cycles when patients reported "very much" toxicity. He questioned the assessment quality in research, toxicity assessment, high level of toxicity, subjective vs. objective toxicity, assessment inside vs. outside hospital, physicians' education in supportive care, and patients' education in supportive care.

The study was funded by Bayer HealthCare Pharmaceuticals and Janssen Research & Development.

Reference

LBA48: Oral rivaroxaban versus standard therapy for the treatment of symptomatic venous thromboembolism in patients with cancer

Anamorelin for the treatment of cancer anorexia-cachexia in NSCLC: Results from the phase III studies ROMANA 1 and 2

Dr Jennifer Temel of the Massachusetts General Hospital, Boston, USA reported that in two global, large-scale phase III studies, 12 weeks of anamorelin was well tolerated, and significantly improved lean body mass, body weight, and anorexia-cachexia symptoms/concerns in advanced NSCLC patients with cachexia.

Cancer anorexia-cachexia syndrome is a common debilitating condition, characterised by decreased body weight, mainly lean body mass and negatively impacts QoL and prognosis. Anamorelin is a novel selective ghrelin receptor agonist with appetite-enhancing and anabolic activity.

ROMANA 1 and 2 were two international, double-blind, phase III trials assessing anamorelin efficacy and safety in patients with unresectable stage III/IV NSCLC, ECOG PS 0-2 and cachexia (≥5% weight loss within prior 6 months or body mass index <20 kg/m2). Patients were randomised (2:1) to anamorelin or placebo, given daily orally for 12 weeks and were permitted to receive chemotherapy while on study.

Co-primary endpoints were change from baseline over 12 weeks in lean body mass and in handgrip strength. Secondary endpoints included change in body weight and in the anorexia-cachexia subdomain of the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire. Safety assessments included lab values and adverse events.

There were no within-study population differences for ROMANA 1 (484 patients) and ROMANA 2 (495 patients). Over 12 weeks, anamorelin significantly increased lean body mass vs. placebo ($p < 0.0001$) in both studies. In ROMANA 1, median change in lean body mass was 1.10 kg for anamorelin vs. -0.44 kg for placebo; similarly, changes in ROMANA 2 were for anamorelin 0.75 kg vs. -0.96 kg for placebo. Change in handgrip strenght was not statistically different between the study arms.

Anamorelin increased body weight ($p < 0.0001$ in both studies) and improved FAACT subdomain scores ($p = 0.0004$ in ROMANA 1; and $p = 0.0016$ in ROMANA 2 study).

The results on OS are pending.

In the anamorelin arm, the most frequent drug-related adverse events were hyperglycemia (5.3%) and nausea (3.8%) for ROMANA 1, hyperglycemia (4.2%) and diabetes (2.1%) for ROMANA 2. Both studies had few drug-related grade ≥3 adverse events (0.9%, 2.7%).

Dr Florian Scotte of the Georges Pompidou European Hospital, Paris, France, who discussed the study results, said that muscle wasting is common in lung cancer patients regardless of body weight. Cancer induced wasting begins early in the course of malignancy and up to 50% of lung cancer patients have severe muscle wasting at diagnosis. In the studies, he questioned an effect on OS, effect on the tumour, methods to assess cachexia/sarcopenia, and long term follow-up.

This study was supported by Helsinn Therapeutics, Inc. (USA).

Reference

1483O_PR: Anamorelin for the treatment of cancer anorexia-cachexia in NSCLC: Results from the phase 3 studies ROMANA 1 and 2

RELATED INFORMATION

Click here to access the Conference abstracts.

Click here to access the meeting webcast page.

Save the date

European Cancer Congress 2015 (ECC 2015), Vienna, Austria, 25-29 September 2015.

Affiliations and Disclosure

Affiliation

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Disclosure

No conflicts of interest to disclose.

Acknowledgment

ESMO would like to thank Drs Gligorov, von Minckwitz, Zhu, Kang, Lenz, Stintzing, Konecny, Krishnansu, Goss, Robert, McArthur, Weber, and Blay for giving their permission to publish images from the studies presented during the ESMO 2014 Congress in the ESMO Scientific report.