2015 EUROPEAN CANCER CONGRESS

25-29 September 2015

Vienna, Austria

SUMMARY

The European Cancer Congress (ECC 2015) combined the 40th European Society for Medical Oncology (ESMO) congress with the 18th congress of the European CanCer Organisation (ECCO) and was held 25 to 29 September, 2015. The meeting was organised in partnership with the European Society of Radiation and Oncology (ESTRO), the European Society of Surgical Oncology (ESSO), the European Academy for Cancer Research (EACR), the European Oncology Nursing Society (EONS), and International Society of Paediatric Oncology (SIOPE). The efforts of all partner organisations were united to continue advancing multidisciplinarity as the way forward to optimise the prevention, diagnosis, treatment, and care of cancer patients by encouraging participants to leverage knowledge, promote education and build awareness for patient-centred oncology.

Contents

SARCOMAS

Phase III sarcoma study final results show patient benefit with trabectedin but not in overall survival

Final overall survival (OS) findings from a phase III trial conducted by Shreyaskumar R. Patel, MD Anderson Cancer Center, Houston, USA, and colleagues were consistent with the interim analysis in showing no significant advantage with trabectedin over dacarbazine in advanced leiomyosarcoma or liposarcoma. The open-label trial, randomised 518 patients with a variety of soft tissue sarcoma histologies in a 2:1 ratio; 345 patients received 1.5 mg/m^2 of trabectedin and 172 patients received 1.0 g/m^2 of dacarbazine once every 3 weeks until disease progression or unacceptable toxicity. Patients in the trabectedin arm also were given 20 mg of i.v. dexamethasone as premedication.

The primary endpoint was OS; an analysis done after 381 deaths had occurred at a median 21-month follow-up showed the OS with trabectedin was median 13.7 months compared with 13.1 months with dacarbazine, HR 0.93; 95% CI 0.75, 1.15 (p = 0.492). However, the difference in median progression-free survival (PFS) was significant; median trabectedin PFS was 4.2 versus 1.5 months with dacarbazine, HR 0.55; 95% CI 0.44, 0.70 (p <0.001). Patients received a median of 4 trabectedin treatment cycles compared with 2 dacarbazine cycles and the median duration of response was 6.5 versus 4.2 months, respectively, HR 0.47 (p = 0.14). The objective response rates were 9.9% with trabectedin versus 6.9% with dacarbazine and the clinical benefit rate (response plus stable disease rate) was 34% and 19%, respectively. While OS findings were consistent across a planned subgroup analysis with that of the overall study population (HR 0.93), multivariate analysis showed that OS was improved by trabectedin for patients receiving just one prior line of chemotherapy versus ≥2 and for those with an ECOG PS of 0 versus 1 (p < 0.05).

Adverse events (AEs) with trabectedin were higher overall versus dacarbazine and included nausea (73% versus 49%), fatigue (67% versus 51%), neutropenia (49% versus 29%), increased ALT levels (45% versus 6%), vomiting (44% versus 21%), anaemia (39% versus 29%), constipation (36% versus 28%), increased AST levels (35% versus 5%), and diarrhoea (34% versus 23%). Grade 3 AEs with the highest frequency in the trabectedin arm versus dacarbazine, respectively, were increased ALT levels (25% versus 1%), neutropenia (21% versus 11%), anaemia (14% versus 11%), and increased AST levels (12% versus 0%). With trabectedin, 16% of patients had grade 4 neutropenia compared with 10% in the dacarbazine group. Treatment-related discontinuation rates were 12.6% and 7.7% with trabectedin and dacarbazine, respectively. There

were treatment-associated deaths within 30 days of the last dose among 2.1% of patients receiving trabectedin but none in the dacarbazine arm; the deaths were related to sepsis/septic shock in 3 patients, while rhabdomyolysis/sepsis, renal failure, renal failure/cardiac arrest, and multi-organ failure each occurred in one patient.

The authors pointed out factors that could have confounded the OS results: 70% of patients in both arms received subsequent therapies and the median time to initiation of subsequent therapy was significantly prolonged with trabectedin compared with dacarbazine (6.8 months versus 3.5 months, HR 0.53; $p < 0.0001$). The possibility that this had a confounding impact was supported by a sensitivity analyses of OS, which showed a consistent favourable trend with trabectedin. These results have also recently been published in the JCO. Patel *et al.* Abstract 3403.

Practice point and future research opportunities

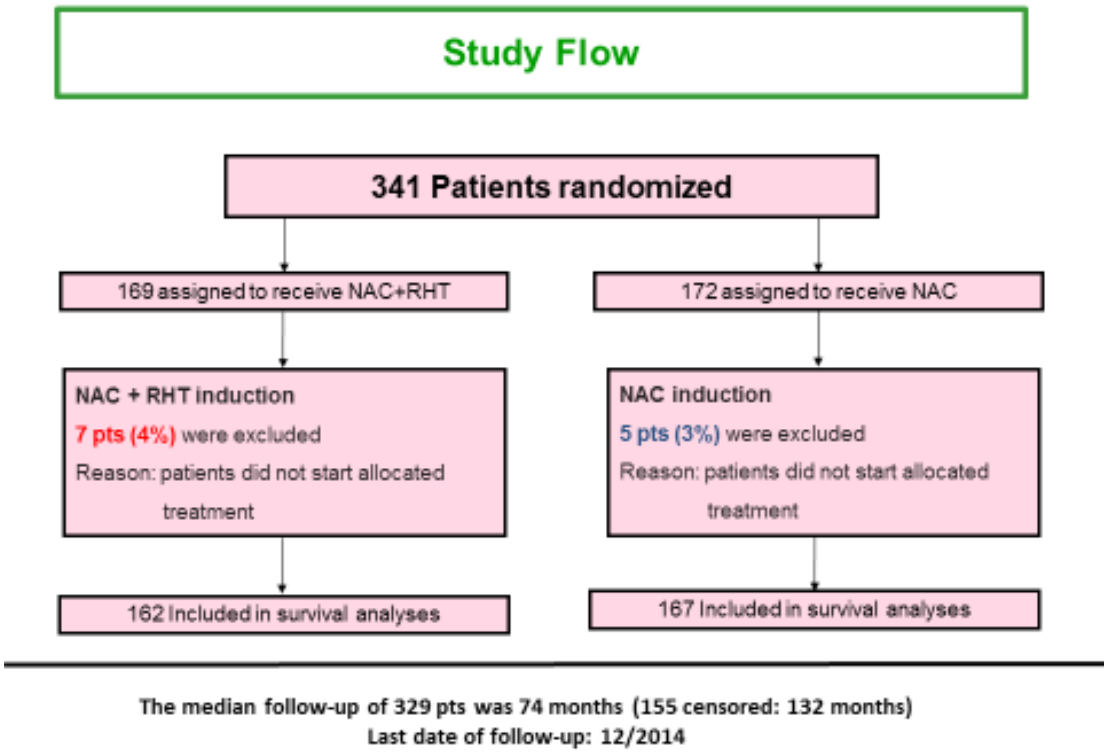
Whereas the final overall survival analysis showed comparable survival with trabectedin or dacarbazine, patients with advanced leiomyosarcoma or liposarcoma achieved clinically meaningful and statistically significant improvement in progression-free survival with trabectedin. Furthermore, the overall survival may have been confounded by use of post-study therapies that were delivered earlier in the dacarbazine arm. In October, 2015, the US Food and Drug Administration approved trabectedin for the treatment of unresectable or metastatic liposarcoma and leiomyosarcoma.

Long-term results show overall survival more than doubled with the addition of regional hyperthermia to neoadjuvant chemotherapy in patients with localised high-risk soft tissue sarcoma

Lead investigator Rolf Issels, München-Großhadern Klinikum Grosshadern, Munich, Germany reported findings of an analysis after long term follow-up of a phase III study showing that regional hyperthermia as an induction treatment added to neoadjuvant chemotherapy enhanced clinical benefit across all measured parametres in patients with localised high-risk soft tissue sarcoma. The randomised, multicentre, phase III EORTC trial of sole neoadjuvant chemotherapy or in combination with regional hyperthermia enrolled patients with localised high-risk soft tissue sarcoma of 5 cm or larger that were FNCLCC grade 2 or 3, that were stratified by site, disease presentation, and centre, then randomised to receive etoposide 125 mg/m², ifosfamide 1500 mg/m² plus adriamycin at 50 mg/m² for 4 cycles or the same regimen plus regional hyperthermia at 42°C for 60 min on days 1 and 4 as induction therapy. Baseline and disease characteristics, including concomitant local surgical and/or radiotherapy interventions were well balanced between study

arms. The primary endpoint of the study was locoregional progression-free survival (LPFS) and secondary endpoints included treatment safety, response, disease-free survival (DFS), and overall survival (OS).

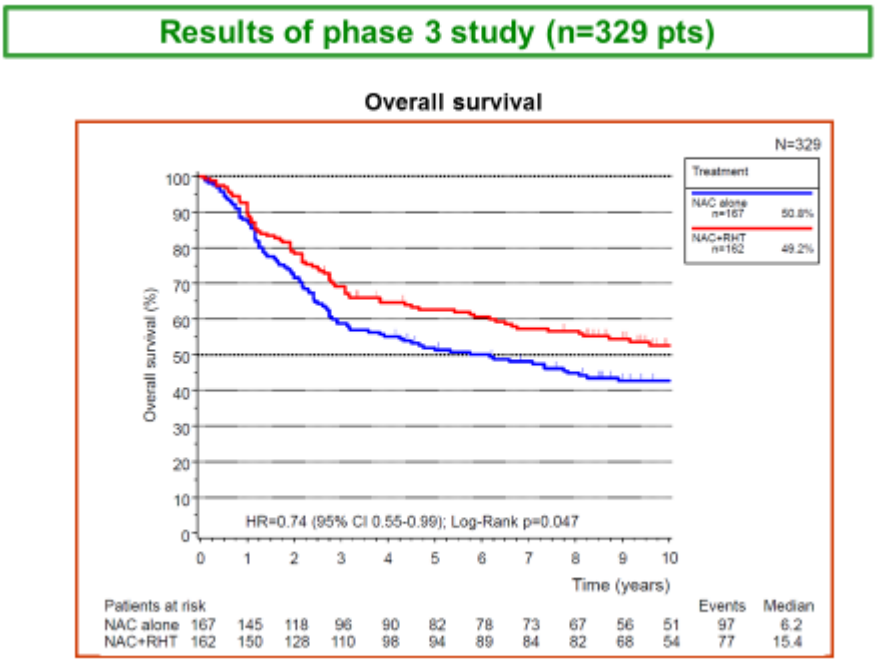
The analysis done after a median follow-up of 74 months on the intent to treat population of 167 patients treated with neoadjuvant chemotherapy versus 162 patients treated with neoadjuvant chemotherapy plus regional hyperthermia showed LPFS rates of 40% versus 51%, and DFS of 34% versus 42%, respectively, HR 0.72; 95% CI 0.55, 0.94 (log rank p = 0.016). The OS analysis also favoured the adjunct hyperthermia arm: Median OS was 15.4 years for patients receiving regional hyperthermia versus 6.2 years for patients receiving only neoadjuvant chemotherapy. At the 5-year follow-up, the OS rate was 63% (95% CI 55%, 70%) versus 51% (95% CI 43%, 59%) in the respective arms and OS was significantly prolonged with regional hyperthermia compared with sole chemotherapy, HR 0.74; 95% CI 0.55, 0.99 (log rank p = 0.047).



Caption: *EORTC 62961/ESHO – Study flow*

Credit: Rolf Issels

By December 2014, 221 (67%) patients overall had relapsed and 174 (53%) had died. After 9 years of follow-up, OS rates of 54% (95% CI 46%, 62%) compared to 43% (95% CI 35%, 50%) were demonstrated in the hyperthermia arm compared to the adjuvant chemotherapy arm, respectively. LPFS also was also significantly higher in the hyperthermia arm compared to the adjuvant chemotherapy arm; HR 0.71; 95% CI 0.54, 0.93 (log rank p = 0.012). The toxicity profile was consistent with prior experience of neoadjuvant chemotherapy and hyperthermia; no unexpected or new safety findings were reported. The authors suggest that the beneficial effects on survival might be linked to the known heat shock related immune effects induced by hyperthermia. EORTC 62961/ESHO, NCT00003052. Issels *et al.* Abstract 13LBA.



Caption: *EORTC 62961/ESHO – Overall survival*

Credit: Rolf Issels

Practice point and future research opportunities

This was a positive trial that met the primary endpoint, locoregional progression-free survival, and demonstrated significantly improved overall survival, in a high-risk population. While confirmation is

warranted, these findings support adding regional hyperthermia to standard neoadjuvant chemotherapy in patients with localised high-risk soft tissue sarcoma.

A French nationwide survey shows improved key parametres after incorporating two expert networks for desmoid tumour management

Nicolas Penel, Oscar Lambret Centre, Lille, France, presented findings showing that the founding of 2 expert networks for desmoid tumour improved the diagnosis and management modalities of a very rare tumour at a national level. He described how the French National Cancer Institute and Patient advocacy Groupe (SOS Desmoide) had supported the labeling of 2 expert networks in 2009: one was the RRePS, which comprised a network of expert pathologists to systematically confirm every suspected case of desmoid tumour, and NetSarc, a network gathering centre with expertise in adult sarcoma and desmoid tumour management. This study analysed the diagnosis modalities from of 903 successive cases from 2010 to 2013 to evaluate the activities of both networks by prospectively collecting data using a nationwide database.

Out of a total of 903 patients identified during this interval, 846 were aged ≥18 years and were eligible for management by NetSarc. Of these, 414 (48.9%) patients were treated by the NetSarc organisation; this rate of patients managed within the network has constantly increased since 2010, from 36.95% to 50.0%. Furthermore, the median time to management by NetSarc centres has decreased from 440 to 67 days ($p < 0.0005$). The predictive factors associated with management by NetSarc centres that emerged were being female, 50.0% women compared with 41.2% men ($p = 0.0016$), and having a soft tissue rather than visceral desmoid tumour (50.8% versus 37.6%; $p = 0.02$). Patients treated within NetSarc were also younger at mean 44 versus 48 years ($p = 0.005$). However, the analysis revealed that management within NetSarc was not related to tumour size or beta-catenin mutational status.

This analysis also revealed that key-indicators of the RRePS constantly improved from 2010 to 2013, as reflected in the number of confirmed cases, which rose from 173 to 273, and the rate of cases diagnosed with microbiopsies, which rose from 30.6% to 40.7%. Additionally, the rate of analysis done on the beta-catenin mutational status increased from 87.8% to 94.0%. Another key indicator, the mean delay for pathological diagnosis confirmation from the date of first biopsy/surgery was seen to consistently decrease over this time from 107 to 47 days. The authors plan a prospective analysis of the impact of these networks upon patient outcome. Penel *et al.* Abstract 3400.

Practice point and future research opportunities

Management of rare tumours, including diagnosis confirmation and prompt management in referral centers remains a public health challenge; however this survey demonstrates how both expert networks improved the overall confirmation of cases, and other indicators, such as time to pathological diagnosis.

RELATED INFORMATION

Click here to access Congress details and programme.

Click here to access the Congress webcast page.

AFFILIATION AND DISCLOSURE

Affiliation

Dr Svetlana Jezdic, ESMO Head Office.

Disclosure

No conflicts of interest to disclose.

ACKNOWLEDGMENT

ESMO would like to thank Virginia Powers, PhD for editorial assistance in preparation of the report.

ESMO would like to thank Drs Jeffrey Ross, Siraj Ali, Christoph Zielinski, Eva Segalov, Toni Choueiri, Richard Cathomas, Paul Nghiem, James Yao, Grant McArthur, and Rolf Issels for giving their permission to publish images from the studies presented during the ECC 2015 in the ESMO media channels.