

Young patients with metastatic colorectal cancer are at high risk of disease progression and death

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Younger patients with colorectal cancer that has spread (metastasised) to other parts of the body represent a high-risk group that is less likely to respond to anti-cancer treatments. Their disease is more likely to progress and they are at greater risk of death than other age groups, according to new research to be presented to the 2013 European Cancer Congress (ECC2013) [1] on Sunday.

An analysis of 20,034 [patients](#) in 24 phase III [clinical trials](#) [2] for colorectal [cancer](#), of which 695 patients (3%) were younger than 40, showed that the youngest and oldest patients had the highest risk of their disease progressing and of dying, compared to middle-aged patients. When compared to 57-year-olds, the youngest patients had a 30% increased risk of dying from the disease, and, when compared to 61-year-olds, they had a 28% increased risk of their disease progressing and metastasising during the first year of follow-up after randomisation and the start of treatment. The oldest patients had a 72% increased risk of death and a 19% increased risk of their disease metastasising compared to the 57 and 61-year-olds during the follow-up period.

Dr Christopher Lieu, MD, an assistant professor at the University of Colorado (USA), will tell the congress: "Although colorectal cancer occurs in only 4.6% of patients who are younger than 50, the incidence of the disease has been increasing at a rate of 1.5% per year from 1992 to 2005 in this age group. The most dramatic increases have been

observed in the 20-29 year-old group, where there has been an annual 5.2% increase in cases in men and a 5.6% increase in women, and in the 30-39 year-old group, where there has been an annual 3% increase in men and a 2% increase in women. [3]

"The reasons why the incidence is increasing in younger patients remain unknown, although [genetic predisposition](#), [environmental factors](#), fewer early cancer detections in this population, or a combination of these factors are thought to play a role. We carried out this study to see whether age was associated with time until cancer progresses or the patient dies. We also wanted to get a better picture of the age-response relationship and identify how risk changes as people age, rather than simply comparing one group (patients younger than 40) with another group (patients older than 40)."

Previous studies in this field have split the population into two mutually exclusive groups, establishing rigid limits between those patients younger than 40 or 50 and those older than that age. The new research, however, did not use such a cut-off approach and it includes data spanning all ages. "The reason why we did this is because we believe that a 49-year-old patient with colorectal cancer may be different than a 20-year-old. By including them in the same group of people younger than 50 years old we might be mistakenly considering them to be the same," Dr Lieu will explain.

Dr Lieu and his colleagues analysed information from a database of clinical trials in advanced colorectal cancer supported by the French "Aide et Recherche en Cancérologie Digestive" Foundation (ARCAD), which includes the 20,034 patients from 24 phase III clinical trials who were on their first treatment for the disease, plus additional patient data from other trials in which patients might be on second or third lines of different treatments, having not responded to their initial therapy.

Out of these patients, 20,011 were evaluable for analysis of survival time and time until the disease progressed. Dr Lieu will say: "Analysis of this incredibly large population of patients has allowed us to answer meaningful questions, such as the outcomes of young versus older patients. Our results show that young age is associated with worse overall survival and progression-free survival. Young patients with metastatic colorectal cancer represent a group who are at high risk for treatment failure."

Despite the comprehensive nature of the study, more research will be required to identify why colorectal cancer in younger people appears to be more aggressive. "Further studies identifying biological differences are warranted," says Dr Lieu. He and his group are currently collaborating along these lines with a research group at the University of Texas MD Anderson Cancer Center (Texas, USA).

ECCO President, Professor Cornelis van de Velde, commented: "While colorectal cancer overwhelmingly occurs in older people, we must not forget that people younger than 50 can develop it too. The study by Lieu and his colleagues is important as it shows that these younger patients may have a worse prognosis if their disease has metastasised. Doctors and patients need to be aware of this so that they are alert to the early symptoms of colorectal cancer, and treatment can be given before the disease has started to spread."

ESMO spokesperson, Professor Erika Martinelli, Assistant Professor in Medical Oncology at Seconda Università Studi di Napoli Policlinico Federico II, Naples, Italy, commented: "Considerable controversy exists concerning the outcome of younger patients with colorectal cancer and it is a critical topic because the incidence of this cancer is increasing in the younger [population](#). Dr Lieu and his colleagues have contributed important scientific evidence from a worldwide collaboration of clinicians and scientists specialising in gastrointestinal cancer, and they

have confirmed that patients younger than 40 have a worse prognosis. These patients have poor overall survival and progression-free survival, and this was not influenced by sex or performance status.

"The conclusions are intriguing because the study has been performed on a large case series of patients (the ARCAD database is one of the largest in gastrointestinal oncology), reinforcing the concept that younger people diagnosed with colorectal cancer survive less well, in spite of being in better overall condition and with fewer other medical problems.

"This evaluation of the prognostic significance of age needs further analysis aimed at identifying any biological characteristics or markers that make the cancer disease of young people more aggressive and less responsive to drugs."

More information: [1] The 2013 European Cancer Congress is the 17th congress of the European Cancer Organisation (ECCO), the 38th congress of the European Society for Medical Oncology (ESMO) and the 32nd congress of European Society for Therapeutic Radiology and Oncology (ESTRO).

[2] All figures correspond to patients' outcome within one year of initiating first-line – the initial – treatment in phase III clinical trials. These trials are designed to assess the effectiveness of medical treatments and their value in clinical practice.

[3] Based on a Surveillance, Epidemiology and End Results (SEER) programme review (National Cancer Institute) of trends in colon cancer from 1992 to 2005 (Cancer Epidemiology, Biomarkers & Prevention. 2009; 18:1695-98).

[4] This study received external funding from the Cancer League of Colorado, USA.

Abstract no: 2158, "The impact of young age on survival in patients with metastatic colorectal cancer: analysis from the ARCAD Clinical Trials Program". Gastrointestinal malignancies – colorectal cancer II proffered papers session, 09.00 hrs CEST, Sunday 29 September 2013, RAI Auditorium.

Provided by ECCO-the European CanCer Organisation

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