Cetuximab Fails to Extend OS in Locally Advanced Esophageal Cancer

Written by Emma Hitt Nichols, PhD

Cetuximab plus chemotherapy and radiation therapy does not improve clinical complete response (cCR) rates or overall survival (OS) in patients with locally advanced esophageal cancer. David H. Ilson, MD, PhD, Memorial Sloan-Kettering Cancer Center, New York, New York, USA, presented data from the Paclitaxel, Cisplatin, and Radiation Therapy With or Without Cetuximab in Treating Patients With Locally Advanced Esophageal Cancer trial [RTOG 0436; Ilson D et al. *Ann Oncol* 2014 (abstr O-0005)].

Cetuximab is a monoclonal antibody that blocks the EGFR and inhibits tumor growth by preventing blood flow to the tumor. The purpose of the RTOG 0436 trial was to determine if the addition of cetuximab to paclitaxel and cisplatin plus radiation therapy would improve outcomes in patients with locally advanced esophageal cancer.

In the Phase 3 RTOG 0436 trial, 328 patients with adenocarcinoma or squamous cell carcinoma of the esophagus were randomly assigned to receive paclitaxel plus cisplatin and radiation (50.4 Gy/1.8 Gy fractions) with or without cetuximab. Patients were eligible if their endoscopic ultrasound (EUS) stage was T1N1M0, T2 to T4 any N M0, or any T or N M1a, and patients were stratified by histology, tumor size, and the presence of celiac lymph nodes. The primary end point of the RTOG 0436 trial was OS. Baseline characteristics were similar among treatment arms, with T3/4 disease present in 80% of patients, N1 in 66%, and celiac lymph nodes in 19%.

During the median follow-up period of 15.4 months, cCR rates were similar between both treatment arms ($p = .72$), regardless of stratification by histology. In patients who achieved cCR, the 12- and 24-m OS rates were, respectively, 79% and 58% compared with 53% and 30% in patients with residual disease ($p < .0001$); however, there was no significant difference between treatment arms.

Dr. Ilson stated that, in his opinion, the data from the RTOG 0436 trial indicated that the addition of cetuximab to concurrent chemotherapy and radiation therapy does not improve cCR rates or prolong OS in patients with esophageal cancer, regardless of histology. Therefore, the data from this trial suggest that there is currently no evidence for the use of EGFR-targeted therapies in addition to concurrent chemotherapy and radiation therapy for the treatment of esophageal cancer.

High Fatty Acids and Low Fiber Intake Is Associated With CRC

Written by Lynne Lederman

Various dietary elements have been linked to the development of colorectal cancer (CRC). It is not known, however, if or how dietary fat components (eg fatty acids) contribute to this disease. In addition, factors like blood lipids could affect how dietary fats contribute to the development of CRC [Kato I et al. *Int J Cancer* 2010; Endo H et al. *Gut* 2009].

Bledar Kraja, MD, PhD, Erasmus Medical Center, Rotterdam, The Netherlands, presented the use of data from the Rotterdam Study to determine whether intake of polyunsaturated fatty acids (PUFAs) and saturated fatty acids (SFAs) is associated with CRC and whether it is affected by levels of dietary fiber or blood lipids [Kraja B et al. *Ann Oncol* 2014 (abstr O-0013)].

The Rotterdam Study, a single-center, population-based, prospective cohort study that enrolled 7983 adults aged ≥ 55 years in a suburb of Rotterdam, The Netherlands, examined the incidence of, prevalence of, and risk factors for chronic disease in the elderly with the objective of improved prevention and treatment. Researchers obtained baseline measurements from 1990 to 1993, and follow-up measurements every 2 to 3 years for the original cohort. In 2000, 3011 subjects aged ≥ 55 years were added; in 2006, 3932 subjects aged ≥ 45 years were added. All subjects are reexamined every 3 to 4 years. The total Rotterdam Study population includes 14,926 participants [Hofman A et al. *Eur J Epidemiol* 2013]. The cohorts and examination cycles are shown in Figure 1.

Dr. Kraja's group looked at data from 4902 subjects aged ≥ 55 years from the first cohort of the Rotterdam Study. Diet was determined by a food frequency questionnaire. CRC was classified using the 10th edition of the International Classification of Diseases. Cox regression models were used to calculate multivariable adjusted hazard ratios (HRs).

Incident cases of CRC ($n = 218$) were identified during a follow-up of 24 years. No evidence of an association between PUFAs intake and CRC was seen. A positive linear relationship was evident, however, between SFAs intake and CRC (HR, 1.02; 95% CI, 1.01 to 1.03). In participants with high dietary-fiber intake (> median), PUFAs intake was associated with an increased risk of CRC (HR, 2.12; 95% CI, 1.04 to 4.29 for the 4th quartile vs the 1st quartile). Among those participants with low fiber intake (< median), SFAs intake was associated with higher CRC risk (HR, 1.52; 95% CI, 1.12 to –2.06 for the 4th quartile vs the 1st quartile). In contrast, a negative