Chairperson's introduction

Cornelis J.H. van de Velde

Professor of Surgery, Leiden University Medical Center, Leiden, The Netherlands

An estimated 1.4 million new cases of colorectal cancer occur each year worldwide, with a poor survival of only 55% of patients alive five years after diagnosis. Patients die mainly from metastatic disease. Survival of patients with metastatic colorectal cancer has dramatically improved over the last decade. Both opportunities for surgery and the efficacy of chemotherapy have improved so that 20 years ago overall survival with best supportive care was less than six months with limited indications for surgery, whereas currently, with modern regimens, overall median survival of over 20 months is demonstrated alongside better understanding of tumour biology and the development of biological therapies. The paper by Cees Verhoef and colleagues [1] discusses the role of surgery of the primary in stage IV colorectal cancer. Non-randomised studies favour resection of the primary tumour, but are subject to case selection. Obviously, the role of surgery in symptomatic patients is a prominent one as opposed to in asymptomatic patients, and its effect on the quality of life is profound. The definition of unresectable metastatic disease has changed over the years as evidence from the liver metastases registry indicates more than 15% five-year survival and clearly an initially unresectable stage for the disease. Trials in both colon and rectal cancer are now underway. Also, in two phase III studies (CAIRO I and CAIRO II) resection of the primary was a strong prognostic factor for survival. Therefore, there is a clear need for randomised trials, although the evidence is accumulating that an aggressive approach, if carried out with acceptable morbidity and low mortality, is worthwhile. Gunnar Folprecht [2] discusses the need for neoadjuvant treatment. FOLFOX was established in the EORTC 40983 trial, but FOLFOXIRI as well as Cetuximab + doublet have shown a high response rate and increased resection rates compared with the control arms. Re-evaluation for resectability should be performed at least at three and six months and resection should be performed as soon as resectability is shown; complete remission should not be awaited. Different studies are discussed as well as the limited relevance of microscopic complete response. Since neoadjuvant treatment increases perioperative morbidity in resectable metastases the need is not established. Isolated liver perfusion and intra-arterial regimens have clearly decreased in popularity as a result of better drugs and less complex systemic combination therapy.

Aimery de Gramont [3] rechallenges the concept of lines of therapy in metastatic colorectal cancer. He discusses cumulative toxicity, for instance, withdrawing oxaliplatin because of neuropathy and reintroducing it later at a fixed interval or at tumour progression. First-, second- and third-line therapies are described, indicating that the most active doublets appeared to be the cornerstone of chemotherapy, followed by the stop and go strategy and complete termination of the chemotherapeutic strategy. Subsequently, the role of targeted therapy is maintenance without chemotherapy. The ultimate goal is to achieve a 30-month median ultimate survival, which after the improvements over the last decade seems a realistic achievement in the coming decade. Finally, as a result of this improved survival Timothy Maughan [4] of Oxford University discusses the selective use of chemotherapy, sequential therapy and a chemotherapy-free interval, especially in patients with a low tumour burden and/or slow growing disease. Identification of *KRAS* and *BRAF* mutations is now undertaken routinely in patients with colorectal cancer to identify patients for treatment with EGFR-targeted monoclonal antibodies. In the largest trial in metastatic cancer, the COIN trial, the overall survival differs markedly by mutation status irrespective of treatment received. The requirement of the oncologist is to have a patient-centric perspective, varying management from standard paradigms to meet the patients' needs.

With these expert views this chapter will provide readers with an overview and clues in the jungle of treatments for advanced colorectal cancer where no guidelines are or will be available.

Conflict of interest statement

The author has no conflict of interest to report.

References

1 Verhoef C, de Wilt JH, Burger JWA, Verheul HMW, Koopman M. Surgery of the primary in stage IV colorectal cancer with unresectable metastases. *Eur J Cancer* 2011;**47**(Suppl 3):S61–6.
2 Folprecht G. Neoadjuvant chemotherapy for non-/resectable metastases. *Eur J Cancer* 2011;**47**(Suppl 3):S52–60.
3 de Gramont A. Re-challenge and the concept of lines of therapy in metastatic colorectal cancer. *Eur J Cancer* 2011;**47**(Suppl 3): S76–84.
4 Maughan TS. The treatment of patients with low tumour burden and/or slow growing disease. *Eur J Cancer* 2011;**47**(Suppl 3): S67–75.