Chairperson's Introduction

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The systemic treatment of advanced colorectal cancer is based upon four chemotherapeutic agents (fluoropyrimidines, oxaliplatin, irinotecan and mitomycin) and three biologic agents (bevacizumab, cetuximab and panitumumab).

The median survival of patients treated in phase III and IV clinical trials is around 2 years with a certain, small percentage of them being able to undergo surgical resection of metastatic disease, leading to long-term disease-free survival.

In most cases requiring treatment right away, the first decision is whether to start with a doublet plus a biologic or with single agent fluoropyrimidine (plus or minus biologics). Potentially resectable cases, along with those with high tumour bulk, rapid clinical course and the presence of tumour-related symptoms, call for the aggressive approach. In all other cases where the quality of life is good with no symptoms, and low tumour bulk at different organ sites, the staged approach of starting "light touch" chemotherapy, and using the doublets upon progression, has been demonstrated to produce no detrimental effect on survival.

The majority of patients receive 2–3 lines of therapy. FOLFOX or XELOX or FOLFIRI plus bevacizumab are the most widely used first-line combinations. The alternative doublet is used in second line treatment. In K-RAS wild type tumours, cetuximab and panitumumab have been demonstrated to prolong life in third-line treatment and beyond. In particular cases, cetuximab may be used along with the doublets in first-line therapy. Unexpectedly, the biologic doublets (bevacizumab + cetuximab or panitumumab) produce detrimental results, thus they should be used in sequence, not together.

The availability of seven drugs and the extension of survival from 6 months (untreated stage IV) to 24 months generate a series of challenges that will be discussed at this session. These include the choice of the biologic for first-line treatment, the choice of the best companion chemotherapy, the search for determinants of activity and resistance to both chemotherapy and biologics, the duration of initial treatment, the continuation of aggressive chemotherapy after an initial aggressive induction, the maintenance treatment with fluoropyrimidines and/or biologics, drug holiday periods, re-challenge with previously used agents along with the definition of "line of treatment". Finally, a separate article will be dedicated to novel agents that are in early or late clinical development and are likely to soon change our paradigm of treatment of this disease where medical oncology has already been so successful in the last 20 years.

Conflict of interest statement

Honoraria from and advisor to Roche, Merck Serono, Bayer, AstraZeneca, Amgen, Sanofi-aventis.