Second-Line Strategies in the Treatment of Patients With Metastatic Colorectal Cancer

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Summary

Given the number of active drugs and combinations available, the choice of second-line therapy in metastatic colorectal cancer can be complicated. It is influenced by many factors, such as the nature of the first-line therapy, the potential toxicity of one regimen vs another, and the overall goal of treatment for the patient. In this chapter, we focus our discussion on the therapeutic strategies that can be used in the treatment of colorectal cancer after the failure of first-line therapy.

Key Words: Chemotherapy; oxaliplatin; irinotecan; cetuximab.

1. INTRODUCTION

The multitude of effective cytotoxic and targeted agents given in different combinations has brought new hope to patients and significant challenges to the treating oncologist (1–8). The sequencing of the different combinations and the incorporation of the targeted agents have to be done in a rational manner that provides the highest efficacy and least toxicity. For this purpose, treating oncologists find themselves faced with the task of assimilating a large body of data and trying to formulate a treatment approach that best suits the patient and allows him or her the benefit of exposure to all or most of the active compounds.

In this chapter, we will focus our discussion on the therapeutic strategies that can be used in the treatment of metastatic colorectal cancer (CRC) after the failure of first-line therapy. Given the number of active drugs and combinations available, the choice of second-line therapy can be complicated, because it is
influenced by many factors such as the nature of the first-line therapy, the potential toxicity of one regimen vs another, and the overall goal of treatment for the patient.

2. OVERVIEW OF SECOND-LINE THERAPEUTIC OPTIONS AFTER FAILURE OF A FRONT-LINE IRINOTECAN-BASED COMBINATION

The most common irinotecan-based combinations used in the first-line treatment of patients with metastatic CRC include infusional 5-FU and leucovorin (LV) with irinotecan (FOLFIRI) or FOLFIRI with bevacizumab (BV). Several second-line treatment options exist in case of failure of FOLFIRI or FOLFIRI/BV. As we review the data related to these options, we will highlight the factors that may favor one over another (Fig. 1).

2.1. FOLFOX

Prior to the incorporation of BV in the first-line treatment of metastatic CRC, Tournigand had shown that the sequence of FOLFIRI followed by 5-FU/LV/oxaliplatin (FOLFOX) was equivalent to FOLFOX followed by FOLFIRI. Both sequences resulted in an overall survival of 21 mo. Specifically, after progression of disease on FOLFIRI, FOLFOX had a response rate of 15% and a progression-free survival (PFS) of 4.2 mo (9). The sequence of FOLFIRI followed by FOLFOX or vice versa is not commonly used anymore given the

Fig. 1. Potential second- and third-line therapies after failure of an innotecan-based regimen. (This sequence, which excludes bevacizumab, may be most appropriate for a patient with contraindications to BV such as a recent myocardial infarction or cerebrovascular accident.)