Best Practice & Research Clinical Gastroenterology 30 (2016) 529–535

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology

2

Chemotherapeutic agents for GI tumor chemoradiotherapy overview of chemotherapeutic agents to be combined with radiotherapy in the GI tract and their potential as radiosensitizers

PD Dr. med. G. Klautke*, Dr. med. K. Müller

Clinic for Radiation Oncology, Chemnitz Medical Center, Germany

Keywords:
Chemoradiotherapy
Radiosensitizers
Mechanism of radiation-intensifying
Gastrointestinal tumors

A B S T R A C T

In the treatment of gastrointestinal tumors, simultaneous radiochemotherapy plays an important role. It is one of the principles of simultaneous radiochemotherapy, applying only chemotherapeutic agents simultaneously to radiation, which are primarily effective in the treated tumor entity, therefore a lot of different agents, like antimetabolites, mostly 5-fluorouracil, platinum derivates (mostly cisplatinum and oxaliplatin), mitomycin C and taxanes are used in simultaneous radiochemotherapy. Most of these have also radiation-intensifying effects. The mechanisms and interactions with ionizing radiation are presented in the article.

Introduction

In the treatment of gastrointestinal tumors, simultaneous chemoradiotherapy plays an important role in neoadjuvant, adjuvant, or definitive treatment approaches. In the definitive treatment situation, chemoradiation is a therapeutic strategy of healing without surgery, but a better functional treatment outcome for the patient. In the neoadjuvant situation, the goal is not downsizing but also a real downstaging or ideally a complete remission, which ultimately improves the prognosis of patients

* Corresponding author.
E-mail address: G.Klautke@skc.de (G. Klautke).

http://dx.doi.org/10.1016/j.bpg.2016.07.001
1521-6918/

significantly. Since radiation dose cannot be increased so easily, the combination partner "chemotherapy" plays a more important role. When in the early 90s only 5-Fu and cisplatin (and possibly also mitomycin C) were the most frequently used substances simultaneously to radiation, the spectrum of possible combination partners has significantly expanded in recent years. Nearly all modern chemotherapeutic agents are used together with radiation. It has to be noted that there should no overlapping toxicities with irradiation expected, and that the chemotherapeutic schedules should have only a moderate hematotoxicity, because prophylactic administration (not therapeutic administration) of growth factors during radiotherapy is contraindicated. Therefore, usually only schedules with two chemotherapeutic agents are used in chemoradiation.

Chemotherapeutic agents in combination with radiation in gastrointestinal tumors

Overview of used chemotherapeutic agents

The combination of 5-Fu and cisplatin or carboplatin was certainly deemed to be the standard for esophageal cancer and tumors of the gastroesophageal junction. No later than since the so-called CROSS study [1], the combination of paclitaxel and carboplatin can also be seen as a possible standard. The current S3 guideline for esophageal cancer also invokes the FOLFOX regimen as a possible simultaneous partner to radiation therapy, although many in practice dispense with folinic acid alongside radiation for toxicity reasons. Less known, but certainly of interest in some cases, is a combination of vinorelbine/cisplatin, which in a matched case control study could show a complete remission rate twice as high as 5-Fu/Cis as part of neoadjuvant chemoradiotherapy [2].

As a rule, there is no adjuvant or postoperative chemoradiation for pancreatic cancer in Europe, other than clinical studies that follow the neoadjuvant approach. Those studies mostly use gemcitabine mono or combined with cisplatin simultaneously with radiation. Valid data for the combination with nab-paclitaxel as part of chemoradiotherapy are not yet known. Perhaps capecitabine is also a useful drug in combination with radiotherapy as demonstrated by the SCALOP trial [3] in the treatment of pancreatic cancer.

Specific adjuvant therapy of bile duct or gallbladder cancer using chemoradiation is not standard therapy, although retrospective analyses definitely indicate considerable survival benefits from chemoradiation for patients with affected lymph nodes [4]. This therapy is mostly platinum-based as well (cisplatin or oxaliplatin).

Chemoradiotherapy for rectal cancer is 5-Fu-based or uses equivalent oral 5-Fu prodrugs, primarily capecitabine and ftorafur (UFT) as well, if necessary. In the neoadjuvant situation, there are sound

Table 1
Overview of used chemotherapeutic schedules in combination with radiation.

Tumor entity	Possible chemotherapeutic combinations concurrent with radiation
Esophageal cancer	5-Fu + Cis or Carbo
	Pac + Carbo
	FOLFOX
Pancreatic cancer	Gem
	Gem + Cis
	Cap
Gallbladder cancer	Gem
	5-Fu + Cis or Carbo
	5-Fu + Ox
Rectal cancer	5-Fu or Cap
	5-Fu (Cap) + Ox
	5-Fu (Cap) + Iri
Anal cancer	5-Fu + Mito C
	5-Fu + Cis

5-Fu = 5-fluorouracil; Cis = Cisplatin; Carbo = Carboplatin; Pac = Paclitaxel; Gem = Gemcitabine; Cap = Capecitabine; Iri = Irinotecan; Mito C = Mitomycin C.