CHAPTER 4
Methods Used in Neoadjuvant Treatment

CHEMOTHERAPEUTIC AGENTS

5-Fluorouracil

The most traditional neoadjuvant regimens have been based on fluoropyrimidines such as 5-Fluorouracil (5-FU). This drug can be administered in 2 ways, bolus or continuous infusion and is usually associated with leucovorin (LV), an analog of folic acid that is used as a modulator to reduce adverse effects.

The usual dose of 5-FU is 225 mg / m2 / day, for 5 days a week. There are retrospective data that justify the preference of 5-FU infusion over bolus administration, since it has shown a greater probability of achieving pathologic complete response (pCR).[153] However, the evidence for the advantages of infusion over bolus is stronger in the adjuvant setting.

Capecitabine

Capecitabine, an oral fluoropyrimidine, at a dose of 825mg / m2 twice a day for 5 days a week, has shown results comparable to those of 5-FU and even fewer metastases after a period of 52 months.[95] However, the pattern of toxicity is somewhat different, with a higher percentage of proctitis and skin involvement of the hands and feet, but also fewer cases of leukopenia with capecitabine.

Oxaliplatin

Although the association of oxaliplatin with 5-FU has been shown to be superior for stage III colon cancer in the adjuvant setting and is in fact currently considered the standard of treatment, its use in neoadjuvant treatment is not yet recommended outside of a clinical trial. A meta-analysis that included 5599 patients from ten randomized clinical trials showed that the addition of oxaliplatin significantly increased the rate of pCR and reduced the risk of metastasis, but did not impact survival or local relapses, with a significant increase in the rate of grade 3 and 4 toxicity.[102]

Irinotecan

Irinotecan has been analyzed in some non-randomized studies with apparent benefits, but only one randomized clinical trial is known, which included only 106 patients randomized to receive a 5-FU infusion with or without irinotecan and two different RT regimens.[152] No differences were observed in either pCR rate or toxicity. It is not recommended outside of a clinical trial at this time.

Monoclonal antibodies

To date, there are no phase III studies evaluating these drugs in the neoadjuvant context.

Radiotherapy techniques

The choice of radiotherapy technique in pelvic tumors is of great importance to reduce toxic effects, since the anterior pelvic structures are rarely compromised, and it is also important to protect intestinal loops that could be located in the field to be irradiated. That is why 4-field techniques are preferred over 2-field irradiation, adding lateral beams that avoid delivering high doses on the mentioned anatomical structures. The incorporation of images into planning and at the time of application has been a very important contribution. Thus, today new external radiotherapy modalities are known for this type of cancer

- 3D conformal radiation therapy (3D-CRT) is a variant that delivers radiation beams from different directions, designed to match the shape of the tumor. This helps limit radiation damage to healthy tissues and better eliminate cancer by focusing the radiation dose on the exact size and shape of the lesion.
- Image-guided radiation therapy is a form of 3D-CRT, in which an image (such as a CT scan) is taken before each treatment. This allows the radiation therapist to adjust the patient's position or refocus the radiation as needed to ensure that the radiation beams are focused exactly on the tumor and that exposure to normal tissues is limited.
- Intensity modulated radiation therapy (IMRT) is similar to 3D-CRT, but it also changes the strength of some of the beams in certain areas. This allows stronger doses to be delivered to certain parts of the tumor and helps reduce damage to nearby organs.

In long-course RT, the recommended doses are usually 45 to 54 Gy in 25 to 30 fractions, usually 1.8 Gy using 3 or 4 fields extending to the mesorectum, presacral region and the lymph nodes along the internal iliac artery and the obturator region. In short-course RT the usual dose is 25 Gy administered in 5 fractions of 5 Gy over 1 week.