CHAPTER 20
Conclusions

- Neoadjuvant therapy has been definitively installed as a therapeutic strategy based on its obvious benefits, which far outweigh the eventual risk of overtreatment. However, neither pelvic RT nor ChT are free of complications, so overindication should be avoided to minimize the consequences of unnecessary therapies.
- Although TME alone had significantly improved rectal cancer treatment outcomes, the addition of RT in selected cases provides an additional benefit.
- Downstaging depends more on the waiting time than on the type of RT regimen chosen (short or long-course).
- TNT increases response, favors adherence to ChT and reduces toxicity, but definitive data on its benefits in terms of survival are still lacking. Consolidation TNT allows an even higher response rate than that achieved with induction ChT.
- When the goal of TNT is to treat micrometastatic disease in high-risk patients, induction ChT could be the preferred option in order not to delay the start of systemic treatment, since no definitive advantages have been demonstrated with ChT consolidation in terms of survival.
- When what is sought is only to preserve the organ or the sphincter, it is more reasonable to start with RT or CRT, evaluate clinical response and, if it is evident but not complete, opt for consolidation ChT. In this way, it will be avoided to administer and expose the risk of ChT to patients who probably never require it.
- Short-course RT followed by consolidation TNT has all the advantages, since it practically does not delay the onset of systemic ChT and achieves very high response rates. For these reasons it appears as an ideal option and is increasingly being considered.
- Neoadjuvant treatment with ChT and without RT cannot be recommended outside of a research protocol.
- There are a growing number of studies supporting the positive impact of IDT meetings on the oncological outcome of the treatment of patients with rectal cancer.
- Given the risk of understaging mesorectal lymph nodes, neoadjuvant treatment may be considered prudent in tumors with cT3N0 staging.
- Other tumor-related findings that should prompt the IDT to evaluate the neoadjuvant indication are:
    - CRM involvement.
    - Suspicious mesorectal lymph nodes.
    - EMVI +.
    - Suspicious LLN.
    - The indication of APR.
    - To avoid a coloanal anastomosis (high-risk patient or pacient refusal).
- HR-MRI is the essential study in clinical staging prior to any rectal cancer treatment, especially in locally advanced tumors.
- Pathologists play a critical role, not only in microscopic evaluation, but also in the proper handling of macroscopic specimens. The neoadjuvant response scores open an interesting line of research in the definition of management after the end of treatment.
- ERUS should not be considered to assess the response to preoperative RT or CRT in order to define management. HR-MRI is the best imaging method available in this setting, but it must be complemented by digital rectal examination and endoscopy, all of which must be performed serially.
- Specifically, current guidelines, both European (ESMO) and American (NCCN), recommend a very wide waiting range (4 to 12 weeks for ESMO and 5 to 12 weeks for NCCN) after completing CRT, to define surgical strategy. This period is valid after short-term regimens in which immediate surgery is also indicated.
- It should be taken into account that cCR does not imply pCR, but rather the latter can occur in cases in which there was an impression of residual tumor both clinically and on imaging. Biopsies are not helpful and the possibility of mesorectal disease should not be overlooked. Confirming the existence of a pCR continues to be one of the IDT's biggest challenges.
- Although there is no definitive evidence, in specific cases properly studied with quality images, a change in the surgical strategy can be considered according to the response to neoadjuvant therapy.
- The current data do not favor TAE in the context of neoadjuvant treatment, since it is extremely difficult to establish with certainty, with the available studies, the level of rectal wall and mesorectum involvement.
- Although NOT is not a standard treatment, it is al-

ready considered in international guidelines and it must be accepted that a patient with cCR, after being duly informed, decide to be included in these protocols. It should be clear that NOT implies to postpone surgery for an indefinite period, which will last only while there is no evidence of tumor regrowth on control studies.
- There is still no universally adopted consensus on a standardized follow-up protocol for these patients.
- The response rate seems to correlate with prognosis. The greater the downstaging, the better the survival.
- Adjuvant therapy in the context of neoadjuvant treatment only seems useful in cases in which nodal disease persists, especially in ypN2. In general, it is not recommended for patients that achieved pCR.
- The decision to use oxaliplatin as adjuvant ChT should be based on yp staging, performance status, and the existence of comorbidities.
- In stage IV, the main objective is systemic control, so neoadjuvant treatment indications are contingent on this, since the initial focus is placed on ChT.
- Ovarian transposition should always be considered in the IDT when deciding to treat with RT a woman of childbearing age with wishes for childbirth.
- If RT has been decided in the IDT for a woman of childbearing age with a desire to have children, ovarian transposition should always be considered.