

Supplementary Methods S1

Pathological data:

Gross examination includes anatomic site, serosal surface or mesorectal completeness, tumor size, pattern of growth (exophytic, ulcerated, infiltrative, annular, diffuse), surgical margins including inked radial resection margin, lymph node dissection (≥ 14 lymph nodes), tumoral implants and other features as perforation, polyps, etc. Representative tissue sections are taken based on protocols (CAP).

Microscopic examination includes histologic type (WHO), histologic grade (for adenocarcinomas NOS G1 well differentiated > 95 gland formation, G2 moderately differentiated 50 to 95% gland formation, high grade $< 50\%$ of glandular differentiation). Mucinous differentiation ($> 50\%$ of extracellular mucin), tumoral invasion depth, surgical margins (deep and mucosal) including radial resection margin, lymphovascular invasion including intramural and extramural muscular veins, perineural infiltration, tumor infiltrating lymphocytes (none; mild to moderate 0-2/HPF and marked ≥ 3 /HPF), tumor budding (based on 0,785 mm² field area) defined as low 0-4 buds, intermediated 5-9 buds and high grade ≥ 10 buds, tumor infiltrating edge (infiltrative, expansive and medullary type), Crohn-like or medullary lymphoid pattern. Total lymph nodes, total metastatic lymph nodes, perinodal tumoral compromise and tumoral implants. Only for this study, mucin was cut-off at 30% instead of 50%.

In addition to the complete histopathological report that will allow define stage and prognosis, we seek for histologic features that are associated with molecular genetic alterations. In all cases, we also include (institutional protocol) histochemical stain for green-light orcein to evaluate muscular veins and immunohistochemical determination of MSI status. Since cases are recruited during a large period, a certificated pathologist reevaluated all of them.