

Cancer of the rectum

Y Bécouarn¹, MP Blanc-Vincent^{1,2}, M Ducreux³, P Lasser³, JB Dubois⁴, M Giovannini⁵ and P Rougier⁶

¹Institut Bergonié, Bordeaux; ²FNCLCC, Paris; ³Institut Gustave Roussy, Villejuif; ⁴Centre Val d'Aurelle Paul-Lamarque, Montpellier; ⁵Institut Paoli-Calmettes, Marseille; ⁶Hôpital Ambroise Paré, Boulogne, France

Primary carcinoma of the rectum accounts for approximately 40% of all colorectal carcinomas registered in France. The standardized incidence of rectal cancer is among the highest in the world at 17.2 per 100 000 males and 8.6 per 100 000 for women.

The anatomical situation of cancer of the rectum presents two particular problems: locoregional recurrence and sphincter preservation. Specialized, multidisciplinary patient management is therefore essential.

This document was validated in December 1998. An update is planned for the year 2001.

DIAGNOSIS

The diagnosis of a rectal cancer is made by histological examination of a fragment of tumour obtained by endoscopic biopsy (standard).

STAGING

Locoregional staging depends on three examinations that are cheap and possible in an outpatient setting: digital examination, rigid rectoscopy and endorectal ultrasonography (standard). The reliability of these examinations depends on the experience of the examiner. A pelvic CT scan (which has replaced intravenous urography) should be considered in the case of extensive disease, as should MRI for large, deeply situated tumours (options). Locoregional staging of a primary cancer of the rectum must be carried out by an experienced multidisciplinary team.

Distant spread is assessed by clinical examination, chest X-ray (AP and lateral), abdominal ultrasound and colonoscopy (standard). A CT scan of the liver can be undertaken if the ultrasound is not satisfactory (option). The measurement of carcino-embryonic antigen (CAE) levels is an option.

PROGNOSTIC FACTORS

The standard prognostic factors that enable a multidisciplinary therapeutic decision to be made are: the presence or absence of distant metastases, the type of rectal surgery undertaken (curative or palliative), the extent of infiltration of the bowel wall by tumour, invasion of adjacent organs by direct extension and the presence or absence of metastatic locoregional nodes.

Other prognostic factors can add to the therapeutic decision-making process. These include clinical factors such as presentation with acute bowel obstruction or perforation and pathological factors such as venous or lymphatic invasion, local neural involvement, the number of nodes examined and the number of metastatic nodes detected.

A minimum of eight nodes should be removed for histological examination (level of evidence C). Biological and genetic markers should only be measured if their prognostic value is being evaluated prospectively.

CLASSIFICATION

The most commonly used tumour classifications are postoperative and based on pathological findings, even though therapeutic decisions must be made before surgery. Therefore, prior to treatment, the TNM classification of the International Union Against Cancer (UICC), which includes information from staging endorectal ultrasonography is recommended. Following primary surgery, the UICC pTNM post-therapeutic classification system takes into account all the histopathological information on which further treatment can be based.

TREATMENT MODALITIES

Surgery

In order to obtain satisfactory tumour clearance, the safe margin between the lower end of the tumour and the rectal stump must be greater than or equal to 2 cm (standard). A minimum of 6–8 nodes should be examined (standard). Surgery with sphincter preservation (anterior resection or colo-anal anastomosis) is possible for upper third cancers and usually for cancers of the middle third of the rectum (option).

A radical resection (abdomino-perineal (A-P) resection) is usually required for tumours of the lower third of the rectum (option). If an A-P resection is undertaken, epiplooplasty to fill the perineal wound is recommended (level of evidence B). For tumours of the lower third of the rectum, or the middle third but palpable by digital examination, excision of the entire mesorectum reduces the risk of locoregional recurrence (level of evidence C). Patients with cancers of the lower third of the rectum should be included in surgical protocols evaluating sphincter preservation.

There is currently no indication for extensive pelvic nodal clearance with the aim of reducing the risk of tumour recurrence (level of evidence B). Procedures conserving the erector nerves, to try and improve a patient's quality of life, are not recommended, as an adverse effect on local tumour control has not yet been excluded (level of evidence B). In cases of colo-anal or colorectal anastomoses, the construction of a colonic pouch to replace the rectal reservoir improves the functional outcome for patients (level of evidence B).

After surgical resection, the pelvis should be packed. This reduces the risk of major complications for patients receiving post-operative irradiation by preventing the interposition of small

intestine (level of evidence B). Laparoscopic surgery is only recommended within prospective randomized studies.

Radiotherapy

Preoperative radiotherapy is indicated for T3 and T4 tumours of the rectum (standard). Preoperative radiotherapy may be indicated for T2 tumours, even though the risk of recurrence appears small after complete surgical resection alone (option). A three- or four-field technique is recommended (level of evidence B). Radiotherapy is contra-indicated if pelvic irradiation has been given previously (standard). Advanced age, psychiatric problems and prior laparotomy are all relative contra-indications to preoperative radiotherapy (option). The minimum recommended preoperative dose is 45 Gy (level of evidence B).

Postoperative radiotherapy must be considered if surgical clearance of tumour is incomplete in the absence of preoperative radiotherapy, or if the tumour has been under-staged preoperatively (standard). The minimum recommended postoperative dose is 50 Gy given as external-beam irradiation.

The place of intraoperative radiotherapy (with or without external-beam radiotherapy) requires evaluation within randomized trials to assess both efficacy and toxicity and to define its role in the treatment of rectal cancers.

Radiotherapy as sole treatment must only be undertaken in patients with inoperable disease or surgical contra-indications. In this case, radiochemotherapy is recommended.

The definitive choice of technique (external, intracavitary or both) depends on the treatment facilities and the experience of the radiotherapy service concerned.

Radiochemotherapy

Combination radiochemotherapy is recommended for the treatment of locoregional disease in patients considered 'inoperable' because of medical reasons or if surgery is refused. Radiotherapy, at a dose of ≥ 55 Gy, is combined with bolus chemotherapy (5-fluorouracil (5-FU) + folinic acid, days 1–5 during weeks 1–5 of radiotherapy), or with continuous infusion 5-FU ($225 \text{ mg m}^{-2} \text{ day}^{-1}$) for the duration of radiotherapy. After 50 Gy, the operability of the patient must be re-assessed.

Therapeutic trials are required to evaluate the place of neo-adjuvant preoperative combination radiochemotherapy. These must address such issues as the optimal efficacy/toxicity ratio of the combination, the compliance with treatment and the role of reportedly effective chemotherapy combinations when given with radiotherapy. If a patient has had surgery and no preoperative irradiation, radiotherapy at a dose of 50 Gy, given in conventional fractions combined with 5-FU given as a continuous infusion, is recommended, especially if there are poor prognostic factors.

Adjuvant chemotherapy

In the adjuvant situation, the indication for chemotherapy and/or immunotherapy has not been standardized; no trial is specific for cancers of the rectum. After resection of any node-positive tumour chemotherapy with six courses of bolus 5-FU plus folinic acid (high or low dose) days 1–5 can be considered (option), if the patient cannot be included in a therapeutic trial evaluating routine adjuvant chemotherapy.

Local treatment of early rectal cancers

Local treatment for small cancers of the rectum is not as well defined as the more classical treatments. This form of treatment is only appropriate for T1 or T2 tumours of ≤ 3 cm that are mobile, node-negative on endorectal ultrasonography and histologically well differentiated. Local treatment looks promising in some studies (level of evidence C), but the results are often difficult to interpret and must be confirmed. If possible, local transanal surgery should be undertaken in order to obtain tissue for histology. Close follow-up of these small cancers post-therapy is essential in view of the risk of local recurrence and/or metastases and because salvage treatment for recurrence is possible. Follow-up should include clinical examination, rectoscopy, endorectal ultrasonography and biopsy of any suspicious lesions. Local treatment should only be considered for selected patients and delivered by specialized teams (level of evidence C).

THERAPEUTIC STRATEGY

T1 N0 M0 tumours

Complete surgical resection with sphincter preservation by a specialist surgeon is the standard treatment (Figures 1 and 2). For T1 sub-peritoneal tumours, the total removal of the mesorectum can be considered. Postoperative external radiotherapy, at appropriate dose, with or without extensive surgery, is indicated if the histology of the excised section shows incomplete clearance and/or the presence of metastatic nodes and/or invasion of the perirectal fat (option).

T2 N0 M0 tumours

Primary, complete surgical resection with preservation of the sphincter by a specialist surgeon should be undertaken if possible (standard) (Figures 1 and 3). Preoperative external radiotherapy is an option. If the local resection is histologically incomplete, additional treatment with radiotherapy with or without extensive surgery can be undertaken (level of evidence C). For T2 sub-peritoneal tumours, total removal of the mesorectum can be considered.

T3 or T4 (or node-positive irrespective of T) M0 tumours

External radiotherapy followed by surgery is standard treatment (Figures 1 and 4). Surgery preserving sphincter function should be undertaken if possible, depending on the situation of the tumour in relation to the sphincter, the volume of tumour and the anatomy of the patient (narrow pelvis, obesity, etc) (standard). Removal of the mesorectum can be considered for sub-peritoneal tumours (option). After resection of a node-positive tumour, six courses of bolus 5-FU/folinic acid days 1–5 can be considered (option).

Patients should be included in prospective randomized clinical trials to determine the precise role and the optimal use of radiotherapy and chemotherapy in this context, such as:

- preoperative chemotherapy and radiotherapy vs preoperative radiotherapy alone
- adjuvant locoregional chemotherapy (intraportal or intraperitoneal) plus systemic chemotherapy vs systemic chemotherapy alone

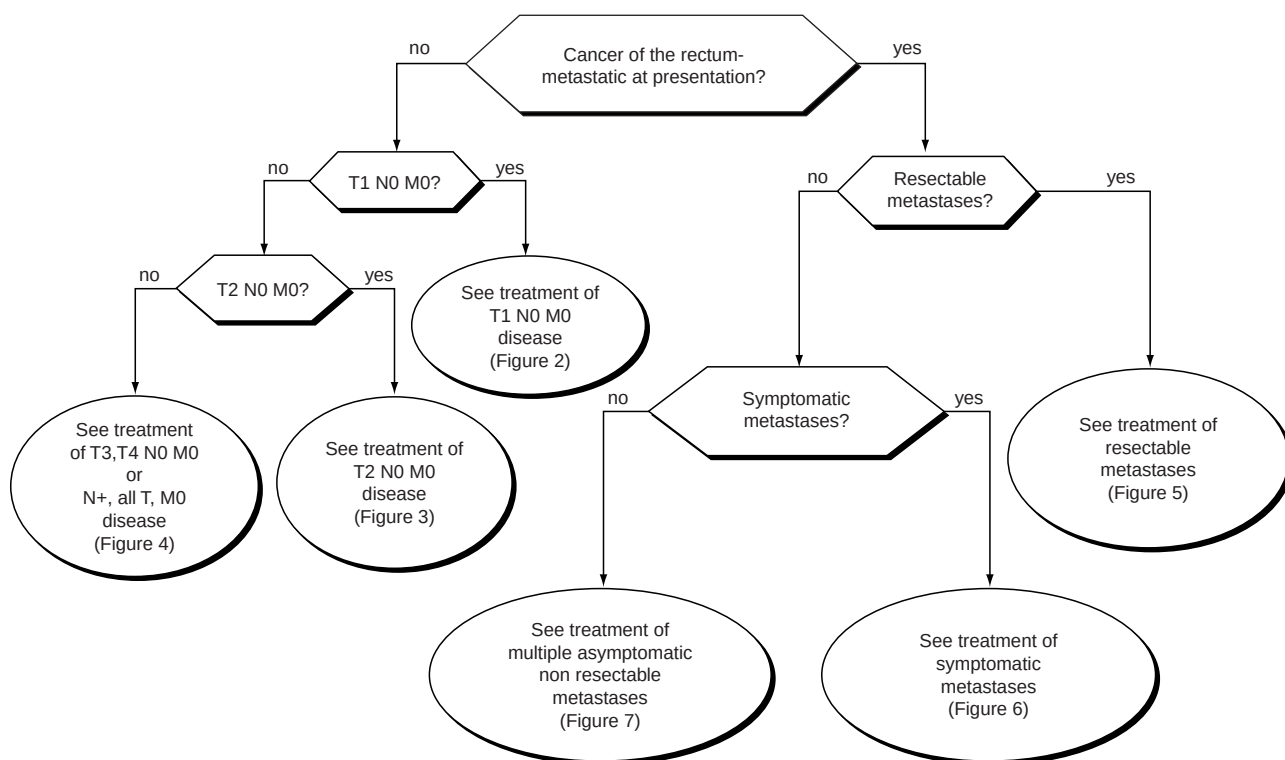


Figure 1 Therapeutic strategy for cancer of the rectum

- preoperative plus intraoperative radiotherapy vs preoperative radiotherapy alone.

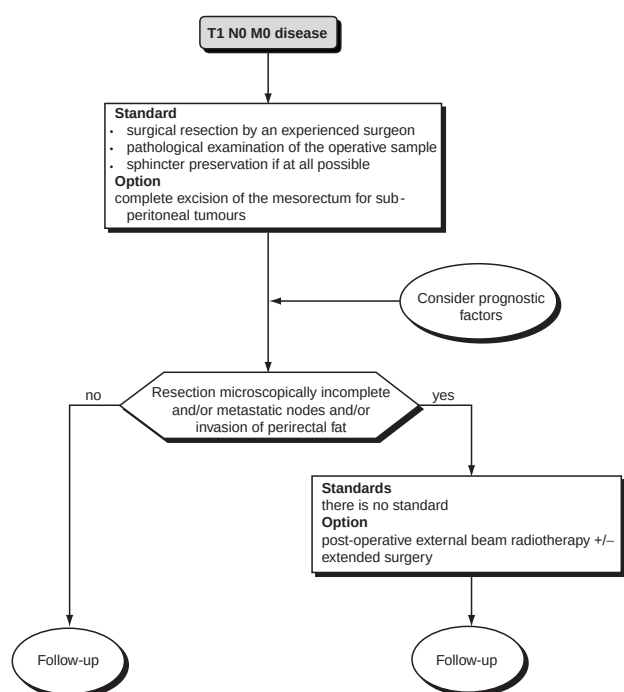


Figure 2 Treatment of T1 N0 M0 disease

Synchronous, resectable (single or multiple) asymptomatic hepatic or pulmonary metastases

Extended surgery can be undertaken. Concurrent rectal and hepatic surgery is standard treatment if the hepatectomy involves less than or equal to three segments (Figures 1 and 5). If this is not possible, a partial hepatectomy can be carried out some time after the rectal surgery, depending on the assessment of disease extent at that time (option). Pulmonary surgery can be undertaken 3 months after the rectal surgery, depending on the assessment of disease spread (option). Additional pelvic radiotherapy according to local stage can be considered if the resection has been complete. Primary systemic chemotherapy, alone or in combination with radiotherapy, can be considered before the rectal surgery (option). Systemic chemotherapy in the interval between the rectal surgery and the hepatic or pulmonary surgery can be considered (option).

Multiple synchronous symptomatic metastases

Palliative chemotherapy is the standard treatment (Figures 1 and 6). This consists of biweekly 5-FU plus a continuous infusion of folinic acid (the de Gramont protocol) with or without oxaliplatin or irinotecan (options).

Specific local treatment is dependent on the clinical situation, for example surgery for stoma formation, radiotherapy, laser therapy, or chemotherapy plus radiotherapy (options). Systemic chemotherapy can be combined with pelvic radiotherapy (option). The 5-FU bolus/continuous infusion folinic acid protocols (as above) are preferable for primary treatment (level of evidence B).

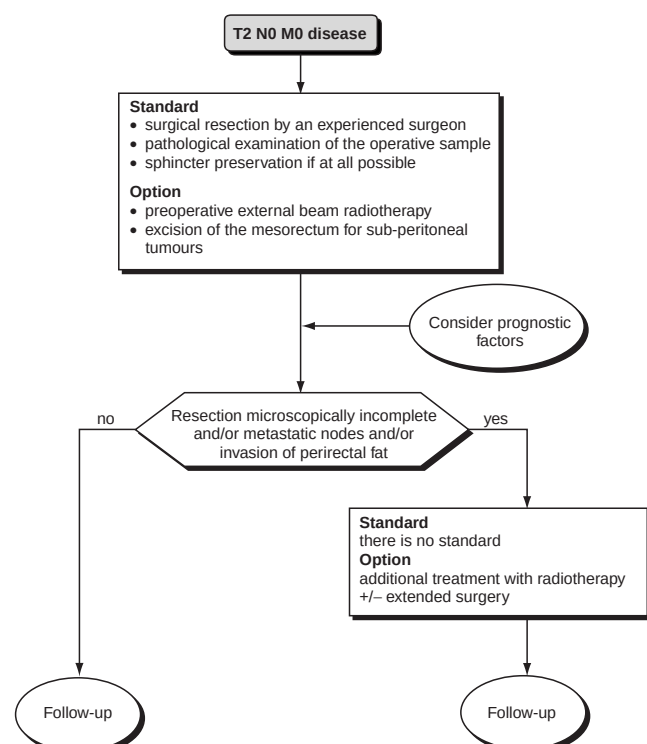


Figure 3 Treatment of T2 N0 M0 disease

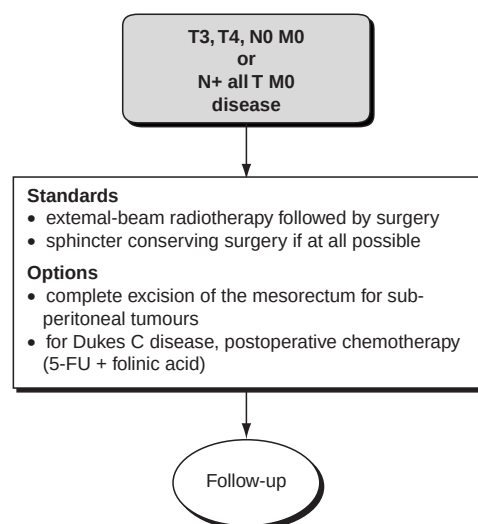


Figure 4 Treatment of non-metastatic T3 T4 N0 or N+ all T disease

Synchronous, multiple, non-resectable, asymptomatic metastases

There is no standard approach. Locoregional treatment (surgery and/or radiotherapy) followed by palliative chemotherapy is possible (option) (Figures 1 and 7). It is recommended that patients be included in prospective randomized trials to determine the precise role of the following therapies:

- hepatic intra-arterial chemotherapy for hepatic metastases
- systemic chemotherapy and pelvic radiotherapy
- palliative systemic chemotherapy.

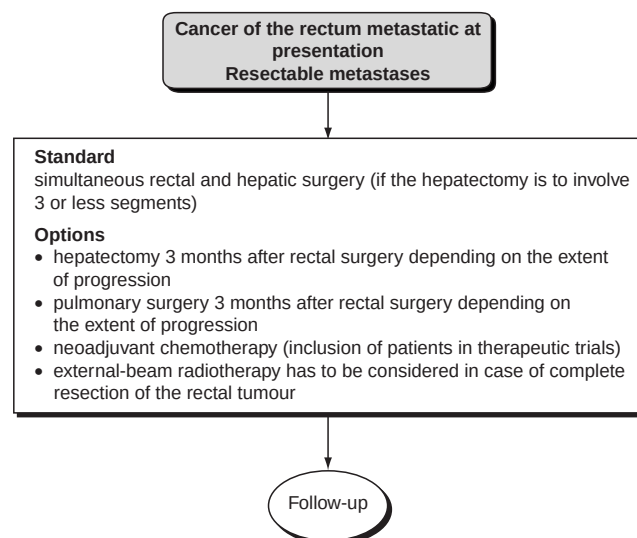


Figure 5 Treatment of disease presenting with resectable metastases

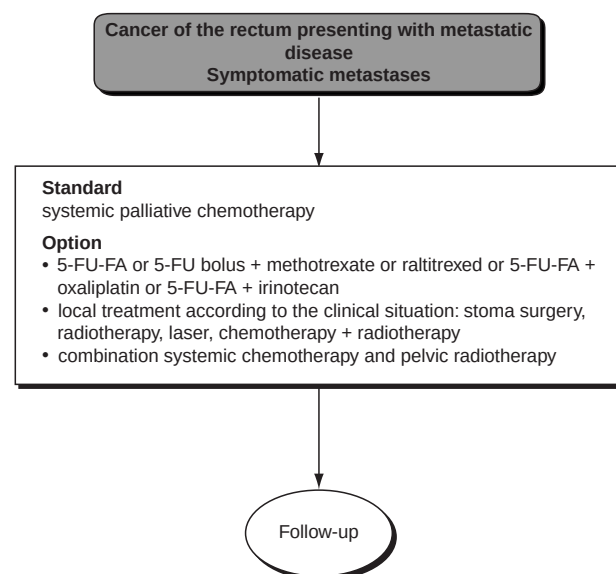


Figure 6 Treatment of disease presenting with symptomatic metastases

FOLLOW-UP

Follow-up after potentially curative surgery for a rectal cancer has the objective of detecting a recurrence or a second cancer as early as possible.

A patient with a poor performance status who is not fit for further surgery should undergo minimal follow-up. The standard examinations for follow-up are: clinical examination, CXR, liver ultrasound and colonoscopy. If the patient has had sphincter-preservation surgery, rectoscopy and/or endorectal ultrasonography can be done (option). If the interpretation of an ultrasound is difficult, a CT scan of the pelvis and/or liver is an option. It is recommended that patients be included in prospective randomized studies to determine the best methods and frequency of follow-up and in particular, to define the role of monitoring carcino-embryonic antigen (CEA) levels.

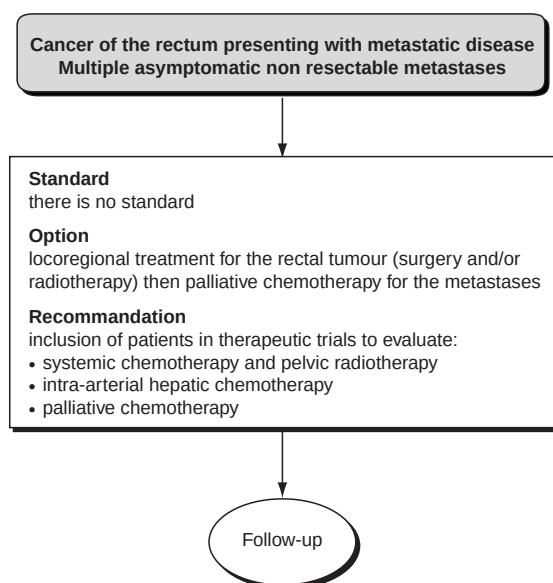


Figure 7 Treatment of disease presenting with asymptomatic non-resectable metastases

CT scanning and MRI are not indicated as routine examinations in the follow-up of rectal cancers. Liver function tests and markers must not be measured as a routine. The observation of an elevated CEA level must be confirmed by repeat testing after a minimal interval of 1 month (standard). If a preoperative colonoscopy was not done, or was incomplete, a postoperative colonoscopy should be undertaken 6 months following treatment (standard). In all cases, a colonoscopy should be done within the year of surgery and repeated as indicated by the results (standard).

INTERNAL REVIEWERS

G Borel (Centre Paul Strauss, Strasbourg), T Conroy (Centre Alexis Vautrin, Vandœuvre-Lès-Nancy), D de Raucourt (Centre

François Baclesse, Caen), JP Ghnassia (Centre Paul Strauss, Strasbourg), JC Horiot (Centre Georges-François Leclerc, Dijon), G Lorimier (Centre Paul Papin, Angers), P Maingon (Centre Georges-François Leclerc, Dijon), C Marchal (Centre Alexis Vautrin, Vandœuvre-Lès-Nancy), J Mihura (Centre Claudius Regaud, Toulouse), G Monges (Institut Paoli Calmettes, Marseille), TD Nguyen (Institut Jean Godinot, Reims), JC Ollier (Centre Paul Strauss, Strasbourg), JP Pignon (Institut Gustave Roussy, Villejuif), M Rivoire (Centre Régional Léon Bérard, Lyon), P Rouanet (Centre Val d'Aurelle, Montpellier), C Schumacher (Centre Paul Strauss, Strasbourg), P Troufléau (Centre Alexis Vautrin, Vandœuvre-Lès-Nancy) and P Wagner (Centre Paul Strauss, Strasbourg).

EXTERNAL REVIEWERS

M Amouretti (Groupe Hospitalier Sud Haut l'Evêque, Pessac), JF Bosset (CHRU Hôpital Jean Minjoz, Besançon), O Bouché (Hôpital Robert Debré, Reims), J Faivre (CHRU Hôpital du Bocage, Dijon), M Gignoux (Hôpital Côte de Nacre, Caen), H. Johanet (Pontoise), F. Lazorthes (CHRU Hôpital Purpan, Toulouse), B Millat (CHU Hôpital Saint-Eloi, Montpellier), H Orfeuvre (Centre Hospitalier Fleyriat, Bourg-en-Bresse), M Parneix (Hôpital Saint-André, Jean Ababdie, Bordeaux), E Pelissier (CHU Hôpital Saint-Jacques, Besançon), A Quinton (Groupe Hospitalier Saint-André Jean Ababdie, Bordeaux), F Rothé-Thomas (Centre Hospitalier, Chambéry), B Roullet (Hôpital Dupuytren, Limoges), JP Suchaud (Centre Hospitalier, Roanne), G de Laroche (Clinique Mutualiste de la Digoñnière, Saint-Etienne), A Botton (Clinique Sainte-Marie, Pontoise), E Calitchi (Boulogne), PL Etienne (Clinique Armoricaïne, Saint-Brieuc), Farcy-Jacquet (Clinique Armoricaïne, Saint-Brieuc), D Fric (Clinique du Mail, Grenoble), G Ganem (Centre Jean Bernard, Le Mans), H Lauche (Clinique Clémentville, Montpellier), A Namias (Centre Gastro-entérologie, Pontoise) and JL Toullec (Cabinet de Gastro-entérologie, La Rochelle).