Carcinoma of the colon is a major cause of cancer death. More than a third of patients with colon carcinoma present with lymph node metastases and more than half of these patients, initially treated for cure, relapse and later die of the disease. Adjuvant therapy is any treatment that is given in addition to a standard cancer treatment to improve the chances of cure.

In 1990, an United States National Institute of Health (consensus conference) reviewed the available evidence and recommended that one year of 5-fluorouracil (5-FU) plus levamisole be offered to all patients with resected Dukes C colon cancer. Since then, adjuvant trials have abandoned a no-treatment control. There have been recent advances in the use of adjuvant therapy in patients with colon cancer following curative resection, but questions remain regarding the optimal adjuvant therapy regimen and its value in certain clinical contexts, for example, Dukes B colon cancer.

Radiotherapy has a limited role in colon cancer although there are special circumstances where T4 tumours, eg. Adherence to abdominal wall bladder may require adjuvant therapy.

15.1 The research evidence for systemic chemotherapy

Several meta-analyses have been performed to examine the benefits of adjuvant chemotherapy in Dukes C colon cancer. Buyse et al summarised the data on randomised trials of adjuvant therapy for Colorectal Cancer up to 1987. This meta-analysis showed no significant difference in the odds of death. However, in the subgroup of patients treated with 5-FU for at least one year, the odds of death were significantly reduced when compared with untreated controls (CR = 0.83, p = 0.03). On further analysis of this subgroup, the risk reduction for death was more pronounced for rectal than for colon cancer patients (38% vs 8%, p = 0.02). The effect by disease stage could not be examined due to lack of standardisation. The authors cautioned about the significance of these findings in subgroup analysis, which could only suggest hypotheses to be tested in clinical trials.

The Dube meta-analysis of 39 trials performed between 1959 and 1993 in both colon and rectal cancers found a 5% improvement in five-year survival for colon cancer and 9% for rectal. The Cancer Care Ontario Practice Guidelines Initiative (CCOPGI) meta-analysis of 32 trials in 1997 found a mortality odds ratio for adjuvant chemotherapy in stage III colon cancer of 0.69 (0.57–0.85). The Colorectal Cancer Collaborative Group has also presented in abstract form a meta-analysis of 50 studies involving 18,000 patients comparing surgery alone with adjuvant chemotherapy. It found that annualised death rates were reduced by 29% (p = 0.0007) for 5-FU regimens modulated by leucovorin and 22% (p = 0.01) for levamisole modulated regimens. Unmodulated 5-FU schedules led to a 6% reduction (p = 0.11). Overall death rate reduction was 11% for all prolonged systemic chemotherapy treatments.

In addition, the Australian Cancer Network and Clinical Oncological Society of Australia Working Party on Adjuvant Therapy for Colon Cancer (Appendix B) considered only randomised controlled trials published after 1987 comparing adjuvant treatments with observation or other treatments after curative surgery in patients with Dukes C colon cancer. That evidence will be considered now.

15.1.1 Early era of adjuvant trials

This group of three trials predates modern treatment schedules. The South Western Oncology Group (SWOG) in the United States compared chemotherapy using (i) 5-FU plus semustine (MF); with (ii) MF plus BCG immunotherapy, or (iii) BCG alone. The negative result of the SWOG trial (no survival benefit detected) was consistent with previous reports.
The NSABP trial C-01 was the first large adjuvant trial in colon carcinoma to detect a benefit for adjuvant therapy, with a borderline statistical significance. It found an 8% absolute improvement in survival for Dukes C (but not B) patients treated with either chemotherapy (semustine, vincristine, 5-FU) or BCG. However, in a recent update of this trial, no benefit from adjuvant chemotherapy was seen at ten years of follow up. However, there was a benefit from the addition of BCG in survival improvement compared to surgery alone (53% vs 46%, p = 0.02). Four other randomised studies have not shown an advantage with BCG and the observed benefit to BCG in the first trial was thought to be most likely due to reduction in deaths from comorbid conditions.

The third trial in this group was a cooperative study from Japan in which patients with either colon or rectal cancer were randomised, after stratification, to either observation or one of two regimens of chemotherapy. The Japanese study used chemotherapy not widely used in Australia: mitomycin C by portal, and peripheral vein injections plus oral 5-FU. Survival results favoured adjuvant therapy over observation, but only in the subgroup of Dukes C patients.

15.1.2 5-fluorouracil and levamisole

These trials inaugurated the modern era of adjuvant treatment involving the use of the ‘immunomodulator’ levamisole or the biochemical modulator of 5-FU, leucovorin (folinic acid).

In the initial Leicester trial, patients were randomised after curative surgery either to observation, 5-FU, or 5-FU plus levamisole. 5-FU was administered intravenously for three days following surgery, and then orally once weekly for six months; levamisole was administered for only three postoperative days. After five years of follow up, the survival of patients randomised to 5-FU plus levamisole was significantly prolonged when compared with 5-FU alone (p = 0.02), or observation (p = 0.045).

Levamisole alone, given intermittently for one year, did not produce a survival benefit in the EORTC trial with Dukes C colon cancer patients, and its effect was inferior to the combination with intravenous 5-FU in the NCCTG trial with Dukes B and C Colorectal Cancer patients. The intergroup trial 0035 detected a significant survival advantage for 5-FU plus levamisole compared with observation. This benefit, amounting to a 30-40% reduction in the rates of recurrence and death, occurred in Dukes C colon cancer patients but not those with Dukes B. The United States Consensus Conference in 1990 recommended this one-year combination of 5-FU plus levamisole as standard care for Dukes C colon cancer patients.

The Netherlands Adjuvant Colorectal Cancer Project (NACCP) also found a significant overall benefit of adjuvant therapy with 5-FU plus levamisole compared with observation in Dukes B and C colon cancer but not for rectal cancer.

In a 1996 meta-analysis of two trials — 5-FU with or without levamisole versus no treatment control arms — the effect of levamisole became non-significant after adjustment for the total planned 5-FU dose. Levamisole is now of historical interest only, as subsequent studies have disproved its efficacy in adjuvant therapy.

15.1.3 5-FU plus leucovorin

These trials compared postoperative observation with adjuvant 5-FU modulated by leucovorin (folinic acid). Folinic acid prolongs the half-life of 5-FU by increasing its enzymatic binding to thymidylate synthetase. Using an individual patient data meta-analysis, the IMPACT (International Mutlicentre Pooled Analysis of Colon Trials) investigators pooled the results from 1493 randomised patients across three similar trials (Italian, French and Canadian) in patients with Dukes B or Dukes C colon cancer. A significant reduction in the rate of recurrence was detected for patients randomised to monthly five-day 5-FU plus high-dose leucovorin compared with control (hazard ratio (HR) 0.65; 95% CI 0.54, 0.78; p<0.0001). After a median follow up of 3.5 years, there was also a reduction in the
risk of death-favouring treatment (HR 0.76; 95% CI 0.61, 0.96; p = 0.018). The benefits were confined to patients with Dukes C disease. Survival at three years was 76% versus 64% favouring treatment in Dukes C patients, and 90% versus 88% in Dukes B.

A similar observation was reported by Francini et al. In this trial, 239 patients with Dukes C or high-risk Dukes B colon cancer were randomised to either observation or 5-FU plus leucovorin following resection. With a median follow up of 4.5 years, the relative reduction in recurrence rate was 35% (95% CI 18%, 52%) and in mortality rate 34% (95% CI 23%, 45%), favouring treatment. At five years, survival was 79% for adjuvant therapy compared with 65% for control (p = 0.0044). When analysed by stage, the benefit was confined to patients with Dukes C disease. For patients with Dukes C disease, five-year survival was 69% versus 43% for adjuvant therapy and control respectively (p = 0.0025); recurrence-free survival was 66% and 41% respectively (p = 0.0016).

A United States Intergroup trial in Dukes B and C colon cancer has also detected an overall significant reduction in recurrence rate (74% vs 58% at five years; p<0.01), and overall survival (74% vs 63%; p = 0.02) favouring six months of 5-FU plus low-dose leucovorin compared with observation. The analysis was not stratified by stage.

The National Surgical Adjuvant Breast Project (NSABP) trial C-03 compared MOF (semustine, vincristine and 5-FU) with a combination of 5-FU plus leucovorin. A significant improvement in disease-free and overall survival was reported for patients treated with 5-FU plus leucovorin. The survival benefit was mainly in Dukes C patients (27% relative reduction in deaths).

Clinical trials have proceeded to compare 5-FU plus leucovorin with regimens containing levamisole and to determine duration of therapy. Six studies have matured in the past four years since the year 2000 and these have established that six months of 5-FU-leucovorin provides a similar benefit to twelve months, and that the addition of levamisole provides no further benefit. The NSABP C-04 study compared 5-FU plus leucovorin given for 36 weeks with 5-FU plus levamisole and 5-FU plus leucovorin plus levamisole each given for one year. Amongst 2151 patients there were no significant disease-free survival (DFS) or overall survival (OS) differences between the individual arms, although on pair-wise comparisons, 5-FU plus leucovorin had a significant advantage over 5-FU plus levamisole in terms of DFS (P = 0.04). A collaborative study between the NCCTG and the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG used a two-by-two factorial design where standard 5-FU plus levamisole was compared with a 3-drug regimen of 5-FU plus low-dose leucovorin plus levamisole, and either regimen given for six or 12 months. This study enrolled 891 eligible patients and showed that 12 months of therapy offered no benefit over six months. There was a survival benefit with the addition of leucovorin in patients who received six months treatment with five-year OS 70% vs 60%, p<0.01. The American Intergroup study INT-0089 randomised 3759 patients to 12 months of 5-FU plus levamisole or six months of 5-FU plus low-dose leucovorin (LDLV), 5-FU plus high-dose leucovorin (HDLV) or 5-FU plus LDLV plus levamisole. Twelve months of 5-FU plus levamisole was found to offer no survival benefit over six months of 5-FU plus leucovorin. The largest study to date, the British QUASAR (quick and simple and reliable) Trial, has randomised 4863 patients between levamisole and placebo added to 5-FU plus leucovorin regimens. Survival was non-significantly inferior with levamisole when compared with placebo (odds ratio 1.10, p = 0.07). The German adjCCA-01 trial randomised 680 Dukes C patients to receive either 12 months of 5-FU plus levamisole or 5-FU plus HDLV. At a median follow up of 82 months, the 5FU plus leucovorin combination significantly improved DFS (P = 0.012) and significantly decreased overall mortality (P = .003) in comparison with 5-FU plus levamisole. A recent reported Israeli trial of 398 Dukes B and C patients comparing 12 months of 5-FU plus HDLV to 5-FU plus levamisole found no difference in eight-year survival.

QUASAR has also demonstrated that there is no difference in outcome between the use of high-dose or low-dose leucovorin. QUASAR also incorporated a non-randomised comparison of weekly versus a four-weekly five-day schedule of administering the treatment. This schedule was determined by
clinician preference. Risk of recurrence and survival were identical, but the weekly schedule was associated with much less toxicity. To date there have been no direct randomised trials comparing weekly bolus 5-FU plus LDFA with the schedule of monthly five-day bolus 5-FU plus LDFA (Mayo) or the six-out-of-eight weekly bolus 5-FU plus HDFA (Roswell Park) schedule.

Updated data from the Italian SITAC-01 study, one of the IMPACT trials, has found that the treatment has had no detectable adverse effect on the patients’ quality of life. Through a computer-simulated model, it has been estimated that adjuvant therapy with the old regimen of 5-FU plus levamisole costs US$2094 per year of life saved. In an Australian study, cost estimates per quality adjusted life-year (QALY) gained vary from A$370 to A$17,500.

15.1.4 Oral fluoropyrimidines

An individual patient meta-analysis of oral fluoropyrimidines (oral 5-FU, Tegafur and Carmofur) versus surgery alone in curatively resected Colorectal Cancers was presented in abstract form in 2001. Six Japanese trials enrolling 9819 patients were reviewed. A significant overall advantage was found for treatment in terms of disease-free survival and overall survival (relative risk 0.83 and 0.91 respectively). A recent updated meta-analysis of three adjuvant oral fluoropyrimidine trials in 5233 patients, performed by the same group, confirmed that DFS and OS were improved regardless of stage, tumour site, age or sex.

The NSABP C-06 study of oral UFT versus bolus monthly five-day 5-FU plus leucovorin has recently been reported in 1608 patients with Dukes B and C colon cancer. There were no differences in either five-year disease-free or overall survivals. Overall toxicity was similar in both arms, as was quality of life.

Capecitabine given in a two-out-of-three week daily schedule for eight cycles has also been compared to the six cycles of bolus monthly five-day 5-FU plus leucovorin schedule in the X-ACT study of 1987 Dukes C resected colon cancer patients. At 3.8 years median follow up there was a superiority of capecitabine in relapse-free survival (p = 0.05) and a trend toward better disease free survival and overall survival. Capecitabine was associated with a better toxicity profile except for more hand-foot syndrome. It also yields a savings in use of medical resources compared to the intravenous therapy. Multivariate analysis found that capecitabine predicted for improved overall survival (HR 0.77, p = 0.02).

15.1.5 Oxaliplatin

Interim results of the MOSAIC study of biweekly 5-FU plus leucovorin with or without oxaliplatin in 2246 patients with Dukes B and C colon cancer have shown a superiority of the oxaliplatin in improving disease-free survival at 37-month follow up (78.2% vs 72.9%, p = 0.002). Improvement in overall survival is yet to be seen and there are concerns regarding the long-term side effects of neuropathy from the oxaliplatin. However, results to date indicate that severe neurotoxicity does resolve over time to a minor residual grade. A pooled analysis of 15 phase III studies of adjuvant therapy for colon cancer studies utilising individual patient data from 12,915 subjects has shown a high correlation of three-year disease-free survival to the five-year overall survival, except for whether the three-year disease-free survival difference is marginal. The NSABP C07 trial, with the same design as MOSAIC in evaluating oxaliplatin, is now completed and the results are awaited.

15.2 Portal vein infusion

Evidence upon which to make treatment recommendations comes from an individual patient data meta-analysis of trials of portal vein infusion in Colorectal Cancer. The analysis of 3499 patients from ten trials detected an 18% reduction in the annual odds of death for all patients treated with portal vein infusion (p = 0.0004). This translates into an absolute reduction in death rate at five years of 6% (p = 0.001). When analysed by stage, patients with Dukes C disease experienced a 5% absolute
improvement in survival at five years (46.9% vs 51.7%; p = 0.2), corresponding to a 17% reduction in the odds of death for patients with Dukes C disease alone (p = ns). When portal vein infusion was compared with systemic chemotherapy with 5-FU alone, there was a 14% reduction in the odds of death with portal vein infusion. However, the difference did not approach conventional levels of significance (p = 0.4) and the systemic therapy regimen (5-FU alone) would be considered inadequate by today’s standards. In the meta-analysis of individual patient data, portal vein infusion was associated with a 28.2% reduction in the odds of hepatic recurrence as the first event for all patients (p = 0.001). This was due mainly to the first hypothesis-generating trial involving 271 patients. For the other nine trials combined, involving 2817 patients, there was a 14% reduction in the odds of hepatic recurrence as the first event, which was not significant (p = 0.2). However, a meta-analysis of all patients treated with portal vein infusion detected an overall 25% decrease in deaths compared with observation (p = 0.0002).

Since then, three important negative trials have been presented. The EORTC/GIVIO/JFCR trial (n = 1235), the Swiss SAKK 40/87 (n = 769) trial, and the UKCCCR AXIS study (N = 3583) study have all shown no differences in survival of portal vein chemotherapy versus observation. These trials all randomised a combination of colon and rectal cancer patients. The AXIS authors combined their trial data with the above meta-analysis to explore differential treatment effects. They found hazard ratios of 0.82 and 1.00 for colon and rectal patients respectively with PVI. Portal vein infusion, however, is associated with technical difficulties of catheter placement and thrombosis. Therefore portal vein chemotherapy cannot be recommended as a standard adjuvant therapy for high-risk colon cancer after resection.

15.3 Adjuvant therapy in Dukes B colon cancer

The question of the role of adjuvant chemotherapy in Dukes B colon cancer had previously been unresolved because individual trials had been insufficiently powered to exclude a small survival advantage. The NSABP meta-analysis of data from the consecutive C01, C02, C03 and C04 adjuvant studies suggested that the relative mortality reduction in Dukes B patients was 30% versus surgery alone. There was a statistically significant reduction in mortality for patients with Dukes B colon cancer who presented without adverse prognostic factors, but not for those with high-risk prognostic factors. However this meta-analysis has been criticised in that the trials spanned a period between 1977 and 1990, chemotherapy schedules varied, and two of the trials did not have observation arms. An updated meta-analysis of six Japanese oral fluoropyrimidine trials involving 9819 patients also found an overall survival risk ratio of 0.84 (p = 0.017) for Dukes B patients. The recent Dutch NACCP trial found a significant five-year survival difference of 78% versus 70% in patients receiving 5-FU plus levamisole compared to control in Dukes B patients. The IMPACT B2 investigators, however, found no significant difference in their pooled analysis of five trials accruing 1016 patients. The CCOPGI meta-analysis in 1997 reviewed 31 randomised trials that tested several forms of adjuvant therapy in resected colon cancer, and concluded that treatment neither improved survival nor delayed relapse.

The United Kingdom QUASAR study randomised 3238 patients with uncertain indication for adjuvant therapy to observation or either five-day four-weekly or 30-weekly treatments of 5-FU (investigators’ choice) and either high- or low-dose leucovorin with or without levamisole. As described previously the trial found no difference between high and low-dose leucovorin and no benefit to levamisole. Ninety-one per cent of the patients were Dukes B stage and 71% were colonic primaries. The trial has found a small magnitude of benefit for chemotherapy over observation. The five-year recurrence rate was 22.2% for chemotherapy versus 26.2% for observation (4% absolute benefit, p = 0.02) and overall survivals of 80.3% and 77.4% respectively (3% absolute benefit, p = 0.02). No benefit of chemotherapy was seen in patients over the age of 70 years. A detailed subset analysis will be performed on more mature data and this, combined with meta-analysis, will help to define the groups that receive the most benefit from adjuvant therapy in this setting.
Factors such as poor histological differentiation, aneuploidy, tumour perforation, bowel obstruction and invasion of surrounding structures are associated with a poorer prognosis. It would be appropriate to discuss and consider adjuvant therapy in these patients.

15.4 Adjuvant treatment in elderly patients

The incidence of colon cancer rises with age. A pooled analysis of 3351 patients enrolled in seven randomised studies of adjuvant chemotherapy with either 5-FU plus leucovorin and 5-FU plus levamisole versus observation was recently published. There was no significant interaction found between age and efficacy of therapy. The toxicity of treatment was not increased in the elderly (age greater than 70) except for leucopenia in patients receiving the outdated 5-FU plus levamisole schedule. This is supported by United States SEER and Medicare population-based data showing 5-FU therapy is associated with significantly reduced mortality in elderly node-positive patients and that this hazard reduction does not diminish with increasing age. In the absence of significant comorbidities, advanced chronological age should not be used to exclude patients from being offered adjuvant chemotherapy.

15.5 Other trials

A number of other adjuvant therapies or techniques have been investigated or are currently being evaluated and at present cannot be recommended as standard.

15.5.1 Protracted infusional 5-FU

Two recent studies have directly compared the administration of protracted venous infusional (PVI) 5-FU with standard bolus monthly five-day 5-FU plus leucovorin for six cycles. Both found a better toxicity profile with PVI 5-FU and similar efficacy. Interestingly, the Saini trial achieved equivalent overall survival and improved time to relapse with only 12 weeks of infusional 5-FU. A five-year update of the later study confirmed no difference in relapse-free or overall survival in the two arms.

15.5.2 Irinotecan

A phase III trial of weekly bolus 5-FU plus leucovorin (FL) versus irinotecan plus 5-FU plus leucovorin (IFL) (CALGB C89803) was conducted on 1264 Dukes C patients. IFL was associated with greater toxicity and in terms of neutropenia, neutropenic fever and death on treatment, with no improvement in overall or failure-free survival over FL. Irinotecan in this schedule is thus not a recommended adjuvant treatment for colon cancer. The results of two randomised studies (PETACC 2 and ACCORD II) of a biweekly schedule of bolus and infusional 5-FU plus leucovorin versus irinotecan plus 5-FU plus leucovorin (FOLFIRI) are awaited. These studies will further define the role of irinotecan in the adjuvant setting.

15.5.3 Intraperitoneal chemotherapy

Chemotherapy delivered by the intraperitoneal route versus surgery alone has been tested in three trials of adjuvant therapy. Intrapertitoneal treatment involves the infusion of drug into the peritoneal cavity, with catheter placement. One trial used a placebo and was to determine safety and not powered for efficacy. Clinical outcomes related to recurrence and survival were reported in the other two trials involving randomised patients with Dukes C or high-risk Dukes B disease. At a median follow up of 4.6 years in the Scheithauer trial, both DFS and overall survival favoured treatment (DFS 75% vs 58%; p = 0.06: overall survival 78% vs 63%; p = 0.05); but the effect was confined to patients with Dukes C disease. In contrast, Vaillant found no difference in overall survival but a reduced disease-free survival in Dukes B patients.
There has been one trial of intravenous 5-FU plus levamisole versus combined intravenous and intraperitoneal 5-FU plus leucovorin in 241 resected Dukes C and high-risk B colon cancer patients. No difference was found in survival of Dukes B patients at four-year follow up. However, for the Dukes C group, a 45% reduction in estimated mortality was seen for the combined treatment arm. These results require further confirmation.

### 15.5.4 Passive immunotherapy

Passive immunotherapy with BCG, with or without chemotherapy, has been tested in several trials. No definitive benefit compared with chemotherapy alone has been observed.

Isenberg et al compared preoperative immunostimulation with bacterial products with a no-treatment control in 101 patients with colon and rectal cancer. At 76 months follow up for all patients, immunostimulation was associated with improved overall survival (91% vs 63%), including 42 Dukes C patients (38% vs 30%). Formal significance tests were not reported, and the sample size was small.

### 15.5.5 Active specific immunotherapy

Hoover et al tested active specific immunotherapy with autologous tumour cells and BCG against observation alone in 80 evaluable patients with high-risk Dukes B and Dukes C colon and rectal cancer. At a median follow up of 93 months, the main analysis could not detect a benefit for treatment, but in a planned subset analysis there was a survival benefit for the 47 patients with colon cancer (47.8% vs 16.7%; HR 3.97; p = 0.02). Rectal cancer patients also received postoperative radiotherapy, whereas colon cancer patients did not. Analyses were not formally stratified and reported by stage. A Dutch study of this treatment in 254 stage II and III colon cancer patients found a significant recurrence-free survival advantage in stage II patients. However, a parallel Eastern Cooperative Oncology Group study E5283 that enrolled 412 patients found no difference in disease-free or overall survival for either stage II or III patients, but there was indication that treatment compliance with effective immunisation results in better survivals. A large multinational study is currently in progress.

### 15.5.6 Alpha interferon

Three randomised studies, the NSABP C-05, a Hellenic Cooperative Group trial and the German FOGT-1 trial have shown no benefit from adding the immunomodulator alpha interferon to either adjuvant 5-FU plus leucovorin or 5-FU plus levamisole chemotherapy protocols.

### 15.5.7 Monoclonal antibody therapy

In a German study, 189 Dukes C patients with resected colon and rectal cancer were randomised to observation alone or to receive five injections of monoclonal antibody 17-1A (edrecolomab). Treated patients had a significant improvement in disease-free and overall survival at both five years and seven years, although the trial was too small for separate analysis of patients with colon (n = 96) and rectal (n = 70) cancers. The results of two large follow-up studies have been conflicting. A three-armed trial of 2761 subjects has shown this monoclonal antibody as monotherapy to be inferior to treatment with 5-FU plus leucovorin and to have no additional benefit to the chemotherapy in adjuvant therapy of Dukes C patients. An American two-armed study of 1839 patients of 5-FU-based therapy (either monthly 5-FU plus LDFA or Moertel 5-FU plus levamisole) with or without edrecolomab found a significant overall survival difference with the addition of the monoclonal antibody. A recent report of CALGB 9581 of edrecolomab versus observation in 1738 patients with Dukes B colon cancer has also found no benefit in overall survival or failure-free survival. The development of this drug has been ceased.
15.5.8 Raltitrexed

Raltitrexed is a specific thymidylate inhibitor synthase active in advanced Colorectal Cancer. The PETACC-1 trial comparing it to a control arm of 5-FU plus leucovorin in the adjuvant setting was terminated early in 1999 when an excess of drug-related deaths in the raltitrexed arm was noted. Thus the specific role of raltitrexed in adjuvant therapy is unknown and it cannot be recommended as standard treatment in this setting.

Who should be considered for adjuvant therapy?

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<thead>
<tr>
<th>Guidelines — Adjuvant therapy</th>
<th>Level of evidence</th>
<th>Practice recommendation</th>
<th>Refs</th>
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<td>People with resected Dukes C, that is, node-positive colon cancer, should be considered for adjuvant therapy.</td>
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<td>Strongly recommend</td>
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What is the value of adjuvant therapy in Dukes B colon cancer?

<table>
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<tr>
<th>Guidelines — Adjuvant therapy</th>
<th>Level of evidence</th>
<th>Practice recommendation</th>
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<tr>
<td>There is a small but statistically significant benefit for the use of adjuvant chemotherapy in Stage II colon cancer. A decision regarding treatment should be made following a discussion of the relative merits and side effects of chemotherapy. High risk sub-groups are more likely to benefit from adjuvant chemotherapy.</td>
<td>II</td>
<td>Recommend</td>
<td>46</td>
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References


