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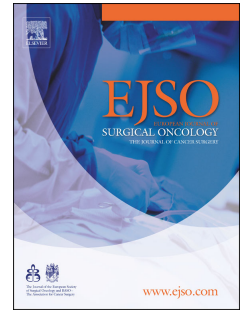
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1 **Primary chemotherapy with or without colonic stent for management of**
2 **irresectable stage IV colorectal cancer**

3 An intention to treat analysis

4

5

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28

29 **ABSTRACT**

30

31

32 **Aim:** Management of patients with irresectable stage IV colorectal cancer is controversial.
33 Since 2000, we have favoured primary chemotherapy with stent insertion in case of
34 obstructive tumor. Our aim was to report the results of this strategy in an unselected
35 consecutive series of patients.

36 **Patients and Methods:** From 2000 to 2007, 68 of 115 consecutive patients admitted with
37 stage IV colorectal cancer were considered irresectable. Data were collected prospectively.
38 Feasibility and outcomes were analysed in an intention to treat basis.

39 **Results:** Of 68 patients, 37 received the intended primary chemotherapy, with stent insertion
40 in 19, 13 required surgery as initial management and 18 patients received supportive care
41 only. Twelve patients in the primary chemotherapy group developed local complication,
42 including bowel obstruction in 9, successfully managed by stent in 6 of them. In patients
43 requiring surgery at presentation, mortality and morbidity were 31% and 77%, respectively.
44 Overall, 41 patients received chemotherapy, of whom, 6 were downstaged to undergo curative
45 resection. Median survival was 6.7 and 15.4 months for the whole series and patients treated
46 by primary chemotherapy, respectively ($p < 0.0001$). On multivariate analysis, age, CEA level,
47 primary chemotherapy and secondary curative resection were independently associated with
48 survival.

49 **Conclusion:** In unselected patients with irresectable stage IV colorectal cancer, primary
50 chemotherapy with or without stent is feasible in more 50% of cases and is associated with a
51 low rate of secondary surgery for complicated primary tumor. This strategy may represent the
52 best palliation in these patients for both duration and quality of survival.

53 **INTRODUCTION**

54

55 At the time of diagnosis, up to 25% of patients with colorectal cancer have synchronous liver
56 metastases.¹ For the majority (70-90%), metastatic disease is not suitable for cure and the
57 main goal is to provide optimal palliation in terms of survival and quality of life.² Except the
58 rare clinical situation of perforated or bleeding primary tumor, which clearly requires
59 immediate bowel surgery, it remains controversial whether first-step primary tumor resection
60 followed by chemotherapy or primary chemotherapy without resection of the primary is the
61 best option.^{3,4} No randomized trial is available to answer this question directly and both
62 strategies are currently practiced. Some argue that the conventional surgical approach, i.e.
63 tumor resection followed by chemotherapy, allows precise abdominal tumor staging, prevents
64 local complications, improves patient's status and efficacy of chemotherapy through a
65 reduction of tumor burden and may favourably impact survival.⁵⁻⁷ In contrast, others favour a
66 more conservative approach, i.e. first-step chemotherapy reserving resection of the primary
67 for the treatment of local complications or with a curative intent if tumor downstaging
68 occurs.⁸⁻¹⁵ The rationale of this approach is the high mortality and morbidity rates associated
69 with bowel resection in a metastatic setting, resulting in an increased risk of delaying or even
70 precluding chemotherapy administration and the relatively low risk of local complication
71 through the effect of systemic therapy on the primary tumor. These retrospective studies
72 however excluded from analysis patients with complicated primary tumor at presentation and
73 those who received supportive care because of poor general conditions. Finally, the long
74 inclusion period in these series introduced an additional bias due to changing in practices and
75 the availability of new diagnostic and therapeutic options over time. Recent advances in both
76 chemotherapy with more effective drugs and the possibility of colon stenting for obstructive

77 tumor have not been studied and may open new perspectives in the treatment of these
78 patients.

79

80 Since 2000, for patients with irresectable stage IV colorectal cancer, our strategy has been to
81 give priority to primary chemotherapy with the use of colonic stent in case of obstructive
82 symptoms reserving bowel resection for other primary tumor related urgent complications or,
83 if sufficient downstaging occurs, for a potentially curative surgery. The aim of this study was
84 to report in an intention to treat fashion, the feasibility and outcomes of this approach in an
85 unselected, consecutive series of patients presenting with newly diagnosed disease.

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87 **PATIENTS AND METHODS**

88

89 *Patients*

90 Between January 2000 and December 2007, 115 consecutive patients with previously
91 untreated stage IV colorectal cancer were admitted in our institution. Sixty eight of them were
92 considered having irresectable metastatic disease at diagnosis and represented our study
93 population (figure 1). Irresectability of metastases was defined as the impossibility to achieve
94 a complete and macroscopically curative resection in one or two stages (in relation to the
95 features of the liver deposits or to the presence of extra-hepatic disease).

96

97 *Management on intention to treat*

98 Since 2000, the strategy of our multidisciplinary oncological committee in such situation has
99 been to give priority to the metastatic disease by using primary chemotherapy with colonic
100 stent insertion in case of obstructive tumor. Resection of the primary tumor was decided for
101 other local complications such as perforation or uncontrolled haemorrhage, when colonic
102 stent was contraindicated or unsuccessful and, secondarily, for a potentially curative surgery
103 if sufficient downstaging had occurred.

104 All patients were staged at admission on evaluation of findings of physical examination,
105 routine laboratory tests, serum CEA level, and helical computed tomography (CT) of the
106 abdomen, pelvis and chest. Colonic stent insertion was considered for patients with
107 obstructive symptoms except for those with middle or low rectal tumours and those with a
108 suspicion of diastatic ischaemia of the cecum or associated small bowel obstruction. All stents
109 were inserted under endoscopy and fluoroscopy by one of the authors (AC) with the
110 previously described technique.¹⁶ In case of other primary tumor related complications
111 requiring immediate surgery, the type of operation was decided upon by the surgeon,

112 depending on the operative findings and the medical condition of the patient. Resection with
113 primary anastomosis was attempted if possible. Patients judged unfit to receive chemotherapy
114 (poor general condition or severe comorbidities) were considered for palliative supportive
115 care.

116

117 *Follow-up*

118 Patients with unresected primary tumors or those with colonic stent were monitored for local
119 complications. Response to chemotherapy was evaluated every 4 cycles and liver metastases
120 were restaged with regard to their resectability. A switch to second-line chemotherapy, with
121 the possible addition of targeted therapies, was decided in cases of grade 3/4 toxicity or
122 disease progression. When liver deposits were secondarily considered suitable for resection, a
123 magnetic resonance imaging of the liver and a positron emission tomography (PET)-CT scan
124 were performed. Specific liver surgical techniques as portal vein embolisation or ligation,
125 radiofrequency ablation or two staged hepatic resection were discussed to allow complete
126 resection of the metastases.

127

128 *Statistical analysis*

129 Data were retrieved from our prospective colorectal database or from patients' charts when
130 missing. All Statistical evaluations were based on the date of the patient's death or the date of
131 last follow-up. Survival probabilities were determined with the Kaplan-Meier method and
132 compared using the log-rank test. Uni- and multivariate analysis of survival was performed by
133 using the log-rank test and a Cox regression mode. A p value of less than 0.05 was considered
134 significant for all tests. Analysis was performed on an intention to treat basis.

135 **RESULTS**

136

137 During the study period, 68 patients with irresectable stage IV colorectal cancer were managed at
138 our institution (table 1). At presentation, 48 patients had a complicated primary tumor:
139 obstruction, n = 39 which was partial in 11 cases and complete in 28 cases; perforation, n = 5;
140 haemorrhage, n = 2 and locally advanced tumor with painful abdominal mass, n = 2. The
141 remaining 20 patients had no or mild symptoms. All patients had liver metastases at the time of
142 diagnosis including 90% with more than 3 nodules and 80% with a bilobar disease. Thirty nine
143 patients had associated extra-hepatic metastases.

144

145 *Primary chemotherapy group*

146 Thirty seven patients underwent primary chemotherapy administration without resection of
147 the primary colorectal tumor as initial management. Among them, 19 had an obstructive
148 primary tumor successfully managed by colonic stent insertion, including 13 cases performed
149 as an emergency procedure. **Chemotherapy was delivered after a median time of 27 days**
150 **(range, 6-74 days) from diagnosis and included folfox, n = 29, folfiri, n = 8 and folfiri**
151 **with bevacizumab, n = 1.** Eighteen patients underwent a switch to a second-line
152 chemotherapy because of grade 3/ 4 toxicity (n = 10) or disease progression (n = 8). The
153 median number of cycles of chemotherapy administrated per patients was 6 (range, 2-18
154 cycles). During the follow-up (median : 12.3 months, range, 1-51 months), 12 of these 37
155 patients were readmitted 1 to 16 months after initial management (median 4.5 months) for a
156 primary tumor related complication. The most prevalent complication was intestinal
157 obstruction observed in 9 patients, including four with obstruction of a previously placed
158 colonic stent due to tumor ingrowth. Six of these 9 obstructive patients were successfully

159 treated by stent insertion, including restenting of an obstructed stent in 2. The remaining 3
160 patients required a colectomy. Three additional patients developed tumor perforation and
161 underwent a colectomy with stoma formation in two cases. Two of these 3 patients had a
162 colonic stent which had been placed 3 and 14 months before the perforation occurred.
163 Overall, 6 patients required urgent colectomy for a late primary tumor related complication
164 with stoma formation in 3 of them.

165

166 *Primary colectomy group*

167 In addition, 13 patients underwent primary tumor resection as initial management for the
168 following local complications: perforation, n = 5; obstruction not suitable for stent, n = 4;
169 hemorrhage, n = 2 and painful abdominal mass related to locally advanced primary tumor, n =
170 2. Four patients died postoperatively. Postoperative morbidity rate was 77%. Anastomotic
171 leak occurred in 3 patients with the need of reoperation for 2 of them and percutaneous CT
172 guided drainage in one. Another patient required reoperation with left nephrectomy for
173 ureteral injury. Among the 9 surviving patients, only 4 could receive postoperative
174 chemotherapy after a median time of 48 days (range, 23-106 days) from hospital discharge.

175

176 *Supportive care group*

177 Finally, for 18 patients, supportive care only was proposed as initial therapy because of their
178 poor general condition or high comorbidities contraindicating the administration of
179 chemotherapy. Among them, 16 had an obstructive primary tumor successfully managed by
180 colonic stent insertion in all but two patients. One patient required emergency laparotomy
181 with diverting colostomy for a failed stent in 1 case and Hartmann procedure for tumor
182 perforation in the other. During the follow-up (median 2.22 months, range 0.5-20 months),
183 two patients were readmitted for a complication 32 and 41 days after stent insertion,

184 respectively and required a colectomy: one developed a late obstruction of the stent due to
185 tumor ingrowth and one had an obstructive acute appendicitis related to a right-sided stent.

186

187 *Outcome and survival*

188 No patient was lost to follow-up. The median follow-up of the whole series was 6.3 months
189 (range, 0.5-51 months). On an intention to treat basis, 41 patients could receive chemotherapy.
190 Among them, 8 became eligible for cure and underwent a laparotomy after a median time of 9
191 months (3-25) from diagnosis. Two of them did not undergo curative resection: one had
192 understaged diffuse hepatic disease discovered at laparotomy and the other underwent liver
193 preparation during colectomy in a two-stage liver resection strategy but failed to complete the
194 second procedure because of hepatic disease progression during the interval. Overall, 6 patients
195 underwent a curative hepatic resection

196 The median survival of the whole series (n = 68), representing the intention-to-treat survival of
197 our strategy, was 6.7 months (95% CI: 3.12-10.22). Median survival was significantly higher in
198 the primary chemotherapy group (15.4 months, 95% CI: 9.48-21.32) compared with the primary
199 resection group (3.37 months, 95% CI: 2.35-4.39) and the supportive group (2.67 months, 95%
200 CI: 1.17-4.16), $p < 0.0001$ (figure 2). On univariate analysis, age, ASA score, CEA level, primary
201 **chemotherapy** and secondary curative resection were significantly correlated with survival
202 (table 2). On multivariate analysis, age, CEA level, primary **chemotherapy** and secondary
203 curative resection were shown to be the only covariates independently influencing survival.
204 Median overall survival of the 6 patients who underwent secondary curative resection was
205 significantly higher (37.1 months, 95% CI: 18.42-55.78) than that of patients who did not
206 undergo curative resection (6.17 months, 95% CI: 4.35-7.98]), $p < 0.0001$. Overall actuarial
207 survivals at 1, 2 and 3 years were respectively 100%, 83% and 67% for the 6 patients who
208 underwent curative hepatic resection.

209 **DISCUSSION**

210

211 This study shows that, on intention to treat, primary chemotherapy with the use of colonic
212 stent for obstructive tumor, in an unselected population of patients with irresectable stage IV
213 colorectal cancer; 1) is possible in more than half of the cases; 2) rarely requires secondary
214 surgery for local complication; 3) may favourably impact survival and enhance the possibility
215 of secondary curative resection.

216

217 *An intention to treat analysis*

218 Patients with irresectable stage IV colorectal cancer have a poor survival and chemotherapy
219 administration, in this palliative context, has been demonstrated to improve both prognosis
220 and quality of life.² However, the possibility of chemotherapy administration depends on the
221 presence of symptoms related to the primary tumor and/ or to the patient's general condition.

222 All published series that addressed the question of prophylactic resection of the primary
223 colorectal tumor in irresectable stage IV patients have focused on asymptomatic patients and
224 on those fit enough to undergo aggressive treatment.⁵⁻¹⁵ **In our unselected patient cohort,**

225 **we found that the specific group of asymptomatic patients accounted for only 26% (18**
226 **patients)** of newly diagnosed cases, the remaining having complicated or symptomatic
227 primary tumor requiring urgent specific management or a poor general condition
228 contraindicating any aggressive treatment. **Colonic stent allowed us to use primary**

229 **chemotherapy in 19 additional patients,** which would have otherwise required primary
230 surgery.¹⁷⁻²⁰ This strategy permitted to use primary chemotherapy, as intended, in 54% of the

231 **patients while only 19% of patients required surgery as initial management.** In the

232 present series, an additional 18% of the patients were judged unfit for chemotherapy

233 administration because of age, comorbidities or terminal disease. This rate is in the range of
234 7% to 37% reported by others.^{7,14}

235

236 *Colonic stent insertion*

237 **Colonic stent as palliative treatment for malignant colorectal obstruction has been**
238 **associated with decreased morbidity, mortality, and stoma formation rate compared**
239 **with emergency surgery.¹⁶⁻²⁰ Although the success rate of stent insertion can reach as**
240 **high as 93%,¹⁶⁻²⁰ colonic perforations leading to acute mortality have been reported²¹**
241 **and large randomized controlled trials as long-term follow-up results are lacking. In the**
242 **present series, colonic stent insertion was associated with low mortality and morbidity**
243 **rates. These low figures may be explained by several factors: balloon dilatation was not**
244 **used during the procedure, stent insertion was performed under endoscopy and**
245 **fluoroscopy and all procedures were performed by one experienced gastroenterologist**
246 **(AC).¹⁶**

247 **Whether systemic chemotherapy may increase the risk of long-term complications of**
248 **colonic stent and particularly the risk of primary tumor perforation has never been**
249 **questioned. Two patients in our series underwent an emergency colectomy because of a**
250 **late tumor perforation by the stent. None of them were on bevacizumab treatment which**
251 **has been reported to cause enteral perforations.²² From our point of view, patients who**
252 **are considered for palliative stenting should not be given angiogenetic inhibitors because**
253 **of the increased risk of colonic perforation. Moreover, this tumor perforation risk under**
254 **chemotherapy could lead to consider palliative SEMS as a « bridge to elective surgery »**
255 **for patients with stabilised metastatic disease.**

256 The short median survival we and others¹⁴ have reported in patients who receive only
257 supportive care also strongly support the need of nonsurgical methods of palliation such as

258 stent insertion when primary tumor related symptoms occur.^{2,14} In our series, 16 of these
259 patients were treated by stent insertion, of whom only 4 required eventual surgery.

260 From our point of view, colonic stent may change the picture of initial management of
261 unselected patients with irresectable stage IV colorectal cancer by drastically reducing the
262 need for palliative surgery for obstruction and stoma formation. For those unfit to receive
263 chemotherapy, this is essential. **The high number of patients with obstructive cancer in
264 the present series (57%) is in part a consequence to our referral pattern of patients
265 specifically referred for stent insertion. This may also reflect a progressive change in
266 surgical practices.**

267

268 *Primary tumor complications under chemotherapy*

269 The potential need for urgent surgical palliation during chemotherapy has also been an
270 argument to advocate first-step bowel resection in unresectable patients.^{3,4} As shown in table
271 3, this complications rate has been reported to range from 9% to 30% and consists mainly in
272 bowel obstruction. When considering the 10 reported series,⁶⁻¹⁵ only 12 of 84 patients who
273 developed bowel obstruction, were treated with colonic stent while the remaining were
274 operated on with significant morbidity and stoma rate ranging from 37% to 100% (table 3). In
275 the present study of unselected patients (> 50% had obstructing symptoms at initial
276 management), local complications and primary tumor obstruction were observed in 32% and
277 24% of patients treated by primary chemotherapy, respectively, but only 16% (6/37) of
278 patients with complications required urgent colectomy. This rate was even lower in symptom-
279 free patients at diagnosis (2/18). Our colonic stent policy, as the use of modern oxaliplatin- or
280 irinotecan-based chemotherapy and its demonstrated effect on the primary tumor²³ may
281 explain this low figure. Moreover, of the 6 patients in the present study who required
282 secondary emergency surgical palliation, none died postoperatively and only 2 experienced

283 postoperative complications. These numbers compare favourably with the mortality and
284 morbidity associated with prophylactic colon resection in the metastatic setting ranging from
285 0% to 4.6% and 19% to 47%, respectively.^{3,4,7,14}

286

287 *Survival analysis*

288 In the present study, patients undergoing primary chemotherapy had a significantly longer
289 survival compared with the two other groups (i.e. primary resection of the primary for
290 complications and supportive care) ($p < 0.0001$). **This difference is not surprising as the
291 three groups were not comparable due to the selection process. The 13 patients who
292 required primary emergency surgery for peritonitis, obstruction or locally advanced
293 tumor had a high postoperative mortality and morbidity of 30 and 77%, respectively
294 and only 4 of the 9 survivors could received postoperative chemotherapy.**

295 The median overall survival of 15.4 months in the primary chemotherapy group is in the
296 range of 7 to 22 months reported by others.^{3,4,7,14} All patients in the present study received
297 oxaliplatin and/ or irinotecan based chemotherapy regimen as a first or second line. Although
298 bevacizumab associated with systemic chemotherapy became the standard of care in
299 metastatic patients during the study period,²⁴ only one patient received this treatment because
300 of the potential risk of perforation when the primary is in place.^{22,25} Recent data suggest that
301 such treatment can be administrated in stage IV colorectal patients provided the primary
302 tumor is asymptomatic and close clinical monitoring is possible.²⁶ For those with *KRAS* wild-
303 type tumors, cetuximab is an alternative of choice.²⁷

304

305 Several studies addressed the prognostic value of primary surgery in stage IV irresectable
306 patients.^{3,4,7,14} All these series included selected patients with asymptomatic primary tumor.

307 By contrast our study is the first to include non selected patients, particularly regarding

308 primary tumor related symptoms and complications at diagnosis. Of interest, the presence of a
309 complicated primary tumor at diagnosis, mostly represented by obstructive symptoms, was
310 not found to be associated with poor survival. This supports our policy of nonsurgical
311 palliation techniques, such as colonic stent, in this context. On the contrary, age > 70 years,
312 poor performance status (ASA score \geq 3) and CEA level > 100 ng/ml at diagnosis were all
313 found to be correlated with survival in the present study. These factors have also been
314 reported to negatively impact survival in patients who underwent resection of the primary as
315 initial management^{5,6,10,28} and cannot be used to favor one or another strategy. **Not**
316 **surprisingly, primary chemotherapy was associated with better survival in univariate**
317 **and multivariate analysis.**

318

319 *Secondary curative resection*

320 It is now well established that patients with initially irresectable metastases may experience
321 tumor downsizing with chemotherapy to such an extent that they become eligible for one- or
322 two-stage resection of both primary and metastases.^{29,30} In the specific context of irresectable
323 synchronous metastases, the secondary resection rate ranges from 4% to 43% depending on
324 the extent of the disease and the type of chemotherapy.^{4,5,7} In the present study, the secondary
325 resection rate was 9% when considering all admitted patients and 15% for those who received
326 chemotherapy and was shown to be an independent variable associated with survival. It
327 should be noted that 3-year actuarial overall survival in the 6 patients who underwent a
328 curative resection was 67%, which is not different from results of resection for initially
329 resectable disease.^{31,32} This aggressive approach combining chemotherapy, resection and
330 specific surgical techniques such as portal vein ligation, two-staged hepatectomy procedure
331 and radiofrequency ablation, offers the only chance of long term survival in these patients.

332

333 **CONCLUSION**

334

335 Half of unselected patients presenting with irresectable stage IV colorectal cancer can be
336 managed by primary chemotherapy provided colonic stent is available. This strategy allows
337 prompt administration of systemic therapy, avoids palliative surgery for primary tumor related
338 complications in more than 80% of them and may be the best palliation for both quality and
339 duration of survival. As chemotherapy, colonic stent should be regarded as standard practice
340 for treating patients with irresectable stage IV colorectal cancer.

341

342

343

344 Conflict of interest statement

345 None to declare.

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473

ACCEPTED MANUSCRIPT

474 **Figure 1:** Evaluation of 115 patients with newly diagnosed stage IV colorectal cancer at our
 475 institution

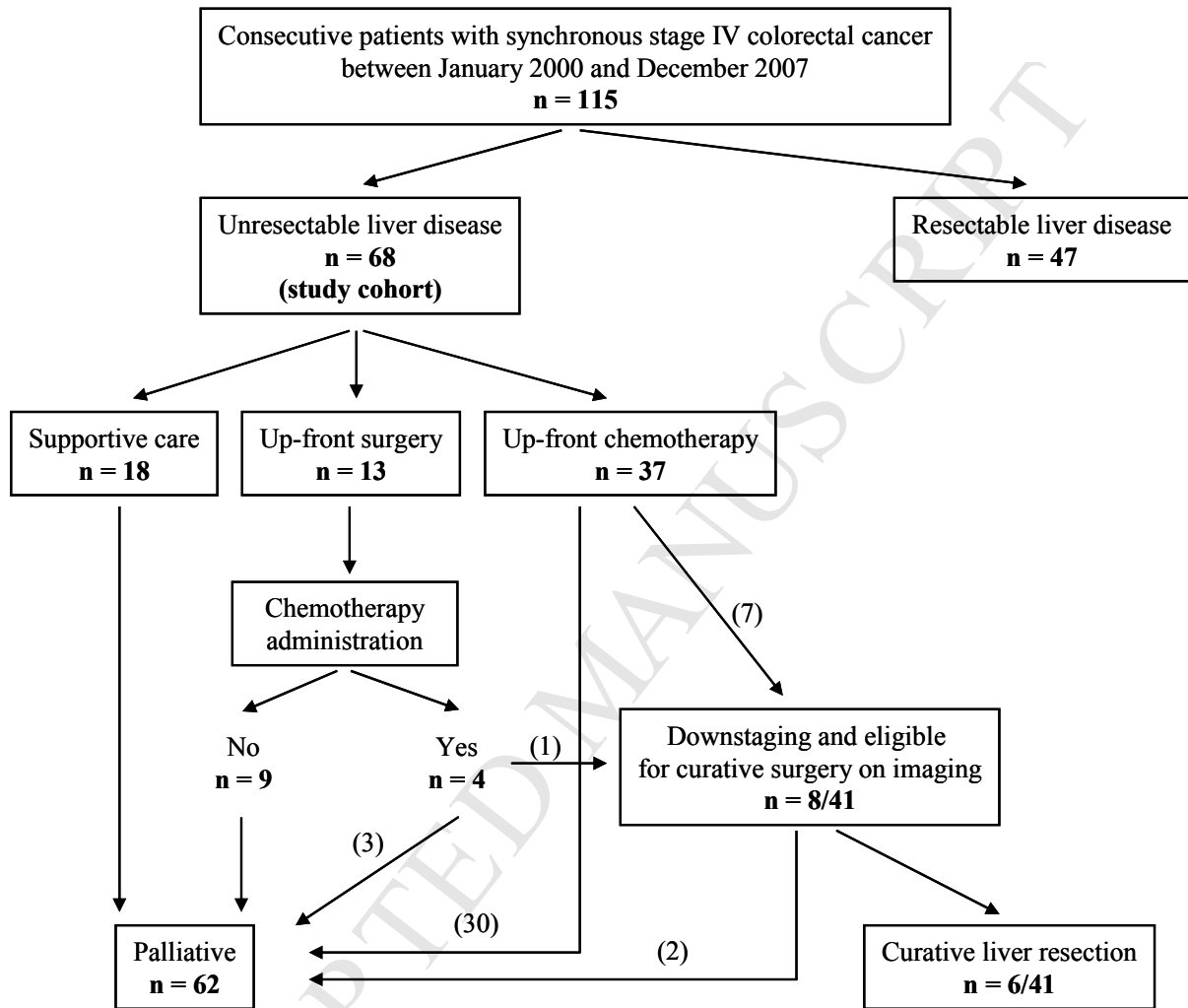
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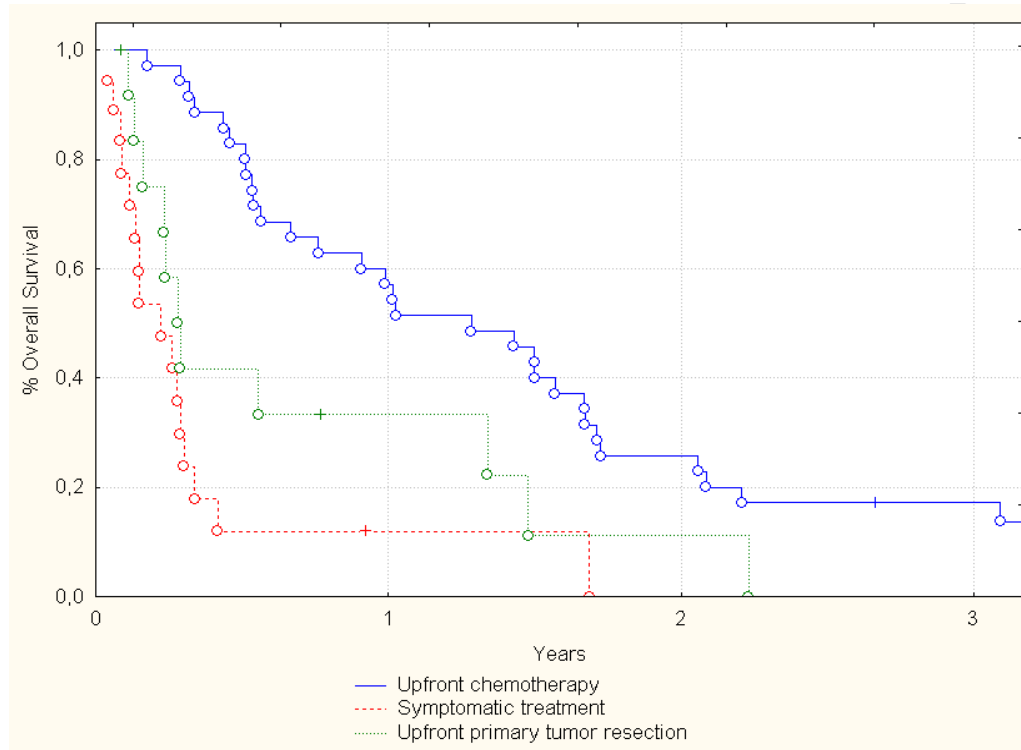
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482 **Figure 2:** Kaplan-Meier overall survival curves after diagnosis of the 68 consecutive patients
483 with irresectable stage IV colorectal cancer according to their initial management
484



523 **Table 1:** Demographic data and tumor characteristics at diagnosis of 68 consecutive and
 524 unselected patients with irresectable stage IV colorectal cancer according to the initial
 525 management
 526

	Total series # (n= 68)
Demographic data	
Age (year, median, range)	69 (35-95)
Age > 70 years	31
Gender (M / F)	37 / 31
BMI (median, range)	23 (14 - 33)
BMI > 30	2
ASA score \geq 3	33
CEA (ng/mL, median, range)	185 (2-3850)
Primary tumor	
Right colon	17
Transverse colon	5
Left colon	7
Sigmoid colon	35
Rectum	4
Liver metastases	
Number (median, range)	9 (1-16)
Number > 3	61
Bilobar	54
Diameter (mm, median, range)	55 (10-100)
Diameter > 5 cm	39
Number of involved segments (median, range)	6 (1-8)
Associated extra-hepatic metastases	
peritoneal	39
Lung	15
Hepatic pedicule lymph node	14
Inter-aorticocava lymph node	10
Bone	8
Mediastinal lymph node	3
Brain	1
Number of involved sites	1
1 site	29
2 sites	6
3 sites	4
Colonic stent	35

527 **Table 2: Univariate and multivariate analysis of overall survival in patients with**
 528 **irresectable stage IV colorectal cancer**

529

	n	Univariate	Multivariate	
		p	p	HR (95% IC)
Age \leq 70 years	37	<0.01	< 0.01	0.27 (0.13 – 0.55)
ASA score < 3	39	0.02	ns	
Non complicated primary tumor*	26	ns		
Number of liver metastases \leq 3	7	ns		
Diameter of liver metastases \leq 5	29	ns		
CEA \leq 100 ng/ml	31	0.02	0.05	0.53 (0.28 – 1.01)
No extrahepatic disease	29	ns		
Primary chemotherapy	37	< 0.01	< 0.01	0.26 (0.12 – 0.56)
Secondary curative hepatic resection	6	< 0.01	< 0.01	0.14 (0.03 – 0.51)
* haemorrhage, perforation, obstruction, or locally advanced primary tumor				

530 **Table 3:** Primary tumor related complications of patients with irresectable stage IV colorectal
 531 cancer treated by primary chemotherapy with particular focus on obstruction.

532

533

	n	Total Complications (%)	Intestinal obstruction (%)	Colonic Stent (n)	Surgery for Obstruction (n)	Stoma formation in Patients Operated on for obstruction (%)
<i>Asymptomatic patients</i>						
Scoggins (1999) ⁸	23	9	100	0	2	100
Sarela (2001) ⁹	24	29	57	2	2	50
Ruo (2003) ⁶	103	29	98	0	29	72
Tebbut (2003) ¹⁰	82	23	58	0	8	37
Michel (2004) ¹¹	23	22	100	0	5	40
Benoist (2005) ¹²	27	15	100	0	4	50
Muratore (2008) ¹³	35	9	33	0	1	100
Galizia (2008) ⁷	23	30	57	3	1	-
Evans (2009) ¹⁴	52	23	25	0	1	100
Poulsides (2009) ¹⁵	233	11	81	7	11	64
<i>Unselected patients</i>						
Present series	37*	32	75 [¶]	6 [†]	3	33

534

535 *19 patients had a stent placed prior to chemotherapy administration

536 [¶]among them, four had a colonic stent in place when obstruction occurred

537 [†]2 patients underwent restenting of an obstructed stent

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