Phase II Study of Capecitabine, Oxaliplatin, and Erlotinib in Previously Treated Patients With Metastatic Colorectal Cancer

Jeffrey A. Meyerhardt, Andrew X. Zhu, Peter C. Enzinger, David P. Ryan, Jeffrey W. Clark, Matthew H. Kulke, Craig C. Earle, Michele Vincitore, Ann Michelini, Susan Sheehan, and Charles S. Fuchs

ABSTRACT

Purpose
To investigate the combination of erlotinib, capecitabine, and oxaliplatin in patients who were previously treated for metastatic colorectal cancer.

Patients and Methods
Patients were eligible if they had metastatic colorectal cancer that progressed, were intolerant to first-line chemotherapy, or had disease recurrence within 1 year of adjuvant therapy for early-stage disease. Each 21-day cycle consisted of daily oral erlotinib at 150 mg, oral capecitabine at 1,000 mg/m² (reduced to 750 mg/m² after the first 13 patients) twice a day on days 1 to 14, and intravenous oxaliplatin at 130 mg/m² on day 1.

Results
Thirty-two patients were enrolled onto this phase II study. By intention-to-treat analyses, eight patients (25%) experienced a partial response and 14 patients (44%) had stable disease for at least 12 weeks. The median progression-free survival was 5.4 months and the median overall survival was 14.7 months. These results were essentially unchanged when limited to the cohort of patients (78%) who received prior irinotecan for metastatic colorectal cancer. Most common grade 3 to 4 toxicities included diarrhea (38%), nausea/emesis (19%), fatigue (16%), dehydration (16%), and dermatitis (13%); grade 3 or 4 toxicities were reduced with a lower starting dose of capecitabine.

Conclusion
The combination of capecitabine, oxaliplatin, and erlotinib seems to have promising activity against metastatic colorectal cancer in patients who received prior chemotherapy, with a relatively higher response rate and progression-free survival compared with previous reports of either infusional FU, leucovorin, and oxaliplatin or capecitabine and oxaliplatin in similar patient populations.

INTRODUCTION
Colorectal cancer is the third most common malignancy and second most frequent cause of cancer-related death in the United States, with 145,290 new cases and 56,290 deaths anticipated in 2005.¹ Nineteen percent of patients with colorectal cancer have metastatic disease at the time of diagnosis² and nearly 50% of patients who are initially diagnosed with localized disease ultimately develop metastases.³ While there have been substantive advances in the treatment of metastatic colorectal cancer over the past 5 years,⁴ median survival for these patients remains under 2 years and less than 5% of patients survive for more than 5 years. New treatment strategies need to be explored.

Cytotoxic chemotherapies active against colorectal cancer include fluoropyrimidines, oxaliplatin, and irinotecan. For most patients with chemotherapy-naive metastatic colorectal cancer, combination therapy that includes a fluoropyrimidine with either oxaliplatin or irinotecan is a reasonable first-line approach.⁵⁻⁸ For patients who receive irinotecan-based therapy as initial treatment, oxaliplatin-based combination therapy is efficacious in second line.⁹ In a large, randomized phase III trial, treatment with a regimen of infusional fluorouracil (FU), leucovorin, and oxaliplatin (FOLFOX) led to a 10% response rate and 4.6 month time-to-tumor progression in patients previously treated with bolus FU, leucovorin, and irinotecan. Borner et al demonstrated similar results substituting capecitabine for infusional FU in a phase II study of 26 patients previously treated for metastatic colorectal cancer (response rate, 15%; 4.2 month time-to-treatment failure).¹⁰
With the introduction of targeted therapies in clinical practice, there is increasing interest in adding such treatments to cytotoxic chemotherapy to improve the efficacy of therapy. The addition of bevacizumab, a monoclonal antibody against the vascular endothelial growth factor, to first-line therapy has been shown to both enhance response rates and improve overall survival. The epidermal growth factor receptor (EGFR) has also emerged as an important therapeutic target in a variety of human cancers. Alterations in the function of EGFR lead to cell growth, invasion, angiogenesis, and metastasis. In colorectal cancer, between 25% and 77% of tumors overexpress EGFR, and overexpression has been associated with a poorer prognosis.

Monoclonal antibodies against EGFR have proven efficacious as monotherapy and in combination with irinotecan in patients previously treated for metastatic disease. In contrast, the oral inhibitors of the EGFR intracellular domain, such as erlotinib and gefitinib, do not appear to have measurable activity against metastatic colorectal cancer as single agents, but may enhance the activity of combination chemotherapy.

Erlotinib is an attractive option for EGFR inhibition due to ease of administration and potentially decreased toxicity relative to the treatment of patients with metastatic colorectal cancer.

**Patients and Methods**

**Patients**

Patients for this study were eligible if they had metastatic colorectal adenocarcinoma previously treated with one prior chemotherapy regimen for metastatic disease and/or recurred within 12 months of completion of adjuvant therapy, had measurable disease by Response Evaluation Criteria in Solid Tumors Group (RECIST), Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2, and adequate hematologic, hepatic, and renal function. Patients could not have been previously treated with oxaliplatin or in an epidermal growth factor inhibitor (prior fluoropyrimidine, including capecitabine, was allowed), had a peripheral neuropathy of grade 2 or greater severity, major surgery in the past 4 weeks, uncontrolled serious medical or psychiatric illness, or concurrent other malignancy (except limited basal cell or squamous cell carcinoma of the skin or in situ cervix carcinoma). In addition, patients lacking physical integrity of the upper gastrointestinal tract or who had a malabsorption syndrome were ineligible. The study was approved by the Dana-Farber/Harvard Cancer Center (Boston, MA) institutional review board. All patients signed informed consent.

**Treatment**

The first patient cohort (13 patients) in the trial received intravenous oxaliplatin 130 mg/m² over 2 hours on day 1, and then began oral capecitabine 1,000 mg/m² twice per day for 14 days. Treatment cycles were repeated every 21 days; erlotinib 150 mg was administered daily throughout the 21-day cycle. Following observations of a high incidence of diarrhea in the first 13 patients (cohort 1), the initial dose of capecitabine was reduced to 750 mg/m² twice per day (cohort 2); doses of oxaliplatin and erlotinib remained the same.

All toxicities were graded according to the National Cancer Institute (NCI; Bethesda, MD) Common Toxicity Criteria (CTC) version 2.0, except for neurotoxicity (which was graded based on an NCI-accepted grading and dose modification schema specific for oxaliplatin). Initiation of a cycle of capecitabine and oxaliplatin required absolute neutrophil count at least 1,500/µL, platelets at least 100,000/µL, and resolution of other toxicities to at least CTC grade 1. Resolution of toxicity was required within 3 weeks of intended start of cycle or patients were withdrawn from the study.

Erlotinib dose was held for up to 14 days for grade 3 or 4 skin toxicities, grade 3 or 4 nausea, grade 3 vomiting, grade 2 or greater diarrhea, and other unanticipated, drug-related adverse effects. Erlotinib was restarted when toxicities resolved to no greater than grade 1 (or skin toxicity was tolerable to patient). For rash, nausea, vomiting, or grade 2 diarrhea, erlotinib could be resumed at the same dose, though a dose reduction was permitted at the clinician’s discretion. For grade 3 or 4 diarrhea, a dose reduction was required. Erlotinib could be continued even if capecitabine and oxaliplatin required a treatment delay if adverse effects were deemed not attributable to erlotinib by the treating clinician. Erlotinib dose reductions were in 50 mg decrements, with the lowest dose to remain on study being 50 mg daily.

Capecitabine dose reductions were required for grade 3 or 4 neutropenia, thrombocytopenia, anemia, grade 2 or 3 hand-foot syndrome; grade 2 or 3 stomatitis; grade 2 or greater diarrhea (despite optimal antidiarheal therapy); or other grade 3 or 4 toxicities by NCI-CTC criteria. For the first cohort of patients (initial dose of capecitabine 1,000 mg/m² twice per day for 14 days), dose reductions were to 750 mg/m², and 500 mg/m². For the second cohort of patients, dose levels were 750 mg/m² (initial dose), 625 mg/m², and 500 mg/m².

Oxaliplatin dose reductions were required for grade 4 neutropenia or anemia, grade 3 or 4 thrombocytopenia, grade 2 parenchymal or dysesthesias persistent between cycles, grade 3 paresthesias or dysesthesias lasting longer than 7 days, grade 3 nausea or emesis or grade 4 emesis (in setting of optimal antinausea therapy), grade 4 diarrhea (despite optimal antidiarheal therapy), or other grade 3 or 4 toxicities by NCI-CTC criteria. Patients on protocol were initially treated with 130 mg/m² of oxaliplatin every 3 weeks; dose level 1 was 100 mg/m² and dose level 2 was 75 mg/m².

Treatment was continued until development of progressive disease by RECIST, unacceptable toxicity, withdrawal of consent, intercurrent illness that prevented continuation of therapy, or changes in the patient’s condition that rendered him or her unable to continue study drugs (as judged by the treating clinician).

**Evaluation**

Baseline tumor measurements by computer tomography were obtained within 21 days before treatment was initiated. Physical examination, toxicity assessment, and laboratory studies were conducted at the start of each 3-week cycle, with the exception of the first cycle when weekly assessments were required. Patients were asked to keep a diary of their self-administration of capecitabine and erlotinib as well as record daily adverse effects.

Repeat imaging was required at 6 weeks and 12 weeks, and then every 9 weeks thereafter. Evaluation of response, stable disease, and disease progression was based on RECIST. Confirmation scans for responders (at

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics (N = 32)</th>
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<tbody>
<tr>
<td>Characteristic</td>
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<tr>
<td>Median age, years</td>
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<td>1</td>
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<td>Received prior adjuvant therapy</td>
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<td>No</td>
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<tr>
<td>Received prior irinotecan</td>
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Abbreviation: ECOG, Eastern Cooperative Oncology Group.
least 30% reduction in the sum of the longest diameters of all measured lesions) were performed at least 4 weeks after the initial scan documenting the reduction.

**Statistical Analysis**

The primary end point of this study was to determine the response rate of the combination of capecitabine, oxaliplatin, and erlotinib in patients with previously treated metastatic colorectal adenocarcinoma. Secondary objectives included assessment of progression-free survival and overall survival of the regimen as well as characterization of toxicities.

Responses were determined by RECIST with an intention-to-treat analysis.24 Progression-free survival was defined as the time between study enrollment and progression of disease or death while on protocol; patients who were withdrawn from the study for other reasons were censored at the discontinuation of study therapy. Overall survival was defined as the time between study enrollment and death. Both progression-free survival and overall survival were estimated by the Kaplan-Meier method.25

Power calculations were based on a phase II two-stage design. The proposed regimen was to be considered worthy for additional investigation in this patient population if a true response rate of 15% or greater and not worthy if 3% or less. A total of 32 eligible patients were entered into the study; 15 in the first stage and 17 in the second stage. The probability of concluding the regimen effective after accruing 32 patients was 84% if the true response rate is 15% and 6% if the true response rate is 3%.

### RESULTS

**Baseline Characteristics**

Between April 2003 and October 2004, 32 patients were enrolled onto this study. One patient came off study before restaging scans being performed. The remaining 31 patients all completed at least one cycle (median, six cycles; range, one cycle to 18 cycles). Primary analyses were based on intent-to-treat; thus, all 32 patients enrolled were included in efficacy and toxicity analyses. The baseline characteristics of the enrolled patients are shown in Table 1. The study cohort was principally male with a median age of 56, and 56% of patients had a baseline ECOG performance status of 0. Eighty-one percent of patients had received one prior chemotherapy regimen for metastatic disease (all but one patient had a prior regimen with irinotecan), and 19% of patients developed disease progression within 12 months of adjuvant chemotherapy. All patients who had previously received chemotherapy for metastatic disease were treated with an irinotecan-containing regimen. Moreover, among all 32 patients, 50% previously received adjuvant therapy.

#### Efficacy

The primary end point for this study was objective response rate (Table 2). By intent-to-treat analysis, eight patients (25%; 95% CI, 10% to 40%) experienced a partial response and 14 patients (44%; 95% CI, 27% to 61%) had stable disease for at least 12 weeks. Among patients who completed at least two cycles of therapy (ie, 6 weeks of treatment), the response rate was 27% and incidence of stable disease for at least 12 weeks was 47%. No differences in response rate or incidence of stable disease were observed between patients who did or did not receive prior irinotecan. Similarly, for the seven patients who progressed within 12 months of adjuvant therapy, two patients (28%) experienced a partial response and three patients (43%) had stable disease.

One half of patients came off therapy (Table 3) due to progression of disease (at least 20% increase in the sum of the longest dimensions of target lesions). Three (9%) additional patients withdrew consent due to clinical evidence of disease progression, nine patients (29%) discontinued study therapy due to toxicity that either required withdrawal or no additional dose reductions were allowable, and three (9%) additional patients withdrew consent due to toxicity that could have either been managed with dose reductions or optimization of

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**Table 2. Efficacy Results**

<table>
<thead>
<tr>
<th>Response</th>
<th>All Patients (N = 32)</th>
<th>Patients Receiving Prior Irinotecan (n = 25)</th>
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<tr>
<td></td>
<td>No.</td>
<td>%</td>
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<tr>
<td>Partial response</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>Stable disease (at least 12 wk)</td>
<td>14</td>
<td>44</td>
</tr>
<tr>
<td>Median progression-free survival (months)</td>
<td>5.4</td>
<td>4.4 to 6.4</td>
</tr>
<tr>
<td>Median overall survival (months)</td>
<td>14.7</td>
<td>7.9 to 21.5</td>
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</tbody>
</table>

**Table 3. Reasons Patients Stopped Protocol Therapy**

<table>
<thead>
<tr>
<th>Event</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery for liver metastases</td>
<td>1</td>
</tr>
<tr>
<td>Progression of disease</td>
<td>16</td>
</tr>
<tr>
<td>Toxicity</td>
<td>9</td>
</tr>
<tr>
<td>Clinical or radiographic disease progression that did not meet RECIST</td>
<td>3</td>
</tr>
<tr>
<td>Toxicity either not treatment related or not requiring withdrawal from study</td>
<td>3</td>
</tr>
</tbody>
</table>

**Fig 1.** Overall survival for entire cohort enrolled.
supportive measures (eg, antidiarrheal medications). One patient proceeded with surgery for isolated liver metastases; this patient only obtained stable disease as a best response to therapy, was on protocol therapy for 4.4 months, and remains alive at 28.7+ months.

The median progression-free survival for the entire patient cohort was 5.4 months (95% CI, 4.4 months to 6.4 months). There was no difference in progression-free survival when the analysis was limited to patients who received prior irinotecan. The median overall survival (Fig 1) for the overall cohort was 14.7 months (95% CI, 7.9 months to 21.5 months). Exclusion of the one patient who underwent surgical resection of liver metastases, who may have had more favorable disease at the onset, did not alter this overall survival estimate.

**Toxicities**

Patients received a median of six cycles of therapy (one cycle is 21 days), with a range from one to 18 cycles. The major grade 3 and 4 toxicities experienced by the patients treated with this regimen are shown in Table 4. Before the dose reduction of capecitabine from 1,000 mg/m² twice a day for 14 days (cohort 1) to 750 mg/m² (cohort 2), 92% of patients experienced at least one grade 3 or 4 toxicity, principally gastrointestinal events, dehydration, and fatigue. After the dose reduction (n = 19 patients), therapy appeared better tolerated, with most subsequent toxicities being characteristic of prolonged therapy with capecitabine and oxaliplatin (eg, neuropathy and bone marrow suppression). These differences are consistent with the fact that patients in cohort 1 received a median of four cycles (range, one to seven), while patients in cohort 2 received a median of six cycles (range, two to 18).

Eighty-eight percent of patients in the entire cohort required a dose reduction of one or more agents while on trial (Table 5). A total of 21 (66% of entire cohort) patients required at least one dose reduction of the erlotinib, of whom eight required two dose reductions (initial dose 150 mg daily, dose level 1 was 100 mg daily and dose level 2 was 50 mg daily). Most reductions were due to diarrhea (71%) and/or dermatitis (33%). Twenty-four patients (75%) required at least one dose reduction of capecitabine (85% of patients in cohort 1, and 68% of those in cohort 2). Eleven of these patients required two dose reductions, the maximum allowable to continue on protocol therapy. Two most common reasons for capecitabine dose reduction were diarrhea (63%), dermatitis (including hand-foot syndrome; 21%), and/or nausea or emesis (21%). Finally, 17 patients (53%) required at least one dose reduction of oxaliplatin; five of those patients required two dose reductions. Dose reductions from oxaliplatin were attributed to nausea or emesis (29%), diarrhea (53%), neuropathy (24%), fatigue (18%), and/or thrombocytopenia (12%).

**DISCUSSION**

In this multi-institution, phase II study of the combination of capecitabine, oxaliplatin, and erlotinib for patients with previously treated metastatic colorectal cancer, we observed a response rate of 25% and median progression-free survival of 5.4 months. The median survival for this population of patients who progressed on first-line chemotherapy or within 12 months of adjuvant therapy was longer than 14 months. Excessive gastrointestinal toxicity was observed in an initial patient cohort; the regimen was better tolerated after the initial dose of capecitabine was reduced from 1,000 mg/m² twice per day for 14 days to 750 mg/m².

Our findings compare favorably with similar regimens with a fluoropyrimidine and oxaliplatin-containing combination in second-line colorectal cancer treatment (Table 6). Regimens with...
infusional FU or capcitabine and oxaliplatin for patients with previously treated metastatic colorectal cancer result in response rates of 10% to 15% and progression-free survival of 4 months to 5 months. Recent data suggest that adding a targeted agent does improve the efficacy of these regimens.10,23,26

Our study does not address whether other means of targeting the EGFR receptor may further enhance activity in this setting. In colorectal cancer, cetuximab and panitumumab (monoclonal antibodies against EGFR) have activity as monotherapy12-14,18-20,22 and cetuximab enhances the activity of irinotecan.16 In contrast, erlotinib and gefitinib do not appear to have measurable activity against metastatic colorectal cancer as single agents.19-21 Nonetheless, oral tyrosine-kinase inhibitors of EGFR may augment the activity of combination chemotherapy against metastatic colorectal cancer. Kuo et al recently reported promising activity (response rate, 33%; median event-free survival, 5.4 months) for the combination of gefitinib, infusional FU, leucovorin, and oxaliplatin (IFX) in patients previously treated for metastatic colorectal cancer.23 Similarly, Delord et al reported a 22% response rate as preliminary results of a phase II study of the combination of bevacizumab, oxaliplatin, and erlotinib.29 The consistency of our results with those of Kuo and Delord and comparison with historical controls suggest that the oral EGFR tyrosine kinase inhibitors may increase the activity of cytotoxic chemotherapy for patients with previously treated metastatic colorectal cancer, though these studies with gefitinib and erlotinib have the limitation of small sample size.

The tolerability of the combination was fair and generally comparable with other studies of capcitabine and oxaliplatin.30,31 In a recent presentation by Hochster et al, capcitabine (at a starting dose of 1,000 mg/m² twice a day for 14 days) with oxaliplatin in previously-un-treated patients with colorectal cancer resulted in 27% grade 3/4 diarrhea, 19% grade 3/4 emesis, 21% grade 3/4 dehydration and 73% any grade 3/4 toxicity. These rates are similar to those in our trial of previously treated patients with the starting dose of 1,000 mg/m² for capcitabine, with the exception of diarrhea. The increased diarrhea in our trial likely reflects an additive toxicity of the capcitabine and erlotinib. In Kuo’s trial of FOLFOX and gefitinib, the rate of grade 3 or 4 diarrhea was 48%.23 Our regimen of capcitabine, oxaliplatin, and erlotinib was better tolerated overall (68% any grade 3/4 toxicity compared with 92%) when the initial dose of capcitabine was dropped to 750 mg/m² twice a day for 14 days, though a 37% grade 3 or 4 diarrhea rate may still be considered high. Nonetheless, regimens of capcitabine and oxaliplatin seem to be more toxic than FOLFOX, particularly at the 1,000 mg/m² twice per day of capcitabine dose,23 which likely contributed to the high rate of dose reductions in this study.

The number of available chemotherapy regimens against metastatic colorectal cancer is rapidly growing. The ultimate question is where this phase II trial fits in this evolving field. A second-line combination with oxaliplatin may not be as useful to oncologists who have shifted their practice to first-line use of oxaliplatin. A phase II study of gefitinib and FOLFOX chemotherapy in previously-un-treated patients with metastatic colorectal cancer demonstrated similar good results when compared with historical controls.32 Since bevacizumab has now been added to chemotherapy for patients with metastatic colorectal cancer, the addition of an oral tyrosine-kinase inhibitor of EGFR to chemotherapy plus bevacizumab remains an important area for additional investigation. Therefore, we are currently enrolling previously untreated patients with metastatic colorectal cancer onto a phase II study of bevacizumab, erlotinib, and FOLFOX.

### Table 6. Efficacy of Select Oxaliplatin-Containing Regimens in Second-Line Therapy for Metastatic Colorectal Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Response Rate (%)</th>
<th>Progression-Free Survival (months)</th>
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</thead>
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<tr>
<td>Rothenberg et al26</td>
<td>152</td>
<td>10</td>
<td>4.6</td>
</tr>
<tr>
<td>Giantonio et al (ECOG 3200)26</td>
<td>FOLFOX</td>
<td>289</td>
<td>9</td>
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<tr>
<td></td>
<td>FOLFOX + bevacizumab</td>
<td>290</td>
<td>22</td>
</tr>
<tr>
<td>Tournigand5</td>
<td>FOLFOX</td>
<td>81</td>
<td>15</td>
</tr>
<tr>
<td>Borner et al10</td>
<td>Capcitabine + oxaliplatin</td>
<td>26</td>
<td>15</td>
</tr>
<tr>
<td>Grothey et al17</td>
<td>Capcitabine + oxaliplatin</td>
<td>33</td>
<td>13</td>
</tr>
<tr>
<td>Kuo et al23</td>
<td>FOLFOX + gefitinib</td>
<td>27</td>
<td>33</td>
</tr>
<tr>
<td>Current study</td>
<td>Capcitabine + oxaliplatin + erlotinib</td>
<td>32</td>
<td>25</td>
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</tbody>
</table>

Abbreviations: FOLFOX, infusional fluorouracil, leucovorin, and oxaliplatin; ECOG, Eastern Cooperative Oncology Group.

### REFERENCES

CAPEOX/Erlotinib for Colorectal Cancer

27. Hochster HS: Capectabine plus oxaliplatin vs irinotecan 5-fluorouracil plus oxaliplatin in the treatment of colorectal cancer Con: Pumpin’ FU (or, avoiding that oral fluorouracil) Clin Adv Hematol Oncol 3:405-406, 2005

Authors’ Disclosures of Potential Conflicts of Interest
Although all authors completed the disclosure declaration, the following authors or their immediate family members indicated a financial interest. No conflict exists for all authors unless noted.

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Genentech (A)
Roche (A)
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