Uracil/Tegafur Plus Oral Calcium Folinate in Advanced Breast Cancer

Published on Physicians Practice (http://www.physicianspractice.com)

Uracil/Tegafur Plus Oral Calcium Folinate in Advanced Breast Cancer

Review Article [1] | July 01, 1999
By Eduardo Richardet, MD, PhD [2], Cecilia Pedraza, MD [3], Elizabeth Mickiewicz, MD [4], Guillermo Lerzo, MD [5], Federico Coppola, MD [6], Alicia Elli, MD [7], Graciela Uranga, MD [8], Silvia Jovtis, MD [9], Mario Bruno, MD [10], Monica Ventriglia, MD [11], Maria Andrea Cuevas, MD [12], Ana Maria Alvarez, MD [13], Luis Alberto Suarez, MD [14], and Luis Fein, MD [15]

Uracil and tegafur (in a molar ratio of 4:1 [UFT]) has proven activity against breast cancer and is delivered in an easy-to-administer oral formulation. Orzel, which combines UFT with the oral biomodulator, calcium folinate, may

Introduction

The overall prognosis for patients with advanced breast cancer who failed a first chemotherapy attempt remains poor. Currently, management with various combination-drug regimens seems to be primarily palliative, producing objective response rates of 20% to 40%. However, these regimens rarely cure and are associated with considerable toxicity.

UFT, an antineoplastic agent containing uracil plus tegafur in a molar ratio of 4:1, has demonstrated activity against colorectal, head and neck, and breast cancers in previous studies.[1-3] In breast cancer, response rates have ranged from 24% to 39%. This notable single-agent activity has resulted in escalation of research into its potential as therapy for breast cancer. UFT plus oral calcium folinate (Orzel) as a biomodulator possesses activity similar to that of intravenous 5-fluorouracil (5-FU) plus calcium folinate, with the additional advantage of oral delivery.[3] Based on this promising background, we designed a phase II protocol to evaluate the feasibility of using UFT plus oral calcium folinate to treat extensively pretreated patients with advanced breast cancer.[4-8]

Patients and Methods

Between June 1997 and April 1998, 24 patients were entered in this phase II tolerability study; only 18 patients were evaluable. Each patient had been previously treated for advanced breast cancer with chemotherapy or hormonal therapy. Prior regimens were based on the anthracyclines, paclitaxel (Taxol), vinorelbine (Navelbine), cyclophosphamide (Cytoxan), methotrexate, mitoxantrone (Novantrone), mitomycin-C (Mutamycin), 5-FU, tamoxifen (Nolvadex), and aminoglutethimide (Cytagren). The patient median age was 62 years (range, 46 to 75 years); Eastern Cooperative Oncology Group (ECOG) performance status was as follows: 0 in two patients; 1 in 14 patients, and 2 in eight patients (Table 1).

Patients were treated with UFT plus oral calcium folinate according to the following schema: 300 mg/m²/day of oral UFT plus 45 mg/day of oral calcium folinate administered every 12 hours for 28 days in cycles repeated every 35 days. Treatment history included UFT plus oral calcium folinate as second-line treatment for three patients (12.5%), as third-line treatment for 10 patients (41.7%), as fourth-line treatment for seven patients (29.2%), and as fifth-line treatment for four patients (16.7%).

Results

Responses

A total of 63 cycles have been administered for a mean of three cycles (range, one to 10 cycles) per patient. Based on this follow-up, we have observed one complete response (5.6%) occurring in soft tissue sites, and four partial responses (22.2%). The overall response rate (complete response + partial response) was 27.8%. Responses were noted in soft tissue, lung, and bone. Disease was
stable in eight patients (44.4%), and progressed in five patients (27.8%). Compliance to treatment protocol was evaluated by means of a patient-completed drug-intake log. Based on these documents, compliance with the prescribed drug regimen appears to be reliable.

**Toxicities**
The toxicity of this regimen was generally mild to moderate (Table 2). Only one patient (5.56%) experienced grade 3 diarrhea during the first drug treatment cycle, which did not recur after the UFT dose was reduced to 250 mg/m²/day. Two patients presented with grade 2 diarrhea (11.11%) and four patients with grade 1 diarrhea (22.22%). Other observed toxicities included grade 2 abdominal pain in one patient (5.56%), grade 2 mucositis in two patients (11.11%), and grade 2 leukopenia in one patient (5.56%). No patient required a treatment delay or withdrawal due to intolerance.

**Conclusions**
Based on our early results, oral administration of UFT plus oral calcium folinate appears to be easily administered and associated with low toxicity. In this study, a UFT plus oral calcium folinate regimen provided therapeutic benefit, accompanied by a good quality-of-life profile. This study continues to recruit patients. The final analysis will determine whether these results are borne out among a larger body of patients over a longer period of observation.

**References:**

**Source URL:**
http://www.physicianspractice.com/review-article/uracil-tegafur-plus-oral-calcium-folinate-advanced-breast-cancer

**Links:**