

REFERENCES

1. Lennard, L., Therapeutic drug monitoring of cytotoxic drug. Br J Clin Pharmacol 52 (2001): 75s-87s.
2. Bocci, G., Danesi, R., Di Paolo, A., Innocenti, F., Allegrini, G., Falcone, F., et al. Comparative pharmacokinetic analysis of 5-fluourouracil and its major metabolite 5-fluoro-5,6-dihydrouracil after conventional and reduced test dose in cancer patients. Clin Cancer Res 6 (2000): 3032-7.
3. Paolo, A. D., Danesi, R., Falcone, A., Cionini, L., Vannozzi, F., Masi, G., et al. Relationship between 5-fluorouracil disposition, toxicity and dihydropyrimidine dehydrogenase activity in cancer patients. Ann Oncol 12 (2001): 1301-6.
4. Young, A.M., Darayanani, S., Kerr, D.J., Can pharmacokinetic monitoring improve clinical use of fluorouracil? Clin pharmacokinetics 36(6) (1999) :391-8.
5. Glimelius, B., Jakobson, A., Graf, W. Bolus injection (2-4 min) versus short- term (10-20 min) infusion of 5-fluorouracil in patients with advanced colorectal cancer: a prospective randomized trial. Eur J Cancer 34(5) (1998): 674-8.
6. Larsson, P.A., Carlsson, G., Gustavsson, B., Graf, W., Glimelius, B. Different intravenous administration techniques for 5-fluorouracil. Acta Oncol 35(2) (1996): 207-12.
7. Milano, G., Etienne, M. C. 5-Fluorouracil. In: L. B. Grochow; M. M. Ames (eds.), A clinician's guide to chemotherapy pharmacokinetics and pharmacodynamics. p.289-300. Baltimore: Williams & Wilkins, 1998.
8. Terret, C.T., Erdociain, E., Guimbaud, R., Boisdrone-Cille, M., McLeod, H. L., Fety-Deporte, R., et al. Dose and time dependencies of 5-fluorouracil pharmacokinetics. Clin Pharmacol Ther 68(3) (2000): 270-9.
9. Gamelin, E., Danquechin-Dorval, E.M., Dumesnil, Y. F., Maillart, P.J., Goudier, M.J., Burtin, P.C., et al. Relationship between 5-fluorouracil (5-FU) dose intensity and therapeutic response in patients with advanced colorectal cancer receiving infusional therapy containing 5-FU. Cancer 77(3) (1996): 441-51.

10. Tebbutt, N.C., Cattell, E., Midgley, R., Cunningham, R., Kerr, D. Systemic treatment of colorectal cancer. *Eur J Cancer* 38 (2002): 1000-15.
11. Laufman, L.R., Krzeczkowske, K.A., Roach, R., Segal, M. Leucovorin plus 5-fluorouracil: an effective treatment for metastatic colon cancer. *J Clin Oncol* 5(9) (1987):1394-400.
12. Gamelin, E., Boisdran-Celle, M., Regimbeau, C., Cailleux, P.E., Alleaume, C., Maillet, M.L., et al. Long term weekly treatment of colorectal metastatic cancer with fluorouracil and leucovorin: results of a multicentric prospective trial of fluorouracil dosage optimization by pharmacokinetic monitoring in 152 patients. *J Clin Oncol* 16(4) (1998): 1470-8.
13. Etienne, M.C., Lagrange, J.L., Dassonville, O., Flemming, R., Thyss, A., Renée, N., et al. Population study of dihydropyrimidine dehydrogenase in cancer patients. *J Clin Oncol* 12(11) (1994): 2248-53.
14. Sohn, D.R., Cho, M.S., Chung, P.J. Dihydropyrimidine dehydrogenase activity in a korean population. *Ther Drug Monitoring* 21(2) April 1999: 152-4.
15. Morsman, J.M., Sludden, J., Ameyaw, M.M., Githang'a, J., Indalo, A., Ofori-Adjei, D., et al. Evaluation of dihydropyrimidine dehydrogenase activity in south-west asian, kenyan and Ghanaian populations. *Br J Clin Pharmacol* 50 (2000):269-72.
16. Chazal, M., Etienne, M.C., Renée, N., Bourgeon, A., Richelme, H., Milano, G. Link between dihydropyrimidine dehydrogenase activity in peripheral blood mononuclear cells and liver. *Clin Cancer Res* 2(3) Mar (1996): 507-10.
17. Saltz, L.B., Minsky, B. Adjuvant therapy of cancers of the colon and rectum. *Surg Clin of N Am* 82 (2002): 1035-58.
18. Davis, L.E. Colorectal cancer. In. Dapiro, J.T., Talbert, R.L., Yee, G.C., Matzke, G.R., Wells, B.G., Posey, L.M. (eds.) *Pharmacotherapy*. p. 2275-2327. New York: McGraw Hill, 2002.
19. Leslie, A., Steele, R.J.C. Management of colorectal cancer. *Postgrad Med J* 78 (2002): 473-8.
20. Cocconi, G., Cunningham, D., Van Cutsem, E., et al. Open, randomized, multicenter trial of raltitrexed versus fluorouracil plus high-dose leucovorin

- in patients with advanced colorectal cancer. J Clin Oncol 16(9) (1993): 2943-52.
21. Grothey, A., Schmoll, H.J. New chemotherapy approaches in colorectal cancer. Curr Opin in Oncol 13 (2001): 275-86.
22. Napier, M.P., Ledermann, J.A. Novel chemotherapeutic agents in colorectal cancer. Eur J Surg Oncol 26 (2000): 605-10.
23. Pazdur, R., Donillard, J.Y., Skilling, J.R., et al. Multicenter phase III study of 5-fluorouracil or UFTTM in patients with metastatic colorectal cancer. Proc Am Soc Clin Oncol 18 (1999): 263a. (abstract)
24. Carmichael, J., Popiela, T., Radstone, D., et al. Randomized comparative study of ORZEL (oral uracil/ tegafur) plus LV vs parenteral 5-FU plus LV in patients with metastatic colorectal cancer. Proc Am Soc Clin Oncol 18 (1999): 264a. (abstract)
25. Ishikawa, T., Utoh, M., Sawada, N., et al. Xeloda (Capecitabine): an orally available tumor-selective fluoro-pyrimidine carbamate. Proc Am Soc Clin Oncol 16 (1997): 208 (abstract).
26. Schuller, J., Cassidy, J., Dumont, E., et al. Preferential activation of capecitabine in tumor following oral administration to colorectal cancer patients. Cancer Chemother Pharmacol 45 (2000): 291-7.
27. Hoff, P. Capecitabine as first line treatment for colorectal cancer (CRC): integrated results of 1207 patients from 2 randomized, phase III studies. On behalf of the capecitabine CRC study group. Ann Oncol 11(suppl 4) (2000) 60. (abstract)
28. Ahmed, F.Y., Johnston, S.J., Cassidy, J., et al. Eniluracil treatment completely inactivates DPD in colorectal tumors. J Clin Oncol 17 (1999): 2439-45.
29. Saltz, L.B., Cox, J.V., Blanke, C., et al. Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. N Eng J Med 343(13) (2000): 905-14.
30. Douillard, J.Y., Cunningham, D., Roth, A.D., et al. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomized trial. Lancet 355 (2000):1041-7.

31. De Gramont, A., Figer, A., Seymour, M., et al. Leucovorin and fluorourcil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. J Clin Oncol 18(16) (2000): 2938-47.
32. Wolmark, N., Fisher, B., Rockette, H., et al. Postoperative adjuvant chemotherapy or BCG for colon cancer: results from NSABP C-01. J Natl Cancer Inst 80 (1988): 30-6. (abstract)
33. Moertel, C.G., Fleming, T.R., Macdonald, J.S., et al. Levamisole and 5-FU for adjuvant therapy of resected colon carcinoma. N Eng J Med 322 (1990): 352-8.
34. Moertel, C.G., Fleming, T.R., Macdonald, J.S., et al. The Intergroup study of 5-FU and levamisole and levamisole and levamisole alone as adjuvant therapy for stage C colon cancer. A final report. Proc Am Soc Clin Oncol 122 (1992): 321-6. (abstract)
35. Moertel, C.G., Fleming, T.R., Macdonald, J.S., et al. Fluorouracil plus levamisole as effective adjuvant therapy after resection of stage III colon carcinoma: A final report. Ann Intern Med 122 (1995): 321-6.
36. International Multicenter Pooled Analysis of Colon cancer Trials.(IMPACT) investigators. Efficacy of adjuvant fluorouracil and folinic acid in colon cancer. Lancet 345 (1995): 939-44.
37. Wolmark, N., Rockette, H., Fisher, M., et al. The benefit of leucovorin modulated fluorouracil as postoperative adjuvant therapy for primary colon cancer: results from National Surgical Adjuvant Breast and Bowel Project protocol C-03. J Clin Oncol 11 (1993): 1879-87.
38. Haller, D.G., Catalano, P.J., Macdonald, J.S., et al. Fluorouracil, leucovorin and levamisole adjuvant therapy for colon cancer: five-year final report of INT-0089. Proc Am Soc Clin 17 (1998):256a (abstract)
39. Wolmark, N., Rockette, H., Mamounas, E.P., et al. Clinical trial to assess the relative efficacy of 5-FU and leucovorin, 5-FU and levamisole and 5-FU/ LV and levamisole in patients with Duke's B and C carcinoma of the colon: Results from National Surgical Adjuvant Breast and Bowel Project C-04. J Clin Oncol 17 (1999): 3553-9.

40. O'Connell, M.J., Laurie, J.A., Kahn, M., et al. Prospectively randomized trial of postoperative adjuvant chemotherapy in patients with high-risk colon cancer. J Clin Oncol 16 (1998): 295-300.
41. QUASAR Collaborative Group. Comparison of fluorouracil with additional levamisole, higher-dose folinic acid or both as adjuvant chemotherapy for colorectal cancer: a randomized trial. Lancet 355 (2000): 1588-96.
42. Porchen, R., Bermann, A., Loffler, T., et al. Fluorouracil plus leucovorin as effective adjuvant chemotherapy in curatively resected stage III colon cancer: results of the trial adjCCA-01. J Clin Oncol 19(6) (2001): 1787-94.
43. Mamounas, E., Wieand, S., Wolmark, N., et al. Comparative efficacy of adjuvant chemotherapy in patients with Duke's B versus Duke's C colon cancer: results from four National Surgical Adjuvant Breast and Bowel Project Adjuvant Studies (C-01, C-02, C-03, and C-04). J Clin Oncol 17(5) (1999): 1349-55.
44. Mamounas, E.P. Adjuvant chemotherapy for stage II colon cancer: the time has come. Eur J Surg Oncol 26 (2000): 725-9.
45. Wein, J., Hahn, E.G., Merkel, S., et al. Adjuvant chemotherapy for stage II (Duke's B) colon cancer: too early for routine use. Eur J Surg Clin 26 (2000): 730-2.
46. The International Multicenters Pooled Analysis of B2 Colon Cancer Trials (IMPACT B2) Investigators. Efficacy of adjuvant fluorouracil and folinic acic in B2 colon cancer. J Clin Oncol 17(5) (1999): 1356-63.
47. Sargent, D.J., Goldberg, R.M., Jacobson, S.D., et al. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. N Eng J Med 345(15) (2001): 1091-7.
48. Douglass, H.D. Jr, Moertel, C.G., Mayer, R.J., et al. Survival after postoperative combination treatment of rectal cancer. N Eng J Med 315 (1986): 1294-5.
49. Fisher, B., Wolmark, N., Rockette, N., et al. Postoperative adjuvant chemotherapy or radiation therapy for rectal cancer: results from NSABP protocol R-01. J Natl Cancer Inst 80 (1988): 21-9 (abstract).

50. Wils, J., Dwyer, P.O., Labianca, R. Adjuvant treatment of colorectal cancer at the turn of the century: European and US perspectives. Ann Oncol 12 (2001): 13-22.
51. Krooke, J.E., Moertel, D.G., Gunderson, L.L., et al. Effective surgical adjuvant therapy for high-risk rectal carcinoma. N Eng J Med 324 (1991): 709-15.
52. O'Connell, M.J., Mortenson, J.A., Wieand, H.S., et al. Improving adjuvant therapy for rectal cancer by combining protracted-infusion fluorouracil with radiation therapy after curative surgery. N Eng J Med 331 (1994): 502-7.
53. Gastrointestinal Tumor Study Group. Radiation therapy and fluorouracil with or without semustine for the treatment of patients with surgical adjuvant adenocarcinoma of the rectum. J Clin Oncol 10 (1992): 549-57.
54. Tepper, J.E., O'Connell, M.J., Petroni, G.R., et al. Adjuvant postoperative fluorouracil-modulated chemotherapy combined with pelvic radiation therapy for rectal cancer: Initial results of Intergroup 0114. J Clin Oncol 15 (1997): 2030-9.
55. Wolmark, N., Wieand, H.S., Hyams, D.N., et al. Randomized trial of postoperative adjuvant chemotherapy with or without radiotherapy for carcinoma of the rectum: National Surgical Adjuvant Breast and Bowel Project protocol R-02. J Natl Cancer Inst 92 (2000): 388-96. (abstract)
56. Camma, C., Giunta, M., Fiorica, F., et al. Prospective radiotherapy for respectable rectal cancer: a meta-analysis. JAMA 284 (2000): 1008-15.
57. Abel, R., Bjornson, D.C., Corrigan, B., Evans, R.P., Hunter, M., Murakami, K.E., et al. Fluorouracil [monograph on CD-ROM]. 2003 Dec.[cited 2004 Jan 5].
58. United States Pharmaceutical convention. USP XXIV. Philadelphia, MD. National publishing (1999) : 736-8.
59. Fraile, R.J., Baker, L.H., Buroker, T.R., et al. Pharmacokinetics of 5-Fluorouracil administrated orally, by rapid intravenous and by slow infusion. Cancer Res 40 (1980): 2223-8.
60. Schalhorm, A., Kuhl, M. Clinical pharmacokinetics of fluorouracil and folinic acid. Semin in Oncol 19(2) (1992): 82-92.

61. Martino, M.M., Martino, R. Clinical studies of three oral prodrugs of 5-fluorouracil (capecitabine, UFT, S-1): a review. *The Oncologist* 7 (2002): 288-323.
62. Aschele, C., Sobrero, A., Faderan, M.A., et al. A novel of resistance to 5-fluorouracil in human colon cancer (HCT-8) sublines following exposure to two different clinically relevant dose schedules. *Cancer Res* 52 (1992):1855-64.
63. Sobrero, A.F., Aschele, C., Bertino, J.R.. Fluorouracil in colorectal cancer- a tale of two drugs: implications for biochemical modulation. *J Clin Oncol* 15 (1997): 368-81.
64. Diasio, R.B., Johnson, M.R. Dihydropyrimidine dehydrogenase: its role in 5-fluorouracil clinical toxicity and tumor resistance. *Clin Cancer Res* 5 (1999): 2672-3.
65. Guimbaud, R., Guichard, S., Dusseau, C., et al. Dihydropyrimidine dehydrogenase activity in normal, inflammatory and tumor tissues of colon and liver in humans. *Cancer Chemother Pharmacol* 45 (2000): 477-82.
66. BC Agency care& research. Fluorouracil.2004 [cited 2004 Feb 11]:[10 screens].
Available from: URL: <http://www.Fluorouracil%20BC%20cancer%20agency.htm>.
67. Thyss, A., Milano, G., Reene, N., et al. Clinical pharmacokinetic study of 5-FU in continuous 5-day infusions for head and neck cancer. *Cancer Chemother Pharmacol* 16 (1986): 64-6.
68. Wattanatorn, W., McLeod, H.L., Macklon, F., et al. Comparison of 5-fluorouracil pharmacokinetics in whole blood, plasma, and red blood cells in patients with colorectal cancer. *Pharmacother* 17(5) (1997): 881-6.
69. Loos, W.J., Bruijn, P., Zuylen, L.V., Verweij, J., et al. Determination of 5-Fluorouracil in microvolumes of human plasma by solvent extraction and high-performance liquid chromatography. *J Chromato B* 735: (1999): 293-7.
70. Escoriaza, J., Aldaz, A., Calvo, E., et al. Simple and sensitive determination of 5-fluorouracil in plasma by high-performance liquid chromatography application to clinical pharmacokinetic studies. *J Chromato B* 736 (1999): 97-102.

71. U.S. department of heath and human services food and drug administration (center for drug evaluation and research (CDER) and center for veterinary medicine (CVM). Guidance for industry; bioanalytical method validation (online). Available from: <http://www.fda.gov/cder/guidance/4252fnl.pdf>. (2001,May).
72. Tomiak, A., Vincent, M., Kocha, W., et al. Standard dose (mayo regimen) 5-fluorouracil and low dose folinic acid: prohibitive toxicity? Am J Clin Oncol. 23(1) (2000): 94-98.



Appendices

ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

Appendices

1. Pharmacokinetic parameters formula from winnonlin software.

$$Ke = (\ln C_1 - \ln C_2) / (t_2 - t_1)$$

$$\text{Half-life} = 0.693/Ke$$

$$Vd = \text{Dose}/Ke \times AUC_{0-\infty}$$

$$Cl = \text{Dose}/AUC_{0-\infty}$$

$$[AUC_{0-t}]_0^t = \sum (C_{n-1} + C_n)(t_n + t_{n-1})/2$$

Ke from winnonlin calculated may not equal to in manual calculated because in winnonlin software used more than 2 point of concentration to select the best fit of calculated value

Table A Eastern Cooperative Oncology Group (ECOG) Performance Status

Performance Status	Description ECOG scale
0	Fully active, able to carry on all predisease activity
1	Restricted in strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature.
2	Out of bed more than 50% of time; ambulatory and capable of self-care, but unable to carry out any work activities
3	In bed more than 50% of time; capable of only limited self-care
4	Bedridden; cannot carry out any self-care, completely disabled

Table B

Common Toxic Criteria version 2, National Institute of Health, National Cancer Institute

Toxicity	Grade			
	0	1	2	3
WBC ($\times 10^3$ g/dL)	≥ 4.0	3.0 – <LLM	2.0-2.9	1.0-1.9
PLT (/ μ L)	WNL	75.0-normal	50.0-74.9	10.0-49.9
Hgb (g/dL)	WNL	10.0-normal	8.0-10.0	6.5-7.9
ANC	≥ 2.0	<1.5-1.9	1.0-1.4	0.5-0.9
Hand-foot syndrome	none	Skin changes or dermatitis without pain (erythema, peeling)	Skin changes with pain, not interfering with function.	Skin changes with pain, interfering with function.
Diarrhea	none	Increase of 2-3 stools/day over pre-Rx baseline	Increase of 4-6 stools/day, nocturnal stools, or moderate cramping	Increase of 7-9 stools/day, incontinence, or severe cramping
Stomatitis	none	Painless ulcers, edema, or ulcers, but can eat	Painful erythema, edema, or ulcers, but can eat	Painful erythema, edema, or ulcers, and cannot eat
				Requires parenteral or enteral support

Table C Response criteria for the evaluation of target lesions

The definitions specifically for the evaluation of target lesions are given below:

Complete Response (CR)	The disappearance of all target lesions with no new lesion forming.
Partial Response (PR)	At least a 30% decrease in the sum of the LD of target lesions, taking as a reference the baseline sum of the LD.
Progressive Disease (PD)	At least a 20% increase in the sum of the LD of target lesions, taking as a reference the smallest sum of the LD recorded since the treatment start, or the appearance of one or more new lesions.
Stable Disease (SD)	The target lesions have neither sufficiently shrunk to quality for PR, nor sufficiently increased in size to quality for PD, taking as reference the smallest sum of the LD since treatment started.



**ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย**

VITAE

Ms. Natthinee Khaonongbua was born on November 14,1973 in Sriracha District of Chonburi Province, Thailand. She graduated with Bachelor Degree in Pharmaceutical Sciences in 1996 from Faculty of Pharmacy, Chiang Mai University. June 2001,she had been enrolled in the Master Degree Program of Clinical Pharmacy at Faculty of Pharmaceutical Sciences, Chulalongkorn University (CU). Currently, she is the staff clinical pharmacist at Department of Pharmacy Service in Lamphun Hospital, Lamphun.

