一、 有研究探討比較 efavirenz 以兩種不同劑量給藥方式於 HIV 治療之有效性與安全性；請仔細閱讀以下之摘要並回答問題： （共25分）

Efficacy of 400 mg efavirenz versus standard 600 mg dose in HIV-infected, antiretroviral-naive adults (ENCORE1): a randomised, double-blind, placebo-controlled, non-inferiority trial. ENCORE1 Study Group.

Background: The optimum dose of key antiretroviral drugs is often overlooked during product development. The ENCORE1 study compared the efficacy and safety of reduced dose efavirenz with standard dose efavirenz in combination with tenofovir and emtricitabine as first-line treatment for HIV infection. An effective and safe reduced dose could yield meaningful cost savings.

Methods: ENCORE1 is a continuing non-inferiority trial in HIV-1-infected antiretroviral-naive adults in 38 clinical sites in 13 countries. Participants (plasma HIV-RNA >1000 $\log_{10}$ copies per mL, CD4 T-cell count 50–500 cells per μL) were randomly assigned by a computer-generated sequence with a blocking factor of four (stratified by clinical site and by screening viral load) to receive tenofovir plus emtricitabine with either a reduced daily dose (400 mg) or a standard dose (600 mg) of efavirenz. Participants, physicians, and all other trial staff were masked to treatment group. The primary endpoint was the difference in proportions of participants with plasma HIV-RNA of less than 200 copies per mL at 48 weeks. Treatment groups were regarded as non-inferior if the lower limit of the 95% CI for the difference in viral load was less than −10% by modified intention-to-treat analysis. Adverse events were summarized by treatment. This trial is registered with ClinicalTrials.gov, number NCT01011413.

Findings: The modified intention-to-treat analysis consisted of 630 patients (efavirenz 400=321; efavirenz 600=309). 32% were women; 37% were African, 33% were Asian, and 30% were white. The mean baseline CD4 cell count was 273 cells per μL (SD 99) and median plasma HIV-RNA was 4.75 $\log_{10}$ copies per mL (IQR 0.88). The proportion of participants with a viral load below 200 copies per mL at week 48 was 94.1% for efavirenz 400 mg and 92.2% for 600 mg (difference 1.85%, 95% CI −2.1 to 5.79). CD4 T-cell counts at week 48 were significantly higher for the 400 mg group than for the 600 mg group (mean difference 25 cells per μL, 95% CI 6–44; p=0.01). We recorded no difference in grade or number of patients reporting adverse events (efavirenz 400=89.1%, efavirenz 600=88.4%; difference 0.75%, 95% CI −4.19 to 5.69; p=0.77). Study drug-related adverse events were significantly more frequent in the 600 mg group than in the 400 mg group (146% [47] vs 118 [37]), difference −10.5%, 95% CI −18.2 to −2.8; p=0.01) and significantly fewer patients with these events stopped treatment (400 mg=6 [2%], 600 mg=18 [6%], difference −3.96%, 95% CI −6.96 to −0.95; p=0.01).

Interpretation: In Our findings suggest that a reduced dose of 400 mg efavirenz is non-inferior to the standard dose of 600 mg, when combined with tenofovir and emtricitabine during 48 weeks in ART-naive adults with HIV-1 infection. Adverse events related to the study drug were more frequent with 600 mg efavirenz than with 400 mg. Lower dose efavirenz should be recommended as part of routine care.

Lancet 2014; 383:1474–1482.

（一） 請以<u>中文</u>簡要敘述此研究之方法與結果。 （10 分）

（二） 一般而言，治療愛滋病毒感染的原則是什麼？ （ 4 分）

（三） Efavirenz 屬於哪一類愛滋病毒藥物？作用機轉是什麼？常見之副作用與交互作用有哪些？應該如何處理與避免？ （11 分）

見背面

二、請就下列處方回答問題：　　（共20分）

臺大醫院 ⊕NTUH

國立臺灣大學醫學院附設醫院

院址：臺北市中山南路七號　臺北市常德街一號

網址：http://ntuh.mc.ntu.edu.tw

2015/02/09　10:45　　臺大醫院門診調劑單

病人姓名　李 XX	先生	領藥窗口	09
年齡　073　性別　M	80 Kg　身份 N01	領藥號碼	L-8173
科別　MED	醫師　朱 XX	病患姓名	李 XX
診斷　250.0	Diabetes	處方日期	2015/02/09
272.4	Hyperlipidemia	病歷號碼	225xxxx
585.3	Chronic kidney disease	結帳號碼	530xxxx
調劑藥師　陳 XX	覆核藥師　周 XX	第　次領藥	

共 05 種

Y 01	Loditon 500 MG (METFORMIN TABLETS)	PO	1 TAB	BID 28 天	56	TAB
Y 02	LASIX 40 MG (FUROSEMIDE TABLETS)	PO	0.5 TAB	BID PC 28 天	28	TAB
Y 03	Glucobay 50 MG (ACARBOS TABLETS)	PO	1 TAB	TID PC 28 天	84	TAB
Y 04	NovoNorm 1 MG (REPAGLINIDE)	PO	1 TAB	TID AC 28 天	84	TAB
Y 05	Crestor Film-coated 10 MG (ROSUVASTATIN CALCIUM TABLETS)	PO	0.5 TAB	QD 28 天	14	TAB

（一）　請問此張處方缺乏那些資訊？ 還需要哪些資訊方能完整評估此處方的適當性？　（ 5 分）

（二）　依據這張處方上的現有資訊，你認為主要有那些用藥問題？ 合理的處方應該是什麼？　（10 分）

（三）　請問該如何發揮專業處理這張處方的用藥問題？ 處理完後，你會重點式提供病友那些衛教內容？　（ 5 分）

接次頁

三、請閱讀短文，並回答下列問題：　（15 分）

Ferric citrate approved as phosphate binder for patients on dialysis

FDA on September 5 approved the marketing of ferric citrate tablets as a means of controlling the serum phosphorus concentration in patients with chronic kidney disease who are undergoing dialysis.

The phosphate binder, which at press time did not have a brand name, will be marketed and distributed by Keryx Biopharmaceuticals Inc.

The drug's ferric ion binds to dietary phosphate in the gastrointestinal tract to form ferric phosphate, which is excreted in stool. By preventing absorption of phosphate, the drug lowers the patient's serum phosphorus concentration.

According to the product's FDA approved labeling, the starting dosage of ferric citrate is two tablets taken three times daily with meals. The dosage can be increased or decreased by one or two tablets at one-week or longer intervals to control a patient's serum phosphorus concentration. No more than 12 tablets should be taken in one day.

Ferric ion can bind to anions other than phosphate. The labeling states that doxycycline doses should be taken at least one hour before ferric citrate tablets. In general, the labeling advises clinicians to consider separating the time of administration of ferric citrate from the administration time for any oral medication whose bioavailability could be reduced by ferric ion and consequently have a "clinically significant effect" on safety or effectiveness.

Some of the iron in ferric citrate may be absorbed from the gastrointestinal tract. The drug is contraindicated inpatients with an iron overload syndrome, such as hemochromatosis. Clinicians are told in the labeling's Warnings and Precautions section to assess patients' iron status before starting ferric citrate therapy and also monitor iron status during therapy.

During clinical trials of the drug, the most common adverse events in patients who received ferric citrate were diarrhea, nausea, constipation, vomiting, and cough.

Thompson, Cheryl A. *AJHP* 2014;71(21):1822.

（一）　請問此新藥之適應症？ 其作用機轉？　（3 分）
（二）　請用拉丁縮寫寫出此藥起使之用法。　（3 分）
（三）　目前有那些藥有相同用途？ 各有何優缺點？　（3 分）
（四）　一般口服鐵劑有哪些成分？ 與此藥有何不同？　（3 分）
（五）　Citrate 在腎衰竭病人使用有何此文未提及的潛在問題？　（3 分）

見背面

四、配合題　　（每格一分，共 20 分）

（一） 請將下列藥品相對應的法定適應症之代碼（**A~Q**），標明題號作答於試卷內之「非選擇題作答區」。[答案可能不只一個，可重複選]　(10%)

題號	藥品	答案	適應症
1.	Amantadine	(1)	**A.** HSV infection
2.	Cotrimoxazole	(2)	**B.** Multiple myeloma
3.	Dapsone	(3)	**C.** Migraine, prophylaxis
4.	Everolimus	(4)	**D.** HBV hepatitis
5.	Foscarnet	(5)	**E.** CMV retinitis
6.	Hydroxychloroquine	(6)	**F.** Transplant rejection
7.	Lamivudine	(7)	**G.** Leprosy
8.	Propranolol	(8)	**H.** Renal cell carcinoma
9.	Thalidomide	(9)	**I.** Influenza A virus influenza
10.	Valganciclovir	(10)	**J.** Pneumocystis pneumonia
			K. Essential tremor
			L. HIV infection
			M. Malaria
			N. Parkinsonism
			O. Lupus erythematosus
			P. *Toxoplasma gondii* encephalitis
			Q. EB virus infection

（二） 請就下列*藥品不良反應*最相關之：1) 具代表性藥品代碼（**A~J**）、 2) 監測該反應之指標代號碼（**a~j**），標明題號依序作答於試卷內。(10%)

題號	*藥品不良反應*	答案	最具代表性藥品	血中監測指標
1.	Thrombocytopenia	(1)	**A.** Alphacalcidol	**a.** Amylase
2.	Hepatotoxicity	(2)	**B.** Amiodarone	**b.** Creatinine
3.	Nephrotoxicity	(3)	**C.** Heparin	**c.** Platelet
4.	Agranulocytosis	(4)	**D.** Fenofibrate	**d.** ALT
5.	Rhabdomyolysis	(5)	**E.** Tacrolimus	**e.** Potassium
6.	Hypothyroidism	(6)	**F.** Foscarnet	**f.** Seg. & band
7.	Pancreatitis	(7)	**G.** Pyrazinamide	**g.** Uric acid
8.	Hyperuricemia	(8)	**H.** Sitagliptin	**h.** Free T_4 & TSH
9.	Hyperkalemia	(9)	**I.** Isoniazid	**i.** Creatinine kinase
10.	Hypercalcemia	(10)	**J.** Ticlopidine	**j.** Calcium

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五、請閱讀文章，並回答下列問題：　（共20分）

CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network

Although there has been substantial hype over the potential of genetic testing to improve medication use, the relatively low uptake of pharmacogenetics into clinical practice provides valuable lessons as to the barriers to implementing "individualized" medicine. Several important pharmacogenetic tests have been available from Clinical Laboratory Improvement Amendments (CLIA)-approved laboratories for many years, and yet their adoption in the clinic remains uncommon. Although there is a paucity of evidence of clinical utility and cost-effectiveness with respect to many of the pharmacogenetic tests, the evidence for a few of them is quite strong. Given this background, why is the extent of clinical adoption so low even for the useful tests that are available and often reimbursed by health-care payers?

Barriers to the adoption of pharmacogenetic tests in clinical practice include the fragmentation of health-care systems that preclude linking a "lifetime" genetic test result with future medical care, the low use of electronic medical records that are vital to linking test results with medication prescribing/dispensing/administration, health-care systems that do not reward the prevention of disease (or adverse drug effects), the lack of sufficient awareness about genomics on the part of many clinicians, and the fact that little of such testing is done preemptively and therefore the results are not available when the prescribing decision is made. Some of these barriers will persist for many years to come.

Clin Pharmacol Ther 2011;89:464–467.

（一）　試簡要敘述此文要旨，並闡述你對此領域之認知。　（10 分）

（二）　Pharmacogenetics 於國內臨床應用之現狀如何？試列舉相關藥品例說明之。　（10 分）

試題隨卷繳回