

vinorelbine had significantly longer progression-free survival than in those given gefitinib. Thus two trials have now compared an EGFR tyrosine kinase inhibitor with chemotherapy in non-small-cell lung cancer,^{1,7} and both challenge widely held notions about specific predictive factors. Caution has also been advised about the use of first-line EGFR tyrosine kinase inhibitors selected by *EGFR* mutations.⁸ Nevertheless, from INTEREST, we now have more than one option to offer patients after first-line chemotherapy. While our understanding of predictive biomarkers develops, the choice of drug is likely to be influenced by patients' views and performance status as well as previous adverse effects.

Important lessons can be learnt from this experience. First, we should not jump to conclusions about specific predictive factors only because they fit the scientific foundations that underpin the design and development of new targeted agents with the fashionable goal of tailoring treatment to the individual patient and the tumour's biology. Also, maybe we were too hasty in adopting docetaxel as a standard second-line therapy on the basis of a small trial⁹ (TAX 317; 55 patients received the safer dose of 75 mg/m²) to allow examination of predictive factors for benefit from chemotherapy against best supportive care. No adequate substitute exists for well-designed, large randomised trials with important clinical and biological outcomes, and ultimately, such

trials have the best chance of changing our practice and our understanding of disease.

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Alternative form of artemether-lumefantrine for infants

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In today's *Lancet*, Salim Abdulla and colleagues, in a non-inferiority randomised trial, compare the efficacy of artemether-lumefantrine dispersible tablets with the crushed commercial tablet in African infants and children with uncomplicated malaria.¹ They conclude that a six-dose regimen with the new dispersible tablet is as efficacious as the crushed tablet, and has a similar safety profile. The long follow-up (28 days) to ascertain parasitological cure rates, in view of the long half-life of lumefantrine, was particularly reassuring.² The dispersible tablet has a sweet cherry flavour and contains the same amount of artemether and lumefantrine as the crushed tablet. The dispersible tablet was developed to facilitate administration to infants and young children.

Artemether-lumefantrine is efficacious in children and adults.^{3–5} Access to prompt and effective treatment

of malaria is the main challenge in Africa, but dose accuracy and adherence to schedule are equally important because adequate therapeutic response depends on them. Many factors can affect adherence to artemisinin-combination therapies, including the bitter taste and tablet formulation of such combinations. The bitter taste may cause children to vomit the drug. The currently used artemether-lumefantrine fixed combination, when prescribed to infants and small children, has to be crushed by mothers at home, which may lead to the loss of active ingredients and thus under-dosing.⁶ Poor adherence to artemether-lumefantrine will also create favourable conditions for the development of drug resistance.⁷ Lack of adherence and compliance by infants and young children is of particular concern because most of malaria's morbidity



Hailay Desta Teklehaimanot

Mother crushing tablet of artemether-lumefantrine for malaria treatment for her child

and mortality in sub-Saharan Africa is in those aged below 5 years.⁸

If the treatment of uncomplicated malaria with artemether-lumefantrine is to affect the control of malaria, the drug must be acceptable and tolerable. There is a need for alternative formulations that offer increased ease of administration and compliance for infants and children. It is not sufficient for a drug to be efficacious. It also has to be suitable and effective under routine operations and accepted by its target population. As exciting as the availability of artemether-lumefantrine is, unless this innovation is combined with developments that ensure maximum effectiveness in children, its impact will continue to be compromised both in terms of its therapeutic outcomes and its lifespan as an effective antimalarial. We could not agree more with Abdulla and colleagues about the need for alternatives to crushed tablets of artemether-lumefantrine. Unless palatable and attractive alternative formulations of artemisinin-combination therapies are available, the challenge of preventing children dying from malaria will continue.

Artemisinin-combination therapies have been in use for more than a decade for the treatment of uncomplicated

malaria in children and adults. However, the research into the development of alternative formulations for children has been limited, and there has not been a single product registered so far that facilitates ease of administration and compliance.^{9,10} At a time when the global malaria community is aiming to mount comprehensive responses to the disease, Abdulla and colleagues' study is timely.

From a public-health perspective, Abdulla and colleagues' results will have consequences for current clinical practice. The use of dispersible tablets will potentially enhance and promote better treatment outcomes, and delay the development of drug resistance at the same time. The effect will be substantial because artemether-lumefantrine is currently one of the most widely used antimalarials in Africa. Further independent studies are needed to convincingly show the efficacy of the new dispersible tablets. However, these new results should also redirect investigators to assess the relative acceptability of dispersible tablets versus crushed tablets.

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