Vinorelbine, methotrexate and fluorouracil (VMF) as first-line therapy in metastatic breast cancer: significance of the time between initiation of adjuvant therapy and of therapy for metastatic breast cancer

We read with interest the article concerning the results of vinorelbine, methotrexate and fluorouracil (VMF) as first line therapy in metastatic breast cancer in the May, 2003 issue of the Annals of Oncology [1]. The study showed that vinorelbine in divided doses (group 1 and group 2) was better tolerated and more efficacious when given once in 3-week cycles. Although responses were not significantly different between the groups, patients in group 1 and group 2 showed better responses than the patients in group 3. This difference may be explained in at least two ways. One is that a higher percentage of patients in group 3 had received CMF regimen as an adjuvant treatment that may lead to the drug resistance. Secondly, the authors did not give the time between initiation of adjuvant treatment and diagnosis and initiation of treatment for metastatic disease, which may affect the response and tolerability of VMF regimen.

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References


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Drs Isik and Altundag argue that differences in patient characteristics may be responsible for the somewhat poorer response rate noted in the third arm of our study, where vinorelbine was given in an undivided dose of 40 mg/m² on day one in contrast to the two other study arms where the dose was divided between days one and eight. While this may be correct we do not think that any firm conclusions on treatment efficacy should be drawn from our study, which was of a randomised phase II design, where tolerability is the primary endpoint and statistical power for the assessment of efficacy is low.

They also point out that heavier pretreatment may be responsible for differences in tolerance between the three study arms. We do not believe this to be the case. Actually, fewer patients in the more toxic arm 3 had received previous adjuvant chemotherapy with the more myelosuppressive FEC regimen than in the two other study arms. There was no significant difference between the groups regarding the time elapsed between the dates of initiation of adjuvant chemotherapy and chemotherapy for overtly metastatic disease.

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Renal tubular damage in rasburicase: risks of alkalisation

It is assumed that tumour lysis syndrome is primarily due to urate precipitation. Due to efficient urate depletion by rasburicase, it is suggested that severe renal damage will be absent [1]. Based on observation of a 7-year-old boy with Burkitt’s lymphoma, needing dialysis, we analysed calcium and phosphate metabolism using rasburicase. The index patient developed anuria, tetany and hyperphosphataemia (8.11 mmol). Creatinin rose from 38 to 188 µmol/l on dialysis. In order to optimise urate excretion, hyperhydration and alkalisation were given during rasburicase administration (7 days). The first 25 consecutive patients treated with rasburicase were analysed for creatinin and phosphate/calcium disturbances in the first weeks of treatment. Twenty-three children had leukaemia or lymphoma, and two patients had bilateral nephroblastoma or hepatoblastoma.

Urate levels were below the detection limit in all serum samples. However, in three patients, urate serum levels <0.25 mmol/l were seen on the first day. In four children with B-cell lymphomas, creatinin levels became abnormal during the rasburicase treatment period, normalising within 5 days. During rasburicase treatment and alkalisation, hypocalcaemia was noted in eight patients. Hyperphosphataemia was noted in the first 3 days after initiating treatment. Hypophosphataemia occurred more often, i.e. in 10 cases. Hypophosphataemia was noted relatively late (1–9 days after treatment started; median at 6 days). In five out of six B-cell cases hypophosphataemia occurred, which is more frequent than in children with other malignancies (P = 0.04).

Our data suggest that tubular damage is common at induction. Since urate depletion was efficient, calcium phosphate precipitation