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To the editor:

The EUTOS CML score aims to support clinical decision-making

Marin et al recently have praised the Sokal score and expressed reluctance in being the first when new ways are tried.[1] Unfortunately, the data they presented do not support their message.

The data of 2060 patients in the European Treatment and Outcome Study (EUTOS) for CML were used to develop and validate the EUTOS score.[2] The objective of the EUTOS score is to support clinical decision-making within the first 18 months after the initiation of treatment with Imatinib. The timeline of 18 months was chosen as our data showed convincingly that patients who did not achieve complete cytogenetic response (CCyR) up to this time point were less likely to achieve a CCyR during the further course of therapy and suffered a considerable risk of progressive disease. Thus, our work was focused on prognosticating as precise and efficient as possible the chance to be in CCyR after 18 months of therapy with Imatinib. Using the percentage of basophiles and the size of the spleen at diagnosis, the score divides the patients into a high-risk and a low-risk group with respect to a failure in meeting the therapeutic target of CCyR at 18 months.

Every third patient in the EUTOS high-risk group did not reach CCyR after 18 months of therapy. The sensitivity and specificity were 23% and 92%, respectively. The positive predictive value (PPV) was 34%. The high-risk group comprises only 11% of all patients. In contrast, the Sokal high-risk group enclosed 21% of the patients and additionally features an intermediate-risk group covering another 38% of the patients which does not reflect the fact that only a small proportion of CML patients today actually progresses. The Sokal high-risk group has a PVV of 25%, a sensitivity of 32%, and a specificity of 86%.

Marin et al in their correspondence did not provide data that contradict our results. Their analyses were focused on 8-year probabilities of overall survival (OS) and progression-free survival (PFS) and 8-year cumulative incidences of CCyR and major molecular remission (MMR) in patients of whom approximately a third were treated with second-generation tyrosine kinase inhibitors. Points in time and endpoints (OS and MMR) were not considered. No reference to CCyR status at 18 months was mentioned. They did not reveal why they chose the hitherto uncommon time of 8 years, in particular when the median observation time was only 5.7 years. Considering this, it would have been very helpful to provide information on the number of patients still under observation at 8 years as well as on the 95% confidence intervals corresponding to the probabilities given in Table 1 of their letter.[1]

Although the EUTOS score was validated in our paper we agree that a prognostic score should be cross-validated with patients not treated within randomized trials. Thus, we plan to test the EUTOS score with patients which were treated outside of studies and documented for the EUTOS CML registry.

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To the editor:

Dietary eicosapentaenoic acid (EPA) to produce antileukemic cyclopentenone prostaglandin J_3?

We read with great interest the article by Hedge et al,[1] reporting that Δ^{12}-prostaglandin (PG) J_3 (Δ^{12}-PGJ_3) has antileukemic activity in mice. Anti-inflammatory and antineoplastic activity has also been reported for 15-deoxy-$\Delta^{12,14}$-prostaglandin J_2 (15d-PGJ_2).[2] We

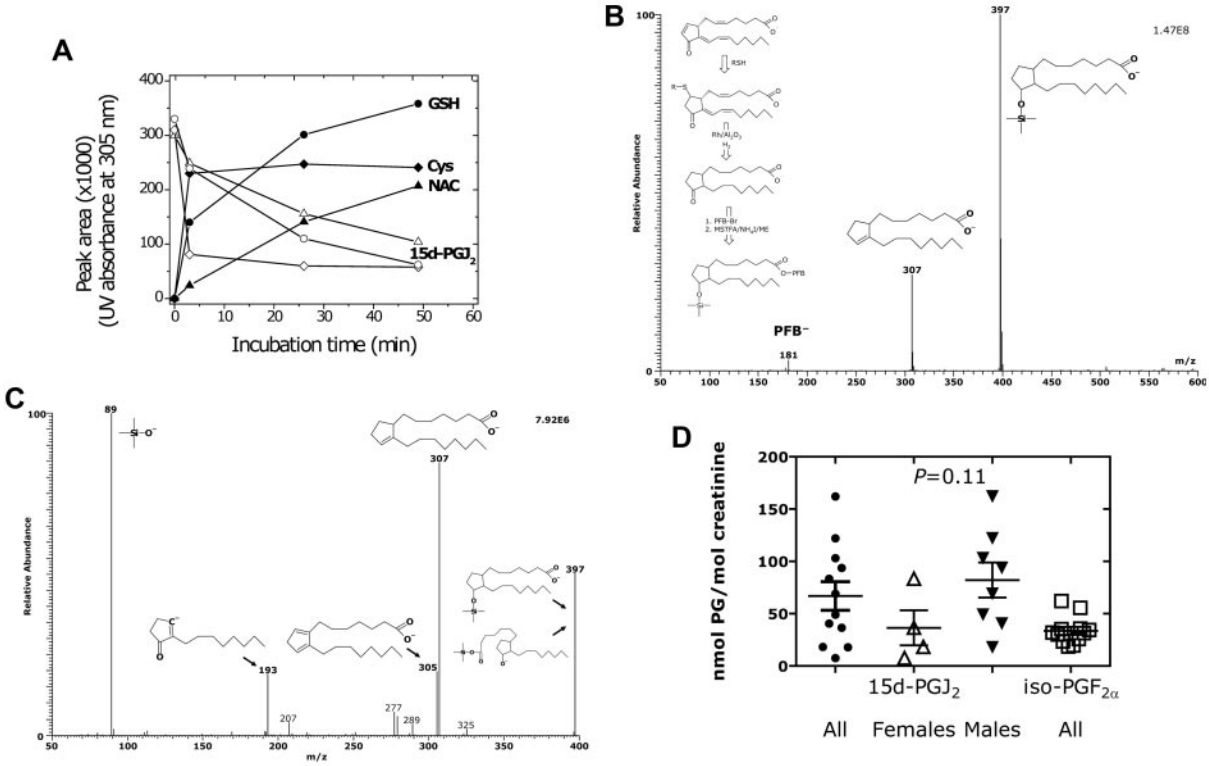

Figure 1. Excretion of 15d-PGJ_2 in human urine and its in vitro conjugation with glutathione, L-cysteine and *N*-acetylcysteine. (A) Reaction of 30μM 15d-PGJ_2 with each 1110μM glutathione (GSH), L-cysteine (Cys) or *N*-acetylcysteine (NAC) in 100mM phosphate buffer (pH 7.4) resulted in formation of the corresponding conjugates and concomitant decrease of 15d-PGJ_2 as measured by high-performance liquid chromatography (HPLC). Retention time was 12.7, 3.6, 2.8 and 1.2 minutes for 15d-PGJ_2 and the 15d-PGJ_2-NAC, 15d-PGJ_2-Cys, and 15d-PGJ_2-GSH conjugates, respectively. Reaction of 15d-PGJ_2 with Cys was accompanied by a shift of the maximum wavelength from 318 nm to 312 nm and an increase in absorbance at 230 nm. (B,C) The HPLC fractions of the above mentioned conjugates were collected and subjected to catalytical hydrogenation/desulfurization as described elsewhere for the cysteinyl leukotriene E_4.[5] After derivatization with pentafluorobenzyl (PFB) bromide (PFB-Br) followed by *N*-methyl-*N*-trimethylsilyl-trifluoroacetamide (MTSFA) in the presence of NH_4I and 2-mercaptoethanol (ME), gas chromatography-mass spectrometry (GC-MS) spectra were generated in the electron-capture negative-ion chemical ionization mode (B). The precursor ion at *m/z* 397 $[M\text{-}PFB]^-$ was subjected to collision-induced dissociation (CID) to generate GC-tandem MS (GC-MS/MS) spectra (C). Expectedly, virtually identical GC-MS and GC-MS/MS mass spectra were obtained from all thiol (RSH) conjugates of 15d-PGJ_2. Inserts in panels B and C indicate schematically part of the analytical procedure used and the proposed structures for the ions obtained. (D) Excretion of 15d-PGJ_2 and the isoprostane 15(*S*)-8-*iso*-$PGF_{2\alpha}$ (iso-$PGF_{2\alpha}$) was measured in fresh spot urine samples of 12 healthy volunteers (4 females) by GC-MS/MS using $^2H_4$-15d-PGJ_2 and $^2H_4$-15(*S*)-8-*iso*-$PGF_{2\alpha}$ as internal standards. 15(*S*)-8-*iso*-$PGF_{2\alpha}$ was extracted from urine (1 mL) by immunoaffinity column chromatography.[6] 15d-PGJ_2 was extracted from acidified (pH 4.5) urine samples by solid-phase extraction and purified by isocratic reverse phase HPLC. In the urine samples no 15d-PGJ_3 was detectable. 15(*S*)-8-*iso*-$PGF_{2\alpha}$ was measured because it is considered a COX-independent metabolite, analogous to 15d-PGJ_2 and 15d-PGJ_3.