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LETTER

Challenges in DPYD Test Implementation in Patients Treated with Fluoropyrimidines are DPYD Genotype Arriving on Time? [Letter]

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Dear editor

I read with great interest the findings published in your journal by Montrasio et al[1] about pharmacogenetic practice of anticancer drugs. However, I would like to share some comments regarding our experience of DPYD genotype implementation in a tertiary hospital this last year.

Due to heterogeneity in drug response and tolerability, up to one-third of those exposed to fluoropyrimidines (FP) are at risk of developing severe adverse events, which impact patient safety, quality of life, and may compromise drug efficacy.[2] DPYD genotyping identifies patients with DPD deficiency who require an initial-dose reduction. As mentioned, after EMA recommendation[3] there has been an increase in the number of test requests; even so, it is not always done on time.

In our hospital, from May 2022 to April 2023, DPYD genotype (rs3918290, rs55886062, rs67376798, rs56038477) was requested in 162 patients being treated with FP for the first time. The test was requested before starting a treatment based on FP in 122 patients (75%), and genotyping was available in 82 (51%) patients.

The proportion of patients who began FP-based treatment with the DPYD test requested and with an available test result were 75% and 47%, respectively. Monthly proportions are shown in Figure 1. The median number of days to obtain genotyping results was eight days (IQR = 4).

Five (3%) naive patients were heterozygous carriers (1 rs56038477, 4 rs67376798), two of whom started treatment with the result available, while the other three started FP treatment before the result was delivered by the laboratory.

Forty-two percent of patients (N=68) started with reduced doses, the reasons for which were: prevention of toxicity in frail patients (N=13), pending genotyping result (N= 52), and DPYD carrier (N=2). In 52 patients, the dose was reduced because the DPYD gene result was not available at the beginning, thereby compromising the efficacy of the treatment, while the reduction was only indicated in the five carriers.

Meanwhile, 21 patients (13%) started treatment at full doses without the availability of the result of their DPYD genotype and could have suffered more toxicity than expected as well as had their safety compromised.

The ultimate goal of pharmacogenetic testing is to achieve greater precision in selecting the right drug for the right patient[4] and reduce the overall burden on the healthcare system. Requesting DPYD genotyping in stages prior to the start of treatment will enable treatment to be started with the DPYD gene variants already genotyped in order to dose prospectively.

The landscape of pharmacogenomic testing is rapidly evolving. While barriers to the implementation of pharmacogenomic testing into clinical practice are multifaceted[5] (systemic, individual, logistical, knowledge-based, etc.) there is a need for increased awareness among oncologists regarding the significance of the test, as much as, develop resources available to support clinicians to implement this testing in their practice.[6] Likewise, it is needed to accelerate the circuits to avoid delays in urgent starting treatment when a 100% dose treatment is required.

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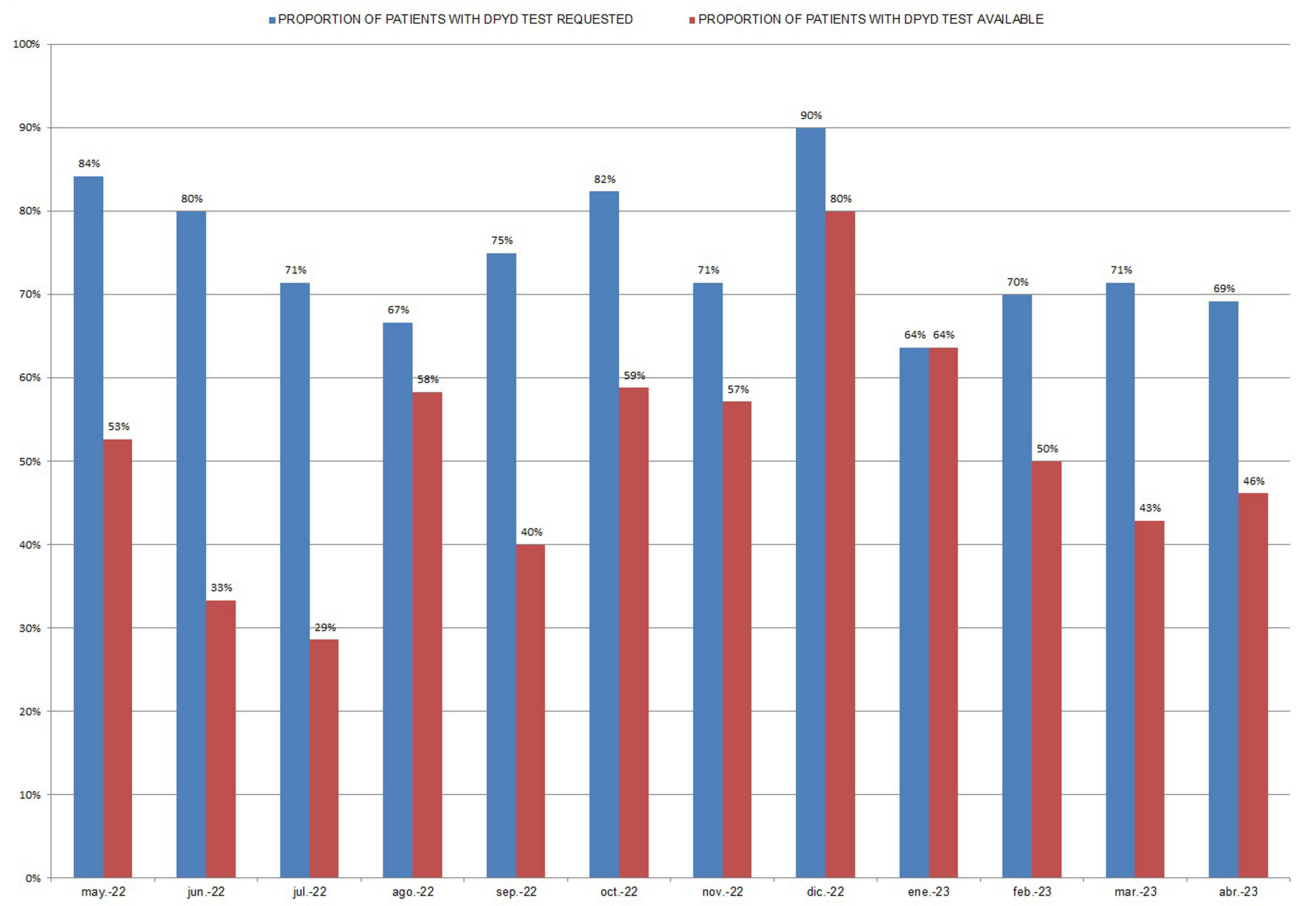

Figure 1 Proportion of patients who began FP-based treatment.

Disclosure

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