We started routine DPYD mutation testing in our hospital in March 2015. DPYD mutation testing was carried out on an ABI 3500 platform using Sanger sequencing. Uptill 31 August 2018 we analysed 1064 consecutive Indian patients who underwent DPYD mutation analysis in our laboratory. The incidence of heterozygous and homozygous DPYD mutation was 25.7% ($n = 273$) and 1.5% ($n = 16$), respectively, which seems much higher than reported in Caucasians. The most common mutations found were heterozygous mutations in exon 13 (c1627A>G) - 12.8% (136); exon 18 (c2194G>A) - 11.4% (121); both exon 18 (c2194G>A) and exon 13 (c1627A>G) - 1.5% (16). Homozygous mutations were found in exon 18 (c2194G>A) - 0.8% (8) and exon 13 (c1627A>G) - 0.8% (8). The incidence of DYPD mutation in the three most common cancers was: head and neck carcinoma 24.4% (142, $n = 583$); gastrointestinal carcinoma 31.8% (125, $n = 393$); oesophageal carcinoma 26.4% (19, $n = 72$).

Furthermore, in the study by Henricks *et al.* [2], the dose modification of 25% was adequate in all except c.1236G>A and c.2846A>T carriers. In our own pilot study, which inspired us to carry out routine DPYD analysis, we saw that with modified doses (a 50% dose reduction) the adverse events with 5-fluorouracil, especially myelosuppression and mucositis, decrease after dose reduction in DPYD-mutated patients [3]. This highlights the importance of carrying out routine DYPD genotyping and modifying the doses according to the CPIC guidelines.

Conflicts of Interest

V. Noronha received grants from Dr. Reddy's Laboratories, Amgen and Sanofi Aventis, outside the submitted work. K. Prabhash received grants from Biocon, Dr. Reddy's Laboratories, Fresenius Kabi India, Alkem Laboratories, Natco Pharma, BDR Pharmaceutics and Roche, outside the submitted work.

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When Can We Discharge Differentiated Thyroid Cancer Patients Who Present With High-Risk Disease and Subsequently Have an Excellent Response to Treatment?

Madam — Further to the publication on low-risk differentiated thyroid cancer (DTC) follow-up [1], the authors wanted to quantify the recurrence rate in DTC patients who present with American Thyroid Association (ATA) high-risk disease and subsequently have an excellent response to treatment (ERST) after dynamic risk stratification (DRS). The only published series include 10 [2] and five patients [3], with no recurrences reported.

We retrospectively analysed DTC patients treated in Leeds between 2001 and 2013, as previously detailed [1]. Of 756 patients stratified into the ERST group, 34 had 'initial ATA high-risk - subsequent DRS low-risk' disease [4,5]. The median follow-up duration was 9.9 (range: 5–17) years. Fifty-nine per cent (20/34) had ERST after total thyroidectomy followed by radioiodine remnant ablation after DRS carried out 6–12 months from treatment completion, whereas 76% (26/34) required additional intervention. Four patients presented with distant metastases – none of whom developed recurrence.

Radiological recurrence occurred in 2/34 (5.9%) patients - one (pT4aN1bM0 papillary thyroid cancer [PTC]) developing biochemical recurrence at 5 years from presentation followed by lung metastases 77 months from diagnosis; the second (pT3N1bM0 PTC) having biochemical recurrence at 3 years followed by regional nodes 38 months from diagnosis. The recurrence rate of ATA low-risk and intermediate-risk disease patients having ERST was 11/722 (1.5%).

This is the largest series of 'initial ATA high-risk - subsequent DRS low-risk' DTC with the longest follow-up duration. The recurrence rate in our group was 5.9% and even if incorrect by a two-fold factor, would remain relatively low. Both recurrences were heralded by biochemical recurrence

* Both have contributed equally.

within 5 years of diagnosis. This group should continue specialist follow-up for at least 5 years, following which discharge to primary care can be considered at the discretion of the thyroid specialist. No conclusion can be drawn on patients presenting with distant metastases as no such patients have been previously described.

Conflict of Interest

G.E. Gerrard has received honoraria for speakers bureau and advisory roles from Genzyme and Eisai Pharmaceuticals.

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