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LETTER TO THE EDITOR

# Sequential treatment with thrombopoietin-receptor agonists (TPO-RAs) in immune thrombocytopenia (ITP): experience in our center

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Dear Editor,

We have read with interest the paper of Mazza et al. [1] reporting their experience with thrombopoietin-receptor agonists (TPO-RAs) in 124 patients with immune thrombocytopenia (ITP). The response to treatment with romiplostim (ROM) and eltrombopag (ELT) is similar to that previously described (Kuter et al. [2], Busell et al. [3]). However, the number of patients in Mazza's study switched from ROM to ELT or vice versa is small. Response was observed in 4 of 7 patients switched to ELT after failure to ROM and in 2 patients who failed to ELT treated with ROM. The response to sequential treatment with TPO-RAs remains an interesting question.

We have evaluated our experience with TPO-RAs in sequential therapy. Between October 2009 and December 2015, 21 patients, 16 woman and 5 men, with ITP were treated with both ROM and ELT. The median age was 60 years. The median time since diagnosis was 4.2 years (range 0–18 years). The median number of previous treatments was 2 (range 1–4). Ten patients (47.6%) were splenectomized. Seventeen patients received ROM as first TPO-RA with 14 patients achieving response (10 complete and 4 partial) according to standard criteria (Rodeghiero et al. Blood 2009 [4]). ELT was the first agonist used in 4 cases and 3 of them achieved response. The reasons for switching were lack of response (4 cases), failure after initial response (9 cases), and poor tolerance or personal preference (8 cases). Response was observed in 13 of 17 patients switched from ROM to ELT, including 2 of 3 non-responders to ROM. Three of 4 patients switched from ELT to ROM responded to treatment. In our experience, only 3 patients showed failure with both drugs. Response rate for patients who switched because of *non-response* or relapsed after transient response was observed in 5 of 9 patients; in contrast, the 8 patients switching because of poor tolerance or personal preference achieved response.

Several authors have reported their experience with sequential treatment with both ROM and ELT. The results of these studies are shown in Table 1. The response observed in our patients is consistent with previous studies. Although most of these publications include a small number of patients, the overall results show a high response rate to the sequential treatment, suggesting a lack of cross-resistance between both drugs. The differences in the pharmacokinetics and the binding site on MPL could explain the absence of cross-resistance between romiplostin and eltrombopag. As regards the reason

**Table 1** Authors who have reported their experience with sequential treatment with both ROM and ELT

| Reference | Romiplostin to eltrombopag | | Eltrombopag to romiplostin | |
|---|---|---|---|---|
| | Patients | Response (%) | Patients | Response (%) |
| Aoki [6] | | | 1 | 1 (100%) |
| Polvorelli [7] | 1 | 1 (100%) | 1 | 1 (100%) |
| D'Arena [8] | 2 | 2 (100%) | | |
| Tsukamoto [9] | | | 6 | 6 (100%) |
| Khelaff [10] | 13 | 6 (54%) | 10 | 8 (80%) |
| Gonzalez-Porras [5] | 51 | 41 (80%) | | |
| Mazza [1] | 7 | 4 (57%) | 2 | 2 (100%) |
| Our series | 17 | 13 (77%) | 4 | 3 (75%) |
| Total | 91 | 67 (74%) | 24 | 21 (88%) |

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for switching drug, our results are similar to those shown by González-Porras et.al [5], observing a higher response rate in those who switched because of reasons other than treatment failure. Our results allow us to conclude that switching from one TPO-RA to the other is an effective option in patients with ITP.

**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

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