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First-line Therapy for Immune Thrombocytopenia: Time for Change

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The treatment landscape for chronic immune thrombocytopenia (ITP) has changed significantly over the last years, with the introduction of TPO-receptor agonists and new immune-modulating drugs. Treatment options for chronic ITP now enable doctors and patients to consider individualized therapy with a current arsenal of 3 types of TPO-RAs, rituximab, splenectomy, mycophenolate mofetil (MMF) and a broad range of newer drugs being in phase 2/3 trials including BTK inhibitors, fostamatinib, FcRn inhibitors and complement inhibitors.[1] Combinations of different therapeutic drugs might even lead to higher efficacy rates.[2]

Despite these advances, first-line treatment of ITP has not changed yet. Current consensus and guidelines recommend corticosteroid monotherapy for first-line treatment of ITP,[3] although their long-term complete response (CR) rates only ranges between 20% and 50%.[4,5] With a therapy being only this moderately successful, it argues for strategies aiming at reaching for more sustained CRs. Indeed, several attempts have already been made in for first-line therapy in ITP, as nicely summarized recently by Gómez-Almaguer et al.[5]

The first issue is the kind of steroid that is used. A recent meta-analysis showed that dexamethasone has equal overall response rates as prednisone, but is superior in sustained response rates after 12 months (relative risk 1.34) without changing adverse event rates.[6]

The combination of corticosteroids with rituximab led to a significant higher sustained response rate after 6 months as compared to corticosteroids alone (58%–76% versus 36%).[5] This was true for both a classical drug dosing as for a low dose rituximab regimen. The superiority of the combination of rituximab and dexamethasone in maintaining a sustained response was confirmed in a meta-analysis (relative risk 0.57).[6] In terms of safety, the adverse events were, in general, mild and balanced between the 2 groups without increase in infections in the rituximab group.[7]

Adding eltrombopag to dexamethasone led to a sustained CR of 57%.[8] A triple therapy of dexamethasone, eltrombopag and rituximab showed a CR rate of 79% after 2 years, although in a very small population.[9]

The combination of all-trans retinoic acid (ATRA) with dexamethasone had a CR rate at 6 months of 68% versus 41% compared with dexamethasone alone, without significant adverse events.[10] Adding MMF to dexamethasone resulted in CR rates of 78% versus 56% in dexamethasone monotherapy after 2 years.[11] In the latter FLIGHT trial, no differences in adverse events were seen (the reported lower quality of life in the MMF group was a nonsignificant difference).[11]

In all, one can say that there is evidence enough that we can do better in increasing the CR rates in first-line ITP. As with second-line therapy, the treatment of choice for acute ITP is one that can be individualized. Every treatment has its side effects, one more than the other, which could be the reason physicians are reluctant to change their current practice. However, preventing patients from developing chronic ITP will probably be far more beneficial in the end. With more immunosuppressive therapies in the horizon for ITP, upfront combination therapies can have a major impact.

AUTHOR CONTRIBUTIONS

REG conceptualized, wrote, and edited the manuscript.

DISCLOSURES

The author has no conflicts of interest to disclose.

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