

EDITORIAL

Combined immunotherapy and countermeasures for immune-related adverse events

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As the saying goes, “good medicine tastes bad,” and for the recently introduced immune checkpoint inhibitors (ICIs), the efficacy and adverse effects often seem to be in proportion^[1,2].

ICIs exert their antitumor effects by activating tumor immunity and disrupting the immune evasion mechanism of tumors; however, they often cause various adverse immunological events that make it impossible to continue treatment. Even in these cases, the therapeutic effects remain for a long time. There are several reports showing that immune-related adverse events (irAEs) are predictors of efficacy, mainly for anti-PD-1 antibodies^[2,3].

As discussed in this issue, combined immunotherapy is now being introduced and has shown high long-term survival rates compared with conventional treatments in malignant melanoma and renal cancer^[4,5]. Takayasu *et al.*, reports an effective case of renal cancer treatment with combined immunotherapy in this volume^[6]. Combined immunotherapy has also been used for lung cancer treatment, which affects a large population. At present, it is not clear whether irAEs can be used as an indicator of efficacy in combined immunotherapy with two ICIs, including ipilimumab, as in monotherapy. This may be especially true in severe cases. In combined immunotherapy, there is a clear increase in serious reactions with all carcinomas. Even at our institution, as shown by Nomizo *et al.*, we have already experienced an increase in the number of serious adverse events, even at this early stage of combined immunotherapy^[7]. If combined immunotherapy is expected to be effective, it is necessary to address these issues comprehensively.

In retrospect, in the era of cell-killing anticancer drugs, the side effects of anticancer drug therapies were handled mainly by the attending physician. However, with the advent of molecular-targeted drugs, collaborations with other departments and professions have become necessary for case management. Furthermore, ICIs, which present with a variety of irAEs, require wider collaboration with other departments, for which comprehensive efforts have been made, including patient education and management by outpatient pharmacy clinics, as reported by Hamatake *et al.*^[8]. This approach needs to be expanded

further for combined immunotherapy. It is unclear at this point whether current combined immunotherapies will take root in lung cancer and other cancer treatments in the future; however, it is clear that immunotherapy will become the mainstay of cancer treatment in the future.

We believe that long-term survival will be the fruit of the accumulated experiences and skills against irAEs.

Conflict of interest

The author declares no potential conflicts of interest.

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