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Original Research

Safety and efficacy of anti-programmed death 1 antibodies in patients with cancer and pre-existing autoimmune or inflammatory disease

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Abstract ***Objective:*** Patients with autoimmune or inflammatory disease (AID) are susceptible to immune-related adverse events (irAEs) when treated with immune check-point inhibitors (ICIs). We decided to analyse the safety and effectiveness of anti-PD-1 antibodies in AID patients and look for an association between the presence of pre-existing AID and the clinical outcome.
Methods: In a prospective study of the REISAMIC registry of grade ≥2 irAEs occurring in ICI-treated patients, we studied the associations between pre-existing AID on one hand and irAE-free survival, overall survival and best objective response rate on the other.
Results: We identified 45 patients with 53 AIDs in REISAMIC. The cancer diagnoses included melanoma (n = 36), non–small-cell lung cancer (n = 6) and others (n = 3). The most frequent pre-existing AIDs were vitiligo (n = 17), psoriasis (n = 12), thyroiditis (n = 7), Sjögren syndrome (n = 4) and rheumatoid arthritis (n = 2). Twenty patients (44.4%) presented with at least one irAE: eleven of these were associated with a pre-existing AID ('AID flare'). Treatment with anti-PD-1 antibodies was maintained in 15 of the 20 patients with an irAE. The IrAE-free survival time was significantly shorter in AID patients (median: 5.4 months) than in AID-free patients (median: 13 months, $p = 2.1 \times 10^{-4}$). The AID and AID-free groups did not differ significantly with regard to the overall survival time and objective response rate (p = 0.38 and 0.098, respectively).
Conclusion: In patients treated with anti-PD-1 antibody, pre-existing AID was associated with a significantly increased risk of irAEs. Our results indicate that cancer treatments with anti-PD-1 antibodies are just as effective in AID patients as they are in AID-free patients.

1. Introduction

The immune check-point inhibitors (ICIs, i.e. antibodies against cytotoxic T-lymphocyte–associated protein 4 [CTLA-4] or programmed death 1 [PD-1]) are effective in the treatment of several types of cancer [1–5]. The clinical success of this immunotherapeutic strategy has confirmed the immune system's role weight in controlling cancer and that the ability of neoplastic cells to hide from the immune system is one of the hallmarks of cancer [6,7].

With anti-CTLA-4 and anti-PD-1 antibodies, oncologists have been confronted with the occurrence of immune-related adverse events (irAEs) [9,8,10,11]. Interestingly, the occurrence of irAE has been linked to greater anti-tumour effectiveness of anti-PD-1 treatment in patients with advanced melanoma and non–small-cell lung cancer (NSCLC) [16–18]. Patients with pre-existing autoimmune and/or inflammatory disease (AID) were initially excluded from clinical trials of ICI because of the possible increase of irAE [12]. Despite this initial reluctance, patients with mild-to-moderate pre-existing AID are now often treated with ICI. Recent studies have shown that both anti-CTLA-4 and anti-PD-1 antibodies can be effective AID patients [13–15]. However, all the data published to date were collected in retrospective studies of small numbers of patients.

Using data from a prospective multicenter registry, we therefore decided to describe and analyse the safety and effectiveness of anti-PD-1 antibodies in patients with a pre-existing AID.

2. Patients and methods

2.1. Patients

We described ICI-treated patients with pre-existing AID and compared them with AID-free patient groups in terms of the occurrence of toxicity, overall survival (OS) and the best overall response rate (ORR). The patients had been included in the prospective REISAMIC registry ('Registry of Severe Adverse Events of Immunomodulating Monoclonal Antibodies in Oncology') between June 1st, 2014, and December 31st, 2016. REISAMIC includes all patients treated with anti-PD-1 antibodies following marketing authorisation, as part of patient access programs for unlicensed medications, or during compassionate use at Gustave Roussy. Exclusion criteria were malignant haematologic disease, a second advanced cancer or a chronic viral infection. The end date for the analysis was set to December 31st, 2016.

Pre-existing AIDs were defined according to the standard diagnostic criteria [19–32]. Diseases not included as AID in the study were atopic diseases, metabolic inflammatory diseases and AIDs caused by infectious diseases or drugs.