The MITCI (phase 1b) study: A novel immunotherapy combination of Coxsackievirus A21 and ipilimumab in patients with advanced melanoma

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Introduction

Coxsackievirus A21 (CVA21) is a novel, low-replicated enterovirus that infects human skin and mucous membranes causing mild to severe disease. The virus has an entry threshold for immune cells and can infect both naïve and activated T cells. The virus can induce tumor cell infection and immune cell infiltration, resulting in tumor regression. In a phase 1b study investigating the safety and efficacy of coxsviruses in patients with advanced melanoma, the primary endpoints were safety and tumor response with 20 of 34 (59%) patients with at least one tumor response. The response rate was 35.1% (12 of 34), with responses observed in both skin and subcutaneous metastases. The median duration of response was 15.1 (95% CI 10.0-19.2) months. In 12% of patients, a true anti-tumor immune response was observed. Data from this study indicates that CVA21 can induce a preferential tumor cell infection, tumor immune cell infiltration, and up-regulation of immune checkpoints, providing a potential new avenue for virus-based therapy.

Patient Characteristics

Response data (preliminary)

Best irRC Overall

Best irRC Overall in patients with or without prior immune checkpoint therapy

Changes in tumor burden by disease stage

Non-injected non-irradiated lesions

Results

Safety and Toxicity

Study Design

Key Inclusion Criteria

1. Patients with metastatic or unresectable stage II, III, or IV melanoma for whom treatment with ipilimumab has failed or is not appropriate, and who are at least 18 years of age or older.
2. Patients who have received prior ipilimumab treatment for melanoma are eligible, as long as the current malignancy is at least 1 year from the previous ipsilateral ipilimumab treatment.
3. Patients must have had a significant decrease in tumor burden with an ipilimumab dose of 3 mg/kg at least 3 months prior to study entry.
4. Patients must be ≥18 years of age.
5. Patients must have a ECOG performance status of 0-1.

Conclusions

The CVA21-1 ipilimumab combination immunotherapy treatment is generally well-tolerated, with the majority of adverse events (AEs) being grade 1 or 2. The most common grade 3 or 4 events were fatigue, pruritus, and sensory neuropathy. The best irRC overall and irPR responses (21% and 3%, respectively) were observed in the 25% of patients who received CVA21 as a single agent. The study showed that the combination of CVA21 and ipilimumab is well-tolerated and has the potential to improve treatment outcomes in patients with advanced melanoma.