■ Sun-269 ■

Atezolizumab induced hypothyroidism in a patient with urothelial carcinoma

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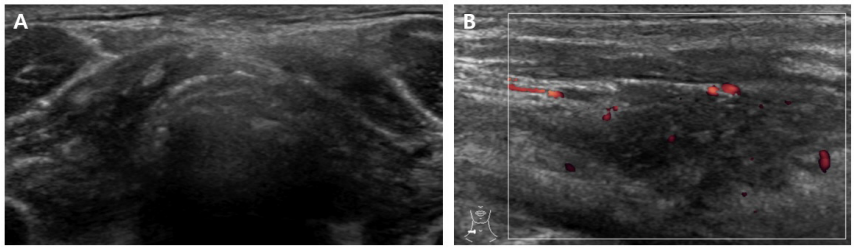
Introduction: Atezolizumab is a PD-L1 inhibitor approved by the US FDA for the treatment of locally advanced urothelial carcinoma(UC). Muscle-invasive UC has a high risk of recurrence. However there are no definitive strategies as adjuvant chemotherapy(AC). One of the ongoing trials compares atezolizumab with observation as AC in patient with muscle-invasive UC after operation. Several cases of pembrolizumab or ipilimumab induced thyroid dysfunction have been reported, but rarely for atezolizumab. Here, we present a case of atezolizumab induced thyroid dysfunction in a patient with UC. **Case:** A 77-year-old male was diagnosed with UC. He underwent two cycles of neoadjuvant GP and received radical cystectomy with ileal conduit. Pathologic staging of T3N0M0 was established after surgery. Then, the patient was enrolled in a clinical trial for AC and assigned into the atezolizumab arm. Before initiation of chemotherapy, his thyroid function was normal[TSH 3.322(0.55-4.78)uIU/ml, Free T4 1.09(0.79-1.86)ng/dL, and total T3 2.945(1.63-3.78)pg/mL)]. After 4 cycles of atezolizumab 1200mg every 3 weeks, overt hypothyroidism was developed. TSH was increased to 127.7uIU/ml. Free T4 and total T3 were decreased to 0.01ng/dL and 1.23pg/mL, respectively. Also, microsomal antibody titer was 6606.3(0-60)U/mL. He developed typical hypothyroid symptoms such as weight gain, puffy eyes, and fatigue. Thyroid US showed diffuse hypoechoic heterogeneous parenchyma, and decreased vascularity on Doppler. The medical history and the temporal relationship with chemotherapy established the clinical diagnosis of atezolizumab induced hypothyroidism. The patient received thyroid hormone replacement therapy(levothyroxine 50ug per day). **Conclusion:** Thyroid dysfunction is one of the most common immune-related adverse events during the course of immune checkpoint blockade therapy. So far, pembrolizumab and ipilimumab induced thyroid dysfunctions have been reported, but rare for the atezolizumab. We described a patient with atezolizumab induced hypothyroidism, who received atezolizumab as AC for muscle-invasive UC. It is important to monitor thyroid function during the course of PDL1 inhibitors.



A. Ultrasound image shows a markedly hypoechoic parenchyma, and the absence of suspicious nodule. B. Decreased vascularity on Doppler was observed.

■ Sun-270 ■

The Effect of Lobeglitazone, A New Thiazolidinedione, on Pancreatic Beta Cells in C57BL/6

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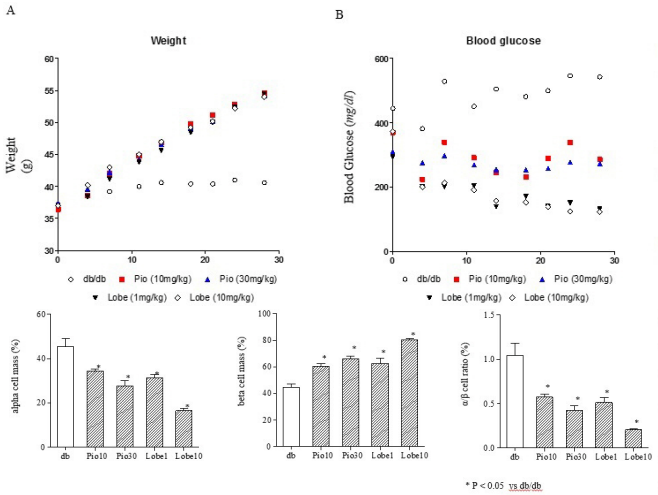
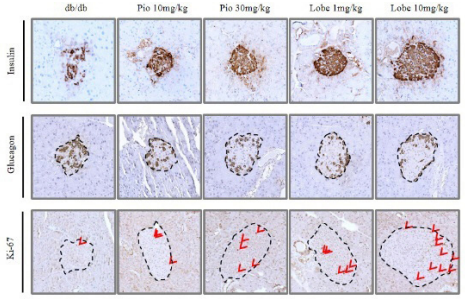
Background/Aims: Thiazolidinediones (TZDs) have been traditionally known as peripheral insulin sensitizer having durability in glycemic control. But studies about direct effects of thiazolidinediones (TZDs) on pancreatic beta cells are not much and results have been controversy. The aim of this study is to find out whether novel TZD, lobeglitazone has beneficial effect on pancreatic beta cells of db/db mice. **Methods:** C57BL/6 db/db mice were treated with pioglitazone or lobeglitazone for 4 weeks. The body weight and blood glucose levels were measured twice a week. Metabolic parameters such as insulin, glucagon and lipid profile of blood were assessed by ELISA. The configuration of pancreatic islets, mass of beta cells and alpha cells were examined by immunohistochemistry, immunofluorescent, and Masson-Trichrome staining. **Results:** In db/db mice treated pioglitazone and lobeglitazone, metabolic parameters were improved than control mice. Islet size, cell proliferation, and beta cell mass were increased and collagen surrounding islets was decreased in pioglitazone and lobeglitazone treated mice. **Conclusions:** Lobeglitazone, the novel TZD, showed the beneficial effects on beta cell survival and function in db/db mice, which was comparable to well-known TZD, pioglitazone. Acknowledgments The study was funded by Chong Kun Dang Pharmaceutical Corporation.





	Triglyceride	Total Cholesterol	LDL Cholesterol
db/db	174.2±6.95	12.76±0.11	6.57±1.56
db/db Pio10-treated	132.8±3.44	12.87±0.27	3.27±0.47
db/db Pio30-treated	122.5±5.59	12.89±0.18	2.93±0.26
db/db Lobe1-treated	103.8±8.36	12.76±0.09	2.64±0.26
db/db Lobe10-treated	96.2±6.36	12.79±0.15	2.74±0.09