March 18th, 2019

Direct Healthcare Professional Communication

TECENTRIQ® (atezolizumab): A New Important Identified Risk: Immune-related Myositis

Dear Healthcare professional,

Roche in agreement with the European Medicines Agency (EMA) would like to inform you of the following:

Summary

- ***Immune-related myositis has now been added as a new important identified risk associated with the use of TECENTRIQ® (atezolizumab).***
- ***It is recommended that TECENTRIQ®(atezolizumab) should be withheld for moderate or severe (Grade 2 or 3) immune-related myositis and permanently discontinued for recurrent severe or life-threatening myositis (recurrent Grade 3 and Grade 4). Please refer the patient to rheumatologist and/or neurologist and consider muscle biopsy and supportive measures as clinically indicated. Corticosteroids treatment with 1-2 mg/kg/day IV methylprednisolone or higher-dose bolus if severely compromised (weakness severely limiting mobility, cardiac function, respiratory function, dysphagia) and/or additional immunosuppressive agents should be administered for > grade 2 events or if event does not improve after initial corticosteroids.***

Background on the safety concern

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC):

- after prior platinum-containing chemotherapy or
- who are considered cisplatin ineligible and whose tumours have a PD-L1 expression ≥ 5%, or
- who are not eligible for any platinum-containing chemotherapy regardless of level of tumor PD-L1 expression.

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy. Patients with EGFR activating mutations or ALK-positive tumour mutations should also have received targeted therapy before receiving Tecentriq.

Myositis or inflammatory myopathies are a group of disorders sharing the common feature of inflammatory muscle injury; dermatomyositis and polymyositis are amongst the most common disorders. Diagnosis is based on clinical (muscle weakness, muscle pain, skin rash in dermatomyositis), biochemical (serum creatine-kinase increase), and imaging (electromyography/MRI) features, and is confirmed with a muscle-biopsy.

A comprehensive analysis was performed across the TECENTRIQ® program and identified cases of immune-related myositis, including biopsy-confirmed cases, in patients that have received atezolizumab. There were 4 cases of myositis with a fatal outcome with some cases suggestive of cardiac involvement (myocarditis or AV blocks). Approximately 19,323 clinical trial patients and 28,975 post-marketing patients have been exposed to TECENTRIQ® (atezolizumab) as of Nov 17, 2018. The incidence of myositis[i] observed across the atezolizumab monotherapy clinical programme was <0.1%. Based on the assessment of all available data, immune-related myositis is considered an important identified risk for TECENTRIQ®(atezolizumab).

Roche is working to update the product label to reflect the risk of immune-related myositis as soon as possible. To further minimize this risk, health care professionals should follow the management guidance detailed above. The benefit-risk profile of atezolizumab in the approved indications remains favourable.

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions in accordance with the national spontaneous reporting system and to Roche at: cac.farmacovigilancia@roche.com

Company contact point

If you have any questions or concerns about the information contained in this letter or the safe and effective use of TECENTRIQ®, please feel free to contact us at: cac.medical_info@roche.com

Sincerely,

Dra. Alexandra Hambelant
Local Safety Responsible
Roche Servicios S.A.

Dr. Daniel Álvarez
Medical Director
Roche Servicios S.A.

[i] Including related terms of dermatomyositis, polymyositis, rhabdomyolysis