Gayane Ghazaryan, Medical Manager

Local Safety Responsible of Hoffmann-La Roche products in Armenia

Direct Healthcare Professional Communication

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

Dear Healthcare professional,

F. Hoffmann-La Roche Ltd. in agreement with the European Medicines Agency> and <the National Competent Authority 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® (atezolizumab) 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%.
- 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 closely with health authorities to update the product label to reflect the risk of immune-related myositis. 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

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Health care professionals should report any adverse events suspected to be associated with the use of TECENTRIQ® (atezolizumab) to: Scientific Centre of Drug and Medical technology Expertise CJSC via following contacts: address: 49/4 Komitas av., 0051 Yerevan, Armenia, phone: +37410231682 (ext: 123), Hot line for ADR reporting: (+374 10) 20-05-05, (+374 96) 22-05-05 email: vigilance@pharm.am

Company contact point

Should you have any questions regarding the use of TECENTRIQ® (atezolizumab), please feel free to contact us: Gayane Ghazaryan: mob.: +374 91 796688/ email: gayaneh.ghazaryan@gmail.com. Or Nune Karapetyan, mob: +374 91 721153/ email: nune.karapetyan.roche@gmail.com. Also direct your reports to Roche Moscow DS Hub via following contacts: tel.: +7-495-229 2999, Fax: +7-495-229 7999/ email: moscow.ds@roche.com; website: www.roche.ru.

Sincerely,

Gayane Ghazaryan, Medical Manager, Local Safety Responsible of Hoffmann-La Roche products in Armenia _____ 02.09.2019

Nune karapetyan, Commercial Lead of Hoffmann-La Roche products in Armenia

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02.09.2019

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