9 November 2020

TECENTRIQ® (atezolizumab), Identified Risk of Severe Cutaneous Adverse Reactions (SCARs) Direct Healthcare Professional Communication (DHPC)

Dear Healthcare professional,

Roche New Zealand, in agreement with Medsafe, would like to inform you of an update to the safety profile of atezolizumab.

Summary

- Severe Cutaneous Adverse Reactions (SCARs) are rare but potentially fatal skin toxicities associated with medication use, including immune checkpoint inhibitors as a class.
- A comprehensive analysis of the data available across the atezolizumab clinical development program has identified a risk of SCARs following atezolizumab use. The incidence rate of SCARs, regardless of severity, from pooled atezolizumab monotherapy and combination therapy company-sponsored clinical studies was 0.7% and 0.6% respectively.
- The NZ atezolizumab Data Sheet will be updated to add a Warning/Precaution, to provide guidance for managing patients with suspected SCARs, and to update the known Adverse Drug Reaction table.

Background on the safety concern

SCARs are a heterogeneous group of immunologically mediated drug eruptions. Although rare, these events are potentially fatal, and are mainly constituted by acute generalised exanthematous pustulosis, Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and drug rash with eosinophilia and systemic symptoms (DRESS). As per epidemiology data, the incidence of SJS and TEN in the general population ranges from 0.8 to 5.3 and 1.2 to 6 per million person-years respectively[i,ii].

A cumulative analysis of the company safety database across the atezolizumab program identified 99 cases, of which 36 cases of SCARs were confirmed by histopathology or specialist diagnosis, in patients who have received atezolizumab. Approximately 23,654 clinical trial patients and 106,316 patients in post-marketing settings have been exposed to atezolizumab as of 17 May 2020. The incidence rates of SCAR, regardless of severity, from pooled atezolizumab monotherapy (N=3178) and combination therapy (N=4371) company-sponsored clinical studies was 0.7% and 0.6% respectively. One fatal case of TEN was reported in a 77 year old female patient who received atezolizumab monotherapy.

It is recommended that:

- For suspected SCARs, the patient should be referred to a dermatologist for further diagnosis and management
- Atezolizumab should be withheld for patients with suspected SJS or TEN
- Atezolizumab should be permanently withdrawn for any grade confirmed SJS or TEN
- Caution should be used when considering the use of atezolizumab in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer agents.

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An update to the NZ atezolizumab prescribing information to include a Warning and Precaution for SCARs, guidelines for discontinuation and further description of the risk will follow this communication. This letter has been disseminated in advance of the NZ Data Sheet update to make you aware of the identified risk and to facilitate prompt management of these risks.

Immune mediated cutaneous adverse reactions, including severe reactions, are considered to be a class effect with immune checkpoint inhibitors[3,4,5].

Before prescribing, please review the full atezolizumab Data Sheet available at www.medsafe.govt.nz.

Further information
If you have any questions or require additional information regarding the use of atezolizumab please contact Roche Medical Information on 0800 276 243 or email auckland.medinfonz@roche.com.

Reporting adverse events

Roche will continue to monitor the safety of atezolizumab through established reporting mechanisms and notify regulatory authorities as per current regulations.

Please report any suspected adverse events via email to Roche Drug Safety at nz.drugsafety@roche.com. Alternatively, this information may be reported to the Centre for Adverse Reactions Monitoring (CARM) in Dunedin by telephone on (03) 479 7247, by fax on (03) 479 7150, online at https://nzphvc.otago.ac.nz/reporting or by email to nzphvc@otago.ac.nz.

Yours sincerely,

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[i] Li LF, Ma C. Epidemiological study of severe cutaneous adverse drug reactions in a city district of China. Clin Exp Dermatol. 2006;31(5):642-647

[ii] Yang MS, Lee JY, Kim J, et al. Incidence of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: A Nationwide Population-Based Study Using National Health Insurance Database in Korea. PLoS One. 2016;11(11):e0165933

3 Jimenez J, Nardone B, Kosche C, et al. Bullous skin disorders associated with PD-1 and PDL-1 inhibitors: Pharmacovigilance analysis of the FDA Adverse Event Reporting System (FAERS) from the Research on Adverse Drug events And Reports (RADAR) Program. J Am. Acad. Dermatology. 2019; 81(4) supp1

4 Zhao, CY, Hwang, SJ, Consuegra, G et al. Anti-programmed cell death-1 therapy-associated bullous disorders: a systematic review of the literature. Melan Res Volume 28(6), p 491-501.

5. Kamińska-Winciorek G, Cybulska-Stopa B, Ługowskadoi I et al. Review paper Principles of prophylactic and therapeutic management of skin toxicity during treatment with checkpoint inhibitors. Adv. Dermatology Allergology. 2019; 36 (4): 382-391

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