MHRA
Regulating Medicines and Medical Devices

MHRA
151 Buckingham Palace Road
London SW1W 9SZ
United Kingdom

mhra.gov.uk

Dr Andrew Harris
Coroner for Inner South District Greater London
Southwark Coroner's Court
1 Tennis Street
Southwark
London SE1 1YD

Thank and copy to LPs
KG 27-6

24th July 2017

Dear Dr Harris,

Coroners and Justice Act 2009 – Regulation 28 Report following the inquest in to the death of Mr Macdonnell
PFD report touching the death of Maurice Macdonnell
Date of death 16.08.2016 / [redacted]

Thank you for your letter of 20th June 2017, received on 26th June 2017, enclosing your Report under Regulation 28 following the inquest into the death of Mr Maurice Macdnnell and the concern raised that there is still a risk that future deaths will occur unless action is taken.

Notification of the death was reported to MHRA as a fatal suspected unexpected serious adverse reaction (SUSAR) within statutory timelines i.e. within 7 days of the trial sponsor becoming aware of the event, in line with Directive 2001/20/EC.

The SUSAR report has been reviewed and the trial sponsor has done due diligence in investigating the cause of death and the potential risk to other patients being treated with nivolumab. The symptoms shown by Mr Macdonell prior to his death are in line with the known safety profile for nivolumab and he was managed in line with the protocol. Other similar events have been noted in the annual safety report reviewed by MHRA and this new information does not alter the safety profile or require any further action for participants in nivolumab clinical trials.

With regard to the possible conflict of interest in reporting the death of Mr Macdonnell and the balance between the risk to the patient from receiving further doses and the benefit from staying in the trial in the interests of research, MHRA has received an opinion from the Health Research Authority (HRA) as conflict of interest lies outside the remit of MHRA for clinical trials. The HRA confirmed that it is common practice for the Principal Investigator in a clinical trial to also be the patient's physician. The duty of care owed by a physician should always be the primary role, above the interests of the trial, and this is generally accepted by physicians participating in clinical trials. These aspects are considered by the Ethics Committee at the time of the initial application of the clinical trial to them, in accordance with the Declaration of Helsinki. We are not aware any concerns were raised for this trial regarding conflict of interest. The HRA have also issued guidance for Ethics Committees on managing potential or perceived competing interests in a clinical trial, and this would have been followed at the time of the initial review and provision of a positive opinion.

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The conflict of interest concern for Mr Macdonnell was also reviewed by an Expert Good Clinical Practice Inspector who raised no concerns from the perspective of MHRA Inspectorate.

MHRA does not consider that any further action is warranted at this time given that the fatal event is not considered a new safety signal and all appropriate mitigation steps are considered to be in place for nivolumab clinical trials. MHRA will continue to monitor all fatal events in the UK for patients participating in clinical trials and who are being treated with nivolumab. Conflict of interest will continue to be reviewed by the Ethics Committee for all clinical trials in line with the HRA guidance.

Yours sincerely

[redacted]
Senior Medical Assessor / Deputy Unit Manager CTU
[redacted]
020 3080 6859