DEVELOPMENT SAFETY UPDATE REPORT

Ruolo prognostico della PET/TC con 18F-FAZA nei gliomi ad alto grado: confronto con la risonanza magnetica e correlazione con i biomarcatori di ipossia

Period Covered: 2016 – 2018

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EXECUTIVE SUMMARY

In the present study, no Serious Adverse Events (SAEs) or Serious Adverse Reactions (SARs) related to the experimentation occurred during the study period. In the present study, only a diagnostic procedure (PET/CT with 18F-FAZA) was added to the patient clinical routine, without altering the treatment and the management of patients with high grade glioma. The death of the 11 patients, at the time of the closure of the study, was expected and due to the progression of the disease.

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1. Introduction

This is the 1st Development Safety Update report for "Ruolo prognostico della PET/TC con 18F-FAZA nei gliomi ad alto grado: confronto con la risonanza magnetica e correlazione con i biomarcatori di ipossia". This report summarises safety data arising from the trial, collected between 08-04-2016 and 09-04-2018, and it has been filled in in accordance with the ICH E2F (DSUR) guideline.
The 18F-fluoroazomycin arabinoside PET radiopharmaceutical (18F-FAZA) is a biomarker of hypoxia. It is of nitromidazole family and once entered in the cells it presents a different behaviour depending on the tissue oxygenation. In particular, in case of hypoxia, it remains trapped in the cell, thus being visible by using PET. All the documentation relative to the 18F-FAZA PET radiopharmaceutical (Medicinal Product Dossier –IMPD-Version 3, January 8 2013) is available in the Nuclear Medicine Department of IRCCS San Raffaele Hospital.

2. Worldwide Marketing Authorisation Status

IMP does not currently have a marketing authorisation.

3. Actions taken in the reporting period for safety reasons during the reporting period

None amendments for safety reasons have been made to this trial.

4. Changes to reference safety information

All the documentation relative to the 18F-FAZA PET radiopharmaceutical (Medicinal Product Dossier –IMPD-Version 3, January 8 2013) is available in the Nuclear Medicine Department of IRCCS San Raffaele Hospital.

5. Inventory of clinical trials ongoing and completed during the reporting period

This DSUR covers a single study: "Ruolo prognostico della PET/TC con 18F-FAZA nei gliomi ad alto grado: confronto con la risonanza magnetica e correlazione con i biomarcatori di ipossia" (EudraCT number: 2015-000679-28)

The primary objectives of this Phase III study were: 1) to guide tumour sampling for a more accurate representation of tumour heterogeneity, and to compare the standard sampling guided by MRI parameters (task1); 2) to predict patient outcome, investigating the correlation between hypoxia immunohistochemical tumour biomarkers with 18F-FAZA PET/CT and MRI parameters (task2); 3) to assess spatial concordance between sites of disease progression/recurrence/radionecrosis and hypoxic portions of the tumours (task3) and 4) to assess the feasibility of 18F-FAZA PET/CT for personalized radiation treatment planning and comparing the standard treatment planning based on MRI (task4).

This study has been conducted at IRCCS San Raffaele Hospital.

This study was planned to enrol 20 adult patients to performed PET study with 18F-FAZA, for the identification of hypoxia, before performing a biopsy or surgical intervention and during follow-up.

Study status:

First Patient First Visit:	08-04-2016
Number of patients screened:	20
Number of patients recruited:	20
Last recruitment date:	12-10-2017
Study closure	09-04-2018

This DSUR only relates to the present study with EudraCT number: 2015-000679-28.

6. Estimated cumulative exposure

a. Cumulative subject exposure in the development program

Demographic data is as follows:

Single arm		Number of subjects		
		Male	Female	Total
Age range (years)	41 - 82	15	5	20

b. Patient exposure from marketing experience

This is not applicable as this is an investigator-led study sponsored by a non-commercial sponsor.

7. Data in line listings and summary tabulations

a. Reference information

The IB served as the reference point for determination for 'expectedness' of all adverse events. The Medical Dictionary for Regulatory Activities (MedDRA) version 13.1 for the coding of adverse events was used.

b. Line listing of Serious Adverse Reactions (SARs) during reporting period

No SARs related to the experimentation occurred during the study period.

c. Cumulative line listings of Serious Adverse Events (SAEs)

No SAEs related to the experimentation occurred during the study period.

8. Significant findings from clinical trials during reporting period

a. Completed clinical trials

Not applicable.

b. Ongoing clinical trials

Not applicable.

c. Long term follow-up

None

d. Other therapeutic use of IMP

Not applicable.

e. New safety data related to combination therapies

Not applicable.

9. Safety findings from non-interventional studies

Not applicable.

10. Other clinical trial/study safety information

Not applicable.

11. Safety findings from marketing experience

Not applicable.

12. Non clinical data

Not applicable.

13. Literature

No significant new safety findings have emerged in the literature for IMP during the reporting period.

14. Other DSURs

Not applicable.

15. Lack of efficacy

Not applicable.

16. Region specific information

Not applicable.

17. Late breaking information

No relevant information was received subsequently to the data-lock for this DSUR.

18. Overall safety assessment

a. Evaluation of the risks

Not applicable.

b. Benefit-risk considerations

Not applicable.

19. Summary of important risks

No relevant risks have emerged during the reporting period.

20. Conclusions

The diagnostic procedure (PET/CT with FAZA) performed to evaluate the presence of tumour hypoxia in glioma patients did not add any risk. During the study period eleven patients dead due to the progression of the disease and it was expected by their status disease.