Development and validation of a method for the analytical control of letermovir by high performance liquid chromatography (HPLC) coupled with UV-visible within a chemotherapy preparation unit

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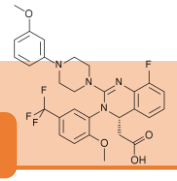

Introduction

Letermovir is an **antiviral** drug indicated for the prophylaxis of cytomegalovirus (CMV) reactivation and CMV disease in adult CMV-seropositive with allogeneic hematopoietic stem cell transplantion, at **standard doses of 480 mg** (without co- ciclosporin prescription) **or 240 mg** (with ciclosporin co-prescription).

Aim

Implementation of a **qualitative and quantitative analytical release control of letermovir by HPLC coupled with a UV-visible detector** in order to secure its preparation within the chemotherapy preparation unit

Material and method

- Letermovir is a ready-to-use solution of 20 mg/ml, to be diluted in a 0.9% NaCl bag of 250 ml, that is **two possible concentrations** (taking into account an overfilling of 18 ml of bags): **0.9 mg/ml and 1.8 mg/ml**.
- Validation of the method in accordance with the international guideline *International Council for Harmonization* (ICH) Q2 (R1) using the following criteria: **linearity, accuracy, repeatability (intra-assay precision) and intermediate precision (between -day precision).**
- **Analysis conditions** by direct injection FIA (*Flow Injection Analysis*):

Wavelength	Mobile phase	Flow rate	Injection volume	Analysis time	Temperature
260 nm	50% water / 50% acetonitrile	1.5 ml/min	30 µL	0.3 min	20°C

- **Calibration range of 5 points carried out on 3 different days**: 0.6 ; 1.0 ; 1.4 ; 1.8 ; 2.0 mg/ml.
- **Quality control (QC) of 4 points repeated 3 times**: 0.6 ; 0.9 ; 1.2 ; 1.6 mg/ml.

Results

y = 26,346 x + 3,196

R^2 = 0,9995

Linear method

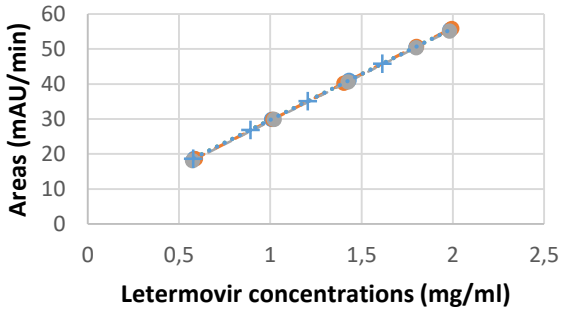

Figure 1: Letermovir assay calibration curve

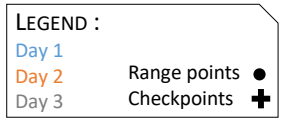

Figure 2: Table of letermovir assay validation parameters

Settings	QC1	QC2	QC3	QC4
Accuracy: recovery rate (%)	**97,0**	**97,5**	**99,9**	**99,3**
Repeatability: variation coefficient (%)	**2,04**	**1,23**	**1,26**	**0,67**
Intermediate precision: variation coefficient (%)	**3,42**	**1,68**	**1,70**	**1,20**

Discussion et conclusion

The method has been validated according to the criteria of the international ICH Q2 (R1) guideline: it is **linear with a correlation coefficient > 0.95, repeatable and precise with variation coefficients < 5% and 8%, and exact with a recovery rate > 90%.** The analytical control of letermovir could thus be deployed routinely within our chemotherapy preparation unit in order to secure the preparation circuit. The development and validation of the analytical control method by UV-Raman spectrometry (QCRx®) has also been implemented.