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Your letter from	Your reference	Our reference	Annex	Date
		FAGG/R&D/VDC	1	

Onderwerp
Titre de l'objet
Subject

Goedkeuring van een klinische proef op 27/08/2018
Approbation d'un essai clinique le 27/08/2018
Authorisation of a clinical trial dated 27/08/2018

A Phase I/IIa study of TG6002 (VV TK-RR-FCU1) administered by intravenous (IV) infusions in combination with oral flucytosine (5-FC) in patients with advanced gastro-intestinal (GI) tumors

EudraCT: 2018-000039-28

Chère Madame,

Conformément à l'article 12 de la Loi du 7 mai 2004 relative aux expérimentations sur la personne humaine, j'ai décidé d'autoriser l'essai clinique ci-dessus mentionné.

Cependant, un suivi doit être apporté aux points mentionnés en annexe.

Salutations sincères,

Pour la Ministre des Affaires sociales et de la Santé publique

Geachte Mevrouw,

In overeenstemming met artikel 12 van de wet van 7 mei 2004 inzake experimenten op de menselijke persoon, heb ik besloten de hierboven vermelde proef goed te keuren.

Niettemin moet er gevolg gegeven worden aan de opmerkingen vermeld in bijlage.

Met de meeste hoogachting,

Voor de Minister van Sociale Zaken en Volksgezondheid

Dr. Greet Musch

In accordance with article 12 of the Law of 7 May 2004 concerning experiments on the human person, I have decided to authorise the above mentioned clinical trial. However, the points as mentioned in annex are to be followed up.

Annex

Quality

Recommendations

The sponsor is recommended to take into consideration the following recommendations during further development of the product. They may be readdressed at the time of assessment of future applications related to this investigational medicinal product:

Drug substance:

R1- The provided answer to Question 3 is partly acceptable since the applicant is only providing a general description of tests and methods used to characterize the DS and not real data as requested. Therefore, the issue is considered as partly resolved at this stage of development and the applicant is recommended to provide CHARACTERIZATION DATA of the VVTG17137 vector (DS) based on which relevant specifications for the release of the vector has been established and set during future application with this IMP.
With regards to impurities (Q3/4), the characterisation data of impurities generated should serve as input into the specification setting for drug substance and drug product along with data from batch analysis. Therefore, it is recommended that relevant (upper) limits of Process-Related Impurities should be set to monitor the residual levels of contaminants of cellular origin.

R2- With regard to compliance with specific guidelines for product specification, the applicant claims that EP 5.14 is not fully required for an investigational medicinal product. This is not agreed since, although the texts are designed to be applicable to approved products, the need for application of part or all of the texts to products used during the different phases of clinical trials is decided by the competent authority.

Safety

Recommendation

The sponsor is recommended to take into consideration the following recommendation during further development of the product. It may be readdressed at the time of assessment of future applications related to this investigational medicinal product.

To be in line with the CTFG Q&A-RSI document (November 2017): http://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2017_11_CTFG_Question_and_Answer_on_Reference_Safety_Information_2017.pdf , the sponsor is highly recommended to state the following in the Reference Safety Information (RSI) section in the IB, if applicable: No SARs are considered expected by the sponsor for the purpose of expedited reporting of SUSARs and identification of SUSARs in the "Cumulative summary tabulation of serious adverse reactions" in the DSUR for the IMP.

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Votre lettre du	Vos références	Nos références	Annexe(s)	Date
		AFMPS/DGPRE/R&D/LSA		

Dossier OGM : B/BE/18/BVW1 (2018-000039-28): A Phase I/IIa study of TG6002 (VV TK-RR-FCU1) administered by intravenous (IV) infusions in combination with oral flucytosine (5-FC) in patients with advanced gastro-intestinal (GI) tumors

Chère Madame Quesnel,

Par la présente, nous vous informons que l'autorisation imposée en vertu de l'arrêté royal du 21 février 2005 règlementant la dissémination volontaire dans l'environnement ainsi que la mise sur le marché d'organismes génétiquement modifiés ou de produits en contenant vous est accordée sur base de l'avis favorable du Conseil de Biosécurité daté du 3 juillet 2018, et ce, aux conditions reprises dans la conclusion de l'avis précité, c'est-à-dire :

"The notifier and the investigators must strictly apply the trial protocol and all the safety instructions as described in the dossier also taking into account the suggestions from the Biosafety Advisory Council for improvement of the personnel instructions.

- *Any protocol amendment has to be previously approved by the Competent Authority.*
- *The notifier is responsible to verify that each study center has qualified personnel experienced in handling infectious material and that the investigator has the required authorisations to perform the clinical trial activities inside the hospital (laboratory, pharmacy, hospital room, consultation room, ...) according to the Regional Decrees transposing Directive 2009/41/EC on Contained use of genetically modified micro-organisms.*
- *The Biosafety Advisory Council should be informed within two weeks when the first patient starts the treatment and the last subject receives the last treatment.*

- *At the latest six months after the last visit of the last patient included in the trial, the notifier must send to the competent authority at the attention of the Biosafety Council a report with details concerning the biosafety aspects of the project. This report will at least contain:*
    - *the total number of patients included in the trial and the number of patients included in Belgium;*
    - *a summary of all adverse events marked by the investigators as probably or definitely related to the study medication;*
    - *a report on the accidental releases, if any, of TG6002."*

Salutations sincères,

Maggie De Block
Ministre des Affaires Sociales et de la Santé publique

Marie Christine Marghem
Ministre de l'Energie, de l'Environnement et du Développement durable