1 ADMINISTRATIVE INFORMATION

EU trial number	2024-511140-37-00
Title of the study	Stereotactic body radiotherapy with or without Darolutamide for OligoRecurrent prostate cancer: a randomized phase II trial (DART).
Name of sponsors	Universitair Ziekenhuis Gent

Has Part I been submitted prior to the submission of Part II?	Yes ☐ No ☒
If Yes	
Is there already a conclusion on part I?	Yes ☐ No ☐ NA ☒

2 GENERAL INFORMATION

Is the CT a low-interventional trial?[1]		Yes ☐ No ☒
First in man ☐, Phase I ☐, II ☐, III ☐, IV ☐ NA ☐		
Is the CT a cluster trial[2]		Yes ☐ No ☒
Is the CT intended to be performed in more than one member state?		Yes ☐ No ☒
Does the CT include healthy volunteers?		Yes ☐ No ☒
Does the CT include	females ?	Yes ☐ No ☒
	males?	Yes ☒ No ☐

[1] If yes – other demands for damage compensation, cfr. Art. 76

[2] If yes – other demands for informed consent, cfr. Art. 30

Which of the following groups are included?	
Adults (18-64 years)	Yes ☒ No ☐
Elderly (>= 65 years)	Yes ☒ No ☐
< 18 years	
Preterm Newborn Infants (up to gestational age < 37 weeks)	Yes ☐ No ☐
Newborns (0-27 days)	Yes ☐ No ☒
Infants and toddlers (28 days - 23 months)	Yes ☐ No ☒
Children (2-11 years)	Yes ☐ No ☒
Adolescents (12-17 years)	Yes ☐ No ☒
Fetuses in utero *(Please note in Belgium it should be checked if an advice of the "Federal commission for the protection of the human embryo" is necessary according to the Law of 11 may 2003.)*	Yes ☐ No ☒
Are there study-specific (outside standard of care) procedures and/or interventions and/or visits beyond the drug application?	Yes ☒ No ☐

3 ASSESSMENT

The trial was already approved by an ethics committee and authorized by the Belgian National Competent Authority under the CTD. As a result, this transitioning application is not re-assessed[3]. The ethics committee who initially approved the trial under the CTD remains responsible until the first substantial modification where the trial should be in compliance with the CTR.

If applicable, wording of remarks from the EC:

[3] Regulation (EU) No 536/2014 Questions & Answers Document, December 2022, paragraph 463.

BE01: certificate of insurance no longer valid and is upon 7 may 2004 law.

-> sponsor has to renew it

BE02: ICF

- **Page 11 of 31**: “Si vous présentez des effets indésirables importants, l'investigateur pourrait estimer nécessaire d'effectuer des tests supplémentaires qui seront considérés comme spécifiques à l'étude.”

-> sponsor should explain who will pay for the additional tests in case of side effects.

- **Page 12 of 31** : Si votre médecin est préoccupé par des élévations des tests sanguins hépatiques et n'est pas sûr qu'elles soient liées au darolutamide, il pourra vous demander de subir des examens supplémentaires pour mieux comprendre la cause des anomalies des tests sanguins hépatiques.
Si les résultats des examens suggèrent une lésion du foie liée au medicament à l'étude, ce dernier sera définitivement arrêté par votre médecin.

-> Sponsor should explain who will pay for the additional tests

- **Page 17 of 31**:

“Les visites et traitements qui résultent d’un effet secondaire sont aussi considérés comme spécifiques à l’étude.”

-> sponsor should add: “Les visites et traitements qui résultent d’un effet secondaire sont aussi considérés comme spécifiques à l’étude **et seront pris en charge par le promoteur**.”

- **Page 14 of 31**: “méthode contraceptive”

-> sponsor should describe what is an efficient contraceptive method, describe the options and provide the patients with condoms, if applicable

- **Page 24 of 31**:

« Je certifie que tous les renseignements que j'ai fournis au sujet de mes antécédents médicaux sont exacts. »
-> sponsor should add :

« Je certifie que tous les renseignements que j'ai fournis au sujet de mes antécédents médicaux sont, **à ma connaissance**, exacts. »

4 ASSESSMENT OF SUBSTANTIAL MODIFICATION ON PART II (SM-XX)

Note: Copy section 4 for each subsequent substantial modification and renumber appropriately (e.g. Next SM will be Section 5)

4.1 The proposed changes are in relation to the following parts of the dossier:

Recruitment arrangement (material, procedure)	☐

ICF(s)	☐
Suitability of the investigators	☐
Suitability of the facilities	☐
Insurance certificate	☐
Compensation to participants	☐
Financial arrangements (contracts, budget for sites)	☐
Compliance with national requirements on Data Protection	☐
Collection, storage, future use of human biological samples	☐
Other patient documents	☐

4.2 Description and assessment of the proposed changes of the SM

Provide a short description of the proposed changes and an assessment of these changes. The table should include the version/number of the ICF(s) and other patient documents proposed for this SM on part II.

Date/version/number of the **ICF(s)**	
Date/version/number of the **other patient documents**	

Is the SM acceptable ?

Yes ☐

No ☐ as a request for additional information (RFI) needs to be resolved

Note for the public reader: The questions from the Ethics committee are available in CTIS for public users.

Please add all questions regarding Part II in CTIS as considerations. The Sponsor does not have access to the draft assessment report. Each consideration must be clear as a stand-alone question. Note: the EC is not obliged to repeat the considerations in this section.

4.3 Final overall conclusion on the substantial modification on part II

The proposed changes are acceptable	☐
The proposed changes are not acceptable	☐
The proposed changes are acceptable subject to conditions	☐
Wording of conditions or rejection as proposed by the EC:	
Wording of recommendation – if any – from the EC: **(recommendations should be used exceptionally)**	