Prospective intervention trial with adjuvant Metformin in girls and boys with classic CAH – METforCAH

Final Report

April 2018

EURDRACT number 2013-002395-40

1. Duration of the study

This is a third party sponsored / investigator initiated trial of which the Agreement between NV Sandoz S.A. and Sponsor (Ghent University Hospital) was signed on 26 11 2015.

The study officially ended on 16 Feb 2018, 30 days after announcement of study end by Sponsor to NV Sandoz S.A.

The reason for early termination of the study is the fact that less than expected patient numbers could be included during the first two years of the study. Therefore, it can be foreseen that, based on pre-study power calculations, insufficient patient numbers will be available at the end of the official inclusion period to ensure meaningful scientific results.

2. Participating centers

Following centers took part in the study:

- Universitair Ziekenhuis Gent, UZG (coordinating center), PI M Cools
- Hôpital Universitaire St Luc, UCL, PI V Beauloye
- Universitair Ziekenhuis Leuven, UZL, PI Kristina Kasteels
- Hôpital Universitaire Mont Godinne, CHU M-G, PI Dominique Beckers
- Hôpital Universitaire Liège, CHUL, PI Anne-Simonne Parent
- Universitair Ziekenhuis Antwerpen, UZA, PI Annick France
- Universitair Ziekenhuis Brussel, UZB, PI Inge Gies

3. Subjects and visits

Center	Subject	Patient	Date IC	First visit	Last visit	Continues MF
UZG	UZG_27	C	05/01/2017	31/08/2016	31/08/2016	NO
	UZG_28	C	05/01/2017	31/08/2016	31/08/2016	NO
	UZG_34	C	27/12/2016	17/05/2016	17/05/2016	NO
	UZG_35	C	18/01/2017	18/01/2017	18/01/2017	NO
UCL	UCL_2	P	21/12/2015	06/01/2016	06/01/2016	YES
	UCL_3	P	02/05/2016	02/05/2016	02/05/2016	YES
	UCL_7	P	24/07/2017	24/07/2017	24/07/2017	YES
	UCL_8	C	17/02/2017	17/02/2017	17/02/2017	NO
	UCL_13	C	18/02/2016	06/05/2016	06/05/2016	NO
	UCL_18	P	23/05/2016	25/05/2016	25/05/2016	YES
UZL	UZL_7	P	24/10/2016	06/02/2017	06/02/2017	NO
	UZL_12	P	06/03/2017	06/03/2017	06/03/2017	YES
CHU M-G	CHU M-G_1	C	08/09/2016	08/09/2016	08/09/2016	NO
	CHU M-G_4	C	18/08/2016	18/08/2016	18/08/2016	NO
CHUL	-	-	-	-	-	
UZA	-	-	-	-	-	
UZB	UZB_18	C	29/09/2016	22/12/2016	22/12/2016	NO

Table 1: overview of included subjects

In total, 6 patients and 9 controls were included during the period Nov 2015 – Jan 2018. Five out of six included patients who started on the study medication Metformin (MF) will continue the medication after termination of the study.

4. Safety

No adverse events or serious adverse events were reported during the study period.

No protocol violations from the planned schedule occurred for the included subjects. The following protocol deviations were logged

- UZG_28: Patient was erroneously included at the age of 17 years, data will not be used for analysis (major)
- UZG_28: version 2 of ICF was signed, version 3 was applicable and was signed afterwards (major)
- UZG_27: version 2 of ICF was signed, version 3 was applicable and was signed afterwards (major)
- UZG_34: version 2 of ICF was signed, version 3 was applicable and was signed afterwards (major)
- UZG_35: fludrocortisone total daily dose divided over three instead of two gifts (minor)

Pre-set numbers were not met during the first two years of the inclusion period, which led to early termination of the study for scientific reasons as specified above.

5. Efficacy

No efficacy results are available as analyses of blood samples will not be performed given the early termination of the study.

6. Publications

No publications will result from this study.

7. Monitoring

Monitoring of the study was performed for the UZ Ghent site, as coordinating center by Bimetra Clinics. The study was performed according to good clinical practice (GCP) and good manufacturing practices (GMP) regulations at all sites.

The monitoring close out visit at UZ Ghent took place on 02 03 2018. Termination of the study was announced to FAGG and the ethical committee of UZG on 16 01 2018. The PI and data manger have announced termination of the study to participating centers, who have subsequently informed their ethical committees.

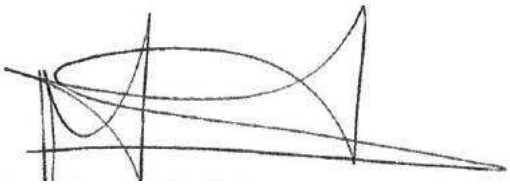
All monitoring details and logs will be stored at UZG for a period of 20 years after termination of the study.

8. Termination of the study

Termination of the study was announced by Sponsor to NV Sandoz S.A. on 16 01 2018, with official termination of the study 30 days later.

According to the Agreement with NV Sandoz S.A. dd 26 11 2015, the following actions were undertaken

- Return of all unused study drug to NV Sandoz S.A. at Sandoz' expense
- Payment of all remaining invoices to participating centers
- Financial report, submitted to NV Sandoz S.A. for approval (annex 1)
- Refund of all unspent funds to NV Sandoz S.A. after termination of the study, based on the financial report (annex 1): 18 257.11 €, based on receipt of invoice by NV Sandoz S.A.



Martine Cools

Principal Investigator

Date: 27 04 2018

Annex II: Approved documents

OVERVIEW APPROVED DOCUMENTS		
Initial submission : - Protocol version 1, 26/03/2013 - ICF Ned version 2, 18/03/2014 - ICF Fr	**Approval EC:** 24/03/2014	**Approval FAGG:** 16/01/2014
Amendment 1: - ICF Fr version 2, 10/07/2014	**Approval EC:** 5/08/2014	**Approval FAGG :** NA
Amendment 2: - Protocol versie 2, 3/12/2014	**Approval EC:** 15/01/2015	**Approval FAGG:** NA
Amendement 3: - Protocol versie 3, 24/09/2015 - Labeling	**Approval EC:** 19/10/2015	**Approval FAGG:** 9/11/2015
Amendement 4: - Toevoegen UZ Leuven	**Approval EC:** 27/06/2016	**Approval EC:** NA
Amendement 5: - Protocol versie 3,1, 14/07/2016 - ICF versie 3, 14/07/2016 (Ned)	**Approval EC:** 12/08/2016	**Approval FAGG:** NA
Amendement 6: - Protocol versie 5 dd 24/10/2016 - ICF versie 4 ouders dd 22/12/2016 (Ned&Fr)	**Approval EC:** 06/01/2017	**Approval FAGG:** NA