Newsletter

GABA-1 & GABA-2 TRIALS

Issue 2 | May 2018

Dear Study Members,
we are glad to release and share with you the second issue of the GABA-1 & GABA-2 newsletter.

This newsletter aims to keep all the people involved in the GABA-1/GABA-2 trials informed regarding the most recent noteworthy updates.

This issue focuses **only on the GABA-1 study** and includes an overview on:

- regulatory status - agreements – sites activation – readiness to patients' enrolment;
- actual patients' enrolment status among the active investigational sites and identified issues;
- nonclinical safety study;
- suggestions for clinical staff.

GABA-1 Highlights

The GABA-1 received **full regulatory approval** in France, Germany, Greece, Italy and The Netherlands.

5 centres are now **fully active** and they are performing **patients' pre-screenings.**

Other 2 will sign their new contracts in few days, for a total of **7 recruiting centres**.

The GABA-1 protocol was authorized by EC in Poland and CA in the United Kingdom.

New CRAs have recently joined the GABA-1 team for French, German, Greek, Dutch and Polish sites, and are providing **full support** to the clinical staff.

Ukraine's CA definitively **rejected** the GABA-1 study.

Dompè Farmaceutici started the **non clinical study** requested by German CA to allow the recruitment of patients from 3 months to 3 years of age.

GABA-1

Regulatory status - Agreements – SIVs – Enrollment readiness

Country	Clinical Site	Protocol approval	Agreem. Status	SIV performed	Ready for Pt enrollment
Albania	Qendra Spitalore Univ Nene Tereza - Tiranë	🙂	⌛	X	★
France	H. Robert Debré - Paris	🙂	✒	✓	★
	H. Necker - Paris		✒	✓	★
	H. La Timone - Marseille		⌛	X	★
	Centre H. Régional Universitaire de Lille		✒	✓	★
Germany	Univ. Klin. Erlangen	🙂	✒	✓	★
Greece	Genicom Nosokomeio Paidon I Agia Sofia	🙂	✒	✓	★
Italy	Az. Osp. – Univ. Consorziale Policlinico di Bari	🙂	✒	✓	★
	Istituto Giannina Gaslini – Genova		⌛	✓	★
Netherlands	Erasmus Universitair Medisch Centrum Rotterdam	🙂	✒	✓	★
	University Medical Center Utrecht		⌛	X	★
Poland	Children's Memorial Health Institute Warsaw	🙂	✒	X	★
UK	Alder Hey Children's Hospital Liverpool	🙂	⌛	X	★

🙂 Approved ⌛ Under finalization ✒ Signed ✓ Yes X No ★ Ready for enrollment

🙂 Waiting for approval ★ Almost ready for enrollment

★ Still work to do

COMMUNICATION

❖ Periodic questionnaire on patient enrollment

A **Patient's enrollment status form** has been created to:

- collect **relevant information** about study enrollment from each centre,
- **understand** which kind of problems/obstacles arise, if any.

The form will be sent monthly for completion by the clinical staff in order to have a constantly **updated picture of the enrollment status at each centre**.

Outcomes

The **Patient's enrollment status form** was forwarded to the following sites:

Clinical site	Country
• H. Robert Debré – Paris • H. Armand Trousseau – Paris • H. Necker - Paris • Centre H. Régional Universitaire de Lille	
• Genicom Nosokomeio Paidon I Agia Sofia	
• Az. Osp. – Univ. Consorziale Policlinico di Bari • Istituto Giannina Gaslini – Genova	
• Erasmus Universitair Medisch Centrum Rotterdam	

To date, no patients have been enrolled in the GABA-1 study.

Some of the returned questionnaires highlighted specific **reasons**, mostly related to lack of Inclusion/Exclusion criteria:

- one patient with pain lasting less than 3 months (Debrè site);
- one patient with intellectual disability and epilepsy (Bari site);
- patients who had already taken tramadol with problems related to safety and efficacy (Necker site).

Many of the sites signed the new agreements or performed the SIV only recently. New useful information will be collected with the next questionnaires.

COMMUNICATION

❖ Monthly Teleconference with GABA-1 Cinical Staff

A dedicated monthly teleconference has been established **every last Friday of the month** to:

- keep the staff of all the sites and the Sponsor **updated about the progress** of the study,
- **discuss hot topics** with GABA-1 and GABA-2 clinical staff.

At the beginning of the enrollment phase of the GABA-1 study, this monthly appointment is a **valuable occasion** to share and discuss every concern or issue arisen, to find better strategies together.

PHARM strongly encourages all the collaborators involved in the GABA-1 study at each site to put every effort to participate to the TC

N.B. Only for this month, the TC has been moved to May 28 at 12.30 CEST.

NONCLINICAL SAFETY STUDY

Following the German Competent Authority's concerns raised in regard to the gabapentin degradation products, it was decided not to recruit patients from 3 months to 3 years of age till new safety data were collected.

The IMP Producer, **Dompè Farmaceutici, has now started the additional non clinical study** requested to determine the **safety** of the so called "impurity A", detected in the Gabapentin IMP, for the youngest population.

The scope of the non clinical study is to achieve an equivalent human safety factor level of 5 with the low dose of impurity A, a safety factor level of 10 with the medium dose, and a safety factor level of 20 with the high dose of impurity A.

If the results of the non clinical study, expected by the end of June, will be favourable in terms of safety, recruitment will be opened again to children below the age of 3 years.

Some suggestions for the clinical staff:

It is important to identify the **origin** of these difficulties, in order to find a **solution**. For example:

- Difficulties linked to I/E Criteria
- Patients involved in other clinical trials
- Problems related to IMPs
- Lack of interest in the study by parents/patients

You have many **options**!

A. Fill in the periodic **Questionnaire on patients enrollment** and send it to the Clinical Operation Manager
B. Discuss it with the Sponsor and the staff of the other clinical sites during the **monthly GABA-1 TC**
C. Contact the Sponsor and we will discuss the best strategies to put in place at your site

Does anyone in your staff need an **eCRF account activation**?

1. After **eCRF training**, send the completed 'account request form' to the data manager to receive your **access credentials**

2. eCRF link: https://trials-ice.advicepharma.com/GABA1/login

1. All the Investigators should **Register** at: https://secure.trainingcampus.net/uas/modules/trees/windex.aspx?rx=c-ssrs.trainingcampus.net
2. Activate and log into your new account
3. Enter «My Activities» section and select the course in **your local language**
4. Attend the course and review the case studies to get your **C-SSRS training certificate**!

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