



Is your baby or child presenting symptoms suggestive of Cow's Milk Allergy?

APTITUDE

A Cow's Milk Allergy Diagnosis Clinical Research Study



**The APTITUDE study is being conducted at approximately
20-30 research centers in US, Canada, Italy and Lithuania**

Overall 230 children are expected to participate in the study



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Panel 10

What is Cow's Milk Allergy (CMA)?

CMA is the most common food allergy in infants. Food allergies may be caused by **allergic mechanisms** producing symptoms within minutes (immediate reaction) to a couple of hours following ingestion of milk products versus **non-allergic mechanisms**, producing symptoms within hours to days (delayed reaction) following the ingestion of milk products, or rarely a combination of both.

The symptoms can include symptoms of the skin (rash, hives, dry, scaly or itchy skin), the digestive system (diarrhoea, vomiting, constipation and reflux), the respiratory system (noisy breathing or wheezing, coughing, runny nose), and other more general allergy symptoms (for example, tiredness, problems sleeping).

With all these different non-specific symptoms, establishing the diagnosis of CMA can be a challenge.

If you suspect your child may be allergic to cow's milk, please discuss with your study doctor who will guide you through the process to a final diagnosis and may propose your participation in the APTITUDE study.

APTITUDE Study

What is the purpose of this research study?

The purpose of this research study is to evaluate the performance of a ready to use an experimental **Patch Test (not approved yet)** for the diagnosis of the **non-IgE form of Cow's Milk Allergy** in children.

Patch testing helps to identify substances (like cow's milk) causing a **delayed-type allergic reaction** and may identify allergens not identified by blood testing or skin prick testing.

This study is a multi-center, Phase II proof of concept study.

200 children with symptoms suggestive of the non-allergic form of Cow's Milk Allergy (CMA) will be enrolled in the study and 30 non-allergic children .



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Jun 04, 2020
Panel 10

Can my child participate in the study?

Your child may be able to take part in this study if:

- Is 1 month to 5 years of age (inclusive)
- Has a history of symptoms that are consistent with the non-allergic form of CMA, characterized by having either:
 - ✓ Two or more gastrointestinal symptoms (vomiting, diarrhoea, persistent distress/colic, regurgitation, constipation), that lasted at least 1 week within 1 month prior to screening or
 - ✓ Blood in their stool
- Has been regularly on a diet containing cow's milk protein during the month prior to the screening visit.

There are other requirements that the study doctor will discuss with you to determine if your child is eligible to participate in this study.

How long is the study?

Your child's participation in the study may last up to approximately 3 months (including a 1 to 2 weeks screening period).

If your child participates in the study, it is important that you:

- ✓ attend all scheduled visits, phone calls, study requirements and complete an electronic daily diary
- ✓ discuss with the study doctor at every visit how your child is feeling

What happens during the study?

Before your child participates in this study, you will receive a study Informed Consent Form (ICF) that provides a detailed description of the study. The study staff will explain anything that you do not understand and answer any questions you may have. Before any study procedure is performed and after all your questions have been answered you will be asked to sign the ICF to confirm your agreement for your child's participation in the study.

During the study you and your child will be asked to perform 7 study visits within 3 months at a maximum and you will have daily phone calls scheduled

with the investigational site to discuss the health of your child, concomitant medication, or any adverse event or any question you may have.

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Protocol Level
Jun 04, 2020
Panel 10

At the study visits, your child will have allergy tests and other health check examination.



Study Periods

Screening Period (1 to 2 weeks)

During the screening visit, the study doctor will talk to you and run some allergy tests to determine if your child is healthy and qualifies for the study.

Diagnosis Period (2 months)

You will visit together with your child the study centre at:

- **Day 1 (inclusion and patch application)**
- **Day 3 (patch removal and patch reading)**
- **Day 4 (patch reading and start of cow's milk protein-free diet)**
- **Day 25 (first hospital food challenge)**
- **Day 37 (second hospital food challenge)**
- **Day 49 (end of study)**

You will have **daily phone calls** with the study center on **Day 26 to 30 and Day 38 to 42** while your child will receive the food challenge formula at home.



At **Day 1** you will be provided with an **electronic diary** wherein you will be asked to report daily your child's symptoms and other important medical information.

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June 1, 2020
Panel 10

What is the study medicinal product?

The investigational medicinal product DBV1605 is a ready to use atopy patch test for diagnostic use containing 2 distinct patches:

- One active patch containing a dry deposit of 180 µg of cow's milk allergen extract.
- One control patch with the same design as the active patch but devoid of any formulation.

On your child's back will be applied the 2 patches (active patch and control patch) for 48 hours (±3 hours).

What other tests will be performed?

Skin Prick Test

At the screening visit a Skin Prick Test containing Cow's milk extract, plus a negative and positive control will be performed in all children to check for immediate allergic reactions to cow's milk, as these children will be excluded from this study.

Allergy skin tests aren't painful and It is a routine procedure commonly performed to detect potential allergies. This type of testing uses very small needles (lancets) that barely penetrate the skin's surface. Your child won't bleed or feel more than mild, momentary discomfort. About 15 minutes after the 3 skin pricks your study doctor will observe your child's skin for signs of immediate allergic reactions. Your child will develop a raised, red, itchy bump (wheal) that may look like a mosquito bite if suffering from an allergic form of CMA.

Your child must not take antiallergic drugs for 1 to 7 days prior to the test according to the advice of your study doctor.

Blood Tests

At screening visit your child will have drawn about 5 ml blood to examine your child's health and to perform a blood test that measures your child's immune system's response to cow milk by measuring the amount of specific cow's milk immunoglobulin E (IgE) antibodies. Children with a positive cow's milk IgE will not be enrolled in this study.

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Protocol Level
June 04, 2020
Panel 10

Cow's Milk Elimination Diet

On Day 4 your child will start a strict cow's milk protein elimination diet for the duration of 3 to 4 consecutive weeks.

- Children aged 1 to 5 months will be fed with Alfamino®, a cow's milk free formula produced by Nestlé Health Science and provided by DBV Technologies.



- Children aged from 6 months to 2 years will be fed with Alfamino® and a complementary cow's milk protein-free diet adapted to their age.
- Children aged 2 to 5 years of age will perform a strict cow's milk elimination diet but will not receive Alfamino®.

Double-Blind, Placebo-Controlled, Food Challenge (DBPCFC)

Alfamino® with cow's milk protein and Alfamino® without cow's milk protein (Placebo)

This test is considered the "gold standard" for diagnosing a food allergy. Your child will receive increasing doses of either cow's milk proteins or a placebo (a harmless substance) in order to assess if symptoms suggestive of CMA appears and at what dose. The cow's milk protein and placebo are given on separate days. Because the allergen and the placebo look alike, neither you nor



your doctor will know which one your child is receiving. That's why this procedure is called "double-blind".

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Protocol Level
Jun 04, 2020
Panel 10

This process ensures that the test results are objective. Neither you or your child's anxiety nor your study doctor's preconceptions can sway the outcome.

Food Challenge Periods

Your child will undergo 2 food challenge periods one being the administration of a placebo formula, the other of a milk protein formula.

Each period will be conducted in 2 separate steps:

The **Hospital Food Challenge** and, if applicable, the **Home Food Challenge** followed by a wash-out period. The order of administration of the 2 formulas will be determined randomly (by chance).

The outcome of each period will be assessed by your study doctor. At the end of the study, the results of the both food challenge periods will be unblinded and your study doctor will communicate to you if your child's suspected CMA was confirmed. With the final diagnosis your study doctor will be able to tell you his recommendations about the further treatment of your child and if the cow's milk free diet should be continued.

Why should I consider my child participating?

Participating in this study is a way to help explore the potential of a new simple and easy to use diagnostic test for Cow's Milk Allergy. This new test may lead to a new way to diagnose and treat CMA and may help doctors and parents in the future.

As a study participant, your child's will be closely monitored under the guidance of a specialist.

Study participation is voluntary, and your child can leave the study at any time. Talk with your study doctor and ask questions about the study if you consider participating.

Sometimes by just asking the simple question: "Could it be cow's milk protein allergy?" you could solve the endless battle that you and your child are going through.



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Panel 10

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This clinical research study is for children who may suffer from Cow's Milk Allergy.

**If you think your child has Cow's Milk Allergy, consider volunteering for the
APTITUDE clinical research study.**



To learn more about the study, please contact _____