SYNOPSIS

INN : CROMOGLICIC ACID

Study number : CR 2594

Study title : Intraindividual randomised double blind comparative study between AARANE * resp. ALLERGOSPASMIN* with old propellant (CFC-containing) and the same combination with new propellant (HFA 227-containing) to assess the prevention of exercise induced asthma in children and adolescents.

CSR date : 25 March 1996

The study results and synopsis are supplied for informational purposes only.

Not all of the study results have necessarily been reviewed by the Regulatory Authorities.

The decision to prescribe and take a product should always be made on the basis of the most recent version of the product information and product package insert in the country of prescription.
### SYNOPSIS
Clinical trial CR 2594 - GER:05/93

<table>
<thead>
<tr>
<th>Name of company:</th>
<th>Fisons Arzneimittel GmbH</th>
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</thead>
<tbody>
<tr>
<td>Name of finished product:</td>
<td>Aarane*</td>
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<tr>
<td>Name of active ingredients:</td>
<td>Sodium cromoglycate and reproterol hydrochloride</td>
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</table>

**Title of study**
Intraindividual randomised double blind comparative study between AARANE* resp. ALLERGOSPASMIN* with old propellant (CFC-containing) and the same combination with new propellant (HFA 227-containing) to assess the prevention of exercise induced asthma in children and adolescents.

**Investigators (centers)**
Dr. med. M. Debelic, Bad Lippspringe (Germany)

**Duration**
4 days

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<th>Clinical phase II</th>
<th>Ref. no. CR 2594</th>
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**Objectives**
It was the aim of the study to examine the protective effect of the fixed drug combination disodium cromoglycate (1 mg) plus reproterolhydrochlorid (0,5 mg) (AARANE* ALLERGOSPASMIN*) delivered in 2 puffs by pressurised aerosol with CFC resp. HFA 227 as propellants on exercise induced asthma.

The primary variable was the maximal fall of FEV1 after exercise

**Methodology**
**Design:** The study was carried out as a crossover double-blind group comparison.

The trial medication was allocated in randomised order. At the beginning of the study two control provocations were carried out:

1. **Control provocation 1:** Baseline measurement without premedication.
2. **Control provocation 2:** Premedication with AARANE*, two puffs were administered by pressurized aerosol.

Only those patients were included in the trial whose FEV1 dropped 20% - 50% after the first control provocation and less than 10% after the second.

If possible, all provocations were carried out on successing days. During the trial days provocation tests were carried out at 30 minutes after inhaling the trial medication.

The exercise was free running over six minutes in a long corridor at a temperature of 18 to 20°C. The running speed was chosen so that the heart rate was 160-180 beats per minute after a four minutes lasting run (submaximal loading).

Therefore the study contains a period of 4 days

**Monitoring:** Lung function, adverse events, blood pressure and pulse on all study days

**Number of subjects**
Total in analysis: 24 patients, study completer per protocol 23 patients

**Diagnosis and inclusion criteria**
Drop of FEV1 of 20-50% after exercise on study day 1 (no medication) and drop of FEV1 of less than 10% after exercise on study day 2 (premedication: AARANE*)

III
Test product | MDI Disodium cromoglycate (1 mg) + reproterol * HCl (0,5 mg) - Fixed drug combination with new propellant HFA 227, 2 puffs via pressurised aerosol.
---|---
Reference | MDI Disodium cromoglycate (1 mg) + reproterol * HCl (0,5 mg) - Fixed Drug combination with old propellant CFC, 2 puffs via pressurised aerosol.
Criteria for Evaluation | Primary variable was the maximum fall of FEV₁ on each study day.
Statistical Methods | Schuirmans’s double-one-sided-t-test procedure.

### Summary of results:

The mean maximum fall of FEV₁ was 135 ± 144 ml under treatment with the CPC-containing formulation and 152 ± 136 ml under treatment with the HFA 227-containing formulation.

Using a range of equivalence of 20% this result was statistically not significant (p = 0.4107).

Due to the fact that all patients showed a 100% protection of EIA which means that there was no fall of FEV₁ after provocation either under treatment with the CPC-containing formulation or the HFA 227-containing formulation and instead a statistically significant result could not be realised, both formulations showed to be equivalent.

There were no reports of adverse events nor any clinical relevant changes in blood pressure or in pulse frequency.

In conclusion it can be accepted that both formulations are equivalent.