Statistical Evaluation of an Application Study with the preparation series

BOVISAN

in the administration forms of capsules, drops and suppositories

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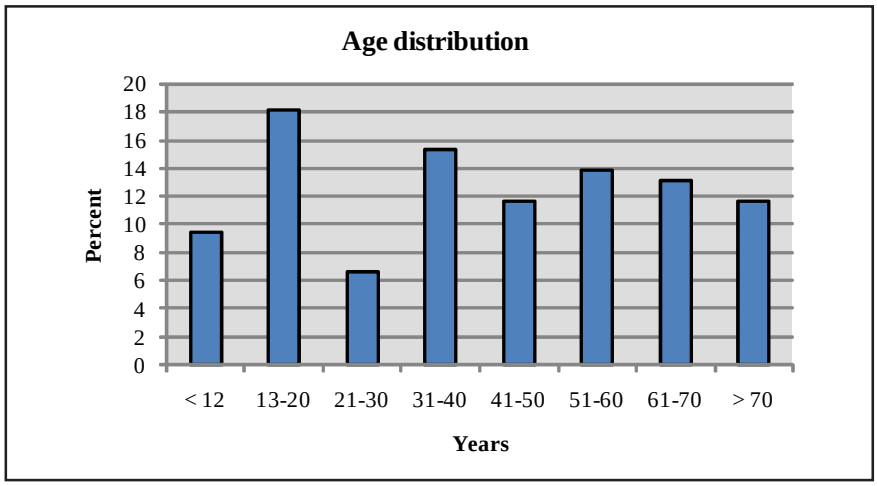
1. Introduction

From January 2002 to March 2006, a total of 137 patients was admitted to an observation study with the preparation series BOVISAN in the administration forms of capsules, drops and suppositories in two internist practices, one surgical practice, one ENT practice and three general practices. The homeopathic test preparation BOVISANconsists of the 5th or 6th decimal dilution of Mycobacterium bovis (BCG), depending on the administration form.

BOVISAN drops contain exclusively Mycobacterium bovis (BCG) 6X dil. in accordance with provision 5a HAB.
1 BOVISAN capsule contains: 330 mg Mycobacterium bovis (BCG) 5X trit. in accordance with provision 6 HAB.
1 BOVISAN suppository contains: 0.2 g Mycobacterium bovis (BCG) 5X trit. in accordance with provision 6 HAB.

The aim of the observation study was to establish the actual application of the preparation and its tolerance under conditions in everyday practice. Further, knowledge concerning the acceptance of the preparation on the market, also amongst children, should be gained.

In accordance with the structure of the study, exclusively descriptive statistical procedures were used. The application of inductive methods was not indicated. An "intention to treat" evaluation was carried out, i.e. all patients were considered, who had received at least one dose of the remedy.



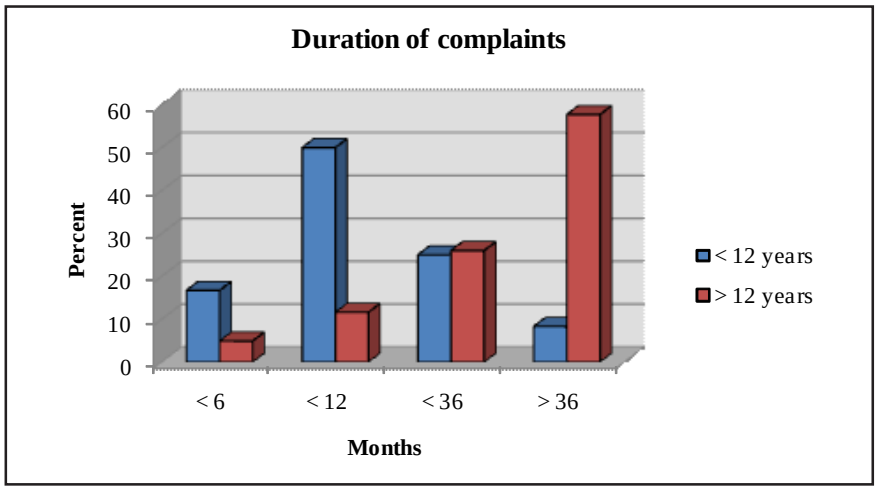
2. Participating patients

137 patients participated in the study, 35% men and 65% women. The age of the patients varied between 6 and 86 years with an average of 41.2 years and a standard deviation of 22.3 years. 9.5% of the patients were younger than 12 years. The biggest age group was that of 13 to 20 years old patients with 18.2%; the smallest group was that of the 21 to 30 years old patients with only 6.6%. The remaining age groups were almost the same size: between 31 and 40 years, there were 15.3%, between 41 and 50 years as well as over 70 years were 11.7% each, and between 61 and 70 years were 13.1% of the patients. In the age distribution, the men with an averave age of 38.6 ± 22.1 years were on average 4 years younger than the women with 42.6 ± 22.2 years.

Height varied between 110 and 190 cm with an average value of 165.2 ± 16.4 cm. Weight varied between 28 and 91 kg with an average of 65.5 ± 14.0 kg.

2.1 Diagnosis and accompanying diseases

The diagnosis leading to prescription had to be recorded in the study protocol. It became apparent that BOVISAN, in accordance with Isopathy, is used in a



Duration of Complaints (Months)	Total Patient Population (%)	Patients < 12 years (%)	Patients > 12 years (%)
< 6	5.9	16.7	4.9
6 - 12	14.8	50.0	11.4
< 36	25.9	25.0	26.0
> 36	53.3	8.3	57.7

very wide area of application. The preferred application was dependent on the age of the patients. In the group of patients under 12 years, BOVISAN was deployed mainly with recurrent tonsillitis, while in the group of patients over 12 years, diseases like hypotonia, rheumatic joint diseases, but also pneumocystis pneumonia and asthma bronchiale were paramount. Medical findings were collected before and after completion of the treatment. Accompanying therapies were to be documented in the survey form.

In order to obtain a measure of the chronic diseases, the patients were asked in the study protocol for how long the disease or complaints had been existent. Time frames were given of less than six months, up to one year, up to three years and more than three years. In 5.9% of the patients, the complaints had existed for less than six months. In 14.8% of the patients, the complaints had existed between six and 12 months, in 25.9% for up to three years. More than half of the patients (53.3%) had suffered from the medical conditions for more than 36 months. Almost the same percentage (50%) had suffered from the complaints for more than six months and less than one year in the group under 12-year-olds and for more than 36 months in the adult group of over 12-year-olds (57.7%). No data were available for two patients.

12 of the 137 patients included in the study had been treated with BOVISAN previously. Without exception, these patients were part of the adult group.

3. Dosage and duration of treatment

3.1 Time of consultation and duration of treatment

Corresponding to the nature of an application study, the doctor was not given a fixed schedule for the final examination. This final examination was carried out after a period of 9 to 1492 days with an average value of 258.6 ± 341.3 days.

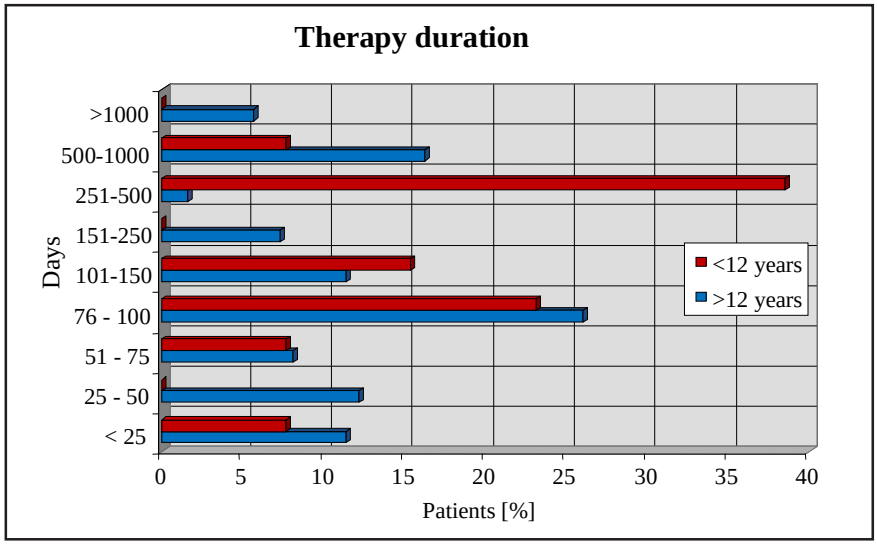
Therapy duration in the children (< 12 years) with 221.7 ± 186.9 days on average was just as long as that in the adult group with 262.5 ± 353.4 days.

3.2 Dosage

Dosage was specified for the individual administration forms according to the package leaflet as follows:

BOVISAN drops
For oral intake: 1 to 3x daily 2 to 5 drops before a meal.
For rubbing in: 2 to 3x weekly 5 to 10 drops into the affected area or the hollow of the elbow.

BOVISAN capsules
Every two weeks, 1 capsule with some liquid either before breakfast or in the evening before bed. An increase to a weekly dose of 2 capsules is possible.



BOVISAN suppositories
2 to 3x weekly 1 suppository before bed.

Referring to the administration forms, capsules were taken in by 57 patients, drops were taken in by 37 patients and rubbed in by 18 patients and suppositories were used by 43 patients. Multiple designations were necessary where several administration forms were combined. The below table shows the medium dose of each administration form. The dosages for drops indicate the daily dose, the dosages for the remaining administration forms indicate the dose per week or two weeks, respectively.

Except from drops for rubbing in, dosage does not differ substantially in the two age groups of younger and older than 12 years. The dosage of drops for rubbing in is about 50% higher in the group of <12 years olds than in the adult group. However, the recommended dose was complied with.

In addition to the monotherapy with only one administration form, also combinations of the different administration forms were deployed in the therapy. In a total of 16 patients (11.7%), different administration forms were combined. Seven Patients received 2 suppositories weekly in addition to the daily intake of drops. By four patients, drops were taken in as well as rubbed in. Further, one patient of this group received 1 capsule weekly in addition. One patient received drops for intake on a daily basis and 1 capsule on a weekly basis. By two patients, drops were rubbed in on a daily basis and in addition, 2 suppositories were used on a weekly basis. Another two patients received 2 suppositories and 1 capsule on a weekly basis. All patients treated with a combination of several admi-

Dosage			
Total population	**Medium Dose**	**Minimum Dose**	**Maximum Dose**
Capsules (weekly)	1.2 ± 0.4	1	2
Capsules (biweekly)	1.0 ± 0	1	1
Suppositories (weekly)	1.5 ± 0.6	1	3
Drops (intake)	9.1 ± 2.0	5	10
Drops (rubbing in)	6.7 ± 3.1	3	10

Dosage				
All patients < 12 years	**Medium Dose**	**Minimum Dose**	**Maximum Dose**	**No. of Patients**
Capsules (weekly)	1.0 ± 0	1	1	3
Suppositories (weekly)	1.8 ± 0.8	1	3	4
Drops (rubbing in)	8.8 ± 2.6	3	10	6

Dosage				
All patients > 12 years	**Medium Dose**	**Minimum Dose**	**Maximum Dose**	**No. of Patients**
Capsules (weekly)	1.2 ± 0.4	1	2	47
Capsules (biweekly)	1.0 ± 0	1	1	7
Suppositories (weekly)	1.5 ± 0.6	1	3	39
Drops (intake)	9.1 ± 2.0	5	10	37
Drops (rubbing in)	5.7 ± 2.7	3	10	12

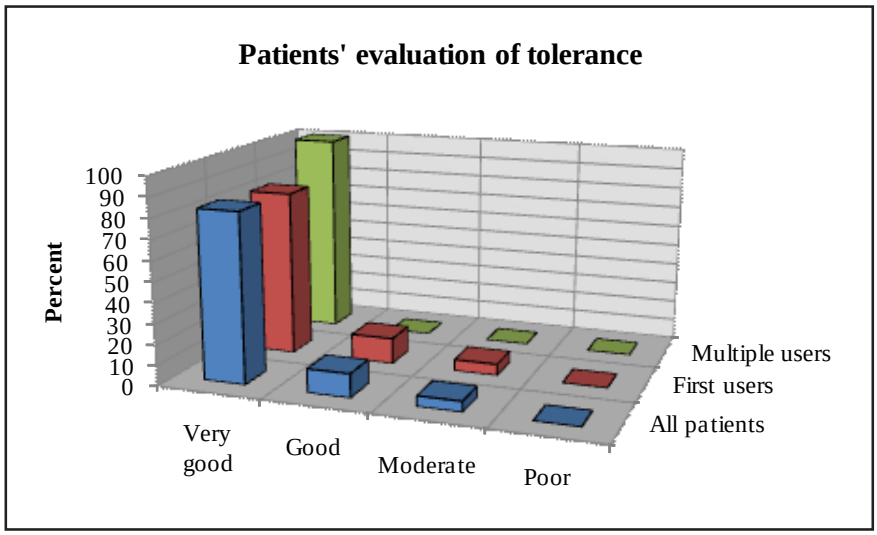
Evaluation of tolerance								
Patient Group	**Patients' evaluation (%)**				**Doctors' evaluation (%)**			
	Very Good	Good	Moderate	Poor	Very Good	Good	Moderate	Poor
All Patients	83.2	11.7	5.1	0	85.4	10.2	4.4	0
First Users	81.6	12.8	5.6	0	84.0	11.2	4.8	0
Multiple Users	100.0	0	0	0	100.0	0	0	0

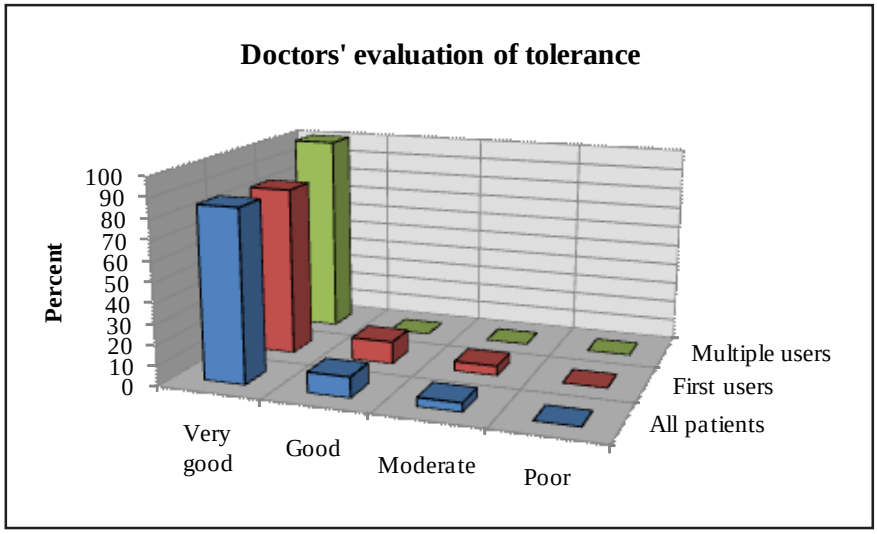
nistration forms were more than 14 years old and thus, belonged to the adult group.

4. Comparison with previous therapy

12 patients had received a previous therapy with one or more administration forms of BOVISAN within the last 5 years. By comparing efficacy and tolerance in the two patient groups of first users and multiple users, evidence for a possible sensitization to the active ingredient should be determined.

In the evaluation of tolerance, multiple use performed better than first use. With a good overall tolerance, in the group of multiple users, both patients and doctors rated tolerance as „very good". From this data, no risk potential concerning a sensitization of the patients to the active ingredient Mycobacterium bovis (BCG) can be identified.





In the group of multiple users, doctors tended to evaluate efficacy better than patients. However, the evaluation of both groups was not significantly different.

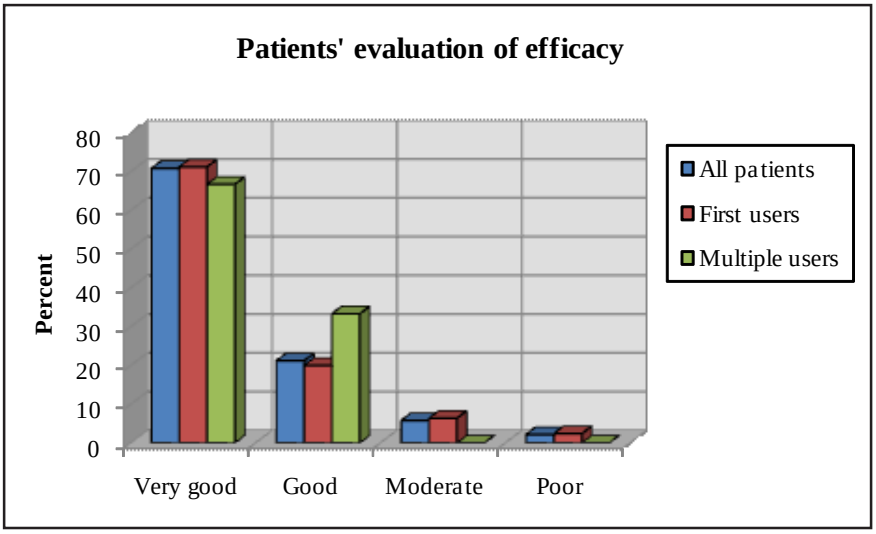
With 121.1 ± 232.7 days, the therapy duration for the multiple users was only half as long as that for the first users with 269.4 ± 351.7 days.

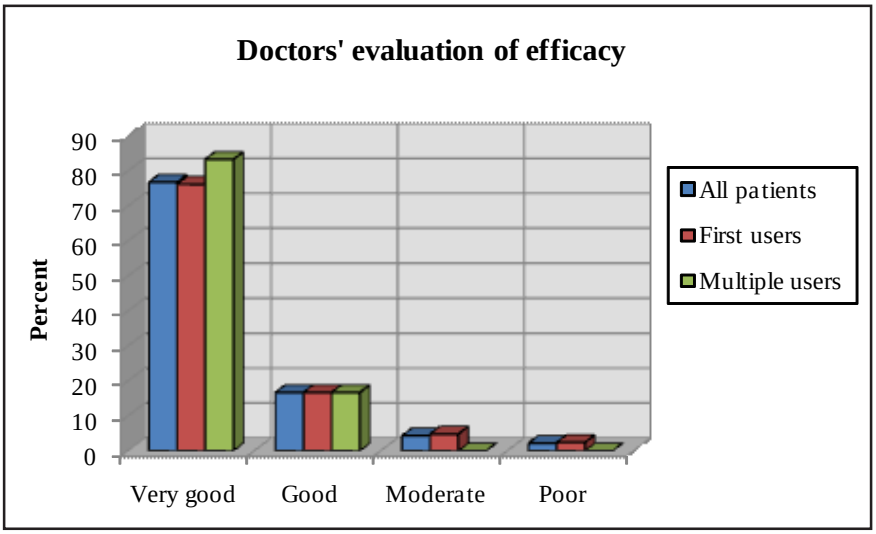
5. Efficacy and tolerance

5.1 Evaluation of efficacy by doctor and patient

In a final assessment, doctors and patients were asked to evaluate efficacy and tolerance. Efficacy could be rated as 'very good', 'good', 'moderate' or having 'no effect'. Further, doctors were asked to evaluate the patients' compliance, which also could be rated as 'very good', 'good', 'moderate' or 'poor'. The evaluation of efficacy showed that 70.8% of the patients found efficacy 'very

Evalulation of efficacy								
Patient Group	**Patients' evaluation (%)**				**Doctors' evaluation (%)**			
	Very Good	Good	Moderate	No Effect	Very Good	Good	Moderate	No Effect
All Patients	70.8	21.2	5.8	2.2	76.8	16.7	4.3	2.2
First Users	71.2	20.0	6.4	2.4	76.2	16.7	4.8	2.4
Multiple Users	66.7	33.3	0	0	83.3	16.7	0	0





good', 21.2% 'good', whilst for 5.8%, the treatment's efficacy was 'moderate', and 2.2% experienced 'no effect'. The result of the doctors' evaluation of efficacy was just as positive as that of the patients. The doctors rated efficacy as 'very good' in 76.8% of the cases, as 'good' in 16.7%, as 'moderate' in 4.3% and as having 'no effect' in 2.2%.

Compliance (N = 132) was rated by the doctors to be 'very good' in 104 patients and 'good' in 26, hence 98.5% of all patients participating in the study were given a 'good' or 'very good' compliance rating. For one patient each, compliance was rated as 'moderate' and 'poor'.

5.2 Evaluation of tolerance by doctor and patient

To conclude the examination, an evaluation of tolerance was submitted by doctors and patients, wherein tolerance could be rated as "very good", "good", "moderate" and "poor". 83.2% of the patients and 85.4% of the doctors rated tolerance as 'very good', while 11.7% of the patients and 10.2% of the doctors attested 'good' tolerance to BOVISAN. 'Moderate' tolerance was stated by 5.1% of the patients and 4.4% of the doctors. 'Poor' tolerance was attested to the preparation in no case.

In the adult group, doctors and patients evaluated the 'very good' tolerance more positively than in the age group of under 12 year-olds, while in the young age group, neither patients nor doctors rated tolerance as 'moderate' or 'poor'.

5.3 Side effects and discontinuation of the therapy

No patient discontinued the therapy with BOVISAN. However, 7 local reactions during the therapy were reported, which will be interpreted in more detail in the following. In a 6 year old boy, an erythema was detected 2 days after embrocation of 3 drops of BOVISAN. The duration of com-

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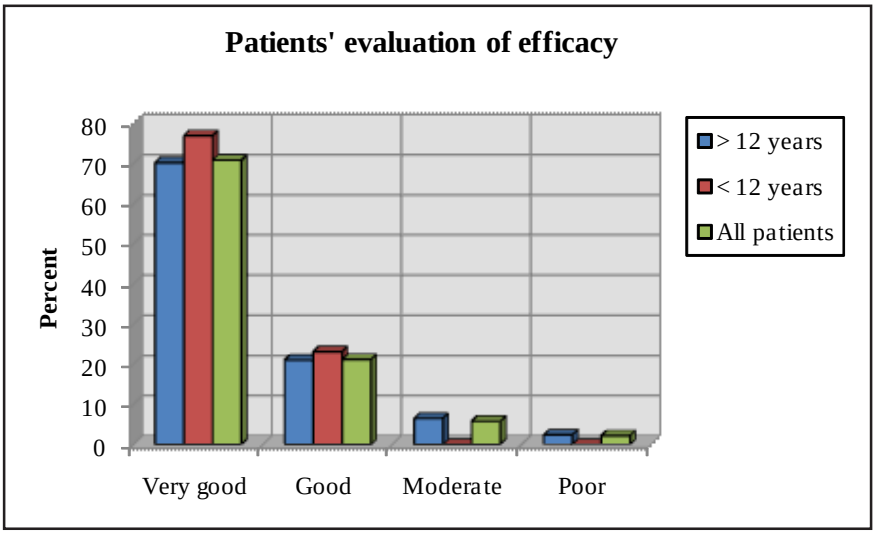
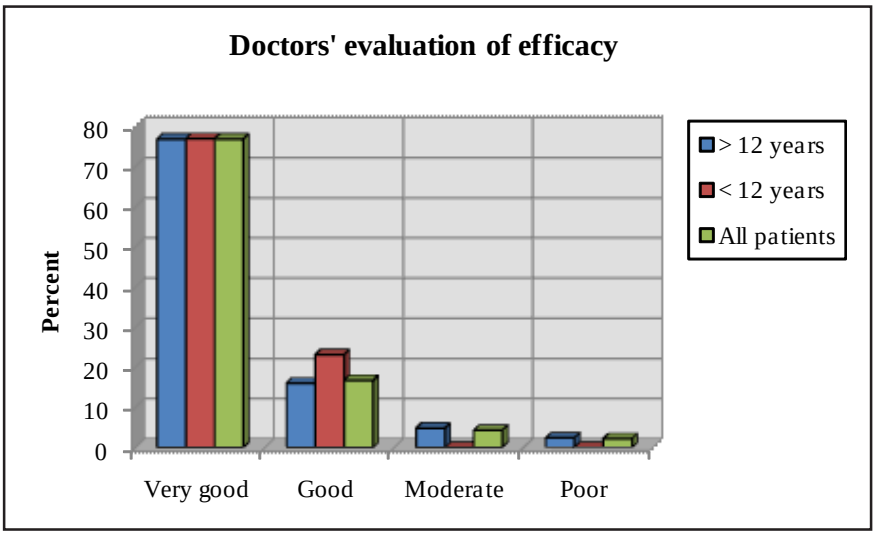
All Patients	70.8	21.2	5.8	2.2	76.8	16.7	4.3	2.2
< 12 years	76.9	23.1	0	0	76.9	23.1	0	0
> 12 years	70.2	21.0	6.5	2.4	76.8	16.0	4.8	2.4





plaints was indicated with „hours". Further intervention was not necessary. A 53 year old man, who had taken in and rubbed in BOVISANdrops, and additionally taken in 1 capsule once a week, complained about a 15-minute perspiration 20 minutes after application, which disappeared without any further measures. Another 65 year old man, who was administered 1 suppository once a week, complained about diarrhoea 1 hour after application. It disappeared without further intervention after 3 hours. A 66 years-old female patient, who was also treated with suppositories, complained about tenesmus 30 minutes after application, which lasted for 1 hour and then disappeared without further intervention. A 35 and a 47 year 'old male patient and a 15 year old female patient complained about a burning sensation in the mouth 3 days and 1 day, respectively, after intake of a capsule. Duration of the complaints was indicated with 2 days and 1 day, respectively. Also in these three cases, no additional therapy was necessary.

In total, no reactions occurred that were difficult to control. All reported side effects were completely reversible.

6. Summary

From January 2002 to March 2006, a total of 137 patients was admitted to an observation study with the preparation series BOVISAN in the administration forms of capsules, drops and suppositories in two internist practices, one surgical practice, one ENT practice and three general practices. The homeopathic investigational preparation BOVISAN consists of the 5th or 6th decimal dilution of Mycobacterium bovis (BCG), depending on the administration form. The age of the patients varied between 6 and 86 years. About 10% of the patients were younger than 12 years.

BOVISAN, in accordance with

Evaluation of tolerance								
Patient Group	**Patients' evaluation (%)**				**Doctors' evaluation (%)**			
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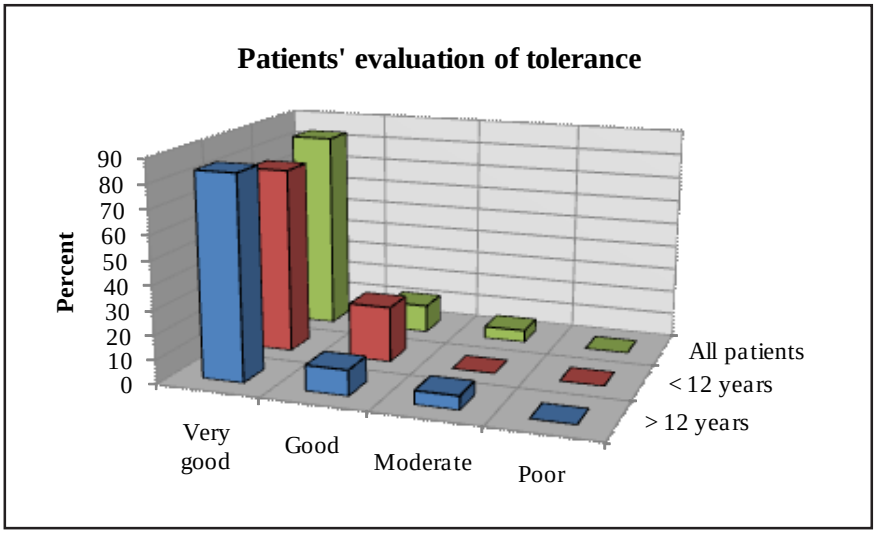

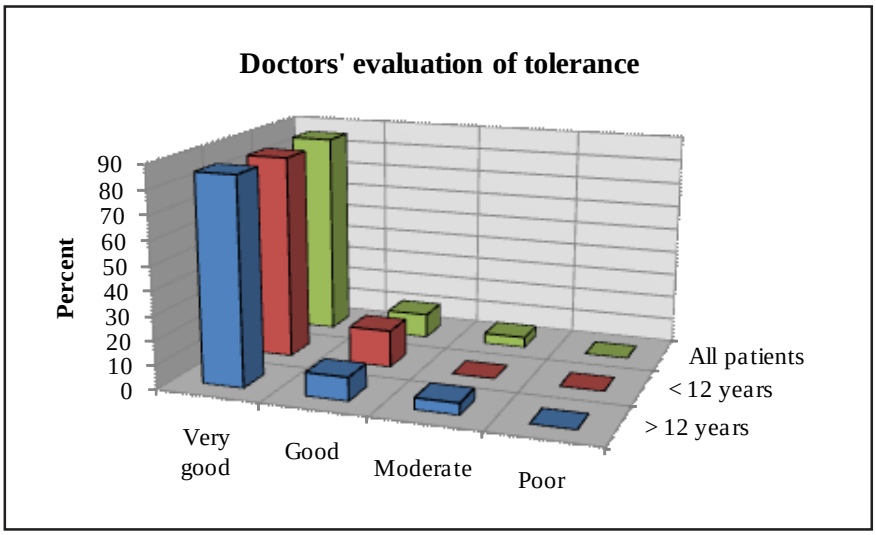

Isopathy, was used in a very wide area of application with the preferred application being dependent on the age of the patients. While in the group of patients under 12 years, BOVISAN was deployed mainly with recurrent tonsillitis, diseases like hypotonia, rheumatic joint diseases, but also pneumocystis pneumonia and asthma bronchiale were paramount in the group of patients over 12 years. Accompanying therapies were to be documented in the survey form.

Therapy duration in the children (< 12 years) was with 221.7 ± 186.9 days on average just as long as that in the adult group with 262.5 ± 353.4 days.

12 patients had received a previous therapy with one or more administration forms of BOVISAN within the last 5 years. No grounds for suspicion of a possible sensitization to the active ingredient could be generated based on these data.

Progress of the treatment was determined by means of a collection of findings before and after completion of the therapy. 92% of the patients and 93.5% of the doctors rated efficacy of the treatment as 'very good' and 'good'. Tolerance was rated as 'very good' and 'good' by 94.9% of the patients and 95.6% of the doctors. No study was discontinued. Side effects and incompatibilities were documented. In total, merely local reactions occurred in 7 patients. All of them were completely reversible without additional therapy. No patient dropped out of the treatment with BOVISAN.

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