A prospective, randomized, double-blind placebo-controlled multi-centre dose-finding study of 3 different regimens of gpASIT+™ administered subcutaneously to adult patients with grass pollen-induced allergic rhinoconjunctivitis

BioTech Tools is developing a new AIT product based on

- Highly purified allergen fragments from natural source (obtained by hydrolysis and purification)
- Short course treatment

First indication: treatment of patients with grass pollen-induced allergic rhinoconjunctivitis with or without controlled asthma.
Clinical development

BTT007, Phase IIa, open, 1 group, n=65
grass pollen allergic patients over 6 weekly visits with 2 injections per visit

• Determination of maximal tolerated dose

• Assessment of change of reactivity to CPT

• gpASIT+™: Max cumulative dose 490 µg
## BTT007 - Treatment schedule

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Baseline
0 µg

6 visits
490 µg
• No case fatality observed

• No use of epinephrine

• Systemic allergic reaction
  • No grade III nor grade IV AWMF
  • Grade I & II AWMF

• Local reaction at the injection site
  • Local reactions were transient, usually resolving by the second day post-injection
  • Size did not increase with the increase of the dose injected.

• Unsolicited adverse events reported were not different from those reported previously for other rhinoconjunctivitis immunotherapies.
Conjunctival Provocation Test (CPT)

- 100 U
  - No reaction = Negative

- 1000 U
  - Negative

- 10000 U
  - Negative
  - Non reactive

- STOP

Positive
BTT007 - Effects of gpASIT+™

Distribution of patient CPT reactivity

- 70% of the patients become non reactive to CPT after 4 injection visits
- Significant reduction of the CPT score after 4 injection visits (p< 0.001)
- 5 fold increase of grass pollen specific IgG4 after 4 injection visits (p<0.001)

Induction of gp-specific IgG4
Clinical development strategy

BTT007, Phase IIa, open

BTT008, Phase IIb, RDBPC, Multicentric, dose-ranging study, n=50 grass pollen allergic patients/group, 5 weekly visits with 2 injections per visit

- 4 groups
  - Placebo
  - gpASIT+™: Max cumulative dose 70-170-370 µg
- Assessment of change of reactivity to CPT
198 patients randomized in 4 groups
- Placebo
- gpASIT+TM-70 µg (cumulative dose)
- gpASIT+TM-170 µg (cumulative dose)
- gpASIT+TM-370 µg (cumulative dose)

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Screened patients N=240

Incl/excl (N=35)
Consent withdrawal (N=6)
Other (N=1)

Randomized patients N=198 (Safety Set)

Group I
Placebo
N=46

Drop-out
N=1 AE

N= 45 completed

Group II
gpASIT-70 µg
N=50

Drop-out
N=1 AE

N=49 completed

Group III
gpASIT-170 µg
N=49

Drop-out
N=2 AEs

N=47 completed

Group IV
gpASIT-370 µg
N=53

Drop-out
N=2 AEs

N=51 completed
• 1 SAE: systemic reaction grade II

• Systemic allergic reactions (AWMF classification):
  • No grade III nor grade IV
  • 14 grade II SR in 12 patients including placebo (No use of epinephrine)
  • 12 grade I SR in 9 patients including placebo
  • No dose effect
Local reaction at the injection site
- Mean value of local reactions far below the critical level of action (5 cm)
- Mean value does not increase with the increase of the dose injected
BTT008 - Effects on CPT reactivity (ITT)

*After 4 treatment visits, patients of 170 µg and 370 µg groups have received 170 µg of gpASIT+™

Significant improvement in reactivity to CPT in the group receiving 170 µg gpASIT+™ after 4 injection visits (p<0.005) and 5 injection visits (p = 0.022)

- 170 µg is the selected dose for the upcoming Phase III study
Plateau effect is noticeable at 170 µg in terms of:

- The percentage of patients with a decrease of reactivity to CPT
- The percentage of patients who become non-reactive to CPT
gpASIT+™ stimulates the production of grass pollen IgG4, with a dose-dependent relationship

Production of blocking antibodies confirmed: respectively 20, 23, and 32% of reduction of complexes binding in patients who received 70, 170, and 370 µg of gpASIT+™

For detailed information, please visit Thematic Poster Session:
  Session no.: LB TPS 7,
  Session date: 09.06.2015
  Session time: 12:00 – 13:30
BTT008 - Conclusions

• A short course treatment with increasing doses of gpASIT+™

• Clinical efficacy of gpASIT+™
  • Dose effect in improvement of reactivity to CPT
  • Statistically significant improvement in the group receiving 170 µg gpASIT+™ (p<0.005 after 4 injection visits, p = 0.022 after 5 injection visits)
  • 170 µg is the selected dose for Phase III study

• Safe and well-tolerated until 100 µg/injection, no grade III nor grade IV SR (AWMF Classification)

• Dose-dependent effect on the immune responses
  • Grass pollen-specific IgG4, IgE
  • Blocking antibodies