**SUPPLEMENTARY FILE**

**A randomized, double-blind, phase III study to compare the efficacy and safety of GB242 and infliximab when administered with methotrexate in patients with active moderate to severe rheumatoid arthritis**

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# Inclusion and exclusion criteria

***Inclusion Criteria***

1. aged 18–75 years, male or female.
2. Had been diagnosed as having RA according to the revised 2010 ACR criteria for at least 3 months prior to Screening.
3. Patients had to have ≥4 swollen and ≥6 tender joints and at least two of the following: erythrocyte sedimentation rate (ESR) >28 mm/h or serum C reactive protein (CRP) concentration >1.0 mg/dl.
4. Patients had to have been receiving methotrexate (MTX) therapy for ≥3 months (stable dose of 10–15 mg/week for ≥4 weeks prior to screening).
5. patients have discontinued Other disease-modifying antirheumatic drugs (DMARDs) (including but not limited to chloroquine, hydroxychloroquine, gold preparation, penicillamine, salazosulfapyridine, azathioprine, cyclophosphamide, cyclosporin A, gold thiosaccharide, kinofin, etc.) for at least 4 weeks except for MTX before entry. If leflumide was administered before, it should be eluted with cholestyramine (8g, 3 times per day) for 11 days, and wait for 4 weeks before enrolling.
6. Before the drug administration, if the patient is taking glucocorticoids, the dose must be stabilized at ≤10 mg/d (equivalent to the dose of prednisone) for at least 4 weeks; if no glucocorticoid is used, no oral administration for at least 4 or no local injection for weeks or 12 weeks.
7. If you have used proprietary Chinese medicines or herbal medicines for the treatment of rheumatoid arthritis (RA) before the study, or received physical therapy, or received live (attenuated) virus/bacterial vaccine, or intravenous injection of immunoglobulin IgG, these treatments Need to stop for at least 4 weeks.
8. if patient have used other biological agents or participated in the clinical trials of other research drugs or marketed drugs before the study drug administration, the patient needs to stop using it for at least 3 months.
9. Female subjects who were not pregnant or nursing at Screening and who were not planning to become pregnant from Screening until 6 months after the last dose of investigational product (IP).
10. Were able to provide informed consent, which had to be obtained prior to any study related procedures.
11. Were able to understand and correctly complete the evaluation form
12. Were able to communicate with the Investigator, understand the implications of taking part in the study and were willing to follow the study requirements.

***Exclusion Criteria***

1. Had been treated previously with any biological agents to treat RA within 3 months before randomization including any tumor necrosis factor inhibitor.
2. were allergic to any auxiliary materials of the study drug or any other mouse or human protein, or have hypersensitivity to immunoglobulin products, have a known history of allergic diseases or are allergic.
3. weigh more than 100 kg
4. Rheumatoid arthritis joint function activity classification is Ⅳ or need to be wheelchair or bedridden.
5. Received interferon treatment within 4 weeks before the study drug administration.
6. Had a positive serological test for Anti-HIV, TP-Ab, hepatitis B (HBV) and hepatitis C (HCV)
7. Patients with known tuberculosis infection and high risk of tuberculosis infection should be excluded. Patients with latent tuberculosis infection (LTBI) who agree to receive preventive anti-tuberculosis drug treatment during the trial period can be selected for this trial, otherwise they should be excluded.

(1) Known tuberculosis infection (any of the following)

A. Active tuberculosis infection or clinical signs and symptoms of suspected tuberculosis (in the lung or outside the lung);

B. Active tuberculosis infection involving any organ system has occurred, or other organ systems have symptoms consistent with tuberculosis infection;

C. Evidence of previous infection found in radiology or other imaging examinations at the time of screening or within 3 months before (old tuberculosis evidence: lung and/or pleural fibrous scars; calcifications in the apex of the lung; hilar and/or mediastinum Lymph node disease; decrease in the volume of the upper lobe of the lung; cavities in the lung).

(2) High risk of tuberculosis infection (any of the following)

A. Known to have been in close contact with patients with active tuberculosis within 3 months before screening;

B. People with low immune function and any signs of latent tuberculosis infection;

C. Stay in a medical service environment or institution with a high risk of tuberculosis infection or tuberculosis infection

(3) Patients with latent tuberculosis infection (LTBI) who agree to be treated with preventive anti-tuberculosis drugs during the trial period can be selected for this trial, otherwise they should be excluded.

LTBI is defined as: there is no sign, symptom or abnormal physical examination suggesting tuberculosis infection, and there is no evidence of tuberculosis infection in the chest radiograph (or other imaging examination), but the gamma interferon test (IGRA) is positive or the results of the 2 IGRA tests are both unclear.

1. Opportunistic infections (herpes zoster, cytomegalovirus, mycoplasma, pneumocystis carinii, histoplasmosis, Candida, Aspergillus, mycobacteria other than Mycobacterium tuberculosis) occurred in the 6 months before screening).
2. A history of chronic infections (such as chronic hepatitis, chronic kidney infection, etc.), recent (within 6 months) serious or life-threatening infections (such as hepatitis, pneumonia, pyelonephritis, etc.), or any current symptoms or Signs suggest that there may be an infection (such as fever, cough, urgency, dysuria, abdominal pain, diarrhea, infected skin wounds, etc.).
3. Patients at high risk of infection (such as leg ulcers, indwelling catheters, persistent or recurrent chest infections, and long-term bedridden or sedentary wheelchair users).
4. Patients with a history of lymphoproliferative disease (including lymphoma or signs or symptoms of lymphoproliferative disease at any time); or splenomegaly.
5. Those who have had or are suffering from malignant tumors within 5 years before screening (except for basal cell carcinoma or squamous cell carcinoma of the skin, and carcinoma in situ of the cervix that have been fully treated and completely cured).
6. Patients who currently have or have had congestive heart failure disease or medical history.
7. Patients who currently have or have had a history of interstitial lung disease.
8. Patients who have or have multiple sclerosis or other central nervous system demyelinating diseases or medical history.
9. There is evidence that the patient has a history of severe, progressive, uncontrolled cardiovascular, cerebrovascular, kidney, liver, hematopoietic system, gastrointestinal tract, endocrine, lung, and neurological diseases, as well as other investigators judge that it inappropriate to join this trial.
10. The abnormal laboratory indicators that need to be excluded include: white blood cell (WBC) <3.0×109/L, neutrophil (ANC) <1.5×109/L, platelet count (PLT) <100×109/L, hemoglobin ( HGB) <85 g/L, alanine aminotransferase (ALT) or aspartate aminotransferase (AST)> 2 times the upper limit of normal (ULN), alkaline phosphatase (ALP)> 2 times ULN, Serum creatinine (Cr)>1.5 times ULN.
11. Have or have had other systemic immune diseases (such as systemic lupus erythematosus, etc.), or inflammatory joint diseases other than rheumatoid arthritis (such as gout, reactive arthritis, psoriatic arthritis, Seronegative spondyloarthropathy, Lyme disease, etc.). Patients with rheumatoid arthritis complicated or secondary to Sjogren’s syndrome are allowed to be included in the group if the investigator judges that it will not affect the drug evaluation.
12. Had a history of artificial joint infection and the artificial joint is still in the body.
13. Had received more than 3 arthroplasties.
14. Had undergone organ transplantation within 6 months before screening.
15. Women who are breastfeeding.
16. Had a long history of alcohol or drug abuse.
17. The patient has insufficient communication, understanding and cooperation skills, or has a low level of education, cannot understand and fill in the relevant forms correctly, has a history of not following the doctor’s prescription, or has other conditions that may interfere with the patient’s compliance (such as: mental illness, Frequent travel, lack of motivation to take the test, etc.).
18. The investigator believes that those with other diseases (such as clinically significant symptoms or abnormal laboratory indicators) are not suitable for participating in this clinical trial.

# Appendix S1. Change of Efficacy Components at Week 30 from Baseline (FAS)

|  |  |  |
| --- | --- | --- |
| Outcome (mean (SD)) | GB242 | INF |
| Tender Joint Count (68 joints) | -8.4 (7.29) | -8.0 (7.06) |
| Swollen Joint Count (66 joints) | -6.7 (5.30) | -6.8 (5.55) |
| Patient pain VAS (mm) | -2.901 (2.4538) | -2.782 (2.5423) |
| VAS from Patient | -2.979 (2.4516) | -2.773 (2.4882) |
| VAS from Physician | -3.347 (2.3106) | -3.172 (2.3690) |
| HAQ-DI | -0.727 (0.7356) | -0.645 (0.7408) |
| CRP | -1.5278 (3.9333) | -1.5236 (3.3493) |
| ESR | -16.972 (24.4759) | -15.926 (24.6992) |

# Appendix S2. ACR20 Response Rate by ADA subgroups at Week 30 (SS)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| 30-week  ADA Result | Treatment | Responders  n (%) | Difference Rate | 95% CI | *P* value |
| Positive | GB242 (N=196) | 115 (58.67%) | 4.42% | (-5.65%, 14.41%) |  |
|  | INF (N=188) | 102 (54.26%) |  |  |  |
|  |  |  |  |  | 0.7408 |
| Negative | GB242 (N=79) | 59 (74.68%) | 8.80% | (-5.42%, 22.79%) |  |
|  | INF (N=85) | 56 (65.88%) |  |  |  |

ADA, anti-drug antibody; CI, confidence interval

The p value is for the interaction term treatment by ADA status from an ANCOVA model, where ACR20 response is the response variable, and treatment, ADA status, treatment by ADA status, and baseline CRP are the independent variables and covariates.

# Appendix S3. ADA and NAb incidence by study visit (safety population)

图形用户界面, 图表

描述已自动生成