Multicenter, dubbelblind, gerandomiseerd, parallel, placebo-gecontroleerd onderzoek om de veiligheid, werkzaamheid en farmacokinetiek tussen 2 orale dosis, 25 mg PG-760564 twee maal daags en 100 mg PG-760564 twee maal daags bij volwassen patienten met reumatoide arthritis die met methotrexaat worden behandeld te vergelijken.

Gepubliceerd: 09-03-2007 Laatst bijgewerkt: 20-05-2024

The objectives of this study are as follows:Primary Efficacy Objective:• To assess the effect of PG-760564 on the proportion of patients meeting the American College of Rheumatology 20 response criteria (ACR 20) at 12 weeks;11Secondary Efficacy...

Ethische beoordeling	Goedgekeurd WMO
Status	Werving nog niet gestart
Type aandoening	Overige aandoening
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON30408

Bron
ToetsingOnline

Verkorte titel
RACER

Aandoening

- Overige aandoening

Synoniemen aandoening
reumatoide atritis

Aandoening

gewrichtsaandoeningen

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor: Procter & Gamble
Overige ondersteuning: farmaceutische industrie

Onderzoeksproduct en/of interventie

Trefwoord: reumatoide artritis

Uitkomstmaten

Primaire uitkomstmaten

The primary efficacy endpoint will be the proportion of patients meeting the

ACR 20 response criteria at 12 weeks.

Secundaire uitkomstmaten

The secondary efficacy endpoints will include:

• ACR 50 and ACR 70 responses at 12 weeks (Appendix 2);

14• Change from baseline in DAS 28 scores at 12 weeks (Appendix 3);

• Change from baseline at 12 weeks in:

o Tender joint count

o Swollen joint count

o Physician*s global assessment

o Patient*s global assessment

o Patient*s assessment of pain

15o HAQ score (Appendix 4)

o Acute phase reactants (ESR and CRP)

o TNF-α, IL-1, and IL-6

o Duration of morning stiffness

o RF titer;

• Time to ACR 20.

Toelichting onderzoek

Achtergrond van het onderzoek

Rheumatoid arthritis (RA) is a chronic inflammatory arthritis with a worldwide prevalence of 0.5% to 1%.1,2 Rheumatoid arthritis causes substantial morbidity: approximately 50% of patients are unable to work within 10 years of disease onset.3 Rheumatoid arthritis is a systemic inflammatory disorder and RA patients may also develop extra-articular manifestations in different organ systems.
The importance of pro-inflammatory cytokines in the pathogenesis of RA has been shown in clinical trials of biologic agents that block tumor necrosis factor alpha (TNF-α) and interleukin-1 (IL-1) activity.4,,,567 Although anti-TNF-α therapies have been reported to increase the risk of infection, they have shown significant efficacy in RA and have set a new standard in the management of RA. There are 3 TNF-α antagonists currently approved for RA in the US.
PG-760564 [2-(4-Fluorophenyl)-6,7-dihydro-3-(2-phenoxy-4-pyrimidinyl)-1H,5H-pyrazolo(1,2-a)pyrazol-1-one] is a cytokine synthesis/release inhibitor with p-38 mitogen-activated protein (MAP) kinase inhibition activity that is being investigated as a treatment for RA. PG-760564 has been shown to inhibit p-38 MAP kinase directly and has been shown to inhibit the release of TNF-α and IL-1 from a number of cell types. Oral administration of PG-760564 was effective in both the prevention and treatment components of the rat collagen-induced RA model. Histological examination of the joints showed statistically significant inhibition of pannus, inflammation, cartilage damage, and bone resorption at 2.5 mg/kg in the treatment model.

Doel van het onderzoek

The objectives of this study are as follows:
Primary Efficacy Objective:
• To assess the effect of PG-760564 on the proportion of patients meeting the American College of Rheumatology 20 response criteria (ACR 20) at 12 weeks;11
Secondary Efficacy Objectives:
• To assess the effect of PG-760564 on the proportion of patients meeting the ACR 50 and ACR 70 responses at 12 weeks;
• To assess the effect of PG-760564 on the change from baseline in 28-joint Disease Activity Score (DAS 28) at 12 weeks;
• To assess the effect of PG-760564 on the change from baseline at 12 weeks in the following parameters:
o Tender joint count
o Swollen joint count
o Physician*s global assessment
o Patient*s global assessment
o Patient*s assessment of pain
o Health Assessment Questionnaire (HAQ) score
o Acute phase reactants [erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)]
o TNF-α, IL-1, and IL-6
o Duration of morning stiffness
o Rheumatoid factor (RF) titer;
• To assess the effect of PG-760564 on time to ACR 20.
Safety Objectives:
• To assess the safety and tolerability of PG-760564 in patients with RA.

Onderzoeksopzet

This will be a 12-week, double-blind, randomized, placebo-controlled, parallel group, multicenter study to evaluate the safety, efficacy, and PK of oral administration of PG-760564 in adult patients with active RA receiving treatment with MTX. The study will be conducted in North America and Europe at approximately 50 to 60 sites. Approximately 270 patients will be randomized, of which 189 are expected to complete the study. If the dropout rate is >30%, up to an additional 30 patients total could be randomized, to ensure 63 completed patients per treatment group. Two oral doses of PG-760564 will be evaluated: 25 mg BID and 100 mg BID.
Due to concomitant treatment with MTX, all patients will be required to take either 5-7 mg/week of folic acid or 2.5 mg/week of folinic acid. Higher doses will not be allowed.

The study will consist of a screening visit followed by a washout period for all disease-modifying antirheumatic drugs (DMARDs) and anti-cytokine therapies except MTX (see Appendix 5). The washout period will be 4 weeks for

sulfasalazine, hydroxychloroquine, azathioprine, D-penicillamine, etanercept, and anakinra, 8 weeks for gold, infliximab, and adalimumab, and 12 weeks for abatacept.
After the washout period, the patients will be randomized if they fulfill all inclusion and exclusion criteria. Patients determined to be eligible will be randomized to receive either 25 mg BID or 100 mg BID of oral PG-760564, or placebo for 12 weeks. There will be 6 treatment visits (Weeks 1, 2, 4, 6, 8, and 12) and a follow-up visit 4 weeks after the last treatment visit (Week 16). Patients will not initiate new therapies until after the 4-week follow-up is completed. Liver function tests will be evaluated at every visit.
If dose-limiting toxicity is seen in patients receiving the 100 mg BID dose (based on recommendation from the IDMC), the 100 mg BID dose will be discontinued and patients in this dose group will have their dose decreased to 50 mg BID. In that case, new patients randomized to the 100 mg BID dose will be given a 50 mg BID dose instead.
The primary efficacy endpoint will be the proportion of patients meeting the ACR 20 response criteria after 12 weeks of treatment.

Onderzoeksproduct en/of interventie

use of PG-760564 en methotrexaat

Inschatting van belasting en risico

-

Contactpersonen

Publiek

Procter & Gamble

Watermanweg 100
3067GG Rotterdam
Nederland

Wetenschappelijk

Procter & Gamble

Watermanweg 100
3067GG Rotterdam
Nederland

Locaties

Landen waar het onderzoek wordt uitgevoerd

Netherlands

Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

-

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

-

Onderzoeksopzet

Opzet

Fase onderzoek:	2
Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo
Doel:	Behandeling / therapie

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-11-2006
Aantal proefpersonen:	30
Type:	Verwachte startdatum

In onderzoek gebruikte producten en hulpmiddelen

Soort:	Geneesmiddel
Merknaam:	metotrexaat
Generieke naam:	metotrexaat
Registratie:	Geregistreerd voor de te bestuderen indicatie/dosering
Soort:	Geneesmiddel
Merknaam:	nog niet bekend
Generieke naam:	PG-760564

Ethische beoordeling

Goedgekeurd WMO

Datum:	09-03-2007
Soort:	Eerste indiening
Toetsingscommissie:	METC Leids Universitair Medisch Centrum (Leiden)

Goedgekeurd WMO

Datum:	14-06-2007
Soort:	Amendement
Toetsingscommissie:	METC Leids Universitair Medisch Centrum (Leiden)

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
EudraCT	EUCTR2006-002216-10-NL
Ander register	geen nummer
CCMO	NL14158.058.06