Clinical responses and patient-reported outcomes to NNC0109-0012 (anti-IL-20 mAb) in rheumatoid arthritis (RA) patients following 12-weeks dosing and 13-weeks follow-up Results from a phase 2a trial

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Disclosures

Ladislav Šenolt
Abbott, Amgen, AstraZeneca, Biotech, Bristol-Myers Squibb, Celgene Corporation, Merck Sharp & Dohme, Novo Nordisk, PAREXEL, Pfizer, UCB

Eva Dokoupilová
Abbott, Amgen, AstraZeneca, Biotech, Eli Lilly, Medimmune, Merck Sharp & Dohme, Novartis, Novo Nordisk, PAREXEL, Pfizer, Procter and Gamble, Sanofi, UCB

Marie Göthberg
Xavier Valencia
Employees of Novo Nordisk A/S

This trial (ID no. NN8226-3875; NCT01282255) was sponsored by Novo Nordisk A/S

Involvement of IL-20 (α) and IL-20R (β) in RA pathogenesis


Potential benefit of anti-IL-20 (α) in RA


Phase 2a clinical trial
Anti-IL-20 mAb (NNC0109-0012, human IgG4)

- Multi-centre, randomised, placebo-controlled, double-blind, parallel group trial, with 12-weeks of treatment and 13-weeks follow-up in RA patients with methotrexate-inadequate responses (MTX-IR)
- Primary endpoint:
  - Change in disease activity (DAS28-CRP) following 12 weekly s.c. doses of 3 mg/kg of NNC0109-0012 (anti-IL-20 mAb) compared with placebo
- Other endpoints:
  - ACR20/50/70
  - Physical function and disability (HAQ-DI), pain (VAS) and patient global assessment of disease activity (PGA)
  - Safety


Bone erosion

Chemokine release and cartilage destruction

Cytokine release

Chemoattraction

Cytokine and chemokine release

Chemokine release and cartilage destruction

Cytokine release

Bone erosion

Chemokine release and cartilage destruction

Cytokine and chemokine release

Chemokine release and cartilage destruction

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Cytokine release
Anti-IL-20 mAb – phase 2a trial

Trial design

Inclusion
RA diagnosis ≥3 months
DAS28-CRP ≥4.5
ESR ≥3
MTX*

MTX = placebo (n=22)

MTX = anti-IL-20 mAb** (n=45)

Assessments: -2 to -1 0 6 12 16 20 25 weeks

Primary endpoint

Weekly dosing Off-drug follow-up

Demographics and baseline characteristics

Table:

<table>
<thead>
<tr>
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<th>Placebo (n=22)</th>
<th>3 mg/kg NNC0109-0012 (n=45)</th>
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<td>Age (years) (min; max)</td>
<td>52.1 (24.6; 69.3)</td>
<td>58.9 (26.2; 76.9)</td>
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<td>Sex, %</td>
<td>72.7/27.3</td>
<td>77.4/22.6</td>
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<td>ESR (mm/hr)*</td>
<td>24.5 (24.4; 36.1)</td>
<td>28.0 (19.8; 36.6)</td>
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<td>RA (years)</td>
<td>6.1 (4.9; 14.2)</td>
<td>4.6 (3.0; 17.3)</td>
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<td>Duration of current MTX (years)*</td>
<td>1.8 (0.1; 7.9)</td>
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<td>Mean MTX dose (mg/week)*</td>
<td>18.8 (9.4; 29.8)</td>
<td>19.2 (7.4; 25.8)</td>
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<td>RF positive, %</td>
<td>63.6</td>
<td>71.1</td>
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<td>ACPA positive, %</td>
<td>68.2</td>
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* = Mean (min; max)

Estimated mean difference at 12 weeks = -0.88 [-1.61; -0.14], p=0.02. Data represent mean +/- SEM

Anti-IL-20 mAb significantly reduces DAS28-CRP from week 1

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*All patients on MTX treatment for at least 12 weeks; stable dose (≥7.5 mg or ≤25 mg/week) for at least 4 weeks prior to screening

**Anti-IL-20 mAb: NNC0109-0012

MTX*
Estimated mean difference at 12 weeks = 1.66 [-2.53; -0.79], p=0.0004. No difference in DAS28-CRP changes between anti-IL-20- and placebo-treated seronegative patients. Data represent mean +/- SEM.

Anti-IL-20 mAb significantly reduces DAS28-CRP from week 1: Seropositive patients

Percent ACR20/50/70 responders over time

Improvements in patient-reported outcomes Seropositive patients

Anti-IL-20 mAb

Adverse events and withdrawals

<table>
<thead>
<tr>
<th>Events (n) in 31 subjects</th>
<th>Placebo (n=14)</th>
<th>NCC0109-0012 (n=17)</th>
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<tbody>
<tr>
<td>AEs</td>
<td>10</td>
<td>45.5, 12</td>
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<tr>
<td>AE withdrawals</td>
<td>1</td>
<td>4.5</td>
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<tr>
<td>Severe AEs</td>
<td>1</td>
<td>4.5</td>
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<tr>
<td>Infections</td>
<td>1</td>
<td>4.5</td>
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<tr>
<td>Injection-site reactions</td>
<td>0</td>
<td>0.0</td>
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<tr>
<td>Total number of withdrawals</td>
<td>2</td>
<td>9.1</td>
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- There were no serious or life-threatening AEs
- All injection-site reactions were mild and transient
- None of the infections were severe and the infections reported were:
  - upper respiratory tract infection, urinary tract infection, bronchitis, herpes simplex, herpes zoster (placebo), cystitis (placebo)
- Withdrawals:
  - Placebo: CDA lymphopenia (1); Withdrawal of consent (1)
  - NCC0109-0012: Withdrawal of consent (1); Violation of exclusion criteria (1)

Conclusion – NCC0109-0012 (anti-IL-20 mAb)
Phase 2a trial in RA MTX-IR patients

- Anti-IL-20 mAb effectively reduced disease activity
- Significant reduction in DAS28-CRP occurred as early as week 1 and further improved to week 12
- In seropositive patients, disease activity and patient-reported outcome improvements were more pronounced and sustained in the follow-up period
- Anti-IL-20 mAb 3mg/kg, s.c., once weekly for 12 weeks was safe and well tolerated
Thank you to investigators in the phase 2a trial (NN8226-3875)

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<thead>
<tr>
<th>Czech Republic</th>
<th>Poland</th>
<th>Romania</th>
<th>Spain</th>
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<tbody>
<tr>
<td>Dr Eva Dokoupilova</td>
<td>Dr Piotr Lesczyński</td>
<td>Dr Simona Rednic</td>
<td>Dr Federic Navarro</td>
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<tr>
<td>Dr Ladislav Šencolt, PI</td>
<td>Dr Maria Głowacka</td>
<td>Dr Bogdan Jantos</td>
<td>Dr José Luis Sueiro</td>
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<td>Dr Petr Víták</td>
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<td>Dr Zuzana Stęfnowa</td>
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