German Rheumatism Research Centre, Epidemiology Unit

Patients & Methods

The German biologics register RABBIT continuously includes RA patients with a new DMARD start after at least one csDMARD failure. Among patients enrolled between 01/2009 and 10/2017 (N=9,455), patients with BMI ≥ 25 and 6 months of follow-up were selected (n=9,245). Effectiveness was measured as the improvement of DAS28-CRP and its components during the first 6 months of treatment.

(i) The obesity effect was assessed by linear regression, adjusting for age, baseline value, disease duration, prior bDMARD failure, glucocorticoid dosage, number of comorbidities, erosions, smoking habits. Missing values were addressed by multiple imputations. CRP levels were log-transformed.

(ii) To assess whether patients received norm dosage, a tolerance interval was defined for TOC and infliximab (INF) (≤ 15% underdosage, ≤ 15% overdosage, ≤ 95% of treatments were dosed as recommended, at least 90% for any particular therapy, also among obese patients (exception: only 78% norm dosage for INF).

Dosage

• 95% of treatments were dosed as recommended, at least ~90% for any particular therapy, also among obese patients (exception: only 78% norm dosage for INF).

TOC underdosage had a significant negative effect on SJC (15% (TOC) ≤ 15%) vs. 0%) and was less likely to ever smoke than men (47% vs. 75%).

Conclusions

Obesity negatively influences the effectiveness in particular of those biologics that target single cytokines, i.e., tumor necrosis factor inhibitors and tocilizumab, while therapies targeting specific immune cell populations are only marginally affected. In tocilizumab, the effect of obesity might be attenuated by a better weight adjustment of its dosage.

Background & Objectives

Obesity in patients with rheumatoid arthritis (RA) affects effectiveness of tumor necrosis factor inhibitors (TNFi), but not abatacept and rituximab. For tocilizumab (TOC), the obesity on drug effectiveness is mediated by gender to some extent. Obesity negatively influences the improvement of DAS28-CRP and its components during the first 6 months of treatment.

Effect of obesity (see figure)

• Among women receiving TNFi, a significant negative effect of obesity on the improvement of CRP levels after 6 months of treatment was observed. The effect in men differed significantly (see circle), possibly influenced by gender specific body fat distributions.

• Among women under TNFi or csDMARDs, obesity significantly affected DAS28-CRP improvement. Such an effect was also observed for TOC, unlike in previous studies.

Results

Patient characteristics (see table)

• Obese RA patients were comparable to non-obese patients in age (both mean 58 years) and gender (women: 75% vs. 74%) at baseline. They were less frequently seropositive (66% vs. 73%), less likely to have joint erosions (40% vs. 52%), but more likely to have ≥ 3 comorbidities (45% vs. 30%).

• Women had worse physical abilities than men (65% vs. 72% of full physical function), particularly among obese patients (58% vs. 68%). They were more likely to have a DAS28-CRP ≥ 5.1 (50% vs. 41%), but had smaller overall CRP values (mean 12 vs. 17 mg/l) and were less likely to ever smoke than men (47% vs. 75%).


Funding: RABBIT is supported by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celltrion, Lilly, MSD Sharp & Dohme, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis, UCB and Hexal AG.

Table: Baseline characteristics of patients in BMI/gender groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal weight (18.5 ≤ BMI &lt; 25)</th>
<th>Overweight (25 ≤ BMI &lt; 30)</th>
<th>Obesity (BMI ≥ 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>n=2716 (80.2%)</td>
<td>n=670 (19.8%)</td>
<td>n=625 (24.8%)</td>
</tr>
<tr>
<td>Age in years</td>
<td>55.6 ± 13.8</td>
<td>57.7 ± 13.5</td>
<td>57.7 ± 10.6</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>4.7 ± 1.1</td>
<td>4.7 ± 1.1</td>
<td>4.4 ± 1.1</td>
</tr>
<tr>
<td>SJC</td>
<td>5.5 ± 2.1</td>
<td>5.3 ± 2.1</td>
<td>5.1 ± 2.1</td>
</tr>
<tr>
<td>Tender joints count (TJC)</td>
<td>7.1 ± 6.2</td>
<td>7.6 ± 6.4</td>
<td>7.4 ± 6.1</td>
</tr>
<tr>
<td>Joint erosions</td>
<td>1552 (57.1%)</td>
<td>1813 (59.3%)</td>
<td>1170 (48.5%)</td>
</tr>
<tr>
<td>% of full physical function</td>
<td>69.2 ± 22</td>
<td>64.2 ± 22</td>
<td>58.2 ± 22</td>
</tr>
</tbody>
</table>

Conclusion:

The German biologics register RABBIT continuously includes RA patients with a new DMARD start after at least one csDMARD failure. Among patients enrolled between 01/2009 and 10/2017 (N=9,455), patients with BMI ≥ 25 and 6 months of follow-up were selected (n=9,245). Effectiveness was measured as the improvement of DAS28-CRP and its components during the first 6 months of treatment.

(i) The obesity effect was assessed by linear regression, adjusting for age, baseline value, disease duration, prior bDMARD failure, glucocorticoid dosage, number of comorbidities, erosions, smoking habits. Missing values were addressed by multiple imputations. CRP levels were log-transformed.

(ii) To assess whether patients received norm dosage, a tolerance interval was defined for TOC and infliximab (INF) (≤ 15% underdosage, ≤ 15% overdosage, ≤ 95% of treatments were dosed as recommended, at least 90% for any particular therapy, also among obese patients (exception: only 78% norm dosage for INF).

Dosage

• 95% of treatments were dosed as recommended, at least ~90% for any particular therapy, also among obese patients (exception: only 78% norm dosage for INF).

TOC underdosage had a significant negative effect on SJC improvement. TOC patients tended to show weight gains, which correlated negatively with change in dosis/kg weight.

Effect of obesity (see figure)

• Among women receiving TNFi, a significant negative effect of obesity on the improvement of CRP levels after 6 months of treatment was observed. The effect in men differed significantly (see circle), possibly influenced by gender specific body fat distributions.

• Among women under TNFi or csDMARDs, obesity significantly affected DAS28-CRP improvement. Such an effect was also observed for TOC, unlike in past studies.


Funding: RABBIT is supported by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celltrion, Lilly, MSD Sharp & Dohme, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis, UCB and Hexal AG.

German Rheumatism Research Centre, Epidemiology Unit

EULAR 2018 SAT0702

Influence of obesity and gender on drug effectiveness in rheumatoid arthritis depends on the outcome considered


1German Rheumatism Research Center Berlin, 2Helios Hospital Vogelsang-Gommern, Vogelsang-Gommern, 3Rheumatologist, Naunhof, 4Rheumatologist, Berlin, 5Charité – Universitätsmedizin Berlin, Berlin, all Germany

Table: Baseline characteristics of patients in BMI/gender  groups

DAS28-CRP

Age in years

% of full physical function

Swollen joints count (SJC)

Sum of comorbidities

Disease duration in years

Joint erosions

Seropositivity (RF or anti-CCP)

1334 (49.1%) 475 (70.9%) 988 (44.1%) 844 (76.7%) 881 (46.5%) 469 (75%)

2119.8 (78%) 504.9 (75.4%) 1620.7 (72.4%) 8183 (74.4%) 1244.6 (65.7%) 429.8 (68.8%)