Results: No differences were seen on comparing the baseline parameters of the 3 groups. In comparison to the baseline, there was significant increase in the BMD in the 3 groups, Denosumab /Zol/Aln at both spine and hip (P = 0.02) at 5-, 3- and 5-years of treatment respectively. In the denosumab group, at 5-years of therapy, there was significant decrease in falls risk score (-1.4, 95% CI = -2.8 to -0.7; P = 0.01), significant improvements in the grip strength (+4.2Kg, P = 0.01), SPFF score (1.2 points; 95% CI = -0.2 to 2.2; P = 0.2), TUG (1.7 seconds; 95% CI = -2.2 to 0.1; P = 0.3) and gait speed (0.1 m/s; 95% CI = 0.03-0.2; P = 0.1). Zol and Aln improved significantly SPFF score (0.9 and 0.8 points; P = 0.4), TUG (1.4 and 13 seconds; P = 0.5) and gait speed (0.2 and 0.3 m/s; P = 0.2) respectively, however, there was no significant change in the falls risk (p = 0.06 and 0.7 respectively).

1-year after stopping Denosumab, there was significant worsening of the falls risk score, grip strength, SPFF score, TUG and gait speed (P = 0.1).

There was no difference in all the measures 1-year after stopping Zol and Aln.

There was no relation to the increase in BMD gained.

Conclusion: Denosumab displayed positive impact and significant improvements in physical performance, grip strength and gait speed. Also, Denosumab, enhanced multidirectional agility as depicted by TUG. Collectively, this would explain the reduction of falls risk which got worse on stopping the medication.

Osteoporosis and sarcopenia share similar risk factors, highlighting muscle-bone interactions, which may result in debilitating consequences, such as falls and fractures. RANK/RANKL/OPG pathway, a key regulator of bone homeostasis, which may result in debilitating consequences, such as falls and fractures. RANK/RANKL/OPG pathway, a key regulator of bone homeostasis, which may result in debilitating consequences, such as falls and fractures. RANK/RANKL/OPG pathway, a key regulator of bone homeostasis, which may result in debilitating consequences, such as falls and fractures.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6521

Clinical symposium axSpA: Treat-to-target in axSpA: myth or reality?

A. Ruyssen-Witrand1,2, V. Rousseau1,2, A. Sommet1,2,3, P. Goupille4, Y. Degboe1,3,5, A. Constantin1,3,5. 10.1136/annrheumdis-2020-eular.3222

Disclosure of Interests: Adeline Ruyssen-Witrand/Grant/research support from: Abbvie, Pfizer, Consultant of: Abbvie, BMS, Lilly, Mylan, Novartis, Pfizer, Sandoz, Sanofi-Genezyme, Vanessa Rousseau: None declared, Agnès Sommet: None declared, Philippe Goupille: Grant/research support from Abbvie, Biogen, BMS, Celgene, Chugui, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Consultant of: Abbvie, Amgen, Biogen, BMS, Chugui, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Speakers bureau: Abbvie, Amgen, Biogen, BMS, Celgene, Chugui, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Yannick Degboe: None declared, Arnaud Constantin: None declared

DOIs: 10.1136/annrheumdis-2020-eular.6521

Background: Response criteria and disease activity status used to assess treat-ment efficacy in axial spondyloarthritis (axSpA) are: the ASAS response criteria (ASAS20; 40; 5/6 and partial remission - PR), BASDAI50 and ASAS-based criteria (clinically important/major improvement –CII/M; low disease activity/ inactive disease –LDA/ID). These outcomes are variably used in RCTs testing biological (b) and targeted-synthetic (ts)DMARDs. However, it remains unknown which are the most discriminative.

Objectives: To compare the ability of different criteria to discriminate between the response to active treatment and placebo in axSpA. Patients with longer symptom duration, higher baseline ASAS- and NSAIDs scores were less often in DF remission, while imaging and biological data did not predict DF remission.

Disclosure of Interests: Adeline Ruyssen-Witrand/Grant/research support from: Abbvie, Pfizer, Consultant of: Abbvie, BMS, Lilly, Mylan, Novartis, Pfizer, Sandoz, Sanofi-Genezyme, Vanessa Rousseau: None declared, Agnès Sommet: None declared, Philippe Goupille: Grant/research support from Abbvie, Biogen, BMS, Celgene, Chugui, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Consultant of: Abbvie, Amgen, Biogen, BMS, Celgene, Chugui, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Speakers bureau: Abbvie, Amgen, Biogen, BMS, Celgene, Chugui, Lilly, Janssen, Medac, MSD France, Nordic Pharma, Novartis, Pfizer, Sanofi and UCB, Yannick Degboe: None declared, Arnaud Constantin: None declared

DOIs: 10.1136/annrheumdis-2020-eular.6521

Disclosure of Interests:

- Adeline Ruyssen-Witrand: None declared
- S. Ramiro: 1, S. Sepriano: 1, B. R. Landewe: 2, D. Van der Heijde: 2, V. Navarro-Compán: 1, Leiden University Medical Center, Leiden, Netherlands;
- Amsterdam Rheumatology Center, Amsterdam, Netherlands;
- University Hospital La Paz, Madrid, Spain

Background: Response criteria and disease activity status used to assess treat-ment efficacy in axial spondyloarthritis (axSpA) are: the ASAS response criteria (ASAS20; 40; 5/6 and partial remission - PR), BASDAI50 and ASAS-based criteria (clinically important/major improvement –CII/M; low disease activity/ inactive disease –LDA/ID). These outcomes are variably used in RCTs testing biological (b) and targeted-synthetic (ts)DMARDs. However, it remains unknown which are the most discriminative.

Objectives: To compare the ability of different criteria to discriminate between the response to active treatment and placebo in axSpA.

Methods: A systematic literature review was performed in Medline and Embase to identify RCTs of b- and tsDMARDs. Placebo-controlled RCTs meeting the primary endpoint were included provided they reported ≥2 response/status cri-teria. Outcomes were collected at the timepoint of primary endpoint assessment (PEA). Risk of bias was evaluated by The Cochrane tool. Meta-analysis with fixed effects model was performed if too few RCTs were available, otherwise random effects meta-analysis was performed. The potential role of outcome reporting bias was assessed.

Results: 29 RCTs fulfilled inclusion criteria. In total, 23/29 RCTs with PEA at 12, 14 or 16 weeks, all at a low risk of bias, could be considered for meta-anal-yis. Other 6 RCTs had later (e.g. 24 weeks) or earlier (e.g. 6 weeks) PEA. Out of the 23 RCTs, only 16 reported at least a minimum set of ASAS20,-40,-PR and BASDAI50 (Table 1): discriminative performances for ASAS40 were >ASAS20>BASDAI50>ASAS-PR. In 11/16 RCTs ASAS5/6 was also included (Table 2): this criterion showed the best performance among ASAS-based response criteria. 8/16 RCTs additionally included some ASAS-based criteria (Table 3). ASAS-CII and -MI showed a much higher discrimination com-pared to the ASAS-based criteria. In only 3 trials could all criteria be compared, with the ASAS-CII and -MI appearing as the most discriminative criteria, fol-lowed by ASAS 5/6 (Table 4).
Conclusion: Response criteria are more discriminative than status criteria. ASAS-DAS-CII and ASDAS-MI showed the best discrimination between treatment/ placebo arms. Using the ASDAS-CII as primary outcome in future RCTs can reduce the number of patients needed to be included while keeping the same statistical power.

Table. Discriminative performances of response and status criteria in RCTs of biological and targeted synthetic DMARDs in axial spondyloarthritis

<table>
<thead>
<tr>
<th>Minimum set of outcomes</th>
<th>Set 1:</th>
<th>Set 2:</th>
<th>Set 3:</th>
<th>Set 4:</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS20</td>
<td>339</td>
<td>334</td>
<td>ASDAS-CII 309</td>
<td>ASDAS-CII 124</td>
</tr>
<tr>
<td>ASAS20, 40</td>
<td>236</td>
<td>216</td>
<td>ASDAS-MI 253</td>
<td>ASDAS-MI 65</td>
</tr>
<tr>
<td>ASAS20, 40, PR</td>
<td>207</td>
<td>186</td>
<td>ASDAS-LDA 196</td>
<td>ASDAS-LDA 48</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 54</td>
<td>178</td>
<td>154</td>
<td>ASDAS-LDA 127</td>
<td>ASDAS-LDA 27</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 58</td>
<td>163</td>
<td>139</td>
<td>ASDAS-LDA 117</td>
<td>ASDAS-LDA 39</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 64</td>
<td>148</td>
<td>124</td>
<td>ASDAS-LDA 117</td>
<td>ASDAS-LDA 34</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 68</td>
<td>133</td>
<td>109</td>
<td>ASDAS-LDA 117</td>
<td>ASDAS-LDA 30</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 72</td>
<td>118</td>
<td>94</td>
<td>ASDAS-LDA 117</td>
<td>ASDAS-LDA 26</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 76</td>
<td>103</td>
<td>79</td>
<td>ASDAS-LDA 117</td>
<td>ASDAS-LDA 22</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 80</td>
<td>88</td>
<td>64</td>
<td>ASDAS-LDA 117</td>
<td>ASDAS-LDA 21</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 84</td>
<td>73</td>
<td>49</td>
<td>ASDAS-LDA 117</td>
<td>ASDAS-LDA 19</td>
</tr>
<tr>
<td>ASAS20, 40, PR, 88</td>
<td>58</td>
<td>34</td>
<td>ASDAS-LDA 117</td>
<td>ASDAS-LDA 17</td>
</tr>
<tr>
<td>Total=16*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Legend: *total of 16 RCTs analysed, with different sets of RCTs within the 16 analysed based on the availability of response criteria. (x): chi-square; RCT= randomized controlled trials; ASAS=Daxial Spondyloarthritis Disease Activity Index; ASDAS = Assessment in SpondyloArthritis International Society; PR= partial remission; CI= clinically important improvement; MI= major improvement; LDA= low disease activity; ID= inactive disease

Disclosurer of Interests: Augusta Ortolan: None declared, Sofia Ramiro: None declared, Alexandre Sepriano: None declared, Robert B.M. Landewé Consultant of: AbbVie; AstraZeneca; Bristol-Myers Squibb; Eli Lilly & Co.; Galapagos NV; Novartis; Pfizer; UCB Pharma; Desirée van der Heijde Consultant of: AbbVie; Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cytoke, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV, Victoria Navarro-Compán Consultant of: Abbvie, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, MSD, Lilly, Novartis, Pfizer, UCB

DOI: 10.1136/annrheumdis-2020-eular.1106

New perspectives on therapeutic immune tolerance.

OP0316 EMERGING BEST-IN-CLASS IL-2 VARIANT HIGHLIGHTS TREG-DIRECTED THERAPY FOR AUTOIMMUNE DISEASE

Y.T. Hsieh1, C. Hubeau1, V. Massa1, W. LI1, S. Frei1, B. Capraro1, A. Umana1, A. Aherrera1, Y. LI1, J. Xu1, L. Rui1.

Background: Impairment or deficiency of regulatory T cells (Treg) is associated with chronic inflammation and autoimmune diseases. Interleukin 2 (IL-2) is dominant effector CD4, CD8 and NK cells. The ratio of Treg/Teff cells achieved as high as 0.4 in mice and 1.2 in monkeys. Both CD4+ and CD8+ Tregs were expanded with preferential increases in memory over naïve subsets. A substantial increase in Treg-suppressive capacity over T effector cells was corroborated by enhanced expression of functional and inhibitory markers, including CD25, Foxp3, PD-1, CTLA-4, Tim3 and ICOS. In DTH and TDAR models, CUG252 strongly inhibited antigen-driven inflammation, B cell maturation, and antibody production. The sustained PK/PD profile supports monthly dosing or better in human body temperature, clinical pathology or signs of vascular leakage were observed. Moreover, CUG252 demonstrated superior manufacturability.

Conclusion: CUG252 demonstrates an emerging best-in-class profile among IL-2 variants. It displayed exquisite Treg-selectivity while retaining potency comparable to wild-type IL-2. It showed strong anti-inflammatory and anti-antibody production efficacy with significantly improved therapeutic index and manufacturability. Its favorable drug-like property and robust preclinical efficacy warrant further evaluation in patients with a variety of inflammation and autoimmune diseases.

References:


Pathological calcification in rheumatic diseases