Adalimumab is effective and well tolerated in treating patients with ankylosing spondylitis who have advanced spinal fusion

Martin Rudwaleit¹, Ignazio Olivieri², Kyriaki A. Boki³, Eduard N. Griep⁴, Pentti Järvinen⁵, Robert L. Wong⁶, Martina Kron⁷, Sonja Kary⁷ and Hartmut Kupper⁷

Introduction

AS is a chronic and progressive rheumatological disease of the spine and extra-axial structures, affecting 0.55% of the European population [1, 2]. The spinal inflammation is primarily characterized by sacroilitis and also further involves axial joints and vertebrae with the formation of intervertebral syndesmophytes or ossceous fusion. In a radiographic grading system, five stages of spinal structural damage have been proposed (Table 1) [3]. Stages I–III are defined by minor to moderate radiographic evidence of structural damage involving <50% of the spine (i.e. 12 vertebrae or less) in two spinal segments or less [3]. Stages IV and V represent advanced AS, with Stage IV being characterized by the involvement of 50% to <80% of the spine in more than two spinal segments (i.e. 13–19 vertebrae) and Stage V being characterized by involvement of ≥80% of the spine (i.e. 20 vertebrae or more) [3]. Stage V disease encompasses patients with widespread spinal fusion and total spinal ankylosis (TSA), which radiographically appears as bamboo spine [3]. Patients with AS are substantially impaired by back pain, primarily at night, and spinal immobility, depending on the degree of structural damage of the spine. It is important to note, however, that degree of spinal involvement does not necessarily correlate with disease activity.

NSAIDs, along with education and physiotherapy, are the recommended treatment for AS, whereas DMARDs have no effect on the spinal signs and symptoms of AS [4]. The therapeutic options for patients with AS who have had unsatisfactory responses to standard treatment have been notably improved by the advent of TNF antagonists, including the TNF-receptor construct etanercept and the monoclonal antibodies infliximab and adalimumab [5–15].

Knowledge regarding the efficacy of anti-TNF therapy in patients with TSA is quite limited because most randomized clinical trials (RCTs) have excluded these severely impaired patients. In a pivotal RCT in patients with AS, adalimumab was efficacious in a subset of 11 patients with total ankylosis [16]. In addition, an open-label study was conducted to evaluate the safety and effectiveness of adalimumab in patients with AS in daily practice [Review of safety and effectiveness with Adalimumab in Patients with active ankylosing SponDylitis (RHAPSODY)]. The RHAPSODY study protocol allowed the inclusion of patients with advanced AS (i.e. Stages IV and V), and this study represents the largest cohort of patients with advanced radiographic AS ever studied in a clinical trial. Here, we report the results of a pre-specified sub-analysis of the effectiveness and safety of adalimumab therapy in patients with advanced stage AS.

Methods

This was an open-label, multicentre study conducted at 211 centres in 15 European countries. Independent ethics committees in all countries where the study was conducted provided approval for each of the participating centres. The principles of the Declaration of Helsinki and the International Conference on Harmonization Guidelines for Good Clinical Practice were applied. Compliance with local laws and customs was ensured by the investigators. Before any study-related procedures were performed, each patient provided written informed consent. The full results of RHAPSODY, as well as the results of a pre-specified sub-analysis of the effect of adalimumab in reducing anterior uveitis flares, are reported elsewhere [17, 18].

Patients

Patients aged ≥18 years with AS according to the modified 1984 New York Criteria for AS [19] were enrolled. Enrolment required active disease based on a Bath AS Disease Activity Index (BASDAI) score ≥4 [20] and previous unsatisfactory therapy with at least one NSAID. If national guidelines were more...
stringent, requiring treatment failure with at least two NSAIDs, they were followed. Patients could continue their current therapy with NSAIDs, DMARDs, analgesics and glucocorticoids (<10 mg/day prednisone equivalent). Treatment with analgesics had to be discontinued 24 h before a study visit, except for patients who received continuous analgesic maintenance therapy. IA injections or infiltrations of joints and tendons were not allowed within 28 days (injections of SI joints within 14 days) before screening or during the study. Patients who had been treated previously with etanercept or infliximab could enter the study, provided that the anti-TNF therapy had been discontinued at least 3 weeks or at least 2 months, respectively, before the first adalimumab injection.

**Study design**

Patients meeting the inclusion and exclusion criteria self-administered 40 mg of adalimumab (Abbott Laboratories, Abbott Park, IL, USA) subcutaneously every other week for 12 weeks. If adalimumab was not yet commercially available for AS, patients could opt to receive treatment for up to 20 weeks. There was no limitation for enrolment of patients with advanced AS or TSA. At baseline, the rheumatologist documented simply the presence (yes) or the absence (no) of advanced spinal ankylosis based on previous radiographs. For patients with advanced AS, the rheumatologist also provided detailed information about presence of syndesmophytes or of intervertebral fusion for each of the 23 vertebrae (from C2/3 to L5/S1). Advanced AS was determined as Stage IV or V spinal involvement. Further, patients with Stage IV disease discontinued at least 3 weeks or at least 2 months, respectively, before the first adalimumab injection.

**Patient disposition, withdrawals and adalimumab treatment duration**

In total, 1250 patients with active AS and mean disease duration of 11 years were enrolled in the study. Of these, the radiographic stage of AS was documented in 1227 patients (Fig. 1). Based on investigator review of previous radiographs, 27% (330) of patients were judged to have advanced AS (i.e. Stage IV or V) and 73% (897) of patients were judged to have spinal involvement that was minor to moderate (i.e. Stages I–III). Additional questionnaires about the radiographs of the spine, which provided detailed information on fusion or syndesmophytes, were available for 211 of the 330 patients with advanced AS, of which 116 had complete data about all three spinal segments. Stage IV spinal involvement was documented in 31 patients, and Stage V spinal involvement was documented in 41 patients. In the remaining 44 patients, the degree of the reported structural changes was less than the Stage IV criteria; therefore, these 44 patients were excluded from the analysis.

During the complete study period (94% of 897) of patients with AS Stages I–III, 6% (2 of 31) of patients with AS Stage IV and no patients with AS Stage V prematurely discontinued treatment with adalimumab; none of the patients with Stage IV disease discontinued treatment with adalimumab because of unsatisfactory therapeutic effect. The mean exposure to adalimumab was 15 weeks in patients with Stages I–III and Stage IV disease, and 14 weeks in patients with Stage V disease. The median treatment duration was 12 weeks across all patient subsets.

**Baseline characteristics**

Compared with patients whose radiographic grade of AS was Stages I–III, patients whose radiographic grade was Stage IV or V tended to be older, have a longer disease duration, be male, and be HLA-B27 positive (Table 2). The disease activity measured by BASDAI was similar between patients with AS Stages I–III and patients with Stage V spinal fusion (Table 3). Among all three subsets, BASDAI disease activity was least in patients with Stage IV spinal involvement. Further, patients with Stage IV disease reported the least degree of disease activity, as measured by baseline scores for nocturnal pain. Patient’s Global Assessment of disease activity, morning stiffness and total back pain, whereas patients with Stage V spinal involvement had the greatest (i.e. worst) scores for these parameters. Impairment of physical function, as assessed by the baseline BASFI score, was greatest for patients achieving optimal sleep on the Medical Outcomes Study (MOS) sleep scale [27].

**Statistical analysis**

Patients who had received at least one injection of adalimumab were included in the analysis. Observed data were used for all analyses of effectiveness with Week 12 as endpoint, whereas safety data were analysed based on the complete treatment period of each patient. Patients with documented absence of advanced AS, which included the three lower stages of the radiographic grading system (<50% spinal involvement in two segments or less), comprised the Stages I–III subset [3]. For inclusion in the advanced AS subsets (i.e. Stages IV and V), radiographs of all three spinal segments had to be available and the respective radiographic signs of AS had to be met [Stage IV: from 50 to <80% spinal involvement (13–19 vertebrae) in more than two spinal segments; Stage V: ≥80% spinal involvement encompassing 20 vertebrae or more] [3]. Descriptive analyses were performed by calculating counts and percentages for qualitative data and by calculating means and standard deviations or medians and minimums–maximums for quantitative data. Changes from baseline to Week 12 were compared with the Wilcoxon signed-rank test.

**Results**

**Patient disposition, withdrawals and adalimumab treatment duration**

<table>
<thead>
<tr>
<th>Table 1. Grading of AS by radiographic stage</th>
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<tbody>
<tr>
<td><strong>Stage IV</strong></td>
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<tr>
<td><strong>Stage IV</strong></td>
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<tr>
<td><strong>Stage III</strong></td>
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<tr>
<td><strong>Stage II</strong></td>
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<tr>
<td><strong>Stage I</strong></td>
</tr>
</tbody>
</table>

Adapted from Braun et al. [3]. aPatients with Stages IV and V spinal involvement were considered to have radiographically advanced AS. bPatients with Stages I–III spinal involvement were not considered to have advanced radiographic AS and were combined for this analysis.
patients with Stage V disease and similar in patients with Stages I–III and Stage IV disease. With respect to restriction of mobility, the baseline BASMI scores in both subgroups of patients with radiographically advanced AS indicated substantial impairment and were considerably greater than the median scores for patients with Stages I–III spinal involvement (Table 3).

Characteristics of advanced spinal involvement

Patients with Stage IV or V disease differed not only by the number of involved vertebrae, but also by the degree of structural damage of the spine, which was more severe in the 41 patients with Stage V disease compared with the 31 patients by Stage IV disease. In patients with Stage IV spinal involvement, the main structural change was the development of syndesmophytes; nevertheless, fusion was reported in a relevant percentage for each intervertebral unit. As anticipated, vertebral fusion predominated in patients with Stage V spinal involvement. The median percentages of fusion calculated for the 23 intervertebral units were 36% in patients with Stage IV disease and 78% in patients with Stage V disease (Fig. 2A and B).

Effectiveness

At Week 12, an ASAS20 response was achieved by 71% of patients with AS Stages I–III compared with 61% and 63% of patients with Stages IV and V spinal involvement, respectively (Fig. 3). Week-12 ASAS40 response rates were 54% for patients with AS Stages I–III, 48% for Stage IV and 54% for Stage V (Fig. 3). ASAS partial remission was experienced by fewer patients with Stage V spinal involvement (7%) compared with patients with Stage IV (26%) and Stages I–III (30%) disease (Fig. 3). Although the rate of achieving a BASDAI 50 response was somewhat less rapid in patients with Stage V disease compared with the two subgroups with less advanced AS (Fig. 4), the percentage of patients achieving a BASDAI 50 response at Week 12 was greatest in the Stage V subgroup (66% Stage V, 58% Stage IV, and 57% Stages I–III) (Fig. 3). The median improvement in BASDAI was similar across all three patient subgroups, with median changes from baseline ranging from −3.5 in the Stage IV subgroup to −3.9 in the Stage V subgroup (Table 3).

All three subgroups experienced improvements in physical function, as measured by median change in BASFI score from baseline to Week 12, and patients with Stage V spinal involvement exhibited the greatest improvement (median change of −2.4 points).

**Table 2.** Baseline characteristics stratified by stage of AS

<table>
<thead>
<tr>
<th></th>
<th>Not advanced AS</th>
<th>Advanced AS</th>
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<tbody>
<tr>
<td></td>
<td>Stages I–III</td>
<td>Stage IV</td>
</tr>
<tr>
<td></td>
<td>(n = 897)</td>
<td>(n = 31)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>605 (67)</td>
<td>27 (87)</td>
</tr>
<tr>
<td>Age, mean ± s.d., years</td>
<td>41.8 ± 10.8</td>
<td>51.9 ± 10.4</td>
</tr>
<tr>
<td>AS duration, mean ± s.d., years</td>
<td>9.4 ± 8.6</td>
<td>14.9 ± 11.9</td>
</tr>
<tr>
<td>HLA-B27 positive, n (%)</td>
<td>717 (82)</td>
<td>24 (88)</td>
</tr>
<tr>
<td>Prior anti-TNF therapy, n (%)</td>
<td>233 (26)</td>
<td>10 (32)</td>
</tr>
<tr>
<td>Use of DMARDs, n (%)</td>
<td>257 (29)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>Use of NSAIDs, n (%)</td>
<td>686 (77)</td>
<td>19 (61)</td>
</tr>
<tr>
<td>Use of glucocorticoids, n (%)</td>
<td>123 (14)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>≥1 swollen peripheral joint, n (%)</td>
<td>201 (22)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Enthesitis, n (%)</td>
<td>485 (54)</td>
<td>12 (39)</td>
</tr>
</tbody>
</table>

Stages I–III are defined as involvement of 12 vertebrae or less (<50% of the spine) in two spinal segments or less; Stage IV is defined as involvement of 13–19 vertebrae (from 50% to <80% of the spine) in more than two spinal segments; Stage V is defined as involvement of ≥20 vertebrae or more (<80% of the spine). Percentage based on observed data.

**Table 3.** Effectiveness of adalimumab at Week 12 stratified by stage of AS (median baseline, Week 12 and change values)

<table>
<thead>
<tr>
<th></th>
<th>Not advanced AS</th>
<th>Advanced AS</th>
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<tbody>
<tr>
<td></td>
<td>Stages I–III</td>
<td>Stage IV</td>
</tr>
<tr>
<td></td>
<td>(n = 897)</td>
<td>(n = 31)</td>
</tr>
<tr>
<td>BASDAIb</td>
<td>6.4</td>
<td>2.5</td>
</tr>
<tr>
<td>BASFIb</td>
<td>5.2</td>
<td>2.4</td>
</tr>
<tr>
<td>Min, max</td>
<td>0, 10.0</td>
<td>0, 10.0</td>
</tr>
<tr>
<td>BASMI</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Morning stiffnessb</td>
<td>6.7</td>
<td>2.4</td>
</tr>
<tr>
<td>Min, max</td>
<td>0, 10.0</td>
<td>0, 10.0</td>
</tr>
<tr>
<td>PaGA</td>
<td>70</td>
<td>23</td>
</tr>
<tr>
<td>Min, max</td>
<td>0, 100</td>
<td>1, 100</td>
</tr>
<tr>
<td>Total back painb</td>
<td>65</td>
<td>20</td>
</tr>
<tr>
<td>Min, max</td>
<td>0, 100</td>
<td>0, 100</td>
</tr>
<tr>
<td>Nocturnal painb</td>
<td>67</td>
<td>19</td>
</tr>
<tr>
<td>CRP, mg/dl</td>
<td>1.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Stages I–III are defined as involvement of 12 vertebrae or less (<50% of the spine) in two spinal segments or less; Stage IV is defined as involvement of 13–19 vertebrae (from 50% to <80% of the spine) in more than two spinal segments; Stage V is defined as involvement of ≥20 vertebrae or more (<80% of the spine). "Change from baseline to Week 12 includes only patients with both baseline and Week 12 data available, whereas baseline and Week-12 data include all patients with available data at the respective time point. P < 0.001 for all changes. Scale of 0–10. VAS of 0–100 mm. CRP reference value 0.4 mg/dl. PaGA: patient’s global assessment of disease activity.**
Although patients in the advanced AS subgroups had greater baseline restriction of mobility compared with patients in the Stages I–III subgroup, the median changes in BASMI from baseline to Week 12 in both groups were equivalent to the improvement observed in patients with Stages I–III AS (Table 3). After 12-week therapy with adalimumab, the greatest improvements in morning stiffness and nocturnal pain were observed in patients with Stage V disease (changes from baseline to Week 12 of −4.7 and −43, respectively) (Table 3). Despite having more impairment at baseline for both measures, patients with Stage V disease achieved Week 12 morning stiffness and nocturnal pain scores (2.5 and 18, respectively) that were comparable to those of the other two subgroups (both 2.4 and 19, respectively). Improvements in total back pain and Patient’s Global Assessment of disease activity, as well as reductions in CRP concentration, were similar in patients with and without advanced AS. Changes from baseline to Week 12 ranged from −32 to −37 for total back pain, from −34 to −41 for Patient’s Global Assessment and from −0.7 to −1.2 mg/dl for CRP (Table 3). The percentage of patients reporting an optimal sleep quality increased from 34% at baseline to 51% at Week 12 in patients with AS Stages I–III and from 38 to 60%, respectively, in patients with Stage V disease.
in clinical practice, and the results should be interpreted within
was an open-label study, designed to mirror the treatment of AS
patients with radiographically advanced AS in RHAPSODY. This
assess the effectiveness and safety of adalimumab in a subset of
clinical trial data in patients with advanced ankylosis, we aimed to
burden associated with AS [28], coupled with the paucity of
Discussion
Throughout the complete study period, 57% (511 of 897) of
patients with AS Stages I–III, 45% (14 of 31) of patients with
Stage IV disease and 32% (13 of 41) of patients with Stage V
disease experienced at least one adverse event. Severe adverse
events were reported for 28 (3%) patients with AS Stages I–III
and for 1 (1%) patient with Stage IV disease; none of the patients
with Stage V spinal involvement experienced any severe adverse
events. A serious infection was documented in three (<1%)
patients with AS Stages I–III (viral infection, otitis and rickettsial
fever) and in one (1%) patient with Stage V disease (cellulitis).
Overall, no infections of the lower respiratory tract were
documented in patients with advanced AS.

The percentage of patients who considered their sleep optimal at
baseline was greatest in patients with Stage IV AS (45%), but this
subgroup did not report improvement in this measure at Week 12
(Fig. 5).

Safety
Throughout the complete study period, 57% (511 of 897) of
patients with AS Stages I–III, 45% (14 of 31) of patients with
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Overall, no infections of the lower respiratory tract were
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Discussion
Considering the pain, functional disability and overall disease
burden associated with AS [28], coupled with the paucity of
clinical trial data in patients with advanced ankylosis, we aimed to
assess the effectiveness and safety of adalimumab in a subset of
patients with radiographically advanced AS in RHAPSODY. This
was an open-label study, designed to mirror the treatment of AS
in clinical practice, and the results should be interpreted within
this context. Nevertheless, this study represents the largest cohort
of patients with advanced radiographic AS ever studied in a
clinical trial, and this study provides evidence that adalimumab is
an effective therapy for patients with advanced radiographic AS
if inflammatory disease activity in such patients is present. After
12 weeks of treatment, the overall pattern of clinical response
in patients with advanced AS, including patients with TSA, was very
similar to that observed in patients whose AS was not radiographically
advanced. Patients with TSA (i.e. bamboo spine) have been
excluded from most of the previous RCTs, except for an
adalimumab RCT that included 11 patients with TSA. Consistent
with our results, those 11 patients achieved improvements in the
signs and symptoms of AS similar to those achieved in the
complete study population when they were treated with adalimumab [16].

The staging of AS used in this study was based on a five-stage
radiographic grading system proposed by Braun et al. [3] in 2002,
in which the most advanced stage (i.e. Stage V) represents a
radiographic state of extended spinal fusion or bamboo spine.
Although some patients with advanced AS may achieve a state of
low disease activity over time (‘burn-out’ AS), other patients
retain a status of high disease activity throughout their disease
courses. Obviously, patients with radiographically advanced AS
but substantial disease activity according to the rheumatologist
and based on the inclusion criteria (BASDAI score ≥4 at
baseline) were selected for this study. The baseline disease activity
in the 41 patients with Stage V radiographic spinal involvement
was quite substantial and similar to that of patients with Stages
I–III disease, as indicated by median BASDAI scores of 6.5 and
6.4 and CRP concentrations of 1.7 and 1.2 mg/dl, respectively.
Moreover, the baseline nocturnal pain and total back pain scores
are also likely to reflect the presence of active inflammation in the
patients with Stage V disease.

In this study, the reductions in the signs and symptoms of AS,
as well as improvements in function and mobility, achieved in
patients with Stage V disease were comparable to those of patients
whose AS was not radiographically advanced. In particular, the
percentage of patients achieving a BASDAI 50 response at Week
12 was greatest in the subset of patients who had Stage V spinal
involvement; 66% of patients with advanced AS in this study
perceived their disease activity to improve by at least 50% on this
composite index that measures fatigue, spinal and peripheral joint
pain, local tenderness and morning stiffness. Likewise, the
ASAS20 and ASAS40 therapeutic response rates in the subset
with Stage V disease were overall comparable to those in patients
with less advanced AS.

The BASFI and BASMI responses in the subgroup with
Stage V disease are also noteworthy, especially considering that
patients with advanced radiographic AS are likely to have some

![Fig. 3. ASAS and BASDAI 50 responses at Week 12, stratified by radiographic stage of AS. Stages I-III are defined as <50% spinal involvement in two segments or less, Stage IV is defined as 50% to <80% spinal involvement (13–19 vertebrae) in more than two spinal segments. Stage V is defined as ≥80% spinal involvement (20 vertebrae or more).](image1)

![Fig. 4. BASDAI 50 response over time, stratified by stage of AS. Stages I-III are defined as <50% spinal involvement in two segments or less. Stage IV is defined as 50% to <80% spinal involvement (13–19 vertebrae) in more than two spinal segments. Stage V is defined as ≥80% spinal involvement (20 vertebrae or more).](image2)

![Fig. 5. MOS optimal sleep at baseline and Week 12, stratified by stage of AS. Stages I–III are defined as <50% spinal involvement in two segments or less. Stage IV is defined as 50% to <80% spinal involvement (13–19 vertebrae) in more than two spinal segments. Stage V is defined as ≥80% spinal involvement (20 vertebrae or more).](image3)
degrees of permanent structural damage and thus may have inherent limitations in the degrees of function and/or mobility that they can recover. Although the Stage V subgroup had greater impairment of physical function and spinal mobility relative to the other subgroups, as indicated by greater BASMI and BASFI scores at baseline, patients with Stage V disease experienced reductions in BASMI and BASFI that were at least as great as those among patients with AS Stages I–III. In particular, the decrease in BASFI (from 7.0 to 4.3 in Stage V patients is remarkable, and indicates that BASFI is determined by both structural damage and also by active inflammation. In a 24-week, placebo-controlled trial of infliximab in a typical population of patients with active AS [9], the median changes in BASFI and BASMI (−1.7 and −1.0, respectively) were found to be significantly different from placebo. In the previous study of adalimumab therapy in patients with TSA, BASMI improvements were not observed until Week 24 and were somewhat smaller (mean changes ranging from −0.5 at Week 24 to −0.8 after 2 years) than the improvements observed in our study [16]. These data provide context in which to interpret the clinical relevance of the BASFI (median change of −2.4) and BASMI (median change of −1.0) improvements in patients with advanced AS in this 12-week study. In future studies, it may be of interest to explore the correlation of these clinically relevant improvements in physical function and spinal mobility with quality-of-life measures in patients with advanced spinal fusion.

Among all three patient subsets, patients with Stage V disease experienced the greatest median improvement in morning stiffness. The presence of morning stiffness responsive to anti-TNF therapy indicates the presence of reversible active inflammation despite osseous fusion of the spine. Despite having greater nocturnal pain at baseline, patients with Stage V spinal involvement reported the greatest improvement in this measure (change of −43 mm from baseline to Week 12) and achieved levels similar to those of patients with less advanced AS at Week 12. With respect to assessments of back pain and disease activity, patients reported similar improvements in these measures regardless of the correlation of these clinically relevant improvements in physical function and spinal mobility with quality-of-life measures in patients with advanced spinal fusion.

A relevant and marked difference in clinical response for patients with Stage V vs patients with Stage IV or Stages I–III AS was observed only in the ASAS partial remission results, in which the remission rate was considerably lower in patients with Stage V spinal involvement. This result is consistent with the findings in the small group of patients with TSA in the previous adalimumab RCT [16] and is likely a consequence of the structural damage affecting physical function and spinal mobility in patients with TSA. Such structural damage is irreversible and precludes these patients from achieving very low absolute scores on the BASFI (one of the domains of the ASAS partial remission criteria), despite experiencing a similar degree of relative improvement as measured by ASAS40 or BASDAI 50.

It is notable that the subset of patients with Stage IV disease generally achieved somewhat lower response rates and less improvement on the effectiveness parameters compared with both the subset with more spinal involvement (i.e. Stage V) and the subset with less spinal involvement (i.e. Stages I–III). In this study, probably by chance, patients with Stage IV disease tended to have lower disease activity at baseline, as measured by median BASDAI, and less pain and morning stiffness even when compared with patients with Stages I–III spinal involvement. Though the median relative improvements were, in general, smaller in patients with Stage IV disease, the absolute median values achieved by these patients in the various outcome parameters (except for BASFI and BASMI) at Week 12 were similar to those of patients with Stages I–III AS. Therefore, the good clinical response observed for patients with Stage IV or V most likely reflects a substantial degree of active inflammation at baseline.

The overall safety profile of adalimumab in the complete RHAPSODY study population [17] was similar to that reported in the pivotal RCT of adalimumab in AS [10]. When stratified by stage of AS, the frequency and quality of adverse events were similar between patients with AS Stages I–III and those with at least Stage IV spinal involvement. Because of the restricted movement of the ribcage, patients with advanced spinal ankylosis may be expected to have a greater susceptibility for infection of the lower airways. In this study, however, no infection of the lower respiratory tract was reported for patients with Stage IV or V disease.

Conclusions

This study represents the largest cohort of patients with advanced radiographic AS ever studied in a clinical trial. After 12 weeks of treatment, adalimumab was effective and well tolerated in patients with advanced AS. Patients with advanced spinal ankylosis, including patients with bamboo spine, experienced improvements in signs and symptoms of AS that were very similar to those of patients without advanced radiographic changes.

Rheumatology key messages

- RHAPSODY enrolled the largest cohort of patients with radiographically advanced AS ever studied in a clinical trial.
- Adalimumab is effective in patients with advanced spinal ankylosis, including patients with bamboo spine.

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