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Secukinumab 150/300 mg Provides Sustained Improvements in the Signs and Symptoms of Active Ankylosing Spondylitis: 3-Year Results from the Phase 3 MEASURE 3 Study

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Objective. Secukinumab 150 mg has demonstrated significant improvement in signs and symptoms of ankylosing spondylitis (AS), with response rates sustained for up to 5 years. Here, we report end-of-study 3-year efficacy and safety results of secukinumab 150 and 300 mg from the MEASURE 3 study.

Methods. A total of 226 patients was randomized to intravenous secukinumab 10 mg/kg (baseline, weeks 2 and 4) followed by subcutaneous (s.c.) secukinumab 300/150 mg every 4 weeks or a matched placebo. At week 16, placebo patients were re-randomized to s.c. secukinumab 300/150 mg. Analysis at week 156 included patients initially randomized to secukinumab and those who switched from placebo to secukinumab at week 16 (any secukinumab 300/150 mg). Outcome measures at week 156 included Assessment of Spondyloarthritis International Society (ASAS) 20/40, Bath Ankylosing Spondylitis Disease Activity Index, ASAS partial remission (PR), ASAS 5/6, and Ankylosing Spondylitis Disease Activity Score–C-reactive protein inactive disease.

Results. The retention rates from weeks 16 to 156 were 80.5% and 80.9% in secukinumab 300 and 150 mg, respectively. ASAS 20/40 response rates at week 156 were 75.0%/56.5% and 68.2%/47.7% for secukinumab 300 and 150 mg, respectively. At week 156, response rates on more stringent clinical end points (eg, ASAS 40, ASAS-PR) were higher with the 300-mg dose, particularly in tumor necrosis factor (TNF)–inadequate responder (IR) patients. No new safety findings were observed.

Conclusion. Secukinumab (300 and 150 mg) provided sustained improvements through 3 years in the signs and symptoms of active AS. Improvements with secukinumab 300 mg were numerically higher compared with the 150-mg dose for some higher hurdle end points and in TNF-IR patients. The safety profile of secukinumab was consistent with previous reports.

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory disease that is characterized by progressive, irreversible structural damage of the spine, sacroiliac, and/or peripheral joints and causes disability and reduced quality of life for patients (1). Tumor necrosis factor (TNF) inhibitors improve signs and symptoms of AS; however, approximately 40% of patients with AS do not respond to anti-TNF

*See Appendix S1.

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therapy (2,3), leading to treatment discontinuation and disease relapse. TNF-inadequate responder (IR) patients are known to be a difficult-to-treat population. Switching to a second or third TNF inhibitor can be an effective strategy in AS (4); however, overall response rates are progressively lower with within-class switching. Other experimental biologic therapies showing promising results in TNF inhibitor–naïve patients, such as rituximab, have demonstrated little benefit in TNF-IR patients (5,6). Recent recommendations of an international task force on treating axial spondyloarthritis (7) indicate that "a major treatment target should be clinical remission/inactive disease," namely, the treating physician should aim to achieve higher hurdle efficacy end points in AS, such as Assessment of Spondyloarthritis International Society (ASAS), partial remission (PR), or Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease.

The proinflammatory cytokine interleukin-17A (IL-17A) plays a pivotal role in the pathogenesis of AS (8). Secukinumab, a fully human monoclonal antibody that directly inhibits IL-17A, has demonstrated significant improvement in the signs and symptoms of patients with AS (9,10), psoriasis (11), and psoriatic arthritis (12–14) and is approved for the treatment of these diseases, offering an alternate therapeutic option for AS patients. MEASURE 3 (NCT02008916), a Phase 3 study, was conducted to assess the efficacy and safety of subcutaneous (s.c.) maintenance therapy with 300- or 150-mg secukinumab following intravenous (i.v.) loading. Study results of up to 52 weeks have been reported previously (10). The primary efficacy end point was met at week 16; the proportion of patients achieving ASAS 20 response criteria was significantly greater in the 300- and 150-mg groups versus the placebo group; both secukinumab doses showed significant improvement versus placebo across all studied secondary end points, except ASAS PR, for which only secukinumab 300 mg was superior to placebo (10). Here we report the long-term end-of-study (3-year) results from MEASURE 3, which evaluated the highest dose of secukinumab used in AS to date.

METHODS

Study design. MEASURE 3 was a randomized, double-blind, double-dummy, placebo-controlled, parallel-group design study conducted at 54 centers in 10 countries. The details of the study design have been published previously (10). Briefly, patients with active AS were randomized to receive i.v. secukinumab 10 mg/kg (baseline, weeks 2 and 4) followed by s.c. secukinumab 300 or 150 mg every 4 weeks (q4w; i.v.→300/150 mg) starting at week 8. Patients in the placebo group were treated according to the same i.v.-to-s.c. administration schedule and were re-randomized at week 16 to receive s.c. secukinumab 300 or 150 mg (1:1) q4w (Supplementary Figure S1). The study was double-blind until the week 52 interim analysis was complete, after which it was open-label through week 152. Patients were stratified according to previous anti-TNF therapy (patients who were naïve to anti-TNF therapy [TNF-naïve] or those with a history of inadequate response or intolerance to no more than one of these agents [TNF-IR]). Approximately 75% of the patients were TNF-naïve. The trial was conducted by the study investigators in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines and was analyzed by the sponsor. All centers received approval from independent ethics committees or institutional review boards. Patients provided written informed consent before starting the study-related procedures. Following completion of the study (LPLV: 11-Dec-2017), the 3-year results have been presented here.

Patients. Eligible patients (18 years or older) included in the study had moderate to severe AS, fulfilling the modified New York criteria with a score of 4 or higher on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; scores range from 0-10), a spinal pain score of 4 or greater (out of 10) in BASDAI item 2, and a total back pain score of 40 mm or greater on a 100-mm visual analog scale, despite treatment with the highest recommended doses of nonsteroidal anti-inflammatory drugs. Previous use of disease-modifying antirheumatic drugs was allowed with washout periods for agents other than sulfasalazine and methotrexate before the initiation of study treatment. Patients could participate if they had an inadequate response to an approved dose of not more than one anti-TNF agent for 3 months or more or if they had unacceptable side effects (hereafter collectively referred to as TNF-IR).

Key exclusion criteria were total spinal ankylosis, evidence of infection or malignancy on chest radiography, active systemic infection within 2 weeks before baseline, and previous treatment with cell-depleting therapies or biologic agents other than anti-TNF agents.

Outcomes. The primary end point was the proportion of patients who met ASAS 20 response criteria at week 16. Outcomes through week 156 included ASAS 20, ASAS 40 response criteria; change from baseline in total BASDAI score; the proportion of patients achieving ASAS PR (a score of 2 units or less in each of the four core ASAS domains), inactive disease (less than 1.3) in Ankylosing Spondylitis Disease Activity Score-C-reactive protein (ASDAS-CRP), as well as 50% or better improvement in the baseline total BASDAI score (BASDAI 50 response), and ASAS 5/6 response (20% or greater improvement in five of the six ASAS response domains). Additionally, the change from baseline in high-sensitivity CRP (hsCRP) level and Bath Ankylosing Spondylitis Functional Index (BASFI) score, and the proportion of patients with a clinically important improvement (1.1 units or more) and a major improvement (2.0 units or more) in ASDAS-CRP were evaluated. Patients initially randomized to secukinumab and those who switched from placebo to secukinumab at week 16 were combined for analyses after week 52. Prespecified subgroup analyses on the basis of anti-TNF history (TNF-naïve vs. TNF-IR) were performed for key efficacy end points. The overall safety and tolerabil-

ity of secukinumab were reported. Routine safety monitoring was performed; treatment-emergent adverse events (AEs) and serious AEs (SAEs) are reported throughout the entire study period.

Statistical analysis. Efficacy data are reported as observed through week 156 by study treatment dose. Summary statistics of categorical variables are based on observed frequencies and percentages; for continuous variables, the mean ± SD are reported. In addition to the observed data, ASAS 20 and ASAS 40 response rates were analyzed using multiple imputation for patients originally randomized to secukinumab to account for any missing data. Analyses stratified by anti-TNF history were prespecified and reported as observed. Following week 52, patients initially randomized to secukinumab and those who switched from placebo to secukinumab at week 16 were combined for analysis (secukinumab: 300 mg, N = 113; and 150 mg, N = 110). Safety end points were evaluated in the safety set, which included all patients who received at least one dose of the study drug; these end points were summarized descriptively. The exposure-adjusted incidence rates (EAIRs per 100 patient-years) are presented for AEs and SAEs. For the safety data during the entire treatment period (from baseline up to the end of follow-up period), the secukinumab dose groups include any patients who received the stated dose of secukinumab and also placebo patients re-randomized to active treatment at week 16. These secukinumab dose groups have been denoted as "Any secukinumab" 300 mg and 150 mg.

RESULTS

Patients. Of the 226 patients randomized, 222 (98.2%) completed the 16-week evaluation period (10). At week 16, 73 patients treated with placebo were re-randomized to s.c. secukinumab 300 mg (n = 37) or 150 mg (n = 36). Three patients randomized to placebo discontinued the study before week

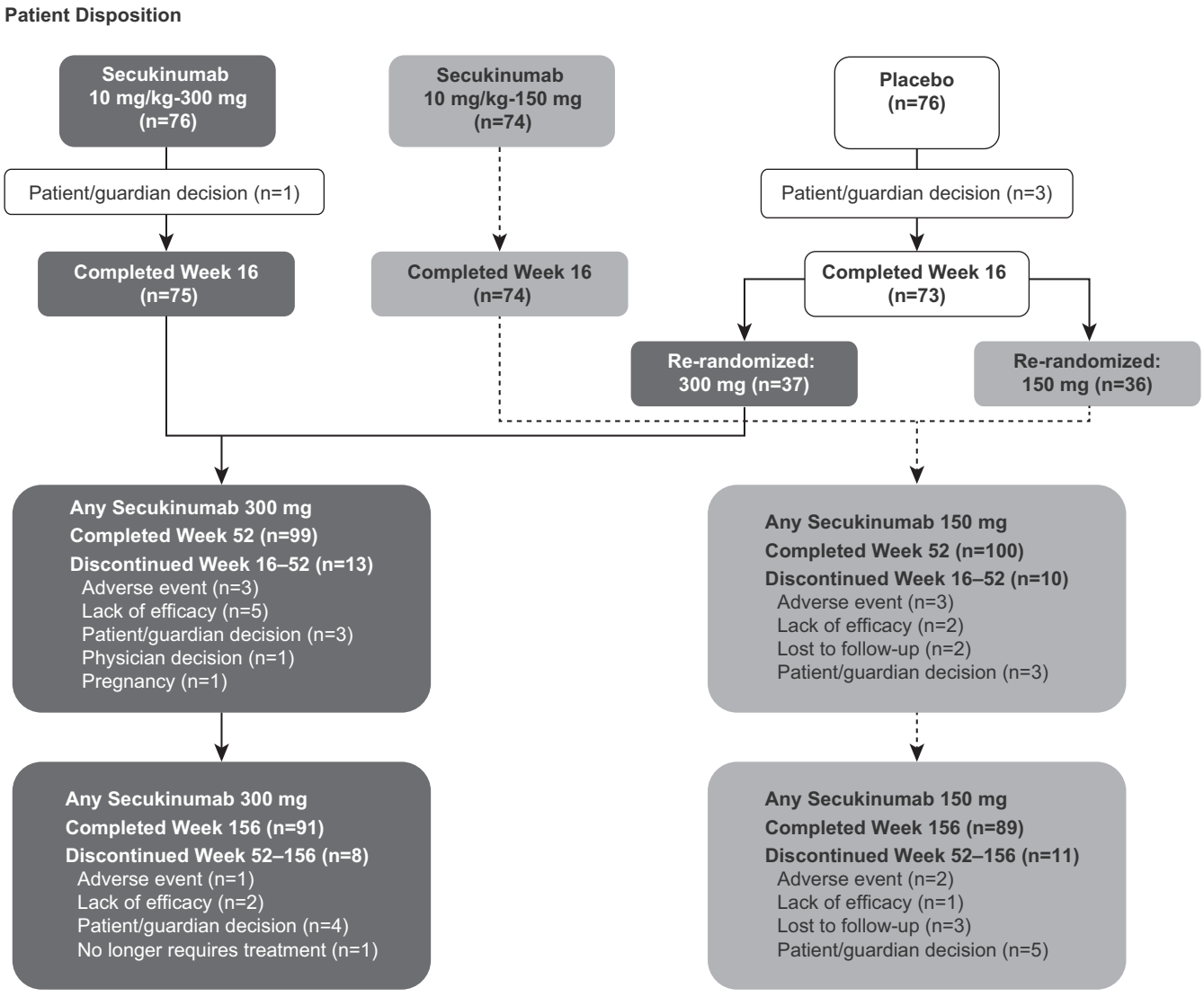

Figure 1. Patient disposition through week 156.

16. Overall, 113 patients on secukinumab 300 mg and 110 on secukinumab 150 mg continued in the study from week 16 onward. The retention rates from weeks 16 to 156 were 80.5% (91 of 113) for secukinumab 300 mg and 80.9% (89 of 110) for secukinumab 150 mg (Figure 1). Demographics and baseline disease characteristics were comparable across the study

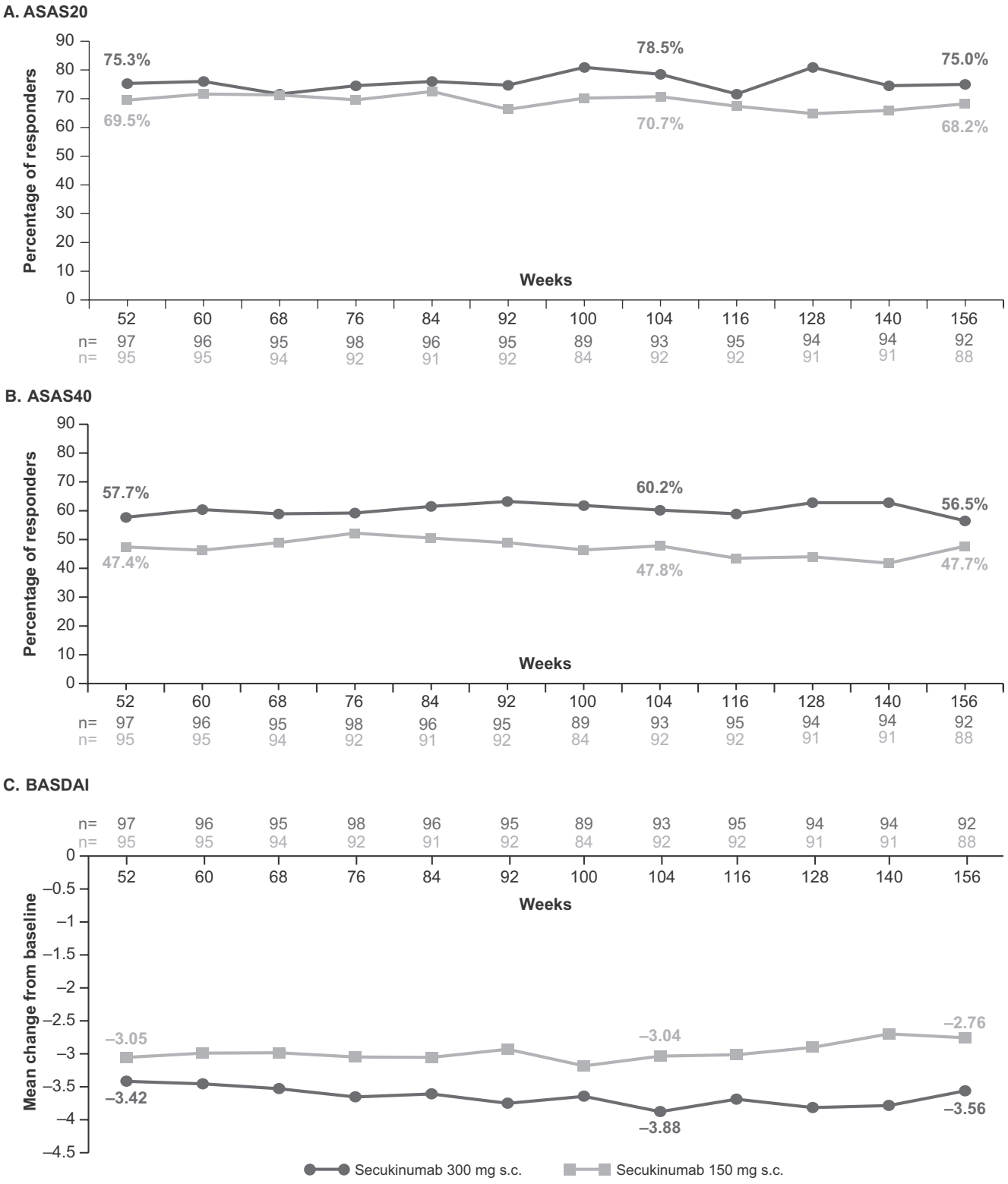

Figure 2. ASAS20/40 response rates and mean change from baseline in BASDAI through week 156. Data are shown as observed through week 156. ASAS20/40, Assessment of Spondyloarthritis International Society criteria for 20%/40% improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; s.c., subcutaneous.

groups [see Supplementary Table S1; and previously reported detail (10)].

Long-term efficacy. The response rates reported through week 52 (10) were sustained to week 156; at week 156, ASAS 20/ASAS 40 response rates were 75.0%/56.5% and 68.2%/47.7% for secukinumab 300 and 150 mg, respectively (Figure 2A and B); responses in patients re-randomized from placebo to secukinumab 300 and 150 mg exhibited similar trends to those in patients receiving active treatment throughout the study beyond week 52 (Supplementary Table S2). At week 156, similar ASAS 20/ASAS 40 response rates were seen using multiple imputation; 74.8%/55.6% and 69.5%/47.6% for secukinumab 300 and 150 mg, respectively (Supplementary Table S3). Furthermore, the

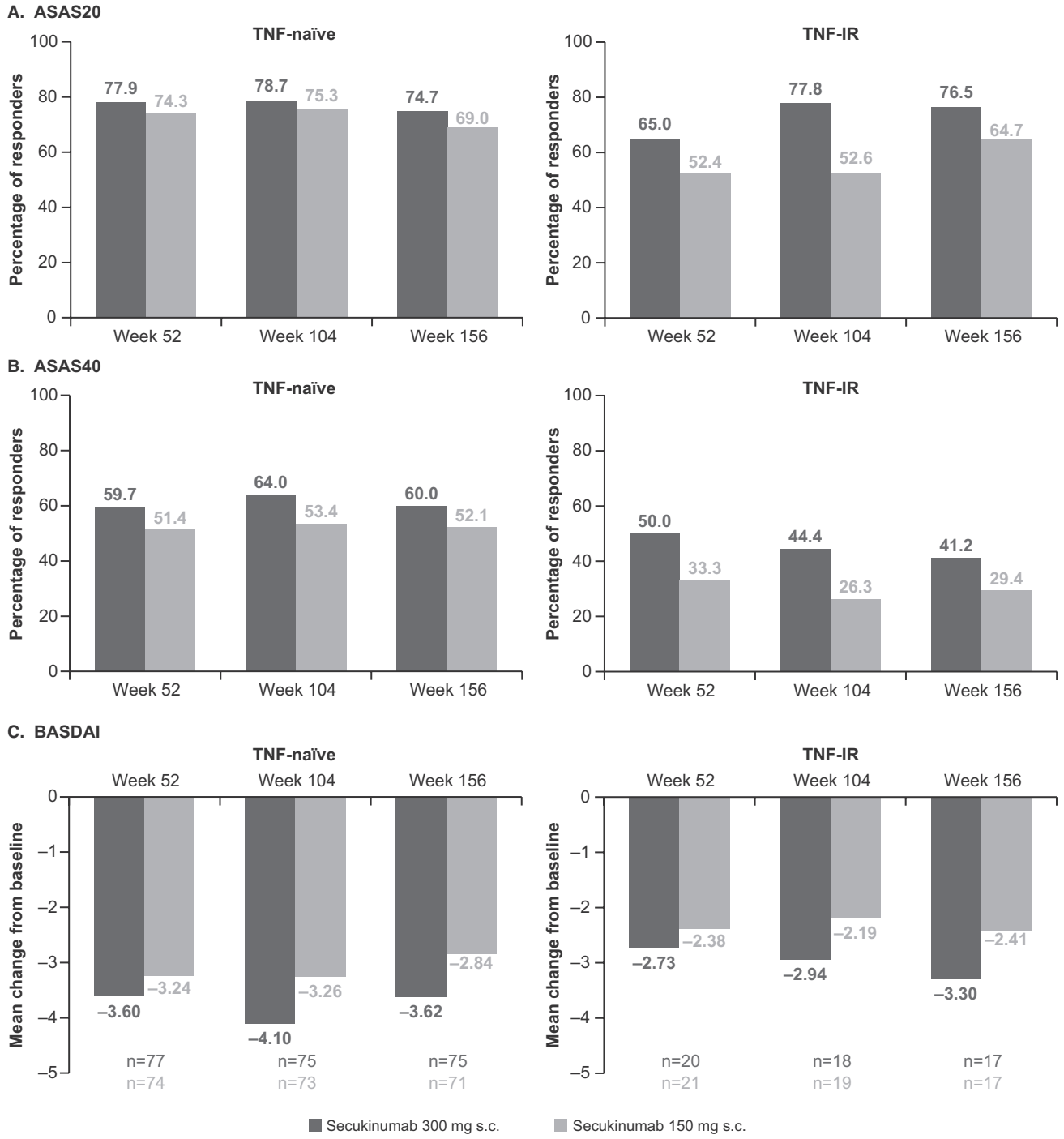

Figure 3. ASAS20/40 response rates and mean change from baseline in BASDAI by TNF status at weeks 52, 104, and 156. Data are shown as observed through week 156. ASAS, Assessment of Spondyloarthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; IR, inadequate response or intolerance; TNF, tumor necrosis factor; s.c., subcutaneous.

improvements observed at week 16 in the individual ASAS component domains were sustained up to week 156 (Supplementary Table S4). The reduction in total BASDAI was maintained through week 156 in both groups (Figure 2C). The mean change from baseline in BASDAI at week 156 was –3.56 with secukinumab 300 mg and –2.76 with secukinumab 150 mg. The median BASDAI scores and the proportions of patients with BASDAI≥4 and spinal pain (BASDAI question #2) 4 or greater through week 156 in patients originally randomized to secukinumab 300 and 150 mg are shown in Supplementary Table S5.

ASAS 20/ASAS 40 response rates and mean change from baseline in BASDAI by anti-TNF status at weeks 52, 104, and 156 are shown in Figure 3. At week 156, ASAS 20/ASAS 40 response rates in TNF-naïve patients were 74.7%/60.0% and 69.0%/52.1% in the secukinumab 300 and 150 mg groups, respectively. The corresponding responses in TNF-IR patients were 76.5%/41.2% and 64.7%/29.4% in the secukinumab 300 and 150 mg groups, respectively (Figure 3A and B). The reduction from baseline in BASDAI observed at week 52 was maintained through week 156 regardless of anti-TNF status with both secukinumab doses (Figure 3C). ASAS PR response rates were sustained through week 156 with both secukinumab doses in the overall population (Figure 4A). Secukinumab 300 mg showed numerically higher responses in this more stringent clinical end point, particularly in TNF-IR patients (Figure 4B).

The proportions of patients achieving ASDAS-CRP inactive disease were 25.8% and 16.8% at week 52 and 25.0% and 18.4% at week 156 with secukinumab 300 and 150 mg, respectively. Both secukinumab dose groups achieved sustained improvements through week 156 across other end points, including BASDAI 50 and ASAS 5/ASAS 6 response; these improvements were observed regardless of anti-TNF status (Table 1). The mean change from baseline in hsCRP was sustained in both secukinumab dose groups from –6.5 and –10.1 at week 52 to –5.0 and –8.6 at week 156 with secukinumab 300 mg and 150 mg, respectively; the reduction was observed regardless of anti-TNF status (Table 1).

Both doses of secukinumab resulted in sustained reduction in ASDAS-CRP through week 156. Mean ASDAS-CRP change from baseline with secukinumab 300/150 mg was –1.6/–1.5, –1.7/–1.5, and –1.6/–1.3 at weeks 52, 104, and 156, respectively. Mean ASDAS-CRP scores at week 156 were 2.16 and 2.49 with secukinumab 300 and 150 mg, respectively. Mean changes from baseline in BASFI with secukinumab 300 and 150 mg were –3.1 and –2.6 at week 52, –3.3 and –2.5 at week 104, and –3.2 and –2.4 at week 156, respectively. Mean BASFI scores at week 156 were 3.45 and 4.21 with secukinumab 300 and 150 mg, respectively. The proportions of patients with a clinically important change (1.1 units or more) and major improvement (2.0 units or more) in ASDAS-CRP at week 52 were 62.9% and 38.1% with secukinumab 300 mg, and 64.2% and 32.6% with secukinumab 150 mg, respectively. These response rates were sustained at week 156 with both secukinumab doses (Table 1).

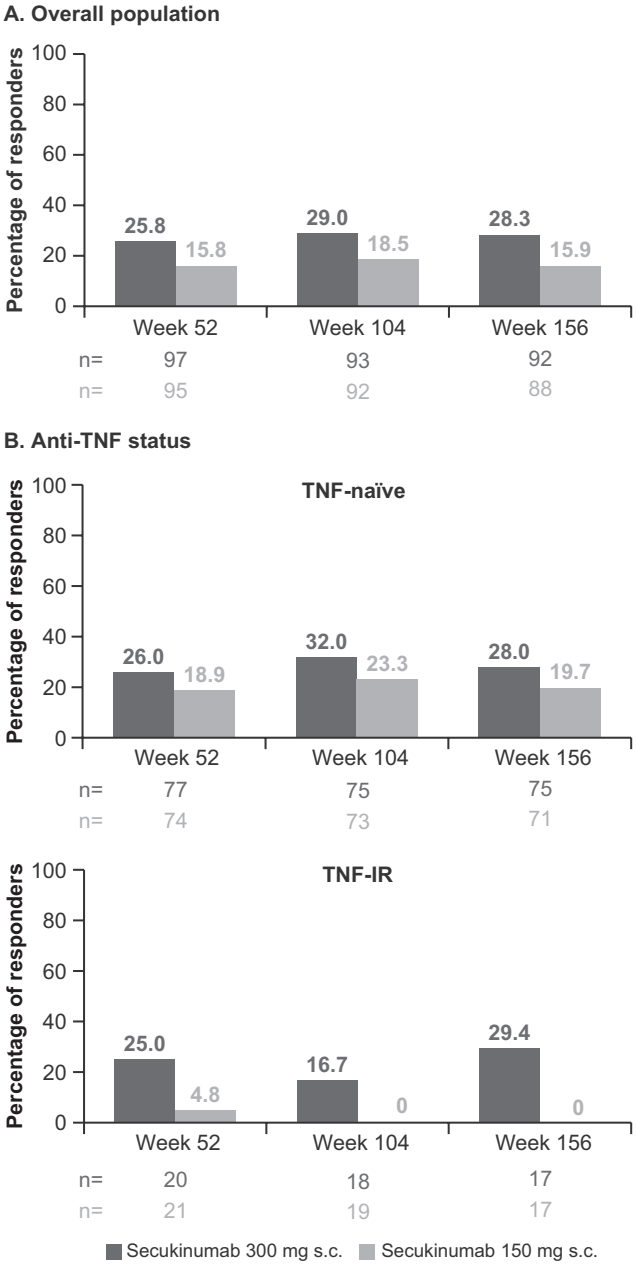

Figure 4. ASAS partial remission response in overall population (**A**) and by TNF status (**B**) at weeks 52, 104, and 156. Data are shown as observed through week 156. ASAS, Assessment of Spondyloarthritis International Society; IR, inadequate response or intolerance; TNF, tumor necrosis factor; s.c., subcutaneous.

Safety. The mean duration of exposure was 980.3 days for Any secukinumab 300 mg and 990.8 days for Any secukinumab 150 mg. The EAIRs of the most common AEs and selected AEs of interest are reported in Table 2. Nasopharyngitis, arthralgia, upper respiratory tract infection, headache, bronchitis, and diarrhea were the most common AEs. The rates of SAEs as well as AEs leading

Table 1. Additional efficacy end points through week 156 in the overall population and by anti-TNF status (observed data)

		Secukinumab 300 mg			Secukinumab 150 mg		
End Points	Week	Overall Population	TNF-Naïve	TNF-IR	Overall Population	TNF-Naïve	TNF-IR
ASAS 5/6, % (n/M)	52	57.7 (56/97)	61.0 (47/77)	45.0 (9/20)	48.4 (46/95)	59.5 (44/74)	9.5 (2/21)
	104	58.1 (54/93)	61.3 (46/75)	44.4 (8/18)	51.1 (47/92)	57.5 (42/73)	26.3 (5/19)
	156	50.0 (46/92)	50.7 (38/75)	47.1 (8/17)	47.7 (42/88)	49.3 (35/71)	41.2 (7/17)
BASDAI 50 response, % (n/M)	52	48.5 (47/97)	50.6 (39/77)	40.0 (8/20)	41.1 (39/95)	45.9 (34/74)	23.8 (5/21)
	104	61.3 (57/93)	65.3 (49/75)	44.4 (8/18)	45.7 (42/92)	52.1 (38/73)	21.1 (4/19)
	156	55.4 (51/92)	57.3 (43/75)	47.1 (8/17)	42.0 (37/88)	45.1 (32/71)	29.4 (5/17)
hsCRP, mean change ± SD (M)	52	−6.5 ± 12.7 (101)	−5.8 ± 11.3 (79)	−9.1 ± 16.7 (22)	−10.1 ± 18.1 (96)	−11.0 ± 16.1 (75)	−6.7 ± 24.1 (21)
	104	−5.4 ± 11.8 (91)	−4.8 ± 11.1 (73)	−7.8 ± 14.5 (18)	−9.9 ± 18.5 (91)	−11.0 ± 18.1 (73)	−5.5 ± 19.9 (18)
	156	−5.0 ± 12.9 (93)	−4.2 ± 12.2 (76)	−5.4 ± 13.4 (17)	−8.6 ± 18.3 (89)	−9.0 ± 18.6 (70)	−5.3 ± 24.6 (19)
ASDAS-CRP inactive disease,[a] % (n/M)	52	25.8 (25/97)	26.0 (20/77)	25.0 (5/20)	16.8 (16/95)	20.3 (15/74)	4.8 (1/21)
	104	34.4 (31/90)	36.1 (26/72)	27.8 (5/18)	17.6 (16/91)	21.9 (16/73)	0 (0/18)
	156	25.0 (23/92)	24.0 (18/75)	29.4 (5/17)	18.4 (16/87)	21.4 (15/70)	5.9 (1/17)
ASDAS clinically important change	52	62.9 (61/97)	ND	ND	64.2 (61/95)	ND	ND
	104	66.7 (60/90)	ND	ND	58.2 (53/91)	ND	ND
	156	66.3 (61/92)	ND	ND	52.9 (46/87)	ND	ND
ASDAS major improvement	52	38.1 (37/97)	ND	ND	32.6 (31/95)	ND	ND
	104	38.9 (35/90)	ND	ND	33.0 (30/91)	ND	ND
	156	35.9 (33/92)	ND	ND	29.9 (26/87)	ND	ND

Abbreviation: ASAS, Assessment of Spondyloarthritis International Society; ASDAS, Ankylosing Spondylitis Disease Activity; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high-sensitivity C-reactive protein; IR, inadequate responder; M, number of patients in the treatment group with evaluation; ND, not done by TNF status; TNF, tumor necrosis factor.
[a]Subgroup analysis not prespecified for ASDAS-CRP inactive disease.

to discontinuation were low and similar between the two secukinumab dose groups (Table 2). *Candida* infections were reported in two (1.8%) patients each in the Any secukinumab 300 and 150 mg groups (Table 2). These included one case each of oral candidiasis, esophageal candidiasis, vulvovaginal candidiasis, and genital candidiasis. All events were of mild to moderate severity, nonserious, and did not lead to study discontinuation. No cases of inflammatory bowel disease (IBD) or Crohn's disease were

Table 2. Safety profile over the entire safety reporting period

Variable	Any Secukinumab, 300 mg (N = 113)[a]	Any Secukinumab, 150 mg (N = 110)[a]	Any Secukinumab, Pooled (N = 223)[a]
Exposure to study treatment: d, mean ± SD	980.3 ± 305.4	990.8 ± 272.5	985.5 ± 289.0
Discontinued due to AEs, n (%)[a]	5 (4.4)	5 (4.5)	10 (4.5)
Treatment-emergent AEs, n (EAIR per 100 patient-years)			
Any AEs	102 (130.6)	98 (129.6)	200 (130.1)
Any serious AEs	11 (3.8)	11 (3.9)	22 (3.8)
Most common AEs[b]			
Nasopharyngitis	27 (10.6)	27 (11.1)	54 (10.8)
Arthralgia	14 (5.0)	14 (5.1)	28 (5.0)
Respiratory tract infection	16 (5.9)	12 (4.3)	28 (5.1)
Headache	14 (5.0)	12 (4.5)	26 (4.7)
Bronchitis	9 (3.1)	14 (5.1)	23 (4.1)
Diarrhea	9 (3.2)	11 (4.0)	20 (3.6)
Selected AEs			
Serious infections	2 (0.7)	2 (0.7)	4 (0.7)
Malignant or unspecified tumors	1 (0.3)	3 (1.0)	4 (0.7)
Candida infections	2 (0.7)	2 (0.7)	4 (0.7)
MACE	1 (0.3)	0	1 (0.2)
Neutropenia[c]			
Grade 3	1	1	2
Grade 4	0	2	2

Abbreviation: AE, adverse event; EAIR, exposure-adjusted incident rate; MACE, major adverse cardiovascular event.
[a]Includes placebo patients who were re-randomized to secukinumab at week 16.
[b]AEs with incidence rate >5 per 100 patient-years or relative frequency >2% in the combined secukinumab group.
[c]No grade 3 or 4 neutropenic laboratory values were reported as AEs or had associated infections; EAIR was not reported.

reported during the study. One major adverse cardiovascular event (myocardial infarction) was confirmed in the Any secukinumab 300 mg group in one patient; the investigator did not suspect a relationship between the event and the study medication.

Treatment-emergent AEs of uveitis were reported in eight patients: five (4.4%) in the Any secukinumab 300 mg group and three (2.7%) in the Any secukinumab 150 mg group, of which four patients had a previous history of uveitis. One new-onset uveitis event led to treatment discontinuation. Serious infections, which include two events of urinary tract infection and one case each of pneumonia and pyelonephritis, were reported in four patients. Grade 3 neutropenia was reported in one patient in each treatment group, and grade 4 neutropenia was reported in two patients in the Any secukinumab 150 mg group. No grade 3/4 neutropenic laboratory values were reported as AEs or had associated infections. Malignant or unspecified tumors were reported for three patients in the Any secukinumab 150 mg group (pancreatic neoplasm, malignant melanoma, and breast cancer) and in one in the Any secukinumab 300 mg group (squamous cell carcinoma). The events, breast cancer and malignant melanoma, were SAEs that led to study treatment discontinuation. No AEs of tuberculosis (new-onset or reactivation) or opportunistic infections were reported in this study. During the entire treatment period, no deaths were reported.

Immunogenicity. Treatment-emergent antidrug antibodies were reported in one patient in the secukinumab 300 mg group at week 52. These were not neutralizing to secukinumab and did not lead to loss of efficacy, pharmacokinetic abnormalities, or associated immunogenicity-related AEs.

The trial was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines by the study investigators and was analyzed by the sponsor. Approval of the protocol by an independent ethics committee/Institutional Review Board (IRB) at each participating center was confirmed by the Sponsor prior to first patient first visit (FPFV). Further information related to ethics approval can be found at https://www.clinicaltrialsregister.eu/ctr-search/search?query=2013-001090-24. A list of Independent Ethics Committees (IECs) or IRBs that approved study along with the list of approval reference numbers for each participating center of this study were provided in supplemental files in the earlier publication (10). Written informed consent was obtained from all patients for participation in the trial and for publication.

DISCUSSION

MEASURE 3 is the third phase 3 study to confirm the efficacy and safety profile of secukinumab in patients with active AS. The primary end point and the majority of secondary end points were met with both doses of secukinumab (150 mg and 300 mg), with the exception of ASAS PR, for which only secukinumab 300 mg was superior to placebo (10).

Here, we report the long-term 3-year efficacy and safety data from MEASURE 3. The two doses of secukinumab showed sustained improvement through 3 years across all efficacy measures, including more stringent criteria of response: ASAS 40, ASDAS inactive disease, and ASAS PR; these findings provide further evidence for the effectiveness of secukinumab as a treatment option for patients with AS. The sustained efficacy of secukinumab in both the TNF-naïve and TNF-IR subgroups is of interest, demonstrating that secukinumab is a suitable long-term treatment option for biologic-naïve patients and for patients who experience an intolerance or IR to anti-TNF agents, who are known to be a more difficult-to-treat population.

The secukinumab 300 mg dose showed numerically higher responses compared with 150 mg through week 156 across the majority of efficacy end points, particularly higher hurdle end points (ASAS 40, ASAS-PR, ASDAS inactive disease) and in TNF-IR patients. This dose is not currently approved for the treatment of AS, although the results of this study indicate some patients benefit from this higher dose.

The safety profile of secukinumab in this study was consistent with that observed in previous trials of secukinumab in AS, psoriatic arthritis, and psoriasis (9–14); no new or unexpected safety findings were reported following long-term administration of secukinumab at this highest dose regimen tested in AS to date. No clinically meaningful difference in safety findings were observed between the 150- and 300-mg doses in this study; based on incidence rates for adverse events (AEs) in the two treatment groups across system organ classes, no dose-dependent mechanism or trend became apparent. Patients with AS are at an increased risk for developing IBD (15). The present study enrolled four patients with a history of IBD and one with a history of Crohn's disease, although no treatment-emergent events of IBD or Crohn's disease were reported during the study. Uveitis is a common extra-articular manifestation of spondyloarthritis, with an estimated prevalence of 33% in patients with ankylosing spondylitis (16,17). The low number of treatment-emergent uveitis events reported in the study is therefore reassuring.

Limitations of this study include that no imaging for the assessment of axial changes was done with this higher maintenance dose of secukinumab. The placebo-controlled period in this study was also limited to 16 weeks for ethical considerations, consistent with clinical studies of other biologics (3,4); therefore, the efficacy and safety of secukinumab compared with the placebo were assessed in the short term only. All long-term analyses were exploratory with an inherent bias in favor of patients remaining in the study. In addition, the response rates observed in TNF-IR patients in this study should be viewed in the context of the relatively small number of TNF-IR patients and the heterogeneity of this subpopulation, which consists of patients who failed TNF inhibitor treatment for reasons including primary lack of efficacy, secondary lack of efficacy, intolerance, or contraindication.

In conclusion, the secukinumab 300 and 150 mg dosing regimens provided sustained improvements in the signs and symptoms of active AS with a favorable and consistent safety profile through 3 years of treatment. Improvements with secukinumab 300 mg were numerically higher compared with the 150-mg dose for higher hurdle efficacy end points and in TNF-IR patients.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual contact, and all authors approved the final version to be published. Dr. Pavelka had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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AVAILABILITY OF DATA AND MATERIAL

Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided are anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations. The trial data availability is according to the criteria and process described on www.clinicalstudydatarequest.com.

Trial details are available at: https://clinicaltrials.gov/ct2/show/NCT02008916,andhttps://www.clinicaltrialsregister.eu/ctr-search/search?query=2013-001090-24, and https://www.novctrd.com/CtrdWeb/searchbystudyid.nov?studyId=AIN457F2314.

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