ABSTRACT NUMBER: 2671

Subcutaneous Abatacept vs Adalimumab Head-to-Head Comparison in Adults with Early, Dual Seropositive Rheumatoid Arthritis, Positive for the Shared Epitope HLA Class II Risk Alleles, and an Inadequate Response to Methotrexate: Results from a Phase 3 Trial

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SESSION INFORMATION

Date: Tuesday, November 19, 2024

Session Type: Abstract Session

Title: Abstracts: RA – Treatment II: Refining Use of Established Therapies

Session Time: 11:00AM-12:30PM

Background/Purpose: For patients (pts) early in their RA disease course, with a clinical profile characterized by inadequate response to MTX (MTX-IR), high titers of ACPA (as measured by anti-CCP2 antibodies) and RF (dual seropositivity) combined with the presence of the shared epitope (SE) HLA risk allele may be predictive of an enhanced response to treatment (tx) with abatacept (ABA) compared with adalimumab (ADA).[1-3]

Methods: The AMPLIFIED trial is a phase 3, randomized, single-blind study evaluating the superiority of ABA compared with ADA in pts who met the ACR/EULAR 2010 criteria for RA (NCT04909801). Pts with (+) or without (−) the SE HLA class II risk alleles were enrolled (the study was powered for the SE+ subset). All pts were on stable background MTX (goal, 15–25 mg/week). No other prior DMARD use was allowed. The primary endpoint was 50% improvement in ACR criteria (ACR50) at week 24 in pts who were SE+. Secondary outcomes included DAS28 (CRP) < 2.6, antibody titers, and adverse events (AEs) at week 24. Post hoc analysis of results stratified by anti-CCP2 titers was performed. Additional analysis compared outcomes, including a range of patient-reported outcomes (PROs), between ABA and ADA tx in

the SE+ subgroup and total study population.

Results: A majority of the total study population (95.9%) completed the single-blind tx period (24 weeks). Baseline demographic and disease characteristics were balanced between tx groups (**Table 1**). Mean baseline anti-CCP2 titers were high and ~65% of pts were SE+. The study failed to meet the primary endpoint: ACR50 rate in the SE+ subset at week 24 was 59% with ABA and 60% with ADA; adjusted odds ratio (aOR; 95% CI): 1.0 (0.6–1.6); *P* = 0.9. The ACR50 rate across the study population was also comparable across txs (59% vs 64% with ABA vs ADA; aOR [95% CI]: 0.8 [0.5–1.3]). DAS28 (CRP) < 2.6 was 44% with ABA vs 47% with ADA; aOR (95% CI): 0.9 (0.5–1.5). ACR responses over time were comparable between the arms in onset and magnitude (**Figure**). PROs were similar between ADA and ABA in the SE+ subgroup and total population (**Table 2**). Mean decrease from baseline to week 24 in autoantibody titers was more notable with ABA vs ADA (anti-CCP2: −196 vs −109 U/mL; RF: −121 vs −27 IU/mL), while the change in CRP was comparable (−6.2 vs −5.7 mg/L) at week 24. Pts with the highest anti-CCP2 levels at baseline trended toward better tx response with ABA compared with ADA. Both drugs were well tolerated with comparable rates of AEs (ABA, 58.0%; ADA, 59.2%) and serious AEs (ABA, 2.4%; ADA, 3.6%). No serious infections were seen with ABA, with 3 seen with ADA. COVID-19 was seen in 12.7% of all pts (all mild). AEs of special interest were similar across ABA and ADA tx groups.

Conclusion: The AMPLIFIED trial failed to confirm the value of autoantibody and SE positivity for predicting response to tx with ABA vs ADA, seen in the prior pilot study.[3] Most pts with early RA tolerated and responded well to both ABA and ADA across all measures, including a broad range of PROs.

References

1. Weinblatt ME, et al. *Arthritis Rheum* 2013;65(1):28–38.
2. Sokolove J, et al. *Ann Rheum Dis* 2016;75(4):709–14.
3. Rigby W, et al. *Arthritis Res Ther* 2021;23:245.

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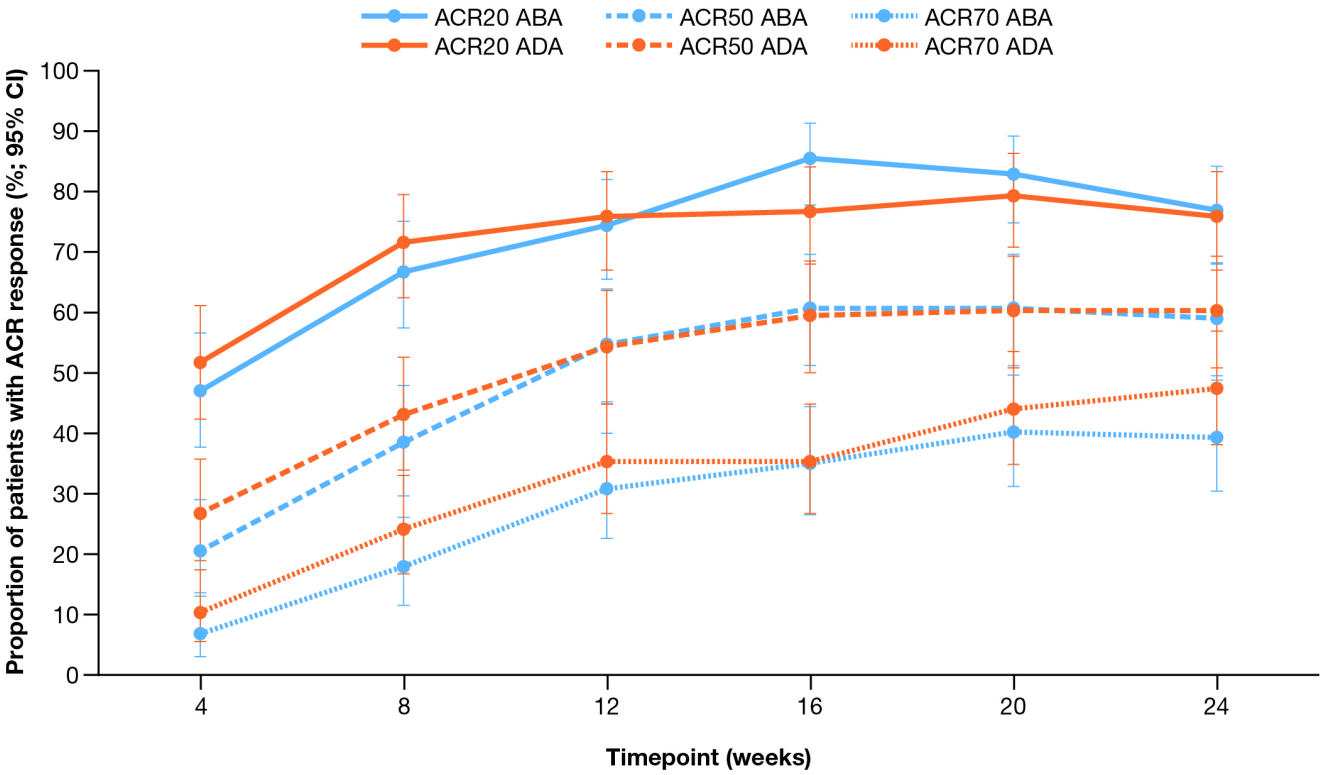
Table 1. Baseline demographics and disease characteristics for all study patients[a]

Variable	Total (N = 338)	Abatacept (n = 169)	Adalimumab (n = 169)
Age, years	48.4 (13.6)	49.3 (13.7)	47.4 (13.4)
Female, n (%)	268 (79.3)	130 (76.9)	138 (81.7)
Geographic region, n (%)			
North America	18 (5.3)	10 (5.9)	8 (4.7)
South America	172 (50.9)	89 (52.7)	83 (49.1)
Asia	36 (10.7)	15 (8.9)	21 (12.4)
Europe	103 (30.5)	51 (30.2)	52 (30.8)
Rest of world	9 (2.7)	4 (2.4)	5 (3.0)

Symptom duration, months	6.1 (2.8)	6.2 (2.7)	5.9 (2.9)
Concomitant glucocorticoid use, n (%)	132 (39.1)	69 (40.8)	63 (37.3)
DAS28 (CRP)	5.2 (1.0)	5.3 (1.0)	5.2 (1.0)
HAQ – Disability index	1.3 (0.7)	1.3 (0.7)	1.3 (0.7)
CRP, mg/L	13.1 (21.1)	12.3 (16.5)	13.8 (24.9)
SE+,[b] n (%)	220 (65.1)	112 (66.3)	108 (63.9)
Anti-CCP2, U/mL	827.1 (1337.3)	752.6 (1321.7)	901.5 (1352.6)
RF, IU/mL	280.4 (600.9)	275.2 (581.6)	285.7 (621.3)

All data are mean (standard deviation) unless otherwise stated.
[a]Modified intention-to-treat population.
[b]≥ 1 SE allele.
SE, shared epitope.

Figure. Proportion of patients with ACR response over time during the single-blind treatment period in the SE+ subset



ABA, abatacept; ACR20/50/70, 20%/50%/70% improvement in ACR criteria; ADA, adalimumab; SE, shared epitope.

Table 2. Adjusted mean change from baseline for PROs in the SE+ subgroup and total population treated with ABA and ADA at week 24

	SE+ subgroup (n=233)		Total population[a] (n=338)	
	Abatacept (n=117)	Adalimumab (n=116)	Abatacept (n=169)	Adalimumab (n=169)
ACR core components				
Patient global assessment (mm)	−39.6 (2.2)	−36.0 (2.3)	−39.1 (1.8)	−36.6 (1.8)
Patient assessment of pain (mm)	−40.9 (2.3)	−37.7 (2.3)	−39.5 (1.9)	−37.0 (1.9)
HAQ–Disability index	−0.9 (0.05)	−0.8 (0.05)	−0.8 (0.04)	−0.8 (0.04)

Work productivity and activity impairment component scores				
Absenteeism	−12.8 (2.8)	−10.2 (2.4)	−11.5 (2.0)	−9.2 (1.9)
Presenteeism	−37.5 (3.5)	−29.5 (3.1)	−34.8 (2.7)	−28.3 (2.5)
Work productivity loss	−27.0 (3.5)	−23.8 (3.0)	−28.3 (2.6)	−24.2 (2.4)
Activity impairment	−33.6 (2.6)	−32.6 (2.5)	−34.6 (2.1)	−33.7 (2.1)
FACIT-F score	9.1 (0.7)	8.6 (0.7)	8.9 (0.6)	8.6 (0.6)
Morning stiffness duration (mins)	−38.1 (2.9)	−34.8 (2.9)	−41.6 (2.4)	−40.0 (2.4)
SF-36 components (scores)				
Physical component summary	10.2 (0.7)	9.6 (0.7)	9.9 (0.6)	9.2 (0.6)
Mental component summary	8.4 (0.8)	7.3 (0.8)	7.6 (0.7)	7.7 (0.7)

All data are adjusted mean change from baseline (standard error).

[a]Total population is the modified intention-to-treat population.

ABA, abatacept; ADA, adalimumab; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; PRO, patient-reported outcome; SE, shared epitope; SF-36, Short-Form 36 health survey questionnaire.

Disclosures: M. Weinblatt: Abbive, 5, Abbvie, 2, Aclaris, 2, Amgen, 2, Aqtual, 2, 5, Bristol Myers Squibb, 2, 5, Canfite, 11, Glaxo Smith Kline, 2, Inmedix, 11, Janssen, 5, Johnson & Johnson, 2, Lilly, 2, Novartis, 2, Pfizer, 2, Prometheus, 2, Rani, 2, Revolo, 2, Sanofi, 2, Sci Rhom, 2, Scipher, 2, 11, Set Point, 2; **P. Emery**: AbbVie, 1, 12, Clinical trials, Activa, 1, AstraZeneca, 1, Boehringer Ingelheim, 1, Bristol Myers Squibb, 1, 12, Clinical trials, Galapagos, 1, Gilead, 1, Immunovant, 1, Janssen, 1, Lilly, 1, 12, Clinical trials, Novartis, 1, 1, 12, Clinical trials, 12, Clinical trials, Pfizer, 12, Clinical trials, Samsung, 12, Clinical trials; **V. Bykerk**: BMS, 5, Pfizer, 1; **A. Cope**: AbbVie, 6, Bristol-Myers Squibb, 2, 5, 6, GSK/ Galvini, 12, Data monitoring committee, Janssen, 2, 5, UCB, 2, 5; **G. Burmester**: AbbVie, 2, Amgen, 2, BMS, 2, Galapagos, 2, Lilly, 2, MSD, 2, Pfizer, 2, Sanofi, 2; **Y. Tanaka**: AbbVie, 6, Asahi-kasei, 6, Astellas, 6, AstraZeneca, 6, Boehringer Ingelheim, 5, 6, Chugai, 5, 6, Daiichi Sankyo, 6, Eisai, 6, Gilead, 6, GSK, 6, Lilly, 6, Pfizer, 6, Taisho, 5, 6, UCB, 6; **G. Citera**: AbbVie, 6, Bristol Myers Squibb, 1, 5, 6, Janssen, 1, 6, Pfizer, 6, Raffo, 6, Roche, 5, 6; **P. Nash**: Amgen, 1, 5, 6, Janssen, 1, 5, 6, Lilly, 1, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, UCB, 1, 5; **Q. Dornic**: Bristol Myers Squibb, 3; **S. Kelly**: Bristol Myers Squibb, 3; **M. Maldonado**: Bristol Myers Squibb, 3.

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