Bimekizumab impact on cardiovascular inflammation markers in moderate to severe plaque psoriasis: Results from phase 3 trials

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Objective

To assess the impact of bimekizumab (BKZ) on cardiovascular (CV) inflammation-associated markers vs placebo (PBO) or ustekinumab (UST) over 16 weeks in the phase 3 BE VIVID trial, or vs secukinumab (SEC) over 48 weeks in the phase 3b BE RADIANT trial.

Introduction

- High levels of inflammatory markers, such as neutrophil/lymphocyte ratio (NLR) and C-reactive protein (CRP) are observed in patients with psoriasis and are associated with poor CV outcomes.[1–3]
- Systemic anti-inflammatory therapies, including interleukin (IL)-17 blockade with SEC or BKZ and IL-12/23 blockade with UST, may reduce levels of CV inflammation-associated markers.[4,5] Consequently, such treatments may reduce mortality risk in patients with psoriasis.
- Dual inhibition of IL-17A and IL-17F with BKZ has shown efficacy in patients with moderate to severe plaque psoriasis.[6,7]

Methods

- Study designs for included trials have been reported previously.[6,7]
- In BE VIVID, patients were randomised to BKZ 320 mg every 4 weeks (Q4W), PBO to Week 16 followed by BKZ Q4W, or UST to Week 52.[6]
- In BE RADIANT, patients were randomised to BKZ 320 mg Q4W to Week 16 followed by BKZ Q4W or Q8W, or SEC 300 mg weekly to Week 4 then Q4W, to Week 48.[7]
- In BE RADIANT, NLR, CRP concentration, and triglyceride-glucose (TyG) index (another marker associated with increased risk of CV disease)[8] were assessed. In BE VIVID, NLR was assessed during the PBO-controlled period (to Week 16); CRP concentration and the components of the TyG index (triglyceride and glucose results, regardless of fasting status) were not systematically collected in BE VIVID.
- Median observed results are reported to Week 16 for BKZ Q4W-, PBO-, and UST-randomised patients from BE VIVID, and to Week 48 for BKZ- and SEC-randomised patients from BE RADIANT. For BE RADIANT, BKZ-randomised patients are presented as BKZ Total, the combined BKZ Q4W and Q8W maintenance doses. Patients are grouped by baseline CRP level (overall, CRP <5mg/L, CRP ≥5 mg/L).
- Data are reported as observed case (OC).

Results

- In BE VIVID, median baseline neutrophil and lymphocyte concentrations were similar for BKZ Q4W-, UST-, and PBO-randomised patients (**Table 1**).
- At Week 16, median NLR was reduced from baseline with BKZ Q4W and UST, and was lower with BKZ Q4W and UST vs PBO (**Figure 1**).
- In BE RADIANT, median baseline neutrophil and lymphocyte concentrations were also similar for BKZ- and SEC-randomised patients (**Table 2**).
- Median NLR was reduced at Week 16 vs baseline with BKZ and SEC (**Figure 2A**), and was comparable with BKZ vs SEC at baseline and Week 16.
  - These results were maintained to Week 48 (**Figure 2A**).
  - Similar reductions in NLR from baseline to Week 16 were observed in subgroups of patients with baseline CRP <5 mg/L and CRP ≥5 mg/L, with both BKZ and SEC (**Figure 2B**).
- Median CRP concentrations were reduced at Week 16 vs baseline with BKZ and SEC (**Figure 3A**). Week 16 CRP was comparable with BKZ vs SEC.
  - These results were also maintained to Week 48 (**Figure 3A**).
  - In patients with baseline CRP ≥5 mg/L there was a large reduction in CRP concentration to Week 16 which was maintained to Week 48 (**Figure 3B**).
  - CRP concentration remained stable from baseline to Week 48 in patients with baseline CRP <5 mg/L (**Figure 3B**).
- The TyG index remained stable over 48 weeks in BKZ- and SEC-treated patients, both overall and in baseline CRP subgroups (**Figure 4**).

Conclusions

BKZ treatment was associated with rapid, stable reductions in CV inflammation-associated biomarkers. At Week 16, NLR was reduced with BKZ vs PBO, and NLR and CRP concentrations were reduced vs baseline, particularly in patients with high CRP at baseline. Both markers remained stable through 1 year of BKZ treatment. TyG index remained stable from baseline to 1 year. Where active comparisons were available, BKZ showed the same trends as SEC and UST.

Summary

Inflammation-associated biomarkers

Three inflammatory markers associated with increased risk of cardiovascular disease were examined

CRP: C-reactive protein

Liver protein that rises in response to inflammation[3]

With BKZ:
Reduced at Week 16
Remained stable to Week 48

NLR: Neutrophil/lymphocyte ratio

Neutrophil count / Lymphocyte count = Increase in proinflammatory neutrophils = NLR increase[1]

With BKZ:
Reduced at Week 16
Remained stable to Week 48

TyG index: Triglyceride-glucose index

Surrogate indicator for insulin resistance, which can cause cardiovascular disease[8]

With BKZ:
Remained stable from baseline to Week 48

Table 1 Median observed neutrophil and lymphocyte concentrations in BE VIVID (OC)

	Median observed neutrophil concentration, 10^9/L (n)			Median observed lymphocyte concentration, 10^9/L (n)		
	BKZ Q4W N=321	PBO N=83	UST N=163	BKZ Q4W N=321	PBO N=83	UST N=163
Baseline	4.40 (321)	4.35 (83)	4.50 (163)	1.72 (321)	1.71 (83)	1.78 (163)
Week 16	3.70 (306)	4.00 (74)	3.98 (156)	1.78 (306)	1.67 (74)	1.82 (156)

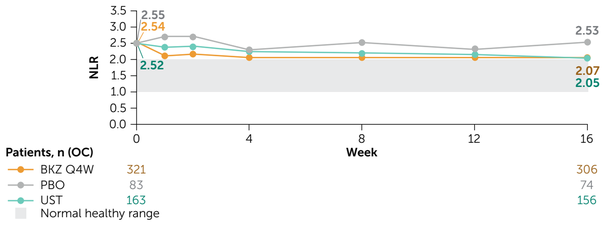
Data presented are for all patients who were randomised at baseline.

Table 2 Median observed neutrophil and lymphocyte concentrations in BE RADIANT (OC)

	Median observed neutrophil concentration, 10^9/L (n)		Median observed lymphocyte concentration, 10^9/L (n)	
	BKZ Total N=373	SEC N=370	BKZ Total N=373	SEC N=370
Baseline	4.57 (373)	4.42 (370)	1.81 (373)	1.88 (370)
Week 16	3.90 (360)	3.87 (352)	1.83 (360)	1.91 (352)
Week 32	3.97 (345)	3.96 (332)	1.83 (345)	1.94 (332)
Week 48	4.08 (337)	4.01 (314)	1.82 (337)	1.94 (314)

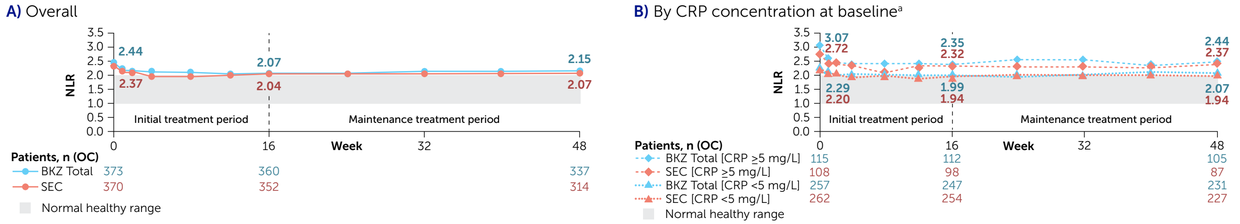
Data presented are for all patients who were randomised at baseline.

Figure 1 Median observed NLR over 16 weeks in BE VIVID (OC)



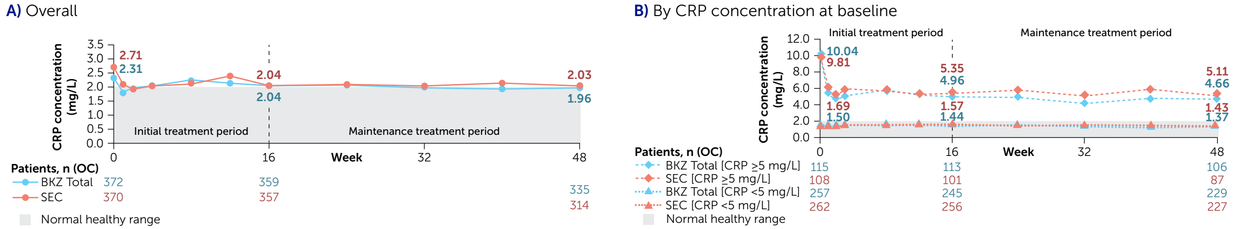
Data are presented by initial randomisation group. Grey shaded region indicates the normal healthy range of NLR values.[9]

Figure 2 Median observed NLR over 48 weeks in BE RADIANT (OC)



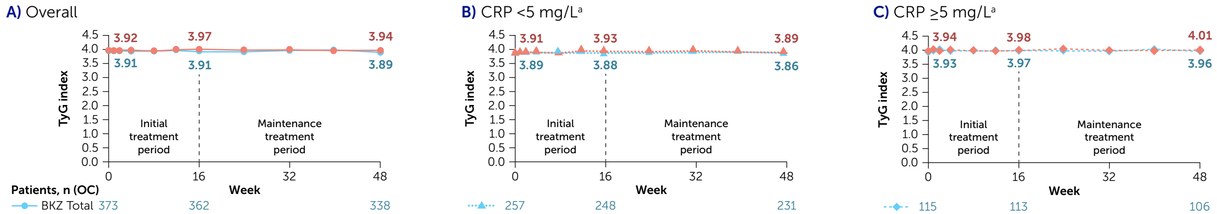
Data presented are for all patients who were randomised at baseline. Grey shaded regions indicate the normal healthy range of NLR values.[9] [a]No numeric CRP concentration at baseline for one patient; this patient was excluded from the final data set.

Figure 3 Median observed CRP concentration over 48 weeks in BE RADIANT (OC)



Data presented are for all patients who were randomised at baseline. Grey shaded regions indicate the normal healthy range of CRP values.[10] No numeric CRP concentration at baseline for one patient; this patient was excluded from the final data set.

Figure 4 Median observed TyG index over 48 weeks in BE RADIANT (OC)



The TyG index was calculated using triglyceride and glucose measurements, regardless of fasting status. Patients with TyG index values above 4.5 are likely to suffer from insulin resistance (cut-off based on fasting measurements).[11] [a]No numeric CRP concentration at baseline for one patient; this patient was excluded from the final data set.

BKZ: bimekizumab; **CRP:** C-reactive protein; **CV:** cardiovascular; **IL:** interleukin; **NLR:** neutrophil/lymphocyte ratio; **OC:** observed case; **PBO:** placebo; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SEC:** secukinumab; **TyG:** triglyceride-glucose index; **UST:** ustekinumab.

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References: [1]Angkananard T et al. Biomed Res Int 2018;2703518; [2]Løfblad L et al. Sci Rep 2021;11:15644; [3]Aktaş Karabay E et al. Ann Dermatol 2019;31:601–10; [4]Terui H & Asano Y. J Clin Med 2023;12:1162; [5]Benson JM et al. mAbs 2011;3:535–45; [6]Reich K et al. Lancet 2021;397:487–98, NCT03370133; [7]Reich K et al. N Engl J Med 2021;385:142–52, NCT03536884; [8]Li S et al. Sci Rep 2019;9:7320; [9]Zahorec R. Bratisl Lek Listy 2021;122:474–88; [10]Ansar W & Ghosh S. Immunol Biol 2013;218:131–42; [11]Salazar J et al. F1000Res 2018;6:1337. **Author Contributions:** Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: **RBW**, **RGL**, **GK**, **BK**, **JGK**, **KE**, **LD**, **OD**, **NC**, **DD**, **BS**; Drafting of the publication, or reviewing it critically for important intellectual content: **RBW**, **RGL**, **GK**, **BK**, **JGK**, **KE**, **LD**, **OD**, **NC**, **DD**, **BS**; Final approval of the publication: **RBW**, **RGL**, **GK**, **BK**, **JGK**, **KE**, **LD**, **OD**, **NC**, **DD**, **BS**. **Author Disclosures: RBW:** Consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, GSK, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma; research grants to his institution from AbbVie, Almirall, Janssen, LEO Pharma, Novartis, and UCB Pharma; honoraria from Astellas, DiCE, GSK, and Union Therapeutics. **RGL:** Principal investigator for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, and UCB Pharma; served on scientific advisory boards for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, Pfizer, and UCB Pharma; provided lectures for AbbVie, Amgen, Celgene, Eli Lilly, LEO Pharma, Merck, Novartis, and Pfizer. **GK:** Received travel grants or honoraria, or has been a consultant member of advisory boards and speaker bureaus or has served as investigator for AbbVie, Actelion, Almirall, Amgen, Baslea, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Hexal-Sandoz, Janssen-Cilag, LEO Pharma, MSD, Novartis, Pfizer, Sanofi, and UCB Pharma. **BK:** Received research support from or been a principal investigator (clinical trials) for AbbVie, Almirall, Janssen, Merck, MoonLake, Novartis, Pfizer, and UCB Pharma; has been a consultant for AbbVie, Almirall, Celgene, Janssen, Merck, MoonLake, Novartis, Pfizer, and UCB Pharma; has received honoraria from AbbVie, Almirall, Celgene, Eli Lilly, Janssen, MoonLake, Novartis, Pfizer, and UCB Pharma; and has been on scientific advisory boards for AbbVie, Almirall, Celgene, Eli Lilly, Janssen, MoonLake, Novartis, Pfizer, and UCB Pharma. **JGK:** Grants paid to institution from AbbVie, Amgen, Akros, Allergan, Avillion, Biogen MA, Boehringer Ingelheim, Botanix, Bristol Myers Squibb, Celgene, Eli Lilly, Exicure, Incytem, Innovaderm, Janssen, LEO Pharma, Novan, Novartis, Paraxel, Pfizer, Regeneron, Sienna, UCB Pharma, and Vitae; personal fees from AbbVie, Aclaris, Allergan, Almirall, Amgen, Arena, Aristea, Asana, Aurigne, BiogenIdec, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Escalier, Galapagos, LEO Pharma, Menlo, Nimbus, Novartis, Pfizer, Sanofi, Sienna, Sun Pharma, UCB Pharma, Valeant, and Ventyx Biosciences. **KE:** Speaker and/or advisor for AbbVie, Almirall, Bristol Myers Squibb, Boehringer Ingelheim, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB Pharma. **LD**, **OD**, **NC**, **DD:** Employees and shareholders of UCB Pharma. **BS:** Consultant (honoraria) for AbbVie, Alamar, Alumis, Almirall, Amgen, Arcutis, Arena, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Capital One, Connect Biopharma, CorEvitas, Dermavant, Eli Lilly, Evelo Biosciences, Immunic Therapeutics, Janssen, Kangpu Pharmaceuticals, LEO Pharma, Maruho, Meiji Seika Pharma, Mindera Health, Monte Carlo, Novartis, Pfizer, Protagonist Therapeutics, Regeneron, Sanofi-Genzyme, Sun Pharma, Takeda/Nimbus, UCB Pharma, Union Therapeutics, VentyxBio, and vTv Therapeutics; stock options from Connect Biopharma and Mindera Health; speaker for AbbVie, Arcutis, Dermavant, Eli Lilly, Incyte, Janssen, Regeneron, and Sanofi-Genzyme; scientific co-director (consulting fee) for CorEvitas Psoriasis Registry; editor-in-chief (honorarium) for Journal of Psoriasis, and Psoriatic Arthritis.

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