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Bimekizumab impact on clinical markers of liver fibrosis and key liver parameters in patients with moderate to severe plaque psoriasis: Long-term pooled data from BE BRIGHT

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Objective

To assess the impact of bimekizumab (BKZ) treatment on clinical markers of liver fibrosis and key liver parameters over 4 years, in patients with moderate to severe psoriasis and high or low risk of liver fibrosis.

Introduction

- Patients with psoriasis are at an increased risk of liver fibrosis.[1]
- Reports suggest treatments which inhibit interleukin (IL)-17F and IL-17A may reduce this risk.[2,3]
- BKZ, a monoclonal IgG1 antibody that selectively inhibits IL-17F and IL-17A,[4] has demonstrated rapid and superior efficacy in the treatment of patients with moderate to severe plaque psoriasis in head-to-head studies versus ustekinumab, adalimumab, and secukinumab, with established long-term durability of response.[5–8]
- It has been reported that clinical markers of liver fibrosis, and mean levels of the key liver enzymes alanine transaminase (ALT) and aspartate transaminase (AST), did not increase over 2 years of BKZ treatment.[10]

Methods

- Data were pooled from the 52-week BE VIVID, and 56-week BE SURE and BE READY phase 3 trials, and their open-label extension (OLE) BE BRIGHT.[6–9]
- Included patients were randomised to BKZ 320 mg every 4 weeks (Q4W) to Week 16, received BKZ Q4W or every 8 weeks (Q8W) thereafter and entered the OLE.
- Data are reported for BKZ dose groups combined (BKZ Total).
- Patients were grouped according to liver fibrosis severity at baseline, estimated using the non-invasive Fibrosis-4 Index (FIB-4, <1.3 [low risk of liver fibrosis] and >1.659 [high risk of liver fibrosis]) and the Aspartate transaminase to Platelet Ratio Index (APRI, <0.5 [absence of advanced fibrosis] and ≥0.5 [presence of advanced fibrosis]).[10]
- Mean FIB-4 and APRI scores, and mean ALT, AST, and platelet levels, are reported through 4 years (Week 196) by baseline liver fibrosis risk.

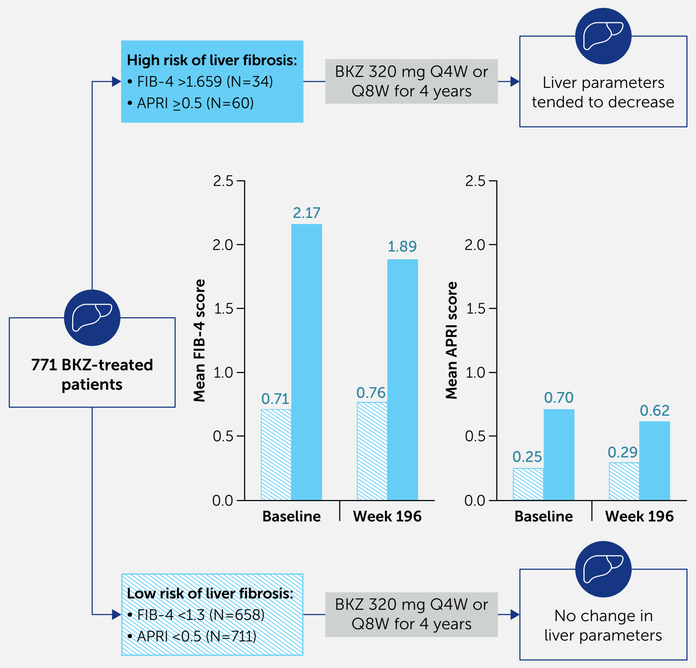
Results

- Overall, 771 patients received continuous BKZ and entered the OLE.
- Baseline characteristics of patient groups by FIB-4 and APRI scores at baseline are reported in **Table 1**.
- Mean FIB-4 scores tended to decrease in high-risk patients, and remained stable in low-risk patients:
  - In patients with high baseline liver fibrosis risk (FIB-4 >1.659; N=34), FIB-4 scores (mean ± standard deviation [SD]) trended towards a decrease from baseline (2.17 ± 0.45) until Year 4 (1.89 ± 0.76) (**Figure 1A**).
  - In patients with low baseline fibrosis risk (FIB-4 <1.3; N=658), mean FIB-4 scores remained consistent from baseline (0.71 ± 0.26) to Year 4 (0.76 ± 0.34) (**Figure 1A**).
- Similar trends were observed for mean ALT and AST levels, whilst mean platelet counts remained consistent over 4 years in both risk groups (**Figures 1B–D**).
- Mean APRI scores tended to decrease in high-risk patients, and remained stable in low-risk patients:
  - In patients with advanced fibrosis at baseline (APRI ≥0.5, N=60), mean APRI scores trended towards a decrease from baseline (0.70 ± 0.26) to Week 16 (0.56 ± 0.31) and remained consistent to Year 4 (0.62 ± 0.61) (**Figure 2**).
  - In patients without advanced fibrosis at baseline (APRI <0.5; N=711), mean APRI scores remained consistent from baseline (0.25 ± 0.09) to Year 4 (0.29 ± 0.14) (**Figure 2**).

Conclusions

These results suggest bimekizumab does not increase the risk of liver fibrosis in patients with psoriasis and a high baseline risk of liver fibrosis. However, these findings are based on a limited number of high-risk patients; further prospective research (including alternative assessments such as stiffness assessment by transient elastography) is needed to fully understand any potential preventative benefit of inhibition of IL-17A and IL-17F with bimekizumab in these patients.

Summary



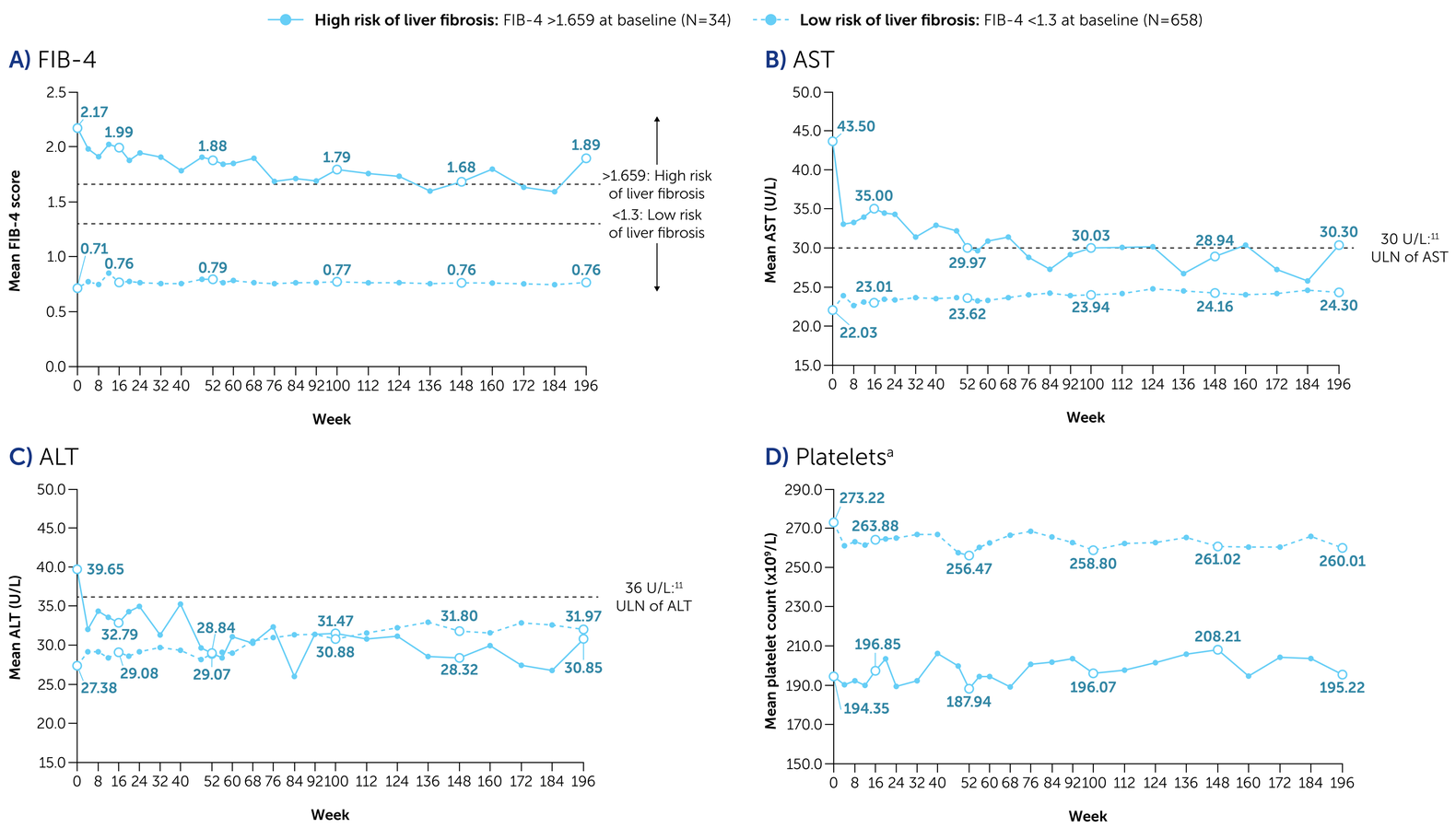
Mean clinical markers of liver fibrosis, **FIB-4** and **APRI scores**, trended towards a **reduction** over 4 years in bimekizumab-treated patients with **high risk of liver fibrosis** at baseline, and **remained consistent** in those with **low risk of liver fibrosis** at baseline.

Table 1 Baseline characteristics

	BKZ Total		BKZ Total	
	High risk of liver fibrosis: FIB-4 >1.659 N=34	Low risk of liver fibrosis: FIB-4 <1.3 N=658	Presence of advanced liver fibrosis: APRI ≥0.5 N=60	Absence of advanced liver fibrosis: APRI <0.5 N=711
Age (years), mean ± SD	60.8 ± 8.3	42.9 ± 12.3	47.1 ± 11.9	45.3 ± 13.6
Sex, male, n (%)	23 (67.6)	470 (71.4)	46 (76.7)	504 (70.9)
Racial group, white, n (%)	32 (94.1)	555 (84.3)	56 (93.3)	600 (84.4)
Weight (kg), mean ± SD	86.5 ± 18.4	89.6 ± 21.6	97.8 ± 19.1	89.0 ± 21.3
Disease duration (years), mean ± SD	24.1 ± 16.1	18.0 ± 11.9	18.4 ± 13.9	18.6 ± 12.6
PASI, mean ± SD	19.8 ± 7.3	21.4 ± 7.8	19.9 ± 7.7	21.2 ± 7.6
BSA (%), mean ± SD	23.9 ± 12.5	27.7 ± 16.1	22.8 ± 13.2	27.4 ± 15.7
IGA,[a] n (%)				
3: moderate	30 (88.2)	422 (64.1)	47 (78.3)	461 (64.8)
4: severe	4 (11.8)	235 (35.7)	13 (21.7)	249 (35.0)
DLQI total, mean ± SD	8.8 ± 5.2	10.5 ± 6.3	10.6 ± 6.1	10.5 ± 6.3
Any prior systemic therapy, n (%)	29 (85.3)	526 (79.9)	43 (71.7)	575 (80.9)
Any prior biologic therapy, n (%)	11 (32.4)	253 (38.4)	22 (36.7)	287 (40.4)
Anti-TNF	2 (5.9)	95 (14.4)	6 (10.0)	107 (15.0)
Anti-IL-17	8 (23.5)	154 (23.4)	16 (26.7)	177 (24.9)
Anti-IL-23	1 (2.9)	32 (4.9)	2 (3.3)	35 (4.9)
Anti-IL-12/23	1 (2.9)	37 (5.6)	4 (6.7)	39 (5.5)
Liver parameters, mean ± SD				
FIB-4	2.2 ± 0.4	0.7 ± 0.3	1.5 ± 0.7	0.8 ± 0.4
APRI	0.7 ± 0.4	0.3 ± 0.1	0.7 ± 0.3	0.3 ± 0.1
ALT (U/L)	39.7 ± 30.6	27.4 ± 17.5	63.0 ± 27.7	25.2 ± 14.0
AST (U/L)	43.5 ± 26.9	22.0 ± 8.4	50.3 ± 19.1	21.5 ± 7.1
Platelets (x10^9/L)	194.4 ± 33.4	273.2 ± 64.5	212.5 ± 43.9	268.8 ± 65.0

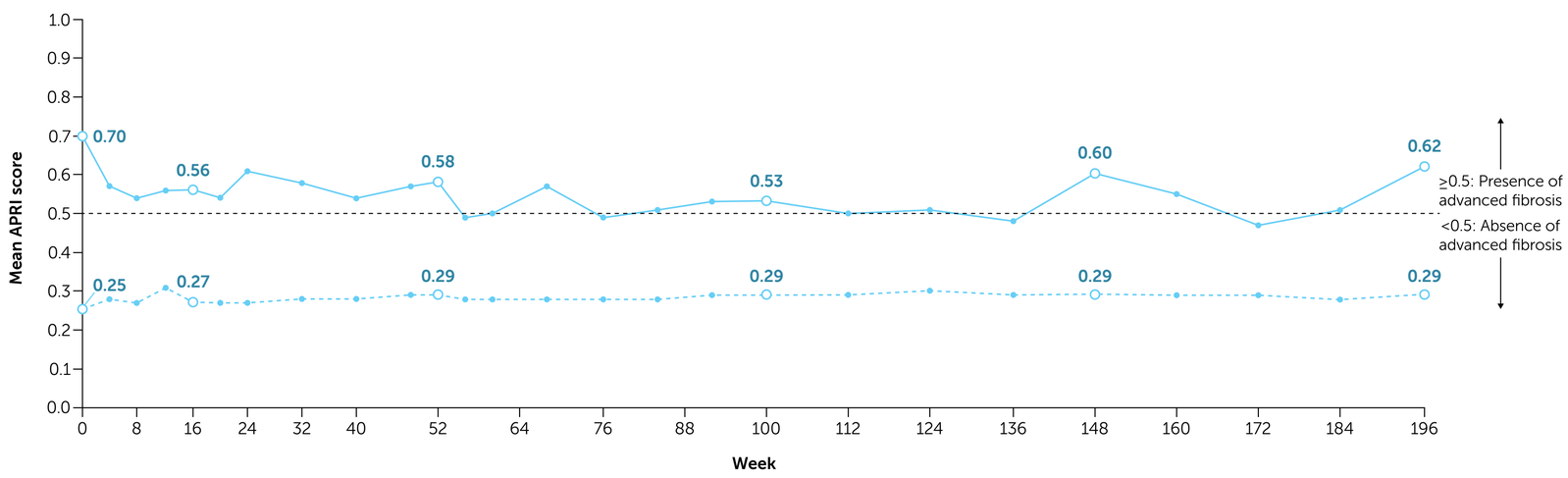
Included patients were randomised to BKZ at baseline and continued to receive BKZ in the maintenance period and OLE.
[a] One patient in the FIB-4 <1.3 and APRI <0.5 groups had an IGA score of 2.

Figure 1 Change in mean clinical markers of liver fibrosis and key liver parameters over 4 years by risk of liver fibrosis (defined by FIB-4 at baseline)



BE VIVID lasted 52 weeks and BE SURE and BE READY lasted 56 weeks; to pool data across studies, Week 52 data presented here are from the Week 52 assessment in BE VIVID and the Week 56 assessment in BE SURE and BE READY, respectively. Data presented after Week 52 are from the BE BRIGHT OLE. Normal reference ranges for liver function tests (represented by the dotted lines) and platelets may vary depending on laboratory and patient characteristics (such as sex and body mass index [BMI]).[11,12] **[a]** Mean platelet counts were within the normal reference range.[12]

Figure 2 Change in mean APRI over 4 years by presence of liver fibrosis (defined by APRI at baseline)



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ALT: alanine transaminase; **APRI:** Aspartate transaminase to Platelet Ratio Index; **AST:** aspartate transaminase; **BKZ:** bimekizumab; **BSA:** body surface area; **BMI:** body mass index; **DLQI:** Dermatology Life Quality Index; **FIB-4:** Fibrosis-4 Index; **IGA:** Investigator's Global Assessment; **IL:** interleukin; **OLE:** open-label extension; **PASI:** Psoriasis Area Severity Index; **Q4W:** every 4 weeks; **Q8W:** every 8 weeks; **SD:** standard deviation; **TNF:** tumour necrosis factor; **U/L:** units per litre; **ULN:** upper limit of normal.

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