Dual neutralization of IL-17A and IL-17F with bimekizumab improves quality of life in patients with moderate-to-severe plaque psoriasis: results from a Phase 2b study and correlation with clinical response

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37th FCD Conference
18–21 October 2018
Las Vegas, NV, USA

Synopsis

- IL-17A and IL-17F are pro-inflammatory cytokines that share ~50% structural homology and overlapping biological function.[1–3] Both IL-17A and IL-17F are expressed at sites of inflammation[4,5] and independently co-operate with other cytokines to mediate inflammation[4] (**Figure 1**)
- Dual neutralization of IL-17A and IL-17F in disease-relevant human cellular systems resulted in lower expression of inflammation-linked genes and pro-inflammatory cytokines as well as greater suppression of immune cell migration when compared with IL-17A blockade alone[4]
- Bimekizumab, a monoclonal IgG1 antibody, potently and selectively neutralizes the biological function of both IL-17A and IL-17F[4,6,7]

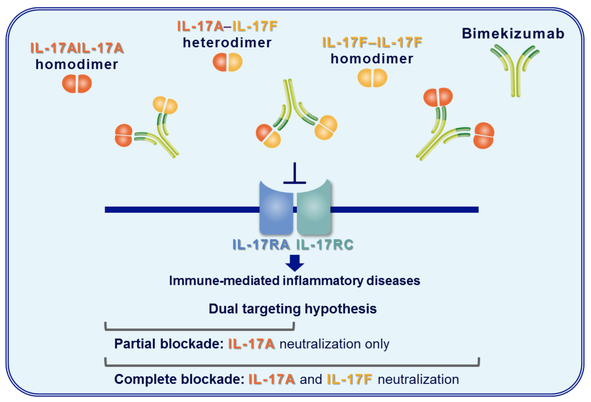

Figure 1. Dual neutralization of IL-17A and IL-17F in immune-mediated inflammatory diseases

BE ABLE 1: summary of key results

- In this Phase 2b, double-blind, placebo-controlled study (NCT02905006), patients with moderate-to-severe plaque psoriasis were randomized (1:1:1:1:1:1) to receive bimekizumab 64 mg, 160 mg, 160 mg with 320 mg loading dose, 320 mg, 480 mg, or placebo every 4 weeks for 12 weeks; the primary objective was to evaluate the dose response of bimekizumab[7]
- There was a significant dose response for Psoriasis Area Severity Index (PASI)90 (P<0.0001) at Week 12. The primary endpoint, PASI90 at Week 12, was achieved by significantly more patients receiving each bimekizumab dose compared with placebo (**Figure 2A**)[7]
- Up to 60.0% of bimekizumab-treated patients achieved complete skin clearance (PASI100) at Week 12 (**Figure 2B**)[7]
- The safety profile of bimekizumab was consistent with previous studies[4,5] with no unexpected safety findings[7]

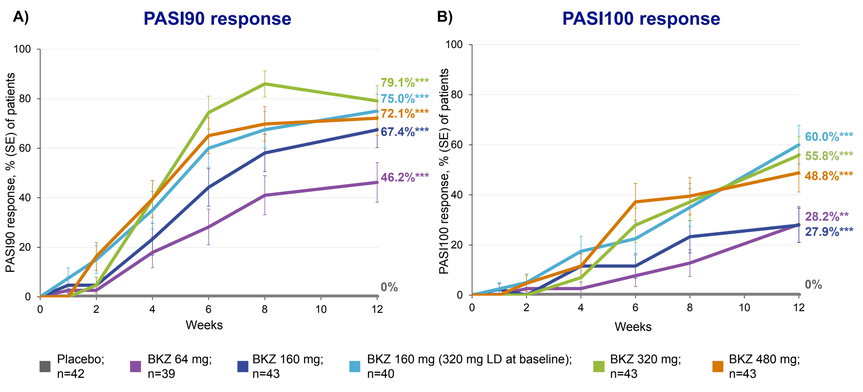

Figure 2A. PASI90 response over time[7]; **Figure 2B.** PASI100 response over time[7], full analysis set (non-responder imputation); **p<0.001, ***p<0.0001 versus placebo (Fisher's exact test); note: no patients receiving placebo achieved PASI90 or PASI100 at any time point; SE, standard error

Objective

To evaluate disease-specific health-related qualify of life (HRQoL) data from the Phase 2b study[7] and its correlation with the absolute PASI and Body Surface Area (BSA) affected

Methods

- Patients completed the Dermatology Life Quality Index (DLQI) questionnaire at baseline, Week 1, Week 2, Week 4, Week 8 and Week 12
- DLQI of 0 or 1 was used to indicate no impact of psoriasis on disease-specific HRQoL; minimal clinically important difference (MCID) was defined as 4-point reduction in DLQI from baseline
- Patients were grouped by absolute PASI (≤1, >1–≤2, >2–≤5, >5) and BSA affected by psoriasis (≤1%; >1–≤3%, >3–≤5%, >5%) to evaluate a possible correlation between clinical response and achievement of DLQI 0 or 1
- Patient demographics and baseline disease characteristics were balanced across treatment groups (mean [SD] DLQI total: 10.7 [6.9]; PASI: 19.1 [6.5]; percentage BSA involvement: 25.1 [13.3])[7]

Results

At the individual patient level, rapid improvements were observed in absolute PASI over time for those receiving bimekizumab. By Week 12, in the three highest bimekizumab dose groups almost all patients had an absolute PASI <2 with the majority of patients at or near zero (Figure 3); PASI improvements were correlated with reductions in DLQI, with the majority of patients achieving a DLQI of 0 or 1 (no impact of psoriasis on disease-specific HRQoL) at Week 12 (Figure 3)

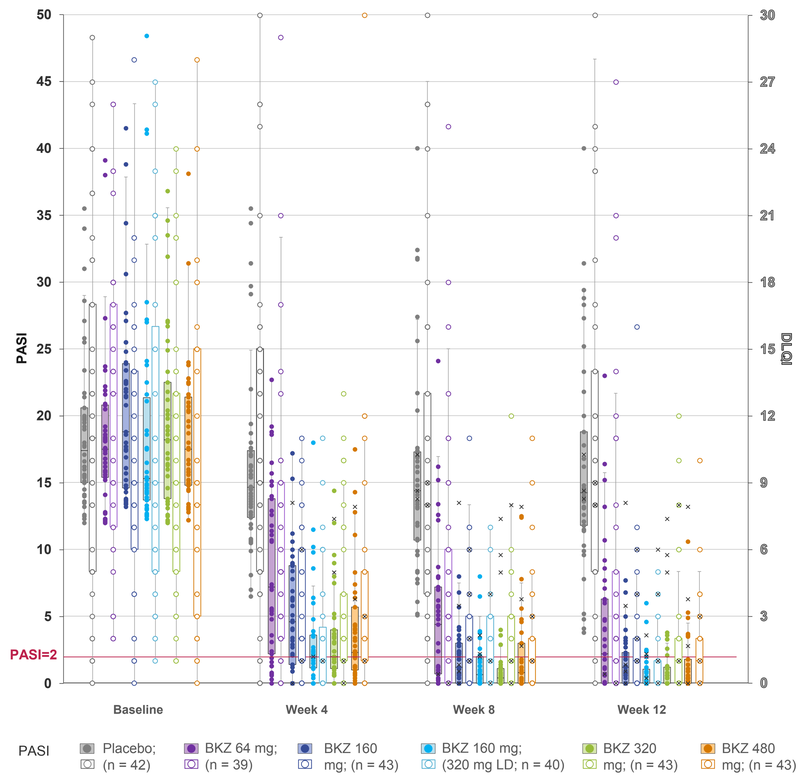

Figure 3. Absolute PASI and DLQI over time (patient-level data); x missing data imputed as last observation carried forward; box plots are first quartile, median and third quartile. Whiskers extend to ±1.5 times the interquartile range. Where the whisker value exceeded the data range, the maximum or minimum value was used, as appropriate

All or nearly all patients with baseline DLQI ≥4 achieved MCID in DLQI at Week 12 in the top three bimekizumab dose groups; 3x MCID and 4x MCID were also achieved by a substantially greater percentage of bimekizumab patients with baseline DLQI ≥12 and ≥16, respectively, compared with placebo (Figure 4A). MCID in DLQI was achieved rapidly and differentiated from placebo after first dose across all bimekizumab groups (Figure 4B)

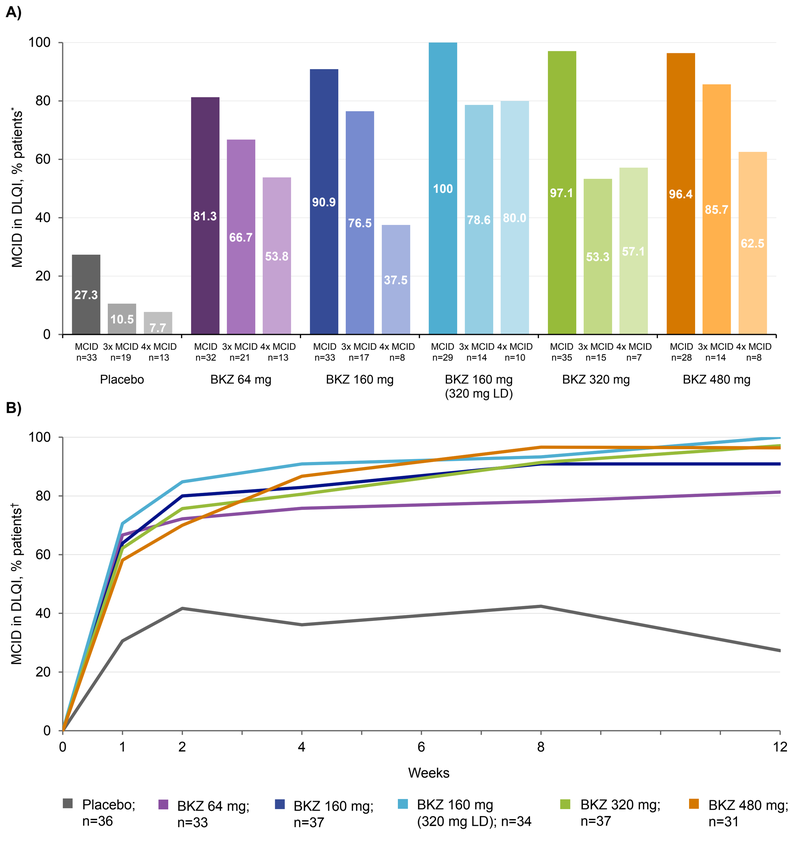

Figure 4A. MCID, 3x MCID and 4x MCID in DLQI at Week 12; **Figure 4B.** MCID in DLQI by visit in patients with baseline DLQI ≥4, full analysis set (observed values); *percentages calculated based on total numbers of evaluable patients at Week 12; †percentages calculated based on total numbers of evaluable patients at each visit

In the pooled bimekizumab group, patients with lower absolute PASI (≤2) more frequently achieved DLQI of 0 or 1 versus those with higher absolute PASI at Week 12 (Figure 5A); similar results were observed at Week 12 in patients with lower BSA versus higher BSA involvement (Figure 5B)

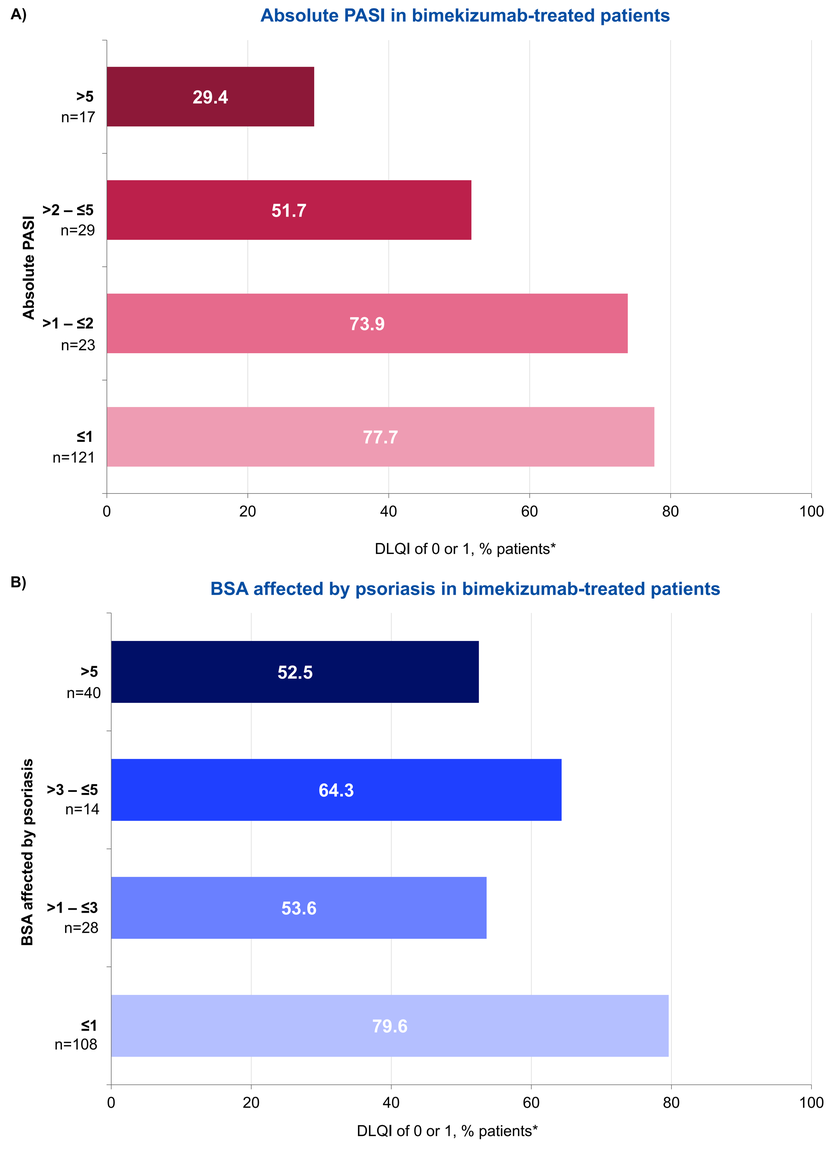

Figure 5A. DLQI of 0 or 1 by absolute PASI at Week 12; **Figure 5B.** DLQI of 0 or 1 by BSA affected by psoriasis at Week 12; combined bimekizumab dose group, full analysis set (observed values); *percentages calculated based on total numbers of evaluable patients at Week 12

Conclusion

- **Dual neutralization of IL-17A and IL-17F with bimekizumab in patients with moderate-to-severe plaque psoriasis was associated with rapid onset of clinically meaningful efficacy, with no unexpected safety findings**
- **Bimekizumab treatment also resulted in rapid improvements in disease-specific quality of life measures in the majority of patients, which correlated with clinical response**
- **These data support achievement of high levels of skin clearance (absolute PASI ≤2) being associated with superior improvements in disease-specific HRQoL**

References

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Disclosures, funding, and acknowledgements

This study was funded by UCB Pharma

KA Papp has received consultant fees from Astellas, AstraZeneca, Baxalta, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, CanFite, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Forward Pharma, Galderma, Genentech, Janssen, Kyowa Hakko Kirin, LEO Pharma, Meiji, Seika Pharma, MSD, Merck Serono, Mitsubishi Pharma, Novartis, Pfizer, Regeneron, Roche, Sanofi/Genzyme, Takeda, UCB, and Valeant; investigator fees from Astellas, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Galderma, Genentech, GSK, Janssen, Kyowa Hakko Kirin, LEO Pharma, MedImmune, MSD, Merck-Serono, Novartis, Pfizer, Regeneron, Roche, Sanofi/Genzyme, Takeda, UCB, and Valeant; speaker fees from Astellas, Celgene, Eli Lilly, Galderma, Kyowa Hakko Kirin, LEO Pharma, MSD, Novartis, Pfizer, and Valeant; has participated in advisory boards for Astellas, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galderma, Janssen, MSD, Novartis, Pfizer, Regeneron, Sanofi/Genzyme, UCB, and Valeant; is a steering committee member for Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Kyowa Hakko Kirin, MSD, Merck-Serono, Novartis, Pfizer, Regeneron, Sanofi/Genzyme, and Valeant; and is a scientific officer for Kyowa Hakko Kirin. **JF Merola** has received honoraria from AbbVie, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, Samumed and UCB. **AB Gottlieb** has received consultant fees, advisory board fees or speaker bureau fees from Janssen Inc.; Celgene Corp., Bristol Myers Squibb Co., Beiersdorf, Inc., Abbvie, UCB, Novartis, Incyte, Lilly, Reddy Labs, Valeant, Dermira, Allergan, Sun Pharmaceutical Industries; and research grants from Janssen, Incyte, Lilly, Novartis, Allergan, LEO. **CEM Griffiths** has received grants and personal fees from AbbVie, Celgene, LEO, Lilly, Janssen, Novartis, Pfizer, and UCB Pharma; grants from Sandoz; personal fees from Almirall and Galderma. CG has received research grants from AbbVie, Celgene, Novartis, Eli Lilly, Janssen, Sandoz, Pfizer, LEO, and UCB. **KK Harris**, **N Cross**, **L Peterson** and **C Cioffi** are employees of UCB. **L Peterson** and **C Cioffi** hold UCB stock or stock options. **A Blauvelt** has received consultant fees from Eli Lilly and Company, Janssen, Regeneron, and Sanofi Genzyme; and a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Allergan, Almirall, Amgen, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Inc., Eli Lilly and Company, Genentech/Roche, GlaxoSmithKline, Janssen, Leo, Merck Sharp & Dohme, Novartis, Pfizer, Purdue Pharma, Regeneron, Sandoz, Sanofi Genzyme, Sienna Pharmaceuticals, Sun Pharma, UCB Pharma, Valeant, and Vidac.

The authors would like to acknowledge Alexandra Webster, MSc, of iMed Comms, an Ashfield Company, for medical writing support that was funded by UCB Pharma in accordance with Good Publication Practice (GPP3) guidelines.