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One-Year Pharmacovigilance Update of Brodalumab

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Efficacy and safety of brodalumab, a fully human anti–interleukin-17 receptor A monoclonal antibody, have been demonstrated in one phase 2 and three phase 3 trials (AMAGINE-1/-2/-3).[1-3] Here, we report an update of brodalumab 1-year pharmacovigilance in the United States (August 15, 2017–August 14, 2018). Observational data reported to Ortho Dermatologics were collected for 826 US patients who received brodalumab within the first 12 months of US Food and Drug Administration approval. Adverse events (AEs) were reported through pharmacovigilance reporting from healthcare providers and patients. AEs were categorized by Medical Dictionary for Regulatory Activities preferred term and system organ class, seriousness, and (company-determined) causality. Brodalumab exposure was estimated by first shipment date to last dose date plus 55 days (ie, 5 half-lives of brodalumab). This calculation may be an underestimation considering these data were derived from a subset of 13 contracted pharmacies. AEs were summarized with descriptive statistics and as exposure-adjusted rates per patient-year (PY).

There were no reports of completed suicides or suicide attempts, major adverse cardiac events, new-onset ulcerative colitis, or new-onset Crohn's disease. Most commonly reported AEs were psoriasis flare, drug ineffectiveness, arthralgia, depression, diarrhea, and pain (Table 1). Reports did not describe therapies patients were transitioning from or duration of time from last therapy to brodalumab initiation. Approximately 78.3% of the cases were reported by non–healthcare provider reporters. For psoriasis flare and drug ineffectiveness, 73% and 72% of AEs, respectively, were patient reported (information was incomplete with regard to prior therapies or length of time on brodalumab).

No reported depression events were serious. Among 11 patients reporting depression, 4 discontinued brodalumab, and 2 had a history of depression (mental health history was not provided in 6 reports). Notably, studies have demonstrated that people with psoriasis are more likely to have depression than those without psoriasis.[4] Of 9 patients reporting diarrhea, 4

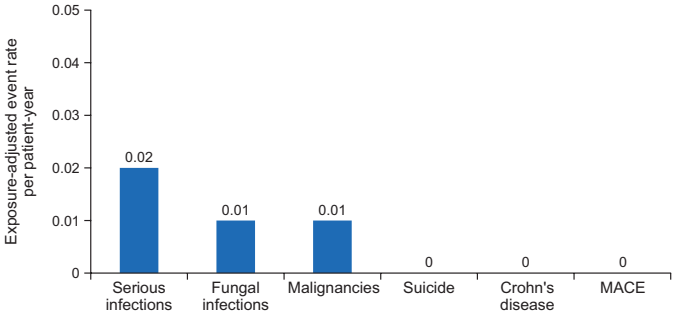
TABLE 1.

Summary of Most Common Adverse Events Reported in the US Pharmacovigilance Monitoring of Brodalumab (August 15, 2017–August 14, 2018)

AE	Event, n (r)[a]	Estimated weeks of brodalumab treatment, mean (min-max)[b]	Event related to brodalumab, n[c]	Discontinuation, n	Patient-reported event, n (%)
Psoriasis flare	26 (0.12)	10.8 (1.7-30.1)	2	2	19 (73)
Drug ineffectiveness	18 (0.08)	15.5 (1.7-52.1)	1	2	13 (72)
Arthralgia	16 (0.07)	4.1 (0.4-10.0)	1	4	13 (81)
Depression	11 (0.05)	14.9 (1.0-35.3)	0	4	5 (45)
Diarrhea	9 (0.04)	6.5 (0.4-12.9)	0	2	4 (44)
Pain	9 (0.04)	5.7 (0.1-12.9)	0	5	5 (55)

Psoriasis flare included the MedDRA categories of "psoriasis," "condition aggravated," and "ill-defined disorder." Drug ineffectiveness included the MedDRA categories of "drug ineffective" and "drug ineffective for unapproved indication." Depression included the MedDRA categories of "depression," "depressive symptoms," and "depressed mood." Pain included the MedDRA categories of "pain" and "pain in extremity."
[a]Analysis was performed on January 11, 2019, for all reports between August 15, 2017 and August 14, 2018. [b]Duration (weeks) of brodalumab treatment was estimated by calculating the number of days from the reported start of brodalumab treatment to the reported end of treatment. If a patient's reported start date included only the month, the start date was determined to be the first day of the month. If a patient's end date included only the month, the end date was determined to be the last day of the month. Patients whose start or end date was unknown were excluded from the calculation. [c]Relatedness to brodalumab was based on company-determined causality.
AE, adverse event; max, maximum duration; MedDRA, Medical Dictionary for Regulatory Activities; min, minimum duration; r, exposure-adjusted rate per patient-year.

FIGURE 1. Exposure-adjusted adverse events of interest per patient-year. Exposure-adjusted event rate per patient-year = number of events/216 patient-years of exposure. MACE, major adverse cardiac event.



were taking other medications potentially causing gastrointestinal upset. Of 9 patients reporting pain, 4 had a history of joint or muscle pain and 4 experienced pain <4 weeks after brodalumab initiation.

Regarding other events of clinical interest, there were 3 reports of malignancy (hepatic, lung, and ovarian; 0.01 events per PY), all considered unrelated to brodalumab. There were 4 reports of serious infections (0.02 events per PY) possibly related to brodalumab, 2 from the same patient (no follow-up information was provided despite multiple requests). There were 2 events of fungal infection (0.01 events per PY) but no reports of serious fungal infection. One nonserious event of oral fungal *Candida* infection was reported; brodalumab was discontinued and symptoms resolved. A nonserious event of vulvovaginal mycotic *Candida* infection was reported; brodalumab was maintained and symptoms resolved (Figure 1).

One-year pharmacovigilance reporting for brodalumab revealed that the most commonly reported AE was psoriasis flare. There were few reports of depression and no reports of suicide attempts, completed suicides, or serious fungal infections. A limitation of this report is that it did not capture all AEs, only those reported to Ortho Dermatologics.

DISCLOSURES

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