One-Year Pharmacovigilance Update of Brodalumab

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SYNOPSIS

- 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]
- There are limited data on the effects of brodalumab treatment in a real-world setting

OBJECTIVE

- To report an update of brodalumab 1-year pharmacovigilance in the United States (August 15, 2017–August 14, 2018)

METHODS

- Observational data were collected for US patients who received brodalumab (N=826) and reported an adverse event (AE) through routine 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)
- AEs were summarized with descriptive statistics and as exposure-adjusted rates per patient-year (PY)
- The analysis was performed on January 11, 2019, for all reports between August 15, 2017, and August 14, 2018

RESULTS

Most commonly reported AEs

- The most commonly reported AEs were psoriasis flare, drug ineffectiveness, arthralgia, depression, diarrhea, and pain (Table 1)
  - Of 9 patients reporting diarrhea, 4 were taking other medications that could potentially cause 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
  - Among 11 patients reporting depression, 4 discontinued brodalumab and 2 had a history of depression (mental health history was not provided in 6 reports); no events of depression were serious

Table 1. Summary of Most Common Adverse Events Reported in the US Pharmacovigilance Monitoring of Brodalumab (August 15, 2017–August 14, 2018)

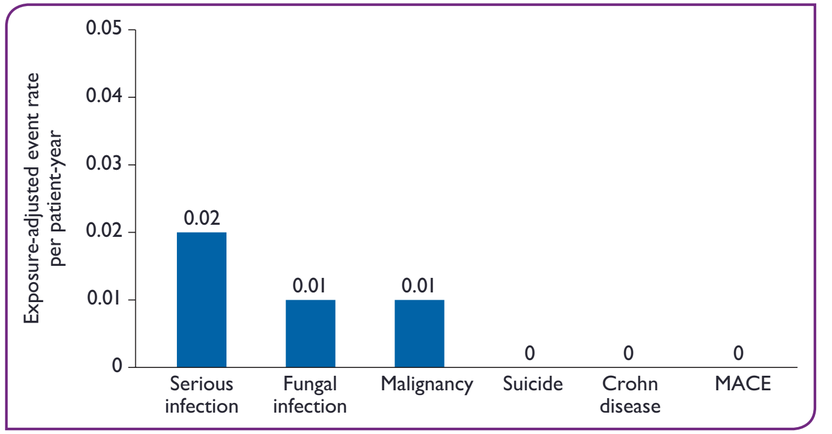
AE	Event, n (r)	Estimated weeks of brodalumab treatment, mean (min-max)[a]	Event related to brodalumab, n	Discontinuation, n
Psoriasis flare	26 (0.12)	10.8 (1.7-30.1)	2	2
Drug ineffectiveness	18 (0.08)	15.5 (1.7-52.1)	1	2
Arthralgia	16 (0.07)	4.1 (0.4-10.0)	1	4
Depression	11 (0.05)	14.9 (1.0-35.3)	0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

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]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. Patients whose start or end date was unknown were excluded from the calculation. AE, adverse event; max, maximum duration; MedDRA, Medical Dictionary for Regulatory Activities; min, minimum duration; r, exposure-adjusted rate per patient-year.

AEs of interest

- There were no reports of completed suicides or suicide attempts, major adverse cardiac events, new-onset ulcerative colitis, or new-onset Crohn disease
- There were 3 reports of malignancy (hepatic, lung, and ovarian; 0.01 events per PY), all considered unrelated to brodalumab (Figure 1)
- There were 4 reports of serious infections (0.02 events per PY; Figure 1) possibly related to brodalumab, with 2 reports in the same patient
- There were 2 events of fungal infection (0.01 events per PY; Figure 1) but no reports of serious fungal infection
  - 1 nonserious event of oral fungal *Candida* infection was reported in which brodalumab was discontinued and symptoms resolved
  - A nonserious event of vulvovaginal mycotic *Candida* infection was reported in which brodalumab was maintained and symptoms resolved

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.

CONCLUSIONS

- **One-year pharmacovigilance reporting for brodalumab revealed that the most commonly reported AE was psoriasis flare**
- **Few patients receiving brodalumab reported depression, and none reported serious fungal infections, suicide attempts, or completed suicides**

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References: 1. Siliq [package insert]. Bridgewater, NJ: Bausch Health US, LLC; 2017. **2.** Lebwohl et al. *N Engl J Med.* 2015;373:1318-1328. **3.** Papp et al. *Br J Dermatol.* 2016;175:273-286.