

Table SI. Reported Cases of DEB Treated with JAK Inhibitors or Dupilumab

| Author                 | Case           | Age/Sex | Diagnosis | Treatment    | Duration(weeks)<br>M(P25,P75) | Baseline<br>VAS score<br>M(P25,P75) | Final<br>VAS score<br>M(P25,P75) | Percent change in pruritus<br>VAS score(%)<br>M(P25,P75) |
|------------------------|----------------|---------|-----------|--------------|-------------------------------|-------------------------------------|----------------------------------|----------------------------------------------------------|
| Zhou, Xingli et al.    | 1              | M/27    | RDEB      | Tofacitinib  | 28                            | 8                                   | 2                                | 75.00%                                                   |
| Chen, K-J et al.       | 1 <sup>1</sup> | F/26    | EBP       | Tofacitinib  | 4                             | 9                                   | 6                                | 33.33%                                                   |
| Jiang, Xingyuan et al. | 1              | M/40    | EBP       | Baricitinib  | 24                            | 8                                   | 3                                | 62.50%                                                   |
| He, Zhe et al.         | 1              | M/28    | EBP       | Baricitinib  | 48                            | 7                                   | 2                                | 71.43%                                                   |
| Kwon, Il Joo et al.    | 1 <sup>2</sup> | F/39    | RDEB      | Baricitinib  | 2                             | 8                                   | 6                                | 25.00%                                                   |
|                        | 2 <sup>3</sup> | M/12    | RDEB      | Upadacitinib | 2                             | 8                                   | 8                                | 0                                                        |
|                        | 3              | F/30    | RDEB      | Upadacitinib | 8                             | 5                                   | 4                                | 20.00%                                                   |
|                        | 4              | F/51    | RDEB      | Baricitinib  | 5                             | 8                                   | 2                                | 75.00%                                                   |
|                        | 5              | F/21    | DDEB      | Baricitinib  | 16                            | 8                                   | 1                                | 87.50%                                                   |
|                        | 6              | M/25    | RDEB      | Upadacitinib | 12                            | 5                                   | 2                                | 60.00%                                                   |
|                        | 7              | F/16    | DDEB      | Upadacitinib | 32                            | 10                                  | 1                                | 90.00%                                                   |
|                        | 8              | F/19    | RDEB      | Baricitinib  | 8                             | 10                                  | 3                                | 70.00%                                                   |

<sup>1</sup> Follow-up was interrupted because of preparation for pregnancy;

<sup>2</sup> concerns about the recurrence of cutaneous squamous cell carcinoma (SCC);

<sup>3</sup> Lack of efficacy;

|                                 |                 |      |      |              |            |        |          |              |
|---------------------------------|-----------------|------|------|--------------|------------|--------|----------|--------------|
|                                 | 9               | M/18 | DDEB | Upadacitinib | 4          | 8      | 7        | 12.50%       |
|                                 | 10              | F/13 | DDEB | Upadacitinib | 4          | 7      | 7        | 0            |
|                                 | 11 <sup>4</sup> | M/30 | DDEB | Baricitinib  | 4          | 8      | 5        | 37.50%       |
|                                 | 12              | M/22 | DDEB | Upadacitinib | 15         | 8      | 2        | 75.00%       |
| Zhang Z, Lin Z.                 | 1               | NA   | EBP  | Upadacitinib | 24         | 10     | 0        | 100%         |
|                                 | 2               | NA   | EBP  | Upadacitinib | 24         | 9      | 1        | 88.89%       |
|                                 | 3               | NA   | EBP  | Upadacitinib | 24         | 8      | 0        | 100%         |
|                                 | 4               | NA   | EBP  | Upadacitinib | 24         | 6      | 1        | 83.33%       |
| Kim N, Jue MS, Huh YJ, et al.   | 1               | F/38 | EBP  | Upadacitinib | 22         | 8      | 1        | 87.50%       |
| Hou, Ping-Chen et al.           | 1               | F/52 | EBP  | Abrocitinib  | 36         | 7      | 0        | 100%         |
|                                 | 2               | F/18 | EBP  | Abrocitinib  | 20         | 4      | 0        | 100%         |
|                                 | 3 <sup>5</sup>  | F/60 | EBP  | Upadacitinib | 36         | 7      | 0        | 100%         |
|                                 | 4               | F/59 | EBP  | Abrocitinib  | 16         | 5      | 0        | 100%         |
|                                 | 5               | M/13 | EBP  | Abrocitinib  | 4          | 4      | 0        | 100%         |
| Current case                    | 1               | M/20 | EBP  | Tofacitinib  | 20         | 8      | 0        | 100%         |
| Summary of JAK inhibitor in DEB | 27              |      |      |              | 16(4.5,24) | 8(7,8) | 2(0,3.5) | 0.75(0.49,1) |
| Wu, Xue-Ge et al.               | 1               | M/13 | EBP  | Dupilumab    | 20         | 7      | 2        | 71.43%       |
|                                 | 2               | F/7  | EBP  | Dupilumab    | 20         | 5      | 3        | 40.00%       |
| Zhou, Amanda G et al.           | 1               | M/15 | EBP  | Dupilumab    | 88         | 8      | 4.5      | 43.75%       |

<sup>4</sup> fatigue and frequent otitis media;

<sup>5</sup> had a slightly elevated lipid profile

|                           |                |      |      |           |    |     |     |        |
|---------------------------|----------------|------|------|-----------|----|-----|-----|--------|
|                           | 2 <sup>6</sup> | F/27 | EBP  | Dupilumab | 24 | 10  | 3   | 70.00% |
| Yang, Dan-Yang et al.     | 1              | M/23 | EBP  | Dupilumab | 17 | 6   | 0   | 100%   |
| Zhao, Caichou et al.      | 1              | F/22 | EBP  | Dupilumab | 14 | 7   | 2   | 71.43% |
| Aala, Wilson Jr F et al.  | 1              | F/25 | DDEB | Dupilumab | 12 | 8   | 3.5 | 56.25% |
|                           | 2              | F/57 | DDEB | Dupilumab | 12 | 8.5 | 3.5 | 58.82% |
|                           | 3              | M/11 | DDEB | Dupilumab | 12 | 7   | 4.5 | 35.71% |
| Caroppo, F et al.         | 1              | F/43 | EBP  | Dupilumab | 12 | 9   | 3   | 66.67% |
| Wang, Yangbin et al.      | 1              | F/10 | EBP  | Dupilumab | 7  | 5.5 | 1.5 | 72.73% |
| Hou, Ping-Chen et al.     | 1              | F/28 | EBP  | Dupilumab | 14 | 7.5 | 2.5 | 66.67% |
|                           | 2              | F/43 | EBP  | Dupilumab | 2  | 6.5 | 3.5 | 46.15% |
|                           | 3              | M/11 | EBP  | Dupilumab | 7  | 7   | 4.5 | 35.71% |
|                           | 4 <sup>7</sup> | F/59 | EBP  | Dupilumab | 8  | 9   | 8   | 11.11% |
|                           | 5 <sup>8</sup> | F/60 | EBP  | Dupilumab | 16 | 8.5 | 3.5 | 58.82% |
| Shehadeh, W et al.        | 1              | F/52 | EBP  | Dupilumab | 12 | 9   | 5   | 44.44% |
| Caroppo, Francesca et al. | 1              | F/1  | RDEB | Dupilumab | 12 | 9   | 2   | 77.78% |
| Bellon, Nathalia et al.   | 1              | F/7  | RDEB | Dupilumab | 52 | 8   | 2   | 75.00% |
|                           | 2              | F/7  | RDEB | Dupilumab | 84 | 8   | 8   | 0      |

<sup>6</sup> The itching worsens before each injection and relieves after adjusting the dose;

<sup>7</sup> Poor response to dupilumab;

<sup>8</sup> Good response to 1st cycle of dupilumab ,Poor response to 2nd cycle of dupilumab;

|                             |    |      |      |           |           |           |        |                 |
|-----------------------------|----|------|------|-----------|-----------|-----------|--------|-----------------|
|                             | 3  | F/3  | RDEB | Dupilumab | 64        | 10        | 2      | 80.00%          |
|                             | 4  | F/4  | RDEB | Dupilumab | 88        | 7         | 4      | 42.86%          |
|                             | 5  | F/12 | RDEB | Dupilumab | 24        | 7         | 3      | 57.14%          |
|                             | 6  | F/18 | RDEB | Dupilumab | 24        | 7         | 4      | 42.86%          |
|                             | 7  | M/9  | RDEB | Dupilumab | 64        | 10        | 3      | 70.00%          |
|                             | 8  | M/21 | DDEB | Dupilumab | 100       | 8         | 3      | 62.50%          |
|                             | 9  | M/9  | DDEB | Dupilumab | 60        | 8         | 2      | 75.00%          |
| Summary of Dupilumab in DEB | 27 |      |      |           | 17(12,56) | 8(7,8.75) | 3(2,4) | 0.59(0.44,0.71) |
| <i>P-value</i>              |    |      |      |           | 0.176     | 0.595     | 0.018  | 0.029*          |

*Note: This table lists all reports found using the Pubmed search tool whose titles included ‘JAK inhibitor’ or ‘Tofacitinib’ or ‘Baricitinib’ or ‘Upadacitinib’ or ‘Abrocitinib’ or ‘dupilumab’ and ‘dystrophic epidermolysis bullosa’. Papers whose patient-specific VAS score were not described were excluded. (Abbreviation:F:Female;M:Male;DEB:dystrophic epidermolysis bullosa;DDEB:dominant dystrophic epidermolysis bullosa;RDEB:recessive dystrophic epidermolysis bullosa;EBP:Dystrophic epidermolysis bullosa pruriginosa ;VAS:Visual analogue scale;JAK inhibitor:Janus kinase inhibitor )\*  $p < 0.05$  for the comparison between JAK inhibitors and Dupilumab, based on Wilcoxon signed-rank test.*

## REFERENCES:

- Zhou X, Geng J, Wang M, Yang J, Zou J, Li W. Novel compound heterozygous mutations of the COL7A1 gene in a Chinese patient with recessive dystrophic epidermolysis bullosa pruriginosa and digestive symptoms successfully treated with tofacitinib. *J Dermatol.* 2024 Jan;51(1):e8-e10. doi: 10.1111/1346-8138.16945
- Chen KJ, Fang S, Ye Q, Jia M. Successful use of tofacitinib in epidermolysis bullosa pruriginosa. *Clin Exp Dermatol.* 2022 Mar;47(3):598-600. doi: 10.1111/ced.14998
- Jiang X, Wang H, Lee M, Lin Z. Epidermolysis Bullosa Pruriginosa Treated With Baricitinib. *JAMA Dermatol.* 2021 Oct 1;157(10):1243-1244. doi: 10.1001/jamadermatol.2021.3174
- He Z, Dong Q, Xi Y, Zheng R. Epidermolysis Bullosa Pruriginosa treated with baricitinib: A case report. *Medicine (Baltimore).* 2024 Jul 5;103(27):e38854. doi: 10.1097/MD.00000000000038854
- Kwon IJ, Kim SE, Kim SC, Lee SE. Efficacy of oral JAK1 or JAK1/2 inhibitor for treating refractory pruritus in dystrophic epidermolysis bullosa: A retrospective case series. *J Dermatol.* 2024 Mar;51(3):441-447. doi: 10.1111/1346-8138.17079
- Zhang Z, Lin Z. Epidermolysis Bullosa Pruriginosa Treated With Upadacitinib. *JAMA Dermatol.* 2024 Oct 1;160(10):1124-1125. doi: 10.1001/jamadermatol.2024.2787
- Kim N, Jue MS, Huh YJ, Sung KJ, Kim H, Kim JE, et al. Epidermolysis bullosa pruriginosa with extensive truncal involvement treated with upadacitinib. *J Eur Acad Dermatol Venereol.* 2023 Feb;37(2):e215-e217. doi: 10.1111/jdv.18487
- Hou PC, Aala W Jr, Tu WT, McGrath JA, Hsu CK. Real-world experience of using dupilumab and JAK inhibitors to manage pruritus in epidermolysis bullosa pruriginosa. *Skin Health Dis.* 2024 Aug 19;4(5):e445. doi: 10.1002/ski2.445
- Wu XG, Yan S, Jiang JQ, Zhou TT, Fang X, Yang H, et al. Successful treatment of epidermolysis bullosa pruriginosa by dupilumab. *J Dermatol.* 2023 Jun;50(6):837-842. doi: 10.1111/1346-8138.16729
- Zhou AG, Little AJ, Antaya RJ. Epidermolysis bullosa pruriginosa treated with dupilumab. *Pediatr Dermatol.* 2021 Mar;38(2):526-527. doi: 10.1111/pde.14493
- Yang DY, Jing WW, Liu X, Li L, Lu T, Li XL. Pruritus Anesis in Dystrophic Epidermolysis Bullosa Pruriginosa with Dupilumab. *Adv Skin Wound Care.* 2024 Feb 1;37(2):1-4. doi: 10.1097/ASW.0000000000000096
- Zhao C, Cao S, Gao X, Xu X, Gu L. Identification of a novel COL7A1 variant associated with dystrophic epidermolysis bullosa pruriginosa responding effectively to dupilumab. *Mol Genet Genomic Med.* 2023 Nov;11(11):e2258. doi: 10.1002/mgg3.2258
- Aala WJF, Hou PC, Hong YK, Lin YC, Lee YR, Tu WT, et al. Dominant dystrophic epidermolysis bullosa is associated with glycolytically active GATA3+ T helper 2 cells which may contribute to pruritus in lesional skin. *Br J Dermatol.* 2024 Jul 16;191(2):252-260. doi: 10.1093/bjd/ljae110
- Caroppo F, Milan E, Giulioni E, Belloni Fortina A. A case of dystrophic epidermolysis bullosa pruriginosa treated with dupilumab. *J Eur Acad Dermatol Venereol.* 2022 May;36(5):e365-e367. doi: 10.1111/jdv.17887
- Wang Y, Zhou M, Zhang L, Zheng S, Hong Y, Gao XH. Amelioration of dystrophic epidermolysis bullosa pruriginosa symptoms with dupilumab: a case report. *Dermatol Ther.* 2021;34(6):e15130. doi:10.1111/dth.15130
- Shehadeh W, Sarig O, Bar J, Sprecher E, Samuelov L. Treatment of epidermolysis bullosa pruriginosa—associated pruritus with dupilumab. *Br J Dermatol.* 2020;182(6):1495–1497. doi:10.1111/bjd.18855
- Caroppo F, Cassalia F, Milan E, Belloni Fortina A. Novel variant c.7795-1G>A of the COL7A1 gene in a 12-month-old female child with recessive dystrophic epidermolysis bullosa treated with dupilumab. *JAAD Case Rep.* 2024;50:79–81. doi:10.1016/j.jdc.2024.06.003
- Bellon N, Bataille P, Bonigen J, et al. Experience of dupilumab treatment in inherited epidermolysis bullosa: a short series. *J Am Acad Dermatol.* 2024;91(2):373–376. doi:10.1016/j.jaad.2024.04.037