

## Considerations for Treating Generalized Pustular Psoriasis (GPP): A Narrative Review

Charles W. Lynde<sup>1</sup>, Vimal H. Prajapati<sup>2</sup>, Melinda J. Gooderham<sup>3</sup>, H. Chih-ho Hong<sup>4</sup>, Mark G. Kirchhof<sup>5</sup>, Perla Lansang<sup>6</sup>, Julien Ringuet<sup>7</sup>, Irina Turchin<sup>8</sup>, Ron Vender<sup>9</sup>, Jensen Yeung<sup>10</sup>, Kim A. Papp<sup>11</sup>

1. Lynde Dermatology, Probitry Medical Research, Markham; Department of Medicine, University of Toronto, Toronto, Ontario, Canada
2. Division of Dermatology, Department of Medicine, University of Calgary, Calgary, Alberta, Canada; Section of Community Pediatrics, Department of Pediatrics, University of Calgary, Calgary, Alberta, Canada; Section of Pediatric Rheumatology, Department of Pediatrics, University of Calgary, Calgary, Alberta, Canada; Dermatology Research Institute, Calgary, Alberta, Canada; Skin Health & Wellness Centre, Calgary, Alberta, Canada; Probitry Medical Research, Calgary, Alberta, Canada
3. SKiN Health, Probitry Medical Research, and Queen's University, Peterborough, Ontario, Canada
4. Division of Dermatology and Skin Science, University of British Columbia; Probitry Medical Research, Surrey, British Columbia, Canada
5. Faculty of Medicine, Division of Dermatology, University of Ottawa, and The Ottawa Hospital, Ottawa, Ontario, Canada
6. Division of Dermatology, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada; Division of Dermatology, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; Division of Dermatology, Women's College Hospital, Toronto, Ontario, Canada; The Hospital for Sick Children, Toronto, Ontario, Canada
7. Centre de Recherche Dermatologique du Québec (CRDQ), Quebec, Canada; Department of Medicine, Division of Dermatology, McGill University, Montreal, Quebec, Canada
8. Brunswick Dermatology Center, Fredericton, New Brunswick, Canada; Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada; Probitry Medical Research, Waterloo, Ontario, Canada
9. Department of Medicine, Division of Dermatology, McMaster University, Hamilton, Ontario, Canada; Dermaterials Research Inc., Hamilton, Ontario, Canada
10. Division of Dermatology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada; Probitry Medical Research, Toronto, Ontario, Canada
11. Probitry Medical Research Inc., Waterloo, Ontario, Canada; Alliance Clinical Trials, Waterloo, Ontario, Canada; Temerty Faculty of Medicine, Division of Dermatology, University of Toronto, Toronto, Ontario, Canada

### Correspondence to:

Charles W. Lynde  
25 Main Street Markham N.  
Markham, ON, L3P 1X3  
Tel: 905-471-7175  
Fax: 905-471-4416  
Email: [derma@lynderma.com](mailto:derma@lynderma.com)

**Supplemental Table 1. Efficacy of plaque-psoriasis approved systemic biologics for the treatment of GPP in adults, as described in case reports and case series.**

Abbreviations: BW, bi-weekly; CR, complete resolution; F, female; IL, interleukin; IV, intravenous; M, male; NOR, no response; NR, not reported; PR, partial response; Q1W, every 1 week; Q2W, every 2 weeks; Q4W, every 4 weeks; Q12W, every 12 weeks; SC, subcutaneous; TNF, tumour necrosis factor

| Target pathway | Treatment  | Publication type | Reference                             | Age/Sex | GPP duration, months | Prior systemic biologic therapies [route, dose, frequency, outcome, time to outcome (days)] | Systemic biologic therapy [route, dose, frequency] | Outcome for systemic biologic therapy | Time to outcome for systemic biologic therapy, days |
|----------------|------------|------------------|---------------------------------------|---------|----------------------|---------------------------------------------------------------------------------------------|----------------------------------------------------|---------------------------------------|-----------------------------------------------------|
| TNF- $\alpha$  | Infliximab | Case Report      | Babuna Kobaner, 2020 <sup>[1]</sup>   | 24/F    | 0.7                  | None                                                                                        | Infliximab [IV, NR, NR]                            | CR                                    | 238                                                 |
|                |            |                  | Chandran, 2010 <sup>[2]</sup>         | 48/F    | 384                  | None                                                                                        | Infliximab [IV, 300 mg, NR]                        | CR                                    | 2                                                   |
|                |            |                  | Dogra, 2019 <sup>[3]</sup>            | 22/M    | NR                   | Secukinumab [SC, 300 mg, Q4W, CR, NR]                                                       | Infliximab [IV, 300 mg, Q8W]                       | CR                                    | 42                                                  |
|                |            |                  | Elewski, 2002 <sup>[4]</sup>          | 39/M    | NR                   | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | CR                                    | 30                                                  |
|                |            |                  | Ito, 2021 <sup>[5]</sup>              | 56/F    | NR                   | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | CR                                    | NR                                                  |
|                |            |                  | Li, 2017 <sup>[6]</sup>               | 25/M    | 1                    | None                                                                                        | Infliximab [IV, 3 mg/kg, Q8W]                      | CR                                    | 3                                                   |
|                |            |                  | Newland, 2002 <sup>[7]</sup>          | 44/F    | 312                  | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | 2                                                   |
|                |            |                  | Osmola-Mankowska, 2014 <sup>[8]</sup> | 31/M    | 48                   | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | NR                                                  |
|                |            |                  | Saito, 2014 <sup>[9]</sup>            | 20/F    | 1                    | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | CR                                    | 540                                                 |
|                |            |                  | Sakai, 2019 <sup>[10]</sup>           | 70/F    | 0.8                  | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | 210                                                 |
|                |            |                  | Samotij, 2021 <sup>[11]</sup>         | 72/F    | 0.5                  | Adalimumab [SC, NR, NR, NOR, NR]                                                            | Infliximab [IV, 5 mg/kg, Q8W]                      | PR                                    | 3                                                   |
|                |            |                  | Sheth, 2009 <sup>[12]</sup>           | 27/F    | 4                    | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | 109                                                 |
|                |            |                  | Smith, 2013 <sup>[13]</sup>           | 33/M    | 0.1                  | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | 4                                                   |
|                |            |                  | Tang, 2012 <sup>[14]</sup>            | 72/M    | 1                    | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | CR                                    | 6                                                   |
|                |            |                  | Varma, 2008 <sup>[15]</sup>           | 44/M    | 60                   | Etanercept [SC, 50 mg, BW, NOR, 120]                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | CR                                    | NR                                                  |
|                |            | Case Series      | Brenner, 2009 <sup>[16]</sup>         | 54/F    | NR                   | Infliximab [IV, 3 mg/kg, NR, CR, NR]; Etanercept [SC, 50 mg, BW, NR, NOR, NR]               | Infliximab [IV, 3 mg/kg, NR]                       | CR                                    | NR                                                  |
|                |            |                  |                                       | 56/F    | NR                   | None                                                                                        | Infliximab [IV, 3 mg/kg, NR]                       | CR                                    | NR                                                  |
|                |            |                  | Kim, 2014 <sup>[17]</sup>             | 41/F    | 36                   | None                                                                                        | Infliximab [IV, 3 mg/kg, Q8W]                      | CR                                    | 2                                                   |
|                |            |                  |                                       | 39/F    | NR                   | None                                                                                        | Infliximab [IV, 3 mg/kg, Q8W]                      | CR                                    | 2                                                   |
|                |            |                  | Kolt-Kaminska, 2021 <sup>[18]</sup>   | 73/F    | 7                    | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | CR                                    | 126                                                 |
|                |            |                  |                                       | 60/M    | NR                   | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | CR                                    | 120                                                 |
|                |            |                  | Routhouska, 2008 <sup>[19]</sup>      | 77/F    | 36                   | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | PR                                    | 360                                                 |
|                |            |                  |                                       | 22/F    | 72                   | Etanercept [SC, 25 mg, BW, NOR, 90]; Adalimumab [SC, 40 mg, Q2W, NOR, NR]                   | Infliximab [IV, 5 mg/kg, Q8W]                      | PR                                    | 126                                                 |
|                |            |                  | Sugiura, 2015 <sup>[20]</sup>         | 39/F    | 348                  | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | CR                                    | 28                                                  |
|                |            |                  |                                       | 36/M    | 312                  | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | NR                                    | NR                                                  |
|                |            |                  |                                       | 29/M    | 276                  | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | CR                                    | 28                                                  |
|                |            |                  |                                       | 65/F    | 144                  | None                                                                                        | Infliximab [IV, 5 mg/kg, Q8W]                      | CR                                    | 28                                                  |
|                |            |                  | Trent, 2004 <sup>[21]</sup>           | 44/F    | NR                   | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | 2                                                   |
|                |            |                  |                                       | 17/F    | NR                   | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | 2                                                   |
|                |            |                  |                                       | 46/F    | NR                   | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | 2                                                   |
|                |            |                  |                                       | 52/F    | NR                   | None                                                                                        | Infliximab [IV, 5 mg/kg, NR]                       | PR                                    | 2                                                   |

|  |            |             |                                       |       |      |                                                                                  |                               |    |     |
|--|------------|-------------|---------------------------------------|-------|------|----------------------------------------------------------------------------------|-------------------------------|----|-----|
|  |            |             | Viguier, 2012 <sup>[22]</sup>         | NR/F  | NR   | None                                                                             | Infliximab [IV, NR, NR]       | CR | 6   |
|  |            |             |                                       | NR/M  | NR   | None                                                                             | Infliximab [IV, NR, NR]       | CR | 3   |
|  |            |             |                                       | NR/F  | NR   | None                                                                             | Infliximab [IV, NR, NR]       | CR | NR  |
|  |            |             |                                       | NR/M  | NR   | None                                                                             | Infliximab [IV, NR, NR]       | CR | 2   |
|  |            |             |                                       | NR/F  | NR   | Etanercept [SC, NR, NR, CR, NR]                                                  | Infliximab [IV, NR, NR]       | CR | 1   |
|  |            |             | Weishaupt, 2007 <sup>[23]</sup>       | NR/F  | NR   | None                                                                             | Infliximab [IV, NR, NR]       | CR | 2   |
|  |            |             |                                       | 24/F  | 204  | None                                                                             | Infliximab [IV, 4 mg/kg, Q8W] | CR | 180 |
|  |            |             |                                       | 18/NR | 84   | None                                                                             | Infliximab [IV, 4 mg/kg, Q8W] | CR | 3   |
|  | Adalimumab | Case Report | Gallo, 2013 <sup>[24]</sup>           | 21/F  | 168  | Infliximab [IV, 6 mg/kg, Q8W, CR, NR]                                            | Adalimumab [SC, 40 mg, Q2W]   | CR | 330 |
|  |            |             | Gkalpakiotis, 2015 <sup>[25]</sup>    | 80/F  | 0.25 | None                                                                             | Adalimumab [SC, 40 mg, Q2W]   | CR | 14  |
|  |            |             | Hay, 2014 <sup>[26]</sup>             | 47/M  | 84   | None                                                                             | Adalimumab [SC, 40 mg, Q2W]   | CR | NR  |
|  |            |             | Jordan, 2009 <sup>[27]</sup>          | 81/F  | NR   | None                                                                             | Adalimumab [SC, 40 mg, Q2W]   | CR | 7   |
|  |            |             | Kimura, 2012 <sup>[28]</sup>          | 36/F  | NR   | None                                                                             | Adalimumab [SC, 40 mg, Q2W]   | CR | 70  |
|  |            |             | Wang, 2014 <sup>[29]</sup>            | 45/M  | 216  | Ustekinumab [SC, 90 mg, Q12W, NOR, NR]                                           | Adalimumab [SC, NR, NR]       | CR | NR  |
|  |            |             | Wang, 2020 <sup>[01]</sup>            | 33/M  | 120  | None                                                                             | Adalimumab [SC, 40 mg, Q2W]   | CR | 56  |
|  |            |             | Zangrilli, 2008 <sup>[31]</sup>       | 50/F  | 120  | Infliximab [IV, 5 mg/kg, NR, PR, NR]                                             | Adalimumab [SC, 40 mg, Q2W]   | CR | 196 |
|  |            | Case Series | Kawakami, 2015 <sup>[32]</sup>        | 43/M  | 12   | Infliximab [IV, 5 mg/kg, Q8W, CR, 91]                                            | Adalimumab [SC, 40 mg, Q2W]   | CR | NR  |
|  |            |             |                                       | 30/F  | NR   | Infliximab [IV, 5 mg/kg, Q8W, CR, 161]                                           | Adalimumab [SC, 40 mg, Q2W]   | CR | NR  |
|  |            |             | Matsumoto, 2017 <sup>[33]</sup>       | 70/F  | 24   | Infliximab [IV, 5 mg/kg, Q8W, CR, NR];<br>Ustekinumab [SC, 90 mg, Q12W, NOR, NR] | Adalimumab [SC, 80 mg, Q2W]   | CR | 60  |
|  |            |             |                                       | 36/F  | 9    | Infliximab [IV, 5 mg/kg, Q8W, CR, NR]                                            | Adalimumab [SC, 80 mg, Q2W]   | CR | NR  |
|  |            |             |                                       | 56/M  | 33   | Infliximab [IV, 5 mg/kg, Q8W, CR, NR]                                            | Adalimumab [SC, 80 mg, Q2W]   | CR | NR  |
|  |            |             |                                       | 43/M  | 4    | Infliximab [IV, 5 mg/kg, Q8W, CR, NR]                                            | Adalimumab [SC, 40 mg, Q2W]   | CR | NR  |
|  |            |             | Viguier, 2012 <sup>[22]</sup>         | NR/M  | NR   | None                                                                             | Adalimumab [SC, NR, NR]       | CR | <28 |
|  |            |             |                                       | NR/M  | NR   | Infliximab [IV, NR, NR, CR]                                                      | Adalimumab [SC, NR, NR]       | NR | NR  |
|  | Etanercept | Case Report | Kamarashev, 2002 <sup>[34]</sup>      | 50/M  | 0.5  | None                                                                             | Etanercept [SC, 50 mg, BW]    | CR | 14  |
|  |            |             | Lo, 2012 <sup>[35]</sup>              | 70/F  | NR   | None                                                                             | Etanercept [SC, 50 mg, BW]    | CR | 7   |
|  |            |             | Mikhail, 2008 <sup>[36]</sup>         | 32/M  | NR   | None                                                                             | Etanercept [SC, 50 mg, Q1W]   | CR | 30  |
|  |            |             | PalomoArellano, 2009 <sup>[37]</sup>  | 49/F  | NR   | None                                                                             | Etanercept [SC, 50 mg, BW]    | CR | 10  |
|  |            |             | Rodriguez-Lomba, 2017 <sup>[38]</sup> | 28/M  | 60   | Infliximab [IV, NR, NR, PR, 720]; Ustekinumab [SC, 90 mg, Q12W, NOR, NR]         | Etanercept [SC, 100 mg, Q1W]  | CR | NR  |
|  |            | Case Series | Esposito, 2008 <sup>[39]</sup>        | 50/F  | 120  | None                                                                             | Etanercept [SC, 50 mg, BW]    | CR | 168 |
|  |            |             |                                       | 75/F  | 132  | Infliximab [IV, 5 mg/kg, Q8W, NOR, NR]                                           | Etanercept [SC, 50 mg, BW]    | CR | 168 |
|  |            |             |                                       | 70/F  | 60   | Infliximab [IV, 5 mg/kg, Q8W, NOR]                                               | Etanercept [SC, 50 mg, BW]    | CR | 336 |
|  |            |             |                                       | 71/F  | 36   | Infliximab [IV, 5 mg/kg, Q8W, CR, NR]                                            | Etanercept [SC, 50 mg, BW]    | CR | 336 |

|       |                    |             |                                      |      |                                                                  |                                                                              |                                      |     |     |
|-------|--------------------|-------------|--------------------------------------|------|------------------------------------------------------------------|------------------------------------------------------------------------------|--------------------------------------|-----|-----|
|       |                    |             |                                      | 18   | 216                                                              | None                                                                         | Etanercept [SC, 50 mg, BW]           | CR  | 168 |
|       |                    |             |                                      | 35/F | 122                                                              | None                                                                         | Etanercept [SC, 50 mg, BW]           | CR  | 168 |
|       |                    |             | Routhouska, 2008 <sup>[19]</sup>     | 72/F | 120                                                              | Infliximab [IV, 5 mg/kg, Q12W, PR, PR, 450]                                  | Etanercept [SC, 25 mg, BW]           | PR  | 60  |
|       |                    |             | Viguier, 2012 <sup>[22]</sup>        | NR/F | NR                                                               | Infliximab [IV, NR, NR, NOR, NR]; Adalimumab [SC, NR, NR, NOR, NR]           | Etanercept [SC, NR, NR]              | CR  | NR  |
|       |                    |             |                                      | NR/F | NR                                                               | Infliximab [IV, NR, NR, CR, NR]; Etanercept [SC, NR, NR, CR, NR]             | Etanercept [SC, NR, NR]              | NOR | NR  |
|       |                    |             | NR/F                                 | NR   | Adalimumab [SC, NR, NR, CR, NR]; Infliximab [IV, NR, NR, CR, NR] | Etanercept [SC, NR, NR]                                                      | NR                                   | NR  |     |
|       | Certolizumab pegol | Case Report | Mizutani, 2020 <sup>[40]</sup>       | 31/F | 180                                                              | None                                                                         | Certolizumab pegol [SC, 200 mg, Q2W] | CR  | NR  |
|       | Golimumab          | Case Report | Narbutt, 2017 <sup>[41]</sup>        | 48/M | 504                                                              | Infliximab [IV, 5 mg/kg, NR, NOR]; Adalimumab [SC, 40 mg, Q2W, NOR, NR]      | Golimumab [SC, NR, NR]               | PR  | NR  |
| IL-17 | Secukinumab        | Case Report | Akaji, 2021 <sup>[42]</sup>          | 38/F | 0.7                                                              | None                                                                         | Secukinumab [SC, 300 mg, NR]         | CR  | 7   |
|       |                    |             | Bohner, 2016 <sup>[43]</sup>         | 50/M | 84                                                               | None                                                                         | Secukinumab [SC, 300 mg, Q1W]        | CR  | 7   |
|       |                    |             | Gabeff, 2019 <sup>[44]</sup>         | 32/F | NR                                                               | Adalimumab [SC, 40 mg, Q2W, NOR, NR]; Infliximab [IV, 5 mg/kg, Q8W, NOR, NR] | Secukinumab [SC, 300 mg, Q4W]        | CR  | 84  |
|       |                    |             | Honma, 2019 <sup>[45]</sup>          | 64/F | 24                                                               | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | NR  |
|       |                    |             | Liu, 2020 <sup>[46]</sup>            | 37/F | 0.1                                                              | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 7   |
|       |                    |             | Miyagawa, 2021 <sup>[47]</sup>       | 75/M | 156                                                              | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 84  |
|       |                    |             | Polesie, 2017 <sup>[48]</sup>        | 44/M | 432                                                              | Anakinra [SC, NR, NR, NOR, NR]; Ustekinumab [SC, 90 mg, Q12W, NOR, NR]       | Secukinumab [SC, 300 mg, Q4W]        | CR  | 21  |
|       |                    |             | Yeung, 2016 <sup>[49]</sup>          | 50/M | NR                                                               | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 21  |
|       |                    | Case Series | Mugheddu, 2017 <sup>[50]</sup>       | 66/M | NR                                                               | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 84  |
|       |                    |             |                                      | 28/M | NR                                                               | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 56  |
|       |                    |             |                                      | 61/M | NR                                                               | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 56  |
|       |                    |             | Sun, 2020 <sup>[51]</sup>            | 21/M | NR                                                               | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 56  |
|       |                    |             |                                      | 18/F | 0.23                                                             | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 56  |
|       |                    |             | Taguchi, 2020 <sup>[52]</sup>        | 48/F | NR                                                               | None                                                                         | Secukinumab [SC, 300 mg, Q4W]        | CR  | 140 |
|       |                    |             | Wilsmann-Theis, 2018 <sup>[53]</sup> | 56/F | 108                                                              | Adalimumab [SC, NR, NR, NR, NR]; Etanercept [NR,                             | Secukinumab [SC, NR, NR]             | PR  | NR  |

|             |              |             |                                     |      |      |                                                                                                                                                  |                                 |    |      |
|-------------|--------------|-------------|-------------------------------------|------|------|--------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|----|------|
|             |              |             |                                     |      |      | NR, NR, NR, NR];<br>Infliximab [IV, NR, NR, NR, NR]                                                                                              |                                 |    |      |
|             |              |             |                                     | 67/F | 216  | Adalimumab [SC, NR, NR, NR, NR]                                                                                                                  | Secukinumab [SC, NR, NR]        | PR | NR   |
|             |              |             |                                     | 72/F | 96   | Adalimumab [SC, NR, NR, NR, NR]; Etanercept [NR, NR, NR, NR, NR];<br>Infliximab [IV, NR, NR, NR, NR]                                             | Secukinumab [SC, NR, NR]        | PR | NR   |
|             |              |             |                                     | 57/M | 0.5  | Adalimumab [SC, NR, NR, NR, NR]                                                                                                                  | Secukinumab [SC, NR, NR]        | PR | NR   |
|             |              |             |                                     | 40/M | 204  | None                                                                                                                                             | Secukinumab [SC, NR, NR]        | PR | NR   |
|             |              |             |                                     | 69/F | 0.25 | None                                                                                                                                             | Secukinumab [SC, NR, NR]        | PR | NR   |
|             |              |             | Xia, 2021 <sup>[54]</sup>           | 32/F | 0.5  | Infliximab [IV, 5 mg/kg, NR, NOR, 1080]                                                                                                          | Secukinumab [SC, 300 mg, Q4W]   | PR | 105  |
|             | Ixezumab     | Case Report | Dattola, 2020 <sup>[55]</sup>       | 32/F | NR   | Adalimumab [SC, 40 mg, Q2W, NOR, NR]; Infliximab [IV, NR, NR, CR, NR]                                                                            | Ixezumab [SC, 80 mg, Q2W]       | CR | 14   |
|             |              |             | Megna, 2022 <sup>[56]</sup>         | 53/F | NR   | None                                                                                                                                             | Ixezumab [SC, 80 mg, Q4W]       | CR | 21   |
|             |              |             | Sawabe, 2019 <sup>[57]</sup>        | 70/M | NR   | Secukinumab [SC, NR, NR, PR, 14]; Infliximab [IV, 5 mg/kg, NR, NOR, NR]                                                                          | Ixezumab [SC, NR, NR]           | PR | 30   |
|             |              |             | Wilmann-Theis, 2018 <sup>[53]</sup> | 37/F | 48   | None                                                                                                                                             | Ixezumab [SC, NR, NR]           | PR | NR   |
|             | Brodalumab   | Case Report | Ichiyama, 2021 <sup>[58]</sup>      | 35/M | NR   | None                                                                                                                                             | Brodalumab [SC, 210 mg, Q2W]    | CR | 7    |
|             | Bimekizumab  | Case Report | Shukuin, 2023 <sup>[59]</sup>       | 69/F | NR   | None                                                                                                                                             | Bimekizumab [NR, NR, NR]        | CR | 14   |
| IL-23       | Guselkumab   | Case Series | Taguchi, 2020 <sup>[53]</sup>       | 28/F | 54   | None                                                                                                                                             | Guselkumab [SC, 50 mg, Q8W]     | CR | 112  |
|             | Risankizumab | Case Report | Okazaki, 2021 <sup>[60]</sup>       | 65/M | 0.3  | Guselkumab [SC, 100 mg, Q8W, NOR, NR];<br>Brodalumab [SC, 210 mg, Q4W, PR, 210]                                                                  | Risankizumab [SC, 150 mg, Q12W] | PR | 112  |
|             |              |             | Pavia, 2022 <sup>[61]</sup>         | 47/F | NR   | None                                                                                                                                             | Risankizumab [SC, 75 mg, NR]    | CR | 18   |
|             |              |             | Ruggiero, 2022 <sup>[62]</sup>      | 38/M | 36   | Ustekinumab [SC, 90 mg, Q12W, NOR, NR];<br>Adalimumab [SC, 80 mg, Q2W, NOR, NR];<br>Ixezumab [SC, NR, NR, PR, 150]                               | Risankizumab [SC, 150 mg, Q12W] | PR | 84   |
| IL-12/IL-23 | Ustekinumab  | Case Report | Dauden, 2010 <sup>[63]</sup>        | 47/M | NR   | None                                                                                                                                             | Ustekinumab [SC, 45 mg, Q12W]   | CR | 84   |
|             |              |             | Storan, 2016 <sup>[64]</sup>        | 90/F | 72   | Adalimumab [SC, 40 mg, Q2W, NOR, 420]                                                                                                            | Ustekinumab [SC, 45 mg, Q12W]   | CR | 28   |
|             |              | Case Series | Arakawa, 2016 <sup>[65]</sup>       | 20/F | 62   | Etanercept [SC, 50 mg, NR, CR, NR]                                                                                                               | Ustekinumab [SC, 90 mg, Q12W]   | CR | 510  |
|             |              |             |                                     | 50/F | 146  | Anakinra [SC, NR, NR, NOR, NR]; Etanercept [SC, 50 mg, NR, CR, NR];<br>Adalimumab [SC, 40 mg, Q2W, CR, NR]; Infliximab [IV, 300 mg, Q8W, CR, NR] | Ustekinumab [SC, 90 mg, Q12W]   | CR | 720  |
|             |              |             |                                     | 20/F | 51   | None                                                                                                                                             | Ustekinumab [SC, 90 mg, Q12W]   | CR | 1320 |

|      |             |             |                                 |      |     |                                                                                                          |                               |    |     |
|------|-------------|-------------|---------------------------------|------|-----|----------------------------------------------------------------------------------------------------------|-------------------------------|----|-----|
|      |             |             |                                 | 50/F | 50  | Adalimumab [SC, 40 mg, Q1W, CR, NR]                                                                      | Ustekinumab [SC, 90 mg, Q12W] | CR | 84  |
|      |             |             | Xia, 2021 <sup>[54]</sup>       | 37/M | 0.7 | Infliximab [IV, 5 mg/kg, NR, NOR, 585]                                                                   | Ustekinumab [SC, 45 mg, Q12W] | PR | NR  |
| IL-1 | Anakinra    | Case Report | Huffmeier, 2014 <sup>[66]</sup> | 47/F | 84  | Etanercept [SC, 50 mg, BW, NOR, NR]; Adalimumab [SC, 40 mg, Q2W, CR, NR]                                 | Anakinra [SC, 100 mg, NR]     | PR | 70  |
|      |             |             | Podlipnik, 2017 <sup>[67]</sup> | 54/M | 84  | Infliximab [IV, 5 mg/kg, NR, PR, 42]                                                                     | Anakinra [SC, 100 mg, NR]     | CR | 365 |
|      |             |             | Viguier, 2010 <sup>[68]</sup>   | 45/F | NR  | Adalimumab [SC, 40 mg, Q2W, NOR, NR]; Infliximab [IV, 300 mg, Q8W, NOR, NR]; Etanercept [NR, NR, PR, 10] | Anakinra [SC, 100 mg, NR]     | PR | 10  |
|      |             |             |                                 | 31/F | 24  | Adalimumab [SC, NR, NR, PR, NR]                                                                          | Anakinra [SC, 100 mg, NR]     | PR | 15  |
|      | Gevokizumab | Case Series | Mansouri, 2015 <sup>[69]</sup>  | 35/M | 6   | Infliximab [IV, 10 mg/kg, Q8W, NOR, NR]                                                                  | Gevokizumab [SC, NR, NR]      | CR | 30  |
|      |             |             |                                 | 59/F | 6   | Etanercept [SC, 50 mg, NR, NOR, NR]; Adalimumab [SC, 40 mg, Q2W, NOR, NR]                                | Gevokizumab [SC, NR, NR]      | PR | 84  |

### Supplementary References

1. Babuna Kobaner G, Polat Ekinci A. Infliximab for the treatment of recalcitrant generalized pustular psoriasis of pregnancy: Report of a challenging case. *Dermatol Ther.* 2020; **33**: e13571.
2. Chandran NS, Chong WS. A dramatic response to a single dose of infliximab as rescue therapy in acute generalized pustular psoriasis of von Zumbusch associated with a neutrophilic cholangitis. *Australas J Dermatol.* 2010; **51**: 29-31.
3. Dogra S, Bishnoi A, Narang T, Handa S. Secukinumab-induced paradoxical pustular psoriasis. *Clin Exp Dermatol.* 2019; **44**: 72-73.
4. Elewski BE. Infliximab for the treatment of severe pustular psoriasis. *J Am Acad Dermatol.* 2002; **47**: 796-797.
5. Ito M, Akutsu K, Isobe M, Okazaki S, Ichiyama S, Hoashi T, et al. Generalized pustular psoriasis complicated with idiopathic retroperitoneal fibrosis successfully treated with infliximab. *J Dermatol.* 2021; **48**: e436-e437.
6. Li M, Dai W, Yan W, Liu Y, Wang L, Li W. A dramatic response to a single dose of infliximab in a patient with prolonged pustular psoriasis derived from inverse psoriasis. *Dermatol Ther.* 2017; **30**: e12492.
7. Newland MR, Weinstein A, Kerdel F. Rapid response to infliximab in severe pustular psoriasis, von Zumbusch type. *Int J Dermatol.* 2002; **41**: 449-452.

8. Osmola-Mańkowska A. Generalised pustular psoriasis: A review of therapeutic approaches. *Przegl Dermatol.* 2014; **6**: 473-476.
9. Saito K, Ito A, Ishikawa K, Shimada H, Takeo N, Hatano Y, et al. Pustular psoriasis occurring after total colectomy for ulcerative colitis and relieved by administration of infliximab. *J Dermatol.* 2014; **41**: 1033-1034.
10. Sakai H, Nomura W, Fukushima H, Sugiura K, Iizuka H. Terbinafine-induced generalized pustular psoriasis in a patient carrying CARD14 mutation. *J Dermatol.* 2019; **46**: e110-e112.
11. Samotij D, Gawron E, Szczęch J, Ostańska E, Reich A. Acrodermatitis continua of Hallopeau evolving into generalized pustular psoriasis following COVID-19: A case report of a successful treatment with infliximab in combination with acitretin. *Biologics.* 2021; **15**: 107-113.
12. Sheth N, Greenblatt DT, Acland K, Barker J, Teixeira F. Generalized pustular psoriasis of pregnancy treated with infliximab. *Clin Exp Dermatol.* 2009; **34**: 521-522.
13. Smith N, Harms KL, Hines AC, Harms PW, Gudjonsson JE, Hristov AC, et al. Acute treatment of generalized pustular psoriasis of von Zumbusch with single-dose infliximab. *J Am Acad Dermatol.* 2013; **68**: e187-9.
14. Tang MM, Spanou Z, Tang H, Schibler F, Pelivani N, Yawalkar N. Rapid downregulation of innate immune cells, interleukin-12 and interleukin-23 in generalized pustular psoriasis with infliximab in combination with acitretin. *Dermatology.* 2012; **225**: 338-343.
15. Varma R, Cantrell W, Elmetts C, Elewski B. Infliximab for the treatment of severe pustular psoriasis: 6 years later. *J Eur Acad Dermatol Venereol.* 2008; **22**: 1253-1254.
16. Brenner M, Molin S, Ruebsam K, Weisenseel P, Ruzicka T, Prinz JC. Generalized pustular psoriasis induced by systemic glucocorticosteroids: four cases and recommendations for treatment. *Br J Dermatol.* 2009; **161**: 964-966.
17. Kim HS, You HS, Cho HH, Kim WJ, Mun JH, Song M, et al. Two cases of generalized pustular psoriasis: successful treatment with infliximab. *Ann Dermatol.* 2014; **26**: 787-788.
18. Kołt-Kamińska M, Żychowska M, Reich A. Infliximab in combination with low-dose acitretin in generalized pustular psoriasis: A report of two cases and review of the literature. *Biologics.* 2021; **15**: 317-327.
19. Routhouska SB, Sheth PB, Korman NJ. Long-term management of generalized pustular psoriasis with infliximab: case series. *J Cutan Med Surg.* 2008; **12**: 184-188.
20. Sugiura K, Endo K, Akasaka T, Akiyama M. Successful treatment with infliximab of sibling cases with generalized pustular psoriasis caused by deficiency of interleukin-36 receptor antagonist. *J Eur Acad Dermatol Venereol.* 2015; **29**: 2054-2056.

21. Trent JT, Kerdel FA. Successful treatment of Von Zumbusch pustular psoriasis with infliximab. *J Cutan Med Surg.* 2004; **8**: 224-228.
22. Viguier M, Aubin F, Delaporte E, Pages C, Paul C, Beylot-Barry M, et al. Efficacy and safety of tumor necrosis factor inhibitors in acute generalized pustular psoriasis. *Arch Dermatol.* 2012; **148**: 1423-1425.
23. Weishaupt C, Metze D, Luger TA, Ständer S. Treatment of pustular psoriasis with infliximab. *J Dtsch Dermatol Ges.* 2007; **5**: 397-399.
24. Gallo E, Llamas-Velasco M, Daudén E, García-Diez A. Refractory generalized pustular psoriasis responsive to a combination of adalimumab and acitretin: Correspondence. *Int J Dermatol.* 2013; **52**: 1610-1611.
25. Gkalpakiotis S, Arenberger P, Gkalpakioti P, Hugo J, Sticova E, Tesinsky P, et al. A case of acute generalized pustular psoriasis of von Zumbusch treated with adalimumab. *J Eur Acad Dermatol Venereol.* 2015; **29**: 2063-2064.
26. Hay RAS, Pan JY. Paradoxical flare of pustular psoriasis triggered by ustekinumab, which responded to adalimumab therapy. *Clin Exp Dermatol.* 2014; **39**: 751-752.
27. Jordan J, Bieber T, Wilsmann-Theis D. Adalimumab: safe and successful in severe pustular psoriasis. *J Eur Acad Dermatol Venereol.* 2009; **23**: 592-593.
28. Kimura U, Kinoshita A, Sekigawa I, Takamori K, Suga Y. Successful treatment with adalimumab in a patient with psoriatic arthritis and generalized pustular psoriasis. *J Dermatol.* 2012; **39**: 1071-1072.
29. Wang TS, Tsai TF. Occurrence of psoriatic plaques on previous adalimumab injection sites during disease relapse in a patient with pustular psoriasis. *J Am Acad Dermatol.* 2014; **71**: e24-6.
30. Wang WM, Shu D, Jiang YY, Jin HZ. Recurrent generalized pustular psoriasis possibly triggered by apremilast. *Chin Med J (Engl).* 2020; **133**: 1259-1260.
31. Zangrilli A, Papoutsaki M, Talamonti M, Chimenti S. Long-term efficacy of adalimumab in generalized pustular psoriasis. *J Dermatolog Treat.* 2008; **19**: 185-187.
32. Kawakami H, Maeda T, Abe N, Matsumoto Y, Mitsunashi Y, Tsuboi R, et al. Efficacy of adalimumab and methotrexate combination therapy on generalized pustular psoriasis patients unresponsive to infliximab monotherapy due to anti-infliximab antibody development. *J Dermatol.* 2015; **42**: 94-95.
33. Matsumoto A, Komine M, Karakawa M, Kishimoto M, Ohtsuki M. Adalimumab administration after infliximab therapy is a successful treatment strategy for generalized pustular psoriasis. *J Dermatol.* 2017; **44**: 202-204.

34. Kamarashev J, Lor P, Forster A, Heinzerling L, Burg G, Nestle FO. Generalised pustular psoriasis induced by cyclosporin a withdrawal responding to the tumour necrosis factor alpha inhibitor etanercept. *Dermatology*. 2002; **205**: 213-216.
35. Lo Schiavo A, Brancaccio G, Puca RV, Caccavale S. Etanercept in the treatment of generalized annular pustular psoriasis. *Ann Dermatol*. 2012; **24**: 233-234.
36. Mikhail M, Weinberg JM, Smith BL. Successful treatment with etanercept of von Zumbusch pustular psoriasis in a patient with human immunodeficiency virus. *Arch Dermatol*. 2008; **144**: 453-456.
37. Palomo AA, Torres ILM, Cervigón GI. Generalized Pustular Psoriasis: Treatment with Etanercept. *Med Cutan Iber Lat Am*. 2009; **37**: 224-226.
38. Rodríguez-Lomba E, Baniandrés O, Cano N, Suárez-Fernández R. Generalised pustular psoriasis and neutrophilic cholangitis: An infrequently reported association with excellent response to tumour necrosis factor inhibitors. *Australas J Dermatol*. 2017; **58**: 70-71.
39. Esposito M, Mazzotta A, Casciello C, Chimenti S. Etanercept at different dosages in the treatment of generalized pustular psoriasis: a case series. *Dermatology*. 2008; **216**: 355-360.
40. Mizutani Y, Mizutani YH, Matsuyama K, Kawamura M, Fujii A, Shu E, et al. Generalized pustular psoriasis in pregnancy, successfully treated with certolizumab pegol. *J Dermatol*. 2020; **47**: e262-e263.
41. Narbutt J, Trelńska M, Woźniacka A, Olejniczak-Staruch I, Lesiak A. Challenges of biological therapy in patients with pustular psoriasis coexisting with psoriatic arthritis. *Przegl Dermatol*. 2017; **2**: 103-111.
42. Akaji K, Nakagawa Y, Kakuda K, Takafuji M, Kiyohara E, Murase C, et al. Generalized pustular psoriasis associated with systemic lupus erythematosus successfully treated with secukinumab. *J Dermatol*. 2021; **48**: e43-e44.
43. Böhner A, Roenneberg S, Eyerich K, Eberlein B, Biedermann T. Acute generalized pustular psoriasis treated with the IL-17A antibody secukinumab. *JAMA Dermatol*. 2016; **152**: 482-484.
44. Gabeff R, Safar R, Leducq S, Maruani A, Sarabay G, Touitou I, et al. Successful therapy with secukinumab in a patient with generalized pustular psoriasis carrying homozygous IL36RN p.His32Arg mutation. *Int J Dermatol*. 2019; **58**: e16-e17.
45. Honma M, Nozaki H, Hayashi K, Iinuma S, Ishida-Yamamoto A. Palmoplantar pustulosis emerged on a case of generalized pustular psoriasis successfully treated by secukinumab. *J Dermatol*. 2019; **46**: e468-e469.
46. Liu N, Zhu L, Cheng Y, Yu N, Yi X, Ding Y. Successful treatment of recurrent pustular psoriasis of pregnancy with secukinumab: A case report. *Acta Derm Venereol*. 2020; **100**: 5860.

47. Miyagawa F, Fukuda K, Mori A, Ogawa K, Asada H. Recurrence of secukinumab-induced eczematous eruptions after guselkumab treatment for pustular psoriasis. *J Dermatol*. 2021; **48**: E498-E499.
48. Polesie S, Lidholm AG. Secukinumab in the treatment of generalized pustular psoriasis: A case report. *Acta Derm Venereol*. 2017; **97**: 124-125.
49. Yeung J, Valbuena V. Successful use of secukinumab in pustular psoriasis. *JAAD Case Rep*. 2016; **2**: 470-472.
50. Mugheddu C, Atzori L, Lappi A, Pau M, Murgia S, Rongioletti F. Successful Secukinumab treatment of generalized pustular psoriasis and erythrodermic psoriasis. *J Eur Acad Dermatol Venereol*. 2017; **31**: e420-e421.
51. Sun ZL, Liu ZL, Xu YY, Zhang XL, Zhang CL, Guan X. Successful treatment of generalized pustular psoriasis with secukinumab: a report of two cases: A report of two cases. *Chin Med J (Engl)*. 2020; **133**: 3015-3016.
52. Taguchi R, Takamura S, Teraki Y. Combination therapy with biologic and colchicine for generalized pustular psoriasis. *Int J Dermatol*. 2020; **59**: e400-e402.
53. Wilsmann-Theis D, Schnell LM, Ralser-Isselstein V, Bieber T, Schon MP, Huffmeier U, et al. Successful treatment with interleukin-17A antagonists of generalized pustular psoriasis in patients without IL36RN mutations. *J Dermatol*. 2018; **45**: 850-854.
54. Xia P, Li YH, Liu Z, et al. Recalcitrant paradoxical pustular psoriasis induced by infliximab: Two case reports. *World J Clin Cases*. 2021; **9**: 3655-3661.
55. Dattola A, Manfreda V, Esposito M, Bianchi L, Giunta A. A case of generalized pustular psoriasis and arthritis treated with ixekizumab. *J Dermatolog Treat*. 2020; **31**: 754-755.
56. Megna M, Abategiovanni L, Annunziata A, Torta G, Peduto T, Fabbrocini G, et al. Generalized pustular psoriasis rapidly and successfully treated with ixekizumab in a Caucasian patient. *Dermatol Ther*. 2022; **35**: e15382.
57. Sawabe Y, Hayashi K, Kamata M, Nagata M, Fukaya S, Fukuyasu A, et al. Case of generalized pustular psoriasis with coexisting mutations in IL36RN and CARD14. *J Dermatol*. 2019; **46**: e368-e370.
58. Ichiyama S, Sugiura K, Hoashi T, Kanda N, Saeki H. Generalized pustular psoriasis with deficiency of interleukin-36 receptor antagonist associated with sensorineural hearing impairment. *J Dermatol*. 2021; **48**: e 470-e471.
59. Shukuin R, Koizumi H, Ebata A, Imai S, Yamashita Y, Ogawa-Momohara M, et al. Successful combination therapy of bimekizumab and granulocyte monocyte adsorption apheresis for generalized pustular psoriasis complicated with microscopic polyangiitis. *J Dermatol*. 2023; **50**: e181-e182.

60. Okazaki S, Hoashi T, Sacki H, Kanda N. A case of autoimmune hepatitis/primary biliary cholangitis overlap syndrome during treatment with brodalumab for generalized pustular psoriasis. *J Nippon Med Sch.* 2021; **88**: 569-573.
61. Pavia G, Gargiulo L, Spinelli F, Avagliano J, Valenti M, Borroni RG, et al. Generalized pustular psoriasis flare in a patient affected by plaque psoriasis after BNT162b2 mRNA COVID-19 vaccine, successfully treated with risankizumab. *J Eur Acad Dermatol Venereol.* 2022; **36**: e502-e505.
62. Ruggiero A, Lauro W, Fabbrocini G, Miano C, Villani A, Marasca C. A case of recalcitrant circinate generalized (Lapière) psoriasis successfully treated with risankizumab. *Case Rep Dermatol.* 2022; **14**: 138-143.
63. Daudén E, Santiago-et-Sánchez-Mateos D, Sotomayor-López E, García-Díez A. Ustekinumab: effective in a patient with severe recalcitrant generalized pustular psoriasis: Correspondence. *Br J Dermatol.* 2010; **163**: 1346-1347.
64. Storan ER, O’Gorman SM, Markham T. Generalized pustular psoriasis treated with ustekinumab. *Clin Exp Dermatol.* 2016; **41**: 689-690.
65. Arakawa A, Ruzicka T, Prinz JC. Therapeutic efficacy of interleukin 12/interleukin 23 blockade in generalized pustular psoriasis regardless of IL36RN mutation status. *JAMA Dermatol.* 2016; **152**: 825-828.
66. Hüffmeier U, Wätzold M, Mohr J, Schön MP, Mössner R. Successful therapy with anakinra in a patient with generalized pustular psoriasis carrying IL36RN mutations. *Br J Dermatol.* 2014; **170**: 202-204.
67. Podlipnik S, de la Mora L, Alsina M, Mascaró JM Jr. Pneumocystis jirovecii pneumonia in a patient with pustular psoriasis with an IL-36RN deficiency treated with infliximab: Case report and review of the literature. *Australas J Dermatol.* 2017; **58**: e44-e47.
68. Viguier M, Guigue P, Pagès C, Smahi A, Bachelez H. Successful treatment of generalized pustular psoriasis with the interleukin-1-receptor antagonist Anakinra: lack of correlation with IL1RN mutations. *Ann Intern Med.* 2010; **153**: 66-67.
69. Mansouri B, Richards L, Menter A. Treatment of two patients with generalized pustular psoriasis with the interleukin-1 $\beta$  inhibitor gevokizumab. *Br J Dermatol.* 2015; **173**: 239-241.