



Subcutaneous immunoglobulin therapy: a new option for patients with primary immunodeficiency diseases

Mai Thị Bích Ngọc



Background

- Primary immunodeficiency diseases (PID): group of over 150 disorders due to defects in critical pathways involved in host defense against infection and immune regulation.
- 50% of PID: defects in antibody production.
- Recurrent and severe bacterial infections, autoimmune disease, inflammatory disorders, and lymphoproliferative disorders.
 - lung damage and shortened life span.

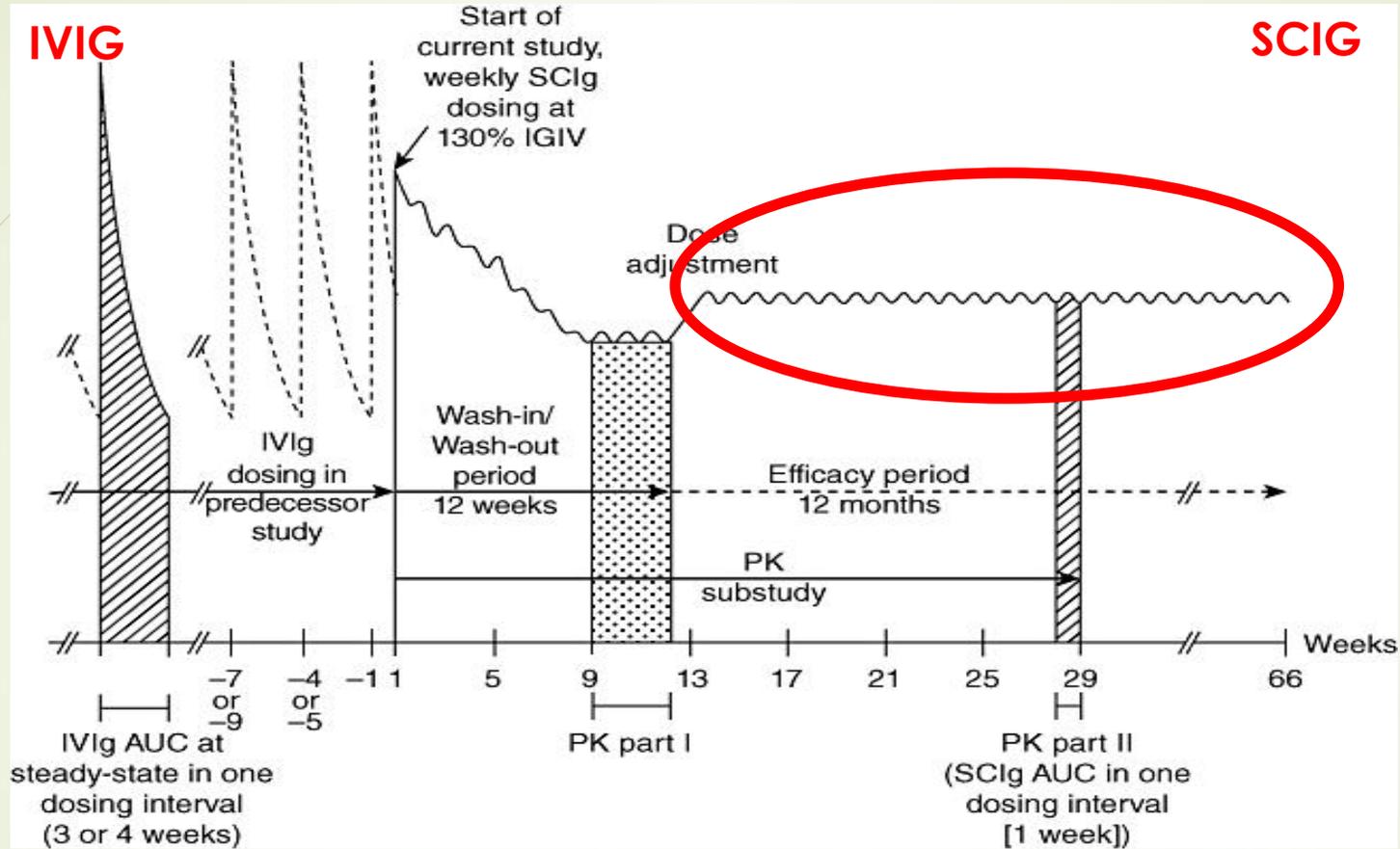


Background

- ▶ Treatment: replacement of immunoglobulin G
 - 1950s: intravenous immunoglobulins (IVIg) every 3–4 weeks
 - 2006: Subcutaneous immunoglobulin

IVIG vs SCIG

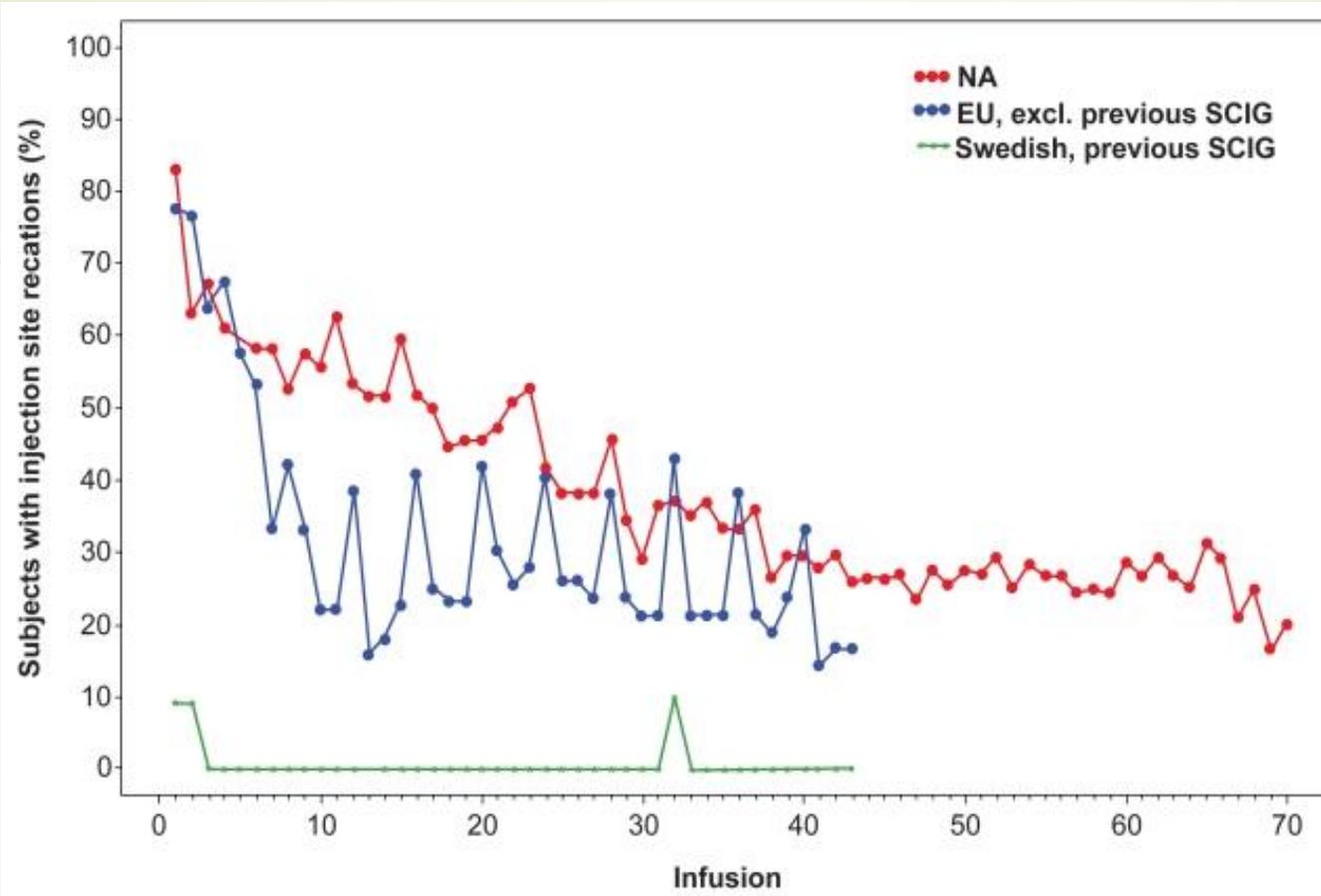
| | IVIG | SCIG |
|----------------------------|---------------------------------------|-------------------------------------|
| Venous access | Yes | No |
| Time of administration | Long | Short (15 – 90 minutes) |
| Frequency | 2-4 weeks | Daily or every 1 – 2 weeks |
| Blood IgG level | Big variation between peak and trough | Higher and more stable trough level |
| Systemic adverse reactions | Many | Few |



Comparison of IgG trough levels

| Adverse event | EU study | US study |
|----------------------|------------------------------|------------------------------|
| | No. (%) of subjects (N = 40) | No. (%) of subjects (N = 21) |
| Arthralgia | 6 (15.0) | 5 (23.8) |
| Abdominal pain upper | 4 (10.0) | 2 (9.5) |
| Abdominal pain | 0 | 3 (14.3) |
| Diarrhea | 4 (10.0) | 3 (14.3) |
| Pyrexia | 4 (10.0) | 2 (9.5) |
| Back pain | 3 (7.5) | 3 (14.3) |
| Headache | 2 (5.0) | 3 (14.3) |
| Fatigue | 1 (2.5) | 5 (23.8) |
| Oropharyngeal pain | 1 (2.5) | 6 (28.6) |
| Anxiety | 0 | 3 (14.3) |
| Nausea | 0 | 4 (19.0) |

Most common adverses



Injection-site reactions over time

The occurrence of injection-site reactions (of any severity) decreases over repeated SCIG administrations in subjects from two clinical trials, in North America (NA) and Europe (EU)

(Chen et al., 2006; O'Neil et al., 2006)

| Year: country | Comparison groups | Outcomes | Preference |
|--------------------|--|--|--|
| 2006 North America | A: SCIG at home vs IVIG hospital B: SCIG home vs IVIG at home | Statistically significant improvements in physical limitations, general health, vitality, health transition, LQI/treatment satisfaction (A); general health (B) SCIG | 81% (A), 69% (B) preferred SCIG |
| 2008 Sweden | SCID at home vs IVIG hospital | Statistically significant improvements in mental health, change in health, family activities and global health at 6 months (CHQ-PF50) | All subjects preferred home SCIG |
| 2010 Germany | SCID at home vs IVIG hospital | Statistically significant improvements in bodily pain, general health perception, vitality (SF-36), family activities, parental emotional and time, general health | 92% preferred SCIG 83% preferred home treatment |
| 2011 Germany | SCID at home vs IVIG hospital | Health-related Quality of Life, LQI improved in SCIG, significant increase in score for convenience | 80% preferred SCIG |

Quality of life studies in PIDD patients switching to SCIG therapy

SCIg: Pump or Push

| PUMP | PUSH |
|-----------------------|------------------------------------|
| Full dose once a week | Smaller dose multiple times a week |
| 25 ml per site | 3 – 20 ml per site |
| 1 – 4 sites | 1 – 2 sites |
| 60 ml syringe | 5,10, 20 ml syringe |



SCIg products

| Product | IgG concentration | IgA content | Stabilizer | Viral inactivation |
|------------------|-------------------|-------------|------------|---|
| Gammagard liquid | 100 mg/mL | 37 mcg/mL | Glycine | Solvent/detergent Nanofiltration Low pH/temperature |
| Gammaked™ | 100 mg/mL | 46 mcg/mL | Glycine | Low pH Caprylate precipitation Depth filtration |
| Gamunex-C | 100 mg/mL | 46 mcg/mL | Glycine | Low pH Caprylate precipitation Depth filtration |
| Hizentra® | 200 mg/mL | <50 mcg/mL | L-proline | Low pH Nanofiltration Depth filtration |



Conclusion

Subcutaneous immunoglobulin therapy is a useful option for many patients because of better tolerability and the freedom to choose when and where they receive their gamma globulin supplementation.