A COMPREHENSIVE ANALYSIS OF THE SAFETY OF A NEW RANGE OF INJECTABLE HYALURONIC ACID PRODUCTS FOR AESTHETIC INDICATIONS

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INTRODUCTION

This review concerns the post-market safety experience of a range of hyaluronic acid (HA) fillers developed by Q-Med AB (Uppsala, Sweden), using Optimal Balance Technology (OBT)™, known as XpresHAn Technology™ in the US (Table 1).[1]

Almost 1 million units were sold (ex-US) during the first 5 years on the market; this volume and duration of use allows for a thorough and accurate evaluation of the safety of these products to be conducted.[2]

SUBJECTS and METHODS

Data Collection:

- The safety dataset was compiled from post-market surveillance (PMS) reports of adverse events (AEs) received since the products were launched in 2011, including any cases reported in the literature
- A total of 302 PMS case reports were included in the analysis
- Available safety data obtained from sponsored clinical studies were also collected and reviewed

Data Analysis:

- Reporting frequencies for PMS reports were calculated based on the number of units of product sold and on the assumption that 1 unit was used per treatment
- AEs classified as related to treatment or as unassessable were considered to be potentially related AEs and were included in the analysis
  - Potentially related adverse events with similar or associated preferred terms were grouped.

REFERENCES

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2. Data on file, Galderma Laboratories, L.P.
3. Farhi D, Trevidic P, Kestemont P, et al. The emervel french survey: a prospective real-practice descriptive study of 1,822 patients treated for facial rejuvenation with a new hyaluronic acid filler. *J Drugs Dermatol*. 2013 May;12(5):e88-e93.
4. FDA Maude database.

RESULTS

- PMS case reports: Of the total number of AEs (from 302 case reports), 771 were classified as potentially related.
  - Overall reporting frequency: 0.033% for the period of 2011 to 2015, within a range between 0.026 to 0.035% per year
  - Five most common events were: swelling (0.016%), mass/induration (0.011%), pain and tenderness (0.007%), erythema (0.006%), and papules/nodules (0.006%)
  - The rare reports of delayed onset events of nodules, swelling or inflammation responded to corticosteroids or hyaluronidase
  - Ten cases were reported as serious (ie, ischemia with or without necrosis, infection, swelling and nodules)
- PMS case reports, continued
  - Time to onset provided for 483 (63%) of the events
    - 68% of AEs had a time to onset within 28 days after treatment, 77% within 60 days, and 90% within 120 days
  - Duration was available for 10% of events
    - Among these events, 85% resolved within 28 days and 95% within 60 days
  - Information on the event outcome showed that 64% were resolved or resolving, but no information was available for 25% of these events
- Reporting frequencies of nodules, inflammatory reactions and granulomas for OBT HA (Table 2)
- Safety data from 7 sponsored interventional clinical studies and 1 observational study were reviewed
  - Studies; 638 subjects followed for 24 weeks to 18 months
    - No related serious adverse events adverse events reported
    - AEs on 3 or more occasions in the entire study population: erythema, hematoma, swelling, pain, papules and telangiectasia
    - Other events reported with lower occurrences were edema, induration, inflammation, pruritus, dermatitis, and skin tightness
- The Emervel French survey, a prospective real-practice descriptive study of 1,822 patients treated with multiple products over 15 months[3]
  - No SAEs reported
  - Immediate post-treatment assessment showed good local tolerability

Table 1. Hyaluronic Acid-Based Injectable Filler Product Range: Original and Rebranded Names

New Name	Original Name	Unit Volumes
Restylane® Refyne	Emervel Classic Lidocaine	1 mL
Restylane® Defyne	Emervel Deep Lidocaine	1 mL
Restylane® Kysse	Emervel Lips Lidocaine	1 mL
Restylane® Volyme	Emervel Volume Lidocaine	1 mL 2 mL
Restylane® Fynesse	Emervel Touch	1 mL

SUMMARY

- There is now a 5-year safety experience to give confidence for use of the OBT range (known as XpresHAn Technology™ in the US) of HA fillers
- There are no new unexpected AEs compared to other established fillers on the market
- Late onset-AEs that are difficult to treat are very rare
- The insight gained from real-world practice is that the use of hyaluronidase with or without corticosteroids can treat rare events such as granulomas, delayed onset nodules, and swelling

Table 2. Reporting Frequencies of Selected Adverse Events

Adverse Events	Emervel (OBT HA)[2,4]
	Reporting rate (%), (n = 922,594) Jan 1, 2011 to Dec 31, 2015
Swelling/Edema	0.0163
Inflammatory reaction	0.003
Papules/Nodules	0.006
Granuloma	0.00043
Hypersensitivity	0.001
Ischemia/Necrosis	0.001

Table 3. Adverse Events Reported After 28 Days[2,4]

Adverse Events	Number	Typical Outcome if Available
Granuloma	5	Typically resolved with hyaluronidase monotherapy or combination therapy
Nodules	13	Typically resolved with hyaluronidase monotherapy or combination therapy
Swelling with or without inflammation	6	Typically resolved with hyaluronidase monotherapy or combination therapy
Swelling preceded by infective episode	4	Recovered after antibiotics

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