

COMBINING OUR STRENGTHS
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Evaluation of ZOSTAVAX® Via the Intradermal Route Using the MicronJet™

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Overview

- ZOSTAVAX® Vaccine Background
- Intradermal Vaccine Delivery
  - MicronJet™
  - Human Skin and Device Depth
- Pre-clinical considerations and studies
- Clinical Design
- Clinical Outcomes
  - Geomean Titers
  - ELISPOT Data
  - Safety
- Conclusions

Public

ZOSTAVAX®



- Vaccine to prevent shingles due to reactivation of varicella
- Administered to ages 50 and older
- Provided by reconstituting a lyophilized cake in a glass vial with sterile diluent (water)
- Subcutaneous administration using a staked needle, single-dose

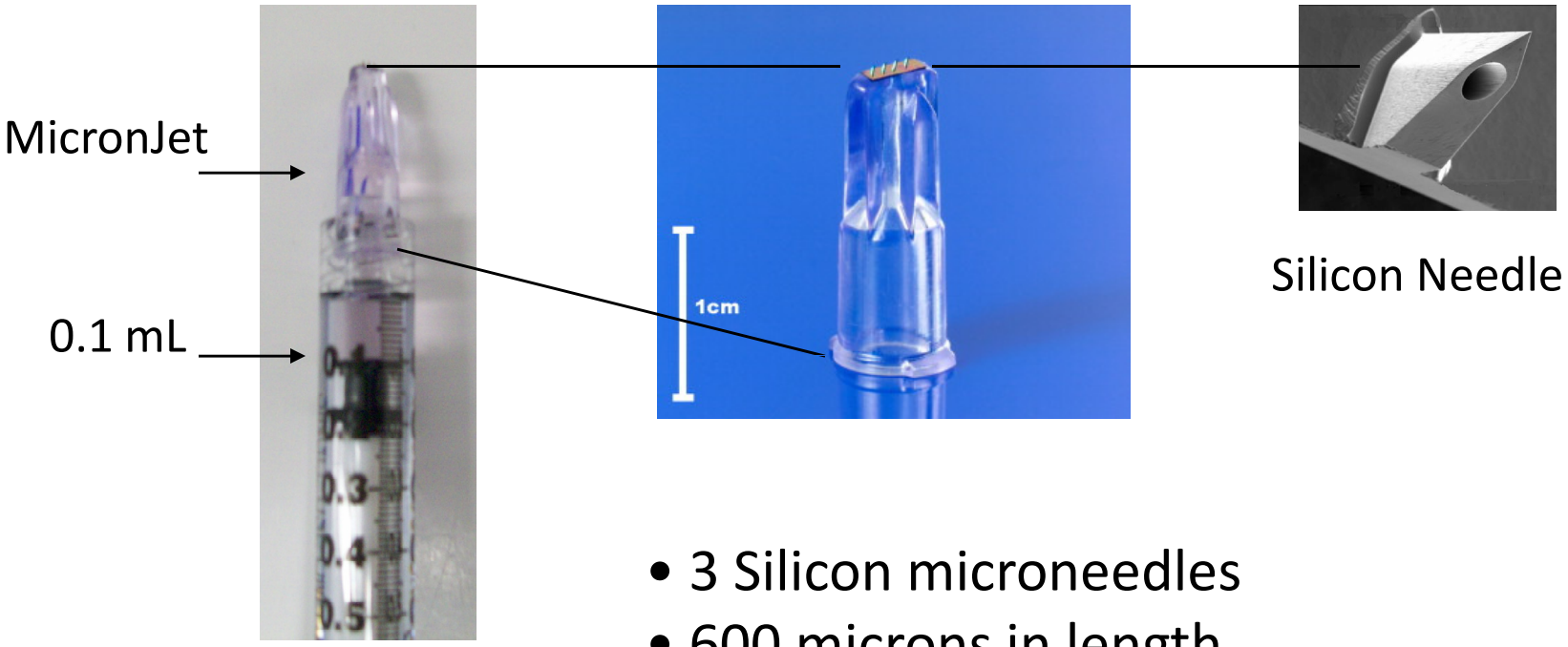
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Intradermal Vaccine Delivery

- Vaccines Delivered Intradermally
  - BCG
  - Fluzone® Intradermal
  - Several rabies vaccines
- Other vaccines being investigated via the intradermal route (www.clinicaltrials.gov)
- We evaluated the intradermal delivery of ZOSTAVAX®

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MicronJet™

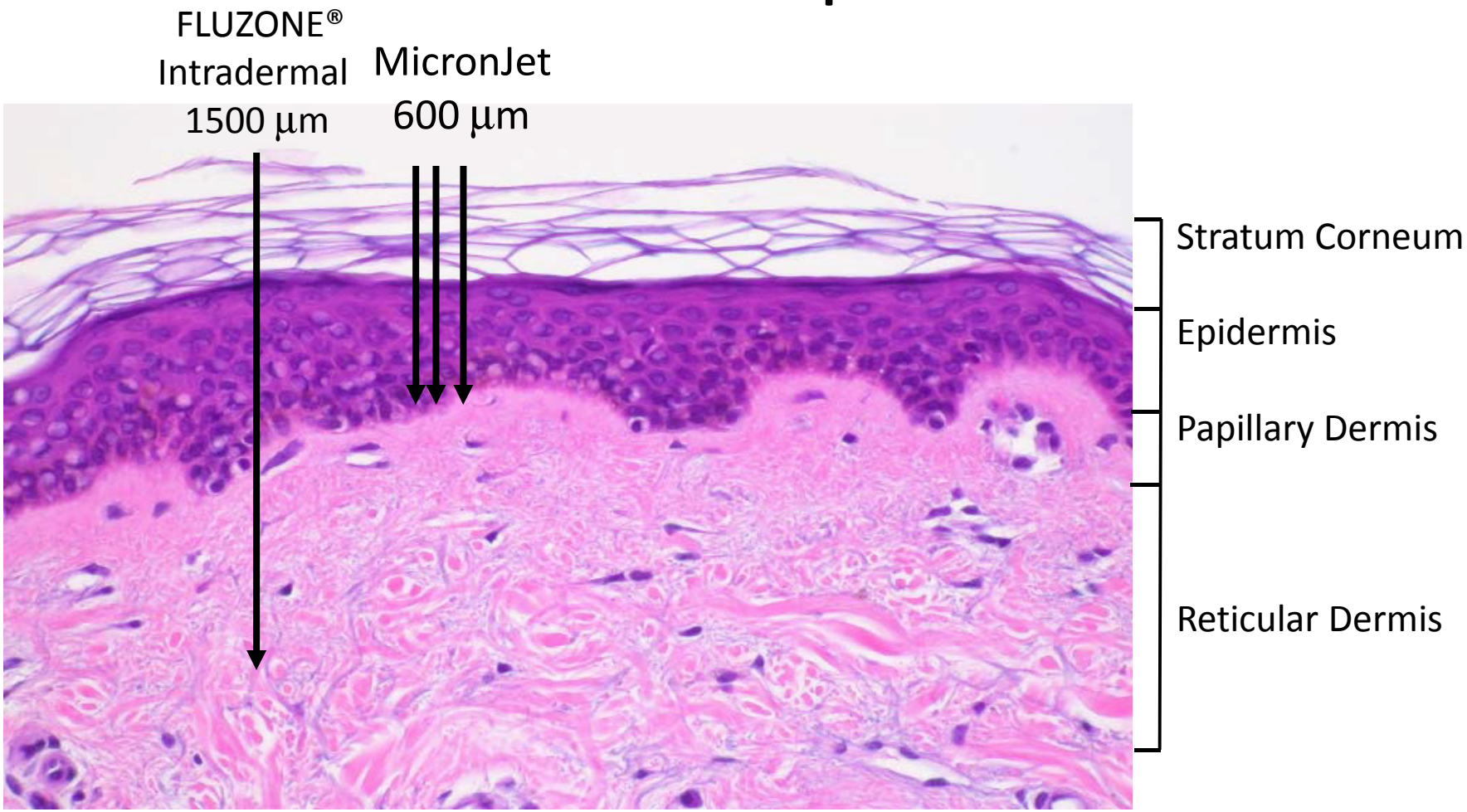


- 3 Silicon microneedles
- 600 microns in length
- Polycarbonate Luer-loc hub
- Attaches to a 1 mL syringe
- Targets epidermis

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Ref. 31, 32

Human Skin and Intradermal Device Depth



(www.istock.com)

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Pre-Clinical Considerations and Studies

- Subcutaneous administration of ZOSTAVAX®
  - ZOSTAVAX® administered by reconstituting 1 vial in 0.7 mL diluent (water)
  - Administer 0.65 mL subcutaneously
- Intradermal administration of ZOSTAVAX®
  - Full-dose, 1/3, 1/10, 1/27 Dose ID
  - Full Dose
    - 0.15 mL maximum volume per injection
    - Re-constituted 2 vials in 0.35 mL diluent each
    - 2 injections of 0.15 mL each
  - 1/3 dose
    - Re-constitution in 0.3 mL water, administer 0.1 mL
  - 1/10 dose
    - Re-constitution in 1 mL water, administer 0.1 mL
  - 1/27 dose
    - Re-constitution in 2.7 mL saline, administer 0.1 mL
  - Performed syringeability studies with all doses and measured vaccine potency

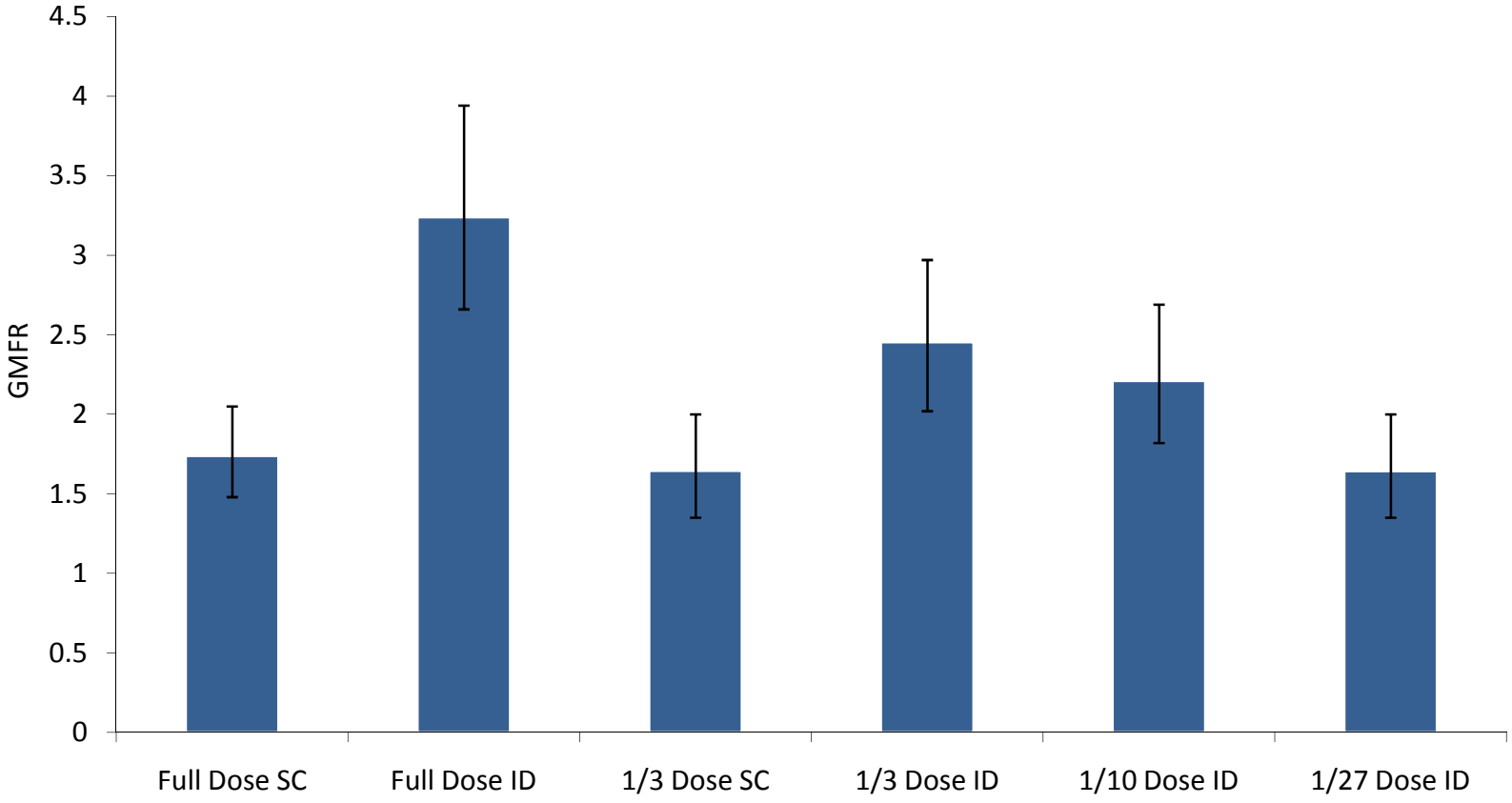
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Clinical Design

- 221 patients enrolled, 3 clinical sites
- Partially Blinded Randomized Trial to evaluate the Immunogenicity and Safety of Zostavax™
- Groups
  - Full-dose SC
  - 1/3 dose SC
  - Full-dose, 1/3, 1/10, 1/27 Dose ID using the MicronJet
- Evaluated a geometric mean fold rise from baseline in VZV-antibodies
- ELISPOT

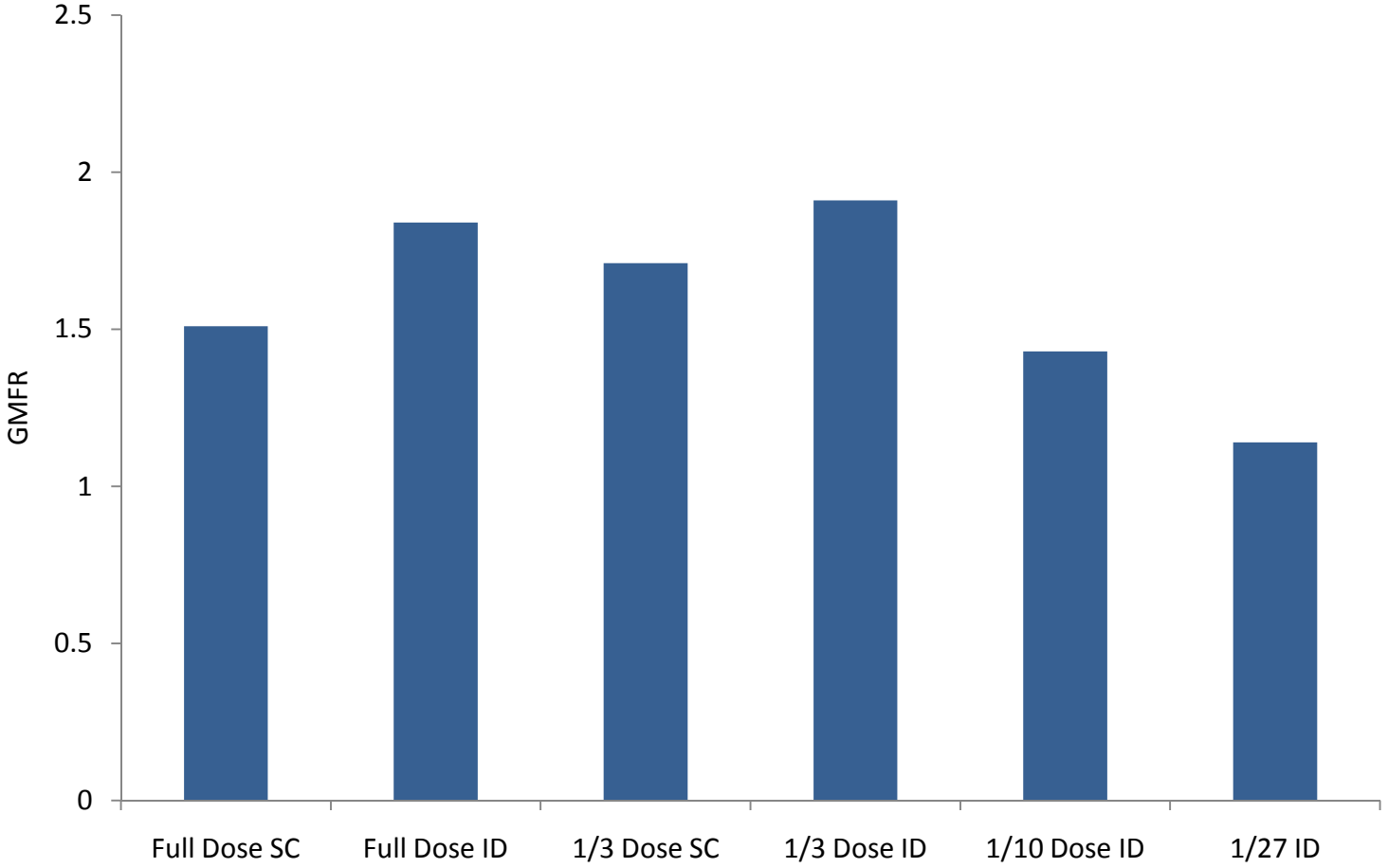
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Titer / Geomean-Fold Rise (GMFR)



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ELISPOT



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SAFETY

- Utilized a Vaccine Report Card
  - Previously validated
  - Subjects recorded daily oral temperatures and injection-site and systemic adverse experiences from Day 1 to 42 Post-vaccination
  - Document injection site reactions (redness, swelling, pain/tenderness) within 5 days of vaccination

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SAFETY (continued)

Table 1. Subjects With Injection Site Adverse Events (Reldays 1 to 5)

	Full SC	1/3 SC	Full ID	1/3 ID	1/10 ID	1/27 ID	Placebo
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Subjects in Population	52	34	34	35	34	34	39
With one of more Injection Site AEs	27 (51.9)	7 (20.6)	27 (79.4)	22 (62.9)	19 (55.9)	19 (55.9)	5 (12.8)
General Disorders and administration site conditions							
Injection site anaesthesia	0 (0)	0 (0)	0 (0)	1 (2.9)	0 (0)	0 (0)	0 (0)
Injection site erythema	16 (30.8)	5 (14.7)	26 (76.5)	20 (57.1)	16 (47.1)	18 (52.9)	4 (10.3)
Injection site haematoma	2 (3.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Injection site induration	5 (9.6)	2 (5.9)	12 (35.3)	12 (34.3)	11 (32.4)	10 (29.4)	1 (2.6)
Injection site pain	15 (28.8)	5 (14.7)	8 (23.5)	9 (25.7)	5 (14.7)	6 (17.6)	0 (0)
Injection site pruritus	1 (1.9)	2 (5.9)	3 (8.8)	3 (8.6)	1 (2.9)	1 (2.9)	0 (0)
Injection site rash	1 (1.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Injection site scab	0 (0)	0 (0)	1 (2.9)	0 (0)	0 (0)	0 (0)	0 (0)
Injection site swelling	13 (25)	4 (11.8)	13 (38.2)	8 (22.9)	6 (17.6)	7 (20.6)	2 (5.1)

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Conclusions

- ZOSTAVAX® delivered intradermally with the MicronJet had a GMFR point estimate that was 2-fold higher when compared to the standard, subcutaneous route
- ZOSTAVAX® delivered intradermally using the MicronJet may result in enhanced immunogenicity when compared to subcutaneous delivery using a staked needle, as measured by gpELISA in adults 50 years and older
  - An efficacy study would be required to establish this point
  - The full dose for the 50-59 age group was atypically low vs. historical data
  - Full dose was administered with the MicronJet with two 0.15 mL doses
- A dose-response was observed for the intradermal route with the MicronJet
- A fraction of the full dose with the MicronJet yielded similar gpELISA and ELISPOT values as compared to the full dose given subcutaneously
- A larger percentage of subjects in ID vaccinations reported injection site erythema and induration when compared to subcutaneous vaccination
- Use of the MicronJet resulted in less injection site pain with the full dose when compared to subcutaneous delivery

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