

Brief overview of use of aluminium salts and other adjuvants for influenza vaccines

Masato Tashiro
National Institute of Infectious Diseases
Japan

Slide 1

M1

Masato, 2009-06-03

Types of aluminium salts used

- Aluminium hydroxide
- Aluminium phosphate
 - Combination of above
- Both widely used in routine paediatric vaccines; DTP, hepatitis B, HiB etc.
Rare aluminium-associated SAEs well documented.

Mode of action

- Still not completely elucidated:
 - Antigen binding and depot effect clearly plays a role.
 - Direct immunostimulatory effect of aluminium via inflammasome and NALP receptor
 - APC death
 - Th2 predominant (serum antibodies > CTL)

Clinical Experience with Split

- CSL
 - Approved pandemic vaccine (Panvax)
 - 150 infants, 590 adults, 196 elderly
- Sanofi Pasteur
 - submitted for approval
 - N= >1 100 adults and elderly (H5N1)
 - Systemic profile identical to seasonal flu vaccine
- Kaketsuken, Japan
 - Phase 1; N=100 adults
 - Much less immunogenic than whole virion

Clinical Experience with whole virion

- Omninvest (Hungary)
 - Approved seasonal vaccine (>15M doses distributed annually)
 - Age >3. No SAE in clinical trials n=1080
 - Approved pandemic vaccine
- GSK
 - Approved pandemic (mock-up) Daronrix
 - n=200

Clinical Experience with whole virion – contd.

- Biken, Kitasato, Kaketuken, DenkaSeiken (Japan):
 - Approved pandemic vaccines (N=1000)
 - Safety studies (N=6,000 adults)
 - 8 hospitalized, but 6 not related.
 - 1 asthmatic, 1 emotional hyperventilation.
 - Prime and cross-boosting tests (N=200 adults)
- Sinovac (China)
 - Approved pandemic vaccines
 - N =522 adults

Polyoxidonium

- Poly-electrolyte polymer
 - Co-polymer N-oxi 1,4-ethylenpiperazine and(N-carboxiethyl) -1,4 ethylenpiperazine bromide
 - Registered as immunomodulator since 1996
 - Used in approved Russian seasonal vaccine Grippol
 - Tested in H5N1 vaccine trials in 2006
 - Safety issue in seasonal vaccine 2006 campaign
 - Allergic reactions (1.5/100,000 children)
 - Possibly observed due to campaign

Virosomes

- Crucell (Berna)
 - Reconstituted HA and NA in liposome membrane
 - Approved seasonal vaccine (Invivac)
 - No published safety concerns for parenteral delivery