GRADE Table 2. What is the effectiveness of live attenuated JE vaccine in preventing JE disease in vaccinees living in JE-endemic areas?

Population : Immunocompetent individuals living in JE-endemic areas
Intervention: One dose of live attenuated JE vaccine
Comparison: Placebo/no vaccination/other JE vaccine
Outcome : JE disease (immunogenicity accepted)

What is the effectiveness of one dose of live attenuated JE vaccine in preventing JE disease in individuals living in JE-endemic areas?				
			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		4 RCTs[1]	4
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious[2]	0
		Indirectness	Serious[3]	-1
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Applicable[4,5]	+1
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**4**
Summary of Findings	**Statement on quality of evidence**			**Evidence supports a high level of confidence that the true effect lies close to that of the estimate of effect on health outcome**
	Conclusion			**Live attenuated JE vaccines elicit seroprotective neutralizing antibody titres.** ***Based on a review of data on CD.JEVAX***

[1]Four clinical studies with 1,256 participants receiving CD.JEVAX were assessed. Seroprotection rates at 28 days post-vaccination in the Philippines study were 92.1% (95% CI: 84.3-96.7) and 90.6 (95% CI: 85.3-94.4); the latter result was in the group administered measles vaccine one month prior (Victor 2014). The seroprotection rate was 97.3% (95% CI: 93.1-99.2) for the live attenuated vaccine when used as a control in a live recombinant JE vaccine RCT in children aged 9 months to 18 years in Thailand (Feroldi 2014). In a similar study in children 12-24 months in Korea, the seroprotection rate was 99.1% (Kim 2013).

[2]In a lot-to-lot consistency study in Bangladesh with vaccine from a new GMP-compliant facility, seroprotection rates ranged between 80.2% (95% CI: 74.0-85.2) to 86.3% (95% CI: 79.8-91.0)(Zaman 2014). Two lots were not equivalent with a seroprotection rate difference of -4.33 (-11.94-3.31). No clinical consequences have been established and it was determined not to downgrade.

[3]Clinical study outcomes are based on an accepted immunological correlate of protection (Hombach 2005).

[4]High seroprotection (>80%) rates post-vaccination, a defined threshold in the WHO Guidance for the Development of Evidence-Based Vaccine-Related Recommendations.

[5]Two effectiveness studies were done in the near-term after vaccination. A case control study in Nepal estimated vaccine effectiveness to be 99.3% (95% CI: 94.9-100) in the one week to one month time period post-vaccination (Bista 2001). A

second case-control study in India estimated vaccine effectiveness to be 94.5% (95% CI: 81.5-98.9) six months following vaccination (Kumar 2009).

Reference List

Clinical Studies in Endemic Settings

Feroldi E, Pancharoen C, Kosalaraksa P, Chokephaibulkit K, Boaz M, Meric C, Hutagalung Y, Bouckenooghe A. Primary immunization of infants and toddlers in Thailand with Japanese encephalitis chimeric virus vaccine in comparison with SA14-14-2: a randomized study of immunogenicity and safety. Pediatr Infect Dis J. 2014 Jun;33(6):643-9.

Kim DS, Houillon G. A randomized study of the immunogenicity and safety of Japanese encephalitis chimeric virus vaccine (JE-CV) in comparison with SA 14-14-2 vaccine in children in South Korea. 8th World Congress of the World Society for Pediatric Infectious Diseases (WSPID) - Nov. 19-22, 2013, Cape Town, South Africa.

Victor J, Gatchalian S, Yao Y, Zhou B, Zhang L, Yoksan S, Yaich M, Neuzil K. Corrigendum to "Comparison of the immunogenicity and safety of measles vaccine administered alone or with live, attenuated Japanese encephalitis SA 14-14-2 vaccine in Philippine infants." Vaccine. 2014 32(2): 306-8.

Zaman K, Naser AM, Power M, Yaich M, Zhang L, Ginsburg AS, Luby SP, Rahman M, Hills S, Bhardwaj M, Flores J. Lot-to-lot consistency of live attenuated SA 14-14-2 Japanese encephalitis vaccine manufactured in a good manufacturing practice facility and non-inferiority with respect to an earlier product. Vaccine. 2014 Sep 18 (epub ahead of print).

Vaccine Effectiveness Studies (<12 months post-vaccination)

Bista MB, Banerjee MK, Shin SH, Tandan JB, Kim MH, Sohn YM, Ohrr HC, Tang JL, Halstead SB. Efficacy of single-dose SA 14-14-2 vaccine against Japanese encephalitis: a case control study. Lancet. 2001 Sep 8;358(9284):791-5.

Kumar R, Tripathi P, Rizvi A. Effectiveness of one dose of SA 14-14-2 vaccine against Japanese encephalitis. N Engl J Med. 2009 Apr 2;360(14):1465-6.

Other

Hombach J, et al. Report on a WHO consultation on immunological endpoints for evaluation of new Japanese encephalitis vaccines, WHO, Geneva, 2-3 September, 2004. Vaccine,2005;23(45):5205-11