

Record of Telephone Conversation, February 25, 2011 - Adenovirus

- Submission Type: BLA Submission ID: 125296/0 Office: OVRR
Product:
Adenovirus Vaccine Live Oral Type 4 and Type 7
Applicant:
Teva Women's Health, Inc.
Telecon Date/Time: 25-Feb-2011 12:30 PM Initiated by FDA? Yes
Telephone Number:
Communication Category(ies):
1. Information Request

Author: HELEN GEMIGNANI
Telecon Summary:
Information Request - Fever
FDA Participants: None
Non-FDA Participants: VALERIE MULLIGAN
Trans-BLA Group: No

Related STNs: None
Related PMCs: None
Telecon Body:

From: Valerie Mulligan [mailto:Valerie.Mulligan@tevausa.com]
Sent: Friday, February 25, 2011 12:30 PM
To: Gemignani, Helen S
Subject: FW: Information Request - Fever

Hi Helen,

As a follow-up to our teleconference of earlier this week, I am providing attachments to address the two items that were requested during the call.

The first request was for information identifying the number of febrile subjects that were recorded within 7 days of receipt of either vaccine or placebo tablets. The attachment "Onset of Febrile ARD" contains that information. Please note that the determination of a febrile condition depended on the subject voluntarily presenting him/herself to the clinic where body temperature could be measured. Data was recorded in degree F with a temperature of greater than or equal to 100.5 deg. F being designated as "febrile" illness.

During the TC, Dr. Schrager had requested clarification as to whether the throat culture data on subject #11077 that tested as "negative" was for adenovirus or some other organism. Per the study protocol, throat swabs were tested for the presence of adenovirus infection only. Additional details on the NHRC analysis may be found in

Appendix 2 - Specimen Collection and Analysis, Protocol DR-ADV-301 (page 305 of the BLA).

I will also briefly address the points raised in your email below, although I believe that we covered these issues during the TC.

1. The templates for the 7-day and 14-day subject diaries are located in Appendix 16.1.2 of CSR DR-ADV-301 (pages 743-6 of the BLA).
2. Fever was not a solicited AE in the study, as the subjects were not equipped with thermometers and so could not measure their temperature or self-diagnose a fever. A temperature measurement could only be done in the clinic.
3. Not applicable (see #2 above).
4. Yes, data on fever was included in the data set. Additional information on fever is presented in the attachment to this email.
5. The definition of fever is "greater than or equal to 100.5 deg F". As noted above, the clinical measurement was recorded as degree F and not degree C.

Finally, for your record, the attendees on the call representing Teva included;

Kathy Reape, M.D. FACOG, VP R&D Teva Women's Health

John Ianacone, Director CMC RA,

----- (b)(6) -----, Associate, RA

Jennifer Henrick, Associate Director, Clinical Program Management

----- (b)(4) -----, Consultant, Statistics

----- (b)(4) -----

Valerie Mulligan, Sr. Director, RA

I trust that this information is sufficient to address the two outstanding items.

Since we will be having a TC later today to talk about the Package Insert, I will hold off on sending you our latest iteration until after that call.

Best wishes,

Valerie

Valerie Mulligan

Sr. Director, Regulatory Affairs

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Response to FDA Request of 2/23/2011

Number of Febrile Episodes of ≥ 100.5 deg F at Day 7: Vaccine vs. Placebo

A total of 151 subjects presented at the clinic with suspected febrile ARD, regardless of whether an adenovirus serotype was eventually identified from a throat swab. Of those, 9 subjects were identified as having had their ARD episode begin prior to enrollment, randomization and receipt of vaccine or placebo, leaving a sample for evaluation of 142 subjects. The table below summarizes the proportion of the 142 subjects in the vaccine and placebo groups with onset of fever classified by time from vaccination in

weeks. Note that because all oral temperatures were recorded in deg F, the definition of fever was an oral temperature of ≥ 100.5 deg F.

The distribution of suspected febrile ARD cases was approximately the same for both vaccine and placebo, with three-fourths or more of all suspected cases being reported more than 2 weeks following vaccination. Less than 10% of all suspected cases were reported within the first week following ingestion of either vaccine or placebo tablets. Since there were 3 times more recruits in the vaccine group, the overall rate of fever is 2-3 times higher in the placebo group at all times in the trial.

Time from Vaccination to Onset of Fever in Febrile ARD Subjects

Treatment Cohort	Febrile ARD Subjects	Within 7 Days	Within 8-14 Days	Within >Than 14 Days
Vaccine (N=3031)	N=72	8 (11.1%)	10 (13.9%)	54 (75.0%)
Placebo (N=1009)	N=70	6 (8.6%)	9 (12.9%)	55 (78.6%)