

**Testimony Before the FDA's Bone, Reproductive,
and Urologic Drug Advisory Committee
Regarding Makena:
A Lack of Substantial Evidence of Effectiveness**

Meena M. Aladdin, Ph.D.

Health Researcher

Public Citizen's Health Research Group

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I have no financial conflicts of interest.

Premarket Clinical Trial 002

- **During the initial review of the NDA for Makena, the lead FDA statistician strongly recommended against the drug's approval, noting the following regarding the single, seriously flawed premarket phase 3 clinical trial:**

“From a statistical perspective, the level of evidence from Study 17P-CT002 is not sufficient to support the effectiveness of 17P. The primary reason is the absence of a second, confirmatory study.... Study 17P-CT002 was not designed for drug approval.”

“The results of the analyses of the 32 and 35 week endpoints suggest their false positive rates could be as great as 1/40.”

Postmarket Confirmatory Trial 003 Fails to Confirms Makena's Effectiveness

- **The PROLONG trial (Trial 003) was a well-designed, well-conducted, appropriately powered, clinical trial, the design of which was mutually agreed upon by the sponsor and FDA.**
- **The trial failed to show a statistically significant treatment effect for Makena on either of the coprimary endpoints:**
 - **Reduction of risk of delivery prior to 35 weeks gestation**
 - **Neonatal morbidity/mortality composite index**
- **Nor did it show any treatment effect on any secondary endpoint.**
- **Upon review of this clinical trial, the FDA concluded:**

In summary, Trial 003 did not demonstrate a treatment benefit of Makena on reducing the neonatal composite index or the rate of spontaneous preterm birth prior to 35 weeks gestation, nor was there evidence of a treatment benefit on the rate of spontaneous preterm birth prior to 37 weeks or 32 weeks gestation.

Sponsor Subgroup's Analyses Fail to Provide Any Evidence of Effectiveness

- **The FDA concluded that the unplanned exploratory subgroup analyses conducted by the Sponsor (stratified by geographic region and race) “do not provide convincing evidence of efficacy over placebo in any subpopulation and there is no statistically significant interaction between Makena and any of these risk factors.”**

Conclusions

Maintaining approval of Makena in the absence of any clinical benefits being demonstrated by Trial 002 or Trial 003 would make a mockery of the more than 50-year legal standard that requires substantial evidence of a drug's effectiveness.

Therefore, Public Citizen strongly urges the committee to recommend that the FDA withdraw approval of Makena from the market, as it fails to provide any clinical benefit.