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Recommendations

10th Summit Meeting Consensus: Recommendations for Regulatory Approval for Hormonal Male Contraception

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The investigators at the Sixth Summit Meeting on Hormonal Male Contraception, Petersberg, Germany, held on July 7–9, 2002, recognized the need for standardized clinical trials to develop a hormonal male method and drafted several recommendations (*Int J Androl*. 2002;25:375).

At the Ninth Summit Meeting on Hormonal Contraception, Nyon, Switzerland, held on October 9–11, 2005, the group of experts reviewed the status of clinical development projects for male hormonal contraception and discussed the need to update the recommendations

The following revised recommendations are the result of this discussion and present the consensus

statement confirmed at the 10th Summit Meeting, New York, NY, October 22–23, 2006.

It is stressed that the following recommendations are valid exclusively for hormonal methods for which the mechanism of action is based on the inhibition of sperm production. Methods with a different mode of action are outside the scope of these recommendations.

The goal of hormonal male contraception is the reversible suppression of spermatogenesis to a level compatible with infertility. In principle, this can be achieved with the use of an androgen alone or an androgen in combination with a gestagen or a GnRH-antagonist. The success of this principle in terms of lowering sperm counts in semen to azoospermia or to severe oligozoospermia has been demonstrated in multiple studies. Some trials demonstrated the contraceptive efficacy of this approach when couples used no other method of contraception. Investigators agree that information gained from preliminary studies on male contraception have reached a stage that hormonal contraceptive products for men should now be proposed for development for general use.

To bring a hormonal method to the market, large-scale clinical trials are required. Because no pharmacological method for male contraception is currently available, this represents a novel effort requiring new recommendations for testing and regulatory approval.

The investigators agreed that the following criteria should be fulfilled:

- In phase II dose-finding studies, the suppression of spermatogenesis can be used as the main parameter. As the surrogate parameter, sperm concentrations, measured according to World Health Organization recommended methods, can be used, and the goal should be ≤1 million/mL.
- After cessation of treatment, each participant should be followed until reversibility of sperm production to criteria that are compatible with normal fertility has been shown. Usually, return to sperm concentrations of at least 20 million/mL provides sufficient evidence of fertility. These figures could be revised, probably downward, as new data on fertility parameters emerge.
- Currently, only men with sperm concentrations ≥20 million/mL should be included. This threshold could be revised, probably downward, in the future as new data on fertility parameters emerge. Participants with known or suspected infertility should not be enrolled in clinical efficacy studies.
- Open-label, noncomparative contraceptive efficacy studies are acceptable if the primary endpoint is not susceptible to bias (eg, pregnancy rate).
- For contraceptive efficacy, 2 independent phase III trials for 1 year beginning when the male volunteer has suppressed to ≤1 million sperm/mL should be completed by 200 men or couples per trial.
- For safety assurance for a new chemical entity, trials are required to involve at least 300–600 men for 6 months at the intended combination and dose, 100 men exposed for 1 year, and a total of 1500 men in phase I–III studies at the minimum.
- Long-term safety will be monitored by postmarketing surveillance.
- The necessary laboratory investigations, especially semen analysis, need to be made under strict quality control.

These recommendations were drafted and approved by the participants in the 10th Summit Meeting on Male Contraception. This statement reflects the opinion of the individuals, but not necessarily the institution with which they are affiliated.

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