



Third Congress of the ICMC May 23rd, 2022, Paris, France

Abstract

Landscape of Non-Hormonal Male Contraceptives

John K. Amory MD, MPH, MSc
Professor of Medicine
Section Head, University of Washington Medical Center
Seattle, WA, USA

Non-hormonal male contraception can be defined as an approach to male contraception that does not utilize the administration of testosterone or compounds that block testosterone secretion. Non-hormonal contraception may have some advantages compared to hormonal male contraceptives as they would likely avoid any impact on testosterone concentrations and therefore not impact sexual function, sex drive or body composition.

There are numerous approaches to non-hormonal male contraception including: 1) drugs that interfere with testicular retinoic acid production or signaling and therefore impair sperm production, 2) drugs that interfere with sperm motility via numerous mechanisms, 3) drugs that alter sperm morphology and 4) reversible blockage of the vas deferens.

Currently, the most advanced of these are in late pre-clinical development but may progress to early clinical testing in the next few years. As new molecular entities, these compounds will require extensive safety testing prior to regulatory approval and clinical introduction.

“Non-Hormonal” Male Contraception-definition

- An approach to reversible male contraception that doesn't primarily involve the administration of hormones or hormone antagonists

“Non-Hormonal” Male Contraception: Pros and Cons

- Advantages:
 - Will not impact testosterone dependent functions (e.g. sexual function, body composition, mood, cholesterol metabolism)
 - Less stigma from negative connotations surrounding testosterone administration (e.g. sports, controlled substance)
 - Oral administration more feasible for some (c.f. classic androgens)
- Disadvantages:
 - Risk of non-reproductive toxicities
 - Risk of sterility
 - Lack of long history of safe clinical use and familiarity to providers

Non-hormonal Male Contraception: Challenges

- Efficacy—
 - ◆ What are the benchmarks for reductions in motility or morphology that correlate with efficacy?
 - ◆ Proposal—“The 99% hypothesis”.
 - ◆ A 99% reduction in sperm concentration roughly equates to a 99% reduction in unintended pregnancy from the WHCI study (Wang presentation)
 - ◆ Non-hormonal male contraceptives acting on motility and morphology should induce a 99% reduction reduction in animal models to “meet the bar” for efficacy testing in humans
- Safety—
 - ◆ No hormonal side effects (good and bad)
 - ◆ Possibility of permanent effects on spermatogenesis (gossypol and ~~and~~ diptolide/triptonide) or unpredictable side effects (e.g. hypokalemia with gossypol) means that large scale testing of these agents (e.g. 10,000 person years of exposure) will be required prior to approval to exclude uncommon adverse effects.