Torsade de pointes/QT prolongation risks with antibiotics: A contemporary analysis of the FDA Adverse Event Reporting System
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OBJECTIVES/SPECIFIC AIMS: Macrolides, linezolid, imipenem-cilastatin, fluoroquinolones, penicillin combinations, and cephalosporins are known to be associated with Torsade de pointes/QT prolongation (TdP/QTTP). Other antibiotics may also lead to TdP/QTTP, but no study has systemically compared TdP/QTTP risks of different antibiotics using recent data. Therefore, the objective of this study was to evaluate the association between TdP/QTTP and antibiotics in recent years using the FDA Adverse Event Report System (FAERS). METHODS/STUDY POPULATION: FAERS reports from January 1, 2015 to December 31, 2017 were analyzed. The Medical Dictionary for Regulatory Activities (MedDRA) was used to identify TdP/QTTP cases. We calculated the Reporting Odds Ratios (RORs) and corresponding 95% confidence intervals (95%CI) for the association between antibiotics and TdP/QTTP. An association was considered to be statistically significant when the lower limit of the 95% CI was greater than 1. RESULTS/ANTICIPATED RESULTS: A total of 2,042,801 reports (including 5,221 TdP/QTTP reports) were considered, after inclusion criteria were applied. Macrolides had the greatest proportion of TdP/QTTP reports, representing 2.9% of all macrolide reports. TdP/QTTP RORs (95%CI) for the antibiotics were (in descending order): macrolides 11.73 (9.74-14.12), linezolid 9.39 (6.45-13.68), amikacin 8.94 (4.22-18.92), imipenem-cilastatin 5.01 (2.38-10.56), fluoroquinolones 4.67 (3.96-5.52), penicillin combinations 3.52 (2.56-4.86), cephalosporins 1.90 (1.14-3.16), metronidazole 1.49 (0.74-2.99), vancomycin 1.26 (0.70-2.28), clindamycin 0.83 (0.27-2.58), trimethoprim-sulfamethoxazole 0.82 (0.31-2.18), and amoxicillin 0.57 (0.18-1.78). DISCUSSION/SIGNIFICANCE OF IMPACT: This study confirms prior evidence for TdP/QTTP risks with macrolides, linezolid, imipenem-cilastatin, fluoroquinolones, penicillin combinations, and cephalosporins. This study provides new evidence for TdP/QTTP risks with amikacin. Macrolides had the highest TdP/QTTP ROR among the antibiotics evaluated in this study.
the mechanical and release characteristics of the rings were thus largely decoupled. DISCUSSION/SIGNIFICANCE OF IMPACT: This is a novel approach to the design and fabrication of intravaginal rings for the treatment of infertility. The use of CAD and the decoupling of release from mechanical properties allows for us to move away from the one-size one-dose fits all approach to IVRs.

The Regulatory Landscape of Products to Treat Opioid Overdose
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OBJECTIVES/SPECIFIC AIMS: Since 1971, Naloxone has been the only FDA approved opioid antagonist indicated for use after opioid overdose. New formulations of Naloxone have been introduced into the market, including an injectable, auto-injector, and nasal spray. However, Naloxone is short-acting and as such often requires multiple doses and may induce severe withdrawal symptoms. This study examines the regulatory framework to understand the evolution of products indicated to treat opioid overdose and the landscape of therapies in development. Furthermore, this study examines how the Food and Drug Administration (FDA) and other government agencies have approached the opioid crisis. METHODS/STUDY POPULATION: A PubMed search of “naloxone AND opioid overdose” with the filter “humans” was conducted to understand Naloxone’s regulatory framework. The term “naloxone” was searched on the Drugs@FDA: Approved Drug Products database. Additionally, “nalmefene” was searched on ClinicalTrials.gov. To examine the opioid antagonist market landscape, a PubMed search of “opioid antagonist AND opioid overdose” with the filters “humans” and “clinical trial,” and a ClinicalTrials.gov search of “opioid antagonist and opioid overdose,” were conducted. Government agency reports were reviewed and cataloged. RESULTS/ANTICIPATED RESULTS: Preliminary findings suggest a lack of innovation in the development of novel opioid antagonists. Most literature review findings focused on already-marketed Naloxone products, including the original injectable approved in 1971, the 2014 Evzio Auto-Injector, and the 2015 Narcan Nasal Spray (Figure 1). For example, there were 14 results yielded from the FDA approvals database, but none of these results represented a new opioid antagonist molecule. A longer-acting opioid antagonist, Nalmefene injectable, was approved in 1995 but has since been removed from the market due to low sales. Our initial ClinicalTrials.gov search using condition “opioid overdose” and other terms “opioid antagonist,” revealed no new studies being conducted on alternative opioid antagonist treatments for opioid overdose. Findings only focused on the distribution, co-dispensing, intervention, pharmacokinetics/pharmacodynamics (PK/PD) of Naloxone (Figure 2). However, a Google search yielded one new trial with an opioid antagonist by Opiant Pharmaceuticals, almost fifty years after FDA’s approval of Naloxone. A ClinicalTrials.gov search was then performed using the search term “nalmefene” to find whether Opiant Pharmaceuticals’ trial was in the ClinicalTrials.gov database. However, the Opiant trial is phase I, and as such does not require reporting on ClinicalTrials.gov. In 2017, the National Institutes of Health (NIH) launched an initiative for longer-acting opioid antagonist formulations. In 2018, Opiant Pharmaceuticals announced positive phase I results for intranasal Nalmefene. The potential return of Nalmefene in intranasal form...