Systematic Review of Regulator-Requested Studies

As randomized clinical trials may not answer every important clinical/regulatory question, noninterventional postauthorization safety/effectiveness studies (PASSs/PAESs) can be important tools to generate real-world evidence (RWE) on the safety and effectiveness of oncology drugs in postapproval settings. Zhang et al. systematically reviewed regulator-requested noninterventional PASSs/PAESs of oncology drugs as of March 2021 and found an increased number of studies requested by regulators, with a vast majority on risk assessment, from 2006 to 2020. This review characterizes the landscape of PASSs/PAESs for oncology drugs. The authors suggest that future efforts are needed to assess how findings of these studies would impact regulatory decisions and improve knowledge of toxicity for clinical/translational development.
See page 155

Using Real-World Data to Emulate Control Arms

In an exploratory study, Tan et al. constructed real-world data (RWD) patient cohorts using retrospective electronic health record (EHR)-derived datasets to emulate the control arms of published clinical trials that supported US Food and Drug Administration approvals of anticancer therapies across multiple tumor types. In a post hoc case study, the authors also evaluated the impact of specific analytic decisions on emulation results. Their findings suggest that the comparability of clinical trial control arms and RWD cohorts may be affected by variability in data source, choice, and availability of relevant prognostic factors for inclusion in the statistical analysis, and RWD cohort construction analytic decisions. Whereas prior efforts have focused on individual tumor types, the authors here evaluate methods for constructing external real-world comparator cohorts across different tumor types. The lessons from this retrospective study may inform future work in retrospectively replicating clinical trial control arms with external data sources, and in designing clinical trials with prospectively constructed EHR-derived RWD cohorts as external comparators.
See page 168

RWE vs. RCT in Crohn’s Disease Treatment

The therapeutic armamentarium in immune-mediated inflammatory diseases, notably Crohn’s disease, dramatically increased in the last decade, but evidence of head-to-head comparisons, add-on therapies, and various ways to stage treatments is lacking, highlighting the need of real-world evidence (RWE) to complement randomized control trial (RCT) outcomes. Kirchgesner et al.’s study aimed to emulate an RCT, the Study of Biologic and Immunomodulator Naive Patients in Crohn’s Disease (SONIC) trial. Based on data of two nationwide samples of insured patients in US commercial insurance databases and the French nationwide health insurance database, this study provides evidence that RWE studies...
can contribute to the assessment of treatment effectiveness for Crohn’s disease in clinical practice. Compared with previous studies emulating RCTs, this study allows assessment of treatment effectiveness in different healthcare schemes and potential prescribing patterns, by using US and French nationwide population-based cohorts.

See page 179

Hypoglycemia in Insulin Secretagogue Users

Using a large healthcare claims database from 5 US states’ Medicaid programs from 1999 to 2011, supplemented with Medicare claims for dual-enrollees, Nam et al. investigated the rate of serious hypoglycemia in insulin secretagogue users with vs. without concomitant use of an ACE inhibitor (ACEI). The results did not suggest that concomitant use of ACEIs was associated with increased rates of serious hypoglycemia in insulin secretagogue users, with the possible exception of glimepiride. These findings may be clinically informative for the treatment of patients with both type 2 diabetes and cardiovascular diseases. The authors posit that widely used drug compendia warning of potential drug-drug interaction (DDI) between sulfonylureas and ACEIs and electronic medical record systems generating interruptive alerts on this potential DDI should consider updating information that was based on relatively small-scale case-control studies and case reports.

See page 218

RWD and RWE in Development of European- Authorized Medicines

Eskola et al. sought to identify and quantify the potential use of RWD/RWE during the pre-authorization phase, as presented in initial marketing authorization applications of new medicines centrally evaluated with a positive opinion in 2018 and 2019 by the European Medicines Agency (EMA). Their findings showed that the use of RWD/RWE in the pre-approval phase is seen in virtually all phases of drug development, but particularly in the Discovery phase (i.e., epidemiology of disease and target population) and in the Lifecycle phase (i.e., establishing the correct safety profile and for pharmacovigilance planning).

See page 310