A Centralized Safety Repository

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Answering key questions on malaria drug delivery
Drug Safety Repository (DSR)

Aims

- To collect and collate safety data from a variety of sources to identify the incidence of adverse reactions and look for new signals of potential harms.

- To develop a framework to allow this surveillance to extend to other drugs & diseases.
Pharmacovigilance systems

**Drug Development**
- Phase II
- Phase III
- Phase IV
- Programmatic use

**Adverse events**

**Key issues**
- Limited exposure
- Not real-life scenarios
- Not real-life populations

**Marketing approval**
- Reliance on (potentially weak) national systems

**Adverse drug reactions** (incl. spontaneous reports)
Pharmacovigilance systems

Drug Development

Phase II

Phase III

Phase IV

Programmatic use

Adverse events

Adverse drug reactions (incl. spontaneous reports)

Key issues

• Limited exposure
• Not real-life scenarios
• Not real-life populations

DRUG SAFETY REPOSITORY
Aggregated data

• Reliance on (potentially weak) national systems
Drug Safety Repository

Key features

● Industry-standard web-based database for collating, recording and reporting events
● Restricted and secure access
● Integrated standardized dictionaries
● Flexible reporting tool
Case processing workflow

Data entry → Coding → Review/Approval → Reporting
Case processing workflow

Data entry → Coding → Review/Approval → Reporting
- Manual data entry
- Electronic upload
- Duplicate checking
Case processing workflow

Data entry → Coding → Review/Approval → Reporting
WHO Drug Dictionary

MedDRA - the Medical Dictionary for Regulatory Affairs

- Integrated into database
- Automated & manual coding
- Drugs
- Diseases
- Events
- Investigations
Case processing workflow

- Data entry checks
- Coding checks
- Missing data
Case processing workflow

- Regulatory & ad hoc reports
- Status reports
- Case lists
- Automated & manual reports
## Reporting – summary tabulations

<table>
<thead>
<tr>
<th>System Organ Class (MedDRA)</th>
<th>Drug 1</th>
<th>Drug 2</th>
<th>Drug 3</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>3446</td>
<td>2931</td>
<td>1288</td>
<td>10792</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>30 (0.9%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>30 (0.4%)</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>1 (0.0%)</td>
<td>2 (0.1%)</td>
<td>0 (0.0%)</td>
<td>3 (0.0%)</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>0 (0.0%)</td>
<td>3 (0.1%)</td>
<td>3 (0.2%)</td>
<td>6 (0.1%)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>12 (0.3%)</td>
<td>155 (5.3%)</td>
<td>32 (2.5%)</td>
<td>199 (2.6%)</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>7 (0.2%)</td>
<td>61 (2.1%)</td>
<td>3 (0.2%)</td>
<td>71 (0.9%)</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>0 (0.0%)</td>
<td>3 (0.1%)</td>
<td>0 (0.0%)</td>
<td>3 (0.0%)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>227 (6.6%)</td>
<td>24 (0.8%)</td>
<td>10 (0.8%)</td>
<td>261 (3.4%)</td>
</tr>
<tr>
<td>Injury, poisoning and procedural complications</td>
<td>5 (0.1%)</td>
<td>0 (0.0%)</td>
<td>1 (0.1%)</td>
<td>6 (0.1%)</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td>6 (0.2%)</td>
<td>3 (0.1%)</td>
<td>2 (0.2%)</td>
<td>11 (0.1%)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>0 (0.0%)</td>
<td>1 (0.0%)</td>
<td>2 (0.2%)</td>
<td>3 (0.0%)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>39 (1.1%)</td>
<td>54 (1.8%)</td>
<td>15 (1.2%)</td>
<td>108 (1.4%)</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>0 (0.0%)</td>
<td>5 (0.2%)</td>
<td>1 (0.1%)</td>
<td>6 (0.1%)</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>0 (0.0%)</td>
<td>2 (0.1%)</td>
<td>0 (0.0%)</td>
<td>2 (0.0%)</td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>2 (0.2%)</td>
<td>2 (0.0%)</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>4 (0.1%)</td>
<td>16 (0.5%)</td>
<td>0 (0.0%)</td>
<td>20 (0.3%)</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>1 (0.0%)</td>
<td>18 (0.6%)</td>
<td>2 (0.2%)</td>
<td>21 (0.3%)</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>2 (0.2%)</td>
<td>2 (0.0%)</td>
</tr>
<tr>
<td>Summary</td>
<td>333 (9.7%)</td>
<td>352 (12.0%)</td>
<td>80 (6.2%)</td>
<td>765 (10.0%)</td>
</tr>
</tbody>
</table>
Reporting - graphs
## Serious events

<table>
<thead>
<tr>
<th>System Organ Class (MedDRA)</th>
<th>Sex</th>
<th>Age Group</th>
<th>Event as reported</th>
<th>Preferred term (MedDRA)</th>
<th>Intensity</th>
<th>First dose to onset</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>FEMALE</td>
<td>Adult</td>
<td>Anaemia</td>
<td>Anaemia</td>
<td>Life threatening</td>
<td>12 weeks 1 day</td>
<td>Recovered</td>
</tr>
<tr>
<td>Congenital, familial and genetic disorders</td>
<td>MALE</td>
<td>Neonate</td>
<td>Cleft palate and lip</td>
<td>Cleft lip and palate</td>
<td>Moderate</td>
<td>NA</td>
<td>Not Recovered</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>FEMALE</td>
<td>Infant</td>
<td>Acute renal failure</td>
<td>Renal failure acute</td>
<td>NA</td>
<td>18 weeks 5 days</td>
<td>Fatal</td>
</tr>
<tr>
<td></td>
<td>FEMALE</td>
<td>Adult</td>
<td>Unable to pass urine</td>
<td>Dysuria</td>
<td>SEVERE</td>
<td>5 days</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

## Non-serious events

<table>
<thead>
<tr>
<th>System Organ Class (MedDRA)</th>
<th>Sex</th>
<th>Pt Id</th>
<th>Event as reported</th>
<th>Preferred term (MedDRA)</th>
<th>Intensity</th>
<th>Onset</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td>MALE</td>
<td>Child</td>
<td>Diarrhoea</td>
<td>Diarrhoea</td>
<td>Moderate</td>
<td>1 day</td>
<td>Recovering</td>
</tr>
<tr>
<td></td>
<td>FEMALE</td>
<td>Adult</td>
<td>Vomiting</td>
<td>Vomiting</td>
<td>Mild</td>
<td>30 minutes</td>
<td>Recovered</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>FEMALE</td>
<td>Adult</td>
<td>Headache</td>
<td>Headache</td>
<td>Moderate</td>
<td>1 day</td>
<td>Recovered</td>
</tr>
<tr>
<td></td>
<td>FEMALE</td>
<td>Adult</td>
<td>Dizziness</td>
<td>Dizziness</td>
<td>Mild</td>
<td>60 minutes</td>
<td>Recovered</td>
</tr>
<tr>
<td>Musculoskeletal and CT disorders</td>
<td>MALE</td>
<td>Adult</td>
<td>Muscle pains</td>
<td>Myalgia</td>
<td>MILD</td>
<td>2 days</td>
<td>Recovered</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>FEMALE</td>
<td>Child</td>
<td>Dark urine</td>
<td>Chromaturia</td>
<td>MILD</td>
<td>4 days</td>
<td>Recovering</td>
</tr>
</tbody>
</table>
Current status

- Validated

- Contains >3000 case reports predominantly from ACTc and MiPc

- Reporting to DSMBs, ethics committees, manufacturers tried and tested

- Providing PV services to other malaria studies

- Standardization and pooled analysis remains a challenge

- Potential future collaborations – other investigators & Consortia, other pooled data initiatives (e.g. WWARN)…..
Thank you for joining us!

Recording will be shared. Please ensure you are on our mailing list:

www.actconsortium.org/newsletter

For any questions or comments, contact

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