DRUG-DRUG INTERACTIONS WITH NIRMATRELVIR/RITONAVIR FOR COVID-19 AND THE ROLE OF HOSPITAL PHARMACISTS

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BACKGROUND AND IMPORTANCE
Nirmatrelvir/ritonavir has recently been approved for treating COVID-19, but an elevated risk of drug-drug interactions (DDI) has been exposed.

AIM AND OBJECTIVES
The aim of this study was to evaluate DDI with nirmatrelvir/ritonavir and the role of hospital pharmacists.

MATERIALS AND METHODS
Retrospective study in a tertiary hospital between May-September 2022. All patients that received nirmatrelvir/ritonavir were included. Data collected: demographic, age-adjusted charlson comorbidity index, medical department, concomitant drugs. All DDI and pharmacy interventions were screened and categorized. Continuous data expressed as median (IQR). U-Mann Whitney for continuous variables and Chi-square for qualitative data.

RESULTS
A total of 48 patients with 350 concomitant drugs were selected. DDI were detected in 26 (54.2%) patients and in 52 (14.9%) drugs. Seven (0-16) concomitant drugs per patient. Female 24(50%), age 69(24-95) years, CHARLSON 5(0-12).

![Graph of DDI category, n(%)]

<table>
<thead>
<tr>
<th>DDI category</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C: monitor therapy</td>
<td>24(46.2)</td>
</tr>
<tr>
<td>D: consider therapy modification</td>
<td>16(30.8)</td>
</tr>
<tr>
<td>X: avoid concomitant use</td>
<td>12(23.1)</td>
</tr>
</tbody>
</table>

![Graph of Medical department with DDI, n(%)]

<table>
<thead>
<tr>
<th>Medical department</th>
<th>DDI, n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency room</td>
<td>3(11.5)</td>
</tr>
<tr>
<td>Pneumology</td>
<td>3(11.5)</td>
</tr>
<tr>
<td>Nephrology</td>
<td>3(11.5)</td>
</tr>
<tr>
<td>Oncology</td>
<td>4(15.4)</td>
</tr>
<tr>
<td>Hematology</td>
<td>6(23.1)</td>
</tr>
</tbody>
</table>

![Graph of ATC of DDI, n (%)]

<table>
<thead>
<tr>
<th>ATC of DDI, n (%)</th>
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</thead>
<tbody>
<tr>
<td>R-respiratory system</td>
</tr>
<tr>
<td>M-musculo-skeletal system</td>
</tr>
<tr>
<td>A-alimentary tract and metabolism</td>
</tr>
<tr>
<td>L-antineoplastic and metabolism</td>
</tr>
<tr>
<td>H-systemic hormonal preparations</td>
</tr>
<tr>
<td>G-genito urinary system</td>
</tr>
<tr>
<td>B-blood and blood forming organs</td>
</tr>
<tr>
<td>C-cardiovascular system</td>
</tr>
<tr>
<td>N-nervous system</td>
</tr>
</tbody>
</table>

![Graph of Pharmacy intervention, n(%)]

<table>
<thead>
<tr>
<th>Pharmacy intervention, n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuation</td>
</tr>
<tr>
<td>Adverse events monitoring</td>
</tr>
<tr>
<td>Dose reduction</td>
</tr>
<tr>
<td>Substitution</td>
</tr>
<tr>
<td>Efficacy monitoring</td>
</tr>
</tbody>
</table>

Statistical significant differences were found with ATC and DDI category (p<0.001): cardiovascular system drugs had more X-category DDI (41.7%) and nervous system drugs had more C-category DDI (60.8%). Hematology department had more patients presenting any DDI (23.1%, p=0.047). No DDI provoked any adverse event during treatment with nirmatrelvir/ritonavir.

CONCLUSION AND RELEVANCE
A high risk for DDI with nirmatrelvir/ritonavir was found, although most of them were mild and none provoked any adverse event. Cardiovascular system drugs showed the most severe DDI. Hematology patients and those receiving nervous system drugs had higher prevalence for DDI. Almost half of pharmacy recommendations were to discontinue the drug presenting the DDI. None of the pharmaceutical interventions induced any adverse event derived from the modification of concomitant treatment during nirmatrelvir/ritonavir administration.

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