Heart failure and atrial tachyarrhythmia on abiraterone: a characterization using pharmacovigilance databases

Authors:
JE Salem¹, BLV Benedicte Lebrun-Vignes², AP Antoine Pariente³, CMS Christian M Shaffer⁴, GGM Gabriel G Malouf⁵, PD Pauline Dureau², CP Camille Potey⁶, CF Christian Funck-Brentano², DMR Dan M Roden⁴, JJM Javid J Moslehiti⁴, MB Marie Bretagne², ¹University Pierre & Marie Curie Paris VI - Paris - France, ²Hospital Pitie-Salpetriere, CIC-Paris Est, pharmacologie médicale - Paris - France, ³University Hospital of Bordeaux - Bordeaux - France, ⁴Vanderbilt University, clinical pharmacology - Nashville - United States of America, ⁵University Hospital of Strasbourg - Strasbourg - France, ⁶CHRU Lille - Lille - France,

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Background: Abiraterone and enzalutamide are recently approved androgen deprivation therapies (ADT) for metastatic prostate cancer. The cardiac safety profile for the two drugs is unknown.

Methods: Using French and World Health Organization (WHO) pharmacovigilance databases, we performed a disproportionality-analysis of suspected adverse-drug-reactions (ADR) to evaluate the reporting-odds-ratio (ROR) of cardiac ADR associated with abiraterone compared to enzalutamide, other ADT used in prostate cancer, and entire database. Clinical and demographic characterization of patients with ADT-induced cardiac ADR was performed.

Results: In the 5,759,781 ADR reports in men, 55,070 pertained to ADT. The ROR of AT for abiraterone was of 4.1[3.1-5.3] vs. enzalutamide, 3.7[3-4.5] vs. other ADT, and 3.2[2.7-3.7] vs. entire database. The corresponding ROR for HF were of 2.5[2-3], 1.5[1.3-1.7], and 2[1.7-2.3], respectively. Mean time to AT and HF onset was shorter on abiraterone (5.2±0.8 and 4.5±0.6 months, respectively) vs. other ADT (13.3±3.2 and 9.2±1.1 months; p<0.05). Cases on abiraterone vs. other ADT were more frequently associated with ≥2 ADR-terms including AT, HF, hypokalemia, hypertension and edema (13.6% vs. 6%, p<10^-4). For abiraterone, age but not dose was associated to reporting of AT/HF vs. any other ADR.

Conclusion: Compared to other ADT, abiraterone was associated with a higher reporting of AT and HF associated with hypokalemia, hypertension and edema. These findings are consistent with the hyper-mineralocorticism induced by abiraterone and not with other ADT.

<table>
<thead>
<tr>
<th>Number (available data)</th>
<th>AT</th>
<th>HF</th>
<th>Hypokalemia</th>
<th>Edema</th>
<th>Hypertension</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>5989</td>
<td>r:0.03</td>
<td>r:0.05</td>
<td>r:0.06</td>
<td>r:0.04</td>
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<tr>
<td>Dose of hydrocortisone equivalent (mg/day)</td>
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<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>r:0.07</td>
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<tr>
<td>Dose of abiraterone (mg/day)</td>
<td>6285</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

Details concerning correlation (r) between clinical covariates and reporting for AT, HF, hypokalemia, edema and hypertension within overall adverse drug reaction on abiraterone (n: 9203) extracted from VigiBase (through 08/2017).
Details concerning correlation (r) between clinical covariates and reporting for AT, HF, hypokalemia, edema and hypertension within overall adverse drug reaction on abiraterone (n: 9203) extracted from VigiBase (through 08/2017).