BACKGROUND AND IMPORTANCE

- Many tyrosine kinase inhibitors interact with the drug-efflux pump P-glycoprotein (P-gp).
- Osimertinib, a P-gp inhibitor, may increase the serum concentration of P-gp substrates. This is essential in digoxin, a drug with a narrow therapeutic index (0.8-1.2 ng/ml) which levels higher than 1.2 ng/ml are associated with an increased risk of death.
- Although this interaction has been described, this is the first case reported.

AIM AND OBJECTIVES

To describe the drug-drug interaction mediated by P-gp between osimertinib and digoxin.

Clinical case

- 77 years-old woman

Permanent atrial fibrillation 🌻 Digoxin
EGFR-mutated NSCLC 🌻 Osimertinib

MATERIAL AND METHODS

- Descriptive case report.
- Data were obtained from computerized clinical records.
- MwPharm++ software was used to analyse serum digoxin concentrations and design a safe and effective dosing regimen.

RESULTS

![Serum digoxin levels and dose variation of digoxin and osimertinib](image)

<table>
<thead>
<tr>
<th>Digoxin dose</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osimertinib dose</td>
<td>125 mcg/day</td>
<td>100 mcg/day</td>
<td>75 mcg/day</td>
<td>50 mcg/day</td>
<td>80 mcg/day</td>
<td>40 mcg/day</td>
</tr>
</tbody>
</table>

Figure: Serum digoxin levels and dose variation of digoxin and osimertinib

CONCLUSION AND RELEVANCE

Therapeutic drug monitoring allowed the detection of increased levels of digoxin. It corresponds with the start of osimertinib treatment, being the P-gp inhibition the most plausible factor for this finding.