DEMOCRATIZING SIMULATIONS IN HEALTHCARE

Vincenzo Carbone, PhD – Product Manager

INTEGRATED PLATFORM FOR PRECISION AND COST-EFFECTIVE ANTI-TUMORAL PHARMACOLOGICAL THERAPY

Innovating the prescriptive process of the oncological drugs by a digital tool for managing patient molecular data, through their translation into prescriptive indications that can pinpoint the best therapy in a cost-effectiveness perspective.
FARMAPRICE PARTNERS

**FARMAPRICE**

Scientific-informatic services company operating in healthcare in the sectors of medical devices and pharma.

Develops e-Health and e-Government solutions to improve the services offered to the healthcare communities.

Excellence in cancer research and medical treatment and assistance to patients.

Carried out the activities of project coordination and dissemination of results.
Optimization of pharmacological therapy in oncology implemented through a correct prescription based on the latest scientific evidence.

Clinically validated guidelines report specific pharmacogenomics-based dose recommendation on single drug-gene interactions.

Lack of IT tools to implement pharmacogenomics results into the workflow of drug prescription for physicians and pharmacists.
RESULTS: GUIDELINES HARMONIZATION AND STANDARDIZATION

CPIC + DPWG + other

DPWG: Dutch Pharmacogenetics Working Group

4 drugs removed because revoked in Italy

3 drugs removed because without CPIC or DPWG guidelines

12 drugs removed because with gene-drug pairs not «actionable»

5 drugs removed due to differences in recommendation between consortium

1 drug removed after its recent guideline publication

1 drug removed due to SNP genotyping analysis problems
RESULTS: SYNOPTIC TABLES CONSTRUCTION

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Genes</td>
<td>Allele</td>
<td>Major Nucleotide Variation</td>
<td>dbSNP RS ID</td>
<td>Effect on protein</td>
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<tr>
<td>2</td>
<td>CYP1A2</td>
<td>*1C</td>
<td>3860G&gt;A</td>
<td>rs2069514</td>
<td>X</td>
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<td>3</td>
<td>CYP1A2</td>
<td>*1F</td>
<td>363C&gt;A</td>
<td>rs762551X</td>
<td>Higher Inducibility</td>
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<tr>
<td>4</td>
<td>CYP2B6</td>
<td>*8</td>
<td>516G&gt;T</td>
<td>rs3745274Q</td>
<td>G172H</td>
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<td>*16</td>
<td>785G&gt;A</td>
<td>rs227934</td>
<td>K252R</td>
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<td>6</td>
<td>CYP2B6</td>
<td>*18</td>
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</table>

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</thead>
<tbody>
<tr>
<td>7</td>
<td>Genes</td>
<td>Allele</td>
<td>Clinically relevant genetic interaction</td>
<td>Gene activity score</td>
<td>Actionable Genotype/Phenotype</td>
</tr>
<tr>
<td>8</td>
<td>CYP2C9</td>
<td>*3</td>
<td>1</td>
<td>2</td>
<td>CYP1A2</td>
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<td>9</td>
<td>CYP2C9</td>
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<tr>
<td>10</td>
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<td>*8</td>
<td>4</td>
<td>CYP2B6</td>
<td>PM</td>
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<tr>
<td>11</td>
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<td>*11</td>
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<td>*12</td>
<td>5</td>
<td>CYP2B6</td>
<td>EM</td>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Drug</td>
<td>Gene</td>
<td>Therapeutic dose recommendation</td>
<td>Note</td>
<td>Classification of evidence</td>
</tr>
<tr>
<td>2</td>
<td>Abacavir</td>
<td>HLA-B</td>
<td>Abacavir is contraindicated.</td>
<td>per depression</td>
<td>S 4</td>
</tr>
<tr>
<td>3</td>
<td>Amitriptyline</td>
<td>CYP2C9</td>
<td>Initiate therapy with recommended starting dose.</td>
<td>per depression</td>
<td>S 4</td>
</tr>
<tr>
<td>4</td>
<td>Amitriptyline</td>
<td>CYP2C9</td>
<td>1) (Initiate therapy with recommended starting dose or) consider alternative drug not metabolized by CYP2C9. Avoid amitriptyline use due to potential for suboptimal response. TCAs without major CYP2C9 metabolism include nor triptyline and desipramine. 2) Consider 30% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.</td>
<td>per depression</td>
<td>M 4</td>
</tr>
<tr>
<td>5</td>
<td>Amitriptyline</td>
<td>CYP2C9</td>
<td>1) (Initiate therapy with recommended starting dose or) consider alternative drug not metabolized by CYP2C9. Avoid amitriptyline use due to potential for suboptimal response. TCAs without major CYP2C9 metabolism include nor triptyline and desipramine. 2) If amitriptyline is warranted, utilize therapeutic drug monitoring to guide dose adjustments.</td>
<td>per depression</td>
<td>O 4</td>
</tr>
<tr>
<td>6</td>
<td>Amitriptyline</td>
<td>CYP2D6</td>
<td>1) Consider alternative drug not metabolized by CYP2D6. 2) If an alternative drug is not possible, consider a 25-40% reduction of recommended starting dose. Utilize therapeutic drug monitoring of amitriptyline and nor triptyline to guide dose adjustment.</td>
<td>per depression</td>
<td>M 3</td>
</tr>
<tr>
<td>7</td>
<td>Amitriptyline</td>
<td>CYP2D6</td>
<td>1) Avoid amitriptyline use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. 2) If amitriptyline is warranted, consider 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring of amitriptyline and nor triptyline to guide dose adjustment.</td>
<td>per depression</td>
<td>S 3</td>
</tr>
<tr>
<td>8</td>
<td>Amitriptyline</td>
<td>CYP2D6</td>
<td>1) Avoid amitriptyline use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. 2) If amitriptyline is warranted, consider titrating to a higher target dose (compared to normal metabolizer) up to 125% increase of the recommended dose. Utilize therapeutic drug monitoring to guide</td>
<td>per depression</td>
<td>S 3</td>
</tr>
</tbody>
</table>
RESULTS: PRESCRIPTION ALGORITHM

Tool for checking and processing genetic data:

- Web interface to upload genetic profile
- Protecting the patient's privacy
- Data validation
- Alert in case of anomalies
- Download formatted and normalized data

- W3C standards
- Papa Parse - CSV Parser for JavaScript
- Microsoft Azure cloud
RESULTS: CLINICAL DECISION SUPPORT SYSTEM

CPIC + DPWG + other

- Configurazione file
- Configurazione principi attivi
- Pazienti
- Profilo genetico germinale
- Melanoma
- Tumore al polmone

FARMAPRICE - Euro BioHighTech 2018
# RESULTS: CLINICAL DECISION SUPPORT SYSTEM

**CPIC + DPWG + other**

<table>
<thead>
<tr>
<th>Gene 1</th>
<th>Gene 2</th>
<th>Messaggio 1° livello</th>
<th>Level of evidence</th>
<th>Warning al medico</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPYD</td>
<td></td>
<td>Attenzione! Pericolo di tossicità severa e potenzialmente fatale per ipersensibilità al farmaco.</td>
<td>⭐⭐⭐</td>
<td>🔄</td>
</tr>
</tbody>
</table>

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**Messaggio 1° livello**

*Attenzione! Pericolo di tossicità severa e potenzialmente fatale per ipersensibilità al farmaco.*

**Messaggio 2° livello**

*Evitare l’utilizzo di 5-FU. Selezionare un farmaco alternativo (tegafur non è un’alternativa in quanto anch’esso metabolizzato dalla DPYD).*

<table>
<thead>
<tr>
<th>Gene 1</th>
<th>Cod. conversione</th>
<th>Level of evidence</th>
<th>Clinical Impact</th>
<th>Warning al medico</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPYD</td>
<td>2′A−2′A</td>
<td>3.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Si raccomanda di eseguire test per SNP: 2′8′4′5′A−T + HapB2</td>
<td>Level of evidence: 3.0</td>
<td>Clinical Impact: F</td>
<td>Warning al medico: Si</td>
<td></td>
</tr>
</tbody>
</table>
RESULTS: ELECTRONIC CLINICAL RECORD

CPIC + DPWG + other

Preservation of the input/output data of the prescription algorithm:

• Registering events
• Connecting through Web Services
• Persisting data in a database
• Security and compliance in healthcare: ISO27001, ISO9001, SOC1, 3, GXP (FDA 21 CFR Part 11), HIPAA

• RESTful API (HTTP + JSON)
• Web-application Proto.io
• Microsoft Azure cloud
RESULTS: FUTURE-PROOF SOLUTION

Ready for integration with:

**Blockchain security**

- Quickly create a blockchain project
- Pre-built, secure and globally available networks and infrastructures
- Integrating blockchain workflows with systems and applications
- Ability to extend functionality using REST-based APIs

**Machine learning and artificial intelligence**

- Creating Artificial Intelligence (AI) via simple interface
- Deploying and sharing of predictive analysis solutions
- Customization using languages such as R or Python
- Advanced Algorithms
- Training the ML model
An innovative platform to translate the latest scientific evidence of new oncology treatments into a personalized therapeutic framework.

- Guarantee excellent assistance to patients
- Suggest correct prescriptions to doctors
- Optimization of guidelines by research centers
- Control of expenditure by healthcare system
- Streamlining drug spending by regulatory bodies
CONTACTS

LUCA EMILI
luca.emili@insilicotrials.com

LORENZO GIOLLO
lorenzo.giollo@insielmercato.it

ERIKA CECCHIN
ececchin@cro.it

THANK YOU FOR YOUR ATTENTION