A Web-based Tool for Patients Cohorts and Clinical Trials Management

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Nowadays, **Clinical research (CR)** generates a large amount of data that must be collected, processed and analyzed, often from centres which are in different places or countries. In order to manage Clinical Trials (CTs) data, CR uses two fundamental instruments:

- Networked Clinical Research (NCR)
  - WWW or VPN connections
- Clinical Data Management Systems (CDMSs)
  - **Electronic Data Capture (EDC)**

On the other side, Clinical Care exploits patient centric systems:

- Electronica Medical Records (EMRs)
- **Electronic Health Records (EHRs)**
Objectives

- To realize an hybrid solution which allows the data integration and management in multicentric 
  **Clinical Trials (CTs)**.
- To preserve EDC features in the data entering process, minimizing data entry operations.
- To maintain the link with patient, as in EHR, permitting the creation of clinical cohorts.
- To develop an user-friendly tool for information extraction.
Entity-Relation approach for database design
High data structuring (Metadata)
Emphasis on the use of standards and codes (LOINC, ICD, normality ranges, units)
Z score* for data standardization
Data sharing and comparison also at semantic level
Web platform

Results: Solution Architecture
Results: Ligurian HIV Clinical Network

This platform provides, in a completely anonymous method for the patient, the management, integration and extraction of data belonging to different types of clinical trials in the field of Infectious Diseases. Currently, there are four ongoing clinical studies:

- **Maraviroc LiHIm-Web**: Case-control study for immune activation and immunoregulation analysis in HIV+ patients undergoing diverse therapies.
- **S. Martino Long-Term**: Immunological evaluations in a cohort of Long Term Non Progressor HIV+ patients never treated with any therapies.
- **ACTeA I Study**: To calculate the real impact of HIV+ patients on Public Health System referring to the Ligurian context.
- **P.HIV-1 M.T. Register**: To monitor the follow up of HIV-1 with maternal transmission infected patients.
Ligurian HIV Clinical Network: Involved Centres

The centres and departments which are participating in the project:

- Infectious Diseases Department of Pietra Ligure Hospital
- Clinical Immunology (CEBR)
- Infectious Diseases Department of Galliera Hospital
- Infectious Diseases Department of Sanremo Hospital
- Infectious Diseases Department of San Martino Hospital
- Immunoregulation (CEBR)
- Infectious Diseases Department of La Spezia Hospital
- Infectious Diseases Department of Alessandria Hospital
- Infectious Diseases Department of Savona Hospital
- Infectious Diseases Department of Torino Hospital
- DISEM University of Genoa
- DIBRIS University of Genoa
### LiHIm-Web Maraviroc: Patients List

<table>
<thead>
<tr>
<th>Id</th>
<th>Patient</th>
<th>Initials</th>
<th>Date of birth</th>
<th>Date HIV positive</th>
<th>Therapeutic lines</th>
<th>Id Center</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LM</td>
<td>11/07/1954</td>
<td>01/02/1991</td>
<td>30th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>2</td>
<td>CG</td>
<td>26/05/1962</td>
<td>24/09/1990</td>
<td>13th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>3</td>
<td>LC</td>
<td>06/11/1967</td>
<td>31/07/1996</td>
<td>11th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>4</td>
<td>RS</td>
<td>05/12/1960</td>
<td>17/04/1990</td>
<td>14th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>5</td>
<td>FS</td>
<td>02/01/1960</td>
<td>28/04/1987</td>
<td>11th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>6</td>
<td>CC</td>
<td>07/08/1953</td>
<td>01/01/1995</td>
<td>13th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>7</td>
<td>RG</td>
<td>11/09/1951</td>
<td>07/03/2000</td>
<td>7th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>8</td>
<td>CG</td>
<td>12/11/1957</td>
<td>05/04/1988</td>
<td>11th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>9</td>
<td>O</td>
<td>12/08/1961</td>
<td>06/10/1989</td>
<td>6th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
<tr>
<td>10</td>
<td>PR</td>
<td>25/05/1961</td>
<td>02/12/1991</td>
<td>11th</td>
<td>DM15</td>
<td>REGISTRY</td>
<td>DELETE details</td>
</tr>
</tbody>
</table>

**Legend**
- Maraviroc (35 Patients)
- Alternative therapy (33 Patients)
- No info (11 Patients)
MARAVIROC LiHIm-Web: Patient’s historical information

LiHIm-Web Maraviroc: anamnestic

Patient LM, ID = 1, anamnestic

- HCV-RNA: 84000 IU/L
- HBV DNA: [491-1352] IU/L
- Nadir CD4: 11 N/mm²
- HIVRNA in to: 45000 Copies/ml
- Framingham Score: 5 %
- HIV risk factors: Addict
- HBV: Ab anti HBC isol

Family history of premature
CHD (CHD in male first-degree relative <5 years):
- YES
- NO
- Not known

MEDINFO HIV Clinical Network is made from MEDINFO, Laboratory of Nanobiotechnology and Medical Informatics (DIST, University of Genoa)
MARAVIROC LiHIm-Web vs ACTeA I-Study: Clinical event’s detail

**LiHIm-Web Maraviroc: Categories examination**

- **Patient DD, ID = 8, T6**
- **Exam Date:** DD / MM / YYYY 18/10/2011
- **Therapeutic line number:** 11

**Actea-I Study: Categories examination**

- **Patient DD, ID = 8, T3**
- **Exam Date:** DD / MM / YYYY 18/10/2011
- **Therapeutic line number:** 11

<table>
<thead>
<tr>
<th>Category</th>
<th>LiHIm-Web Maraviroc</th>
<th>Actea-I Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenotype and viremy</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Carbohydrate metabolism</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Cardiovascular profile</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Liver function</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Renal function</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Oxidative stress</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>NK phenotype</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>HAART therapies</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Inflammation parameters</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>CBC with differential</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Monocyte populations</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Inflammatory mediators</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Lymphocyte proliferation</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
<tr>
<td>Physical Examination</td>
<td>View / Insert results</td>
<td>View / Insert results</td>
</tr>
</tbody>
</table>

MIE2012, Pisa 26-29 August 2012
MARAVIROC LiHIIm-Web vs ACTeA I-Study: Clinical category’s detail

**LiHIIm-Web Malaviroc: Phenotype and viremy**

- **Patient DD, ID = 8, Examination of 18/10/2011**
  - T6, therapeutic Line number = II
  - TCD3: 1055, % TCD3: 77.2
  - TCD4: 408, % TCD4: 29.9
  - TCD8: 643, % TCD8: 47
  - HIVRNA: 9
  - Report TCD4/TCD8: 0.6

**Actea-I Study: Phenotype and viremy**

- **Patient DD, ID = 8, Examination of 18/10/2011**
  - T3, therapeutic Line number = II
  - TCD3: 752-2168, % TCD3: 60-85
  - TCD4: 408, % TCD4: 29.9
  - TCD8: 225-1187, % TCD8: 16-43
  - HIVRNA: 9 copies/µl
  - HIVRNA <20 copies: YES
  - HIVRNA ≥20 copies: NO

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MARAVIROC LiHIm-Web: Data extraction criteria examples
Ligurian HIV Clinical Network: Recorded data (July ‘11-June ‘12)

Approximately 230 HIV+ Positive patients were archived with the following information:

<table>
<thead>
<tr>
<th>Type of clinical event</th>
<th>Archived clinical events</th>
<th>Records</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood sample</td>
<td>535</td>
<td>17720</td>
</tr>
<tr>
<td>Historical information</td>
<td>231</td>
<td>1685</td>
</tr>
<tr>
<td>Therapy</td>
<td>177</td>
<td>926</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>95</td>
<td>602</td>
</tr>
<tr>
<td>Hospital discharge</td>
<td>93</td>
<td>1803</td>
</tr>
</tbody>
</table>


Conclusions and future developments

In conclusion:
- The web-based tool achieves the right level of integration between EDC and EHR.
- The project satisfies clinicians and health patients’ needs managing both CTs and longitudinal follow ups.
- The structure is general and usable for different medical domains.

For the future:
- To test the HL7 interface for data import/export.
- To realize a web based tool which dynamically and automatically builds web pages’ contents from the recorded information in the database.
Thanks for your attention!

Any questions?
Extraction algorithm

Filtering and selection on demographical characteristics

Filtering and selection on features independent of time

Filtering and selection on clinical features dependent on time

Results

Dynamically constructing a query which extracts the patients with the right features

Sliding the patients’ list and by dynamically constructing queries for each patient

Sliding the patients’ list and by dynamically constructing queries for each patient

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MARAVIROC LiHIm-Web: Data extraction tool

LiHIm-Web Maraviroc: Data Extraction

Try extraction for: Patient  Tn

Therapy: Ongoing  Tn selected: T12  Criterion comparison: ≥ ≤ Select: Most recent reporting

Condition to add on: Clinical parameters

Categories: Phenotype and viremia

Clinical parameters: HIVRNA

View: YES  NO

Comparison criteria: ≥ ≤

Value: 40 [Copies/ml (0-40)]
Z-Score* transformation

\[ X_{\downarrow s} = L_{\downarrow s} + (X - L_{\downarrow x}) (U_{\downarrow s} - L_{\downarrow s}) / (U_{\downarrow x} - L_{\downarrow x}) \]

- \( X \) is an assay value
- \( L_{\downarrow x}, U_{\downarrow x} \) are the corresponding reference range of \( X \)
- \( L_{\downarrow s}, U_{\downarrow s} \) are the corresponding reference range of the standard centre (mainly represented centre)
- \( X_{\downarrow s} \) is the standardized value