Pharmacist

Industrial Vision of Clinical trials

Vision of International Clinical Research
(Leem Study)
Clinical Trials are by definition the only way to get Marketing Authorization Approval of a new Medicine.

But Clinical Trials are a part of a long Pharmaceutical Process from Research and Development... to approval and launch:

- 8 to 12 years process
- A very complex process – 1 molecule on 10 000
- A costly process: 1 to 1.5B$ for a new Entity
- A risky process: how to finance R&D with a limited number of marketed medicines
Pharmacist Industrial Vision of Clinical trials

- A lot of candidates
  - very few Products to Launch

10,000 candidates

RESEARCH

100 candidates

PRE-CLINICAL

10 molecules

CLINICAL TRIALS

LAUNCH/PV

1 product

JP PACCIONI EIPG April 11th, 2014
Synthesis of 6 surveys conducted by Leem since 2002 and 2012
Clinical Research: a major issue for French attractiveness within an increasingly competitive environment

- Survey performed by the Leem every 2 years in association with Publicis Healthcare Consulting to conduct a situation analysis of France’s position in international clinical research (quantitative aspects and qualitative perception)

- Exceptional and unique scope of available data in Europe thanks to 6 surveys conducted since 2002
  - International studies of development (Phase II et III) with French participation

Since 2004, nearly 500 studies, over 1 million patients included

Synthesis of 6 surveys conducted by Leem since 2002 and 2012
The survey representativeness increased steadily between 2002 and 2012 to reach 30 laboratories.

Evolution of participation in the survey between 2002 and 2012

- 2002: 11 companies, 44% participation
- 2004: 10 companies, 36% participation
- 2006: 61% participation
- 2008: 62% participation
- 2010: 72% participation
- 2012: 68% participation

The survey 2012 only contains qualitative data.
2012 survey: a significant sample

30 pharmaceutical companies involved in the 2012 survey

- Abbott
- Actelion
- Amgen
- Astellas
- AstraZeneca
- Bayer
- Biogen
- BMS
- Boehringer Ingelheim
- Celgene
- Daiichi-Sankyo
- Gilead
- GlaxoSmithKline
- Ipsen
- Janssen
- Léo Pharma
- LFB
- Lilly
- Lundbeck
- Merck Serono
- MSD
- Novartis
- NovoNordisk
- Pfizer
- Pierre Fabre
- Roche
- Sanofi
- Sanofi Pasteur
- SPMSD
- Takeda

Note: Loss of 3 laboratories: Cephalon, Cytheris, Servier
and merger between Pfizer-Wyeth / MSD-Schering Plough / Takeda-Nycomed

For France

- 559 studies (vs 415 en 2010) Of which 110 studies de phases I et II
- 22 114 patients (vs 22 095 en 2010)
- 3 152 centers (vs 2 433 en 2010)

For international comparison

- 420 studies (vs 328 en 2010)
- 246 895 patients (vs 249 704 en 2010)
- 32 965 centers (vs 24 337 en 2010)

Synthesis of 6 surveys conducted by Leem since 2002 and 2012
US-Canada has increased significantly as they are now involved in nearly 4 studies out of 5.

Synthesis of 6 surveys conducted by Leem since 2002 and 2012
In Europe, participation of Western European countries is quite close, in overall decrease.

**Average Number of patients per center and per year**

<table>
<thead>
<tr>
<th>Year</th>
<th>Scandinavia</th>
<th>Germany</th>
<th>Spain</th>
<th>France</th>
<th>United Kingdom</th>
<th>Italy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>9.4</td>
<td>9.4</td>
<td>7.2</td>
<td>7.2</td>
<td>6.3</td>
<td>5.6</td>
</tr>
<tr>
<td>2006</td>
<td>7.8</td>
<td>6.5</td>
<td>6.0</td>
<td>6.5</td>
<td>5.6</td>
<td>5.2</td>
</tr>
<tr>
<td>2008</td>
<td>8.3</td>
<td>8.1</td>
<td>8.1</td>
<td>7.8</td>
<td>7.6</td>
<td>4.8</td>
</tr>
<tr>
<td>2010</td>
<td>9.7</td>
<td>6.7</td>
<td>6.7</td>
<td>5.2</td>
<td>4.8</td>
<td>4.0</td>
</tr>
<tr>
<td>2012</td>
<td>6.3</td>
<td>6.3</td>
<td>6.3</td>
<td>4.8</td>
<td>4.8</td>
<td>4.0</td>
</tr>
</tbody>
</table>

*Synthesis of 6 surveys conducted by Leem since 2002 and 2012.*
At the European level, the analysis per phase revealed a higher rate of phase II studies in France.

Phase II and III distribution (2012)

- Germany: 296 studies, 27% Phase II, 73% Phase III
- Spain: 245 studies, 27% Phase II, 73% Phase III
- France: 402 studies, 33% Phase II, 67% Phase III
- Italy: 246 studies, 30% Phase II, 70% Phase III
- United Kingdom: 197 studies, 24% Phase II, 76% Phase III
- Scandinavia: 181 studies, 22% Phase II, 78% Phase III

- But with a higher proportion of phase III studies in each country
- Involvement of France in Oncology and Rare Diseases Phase II

Synthesis of 6 surveys conducted by Leem since 2002 and 2012
Variations in timelines approval from the different authorities are different

Median timelines to obtain the approval by ANSM (in days)

- Not analyzed

<table>
<thead>
<tr>
<th>Year</th>
<th>2006</th>
<th>2008</th>
<th>2010</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>53</td>
<td>56</td>
<td>49</td>
<td>-12.5%</td>
</tr>
</tbody>
</table>

Median timelines to obtain the approval by EC (in days)

- Not analyzed

<table>
<thead>
<tr>
<th>Year</th>
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<th>2008</th>
<th>2010</th>
<th>2012</th>
</tr>
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<tbody>
<tr>
<td>Value</td>
<td>50</td>
<td>49</td>
<td>51</td>
<td>54</td>
</tr>
</tbody>
</table>

Phase I, II, III and IV for regulatory purpose

Synthesis of 6 surveys conducted by Leem since 2002 and 2012
Hospital contracts (first contract) timelines dropped significantly from 2006 to 2010 and have since remained stable.

Median deadline to obtain the signature of the first hospital contract (in days)

- 2006: 140 days
- 2008: 124.5 days (-11%)
- 2010: 112 days (-10%)
- 2012: 111 days

Synthesis of 6 surveys conducted by Leem since 2002 and 2012.
France recruited 6.5% of total patients and ranks behind USA, Eastern Europe, Asia, Latin America but also Germany

<table>
<thead>
<tr>
<th>Number of studies</th>
<th>Number of patients</th>
<th>Ratio recruited patients/1 000 000 hab</th>
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<tbody>
<tr>
<td>France</td>
<td>420</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>310</td>
<td></td>
</tr>
<tr>
<td>Other West. Eur</td>
<td>301</td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>293</td>
<td></td>
</tr>
<tr>
<td>Est Europe</td>
<td>280</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>258</td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>257</td>
<td></td>
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<tr>
<td>Canada</td>
<td>237</td>
<td></td>
</tr>
<tr>
<td>Australasia</td>
<td>215</td>
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<tr>
<td>United Kingdom</td>
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</tr>
<tr>
<td>Asia</td>
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<tr>
<td>Scandinavia</td>
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<tr>
<td>Latin Am.</td>
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<td></td>
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<tr>
<td>Africa and Mid.East.</td>
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<tr>
<td>Europe</td>
<td>420</td>
<td></td>
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<tr>
<td>World</td>
<td>420</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Number</th>
<th>%</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>47 333</td>
<td>19.2%</td>
<td>153</td>
</tr>
<tr>
<td>Est Europe</td>
<td>36 970</td>
<td>15.0%</td>
<td>113</td>
</tr>
<tr>
<td>Asia</td>
<td>25 368</td>
<td>10.3%</td>
<td>7</td>
</tr>
<tr>
<td>Germany</td>
<td>22 047</td>
<td>8.9%</td>
<td>270</td>
</tr>
<tr>
<td>Latin Am.</td>
<td>20 743</td>
<td>8.4%</td>
<td>293</td>
</tr>
<tr>
<td>Other West. Eur</td>
<td>19 930</td>
<td>8.1%</td>
<td>39</td>
</tr>
<tr>
<td>France</td>
<td>16 092</td>
<td>6.5%</td>
<td>246</td>
</tr>
<tr>
<td>Canada</td>
<td>10 847</td>
<td>4.4%</td>
<td>317</td>
</tr>
<tr>
<td>Scandinavia</td>
<td>10 770</td>
<td>4.4%</td>
<td>423</td>
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<tr>
<td>Spain</td>
<td>9 672</td>
<td>3.9%</td>
<td>206</td>
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<tr>
<td>Australasia</td>
<td>8 761</td>
<td>3.5%</td>
<td>114</td>
</tr>
<tr>
<td>Italy</td>
<td>8 029</td>
<td>3.3%</td>
<td>133</td>
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<tr>
<td>United Kingdom</td>
<td>7 048</td>
<td>2.9%</td>
<td>17</td>
</tr>
<tr>
<td>Afr. Moyen Or.</td>
<td>3 285</td>
<td>1.3%</td>
<td>55</td>
</tr>
</tbody>
</table>

As only studies involving France were included, the number of studies France took part in is the highest by definition

**In comparison with the 2010 survey**

- An increase for:
  - The USA: 19.2% vs 15.4%
  - Asia: 10.3% vs 7.8%
- A decrease for Europe: 52.9% vs 60.8%
- No variation for Germany: 8.9% vs 9%
- Also a decrease for:
  - Eastern Europe: 15.0% vs 21.6%
  - France: 6.5% vs 7.6%

*Synthesis of 6 surveys conducted by Leem since 2002 and 2012*
Conclusion of the 2012 survey

- Global decrease of Europe in international competition
- France remains in the average of the European countries at a growing distance from Germany, but still with some advantages
- Some alarming signals which calls for the mobilization of all stakeholders
  - Collapse of some therapeutic areas
  - EC and Hospital contracts timelines
  - Deterioration of the perception of administrative simplicity

Synthesis of 6 surveys conducted by Leem since 2002 and 2012
Reinforce our mobilization efforts at all levels

- A mobilization of all Member States and of the European Commission
  - To adopt an European Regulation which really simplifies processes and shortens timelines
  - To set up a positive environment for clinical research, in particular a reflection on a European certified training for investigators
- A better focus in France
  - Hospitals for a simplification of hospitals contractualization and the setting up of efficient organizations (CenGeps actions)
  - Regulatory Authorities (ANSM, EC) to keep competitive timelines
  - Investigators to improve feasibility studies and GCP training
  - Patients to favor their inclusion in clinical trials

Synthesis of 6 surveys conducted by Leem since 2002 and 2012
Thanks for your attention